

This NASA image is a composite of several satellite-based views of Earth. To make the whole-Earth image, NASA scientists combine observations of different parts of the planet.  
(credit:  
NASA/GSFC/NOAA/USGS)

Viewed from space, Earth offers no clues about the diversity of life forms that reside there. The first forms of life on Earth are thought to have been microorganisms that existed for billions of years in the ocean before plants and animals appeared. The mammals, birds, and flowers so familiar to us are all relatively recent, originating 130 to 200 million years ago. Humans have inhabited

this planet for only the last 2.5 million years, and only in the last 200,000 years have humans started looking like we do today.

- Summarize the steps of the scientific method
- Compare inductive reasoning with deductive reasoning
- Describe the goals of basic science and applied science

Formerly called blue-green algae, these (a) cyanobacteria, shown here at 300x magnification under a light microscope, are some of Earth's oldest life forms. These (b) stromatolites along the shores of Lake Thetis in Western Australia are ancient structures formed by the layering of cyanobacteria in shallow waters. (credit a: modification of work by NASA; credit b: modification of work by Ruth Ellison; scale-bar data from Matt

Russell)

What is biology? In simple terms, biology is the study of living organisms and their interactions with one another and their environments. This is a very broad definition because the scope of biology is vast. Biologists may study anything from the microscopic or submicroscopic view of a cell to ecosystems and the whole living planet ([\[link\]](#)). Listening to the daily news, you will quickly realize how many aspects of biology are discussed every day. For example, recent news topics include *Escherichia coli* ([\[link\]](#)) outbreaks in spinach and *Salmonella* contamination in peanut butter. Other subjects include efforts toward finding a cure for AIDS, Alzheimer's disease, and cancer. On a global scale, many researchers are committed to finding ways to protect the planet, solve environmental issues, and reduce the effects of climate change. All of these diverse endeavors are related to different facets of the discipline of biology.

*Escherichia coli* (*E. coli*) bacteria, seen in this scanning electron micrograph, are normal residents of our digestive tracts that aid in the absorption of vitamin K and other nutrients. However, virulent strains are sometimes responsible for disease outbreaks. (credit: Eric Erbe,

digital colorization by Christopher Pooley, both of USDA, ARS,

EMU)

## **The Process of Science**

Biology is a science, but what exactly is science? What does the study of biology share with other scientific disciplines? Science (from the Latin *scientia*, meaning “knowledge”) can be defined as knowledge that covers general truths or the operation of general laws, especially when acquired and tested by the scientific method. It becomes clear from this definition that the application of the scientific method plays a major role in science. The scientific method is a method of research with defined steps that include experiments and careful observation.

The steps of the scientific method will be examined in detail later, but one of the most important aspects of this method is the testing of hypotheses by means of repeatable experiments. A hypothesis is a suggested explanation for an event, which can be tested. Although using the scientific method is inherent to science, it is inadequate in determining what science is. This is because it is relatively easy to apply the scientific method to disciplines such as physics and chemistry, but when it comes to disciplines like archaeology, psychology, and geology, the scientific method becomes less applicable as it becomes more difficult to repeat experiments.

These areas of study are still sciences, however. Consider archeology—even though one cannot perform repeatable experiments, hypotheses may still be supported. For instance, an archeologist can hypothesize that an ancient culture existed based on finding a piece of pottery. Further hypotheses could be made about various characteristics of this culture, and these hypotheses may be found to be correct or false through continued support or contradictions from other findings. A hypothesis may become a verified theory. A theory is a tested and confirmed explanation for observations or phenomena. Science may be better defined as fields of study that attempt to comprehend the nature of the universe.

## **Natural Sciences**

What would you expect to see in a museum of natural sciences? Frogs? Plants? Dinosaur skeletons? Exhibits about how the brain functions? A planetarium? Gems and minerals? Or, maybe all of the above? Science includes such diverse fields as astronomy, biology, computer sciences, geology, logic, physics, chemistry, and mathematics ([link](#)). However, those fields of science related to the physical world and its phenomena and processes are considered natural sciences. Thus, a museum of natural sciences might contain any of the items listed above.

The diversity of scientific fields includes astronomy, biology, computer science, geology, logic, physics, chemistry, mathematics, and many other fields. (credit: "Image

Editor"/Flickr)

There is no complete agreement when it comes to defining what the natural sciences include, however. For some experts, the natural sciences are astronomy, biology, chemistry, earth science, and physics. Other scholars choose to divide natural sciences into life sciences, which study living things and include biology, and physical sciences, which study nonliving matter and include astronomy, geology, physics, and chemistry. Some disciplines such as biophysics and biochemistry build on both life and physical sciences and are interdisciplinary. Natural sciences are sometimes referred to as "hard science" because they rely on the use of quantitative data; social sciences that study society and human behavior are more likely to use qualitative assessments to drive investigations and findings.

Not surprisingly, the natural science of biology has many branches or subdisciplines. Cell biologists study cell structure and function, while biologists who study anatomy investigate the structure of an entire organism. Those biologists studying physiology, however, focus on the internal functioning of an organism. Some areas of biology focus on only particular types of living things. For example, botanists explore plants, while zoologists specialize in animals.

## **Scientific Reasoning**

One thing is common to all forms of science: an ultimate goal “to know.” Curiosity and inquiry are the driving forces for the development of science. Scientists seek to understand the world and the way it operates. To do this, they use two methods of logical thinking: inductive reasoning and deductive reasoning.

Inductive reasoning is a form of logical thinking that uses related observations to arrive at a general conclusion. This type of reasoning is common in descriptive science. A life scientist such as a biologist makes observations and records them. These data can be qualitative or quantitative, and the raw data can be supplemented with drawings, pictures, photos, or videos. From many observations, the scientist can infer conclusions (inductions) based on evidence. Inductive reasoning involves formulating generalizations inferred from careful observation and the analysis of a large amount of data. Brain studies provide an example. In this type of research, many live brains are observed while people are doing a specific activity, such as viewing images of food. The part of the brain that “lights up” during this activity is then predicted to be the part controlling the response to the selected stimulus, in this case, images of food. The “lighting up” of the various areas of the brain is caused by excess absorption of radioactive sugar derivatives by active areas of the brain. The resultant increase in radioactivity is observed by a scanner. Then, researchers can stimulate that part of the brain to see if similar responses result.

Deductive reasoning or deduction is the type of logic used in hypothesis-based science. In deductive reason, the pattern of thinking moves in the opposite direction as compared to inductive reasoning. Deductive reasoning is a form of logical thinking that uses a general principle or law to forecast specific results. From those general principles, a scientist can extrapolate and predict the specific results that would be valid as long as the general principles are valid. Studies in climate change can illustrate this type of reasoning. For example, scientists may predict that if the climate becomes warmer in a particular region, then the distribution of plants and animals should change. These predictions have been made and tested, and many such changes have been found, such as the modification of arable areas for agriculture, with change based on temperature averages.

Both types of logical thinking are related to the two main pathways of scientific study: descriptive science and hypothesis-based science. Descriptive (or discovery) science, which is usually inductive, aims to observe, explore, and discover, while hypothesis-based science, which is usually deductive, begins with a specific question or problem and a potential answer or solution that can be tested. The boundary between these two forms of study is often blurred, and most scientific endeavors combine both approaches. The fuzzy boundary becomes apparent when thinking about how easily observation can lead to specific questions. For example, a gentleman in the 1940s observed that the burr seeds that stuck to his clothes and his dog’s fur had a tiny hook structure. On closer inspection, he discovered that the burrs’ gripping device was more reliable than a zipper. He eventually developed a company and produced the hook-and-loop fastener popularly known today as Velcro. Descriptive science and hypothesis-based science are in continuous dialogue.

## **The Scientific Method**

Biologists study the living world by posing questions about it and seeking science-based responses. This approach is common to other sciences as well and is often referred to as the scientific method. The scientific method was used even in ancient times, but it was first documented by England’s Sir Francis Bacon (1561–1626) ([link](#)), who set up inductive

methods for scientific inquiry. The scientific method is not exclusively used by biologists but can be applied to almost all fields of study as a logical, rational problem-solving method.

Sir Francis Bacon (1561–1626) is credited with being the first to define the scientific method.

(credit: Paul van Somer)

The scientific process typically starts with an observation (often a problem to be solved) that leads to a question. Let's think about a simple problem that starts with an observation and apply the scientific method to solve the problem. One Monday morning, a student arrives at class and quickly discovers that the classroom is too warm. That is an observation that also describes a problem: the classroom is too warm. The student then asks a question: "Why is the classroom so warm?"

### **Proposing a Hypothesis**

Recall that a hypothesis is a suggested explanation that can be tested. To solve a problem, several hypotheses may be proposed. For example, one hypothesis might be, "The classroom is warm because no one turned on the air conditioning." But there could be other responses to the question, and therefore other hypotheses may be proposed. A second hypothesis might be, "The classroom is warm because there is a power failure, and so the air conditioning doesn't work."

Once a hypothesis has been selected, the student can make a prediction. A prediction is similar to a hypothesis but it typically has the format "If . . . then . . . ." For example, the prediction for the first hypothesis might be, "*If* the student turns on the air conditioning, *then* the classroom will no longer be too warm."

### **Testing a Hypothesis**

A valid hypothesis must be testable. It should also be falsifiable, meaning that it can be disproven by experimental results. Importantly, science does not claim to "prove" anything because scientific understandings are always subject to modification with further information. This step—openness to disproving ideas—is what distinguishes sciences from non-sciences. The presence of the supernatural, for instance, is neither testable nor falsifiable. To test a hypothesis, a researcher will conduct one or more experiments designed to eliminate one or more of the hypotheses. Each experiment will have one or more variables and one or more controls. A variable is any part of the experiment that can vary or change during the experiment. The control group contains every feature of the experimental group except it is not given the manipulation that is hypothesized about. Therefore, if the results of the experimental group differ from the control group, the difference must be due to the

hypothesized manipulation, rather than some outside factor. Look for the variables and controls in the examples that follow. To test the first hypothesis, the student would find out if the air conditioning is on. If the air conditioning is turned on but does not work, there should be another reason, and this hypothesis should be rejected. To test the second hypothesis, the student could check if the lights in the classroom are functional. If so, there is no power failure and this hypothesis should be rejected. Each hypothesis should be tested by carrying out appropriate experiments. Be aware that rejecting one hypothesis does not determine whether or not the other hypotheses can be accepted; it simply eliminates one hypothesis that is not valid ([\[link\]](#)). Using the scientific method, the hypotheses that are inconsistent with experimental data are rejected.

While this “warm classroom” example is based on observational results, other hypotheses and experiments might have clearer controls. For instance, a student might attend class on Monday and realize she had difficulty concentrating on the lecture. One observation to explain this occurrence might be, “When I eat breakfast before class, I am better able to pay attention.” The student could then design an experiment with a control to test this hypothesis.

In hypothesis-based science, specific results are predicted from a general premise. This type of reasoning is called deductive reasoning: deduction proceeds from the general to the particular. But the reverse of the process is also possible: sometimes, scientists reach a general conclusion from a number of specific observations. This type of reasoning is called inductive reasoning, and it proceeds from the particular to the general. Inductive and deductive reasoning are often used in tandem to advance scientific knowledge ([\[link\]](#)). In recent years a new approach of testing hypotheses has developed as a result of an exponential growth of data deposited in various databases. Using computer algorithms and statistical analyses of data in databases, a new field of so-called “data research” (also referred to as “in silico” research) provides new methods of data analyses and their interpretation. This will increase the demand for specialists in both biology and computer science, a promising career opportunity.

#### Art Connection

The scientific method consists of a series of well-defined steps. If a hypothesis is not supported by experimental data, a new hypothesis can be

proposed.

In the example below, the scientific method is used to solve an everyday problem. Order the scientific method steps (numbered items) with the process of solving the everyday problem (lettered items). Based on the results of the experiment, is the hypothesis correct? If it is incorrect, propose some alternative hypotheses.

1. Observation
  2. Question
  3. Hypothesis (answer)
  4. Prediction
  5. Experiment
  6. Result
- 
- a. There is something wrong with the electrical outlet.
  - b. If something is wrong with the outlet, my coffeemaker also won't work when plugged into it.
  - c. My toaster doesn't toast my bread.
  - d. I plug my coffee maker into the outlet.
  - e. My coffeemaker works.
  - f. Why doesn't my toaster work?

#### Art Connection

Scientists use two types of reasoning, inductive and deductive reasoning, to advance scientific knowledge. As is the case in this example, the conclusion from inductive reasoning can often become the premise for inductive

reasoning.

Decide if each of the following is an example of inductive or deductive reasoning.

1. All flying birds and insects have wings. Birds and insects flap their wings as they move through the air. Therefore, wings enable flight.
2. Insects generally survive mild winters better than harsh ones. Therefore, insect pests will become more problematic if global temperatures increase.
3. Chromosomes, the carriers of DNA, separate into daughter cells during cell division. Therefore, DNA is the genetic material.

4. Animals as diverse as humans, insects, and wolves all exhibit social behavior. Therefore, social behavior must have an evolutionary advantage.

The scientific method may seem too rigid and structured. It is important to keep in mind that, although scientists often follow this sequence, there is flexibility. Sometimes an experiment leads to conclusions that favor a change in approach; often, an experiment brings entirely new scientific questions to the puzzle. Many times, science does not operate in a linear fashion; instead, scientists continually draw inferences and make generalizations, finding patterns as their research proceeds. Scientific reasoning is more complex than the scientific method alone suggests. Notice, too, that the scientific method can be applied to solving problems that aren't necessarily scientific in nature.

## **Two Types of Science: Basic Science and Applied Science**

The scientific community has been debating for the last few decades about the value of different types of science. Is it valuable to pursue science for the sake of simply gaining knowledge, or does scientific knowledge only have worth if we can apply it to solving a specific problem or to bettering our lives? This question focuses on the differences between two types of science: basic science and applied science.

Basic science or “pure” science seeks to expand knowledge regardless of the short-term application of that knowledge. It is not focused on developing a product or a service of immediate public or commercial value. The immediate goal of basic science is knowledge for knowledge's sake, though this does not mean that, in the end, it may not result in a practical application.

In contrast, applied science or “technology,” aims to use science to solve real-world problems, making it possible, for example, to improve a crop yield, find a cure for a particular disease, or save animals threatened by a natural disaster ([link](#)). In applied science, the problem is usually defined for the researcher.

After Hurricane Ike struck the Gulf Coast in 2008, the U.S. Fish and Wildlife Service rescued this brown pelican. Thanks to applied science, scientists knew how to rehabilitate the bird.

(credit: FEMA)

Some individuals may perceive applied science as “useful” and basic science as “useless.” A question these people might pose to a scientist advocating knowledge acquisition would be, “What for?” A careful look at the history of science, however, reveals that basic knowledge has resulted in many remarkable applications of great value. Many scientists think that a basic understanding of science is necessary before an application is developed; therefore, applied science relies on the results generated through basic science. Other scientists think that it is time to move on from basic science and instead to find solutions to actual problems. Both approaches are valid. It is true that there are problems that demand immediate attention; however, few solutions would be found without the help of the wide knowledge foundation generated through basic science.

One example of how basic and applied science can work together to solve practical problems occurred after the discovery of DNA structure led to an understanding of the molecular mechanisms governing DNA replication. Strands of DNA, unique in every human, are found in our cells, where they provide the instructions necessary for life. During DNA replication, DNA makes new copies of itself, shortly before a cell divides. Understanding the mechanisms of DNA replication enabled scientists to develop laboratory techniques that are now used to identify genetic diseases, pinpoint individuals who were at a crime scene, and determine paternity. Without basic science, it is unlikely that applied science would exist.

Another example of the link between basic and applied research is the Human Genome Project, a study in which each human chromosome was analyzed and mapped to determine the precise sequence of DNA subunits and the exact location of each gene. (The gene is the basic unit of heredity; an individual’s complete collection of genes is his or her genome.) Other less complex organisms have also been studied as part of this project in order to gain a better understanding of human chromosomes. The Human Genome Project ([link](#)) relied on basic research carried out with simple organisms and, later, with the human genome. An important end goal eventually became using the data for applied research, seeking cures and early diagnoses for genetically related diseases.

The Human Genome Project was a 13-year collaborative effort among researchers working in several different fields of science. The project, which sequenced the entire human genome, was completed in 2003. (credit: the U.S. Department of Energy Genome Programs)

(<http://genomics.energy.gov>)

While research efforts in both basic science and applied science are usually carefully planned, it is important to note that some discoveries are made by serendipity, that is, by means of a fortunate accident or a lucky surprise. Penicillin was discovered when biologist Alexander Fleming accidentally left a petri dish of *Staphylococcus* bacteria open. An unwanted mold grew on the dish, killing the bacteria. The mold turned out to be *Penicillium*, and a new antibiotic was discovered. Even in the highly organized world of science, luck—when combined with an observant, curious mind—can lead to unexpected breakthroughs.

## **Reporting Scientific Work**

Whether scientific research is basic science or applied science, scientists must share their findings in order for other researchers to expand and build upon their discoveries. Collaboration with other scientists—when planning, conducting, and analyzing results—are all important for scientific research. For this reason, important aspects of a scientist's work are communicating with peers and disseminating results to peers. Scientists can share results by presenting them at a scientific meeting or conference, but this approach can reach only the select few who are present. Instead, most scientists present their results in peer-reviewed manuscripts that are published in scientific journals. Peer-reviewed manuscripts are scientific papers that are reviewed by a scientist's colleagues, or peers. These colleagues are qualified individuals, often experts in the same research area, who judge whether or not the scientist's work is suitable for publication. The process of peer review helps to ensure that the research described in a scientific paper or grant proposal is original, significant, logical, and thorough. Grant proposals, which are requests for research funding, are also subject to peer review. Scientists publish their work so other scientists can reproduce their experiments under similar or different conditions to expand on the findings. The experimental results must be consistent with the findings of other scientists.

A scientific paper is very different from creative writing. Although creativity is required to design experiments, there are fixed guidelines when it comes to presenting scientific results.

First, scientific writing must be brief, concise, and accurate. A scientific paper needs to be succinct but detailed enough to allow peers to reproduce the experiments.

The scientific paper consists of several specific sections—introduction, materials and methods, results, and discussion. This structure is sometimes called the “IMRaD” format. There are usually acknowledgment and reference sections as well as an abstract (a concise summary) at the beginning of the paper. There might be additional sections depending on the type of paper and the journal where it will be published; for example, some review papers require an outline.

The introduction starts with brief, but broad, background information about what is known in the field. A good introduction also gives the rationale of the work; it justifies the work carried out and also briefly mentions the end of the paper, where the hypothesis or research question driving the research will be presented. The introduction refers to the published scientific work of others and therefore requires citations following the style of the journal. Using the work or ideas of others without proper citation is considered plagiarism.

The materials and methods section includes a complete and accurate description of the substances used, and the method and techniques used by the researchers to gather data. The description should be thorough enough to allow another researcher to repeat the experiment and obtain similar results, but it does not have to be verbose. This section will also include information on how measurements were made and what types of calculations and statistical analyses were used to examine raw data. Although the materials and methods section gives an accurate description of the experiments, it does not discuss them.

Some journals require a results section followed by a discussion section, but it is more common to combine both. If the journal does not allow the combination of both sections, the results section simply narrates the findings without any further interpretation. The results are presented by means of tables or graphs, but no duplicate information should be presented. In the discussion section, the researcher will interpret the results, describe how variables may be related, and attempt to explain the observations. It is indispensable to conduct an extensive literature search to put the results in the context of previously published scientific research. Therefore, proper citations are included in this section as well.

Finally, the conclusion section summarizes the importance of the experimental findings. While the scientific paper almost certainly answered one or more scientific questions that were stated, any good research should lead to more questions. Therefore, a well-done scientific paper leaves doors open for the researcher and others to continue and expand on the findings.

Review articles do not follow the IMRAD format because they do not present original scientific findings, or primary literature; instead, they summarize and comment on findings that were published as primary literature and typically include extensive reference sections.

## **Section Summary**

Biology is the science that studies living organisms and their interactions with one another and their environments. Science attempts to describe and understand the nature of the universe in whole or in part by rational means. Science has many fields; those fields related to the physical world and its phenomena are considered natural sciences.

Science can be basic or applied. The main goal of basic science is to expand knowledge without any expectation of short-term practical application of that knowledge. The primary goal of applied research, however, is to solve practical problems.

Two types of logical reasoning are used in science. Inductive reasoning uses particular results to produce general scientific principles. Deductive reasoning is a form of logical thinking that predicts results by applying general principles. The common thread throughout scientific research is the use of the scientific method, a step-based process that consists of making observations, defining a problem, posing hypotheses, testing these hypotheses, and drawing one or more conclusions. The testing uses proper controls. Scientists present their results in peer-reviewed scientific papers published in scientific journals. A scientific research paper consists of several well-defined sections: introduction, materials and methods, results, and, finally, a concluding discussion. Review papers summarize the research done in a particular field over a period of time.

## Art Connections

[\[link\]](#) In the example below, the scientific method is used to solve an everyday problem. Order the scientific method steps (numbered items) with the process of solving the everyday problem (lettered items). Based on the results of the experiment, is the hypothesis correct? If it is incorrect, propose some alternative hypotheses.

1. Observation
  2. Question
  3. Hypothesis (answer)
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- 
- a. There is something wrong with the electrical outlet.
  - b. If something is wrong with the outlet, my coffeemaker also won't work when plugged into it.
  - c. My toaster doesn't toast my bread.
  - d. I plug my coffee maker into the outlet.
  - e. My coffeemaker works.
  - f. Why doesn't my toaster work?

[\[link\]](#) 1: C; 2: F; 3: A; 4: B; 5: D; 6: E. The original hypothesis is incorrect, as the coffeemaker works when plugged into the outlet. Alternative hypotheses include that the toaster might be broken or that the toaster wasn't turned on.

[\[link\]](#) Decide if each of the following is an example of inductive or deductive reasoning.

1. All flying birds and insects have wings. Birds and insects flap their wings as they move through the air. Therefore, wings enable flight.
2. Insects generally survive mild winters better than harsh ones. Therefore, insect pests will become more problematic if global temperatures increase.
3. Chromosomes, the carriers of DNA, separate into daughter cells during cell division. Therefore, DNA is the genetic material.

4. Animals as diverse as humans, insects, and wolves all exhibit social behavior. Therefore, social behavior must have an evolutionary advantage.

[\[link\]](#) 1: inductive; 2: deductive; 3: deductive; 4: inductive.

## Review Questions

The first forms of life on Earth were \_\_\_\_\_.

- a. plants
- b. microorganisms
- c. birds
- d. dinosaurs

B

A suggested and testable explanation for an event is called a \_\_\_\_\_.

- a. hypothesis
- b. variable
- c. theory
- d. control

A

Which of the following sciences is not considered a natural science?

- a. biology
- b. astronomy
- c. physics
- d. computer science

D

The type of logical thinking that uses related observations to arrive at a general conclusion is called \_\_\_\_\_.

- a. deductive reasoning
- b. the scientific method
- c. hypothesis-based science
- d. inductive reasoning

D

The process of \_\_\_\_\_ helps to ensure that a scientist's research is original, significant, logical, and thorough.

- a. publication
- b. public speaking
- c. peer review

- d. the scientific method

C

A person notices that her houseplants that are regularly exposed to music seem to grow more quickly than those in rooms with no music. As a result, she determines that plants grow better when exposed to music. This example most closely resembles which type of reasoning?

- a. inductive reasoning
- b. deductive reasoning
- c. neither, because no hypothesis was made
- d. both inductive and deductive reasoning

A

### **Free Response**

Although the scientific method is used by most of the sciences, it can also be applied to everyday situations. Think about a problem that you may have at home, at school, or with your car, and apply the scientific method to solve it.

Answers will vary, but should apply the steps of the scientific method. One possibility could be a car which doesn't start. The hypothesis could be that the car doesn't start because the battery is dead. The experiment would be to change the battery or to charge the battery and then check whether the car starts or not. If it starts, the problem was due to the battery, and the hypothesis is accepted.

Give an example of how applied science has had a direct effect on your daily life.

Answers will vary. One example of how applied science has had a direct effect on daily life is the presence of vaccines. Vaccines to prevent diseases such as polio, measles, tetanus, and even influenza affect daily life by contributing to individual and societal health.

Name two topics that are likely to be studied by biologists, and two areas of scientific study that would fall outside the realm of biology.

Answers will vary. Topics that fall inside the area of biological study include how diseases affect human bodies, how pollution impacts a species' habitat, and how plants respond to their environments. Topics that fall outside of biology (the "study of life") include how metamorphic rock is formed and how planetary orbits function.

Thinking about the topic of cancer, write a basic science question and an applied science question that a researcher interested in this topic might ask

Answers will vary. Basic science: What evolutionary purpose might cancer serve? Applied science: What strategies might be found to prevent cancer from reproducing at the cellular level?

### **Glossary**

abstract

opening section of a scientific paper that summarizes the research and conclusions

applied science

form of science that aims to solve real-world problems

basic science

science that seeks to expand knowledge and understanding regardless of the short-term application of that knowledge

biology

the study of living organisms and their interactions with one another and their environments

conclusion

section of a scientific paper that summarizes the importance of the experimental findings

control

part of an experiment that does not change during the experiment

deductive reasoning

form of logical thinking that uses a general inclusive statement to forecast specific results

descriptive science

(also, discovery science) form of science that aims to observe, explore, and investigate

discussion

section of a scientific paper in which the author interprets experimental results, describes how variables may be related, and attempts to explain the phenomenon in question

falsifiable

able to be disproven by experimental results

hypothesis

suggested explanation for an observation, which can be tested

hypothesis-based science

form of science that begins with a specific question and potential testable answers

inductive reasoning

form of logical thinking that uses related observations to arrive at a general conclusion

introduction

opening section of a scientific paper, which provides background information about what was known in the field prior to the research reported in the paper

life science

field of science, such as biology, that studies living things

materials and methods

section of a scientific paper that includes a complete description of the substances, methods, and techniques used by the researchers to gather data

natural science  
field of science that is related to the physical world and its phenomena and processes

peer-reviewed manuscript  
scientific paper that is reviewed by a scientist's colleagues who are experts in the field of study

physical science  
field of science, such as geology, astronomy, physics, and chemistry, that studies nonliving matter

plagiarism  
using other people's work or ideas without proper citation, creating the false impression that those are the author's original ideas

results  
section of a scientific paper in which the author narrates the experimental findings and presents relevant figures, pictures, diagrams, graphs, and tables, without any further interpretation

review article  
paper that summarizes and comments on findings that were published as primary literature

science  
knowledge that covers general truths or the operation of general laws, especially when acquired and tested by the scientific method

scientific method  
method of research with defined steps that include observation, formulation of a hypothesis, testing, and confirming or falsifying the hypothesis

serendipity  
fortunate accident or a lucky surprise

theory  
tested and confirmed explanation for observations or phenomena

variable  
part of an experiment that the experimenter changes

### Themes and Concepts of Biology

By the end of this section, you will be able to:

- Identify and describe the properties of life
- Describe the levels of organization among living things
- Recognize and interpret a phylogenetic tree
- List examples of different sub disciplines in biology

Biology is the science that studies life, but what exactly is life? This may sound like a silly question with an obvious response, but it is not always easy to define life. For example, a branch of biology called virology studies viruses, which exhibit some of the characteristics of living entities but lack others. It turns out that

although viruses can attack living organisms, cause diseases, and even reproduce, they do not meet the criteria that biologists use to define life. Consequently, virologists are not biologists, strictly speaking. Similarly, some biologists study the early molecular evolution that gave rise to life; since the events that preceded life are not biological events, these scientists are also excluded from biology in the strict sense of the term.

From its earliest beginnings, biology has wrestled with three questions: What are the shared properties that make something “alive”? And once we know something is alive, how do we find meaningful levels of organization in its structure? And, finally, when faced with the remarkable diversity of life, how do we organize the different kinds of organisms so that we can better understand them? As new organisms are discovered every day, biologists continue to seek answers to these and other questions.

## **Properties of Life**

All living organisms share several key characteristics or functions: order, sensitivity or response to the environment, reproduction, adaptation, growth and development, regulation, homeostasis, energy processing, and evolution. When viewed together, these nine characteristics serve to define life.

### **Order**

A toad represents a highly organized structure consisting of cells, tissues, organs, and organ systems. (credit: “Ivengo”/Wikimedia

Commons)

Organisms are highly organized, coordinated structures that consist of one or more cells. Even very simple, single-celled organisms are remarkably complex: inside each cell, atoms make up molecules; these in turn make up cell organelles and other cellular inclusions. In multicellular organisms ([link](#)), similar cells form tissues. Tissues, in turn, collaborate to

create organs (body structures with a distinct function). Organs work together to form organ systems.

### **Sensitivity or Response to Stimuli**

The leaves of this sensitive plant (*Mimosa pudica*) will instantly droop and fold when touched. After a few minutes, the plant returns to normal. (credit: Alex

Lomas)

Organisms respond to diverse stimuli. For example, plants can bend toward a source of light, climb on fences and walls, or respond to touch ([\[link\]](#)). Even tiny bacteria can move toward or away from chemicals (a process called *chemotaxis*) or light (*phototaxis*). Movement toward a stimulus is considered a positive response, while movement away from a stimulus is considered a negative response.

Link to Learning

Watch [this video](#) to see how plants respond to a stimulus—from opening to light, to wrapping a tendril around a branch, to capturing prey.

### **Reproduction**

Single-celled organisms reproduce by first duplicating their DNA, and then dividing it equally as the cell prepares to divide to form two new cells. Multicellular organisms often produce specialized reproductive germline cells that will form new individuals. When reproduction occurs, genes containing DNA are passed along to an organism's offspring.

These genes ensure that the offspring will belong to the same species and will have similar characteristics, such as size and shape.

### **Growth and Development**

Organisms grow and develop following specific instructions coded for by their genes. These genes provide instructions that will direct cellular growth and development, ensuring that a species' young ([link](#)) will grow up to exhibit many of the same characteristics as its parents.

Although no two look alike, these kittens have inherited genes from both parents and share many of the same characteristics. (credit: Rocky Mountain Feline

Rescue)

### **Regulation**

Even the smallest organisms are complex and require multiple regulatory mechanisms to coordinate internal functions, respond to stimuli, and cope with environmental stresses. Two examples of internal functions regulated in an organism are nutrient transport and blood flow. Organs (groups of tissues working together) perform specific functions, such as carrying oxygen throughout the body, removing wastes, delivering nutrients to every cell, and cooling the body.

### **Homeostasis**

Polar bears (*Ursus maritimus*) and other mammals living in ice-covered regions maintain their body temperature by generating heat and reducing heat loss through thick fur and a

dense layer of fat under their skin. (credit:

“longhorndave”/Flickr)

In order to function properly, cells need to have appropriate conditions such as proper temperature, pH, and appropriate concentration of diverse chemicals. These conditions may, however, change from one moment to the next. Organisms are able to maintain internal conditions within a narrow range almost constantly, despite environmental changes, through homeostasis (literally, “steady state”)—the ability of an organism to maintain constant internal conditions. For example, an organism needs to regulate body temperature through a process known as thermoregulation. Organisms that live in cold climates, such as the polar bear ([link](#)), have body structures that help them withstand low temperatures and conserve body heat. Structures that aid in this type of insulation include fur, feathers, blubber, and fat. In hot climates, organisms have methods (such as perspiration in humans or panting in dogs) that help them to shed excess body heat.

### **Energy Processing**

The California condor (*Gymnogyps californianus*) uses chemical energy derived from food to power flight. California condors are an endangered species; this bird has a wing tag that helps biologists identify the individual. (credit: Pacific Southwest Region U.S. Fish and Wildlife

Service)

All organisms use a source of energy for their metabolic activities. Some organisms capture energy from the sun and convert it into chemical energy in food; others use chemical energy in molecules they take in as food ([link](#)).

## **Levels of Organization of Living Things**

Living things are highly organized and structured, following a hierarchy that can be examined on a scale from small to large. The atom is the smallest and most fundamental unit of matter. It consists of a nucleus surrounded by electrons. Atoms form molecules. A molecule is a chemical structure consisting of at least two atoms held together by one or more chemical bonds. Many molecules that are biologically important are macromolecules, large molecules that are typically formed by polymerization (a polymer is a large molecule that is made by combining smaller units called monomers, which are simpler than macromolecules). An example of a macromolecule is deoxyribonucleic acid (DNA) ([link](#)), which contains the instructions for the structure and functioning of all living organisms.

All molecules, including this DNA molecule, are composed of atoms. (credit:

“brian0918”/Wikimedia Commons)  
Link to Learning

Watch [this video](#) that animates the three-dimensional structure of the DNA molecule shown in [link](#).

Some cells contain aggregates of macromolecules surrounded by membranes; these are called organelles. Organelles are small structures that exist within cells. Examples of organelles include mitochondria and chloroplasts, which carry out indispensable functions: mitochondria produce energy to power the cell, while chloroplasts enable green plants to utilize the energy in sunlight to make sugars. All living things are made of cells; the cell itself

is the smallest fundamental unit of structure and function in living organisms. (This requirement is why viruses are not considered living: they are not made of cells. To make new viruses, they have to invade and hijack the reproductive mechanism of a living cell; only then can they obtain the materials they need to reproduce.) Some organisms consist of a single cell and others are multicellular. Cells are classified as prokaryotic or eukaryotic. Prokaryotes are single-celled or colonial organisms that do not have membrane-bound nuclei; in contrast, the cells of eukaryotes do have membrane-bound organelles and a membrane-bound nucleus.

In larger organisms, cells combine to make tissues, which are groups of similar cells carrying out similar or related functions. Organs are collections of tissues grouped together performing a common function. Organs are present not only in animals but also in plants. An organ system is a higher level of organization that consists of functionally related organs. Mammals have many organ systems. For instance, the circulatory system transports blood through the body and to and from the lungs; it includes organs such as the heart and blood vessels. Organisms are individual living entities. For example, each tree in a forest is an organism. Single-celled prokaryotes and single-celled eukaryotes are also considered organisms and are typically referred to as microorganisms.

All the individuals of a species living within a specific area are collectively called a population. For example, a forest may include many pine trees. All of these pine trees represent the population of pine trees in this forest. Different populations may live in the same specific area. For example, the forest with the pine trees includes populations of flowering plants and also insects and microbial populations. A community is the sum of populations inhabiting a particular area. For instance, all of the trees, flowers, insects, and other populations in a forest form the forest's community. The forest itself is an ecosystem. An ecosystem consists of all the living things in a particular area together with the abiotic, non-living parts of that environment such as nitrogen in the soil or rain water. At the highest level of organization ([link](#)), the biosphere is the collection of all ecosystems, and it represents the zones of life on earth. It includes land, water, and even the atmosphere to a certain extent.

#### Art Connection

The biological levels of organization of living things are shown. From a single organelle to the entire biosphere, living organisms are parts of a highly structured hierarchy. (credit "organelles": modification of work by Umberto Salvagnin; credit "cells": modification of work by Bruce Wetzels, Harry Schaefer/ National Cancer Institute; credit "tissues": modification of work by Kilbad; Fama Clamosa; Mikael Häggström; credit "organs": modification of work by Mariana Ruiz Villareal; credit "organisms": modification of work by "Crystal"/Flickr; credit "ecosystems": modification of work by US Fish and Wildlife Service)

Headquarters; credit “biosphere”: modification of work by

NASA)

Which of the following statements is false?

- a. Tissues exist within organs which exist within organ systems.
- b. Communities exist within populations which exist within ecosystems.
- c. Organelles exist within cells which exist within tissues.
- d. Communities exist within ecosystems which exist in the biosphere.

## **The Diversity of Life**

The fact that biology, as a science, has such a broad scope has to do with the tremendous diversity of life on earth. The source of this diversity is evolution, the process of gradual change during which new species arise from older species. Evolutionary biologists study the evolution of living things in everything from the microscopic world to ecosystems.

The evolution of various life forms on Earth can be summarized in a phylogenetic tree ([link](#)). A phylogenetic tree is a diagram showing the evolutionary relationships among biological species based on similarities and differences in genetic or physical traits or both. A phylogenetic tree is composed of nodes and branches. The internal nodes represent ancestors and are points in evolution when, based on scientific evidence, an ancestor is thought to have diverged to form two new species. The length of each branch is proportional to the time elapsed since the split.

This phylogenetic tree was constructed by microbiologist Carl Woese using data obtained from sequencing ribosomal RNA genes. The tree shows the separation of living organisms into three domains: Bacteria, Archaea, and Eukarya. Bacteria and Archaea are prokaryotes, single-celled organisms lacking intracellular organelles. (credit: Eric Gaba; NASA

## Astrobiology

Institute)  
Evolution Connection

**Carl Woese and the Phylogenetic Tree** In the past, biologists grouped living organisms into five kingdoms: animals, plants, fungi, protists, and bacteria. The organizational scheme was based mainly on physical features, as opposed to physiology, biochemistry, or molecular biology, all of which are used by modern systematics. The pioneering work of American microbiologist Carl Woese in the early 1970s has shown, however, that life on Earth has evolved along three lineages, now called domains—Bacteria, Archaea, and Eukarya. The first two are prokaryotic cells with microbes that lack membrane-enclosed nuclei and organelles. The third domain contains the eukaryotes and includes unicellular microorganisms together with the four original kingdoms (excluding bacteria). Woese defined Archaea as a new domain, and this resulted in a new taxonomic tree ([\[link\]](#)). Many organisms belonging to the Archaea domain live under extreme conditions and are called extremophiles. To construct his tree, Woese used genetic relationships rather than similarities based on morphology (shape).

Woese's tree was constructed from comparative sequencing of the genes that are universally distributed, present in every organism, and conserved (meaning that these genes have remained essentially unchanged throughout evolution). Woese's approach was revolutionary because comparisons of physical features are insufficient to differentiate between the prokaryotes that appear fairly similar in spite of their tremendous biochemical diversity and genetic variability ([\[link\]](#)). The comparison of homologous DNA and RNA sequences

provided Woese with a sensitive device that revealed the extensive variability of prokaryotes, and which justified the separation of the prokaryotes into two domains: bacteria and archaea.

These images represent different domains. The (a) bacteria in this micrograph belong to Domain Bacteria, while the (b) extremophiles (not visible) living in this hot vent belong to Domain Archaea. Both the (c) sunflower and (d) lion are part of Domain Eukarya. (credit a: modification of work by Drew March; credit b: modification of work by Steve Jurvetson; credit c: modification of work by Michael Arrighi; credit d: modification of work by Leszek

Leszcynski)

## **Branches of Biological Study**

The scope of biology is broad and therefore contains many branches and subdisciplines. Biologists may pursue one of those subdisciplines and work in a more focused field. For instance, molecular biology and biochemistry study biological processes at the molecular and chemical level, including interactions among molecules such as DNA, RNA, and proteins, as well as the way they are regulated. Microbiology, the study of microorganisms, is the study of the structure and function of single-celled organisms. It is quite a broad branch itself, and depending on the subject of study, there are also microbial physiologists, ecologists, and geneticists, among others.

### Career Connection

**Forensic Scientist** Forensic science is the application of science to answer questions related to the law. Biologists as well as chemists and biochemists can be forensic scientists. Forensic scientists provide scientific evidence for use in courts, and their job involves examining trace materials associated with crimes. Interest in forensic science has increased in the last few years, possibly because of popular television shows that feature forensic scientists on the job. Also, the development of molecular techniques and the establishment of DNA databases have

expanded the types of work that forensic scientists can do. Their job activities are primarily related to crimes against people such as murder, rape, and assault. Their work involves analyzing samples such as hair, blood, and other body fluids and also processing DNA ([link](#)) found in many different environments and materials. Forensic scientists also analyze other biological evidence left at crime scenes, such as insect larvae or pollen grains. Students who want to pursue careers in forensic science will most likely be required to take chemistry and biology courses as well as some intensive math courses.

This forensic scientist works in a DNA extraction room at the U.S. Army Criminal Investigation Laboratory at Fort Gillem, GA. (credit: United States Army CID Command

Public Affairs)

Another field of biological study, neurobiology, studies the biology of the nervous system, and although it is considered a branch of biology, it is also recognized as an interdisciplinary field of study known as neuroscience. Because of its interdisciplinary nature, this subdiscipline studies different functions of the nervous system using molecular, cellular, developmental, medical, and computational approaches.

Researchers work on excavating dinosaur fossils at a site in Castellón, Spain. (credit: Mario

Modesto)

Paleontology, another branch of biology, uses fossils to study life's history ([link](#)). Zoology and botany are the study of animals and plants, respectively. Biologists can also specialize as biotechnologists, ecologists, or physiologists, to name just a few areas. This is just a small sample of the many fields that biologists can pursue.

Biology is the culmination of the achievements of the natural sciences from their inception to today. Excitingly, it is the cradle of emerging sciences, such as the biology of brain activity, genetic engineering of custom organisms, and the biology of evolution that uses the laboratory tools of molecular biology to retrace the earliest stages of life on earth. A scan of news headlines—whether reporting on immunizations, a newly discovered species, sports doping, or a genetically-modified food—demonstrates the way biology is active in and important to our everyday world.

## Section Summary

Biology is the science of life. All living organisms share several key properties such as order, sensitivity or response to stimuli, reproduction, growth and development, regulation, homeostasis, and energy processing. Living things are highly organized parts of a hierarchy that includes atoms, molecules, organelles, cells, tissues, organs, and organ systems. Organisms, in turn, are grouped as populations, communities, ecosystems, and the biosphere. The great diversity of life today evolved from less-diverse ancestral organisms over billions of years. A diagram called a phylogenetic tree can be used to show evolutionary relationships among organisms.

Biology is very broad and includes many branches and subdisciplines. Examples include molecular biology, microbiology, neurobiology, zoology, and botany, among others.

## Art Connections

[link](#) Which of the following statements is false?

- a. Tissues exist within organs which exist within organ systems.
- b. Communities exist within populations which exist within ecosystems.
- c. Organelles exist within cells which exist within tissues.
- d. Communities exist within ecosystems which exist in the biosphere.

[\[link\]](#) Communities exist within populations which exist within ecosystems.

## Review Questions

The smallest unit of biological structure that meets the functional requirements of “living” is the \_\_\_\_\_.

- a. organ
- b. organelle
- c. cell
- d. macromolecule

C

Viruses are not considered living because they \_\_\_\_\_.

- a. are not made of cells
- b. lack cell nuclei
- c. do not contain DNA or RNA
- d. cannot reproduce

A

The presence of a membrane-enclosed nucleus is a characteristic of \_\_\_\_\_.

- a. prokaryotic cells
- b. eukaryotic cells
- c. living organisms
- d. bacteria

B

A group of individuals of the same species living in the same area is called a(n) \_\_\_\_\_.

- a. family
- b. community
- c. population
- d. ecosystem

C

Which of the following sequences represents the hierarchy of biological organization from the most inclusive to the least complex level?

- a. organelle, tissue, biosphere, ecosystem, population

- b. organ, organism, tissue, organelle, molecule
- c. organism, community, biosphere, molecule, tissue, organ
- d. biosphere, ecosystem, community, population, organism

D

Where in a phylogenetic tree would you expect to find the organism that had evolved most recently?

- a. at the base
- b. within the branches
- c. at the nodes
- d. at the branch tips

D

### **Free Response**

Select two items that biologists agree are necessary in order to consider an organism “alive.” For each, give an example of a non-living object that otherwise fits the definition of “alive,”

Answers will vary. Layers of sedimentary rock have order but are not alive. Technology is capable of regulation but is not, of itself, alive.

Consider the levels of organization of the biological world, and place each of these items in order from smallest level of organization to most encompassing: skin cell, elephant, water molecule, planet Earth, tropical rainforest, hydrogen atom, wolf pack, liver.

Smallest level of organization to largest: hydrogen atom, water molecule, skin cell, liver, elephant, wolf pack, tropical rainforest, planet Earth

You go for a long walk on a hot day. Give an example of a way in which homeostasis keeps your body healthy.

During your walk, you may begin to perspire, which cools your body and helps your body to maintain a constant internal temperature. You might also become thirsty and pause long enough for a cool drink, which will help to restore the water lost during perspiration.

Using examples, explain how biology can be studied from a microscopic approach to a global approach.

Researchers can approach biology from the smallest to the largest, and everything in between. For instance, an ecologist may study a population of individuals, the population’s community, the community’s ecosystem, and the ecosystem’s part in the biosphere. When studying an individual organism, a biologist could examine the cell and its organelles, the tissues that the cells make up, the organs and their respective organ systems, and the sum total—the organism itself.

### **Glossary**

atom  
smallest and most fundamental unit of matter

biochemistry  
study of the chemistry of biological organisms

biosphere  
collection of all the ecosystems on Earth

botany  
study of plants

cell  
smallest fundamental unit of structure and function in living things

community  
set of populations inhabiting a particular area

ecosystem  
all the living things in a particular area together with the abiotic, nonliving parts of that environment

eukaryote  
organism with cells that have nuclei and membrane-bound organelles

evolution  
process of gradual change during which new species arise from older species and some species become extinct

homeostasis  
ability of an organism to maintain constant internal conditions

macromolecule  
large molecule, typically formed by the joining of smaller molecules

microbiology  
study of the structure and function of microorganisms

molecule  
chemical structure consisting of at least two atoms held together by one or more chemical bonds

molecular biology  
study of biological processes and their regulation at the molecular level, including interactions among molecules such as DNA, RNA, and proteins

neurobiology  
study of the biology of the nervous system

organ  
collection of related tissues grouped together performing a common function

organ system  
level of organization that consists of functionally related interacting organs

organelle  
small structures that exist within cells and carry out cellular functions

organism  
individual living entity

paleontology  
study of life's history by means of fossils

phylogenetic tree

diagram showing the evolutionary relationships among various biological species based on similarities and differences in genetic or physical traits or both; in essence, a hypothesis concerning evolutionary connections

population

all of the individuals of a species living within a specific area

prokaryote

single-celled organism that lacks organelles and does not have nuclei surrounded by a nuclear membrane

tissue

group of similar cells carrying out related functions

zoology

study of animals

Atoms are the building blocks of molecules found in the universe—air, soil, water, rocks . . . and also the cells of all living organisms. In this model of an organic molecule, the atoms of carbon (black), hydrogen (white), nitrogen (blue), oxygen (red), and sulfur (yellow) are shown in proportional atomic size. The silver rods indicate chemical bonds. (credit: modification of work by Christian

Guthier)

Elements in various combinations comprise all matter, including living things. Some of the most abundant elements in living organisms include carbon, hydrogen, nitrogen, oxygen, sulfur, and phosphorus. These form the nucleic acids, proteins, carbohydrates, and lipids that are the fundamental components of living matter. Biologists must understand these important building blocks and the unique structures of the atoms that make up molecules, allowing for the formation of cells, tissues, organ systems, and entire organisms.

All biological processes follow the laws of physics and chemistry, so in order to understand how biological systems work, it is important to understand the underlying physics and chemistry. For example, the flow of blood within the circulatory system follows the laws of physics that regulate the modes of fluid flow. The breakdown of the large, complex molecules of food into smaller molecules—and the conversion of these to release energy to be stored in adenosine

triphosphate (ATP)—is a series of chemical reactions that follow chemical laws. The properties of water and the formation of hydrogen bonds are key to understanding living processes. Recognizing the properties of acids and bases is important, for example, to our understanding of the digestive process. Therefore, the fundamentals of physics and chemistry are important for gaining insight into biological processes.

### Atoms, Isotopes, Ions, and Molecules: The Building Blocks

By the end of this section, you will be able to:

- Define matter and elements
- Describe the interrelationship between protons, neutrons, and electrons
- Compare the ways in which electrons can be donated or shared between atoms
- Explain the ways in which naturally occurring elements combine to create molecules, cells, tissues, organ systems, and organisms

At its most fundamental level, life is made up of matter. Matter is any substance that occupies space and has mass. Elements are unique forms of matter with specific chemical and physical properties that cannot be broken down into smaller substances by ordinary chemical reactions. There are 118 elements, but only 92 occur naturally. The remaining elements are synthesized in laboratories and are unstable.

Each element is designated by its chemical symbol, which is a single capital letter or, when the first letter is already “taken” by another element, a combination of two letters. Some elements follow the English term for the element, such as C for carbon and Ca for calcium. Other elements’ chemical symbols derive from their Latin names; for example, the symbol for sodium is Na, referring to *natrium*, the Latin word for sodium.

The four elements common to all living organisms are oxygen (O), carbon (C), hydrogen (H), and nitrogen (N). In the non-living world, elements are found in different proportions, and some elements common to living organisms are relatively rare on the earth as a whole, as shown in [\[link\]](#). For example, the atmosphere is rich in nitrogen and oxygen but contains little carbon and hydrogen, while the earth’s crust, although it contains oxygen and a small amount of hydrogen, has little nitrogen and carbon. In spite of their differences in abundance, all elements and the chemical reactions between them obey the same chemical and physical laws regardless of whether they are a part of the living or non-living world.

#### **Approximate Percentage of Elements in Living Organisms (Humans) Compared to the Non-living World**

<b>Element</b>	<b>Life (Humans)</b>	<b>Atmosphere</b>	<b>Earth’s Crust</b>
Oxygen (O)	65%	21%	46%
Carbon (C)	18%	trace	trace
Hydrogen (H)	10%	trace	0.1%
Nitrogen (N)	3%	78%	trace

### **The Structure of the Atom**

To understand how elements come together, we must first discuss the smallest component or building block of an element, the atom. An atom is the smallest unit of matter that retains all of the chemical properties of an element. For example, one gold atom has all of the properties of gold in that it is a solid metal at room temperature. A gold coin is simply a very large number of gold atoms molded into the shape of a coin and containing small amounts of other elements known as impurities. Gold atoms cannot be broken down into anything smaller while still retaining the properties of gold.

An atom is composed of two regions: the nucleus, which is in the center of the atom and contains protons and neutrons, and the outermost region of the atom which holds its electrons in orbit around the nucleus, as illustrated in [\[link\]](#). Atoms contain protons, electrons, and neutrons, among other subatomic particles. The only exception is hydrogen (H), which is made of one proton and one electron with no neutrons.

Elements, such as helium, depicted here, are made up of atoms. Atoms are made up of protons and neutrons located within the nucleus, with electrons in orbitals surrounding the

nucleus.

Protons and neutrons have approximately the same mass, about  $1.67 \times 10^{-24}$  grams. Scientists arbitrarily define this amount of mass as one atomic mass unit (amu) or one Dalton, as shown in [\[link\]](#). Although similar in mass, protons and neutrons differ in their electric charge. A proton is positively charged whereas a neutron is uncharged. Therefore, the number of neutrons in an atom contributes significantly to its mass, but not to its charge. Electrons are much smaller in mass than protons, weighing only  $9.11 \times 10^{-28}$  grams, or about 1/1800 of an atomic mass unit. Hence, they do not contribute much to an element's overall atomic mass. Therefore, when considering atomic mass, it is customary to ignore the mass of any electrons and calculate the atom's mass based on the number of protons and neutrons alone. Although not significant contributors to mass, electrons do contribute greatly to the atom's charge, as each electron has a negative charge equal to the positive charge of a proton. In uncharged, neutral atoms, the number of electrons orbiting the nucleus is equal to the number of protons inside the nucleus. In these atoms, the positive and negative charges cancel each other out, leading to an atom with no net charge.

Accounting for the sizes of protons, neutrons, and electrons, most of the volume of an atom—greater than 99 percent—is, in fact, empty space. With all this empty space, one might ask why so-called solid objects do not just pass through one another. The reason they do not is that the electrons that surround all atoms are negatively charged and negative charges repel each other.

### Protons, Neutrons, and Electrons

	Charge	Mass (amu)	Location
Proton	+1	1	nucleus
Neutron	0	1	nucleus
Electron	-1	0	orbitals

### Atomic Number and Mass

Atoms of each element contain a characteristic number of protons and electrons. The number of protons determines an element's atomic number and is used to distinguish one element from another. The number of neutrons is variable, resulting in isotopes, which are different forms of the same atom that vary only in the number of neutrons they possess. Together, the number of protons and the number of neutrons determine an element's mass number, as illustrated in [\[link\]](#). Note that the small contribution of mass from electrons is disregarded in calculating the mass number. This approximation of mass can be used to easily calculate how many neutrons an element has by simply subtracting the number of protons from the mass number. Since an element's isotopes will have slightly different mass numbers, scientists also determine the atomic mass, which is the calculated mean of the mass number for its naturally occurring isotopes. Often, the resulting number contains a fraction. For example, the atomic mass of chlorine (Cl) is 35.45 because chlorine is composed of several isotopes, some (the majority) with atomic mass 35 (17 protons and 18 neutrons) and some with atomic mass 37 (17 protons and 20 neutrons).

#### Art Connection

Carbon has an atomic number of six, and two stable isotopes with mass numbers of twelve and thirteen, respectively. Its relative atomic mass is

How many neutrons do carbon-12 and carbon-13 have, respectively?

## Isotopes

Isotopes are different forms of an element that have the same number of protons but a different number of neutrons. Some elements—such as carbon, potassium, and uranium—have naturally occurring isotopes. Carbon-12 contains six protons, six neutrons, and six electrons; therefore, it has a mass number of 12 (six protons and six neutrons). Carbon-14 contains six protons, eight neutrons, and six electrons; its atomic mass is 14 (six protons and eight neutrons). These two alternate forms of carbon are isotopes. Some isotopes may emit neutrons, protons, and electrons, and attain a more stable atomic configuration (lower level of potential energy); these are radioactive isotopes, or radioisotopes. Radioactive decay (carbon-14 decaying to eventually become nitrogen-14) describes the energy loss that occurs when an unstable atom's nucleus releases radiation.

### Evolution Connection

**Carbon Dating** Carbon is normally present in the atmosphere in the form of gaseous compounds like carbon dioxide and methane. Carbon-14 ( $^{14}\text{C}$ ) is a naturally occurring radioisotope that is created in the atmosphere from atmospheric  $^{14}\text{N}$  (nitrogen) by the addition of a neutron and the loss of a proton because of cosmic rays. This is a continuous process, so more  $^{14}\text{C}$  is always being created. As a living organism incorporates  $^{14}\text{C}$  initially as carbon dioxide fixed in the process of photosynthesis, the relative amount of  $^{14}\text{C}$  in its body is equal to the concentration of  $^{14}\text{C}$  in the atmosphere. When an organism dies, it is no longer ingesting  $^{14}\text{C}$ , so the ratio between  $^{14}\text{C}$  and  $^{12}\text{C}$  will decline as  $^{14}\text{C}$  decays gradually to  $^{14}\text{N}$  by a process called beta decay—the emission of electrons or positrons. This decay gives off energy in a slow process.

After approximately 5,730 years, half of the starting concentration of  $^{14}\text{C}$  will have been converted back to  $^{14}\text{N}$ . The time it takes for half of the original concentration of an isotope to decay back to its more stable form is called its half-life. Because the half-life of  $^{14}\text{C}$  is long, it is used to date formerly living objects such as old bones or wood. Comparing the ratio of the  $^{14}\text{C}$  concentration found in an object to the amount of  $^{14}\text{C}$  detected in the atmosphere, the amount of the isotope that has not yet decayed can be determined. On the basis of this amount, the age of the material, such as the pygmy mammoth shown in [\[link\]](#), can be calculated with accuracy if it is not much older than about 50,000 years. Other elements have isotopes with different half lives. For example,  $^{40}\text{K}$  (potassium-40) has a half-life of 1.25 billion years, and  $^{235}\text{U}$  (Uranium 235) has a half-life of about 700 million years. Through the use of radiometric dating, scientists can study the age of fossils or other remains of extinct organisms to understand how organisms have evolved from earlier species.

The age of carbon-containing remains less than about 50,000 years old, such as this pygmy mammoth, can be determined using carbon dating. (credit: Bill Faulkner,

NPS)

[Link to Learning](#)

To learn more about atoms, isotopes, and how to tell one isotope from another, run the simulation.

Water

By the end of this section, you will be able to:

- Describe the properties of water that are critical to maintaining life
- Explain why water is an excellent solvent
- Provide examples of water's cohesive and adhesive properties
- Discuss the role of acids, bases, and buffers in homeostasis

Why do scientists spend time looking for water on other planets? Why is water so important? It is because water is essential to life as we know it. Water is one of the more abundant molecules and the one most critical to life on Earth. Approximately 60–70 percent of the human body is made up of water. Without it, life as we know it simply would not exist.

The polarity of the water molecule and its resulting hydrogen bonding make water a unique substance with special properties that are intimately tied to the processes of life. Life originally evolved in a watery environment, and most of an organism's cellular chemistry and metabolism occur inside the watery contents of the cell's cytoplasm. Special properties of

water are its high heat capacity and heat of vaporization, its ability to dissolve polar molecules, its cohesive and adhesive properties, and its dissociation into ions that leads to the generation of pH. Understanding these characteristics of water helps to elucidate its importance in maintaining life.

## **Water's Polarity**

One of water's important properties is that it is composed of polar molecules: the hydrogen and oxygen within water molecules (H<sub>2</sub>O) form polar covalent bonds. While there is no net charge to a water molecule, the polarity of water creates a slightly positive charge on hydrogen and a slightly negative charge on oxygen, contributing to water's properties of attraction. Water's charges are generated because oxygen is more electronegative than hydrogen, making it more likely that a shared electron would be found near the oxygen nucleus than the hydrogen nucleus, thus generating the partial negative charge near the oxygen.

As a result of water's polarity, each water molecule attracts other water molecules because of the opposite charges between water molecules, forming hydrogen bonds. Water also attracts or is attracted to other polar molecules and ions. A polar substance that interacts readily with or dissolves in water is referred to as hydrophilic (hydro- = "water"; -philic = "loving"). In contrast, non-polar molecules such as oils and fats do not interact well with water, as shown in [\[link\]](#) and separate from it rather than dissolve in it, as we see in salad dressings containing oil and vinegar (an acidic water solution). These nonpolar compounds are called hydrophobic (hydro- = "water"; -phobic = "fearing").

Oil and water do not mix. As this macro image of oil and water shows, oil does not dissolve in water but forms droplets instead. This is due to it being a nonpolar compound. (credit:

Gautam Dogra).

## **Water's States: Gas, Liquid, and Solid**

The formation of hydrogen bonds is an important quality of the liquid water that is crucial to life as we know it. As water molecules make hydrogen bonds with each other, water takes on

some unique chemical characteristics compared to other liquids and, since living things have a high water content, understanding these chemical features is key to understanding life. In liquid water, hydrogen bonds are constantly formed and broken as the water molecules slide past each other. The breaking of these bonds is caused by the motion (kinetic energy) of the water molecules due to the heat contained in the system. When the heat is raised as water is boiled, the higher kinetic energy of the water molecules causes the hydrogen bonds to break completely and allows water molecules to escape into the air as gas (steam or water vapor). On the other hand, when the temperature of water is reduced and water freezes, the water molecules form a crystalline structure maintained by hydrogen bonding (there is not enough energy to break the hydrogen bonds) that makes ice less dense than liquid water, a phenomenon not seen in the solidification of other liquids.

Water's lower density in its solid form is due to the way hydrogen bonds are oriented as it freezes: the water molecules are pushed farther apart compared to liquid water. With most other liquids, solidification when the temperature drops includes the lowering of kinetic energy between molecules, allowing them to pack even more tightly than in liquid form and giving the solid a greater density than the liquid.

The lower density of ice, illustrated and pictured in [\[link\]](#), an anomaly, causes it to float at the surface of liquid water, such as in an iceberg or in the ice cubes in a glass of ice water. In lakes and ponds, ice will form on the surface of the water creating an insulating barrier that protects the animals and plant life in the pond from freezing. Without this layer of insulating ice, plants and animals living in the pond would freeze in the solid block of ice and could not survive. The detrimental effect of freezing on living organisms is caused by the expansion of ice relative to liquid water. The ice crystals that form upon freezing rupture the delicate membranes essential for the function of living cells, irreversibly damaging them. Cells can only survive freezing if the water in them is temporarily replaced by another liquid like glycerol.

Hydrogen bonding makes ice less dense than liquid water. The (a) lattice structure of ice makes it less dense than the freely flowing molecules of liquid water, enabling it to (b) float on water. (credit a: modification of work by Jane Whitney, image created using Visual

Molecular Dynamics (VMD) software<sup>1</sup>; credit b: modification of work by Carlos

Ponte)  
Link to Learning

Click [here](#) to see a 3-D animation of the structure of an ice lattice. (Image credit: Jane Whitney. Image created using Visual Molecular Dynamics VMD software.<sup>2</sup>)

## **Water's High Heat Capacity**

Water's high heat capacity is a property caused by hydrogen bonding among water molecules. Water has the highest specific heat capacity of any liquids. Specific heat is defined as the amount of heat one gram of a substance must absorb or lose to change its temperature by one degree Celsius. For water, this amount is one calorie. It therefore takes water a long time to heat and long time to cool. In fact, the specific heat capacity of water is about five times more than that of sand. This explains why the land cools faster than the sea. Due to its high heat capacity, water is used by warm blooded animals to more evenly disperse heat in their bodies: it acts in a similar manner to a car's cooling system, transporting heat from warm places to cool places, causing the body to maintain a more even temperature.

## Water's Heat of Vaporization

Water also has a high heat of vaporization, the amount of energy required to change one gram of a liquid substance to a gas. A considerable amount of heat energy (586 cal) is required to accomplish this change in water. This process occurs on the surface of water. As liquid water heats up, hydrogen bonding makes it difficult to separate the liquid water molecules from each other, which is required for it to enter its gaseous phase (steam). As a result, water acts as a heat sink or heat reservoir and requires much more heat to boil than does a liquid such as ethanol (grain alcohol), whose hydrogen bonding with other ethanol molecules is weaker than water's hydrogen bonding. Eventually, as water reaches its boiling point of 100° Celsius (212° Fahrenheit), the heat is able to break the hydrogen bonds between the water molecules, and the kinetic energy (motion) between the water molecules allows them to escape from the liquid as a gas. Even when below its boiling point, water's individual molecules acquire enough energy from other water molecules such that some surface water molecules can escape and vaporize: this process is known as evaporation.

The fact that hydrogen bonds need to be broken for water to evaporate means that a substantial amount of energy is used in the process. As the water evaporates, energy is taken up by the process, cooling the environment where the evaporation is taking place. In many living organisms, including in humans, the evaporation of sweat, which is 90 percent water, allows the organism to cool so that homeostasis of body temperature can be maintained.

## Water's Solvent Properties

Since water is a polar molecule with slightly positive and slightly negative charges, ions and polar molecules can readily dissolve in it. Therefore, water is referred to as a solvent, a substance capable of dissolving other polar molecules and ionic compounds. The charges associated with these molecules will form hydrogen bonds with water, surrounding the particle with water molecules. This is referred to as a sphere of hydration, or a hydration shell, as illustrated in [\[link\]](#) and serves to keep the particles separated or dispersed in the water.

When ionic compounds are added to water, the individual ions react with the polar regions of the water molecules and their ionic bonds are disrupted in the process of dissociation. Dissociation occurs when atoms or groups of atoms break off from molecules and form ions. Consider table salt (NaCl, or sodium chloride): when NaCl crystals are added to water, the molecules of NaCl dissociate into Na<sup>+</sup> and Cl<sup>-</sup> ions, and spheres of hydration form around the ions, illustrated in [\[link\]](#). The positively charged sodium ion is surrounded by the partially negative charge of the water molecule's oxygen. The negatively charged chloride ion is surrounded by the partially positive charge of the hydrogen on the water molecule.

When table salt (NaCl) is mixed in water, spheres of hydration are formed around the

ions.

### **Water's Cohesive and Adhesive Properties**

Have you ever filled a glass of water to the very top and then slowly added a few more drops? Before it overflows, the water forms a dome-like shape above the rim of the glass. This water can stay above the glass because of the property of cohesion. In cohesion, water molecules are attracted to each other (because of hydrogen bonding), keeping the molecules together at the liquid-gas (water-air) interface, although there is no more room in the glass.

Cohesion allows for the development of surface tension, the capacity of a substance to withstand being ruptured when placed under tension or stress. This is also why water forms droplets when placed on a dry surface rather than being flattened out by gravity. When a small scrap of paper is placed onto the droplet of water, the paper floats on top of the water droplet even though paper is denser (heavier) than the water. Cohesion and surface tension keep the hydrogen bonds of water molecules intact and support the item floating on the top. It's even possible to "float" a needle on top of a glass of water if it is placed gently without breaking the surface tension, as shown in [\[link\]](#).

The weight of the needle is pulling the surface downward; at the same time, the surface tension is pulling it up, suspending it on the surface of the water and keeping it from sinking.

Notice the indentation in the water around the needle. (credit: Cory

Zanker)

These cohesive forces are related to water's property of adhesion, or the attraction between water molecules and other molecules. This attraction is sometimes stronger than water's cohesive forces, especially when the water is exposed to charged surfaces such as those found on the inside of thin glass tubes known as capillary tubes. Adhesion is observed when water "climbs" up the tube placed in a glass of water: notice that the water appears to be higher on the sides of the tube than in the middle. This is because the water molecules are attracted to the charged glass walls of the capillary more than they are to each other and therefore adhere to it. This type of adhesion is called capillary action, and is illustrated in [\[link\]](#).

Capillary action in a glass tube is caused by the adhesive forces exerted by the internal surface of the glass exceeding the cohesive forces between the water molecules themselves. (credit: modification of work by Pearson-Scott Foresman, donated to the Wikimedia

Foundation)

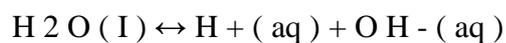
Why are cohesive and adhesive forces important for life? Cohesive and adhesive forces are important for the transport of water from the roots to the leaves in plants. These forces create a “pull” on the water column. This pull results from the tendency of water molecules being evaporated on the surface of the plant to stay connected to water molecules below them, and so they are pulled along. Plants use this natural phenomenon to help transport water from their roots to their leaves. Without these properties of water, plants would be unable to receive the water and the dissolved minerals they require. In another example, insects such as the water strider, shown in [\[link\]](#), use the surface tension of water to stay afloat on the surface layer of water and even mate there.

Water’s cohesive and adhesive properties allow this water strider (*Gerris* sp.) to stay afloat.

(credit: Tim Vickers)

## **pH, Buffers, Acids, and Bases**

The pH of a solution indicates its acidity or alkalinity.



litmus or pH paper, filter paper that has been treated with a natural water-soluble dye so it can be used as a pH indicator, to test how much acid (acidity) or base (alkalinity) exists in a solution. You might have even used some to test whether the water in a swimming pool is properly treated. In both cases, the pH test measures the concentration of hydrogen ions in a given solution.

Hydrogen ions are spontaneously generated in pure water by the dissociation (ionization) of a small percentage of water molecules into equal numbers of hydrogen ( $\text{H}^+$ ) ions and hydroxide ( $\text{OH}^-$ ) ions. While the hydroxide ions are kept in solution by their hydrogen bonding with other water molecules, the hydrogen ions, consisting of naked protons, are immediately attracted to un-ionized water molecules, forming hydronium ions ( $\text{H}_3\text{O}^+$ ). Still, by convention, scientists refer to hydrogen ions and their concentration as if they were free in this state in liquid water.

The concentration of hydrogen ions dissociating from pure water is  $1 \times 10^{-7}$  moles  $H^+$  ions per liter of water. Moles (mol) are a way to express the amount of a substance (which can be atoms, molecules, ions, etc), with one mole being equal to  $6.02 \times 10^{23}$  particles of the substance. Therefore, 1 mole of water is equal to  $6.02 \times 10^{23}$  water molecules. The pH is calculated as the negative of the base 10 logarithm of this concentration. The  $\log_{10}$  of  $1 \times 10^{-7}$  is  $-7.0$ , and the negative of this number (indicated by the “p” of “pH”) yields a pH of 7.0, which is also known as neutral pH. The pH inside of human cells and blood are examples of two areas of the body where near-neutral pH is maintained.

Non-neutral pH readings result from dissolving acids or bases in water. Using the negative logarithm to generate positive integers, high concentrations of hydrogen ions yield a low pH number, whereas low levels of hydrogen ions result in a high pH. An acid is a substance that increases the concentration of hydrogen ions ( $H^+$ ) in a solution, usually by having one of its hydrogen atoms dissociate. A base provides either hydroxide ions ( $OH^-$ ) or other negatively charged ions that combine with hydrogen ions, reducing their concentration in the solution and thereby raising the pH. In cases where the base releases hydroxide ions, these ions bind to free hydrogen ions, generating new water molecules.

The stronger the acid, the more readily it donates  $H^+$ . For example, hydrochloric acid (HCl) completely dissociates into hydrogen and chloride ions and is highly acidic, whereas the acids in tomato juice or vinegar do not completely dissociate and are considered weak acids. Conversely, strong bases are those substances that readily donate  $OH^-$  or take up hydrogen ions. Sodium hydroxide (NaOH) and many household cleaners are highly alkaline and give up  $OH^-$  rapidly when placed in water, thereby raising the pH. An example of a weak basic solution is seawater, which has a pH near 8.0, close enough to neutral pH that marine organisms adapted to this saline environment are able to thrive in it.

The pH scale is, as previously mentioned, an inverse logarithm and ranges from 0 to 14 ([link](#)). Anything below 7.0 (ranging from 0.0 to 6.9) is acidic, and anything above 7.0 (from 7.1 to 14.0) is alkaline. Extremes in pH in either direction from 7.0 are usually considered inhospitable to life. The pH inside cells (6.8) and the pH in the blood (7.4) are both very close to neutral. However, the environment in the stomach is highly acidic, with a pH of 1 to 2. So how do the cells of the stomach survive in such an acidic environment? How do they homeostatically maintain the near neutral pH inside them? The answer is that they cannot do it and are constantly dying. New stomach cells are constantly produced to replace dead ones, which are digested by the stomach acids. It is estimated that the lining of the human stomach is completely replaced every seven to ten days.

The pH scale measures the concentration of hydrogen ions ( $H^+$ ) in a solution. (credit:

modification of work by Edward Stevens)

[Link to Learning](#)

Watch this video for a straightforward explanation of pH and its logarithmic scale.

Carbon

By the end of this section, you will be able to:

- Explain why carbon is important for life
- Describe the role of functional groups in biological molecules

Cells are made of many complex molecules called macromolecules, such as proteins, nucleic acids (RNA and DNA), carbohydrates, and lipids. The macromolecules are a subset of organic molecules (any carbon-containing liquid, solid, or gas) that are especially important for life. The fundamental component for all of these macromolecules is carbon. The carbon atom has unique properties that allow it to form covalent bonds to as many as four different atoms, making this versatile element ideal to serve as the basic structural component, or “backbone,” of the macromolecules.

Individual carbon atoms have an incomplete outermost electron shell. With an atomic number of 6 (six electrons and six protons), the first two electrons fill the inner shell, leaving four in the second shell. Therefore, carbon atoms can form up to four covalent bonds with other atoms to satisfy the octet rule. The methane molecule provides an example: it has the chemical formula  $CH_4$ . Each of its four

hydrogen atoms forms a single covalent bond with the carbon atom by sharing a pair of electrons. This results in a filled outermost shell.

## Hydrocarbons

Hydrocarbons are organic molecules consisting entirely of carbon and hydrogen, such as methane (CH<sub>4</sub>) described above. We often use hydrocarbons in our daily lives as fuels—like the propane in a gas grill or the butane in a lighter. The many covalent bonds between the atoms in hydrocarbons store a great amount of energy, which is released when these molecules are burned (oxidized). Methane, an excellent fuel, is the simplest hydrocarbon molecule, with a central carbon atom bonded to four different hydrogen atoms, as illustrated in [\[link\]](#). The geometry of the methane molecule, where the atoms reside in three dimensions, is determined by the shape of its electron orbitals. The carbons and the four hydrogen atoms form a shape known as a tetrahedron, with four triangular faces; for this reason, methane is described as having tetrahedral geometry.

Methane has a tetrahedral geometry, with each of the four hydrogen atoms spaced 109.5°

apart.

As the backbone of the large molecules of living things, hydrocarbons may exist as linear carbon chains, carbon rings, or combinations of both. Furthermore, individual carbon-to-carbon bonds may be single, double, or triple covalent bonds, and each type of bond affects the geometry of the molecule in a specific way. This three-dimensional shape or conformation of the large molecules of life (macromolecules) is critical to how they function.

## Hydrocarbon Chains

Hydrocarbon chains are formed by successive bonds between carbon atoms and may be branched or unbranched. Furthermore, the overall geometry of the molecule is altered by the

different geometries of single, double, and triple covalent bonds, illustrated in [\[link\]](#). The hydrocarbons ethane, ethene, and ethyne serve as examples of how different carbon-to-carbon bonds affect the geometry of the molecule. The names of all three molecules start with the prefix “eth-,” which is the prefix for two carbon hydrocarbons. The suffixes “-ane,” “-ene,” and “-yne” refer to the presence of single, double, or triple carbon-carbon bonds, respectively. Thus, propane, propene, and propyne follow the same pattern with three carbon molecules, butane, butene, and butyne for four carbon molecules, and so on. Double and triple bonds change the geometry of the molecule: single bonds allow rotation along the axis of the bond, whereas double bonds lead to a planar configuration and triple bonds to a linear one. These geometries have a significant impact on the shape a particular molecule can assume.

When carbon forms single bonds with other atoms, the shape is tetrahedral. When two carbon atoms form a double bond, the shape is planar, or flat. Single bonds, like those found in ethane, are able to rotate. Double bonds, like those found in ethene cannot rotate, so the

atoms on either side are locked in place.

## **Hydrocarbon Rings**

So far, the hydrocarbons we have discussed have been aliphatic hydrocarbons, which consist of linear chains of carbon atoms. Another type of hydrocarbon, aromatic hydrocarbons, consists of closed rings of carbon atoms. Ring structures are found in hydrocarbons, sometimes with the presence of double bonds, which can be seen by comparing the structure of cyclohexane to benzene in [\[link\]](#). Examples of biological molecules that incorporate the benzene ring include some amino acids and cholesterol and its derivatives, including the hormones estrogen and testosterone. The benzene ring is also found in the herbicide 2,4-D. Benzene is a natural component of crude oil and has been classified as a carcinogen. Some hydrocarbons have both aliphatic and aromatic portions; beta-carotene is an example of such a hydrocarbon.

Carbon can form five- and six-membered rings. Single or double bonds may connect the carbons in the ring, and nitrogen may be substituted for

carbon.

## Isomers

The three-dimensional placement of atoms and chemical bonds within organic molecules is central to understanding their chemistry. Molecules that share the same chemical formula but differ in the placement (structure) of their atoms and/or chemical bonds are known as isomers. Structural isomers (like butane and isobutene shown in [link a](#)) differ in the placement of their covalent bonds: both molecules have four carbons and ten hydrogens ( $C_4H_{10}$ ), but the different arrangement of the atoms within the molecules leads to differences in their chemical properties. For example, due to their different chemical properties, butane is suited for use as a fuel for cigarette lighters and torches, whereas isobutene is suited for use as a refrigerant and a propellant in spray cans.

Geometric isomers, on the other hand, have similar placements of their covalent bonds but differ in how these bonds are made to the surrounding atoms, especially in carbon-to-carbon double bonds. In the simple molecule butene ( $C_4H_8$ ), the two methyl groups ( $CH_3$ ) can be on either side of the double covalent bond central to the molecule, as illustrated in [link b](#). When the carbons are bound on the same side of the double bond, this is the *cis* configuration; if they are on opposite sides of the double bond, it is a *trans* configuration. In the *trans* configuration, the carbons form a more or less linear structure, whereas the carbons in the *cis* configuration make a bend (change in direction) of the carbon backbone.

### Art Connection

Molecules that have the same number and type of atoms arranged differently are called isomers. (a) Structural isomers have a different covalent arrangement of atoms. (b) Geometric isomers have a different arrangement of atoms around a double bond. (c) Enantiomers are

mirror images of each other.

Which of the following statements is false?

- Molecules with the formulas  $\text{CH}_3\text{CH}_2\text{COOH}$  and  $\text{C}_3\text{H}_6\text{O}_2$  could be structural isomers.
- Molecules must have a double bond to be *cis-trans* isomers.
- To be enantiomers, a molecule must have at least three different atoms or groups connected to a central carbon.
- To be enantiomers, a molecule must have at least four different atoms or groups connected to a central carbon.

In triglycerides (fats and oils), long carbon chains known as fatty acids may contain double bonds, which can be in either the *cis* or *trans* configuration, illustrated in [\[link\]](#). Fats with at least one double bond between carbon atoms are unsaturated fats. When some of these bonds are in the *cis* configuration, the resulting bend in the carbon backbone of the chain means that triglyceride molecules cannot pack tightly, so they remain liquid (oil) at room temperature. On the other hand, triglycerides with *trans* double bonds (popularly called trans fats), have relatively linear fatty acids that are able to pack tightly together at room temperature and form solid fats. In the human diet, trans fats are linked to an increased risk of cardiovascular disease, so many food manufacturers have reduced or eliminated their use in recent years. In contrast to unsaturated fats, triglycerides without double bonds between carbon atoms are called saturated fats, meaning that they contain all the hydrogen atoms available. Saturated fats are a solid at room temperature and usually of animal origin.

These space-filling models show a *cis* (oleic acid) and a *trans* (eliadic acid) fatty acid. Notice the bend in the molecule cause by

the *cis* configuration.

## **Enantiomers**

Enantiomers are molecules that share the same chemical structure and chemical bonds but differ in the three-dimensional placement of atoms so that they are mirror images. As shown in [\[link\]](#), an amino acid alanine example, the two structures are non-superimposable. In nature, only the L-forms of amino acids are used to make proteins. Some D forms of amino acids are seen in the cell walls of bacteria, but never in their proteins. Similarly, the D-form of glucose is the main product of photosynthesis and the L-form of the molecule is rarely seen in nature.

D-alanine and L-alanine are examples of enantiomers or mirror images. Only the L-forms of

amino acids are used to make proteins.

## Functional Groups

Functional groups are groups of atoms that occur within molecules and confer specific chemical properties to those molecules. They are found along the “carbon backbone” of macromolecules. This carbon backbone is formed by chains and/or rings of carbon atoms with the occasional substitution of an element such as nitrogen or oxygen. Molecules with other elements in their carbon backbone are substituted hydrocarbons.

The functional groups in a macromolecule are usually attached to the carbon backbone at one or several different places along its chain and/or ring structure. Each of the four types of macromolecules—proteins, lipids, carbohydrates, and nucleic acids—has its own characteristic set of functional groups that contributes greatly to its differing chemical properties and its function in living organisms.

A functional group can participate in specific chemical reactions. Some of the important functional groups in biological molecules are shown in [\[link\]](#); they include: hydroxyl, methyl, carbonyl, carboxyl, amino, phosphate, and sulfhydryl. These groups play an important role in the formation of molecules like DNA, proteins, carbohydrates, and lipids. Functional groups are usually classified as hydrophobic or hydrophilic depending on their charge or polarity characteristics. An example of a hydrophobic group is the non-polar methane molecule. Among the hydrophilic functional groups is the carboxyl group found in amino acids, some amino acid side chains, and the fatty acids that form triglycerides and phospholipids. This carboxyl group ionizes to release hydrogen ions ( $H^+$ ) from the COOH group resulting in the negatively charged  $COO^-$  group; this contributes to the hydrophilic nature of whatever molecule it is found on. Other functional groups, such as the carbonyl group, have a partially negatively charged oxygen atom that may form hydrogen bonds with water molecules, again making the molecule more hydrophilic.

The functional groups shown here are found in many different biological

molecules.

Hydrogen bonds between functional groups (within the same molecule or between different molecules) are important to the function of many macromolecules and help them to fold properly into and maintain the appropriate shape for functioning. Hydrogen bonds are also involved in various recognition processes, such as DNA complementary base pairing and the binding of an enzyme to its substrate, as illustrated in [\[link\]](#).

Hydrogen bonds connect two strands of DNA together to create the double-helix

structure.

## Section Summary

The unique properties of carbon make it a central part of biological molecules. Carbon binds to oxygen, hydrogen, and nitrogen covalently to form the many molecules important for cellular function. Carbon has four electrons in its outermost shell and can form four bonds. Carbon and hydrogen can form hydrocarbon chains or rings. Functional groups are groups of atoms that confer specific properties to hydrocarbon (or substituted hydrocarbon) chains or rings that define their overall chemical characteristics and function.

## Art Connections

[\[link\]](#) Which of the following statements is false?

- Molecules with the formulas  $\text{CH}_3\text{CH}_2\text{COOH}$  and  $\text{C}_3\text{H}_6\text{O}_2$  could be structural isomers.
- Molecules must have a double bond to be *cis-trans* isomers.
- To be enantiomers, a molecule must have at least three different atoms or groups connected to a central carbon.
- To be enantiomers, a molecule must have at least four different atoms or groups connected to a central carbon.

[\[link\]](#) C

## Review Questions

Each carbon molecule can bond with as many as \_\_\_\_\_ other atom(s) or molecule(s).

- a. one
- b. two
- c. six
- d. four

D

Which of the following is not a functional group that can bond with carbon?

- a. sodium
- b. hydroxyl
- c. phosphate
- d. carbonyl

A

## Free Response

What property of carbon makes it essential for organic life?

Carbon is unique and found in all living things because it can form up to four covalent bonds between atoms or molecules. These can be nonpolar or polar covalent bonds, and they allow for the formation of long chains of carbon molecules that combine to form proteins and DNA.

Compare and contrast saturated and unsaturated triglycerides.

Saturated triglycerides contain no double bonds between carbon atoms; they are usually solid at room temperature. Unsaturated triglycerides contain at least one double bond between carbon atoms and are usually liquid at room temperature.

## Glossary

aliphatic hydrocarbon

hydrocarbon consisting of a linear chain of carbon atoms

aromatic hydrocarbon

hydrocarbon consisting of closed rings of carbon atoms

enantiomers

molecules that share overall structure and bonding patterns, but differ in how the atoms are three dimensionally placed such that they are mirror images of each other

functional group

group of atoms that provides or imparts a specific function to a carbon skeleton

geometric isomer

isomer with similar bonding patterns differing in the placement of atoms alongside a double covalent bond

hydrocarbon

molecule that consists only of carbon and hydrogen

isomers

molecules that differ from one another even though they share the same chemical formula

organic molecule

any molecule containing carbon (except carbon dioxide)

structural isomers

molecules that share a chemical formula but differ in the placement of their chemical bonds

substituted hydrocarbon

hydrocarbon chain or ring containing an atom of another element in place of one of the backbone carbons

Introduction

class="introduction" class="summary" title="Sections Summary" class="art-exercise" title="Art Connections" class="multiple-choice" title="Multiple Choice" class="free-response" title="Free Response" Foods such as bread, fruit, and cheese are rich sources of

biological macromolecules. (credit: modification of work by Bengt Nyman)

Food provides the body with the nutrients it needs to survive. Many of these critical nutrients are biological macromolecules, or large molecules, necessary for life. These macromolecules (polymers) are built from different combinations of smaller organic molecules (monomers). What specific types of biological macromolecules do living things require? How are these molecules formed? What functions do they serve? In this chapter, these questions will be explored.

Synthesis of Biological Macromolecules

By the end of this section, you will be able to:

- Understand the synthesis of macromolecules
- Explain dehydration (or condensation) and hydrolysis reactions

As you've learned, biological macromolecules are large molecules, necessary for life, that are built from smaller organic molecules. There are four major classes of biological macromolecules (carbohydrates, lipids, proteins, and nucleic acids); each is an important cell component and performs a wide array of functions. Combined, these molecules make up the majority of a cell's dry mass (recall that water makes up the majority of its complete mass). Biological macromolecules are

organic, meaning they contain carbon. In addition, they may contain hydrogen, oxygen, nitrogen, and additional minor elements.

## **Dehydration Synthesis**

Most macromolecules are made from single subunits, or building blocks, called monomers. The monomers combine with each other using covalent bonds to form larger molecules known as polymers. In doing so, monomers release water molecules as byproducts. This type of reaction is known as dehydration synthesis, which means “to put together while losing water.”

In the dehydration synthesis reaction depicted above, two molecules of glucose are linked together to form the disaccharide maltose. In the process, a water molecule is formed.

In a dehydration synthesis reaction ([link](#)), the hydrogen of one monomer combines with the hydroxyl group of another monomer, releasing a molecule of water. At the same time, the

monomers share electrons and form covalent bonds. As additional monomers join, this chain of repeating monomers forms a polymer. Different types of monomers can combine in many configurations, giving rise to a diverse group of macromolecules. Even one kind of monomer can combine in a variety of ways to form several different polymers: for example, glucose monomers are the constituents of starch, glycogen, and cellulose.

## **Hydrolysis**

Polymers are broken down into monomers in a process known as hydrolysis, which means “to split water,” a reaction in which a water molecule is used during the breakdown ([link](#)). During these reactions, the polymer is broken into two components: one part gains a hydrogen atom ( $H^+$ ) and the other gains a hydroxyl molecule ( $OH^-$ ) from a split water molecule.

In the hydrolysis reaction shown here, the disaccharide maltose is broken down to form two glucose monomers with the addition of a water molecule. Note that this reaction is the reverse of the synthesis reaction shown

in [\[link\]](#).

Dehydration and hydrolysis reactions are catalyzed, or “sped up,” by specific enzymes; dehydration reactions involve the formation of new bonds, requiring energy, while hydrolysis reactions break bonds and release energy. These reactions are similar for most macromolecules, but each monomer and polymer reaction is specific for its class. For example, in our bodies, food is hydrolyzed, or broken down, into smaller molecules by catalytic enzymes in the digestive system. This allows for easy absorption of nutrients by cells in the intestine. Each macromolecule is broken down by a specific enzyme. For instance, carbohydrates are broken down by amylase, sucrase, lactase, or maltase. Proteins are broken down by the enzymes pepsin and peptidase, and by hydrochloric acid. Lipids are broken down by lipases. Breakdown of these macromolecules provides energy for cellular activities.

Link to Learning

Visit [this site](#) to see visual representations of dehydration synthesis and hydrolysis.

## Section Summary

Proteins, carbohydrates, nucleic acids, and lipids are the four major classes of biological macromolecules—large molecules necessary for life that are built from smaller organic molecules. Macromolecules are made up of single units known as monomers that are joined by covalent bonds to form larger polymers. The polymer is more than the sum of its parts: it acquires new characteristics, and leads to an osmotic pressure that is much lower than that formed by its ingredients; this is an important advantage in the maintenance of cellular osmotic conditions. A monomer joins with another monomer with the release of a water molecule, leading to the formation of a covalent bond. These types of reactions are known as dehydration or condensation reactions. When polymers are broken down into smaller units (monomers), a molecule of water is used for each bond broken by these reactions; such reactions are known as hydrolysis reactions. Dehydration and hydrolysis reactions are similar for all macromolecules, but each monomer and polymer reaction is specific to its class. Dehydration reactions typically require an investment of energy for new bond formation, while hydrolysis reactions typically release energy by breaking bonds.

## Review Questions

Dehydration synthesis leads to formation of

- monomers
- polymers
- water and polymers
- none of the above

C

During the breakdown of polymers, which of the following reactions takes place?

- hydrolysis
- dehydration
- condensation
- covalent bond

A

## Free Response

Why are biological macromolecules considered organic?

Biological macromolecules are organic because they contain carbon.

What role do electrons play in dehydration synthesis and hydrolysis?

In a dehydration synthesis reaction, the hydrogen of one monomer combines with the hydroxyl group of another monomer, releasing a molecule of water. This creates an opening in the outer shells of atoms in the monomers, which can share electrons and form covalent bonds.

## **Glossary**

biological macromolecule

large molecule necessary for life that is built from smaller organic molecules

dehydration synthesis

(also, condensation) reaction that links monomer molecules together, releasing a molecule of water for each bond formed

hydrolysis

reaction causes breakdown of larger molecules into smaller molecules with the utilization of water

monomer

smallest unit of larger molecules called polymers

polymer

chain of monomer residues that is linked by covalent bonds; polymerization is the process of polymer formation from monomers by condensation

Carbohydrates

By the end of this section, you will be able to:

- Discuss the role of carbohydrates in cells and in the extracellular materials of animals and plants
- Explain the classifications of carbohydrates
- List common monosaccharides, disaccharides, and polysaccharides

Most people are familiar with carbohydrates, one type of macromolecule, especially when it comes to what we eat. To lose weight, some individuals adhere to “low-carb” diets. Athletes, in contrast, often “carb-load” before important competitions to ensure that they have enough energy to compete at a high level. Carbohydrates are, in fact, an essential part of our diet; grains, fruits, and vegetables are all natural sources of carbohydrates. Carbohydrates provide energy to the body, particularly through glucose, a simple sugar that is a component of starch and an ingredient in many staple foods. Carbohydrates also have other important functions in humans, animals, and plants.

## **Molecular Structures**

Carbohydrates can be represented by the stoichiometric formula  $(\text{CH}_2\text{O})_n$ , where  $n$  is the number of carbons in the molecule. In other words, the ratio of carbon to hydrogen to oxygen is 1:2:1 in carbohydrate molecules. This formula also explains the origin of the term “carbohydrate”: the components are carbon (“carbo”) and the components of water (hence, “hydrate”). Carbohydrates are classified into three subtypes: monosaccharides, disaccharides, and polysaccharides.

### **Monosaccharides**

Monosaccharides (mono- = “one”; sacchar- = “sweet”) are simple sugars, the most common of which is glucose. In monosaccharides, the number of carbons usually ranges from three to seven. Most monosaccharide names end with the suffix -ose. If the sugar has an aldehyde group (the functional group with the structure  $\text{R-CHO}$ ), it is known as an aldose, and if it has a ketone group (the functional group with the structure  $\text{RC(=O)R'}$ ), it is known as a ketose. Depending on the number of carbons in the sugar, they also may be known as trioses (three carbons), pentoses (five carbons), and or hexoses (six carbons). See [\[link\]](#) for an illustration of the monosaccharides.

Monosaccharides are classified based on the position of their carbonyl group and the number of carbons in the backbone. Aldoses have a carbonyl group (indicated in green) at the end of the carbon chain, and ketoses have a carbonyl group in the middle of the carbon chain. Trioses, pentoses, and hexoses have three, five, and six carbon backbones,

respectively.

The chemical formula for glucose is  $\text{C}_6\text{H}_{12}\text{O}_6$ . In humans, glucose is an important source of energy. During cellular respiration, energy is released from glucose, and that energy is used to help make adenosine triphosphate (ATP). Plants synthesize glucose using carbon dioxide and water, and glucose in turn is used for energy requirements for the plant. Excess glucose is

often stored as starch that is catabolized (the breakdown of larger molecules by cells) by humans and other animals that feed on plants.

Galactose (part of lactose, or milk sugar) and fructose (found in sucrose, in fruit) are other common monosaccharides. Although glucose, galactose, and fructose all have the same chemical formula ( $C_6H_{12}O_6$ ), they differ structurally and chemically (and are known as isomers) because of the different arrangement of functional groups around the asymmetric carbon; all of these monosaccharides have more than one asymmetric carbon ([\[link\]](#)).

#### Art Connection

Glucose, galactose, and fructose are all hexoses. They are structural isomers, meaning they have the same chemical formula ( $C_6H_{12}O_6$ ) but a different arrangement of

atoms.

What kind of sugars are these, aldose or ketose?

Glucose, galactose, and fructose are isomeric monosaccharides (hexoses), meaning they have the same chemical formula but have slightly different structures. Glucose and galactose are aldoses, and fructose is a ketose.

Monosaccharides can exist as a linear chain or as ring-shaped molecules; in aqueous solutions they are usually found in ring forms ([\[link\]](#)). Glucose in a ring form can have two different arrangements of the hydroxyl group (OH) around the anomeric carbon (carbon 1 that becomes asymmetric in the process of ring formation). If the hydroxyl group is below carbon number 1 in the sugar, it is said to be in the alpha ( $\alpha$ ) position, and if it is above the plane, it is said to be in the beta ( $\beta$ ) position.

Five and six carbon monosaccharides exist in equilibrium between linear and ring forms. When the ring forms, the side chain it closes on is locked into an  $\alpha$  or  $\beta$  position. Fructose and

ribose also form rings, although they form five-membered rings as opposed to the six-

membered ring of glucose.

### **Disaccharides**

Disaccharides (di- = “two”) form when two monosaccharides undergo a dehydration reaction (also known as a condensation reaction or dehydration synthesis). During this process, the hydroxyl group of one monosaccharide combines with the hydrogen of another monosaccharide, releasing a molecule of water and forming a covalent bond. A covalent bond formed between a carbohydrate molecule and another molecule (in this case, between two monosaccharides) is known as a glycosidic bond ([\[link\]](#)). Glycosidic bonds (also called glycosidic linkages) can be of the alpha or the beta type.

Sucrose is formed when a monomer of glucose and a monomer of fructose are joined in a dehydration reaction to form a glycosidic bond. In the process, a water molecule is lost. By convention, the carbon atoms in a monosaccharide are numbered from the terminal carbon closest to the carbonyl group. In sucrose, a glycosidic linkage is formed between carbon 1 in

glucose and carbon 2 in

fructose.

Common disaccharides include lactose, maltose, and sucrose ([link](#)). Lactose is a disaccharide consisting of the monomers glucose and galactose. It is found naturally in milk. Maltose, or malt sugar, is a disaccharide formed by a dehydration reaction between two glucose molecules. The most common disaccharide is sucrose, or table sugar, which is composed of the monomers glucose and fructose.

Common disaccharides include maltose (grain sugar), lactose (milk sugar), and sucrose (table

sugar).

### **Polysaccharides**

A long chain of monosaccharides linked by glycosidic bonds is known as a polysaccharide (poly- = “many”). The chain may be branched or unbranched, and it may contain different types of monosaccharides. The molecular weight may be 100,000 daltons or more depending on the number of monomers joined. Starch, glycogen, cellulose, and chitin are primary examples of polysaccharides.

Starch is the stored form of sugars in plants and is made up of a mixture of amylose and amylopectin (both polymers of glucose). Plants are able to synthesize glucose, and the excess glucose, beyond the plant’s immediate energy needs, is stored as starch in different plant parts, including roots and seeds. The starch in the seeds provides food for the embryo as it germinates and can also act as a source of food for humans and animals. The starch that is consumed by humans is broken down by enzymes, such as salivary amylases, into smaller molecules, such as maltose and glucose. The cells can then absorb the glucose.

Starch is made up of glucose monomers that are joined by  $\alpha$  1-4 or  $\alpha$  1-6 glycosidic bonds. The numbers 1-4 and 1-6 refer to the carbon number of the two residues that have joined to form the bond. As illustrated in [\[link\]](#), amylose is starch formed by unbranched chains of glucose monomers (only  $\alpha$  1-4 linkages), whereas amylopectin is a branched polysaccharide ( $\alpha$  1-6 linkages at the branch points).

Amylose and amylopectin are two different forms of starch. Amylose is composed of unbranched chains of glucose monomers connected by  $\alpha$  1,4 glycosidic linkages. Amylopectin is composed of branched chains of glucose monomers connected by  $\alpha$  1,4 and  $\alpha$  1,6 glycosidic linkages. Because of the way the subunits are joined, the glucose chains

have a helical structure. Glycogen (not shown) is similar in structure to amylopectin but more

highly branched.

Glycogen is the storage form of glucose in humans and other vertebrates and is made up of monomers of glucose. Glycogen is the animal equivalent of starch and is a highly branched molecule usually stored in liver and muscle cells. Whenever blood glucose levels decrease, glycogen is broken down to release glucose in a process known as glycogenolysis.

Cellulose is the most abundant natural biopolymer. The cell wall of plants is mostly made of cellulose; this provides structural support to the cell. Wood and paper are mostly cellulosic in nature. Cellulose is made up of glucose monomers that are linked by  $\beta$  1-4 glycosidic bonds ([link](#)).

In cellulose, glucose monomers are linked in unbranched chains by  $\beta$  1-4 glycosidic linkages. Because of the way the glucose subunits are joined, every glucose monomer is flipped

relative to the next one resulting in a linear, fibrous

structure.

As shown in [\[link\]](#), every other glucose monomer in cellulose is flipped over, and the monomers are packed tightly as extended long chains. This gives cellulose its rigidity and high tensile strength—which is so important to plant cells. While the  $\beta$  1-4 linkage cannot be broken down by human digestive enzymes, herbivores such as cows, koalas, and buffalos are able, with the help of the specialized flora in their stomach, to digest plant material that is rich in cellulose and use it as a food source. In these animals, certain species of bacteria and protists reside in the rumen (part of the digestive system of herbivores) and secrete the enzyme cellulase. The appendix of grazing animals also contains bacteria that digest cellulose, giving it an important role in the digestive systems of ruminants. Cellulases can break down cellulose into glucose monomers that can be used as an energy source by the animal. Termites are also able to break down cellulose because of the presence of other organisms in their bodies that secrete cellulases.

Carbohydrates serve various functions in different animals. Arthropods (insects, crustaceans, and others) have an outer skeleton, called the exoskeleton, which protects their internal body parts (as seen in the bee in [\[link\]](#)). This exoskeleton is made of the biological macromolecule chitin, which is a polysaccharide-containing nitrogen. It is made of repeating units of N-acetyl- $\beta$ -d-glucosamine, a modified sugar. Chitin is also a major component of fungal cell walls; fungi are neither animals nor plants and form a kingdom of their own in the domain Eukarya.

Insects have a hard outer exoskeleton made of chitin, a type of polysaccharide. (credit: Louise

Docker)

#### Career Connections

Registered Dietitian Obesity is a worldwide health concern, and many diseases such as diabetes and heart disease are becoming more prevalent because of obesity. This is one of the reasons why registered dietitians are increasingly sought after for advice. Registered dietitians help plan nutrition programs for individuals in various settings. They often work with patients in health care facilities, designing nutrition plans to treat and prevent diseases. For example, dietitians may teach a patient with diabetes how to manage blood sugar levels by eating the correct types and amounts of carbohydrates. Dietitians may also work in nursing homes, schools, and private practices.

To become a registered dietitian, one needs to earn at least a bachelor's degree in dietetics, nutrition, food technology, or a related field. In addition, registered dietitians must complete a supervised internship program and pass a national exam. Those who pursue careers in dietetics take courses in nutrition, chemistry, biochemistry, biology, microbiology, and human physiology. Dietitians must become experts in the chemistry and physiology (biological functions) of food (proteins, carbohydrates, and fats).

### **Benefits of Carbohydrates**

Are carbohydrates good for you? People who wish to lose weight are often told that carbohydrates are bad for them and should be avoided. Some diets completely forbid carbohydrate consumption, claiming that a low-carbohydrate diet helps people to lose weight faster. However, carbohydrates have been an important part of the human diet for thousands of years; artifacts from ancient civilizations show the presence of wheat, rice, and corn in our ancestors' storage areas.

Carbohydrates should be supplemented with proteins, vitamins, and fats to be parts of a well-balanced diet. Calorie-wise, a gram of carbohydrate provides 4.3 Kcal. For comparison, fats provide 9 Kcal/g, a less desirable ratio. Carbohydrates contain soluble and insoluble elements; the insoluble part is known as fiber, which is mostly cellulose. Fiber has many

uses; it promotes regular bowel movement by adding bulk, and it regulates the rate of consumption of blood glucose. Fiber also helps to remove excess cholesterol from the body: fiber binds to the cholesterol in the small intestine, then attaches to the cholesterol and prevents the cholesterol particles from entering the bloodstream, and then cholesterol exits the body via the feces. Fiber-rich diets also have a protective role in reducing the occurrence of colon cancer. In addition, a meal containing whole grains and vegetables gives a feeling of fullness. As an immediate source of energy, glucose is broken down during the process of cellular respiration, which produces ATP, the energy currency of the cell. Without the consumption of carbohydrates, the availability of “instant energy” would be reduced. Eliminating carbohydrates from the diet is not the best way to lose weight. A low-calorie diet that is rich in whole grains, fruits, vegetables, and lean meat, together with plenty of exercise and plenty of water, is the more sensible way to lose weight.

Link to Learning

For an additional perspective on carbohydrates, explore “Biomolecules: the Carbohydrates” through this [interactive animation](#).

## Section Summary

Carbohydrates are a group of macromolecules that are a vital energy source for the cell and provide structural support to plant cells, fungi, and all of the arthropods that include lobsters, crabs, shrimp, insects, and spiders. Carbohydrates are classified as monosaccharides, disaccharides, and polysaccharides depending on the number of monomers in the molecule. Monosaccharides are linked by glycosidic bonds that are formed as a result of dehydration reactions, forming disaccharides and polysaccharides with the elimination of a water molecule for each bond formed. Glucose, galactose, and fructose are common monosaccharides, whereas common disaccharides include lactose, maltose, and sucrose. Starch and glycogen, examples of polysaccharides, are the storage forms of glucose in plants and animals, respectively. The long polysaccharide chains may be branched or unbranched. Cellulose is an example of an unbranched polysaccharide, whereas amylopectin, a constituent of starch, is a highly branched molecule. Storage of glucose, in the form of polymers like starch or glycogen, makes it slightly less accessible for metabolism; however, this prevents it from leaking out of the cell or creating a high osmotic pressure that could cause excessive water uptake by the cell.

## Art Connections

[\[link\]](#) What kind of sugars are these, aldose or ketose?

[\[link\]](#) Glucose and galactose are aldoses. Fructose is a ketose.

## Review Questions

An example of a monosaccharide is \_\_\_\_\_.

- a. fructose
- b. glucose
- c. galactose
- d. all of the above

D

Cellulose and starch are examples of:

- a. monosaccharides
- b. disaccharides
- c. lipids
- d. polysaccharides

D

Plant cell walls contain which of the following in abundance?

- a. starch
- b. cellulose
- c. glycogen
- d. lactose

B

Lactose is a disaccharide formed by the formation of a \_\_\_\_\_ bond between glucose and \_\_\_\_\_.

- a. glycosidic; lactose
- b. glycosidic; galactose
- c. hydrogen; sucrose
- d. hydrogen; fructose

B

### **Free Response**

Describe the similarities and differences between glycogen and starch.

Glycogen and starch are polysaccharides. They are the storage form of glucose. Glycogen is stored in animals in the liver and in muscle cells, whereas starch is stored in the roots, seeds, and leaves of plants. Starch has two different forms, one unbranched (amylose) and one branched (amylopectin), whereas glycogen is a single type of a highly branched molecule.

Why is it impossible for humans to digest food that contains cellulose?

The  $\beta$  1-4 glycosidic linkage in cellulose cannot be broken down by human digestive enzymes. Herbivores such as cows, koalas, and buffalos are able to digest grass that is rich in

cellulose and use it as a food source because bacteria and protists in their digestive systems, especially in the rumen, secrete the enzyme cellulase. Cellulases can break down cellulose into glucose monomers that can be used as an energy source by the animal.

## Glossary

### carbohydrate

biological macromolecule in which the ratio of carbon to hydrogen and to oxygen is 1:2:1; carbohydrates serve as energy sources and structural support in cells and form the a cellular exoskeleton of arthropods

### cellulose

polysaccharide that makes up the cell wall of plants; provides structural support to the cell

### chitin

type of carbohydrate that forms the outer skeleton of all arthropods that include crustaceans and insects; it also forms the cell walls of fungi

### disaccharide

two sugar monomers that are linked together by a glycosidic bond

### glycogen

storage carbohydrate in animals

### glycosidic bond

bond formed by a dehydration reaction between two monosaccharides with the elimination of a water molecule

### monosaccharide

single unit or monomer of carbohydrates

### polysaccharide

long chain of monosaccharides; may be branched or unbranched

### starch

storage carbohydrate in plants

## Lipids

By the end of this section, you will be able to:

- Describe the four major types of lipids
- Explain the role of fats in storing energy
- Differentiate between saturated and unsaturated fatty acids
- Describe phospholipids and their role in cells
- Define the basic structure of a steroid and some functions of steroids
- Explain the how cholesterol helps to maintain the fluid nature of the plasma membrane

Lipids include a diverse group of compounds that are largely nonpolar in nature. This is because they are hydrocarbons that include mostly nonpolar carbon–carbon or carbon–hydrogen bonds. Non-polar molecules are hydrophobic (“water fearing”), or insoluble in water. Lipids perform many different functions in a cell. Cells store energy for long-term use in the form of fats. Lipids also provide

insulation from the environment for plants and animals ([link](#)). For example, they help keep aquatic birds and mammals dry when forming a protective layer over fur or feathers because of their water-repellant hydrophobic nature. Lipids are also the building blocks of many hormones and are an important constituent of all cellular membranes. Lipids include fats, oils, waxes, phospholipids, and steroids.

Hydrophobic lipids in the fur of aquatic mammals, such as this river otter, protect them from

the elements. (credit: Ken Bosma)

## **Fats and Oils**

A fat molecule consists of two main components—glycerol and fatty acids. Glycerol is an organic compound (alcohol) with three carbons, five hydrogens, and three hydroxyl (OH) groups. Fatty acids have a long chain of hydrocarbons to which a carboxyl group is attached, hence the name “fatty acid.” The number of carbons in the fatty acid may range from 4 to 36; most common are those containing 12–18 carbons. In a fat molecule, the fatty acids are attached to each of the three carbons of the glycerol molecule with an ester bond through an oxygen atom ([link](#)).

Triacylglycerol is formed by the joining of three fatty acids to a glycerol backbone in a dehydration reaction. Three molecules of water are released in the

process.

During this ester bond formation, three water molecules are released. The three fatty acids in the triacylglycerol may be similar or dissimilar. Fats are also called triacylglycerols or triglycerides because of their chemical structure. Some fatty acids have common names that specify their origin. For example, palmitic acid, a saturated fatty acid, is derived from the palm tree. Arachidic acid is derived from *Arachis hypogea*, the scientific name for groundnuts or peanuts.

Fatty acids may be saturated or unsaturated. In a fatty acid chain, if there are only single bonds between neighboring carbons in the hydrocarbon chain, the fatty acid is said to be saturated. Saturated fatty acids are saturated with hydrogen; in other words, the number of hydrogen atoms attached to the carbon skeleton is maximized. Stearic acid is an example of a saturated fatty acid ([link](#))

Stearic acid is a common saturated fatty acid.

When the hydrocarbon chain contains a double bond, the fatty acid is said to be unsaturated. Oleic acid is an example of an unsaturated fatty acid ([link](#)).

Oleic acid is a common unsaturated fatty acid.

Most unsaturated fats are liquid at room temperature and are called oils. If there is one double bond in the molecule, then it is known as a monounsaturated fat (e.g., olive oil), and if there is more than one double bond, then it is known as a polyunsaturated fat (e.g., canola oil).

When a fatty acid has no double bonds, it is known as a saturated fatty acid because no more hydrogen may be added to the carbon atoms of the chain. A fat may contain similar or different fatty acids attached to glycerol. Long straight fatty acids with single bonds tend to get packed tightly and are solid at room temperature. Animal fats with stearic acid and palmitic acid (common in meat) and the fat with butyric acid (common in butter) are examples of saturated fats. Mammals store fats in specialized cells called adipocytes, where globules of fat occupy most of the cell's volume. In plants, fat or oil is stored in many seeds and is used as a source of energy during seedling development. Unsaturated fats or oils are usually of plant origin and contain *cis* unsaturated fatty acids. *Cis* and *trans* indicate the configuration of the molecule around the double bond. If hydrogens are present in the same

plane, it is referred to as a cis fat; if the hydrogen atoms are on two different planes, it is referred to as a trans fat. The *cis* double bond causes a bend or a “kink” that prevents the fatty acids from packing tightly, keeping them liquid at room temperature ([link](#)). Olive oil, corn oil, canola oil, and cod liver oil are examples of unsaturated fats. Unsaturated fats help to lower blood cholesterol levels whereas saturated fats contribute to plaque formation in the arteries.

Saturated fatty acids have hydrocarbon chains connected by single bonds only. Unsaturated fatty acids have one or more double bonds. Each double bond may be in a *cis* or *trans* configuration. In the *cis* configuration, both hydrogens are on the same side of the hydrocarbon chain. In the *trans* configuration, the hydrogens are on opposite sides. A *cis* double bond causes a kink in the

chain.

### **Trans Fats**

In the food industry, oils are artificially hydrogenated to make them semi-solid and of a consistency desirable for many processed food products. Simply speaking, hydrogen gas is bubbled through oils to solidify them. During this hydrogenation process, double bonds of the *cis*- conformation in the hydrocarbon chain may be converted to double bonds in the *trans*- conformation.

Margarine, some types of peanut butter, and shortening are examples of artificially hydrogenated trans fats. Recent studies have shown that an increase in trans fats in the human

diet may lead to an increase in levels of low-density lipoproteins (LDL), or “bad” cholesterol, which in turn may lead to plaque deposition in the arteries, resulting in heart disease. Many fast food restaurants have recently banned the use of trans fats, and food labels are required to display the trans fat content.

## **Omega Fatty Acids**

Essential fatty acids are fatty acids required but not synthesized by the human body. Consequently, they have to be supplemented through ingestion via the diet. Omega-3 fatty acids (like that shown in [link](#)) fall into this category and are one of only two known for humans (the other being omega-6 fatty acid). These are polyunsaturated fatty acids and are called omega-3 because the third carbon from the end of the hydrocarbon chain is connected to its neighboring carbon by a double bond.

Alpha-linolenic acid is an example of an omega-3 fatty acid. It has three *cis* double bonds and, as a result, a curved shape. For clarity, the carbons are not shown. Each singly bonded carbon has two hydrogens associated with it, also not

shown.

The farthest carbon away from the carboxyl group is numbered as the omega ( $\omega$ ) carbon, and if the double bond is between the third and fourth carbon from that end, it is known as an omega-3 fatty acid. Nutritionally important because the body does not make them, omega-3 fatty acids include alpha-linoleic acid (ALA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA), all of which are polyunsaturated. Salmon, trout, and tuna are good sources of omega-3 fatty acids. Research indicates that omega-3 fatty acids reduce the risk of sudden death from heart attacks, reduce triglycerides in the blood, lower blood pressure, and prevent thrombosis by inhibiting blood clotting. They also reduce inflammation, and may help reduce the risk of some cancers in animals.

Like carbohydrates, fats have received a lot of bad publicity. It is true that eating an excess of fried foods and other “fatty” foods leads to weight gain. However, fats do have important functions. Many vitamins are fat soluble, and fats serve as a long-term storage form of fatty

acids: a source of energy. They also provide insulation for the body. Therefore, “healthy” fats in moderate amounts should be consumed on a regular basis.

## **Waxes**

Wax covers the feathers of some aquatic birds and the leaf surfaces of some plants. Because of the hydrophobic nature of waxes, they prevent water from sticking on the surface ([link](#)). Waxes are made up of long fatty acid chains esterified to long-chain alcohols.

Waxy coverings on some leaves are made of lipids. (credit: Roger

Griffith)

## **Phospholipids**

Phospholipids are major constituents of the plasma membrane, the outermost layer of animal cells. Like fats, they are composed of fatty acid chains attached to a glycerol or sphingosine backbone. Instead of three fatty acids attached as in triglycerides, however, there are two fatty acids forming diacylglycerol, and the third carbon of the glycerol backbone is occupied by a modified phosphate group ([link](#)). A phosphate group alone attached to a diacylglycerol does not qualify as a phospholipid; it is phosphatidate (diacylglycerol 3-phosphate), the precursor of phospholipids. The phosphate group is modified by an alcohol. Phosphatidylcholine and phosphatidylserine are two important phospholipids that are found in plasma membranes.

A phospholipid is a molecule with two fatty acids and a modified phosphate group attached to a glycerol backbone. The phosphate may be modified by the addition of charged or polar chemical groups. Two chemical groups that may modify the phosphate, choline and serine, are shown here. Both choline and serine attach to the phosphate group at the position labeled

R via the hydroxyl group indicated in

green.

A phospholipid is an amphipathic molecule, meaning it has a hydrophobic and a hydrophilic part. The fatty acid chains are hydrophobic and cannot interact with water, whereas the phosphate-containing group is hydrophilic and interacts with water ([link](#)).

The phospholipid bilayer is the major component of all cellular membranes. The hydrophilic head groups of the phospholipids face the aqueous solution. The hydrophobic tails are

sequestered in the middle of the bilayer.

The head is the hydrophilic part, and the tail contains the hydrophobic fatty acids. In a membrane, a bilayer of phospholipids forms the matrix of the structure, the fatty acid tails of phospholipids face inside, away from water, whereas the phosphate group faces the outside, aqueous side ([link](#)).

Phospholipids are responsible for the dynamic nature of the plasma membrane. If a drop of phospholipids is placed in water, it spontaneously forms a structure known as a micelle, where the hydrophilic phosphate heads face the outside and the fatty acids face the interior of this structure.

## **Steroids**

Unlike the phospholipids and fats discussed earlier, steroids have a fused ring structure. Although they do not resemble the other lipids, they are grouped with them because they are also hydrophobic and insoluble in water. All steroids have four linked carbon rings and several of them, like cholesterol, have a short tail ([link](#)). Many steroids also have the –OH functional group, which puts them in the alcohol classification (sterols).

Steroids such as cholesterol and cortisol are composed of four fused hydrocarbon

rings.

Cholesterol is the most common steroid. Cholesterol is mainly synthesized in the liver and is the precursor to many steroid hormones such as testosterone and estradiol, which are secreted by the gonads and endocrine glands. It is also the precursor to Vitamin D. Cholesterol is also the precursor of bile salts, which help in the emulsification of fats and their subsequent absorption by cells. Although cholesterol is often spoken of in negative terms by lay people, it is necessary for proper functioning of the body. It is a component of the plasma membrane of animal cells and is found within the phospholipid bilayer. Being the outermost structure in animal cells, the plasma membrane is responsible for the transport of materials and cellular recognition and it is involved in cell-to-cell communication.

Link to Learning

For an additional perspective on lipids, explore the interactive animation [“Biomolecules: The Lipids”](#)

## Section Summary

Lipids are a class of macromolecules that are nonpolar and hydrophobic in nature. Major types include fats and oils, waxes, phospholipids, and steroids. Fats are a stored form of energy and are also known as triacylglycerols or triglycerides. Fats are made up of fatty acids and either glycerol or sphingosine. Fatty acids may be unsaturated or saturated, depending on the presence or absence of double bonds in the hydrocarbon chain. If only single bonds are present, they are known as saturated fatty acids. Unsaturated fatty acids may have one or more double bonds in the hydrocarbon chain. Phospholipids make up the matrix of membranes. They have a glycerol or sphingosine backbone to which two fatty acid chains and a phosphate-containing group are attached. Steroids are another class of lipids. Their basic structure has four fused carbon rings. Cholesterol is a type of steroid and is an important constituent of the plasma membrane, where it helps to maintain the fluid nature of the membrane. It is also the precursor of steroid hormones such as testosterone.

## Review Questions

Saturated fats have all of the following characteristics except:

- they are solid at room temperature
- they have single bonds within the carbon chain
- they are usually obtained from animal sources
- they tend to dissolve in water easily

D

Phospholipids are important components of \_\_\_\_\_.

- the plasma membrane of animal cells
- the ring structure of steroids
- the waxy covering on leaves
- the double bond in hydrocarbon chains

A

## Free Response

Explain at least three functions that lipids serve in plants and/or animals.

Fat serves as a valuable way for animals to store energy. It can also provide insulation. Waxes can protect plant leaves and mammalian fur from getting wet. Phospholipids and steroids are important components of animal cell membranes, as well as plant, fungal, and bacterial membranes.

Why have trans fats been banned from some restaurants? How are they created?

Trans fats are created artificially when hydrogen gas is bubbled through oils to solidify them. The double bonds of the *cis* conformation in the hydrocarbon chain may be converted to double bonds in the *trans* configuration. Some restaurants are banning trans fats because they cause higher levels of LDL, or “bad” cholesterol.

## Glossary

lipid

macromolecule that is nonpolar and insoluble in water

omega fat

type of polyunsaturated fat that is required by the body; the numbering of the carbon omega starts from the methyl end or the end that is farthest from the carboxylic end

phospholipid

major constituent of the membranes; composed of two fatty acids and a phosphate-containing group attached to a glycerol backbone

saturated fatty acid

long-chain of hydrocarbon with single covalent bonds in the carbon chain; the number of hydrogen atoms attached to the carbon skeleton is maximized

steroid

type of lipid composed of four fused hydrocarbon rings forming a planar structure

trans fat

fat formed artificially by hydrogenating oils, leading to a different arrangement of double bond(s) than those found in naturally occurring lipids

triacylglycerol (also, triglyceride)

fat molecule; consists of three fatty acids linked to a glycerol molecule

unsaturated fatty acid

long-chain hydrocarbon that has one or more double bonds in the hydrocarbon chain

wax

lipid made of a long-chain fatty acid that is esterified to a long-chain alcohol; serves as a protective coating on some feathers, aquatic mammal fur, and leaves

Proteins

By the end of this section, you will be able to:

- Describe the functions proteins perform in the cell and in tissues
- Discuss the relationship between amino acids and proteins
- Explain the four levels of protein organization
- Describe the ways in which protein shape and function are linked

Proteins are one of the most abundant organic molecules in living systems and have the most diverse range of functions of all macromolecules. Proteins may be structural, regulatory, contractile, or protective; they may serve in transport, storage, or membranes; or they may be toxins or enzymes. Each cell in a living system may contain thousands of proteins, each with a unique function. Their structures, like their functions, vary greatly. They are all, however, polymers of amino acids, arranged in a linear sequence.

### Types and Functions of Proteins

Enzymes, which are produced by living cells, are catalysts in biochemical reactions (like digestion) and are usually complex or conjugated proteins. Each enzyme is specific for the substrate (a reactant that binds to an enzyme) it acts on. The enzyme may help in breakdown, rearrangement, or synthesis reactions. Enzymes that break down their substrates are called catabolic enzymes, enzymes that build more complex molecules from their substrates are called anabolic enzymes, and enzymes that affect the rate of reaction are called catalytic enzymes. It should be noted that all enzymes increase the rate of reaction and, therefore, are considered to be organic catalysts. An example of an enzyme is salivary amylase, which hydrolyzes its substrate amylose, a component of starch.

Hormones are chemical-signaling molecules, usually small proteins or steroids, secreted by endocrine cells that act to control or regulate specific physiological processes, including growth, development, metabolism, and reproduction. For example, insulin is a protein hormone that helps to regulate the blood glucose level. The primary types and functions of proteins are listed in [\[link\]](#).

Protein Types and Functions		
Type	Examples	Functions
Digestive Enzymes	Amylase, lipase, pepsin, trypsin	Help in digestion of food by catabolizing nutrients into monomeric units
Transport	Hemoglobin, albumin	Carry substances in the blood or lymph throughout the body
Structural	Actin, tubulin, keratin	Construct different structures, like the cytoskeleton
Hormones	Insulin, thyroxine	Coordinate the activity of different body systems
Defense	Immunoglobulins	Protect the body from foreign pathogens
Contractile	Actin, myosin	Effect muscle contraction
Storage	Legume storage proteins, egg white (albumin)	Provide nourishment in early development of the embryo and the seedling

Proteins have different shapes and molecular weights; some proteins are globular in shape whereas others are fibrous in nature. For example, hemoglobin is a globular protein, but collagen, found in our skin, is a fibrous protein. Protein shape is critical to its function, and this shape is maintained by many different types of chemical bonds. Changes in temperature, pH, and exposure to chemicals may lead to permanent changes in the shape of the protein, leading to loss of function, known as denaturation. All proteins are made up of different arrangements of the same 20 types of amino acids.

## Amino Acids

Amino acids are the monomers that make up proteins. Each amino acid has the same fundamental structure, which consists of a central carbon atom, also known as the alpha ( $\alpha$ ) carbon, bonded to an amino group ( $\text{NH}_2$ ), a carboxyl group ( $\text{COOH}$ ), and to a hydrogen atom. Every amino acid also has another atom or group of atoms bonded to the central atom known as the R group ([link](#)).

Amino acids have a central asymmetric carbon to which an amino group, a carboxyl group, a hydrogen atom, and a side chain (R group) are

attached.

The name "amino acid" is derived from the fact that they contain both amino group and carboxyl-acid-group in their basic structure. As mentioned, there are 20 amino acids present in proteins. Nine of these are considered essential amino acids in humans because the human body cannot produce them and they are obtained from the diet. For each amino acid, the R group (or side chain) is different ([link](#)).

Art Connection

There are 20 common amino acids commonly found in proteins, each with a different R group (variant group) that determines its chemical

nature.

Which categories of amino acid would you expect to find on the surface of a soluble protein, and which would you expect to find in the interior? What distribution of amino acids would you expect to find in a protein embedded in a lipid bilayer?

The chemical nature of the side chain determines the nature of the amino acid (that is, whether it is acidic, basic, polar, or nonpolar). For example, the amino acid glycine has a hydrogen atom as the R group. Amino acids such as valine, methionine, and alanine are nonpolar or hydrophobic in nature, while amino acids such as serine, threonine, and cysteine are polar and have hydrophilic side chains. The side chains of lysine and arginine are positively charged, and therefore these amino acids are also known as basic amino acids. Proline has an R group that is linked to the amino group, forming a ring-like structure. Proline is an exception to the standard structure of an amino acid since its amino group is not separate from the side chain ([\[link\]](#)).

Amino acids are represented by a single upper case letter or a three-letter abbreviation. For example, valine is known by the letter V or the three-letter symbol val. Just as some fatty acids are essential to a diet, some amino acids are necessary as well. They are known as essential amino acids, and in humans they include isoleucine, leucine, and cysteine. Essential amino acids refer to those necessary for construction of proteins in the body, although not produced by the body; which amino acids are essential varies from organism to organism.

The sequence and the number of amino acids ultimately determine the protein's shape, size, and function. Each amino acid is attached to another amino acid by a covalent bond, known as a peptide bond, which is formed by a dehydration reaction. The carboxyl group of one amino acid and the amino group of the incoming amino acid combine, releasing a molecule of water. The resulting bond is the peptide bond ([link](#)).

Peptide bond formation is a dehydration synthesis reaction. The carboxyl group of one amino acid is linked to the amino group of the incoming amino acid. In the process, a molecule of

water is released.

The products formed by such linkages are called peptides. As more amino acids join to this growing chain, the resulting chain is known as a polypeptide. Each polypeptide has a free amino group at one end. This end is called the N terminal, or the amino terminal, and the other end has a free carboxyl group, also known as the C or carboxyl terminal. While the terms polypeptide and protein are sometimes used interchangeably, a polypeptide is technically a polymer of amino acids, whereas the term protein is used for a polypeptide or polypeptides that have combined together, often have bound non-peptide prosthetic groups, have a distinct shape, and have a unique function. After protein synthesis (translation), most proteins are modified. These are known as post-translational modifications. They may undergo cleavage, phosphorylation, or may require the addition of other chemical groups. Only after these modifications is the protein completely functional.

Link to Learning

Click through the steps of protein synthesis in this [interactive tutorial](#).

## Evolution Connection

The Evolutionary Significance of Cytochrome c  
Cytochrome c is an important component of the electron transport chain, a part of cellular respiration, and it is normally found in the cellular organelle, the mitochondrion. This protein has a heme prosthetic group, and the central iron of the heme gets alternately reduced and oxidized during electron transfer. Because this essential protein's role in producing cellular energy is crucial, it has changed very little over millions of years. Protein sequencing has shown that there is a considerable amount of cytochrome c amino acid sequence homology among different species; in other words, evolutionary kinship can be assessed by measuring the similarities or differences among various species' DNA or protein sequences.

Scientists have determined that human cytochrome c contains 104 amino acids. For each cytochrome c molecule from different organisms that has been sequenced to date, 37 of these amino acids appear in the same position in all samples of cytochrome c. This indicates that there may have been a common ancestor. On comparing the human and chimpanzee protein sequences, no sequence difference was found. When human and rhesus monkey sequences were compared, the single difference found was in one amino acid. In another comparison, human to yeast sequencing shows a difference in the 44th position.

## Protein Structure

As discussed earlier, the shape of a protein is critical to its function. For example, an enzyme can bind to a specific substrate at a site known as the active site. If this active site is altered because of local changes or changes in overall protein structure, the enzyme may be unable to bind to the substrate. To understand how the protein gets its final shape or conformation, we need to understand the four levels of protein structure: primary, secondary, tertiary, and quaternary.

### Primary Structure

The unique sequence of amino acids in a polypeptide chain is its primary structure. For example, the pancreatic hormone insulin has two polypeptide chains, A and B, and they are linked together by disulfide bonds. The N terminal amino acid of the A chain is glycine, whereas the C terminal amino acid is asparagine ([link](#)). The sequences of amino acids in the A and B chains are unique to insulin.

Bovine serum insulin is a protein hormone made of two peptide chains, A (21 amino acids long) and B (30 amino acids long). In each chain, primary structure is indicated by three-letter abbreviations that represent the names of the amino acids in the order they are present. The amino acid cysteine (cys) has a sulfhydryl (SH) group as a side chain. Two sulfhydryl groups can react in the presence of oxygen to form a disulfide (S-S) bond. Two disulfide bonds connect the A and B chains together, and a third helps the A chain fold into the correct

shape. Note that all disulfide bonds are the same length, but are drawn different sizes for

clarity.

The unique sequence for every protein is ultimately determined by the gene encoding the protein. A change in nucleotide sequence of the gene's coding region may lead to a different amino acid being added to the growing polypeptide chain, causing a change in protein structure and function. In sickle cell anemia, the hemoglobin  $\beta$  chain (a small portion of which is shown in [\[link\]](#)) has a single amino acid substitution, causing a change in protein structure and function. Specifically, the amino acid glutamic acid is substituted by valine in the  $\beta$  chain. What is most remarkable to consider is that a hemoglobin molecule is made up of two alpha chains and two beta chains that each consist of about 150 amino acids. The molecule, therefore, has about 600 amino acids. The structural difference between a normal hemoglobin molecule and a sickle cell molecule—which dramatically decreases life expectancy—is a single amino acid of the 600. What is even more remarkable is that those 600 amino acids are encoded by three nucleotides each, and the mutation is caused by a single base change (point mutation), 1 in 1800 bases.

The beta chain of hemoglobin is 147 residues in length, yet a single amino acid substitution leads to sickle cell anemia. In normal hemoglobin, the amino acid at position seven is

glutamate. In sickle cell hemoglobin, this glutamate is replaced by a

valine.

Because of this change of one amino acid in the chain, hemoglobin molecules form long fibers that distort the biconcave, or disc-shaped, red blood cells and assume a crescent or “sickle” shape, which clogs arteries ([link](#)). This can lead to myriad serious health problems such as breathlessness, dizziness, headaches, and abdominal pain for those affected by this disease.

In this blood smear, visualized at 535x magnification using bright field microscopy, sickle cells are crescent shaped, while normal cells are disc-shaped. (credit: modification of work by Ed Uthman; scale-bar data from Matt

Russell)

**Secondary Structure**

The local folding of the polypeptide in some regions gives rise to the secondary structure of the protein. The most common are the  $\alpha$ -helix and  $\beta$ -pleated sheet structures ([\[link\]](#)). Both structures are the  $\alpha$ -helix structure—the helix held in shape by hydrogen bonds. The hydrogen bonds form between the oxygen atom in the carbonyl group in one amino acid and another amino acid that is four amino acids farther along the chain.

The  $\alpha$ -helix and  $\beta$ -pleated sheet are secondary structures of proteins that form because of hydrogen bonding between carbonyl and amino groups in the peptide backbone. Certain amino acids have a propensity to form an  $\alpha$ -helix, while others have a propensity to form a  $\beta$ -

pleated sheet.

Every helical turn in an alpha helix has 3.6 amino acid residues. The R groups (the variant groups) of the polypeptide protrude out from the  $\alpha$ -helix chain. In the  $\beta$ -pleated sheet, the “pleats” are formed by hydrogen bonding between atoms on the backbone of the polypeptide chain. The R groups are attached to the carbons and extend above and below the folds of the pleat. The pleated segments align parallel or antiparallel to each other, and hydrogen bonds form between the partially positive nitrogen atom in the amino group and the partially negative oxygen atom in the carbonyl group of the peptide backbone. The  $\alpha$ -helix and  $\beta$ -pleated sheet structures are found in most globular and fibrous proteins and they play an important structural role.

### **Tertiary Structure**

The unique three-dimensional structure of a polypeptide is its tertiary structure ([\[link\]](#)). This structure is in part due to chemical interactions at work on the polypeptide chain. Primarily, the interactions among R groups creates the complex three-dimensional tertiary structure of a protein. The nature of the R groups found in the amino acids involved can counteract the formation of the hydrogen bonds described for standard secondary structures. For example, R groups with like charges are repelled by each other and those with unlike charges are

attracted to each other (ionic bonds). When protein folding takes place, the hydrophobic R groups of nonpolar amino acids lay in the interior of the protein, whereas the hydrophilic R groups lay on the outside. The former types of interactions are also known as hydrophobic interactions. Interaction between cysteine side chains forms disulfide linkages in the presence of oxygen, the only covalent bond forming during protein folding.

The tertiary structure of proteins is determined by a variety of chemical interactions. These include hydrophobic interactions, ionic bonding, hydrogen bonding and disulfide

linkages.

All of these interactions, weak and strong, determine the final three-dimensional shape of the protein. When a protein loses its three-dimensional shape, it may no longer be functional.

### **Quaternary Structure**

In nature, some proteins are formed from several polypeptides, also known as subunits, and the interaction of these subunits forms the quaternary structure. Weak interactions between the subunits help to stabilize the overall structure. For example, insulin (a globular protein) has a combination of hydrogen bonds and disulfide bonds that cause it to be mostly clumped into a ball shape. Insulin starts out as a single polypeptide and loses some internal sequences in the presence of post-translational modification after the formation of the disulfide linkages that hold the remaining chains together. Silk (a fibrous protein), however, has a  $\beta$ -pleated sheet structure that is the result of hydrogen bonding between different chains.

The four levels of protein structure (primary, secondary, tertiary, and quaternary) are illustrated in [\[link\]](#).

The four levels of protein structure can be observed in these illustrations. (credit: modification of work by National Human Genome Research

Institute)

## **Denaturation and Protein Folding**

Each protein has its own unique sequence and shape that are held together by chemical interactions. If the protein is subject to changes in temperature, pH, or exposure to chemicals, the protein structure may change, losing its shape without losing its primary sequence in what is known as denaturation. Denaturation is often reversible because the primary structure of the polypeptide is conserved in the process if the denaturing agent is removed, allowing the protein to resume its function. Sometimes denaturation is irreversible, leading to loss of function. One example of irreversible protein denaturation is when an egg is fried. The albumin protein in the liquid egg white is denatured when placed in a hot pan. Not all proteins are denatured at high temperatures; for instance, bacteria that survive in hot springs have proteins that function at temperatures close to boiling. The stomach is also very acidic, has a low pH, and denatures proteins as part of the digestion process; however, the digestive enzymes of the stomach retain their activity under these conditions.

Protein folding is critical to its function. It was originally thought that the proteins themselves were responsible for the folding process. Only recently was it found that often they receive assistance in the folding process from protein helpers known as chaperones (or chaperonins) that associate with the target protein during the folding process. They act by preventing

aggregation of polypeptides that make up the complete protein structure, and they disassociate from the protein once the target protein is folded.

Link to Learning

For an additional perspective on proteins, view [this animation](#) called “Biomolecules: The Proteins.”

## Section Summary

Proteins are a class of macromolecules that perform a diverse range of functions for the cell. They help in metabolism by providing structural support and by acting as enzymes, carriers, or hormones. The building blocks of proteins (monomers) are amino acids. Each amino acid has a central carbon that is linked to an amino group, a carboxyl group, a hydrogen atom, and an R group or side chain. There are 20 commonly occurring amino acids, each of which differs in the R group. Each amino acid is linked to its neighbors by a peptide bond. A long chain of amino acids is known as a polypeptide.

Proteins are organized at four levels: primary, secondary, tertiary, and (optional) quaternary. The primary structure is the unique sequence of amino acids. The local folding of the polypeptide to form structures such as the  $\alpha$  helix and  $\beta$ -pleated sheet constitutes the secondary structure. The overall three-dimensional structure is the tertiary structure. When two or more polypeptides combine to form the complete protein structure, the configuration is known as the quaternary structure of a protein. Protein shape and function are intricately linked; any change in shape caused by changes in temperature or pH may lead to protein denaturation and a loss in function.

## Art Connections

[\[link\]](#) Which categories of amino acid would you expect to find on the surface of a soluble protein, and which would you expect to find in the interior? What distribution of amino acids would you expect to find in a protein embedded in a lipid bilayer?

[\[link\]](#) Polar and charged amino acid residues (the remainder after peptide bond formation) are more likely to be found on the surface of soluble proteins where they can interact with water, and nonpolar (e.g., amino acid side chains) are more likely to be found in the interior where they are sequestered from water. In membrane proteins, nonpolar and hydrophobic amino acid side chains associate with the hydrophobic tails of phospholipids, while polar and charged amino acid side chains interact with the polar head groups or with the aqueous solution. However, there are exceptions. Sometimes, positively and negatively charged amino acid side chains interact with one another in the interior of a protein, and polar or charged amino acid side chains that interact with a ligand can be found in the ligand binding pocket.

## Review Questions

The monomers that make up proteins are called \_\_\_\_\_.

- a. nucleotides
- b. disaccharides
- c. amino acids
- d. chaperones

C

The  $\alpha$  helix and the  $\beta$ -pleated sheet are part of which protein structure?

- a. primary
- b. secondary
- c. tertiary
- d. quaternary

B

## Free Response

Explain what happens if even one amino acid is substituted for another in a polypeptide chain. Provide a specific example.

A change in gene sequence can lead to a different amino acid being added to a polypeptide chain instead of the normal one. This causes a change in protein structure and function. For example, in sickle cell anemia, the hemoglobin  $\beta$  chain has a single amino acid substitution—the amino acid glutamic acid in position six is substituted by valine. Because of this change, hemoglobin molecules form aggregates, and the disc-shaped red blood cells assume a crescent shape, which results in serious health problems.

Describe the differences in the four protein structures.

The sequence and number of amino acids in a polypeptide chain is its primary structure. The local folding of the polypeptide in some regions is the secondary structure of the protein. The three-dimensional structure of a polypeptide is known as its tertiary structure, created in part by chemical interactions such as hydrogen bonds between polar side chains, van der Waals interactions, disulfide linkages, and hydrophobic interactions. Some proteins are formed from multiple polypeptides, also known as subunits, and the interaction of these subunits forms the quaternary structure.

## Glossary

alpha-helix structure ( $\alpha$ -helix)

type of secondary structure of proteins formed by folding of the polypeptide into a helix shape with hydrogen bonds stabilizing the structure

amino acid

monomer of a protein; has a central carbon or alpha carbon to which an amino group, a carboxyl group, a hydrogen, and an R group or side chain is attached; the R group is different for all 20 amino acids

beta-pleated sheet ( $\beta$ -pleated)

secondary structure found in proteins in which “pleats” are formed by hydrogen bonding between atoms on the backbone of the polypeptide chain

chaperone

(also, chaperonin) protein that helps nascent protein in the folding process

denaturation

loss of shape in a protein as a result of changes in temperature, pH, or exposure to chemicals

enzyme

catalyst in a biochemical reaction that is usually a complex or conjugated protein

hormone

chemical signaling molecule, usually protein or steroid, secreted by endocrine cells that act to control or regulate specific physiological processes

peptide bond

bond formed between two amino acids by a dehydration reaction

polypeptide

long chain of amino acids linked by peptide bonds

primary structure

linear sequence of amino acids in a protein

protein

biological macromolecule composed of one or more chains of amino acids

quaternary structure

association of discrete polypeptide subunits in a protein

secondary structure

regular structure formed by proteins by intramolecular hydrogen bonding between the oxygen atom of one amino acid residue and the hydrogen attached to the nitrogen atom of another amino acid residue

tertiary structure

three-dimensional conformation of a protein, including interactions between secondary structural elements; formed from interactions between amino acid side chains

Nucleic Acids

By the end of this section, you will be able to:

- Describe the structure of nucleic acids and define the two types of nucleic acids
- Explain the structure and role of DNA
- Explain the structure and roles of RNA

Nucleic acids are the most important macromolecules for the continuity of life. They carry the genetic blueprint of a cell and carry instructions for the functioning of the cell.

## **DNA and RNA**

The two main types of nucleic acids are deoxyribonucleic acid (DNA) and ribonucleic acid (RNA). DNA is the genetic material found in all living organisms, ranging from single-celled bacteria to multicellular mammals. It is found in the nucleus of eukaryotes and in the organelles, chloroplasts, and mitochondria. In prokaryotes, the DNA is not enclosed in a membranous envelope.

The entire genetic content of a cell is known as its genome, and the study of genomes is genomics. In eukaryotic cells but not in prokaryotes, DNA forms a complex with histone proteins to form chromatin, the substance of eukaryotic chromosomes. A chromosome may contain tens of thousands of genes. Many genes contain the information to make protein products; other genes code for RNA products. DNA controls all of the cellular activities by turning the genes “on” or “off.”

The other type of nucleic acid, RNA, is mostly involved in protein synthesis. The DNA molecules never leave the nucleus but instead use an intermediary to communicate with the rest of the cell. This intermediary is the messenger RNA (mRNA). Other types of RNA—like rRNA, tRNA, and microRNA—are involved in protein synthesis and its regulation.

DNA and RNA are made up of monomers known as nucleotides. The nucleotides combine with each other to form a polynucleotide, DNA or RNA. Each nucleotide is made up of three components: a nitrogenous base, a pentose (five-carbon) sugar, and a phosphate group ([link](#)). Each nitrogenous base in a nucleotide is attached to a sugar molecule, which is attached to one or more phosphate groups.

A nucleotide is made up of three components: a nitrogenous base, a pentose sugar, and one or more phosphate groups. Carbon residues in the pentose are numbered 1' through 5' (the prime distinguishes these residues from those in the base, which are numbered without using a prime notation). The base is attached to the 1' position of the ribose, and the phosphate is attached to the 5' position. When a polynucleotide is formed, the 5' phosphate of the incoming nucleotide attaches to the 3' hydroxyl group at the end of the growing chain. Two types of pentose are found in nucleotides, deoxyribose (found in DNA) and ribose (found in RNA). Deoxyribose is similar in structure to ribose, but it has an H instead of an OH at the 2' position. Bases can be divided into two categories: purines and pyrimidines. Purines have a double ring structure, and pyrimidines have a single

ring.

The nitrogenous bases, important components of nucleotides, are organic molecules and are so named because they contain carbon and nitrogen. They are bases because they contain an amino group that has the potential of binding an extra hydrogen, and thus, decreases the hydrogen ion concentration in its environment, making it more basic. Each nucleotide in DNA contains one of four possible nitrogenous bases: adenine (A), guanine (G) cytosine (C), and thymine (T).

Adenine and guanine are classified as purines. The primary structure of a purine is two carbon-nitrogen rings. Cytosine, thymine, and uracil are classified as pyrimidines which have a single carbon-nitrogen ring as their primary structure ([link](#)). Each of these basic carbon-nitrogen rings has different functional groups attached to it. In molecular biology shorthand, the nitrogenous bases are simply known by their symbols A, T, G, C, and U. DNA contains A, T, G, and C whereas RNA contains A, U, G, and C.

The pentose sugar in DNA is deoxyribose, and in RNA, the sugar is ribose ([\[link\]](#)). The difference between the sugars is the presence of the hydroxyl group on the second carbon of the ribose and hydrogen on the second carbon of the deoxyribose. The carbon atoms of the sugar molecule are numbered as 1', 2', 3', 4', and 5' (1' is read as "one prime"). The phosphate residue is attached to the hydroxyl group of the 5' carbon of one sugar and the hydroxyl group of the 3' carbon of the sugar of the next nucleotide, which forms a 5'–3' phosphodiester linkage. The phosphodiester linkage is not formed by simple dehydration reaction like the other linkages connecting monomers in macromolecules: its formation involves the removal of two phosphate groups. A polynucleotide may have thousands of such phosphodiester linkages.

## DNA Double-Helix Structure

DNA has a double-helix structure ([\[link\]](#)). The sugar and phosphate lie on the outside of the helix, forming the backbone of the DNA. The nitrogenous bases are stacked in the interior, like the steps of a staircase, in pairs; the pairs are bound to each other by hydrogen bonds. Every base pair in the double helix is separated from the next base pair by 0.34 nm. The two strands of the helix run in opposite directions, meaning that the 5' carbon end of one strand will face the 3' carbon end of its matching strand. (This is referred to as antiparallel orientation and is important to DNA replication and in many nucleic acid interactions.)

Native DNA is an antiparallel double helix. The phosphate backbone (indicated by the curvy lines) is on the outside, and the bases are on the inside. Each base from one strand interacts via hydrogen bonding with a base from the opposing strand. (credit: Jerome Walker/Dennis

Myts)

Only certain types of base pairing are allowed. For example, a certain purine can only pair with a certain pyrimidine. This means A can pair with T, and G can pair with C, as shown in [\[link\]](#). This is known as the base complementary rule. In other words, the DNA strands are complementary to each other. If the sequence of one strand is AATTGGCC, the complementary strand would have the sequence TTAACCGG. During DNA replication, each strand is copied, resulting in a daughter DNA double helix containing one parental DNA strand and a newly synthesized strand.

### Art Connection

In a double stranded DNA molecule, the two strands run antiparallel to one another so that one strand runs 5' to 3' and the other 3' to 5'. The phosphate backbone is located on the

outside, and the bases are in the middle. Adenine forms hydrogen bonds (or base pairs) with thymine, and guanine base pairs with

cytosine.

A mutation occurs, and cytosine is replaced with adenine. What impact do you think this will have on the DNA structure?

## **RNA**

Ribonucleic acid, or RNA, is mainly involved in the process of protein synthesis under the direction of DNA. RNA is usually single-stranded and is made of ribonucleotides that are linked by phosphodiester bonds. A ribonucleotide in the RNA chain contains ribose (the pentose sugar), one of the four nitrogenous bases (A, U, G, and C), and the phosphate group.

There are four major types of RNA: messenger RNA (mRNA), ribosomal RNA (rRNA), transfer RNA (tRNA), and microRNA (miRNA). The first, mRNA, carries the message from DNA, which controls all of the cellular activities in a cell. If a cell requires a certain protein to be synthesized, the gene for this product is turned “on” and the messenger RNA is synthesized in the nucleus. The RNA base sequence is complementary to the coding sequence of the DNA from which it has been copied. However, in RNA, the base T is absent and U is present instead. If the DNA strand has a sequence AATTGCGC, the sequence of the complementary RNA is UUAACGCG. In the cytoplasm, the mRNA interacts with ribosomes and other cellular machinery ([link](#)).

A ribosome has two parts: a large subunit and a small subunit. The mRNA sits in between the two subunits. A tRNA molecule recognizes a codon on the mRNA, binds to it by

complementary base pairing, and adds the correct amino acid to the growing peptide

chain.

The mRNA is read in sets of three bases known as codons. Each codon codes for a single amino acid. In this way, the mRNA is read and the protein product is made. Ribosomal RNA (rRNA) is a major constituent of ribosomes on which the mRNA binds. The rRNA ensures the proper alignment of the mRNA and the ribosomes; the rRNA of the ribosome also has an enzymatic activity (peptidyl transferase) and catalyzes the formation of the peptide bonds between two aligned amino acids. Transfer RNA (tRNA) is one of the smallest of the four types of RNA, usually 70–90 nucleotides long. It carries the correct amino acid to the site of protein synthesis. It is the base pairing between the tRNA and mRNA that allows for the correct amino acid to be inserted in the polypeptide chain. microRNAs are the smallest RNA molecules and their role involves the regulation of gene expression by interfering with the expression of certain mRNA messages. [\[link\]](#) summarizes features of DNA and RNA.

### **Features of DNA and RNA**

	<b>DNA</b>	<b>RNA</b>
Function	Carries genetic information	Involved in protein synthesis
Location	Remains in the nucleus	Leaves the nucleus
Structure	Double helix	Usually single-stranded
Sugar	Deoxyribose	Ribose
Pyrimidines	Cytosine, thymine	Cytosine, uracil
Purines	Adenine, guanine	Adenine, guanine

Even though the RNA is single stranded, most RNA types show extensive intramolecular base pairing between complementary sequences, creating a predictable three-dimensional structure essential for their function.

As you have learned, information flow in an organism takes place from DNA to RNA to protein. DNA dictates the structure of mRNA in a process known as transcription, and RNA dictates the structure of protein in a process known as translation. This is known as the Central Dogma of Life, which holds true for all organisms; however, exceptions to the rule occur in connection with viral infections.

Link to Learning

To learn more about DNA, explore the [Howard Hughes Medical Institute BioInteractive animations](#) on the topic of DNA.

## Section Summary

Nucleic acids are molecules made up of nucleotides that direct cellular activities such as cell division and protein synthesis. Each nucleotide is made up of a pentose sugar, a nitrogenous base, and a phosphate group. There are two types of nucleic acids: DNA and RNA. DNA carries the genetic blueprint of the cell and is passed on from parents to offspring (in the form of chromosomes). It has a double-helical structure with the two strands running in opposite directions, connected by hydrogen bonds, and complementary to each other. RNA is single-stranded and is made of a pentose sugar (ribose), a nitrogenous base, and a phosphate group. RNA is involved in protein synthesis and its regulation. Messenger RNA (mRNA) is copied from the DNA, is exported from the nucleus to the cytoplasm, and contains information for the construction of proteins. Ribosomal RNA (rRNA) is a part of the ribosomes at the site of protein synthesis, whereas transfer RNA (tRNA) carries the amino acid to the site of protein synthesis. microRNA regulates the use of mRNA for protein synthesis.

## Art Connections

[\[link\]](#) A mutation occurs, and cytosine is replaced with adenine. What impact do you think this will have on the DNA structure?

[\[link\]](#) Adenine is larger than cytosine and will not be able to base pair properly with the guanine on the opposing strand. This will cause the DNA to bulge. DNA repair enzymes may recognize the bulge and replace the incorrect nucleotide.

## Review Questions

A nucleotide of DNA may contain \_\_\_\_\_.

- ribose, uracil, and a phosphate group
- deoxyribose, uracil, and a phosphate group
- deoxyribose, thymine, and a phosphate group

- d. ribose, thymine, and a phosphate group

C

The building blocks of nucleic acids are \_\_\_\_\_.

- a. sugars
- b. nitrogenous bases
- c. peptides
- d. nucleotides

D

### Free Response

What are the structural differences between RNA and DNA?

DNA has a double-helix structure. The sugar and the phosphate are on the outside of the helix and the nitrogenous bases are in the interior. The monomers of DNA are nucleotides containing deoxyribose, one of the four nitrogenous bases (A, T, G and C), and a phosphate group. RNA is usually single-stranded and is made of ribonucleotides that are linked by phosphodiester linkages. A ribonucleotide contains ribose (the pentose sugar), one of the four nitrogenous bases (A,U, G, and C), and the phosphate group.

What are the four types of RNA and how do they function?

The four types of RNA are messenger RNA, ribosomal RNA, transfer RNA, and microRNA. Messenger RNA carries the information from the DNA that controls all cellular activities. The mRNA binds to the ribosomes that are constructed of proteins and rRNA, and tRNA transfers the correct amino acid to the site of protein synthesis. microRNA regulates the availability of mRNA for translation.

### Glossary

deoxyribonucleic acid (DNA)

double-helical molecule that carries the hereditary information of the cell

messenger RNA (mRNA)

RNA that carries information from DNA to ribosomes during protein synthesis

nucleic acid

biological macromolecule that carries the genetic blueprint of a cell and carries instructions for the functioning of the cell

nucleotide

monomer of nucleic acids; contains a pentose sugar, one or more phosphate groups, and a nitrogenous base

phosphodiester

linkage covalent chemical bond that holds together the polynucleotide chains with a phosphate group linking two pentose sugars of neighboring nucleotides

polynucleotide

long chain of nucleotides

purine

type of nitrogenous base in DNA and RNA; adenine and guanine are purines

pyrimidine

type of nitrogenous base in DNA and RNA; cytosine, thymine, and uracil are pyrimidines

ribonucleic acid (RNA)

single-stranded, often internally base paired, molecule that is involved in protein synthesis

ribosomal RNA (rRNA)

RNA that ensures the proper alignment of the mRNA and the ribosomes during protein synthesis and catalyzes the formation of the peptide linkage

transcription

process through which messenger RNA forms on a template of DNA

transfer RNA (tRNA)

RNA that carries activated amino acids to the site of protein synthesis on the ribosome

translation

process through which RNA directs the formation of protein

Introduction

class="introduction" class="summary" title="Sections Summary" class="art-exercise" title="Art Connections" class="multiple-choice" title="Multiple Choice" class="free-response" title="Free Response"(a) Nasal sinus cells (viewed with a light microscope), (b) onion cells (viewed with a light microscope), and (c) *Vibrio tasmaniensis* bacterial cells (seen through a scanning electron microscope) are from very different organisms, yet all share certain characteristics of basic cell structure. (credit a: modification of work by Ed Uthman, MD; credit b: modification of work by Umberto Salvagnin; credit c: modification of work by Anthony D'Onofrio, William H. Fowle, Eric J. Stewart, and Kim Lewis of the Lewis Lab at Northeastern University; scale-bar data from Matt

Russell)

Close your eyes and picture a brick wall. What is the basic building block of that wall? A single brick, of course. Like a brick wall, your body is composed of basic building blocks, and the building blocks of your body are cells.

Your body has many kinds of cells, each specialized for a specific purpose. Just as a home is made from a variety of building materials, the human body is constructed from many cell types. For example, epithelial cells protect the surface of the body and cover the organs and body cavities within. Bone cells help to support and protect the body. Cells of the immune system fight invading bacteria. Additionally, blood and blood cells carry nutrients and oxygen throughout the body while removing carbon dioxide. Each of these cell types plays a vital role during the growth, development, and day-to-day maintenance of the body. In spite of their enormous variety, however, cells from all organisms—even ones as diverse as bacteria, onion, and human—share certain fundamental characteristics.

Studying Cells

By the end of this section, you will be able to:

- Describe the role of cells in organisms
- Compare and contrast light microscopy and electron microscopy
- Summarize cell theory

A cell is the smallest unit of a living thing. A living thing, whether made of one cell (like bacteria) or many cells (like a human), is called an organism. Thus, cells are the basic building blocks of all organisms.

Several cells of one kind that interconnect with each other and perform a shared function form tissues, several tissues combine to form an organ (your stomach, heart, or brain), and several organs make up an organ system (such as the digestive system, circulatory system, or nervous system). Several systems that function together form an organism (like a human being). Here, we will examine the structure and function of cells.

There are many types of cells, all grouped into one of two broad categories: prokaryotic and eukaryotic. For example, both animal and plant cells are classified as eukaryotic cells, whereas bacterial cells are classified as prokaryotic. Before discussing the criteria for determining whether a cell is prokaryotic or eukaryotic, let's first examine how biologists study cells.

## **Microscopy**

Cells vary in size. With few exceptions, individual cells cannot be seen with the naked eye, so scientists use microscopes (micro- = "small"; -scope = "to look at") to study them. A microscope is an instrument that magnifies an object. Most photographs of cells are taken with a microscope, and these images can also be called micrographs.

The optics of a microscope's lenses change the orientation of the image that the user sees. A specimen that is right-side up and facing right on the microscope slide will appear upside-down and facing left when viewed through a microscope, and vice versa. Similarly, if the slide is moved left while looking through the microscope, it will appear to move right, and if moved down, it will seem to move up. This occurs because microscopes use two sets of lenses to magnify the image. Because of the manner by which light travels through the lenses, this system of two lenses produces an inverted image (binocular, or dissecting microscopes, work in a similar manner, but include an additional magnification system that makes the final image appear to be upright).

## **Light Microscopes**

To give you a sense of cell size, a typical human red blood cell is about eight millionths of a meter or eight micrometers (abbreviated as eight  $\mu\text{m}$ ) in diameter; the head of a pin is about two thousandths of a meter (two mm) in diameter. That means about 250 red blood cells could fit on the head of a pin.

Most student microscopes are classified as light microscopes ([link](#)**a**). Visible light passes and is bent through the lens system to enable the user to see the specimen. Light microscopes are advantageous for viewing living organisms, but since individual cells are generally transparent, their components are not distinguishable unless they are colored with special stains. Staining, however, usually kills the cells.

Light microscopes commonly used in the undergraduate college laboratory magnify up to approximately 400 times. Two parameters that are important in microscopy are magnification and resolving power. Magnification is the process of enlarging an object in appearance. Resolving power is the ability of a microscope to distinguish two adjacent structures as separate: the higher the resolution, the better the clarity and detail of the image. When oil immersion lenses are used for the study of small objects, magnification is usually increased to 1,000 times. In order to gain a better understanding of cellular structure and function, scientists typically use electron microscopes.

(a) Most light microscopes used in a college biology lab can magnify cells up to approximately 400 times and have a resolution of about 200 nanometers. (b) Electron microscopes provide a much higher magnification, 100,000x, and have a resolution of 50 picometers. (credit a: modification of work by "GcG"/Wikimedia Commons; credit b:

modification of work by Evan Bench)

### **Electron Microscopes**

In contrast to light microscopes, electron microscopes ([link](#)**b**) use a beam of electrons instead of a beam of light. Not only does this allow for higher magnification and, thus, more detail ([link](#)), it also provides higher resolving power. The method used to prepare the specimen for viewing with an electron microscope kills the specimen. Electrons have short wavelengths (shorter than photons) that move best in a vacuum, so living cells cannot be viewed with an electron microscope.

In a scanning electron microscope, a beam of electrons moves back and forth across a cell's surface, creating details of cell surface characteristics. In a transmission electron microscope, the electron beam penetrates the cell and provides details of a cell's internal structures. As you might imagine, electron microscopes are significantly more bulky and expensive than light microscopes.

(a) These *Salmonella* bacteria appear as tiny purple dots when viewed with a light microscope. (b) This scanning electron microscope micrograph shows *Salmonella* bacteria (in red) invading human cells (yellow). Even though subfigure (b) shows a different *Salmonella* specimen than subfigure (a), you can still observe the comparative increase in magnification and detail. (credit a: modification of work by CDC/Armed Forces Institute of Pathology, Charles N. Farmer, Rocky Mountain Laboratories; credit b: modification of work by NIAID, NIH; scale-bar data from Matt

Russell)  
Link to Learning

For another perspective on cell size, try the HowBig interactive at [this site](#).

## Cell Theory

The microscopes we use today are far more complex than those used in the 1600s by Antony van Leeuwenhoek, a Dutch shopkeeper who had great skill in crafting lenses. Despite the limitations of his now-ancient lenses, van Leeuwenhoek observed the movements of protista (a type of single-celled organism) and sperm, which he collectively termed “animalcules.”

In a 1665 publication called *Micrographia*, experimental scientist Robert Hooke coined the term “cell” for the box-like structures he observed when viewing cork tissue through a lens. In the 1670s, van Leeuwenhoek discovered bacteria and protozoa. Later advances in lenses, microscope construction, and staining techniques enabled other scientists to see some components inside cells.

By the late 1830s, botanist Matthias Schleiden and zoologist Theodor Schwann were studying tissues and proposed the unified cell theory, which states that all living things are composed of one or more cells, the cell is the basic unit of life, and new cells arise from existing cells. Rudolf Virchow later made important contributions to this theory.

Career Connection

Cytotechnologist Have you ever heard of a medical test called a Pap smear ([link](#))? In this test, a doctor takes a small sample of cells from the uterine cervix of a patient and sends it to a medical lab where a cytotechnologist stains the cells and examines them for any changes that could indicate cervical cancer or a microbial infection.

Cytotechnologists (cyto- = “cell”) are professionals who study cells via microscopic examinations and other laboratory tests. They are trained to determine which cellular changes are within normal limits and which are abnormal. Their focus is not limited to cervical cells; they study cellular specimens that come from all organs. When they notice abnormalities, they consult a pathologist, who is a medical doctor who can make a clinical diagnosis.

Cytotechnologists play a vital role in saving people’s lives. When abnormalities are discovered early, a patient’s treatment can begin sooner, which usually increases the chances of a successful outcome.

These uterine cervix cells, viewed through a light microscope, were obtained from a Pap smear. Normal cells are on the left. The cells on the right are infected with human papillomavirus (HPV). Notice that the infected cells are larger; also, two of these cells each have two nuclei instead of one, the normal number. (credit: modification of work by Ed Uthman, MD; scale-bar data from Matt

Russell)

## **Section Summary**

A cell is the smallest unit of life. Most cells are so tiny that they cannot be seen with the naked eye. Therefore, scientists use microscopes to study cells. Electron microscopes provide higher magnification, higher resolution, and more detail than light microscopes. The unified cell theory states that all organisms are composed of one or more cells, the cell is the basic unit of life, and new cells arise from existing cells.

## **Review Questions**

When viewing a specimen through a light microscope, scientists use \_\_\_\_\_ to distinguish the individual components of cells.

- a. a beam of electrons
- b. radioactive isotopes
- c. special stains
- d. high temperatures

C

The \_\_\_\_\_ is the basic unit of life.

- a. organism
- b. cell
- c. tissue
- d. organ

B

### **Free Response**

In your everyday life, you have probably noticed that certain instruments are ideal for certain situations. For example, you would use a spoon rather than a fork to eat soup because a spoon is shaped for scooping, while soup would slip between the tines of a fork. The use of ideal instruments also applies in science. In what situation(s) would the use of a light microscope be ideal, and why?

A light microscope would be ideal when viewing a small living organism, especially when the cell has been stained to reveal details.

In what situation(s) would the use of a scanning electron microscope be ideal, and why?

A scanning electron microscope would be ideal when you want to view the minute details of a cell's surface, because its beam of electrons moves back and forth over the surface to convey the image.

In what situation(s) would a transmission electron microscope be ideal, and why?

A transmission electron microscope would be ideal for viewing the cell's internal structures, because many of the internal structures have membranes that are not visible by the light microscope.

What are the advantages and disadvantages of each of these types of microscopes?

The advantages of light microscopes are that they are easily obtained, and the light beam does not kill the cells. However, typical light microscopes are somewhat limited in the amount of detail they can reveal. Electron microscopes are ideal because you can view intricate details, but they are bulky and costly, and preparation for the microscopic examination kills the specimen.

## Glossary

cell theory

see unified cell theory

electron microscope

an instrument that magnifies an object using a beam of electrons passed and bent through a lens system to visualize a specimen

light microscope

an instrument that magnifies an object using a beam visible light passed and bent through a lens system to visualize a specimen

microscope

an instrument that magnifies an object

unified cell theory

a biological concept that states that all organisms are composed of one or more cells; the cell is the basic unit of life; and new cells arise from existing cells

### Prokaryotic Cells

By the end of this section, you will be able to:

- Name examples of prokaryotic and eukaryotic organisms
- Compare and contrast prokaryotic cells and eukaryotic cells
- Describe the relative sizes of different kinds of cells
- Explain why cells must be small

Cells fall into one of two broad categories: prokaryotic and eukaryotic. Only the predominantly single-celled organisms of the domains Bacteria and Archaea are classified as prokaryotes (pro- = “before”; -kary- = “nucleus”). Animals, plants, fungi, and protists are all eukaryotes (eu- = “true”) and are made up of eukaryotic cells.

## Components of Prokaryotic Cells

All cells share four common components: 1) a plasma membrane, an outer covering that separates the cell’s interior from its surrounding environment; 2) cytoplasm, consisting of a jelly-like cytosol within the cell in which other cellular components are found; 3) DNA, the genetic material of the cell; and 4) ribosomes, which synthesize proteins. However, prokaryotes differ from eukaryotic cells in several ways.

A prokaryote is a simple, mostly single-celled (unicellular) organism that lacks a nucleus, or any other membrane-bound organelle. We will shortly come to see that this is significantly different in eukaryotes. Prokaryotic DNA is found in a central part of the cell: the nucleoid ([link](#)).

This figure shows the generalized structure of a prokaryotic cell. All prokaryotes have chromosomal DNA localized in a nucleoid, ribosomes, a cell membrane, and a cell wall. The

other structures shown are present in some, but not all,

bacteria.

Most prokaryotes have a peptidoglycan cell wall and many have a polysaccharide capsule ([link](#)). The cell wall acts as an extra layer of protection, helps the cell maintain its shape, and prevents dehydration. The capsule enables the cell to attach to surfaces in its environment. Some prokaryotes have flagella, pili, or fimbriae. Flagella are used for locomotion. Pili are used to exchange genetic material during a type of reproduction called conjugation. Fimbriae are used by bacteria to attach to a host cell.

### Career Connection

**Microbiologist**The most effective action anyone can take to prevent the spread of contagious illnesses is to wash his or her hands. Why? Because microbes (organisms so tiny that they can only be seen with microscopes) are ubiquitous. They live on doorknobs, money, your hands, and many other surfaces. If someone sneezes into his hand and touches a doorknob, and afterwards you touch that same doorknob, the microbes from the sneezer's mucus are now on your hands. If you touch your hands to your mouth, nose, or eyes, those microbes can enter your body and could make you sick.

However, not all microbes (also called microorganisms) cause disease; most are actually beneficial. You have microbes in your gut that make vitamin K. Other microorganisms are used to ferment beer and wine.

Microbiologists are scientists who study microbes. Microbiologists can pursue a number of careers. Not only do they work in the food industry, they are also employed in the veterinary and medical fields. They can work in the pharmaceutical sector, serving key roles in research and development by identifying new sources of antibiotics that could be used to treat bacterial infections.

Environmental microbiologists may look for new ways to use specially selected or genetically engineered microbes for the removal of pollutants from soil or groundwater, as

well as hazardous elements from contaminated sites. These uses of microbes are called bioremediation technologies. Microbiologists can also work in the field of bioinformatics, providing specialized knowledge and insight for the design, development, and specificity of computer models of, for example, bacterial epidemics.

### **Cell Size**

At 0.1 to 5.0  $\mu\text{m}$  in diameter, prokaryotic cells are significantly smaller than eukaryotic cells, which have diameters ranging from 10 to 100  $\mu\text{m}$  ([link](#)). The small size of prokaryotes allows ions and organic molecules that enter them to quickly diffuse to other parts of the cell. Similarly, any wastes produced within a prokaryotic cell can quickly diffuse out. This is not the case in eukaryotic cells, which have developed different structural adaptations to enhance intracellular transport.

This figure shows relative sizes of microbes on a logarithmic scale (recall that each unit of increase in a logarithmic scale represents a 10-fold increase in the quantity being measured).

Small size, in general, is necessary for all cells, whether prokaryotic or eukaryotic. Let's examine why that is so. First, we'll consider the area and volume of a typical cell. Not all cells are spherical in shape, but most tend to approximate a sphere. You may remember from your high school geometry course that the formula for the surface area of a sphere is  $4\pi r^2$ , while the formula for its volume is  $\frac{4\pi r^3}{3}$ . Thus, as the radius of a cell increases, its surface area increases as the square of its radius, but its volume increases as the cube of its radius (much more rapidly). Therefore, as a cell increases in size, its surface area-to-volume ratio decreases. This same principle would apply if the cell had the shape of a cube ([link](#)). If the cell grows too large, the plasma membrane will not have sufficient surface area to support the rate of diffusion required for the increased volume. In other words, as a cell grows, it becomes less efficient. One way to become more efficient is to divide; another way is to develop organelles that perform specific tasks. These adaptations lead to the development of more sophisticated cells called eukaryotic cells.

### Art Connection

Notice that as a cell increases in size, its surface area-to-volume ratio decreases. When there is insufficient surface area to support a cell's increasing volume, a cell will either divide or die. The cell on the left has a volume of  $1 \text{ mm}^3$  and a surface area of  $6 \text{ mm}^2$ , with a surface area-to-volume ratio of 6 to 1, whereas the cell on the right has a volume of  $8 \text{ mm}^3$  and a surface area of  $24 \text{ mm}^2$ , with a surface area-to-volume ratio of 3 to

1.

Prokaryotic cells are much smaller than eukaryotic cells. What advantages might small cell size confer on a cell? What advantages might large cell size have?

### Section Summary

Prokaryotes are predominantly single-celled organisms of the domains Bacteria and Archaea. All prokaryotes have plasma membranes, cytoplasm, ribosomes, and DNA that is not membrane-bound. Most have peptidoglycan cell walls and many have polysaccharide capsules. Prokaryotic cells range in diameter from  $0.1$  to  $5.0 \text{ }\mu\text{m}$ .

As a cell increases in size, its surface area-to-volume ratio decreases. If the cell grows too large, the plasma membrane will not have sufficient surface area to support the rate of diffusion required for the increased volume.

### Art Connections

[\[link\]](#) Prokaryotic cells are much smaller than eukaryotic cells. What advantages might small cell size confer on a cell? What advantages might large cell size have?

[\[link\]](#) Substances can diffuse more quickly through small cells. Small cells have no need for organelles and therefore do not need to expend energy getting substances across organelle membranes. Large cells have organelles that can separate cellular processes, enabling them to build molecules that are more complex.

### Review Questions

Prokaryotes depend on \_\_\_\_\_ to obtain some materials and to get rid of wastes.

- a. ribosomes
- b. flagella
- c. cell division
- d. diffusion

D

Bacteria that lack fimbriae are less likely to \_\_\_\_\_.

- a. adhere to cell surfaces
- b. swim through bodily fluids
- c. synthesize proteins
- d. retain the ability to divide

A

### Free Response

Antibiotics are medicines that are used to fight bacterial infections. These medicines kill prokaryotic cells without harming human cells. What part or parts of the bacterial cell do you think antibiotics target? Why?

The cell wall would be targeted by antibiotics as well as the bacteria's ability to replicate. This would inhibit the bacteria's ability to reproduce, and it would compromise its defense mechanisms.

Explain why not all microbes are harmful.

Some microbes are beneficial. For instance, *E. coli* bacteria populate the human gut and help break down fiber in the diet. Some foods such as yogurt are formed by bacteria.

## Glossary

### nucleoid

central part of a prokaryotic cell in which the chromosome is found

### prokaryote

unicellular organism that lacks a nucleus or any other membrane-bound organelle

### Eukaryotic Cells

By the end of this section, you will be able to:

- Describe the structure of eukaryotic cells
- Compare animal cells with plant cells
- State the role of the plasma membrane
- Summarize the functions of the major cell organelles

Have you ever heard the phrase “form follows function?” It’s a philosophy practiced in many industries. In architecture, this means that buildings should be constructed to support the activities that will be carried out inside them. For example, a skyscraper should be built with several elevator banks; a hospital should be built so that its emergency room is easily accessible.

Our natural world also utilizes the principle of form following function, especially in cell biology, and this will become clear as we explore eukaryotic cells ([\[link\]](#)). Unlike prokaryotic cells, eukaryotic cells have: 1) a membrane-bound nucleus; 2) numerous membrane-bound organelles such as the endoplasmic reticulum, Golgi apparatus, chloroplasts, mitochondria, and others; and 3) several, rod-shaped chromosomes. Because a eukaryotic cell’s nucleus is surrounded by a membrane, it is often said to have a “true nucleus.” The word “organelle” means “little organ,” and, as already mentioned, organelles have specialized cellular functions, just as the organs of your body have specialized functions.

At this point, it should be clear to you that eukaryotic cells have a more complex structure than prokaryotic cells. Organelles allow different functions to be compartmentalized in different areas of the cell. Before turning to organelles, let’s first examine two important components of the cell: the plasma membrane and the cytoplasm.

### Art Connection

These figures show the major organelles and other cell components of (a) a typical animal cell and (b) a typical eukaryotic plant cell. The plant cell has a cell wall, chloroplasts, plastids, and a central vacuole—structures not found in animal cells. Plant cells do not have lysosomes or

centrosomes.

If the nucleolus were not able to carry out its function, what other cellular organelles would be affected?

### **The Plasma Membrane**

Like prokaryotes, eukaryotic cells have a plasma membrane ( [link](#) ), a phospholipid bilayer with embedded proteins that separates the internal contents of the cell from its surrounding environment. A phospholipid is a lipid molecule with two fatty acid chains and a phosphate-containing group. The plasma membrane controls the passage of organic molecules, ions, water, and oxygen into and out of the cell. Wastes (such as carbon dioxide and ammonia) also leave the cell by passing through the plasma membrane.

The eukaryotic plasma membrane is a phospholipid bilayer with proteins and cholesterol embedded in it.

The plasma membranes of cells that specialize in absorption are folded into fingerlike projections called microvilli (singular = microvillus); ([link](#)). Such cells are typically found lining the small intestine, the organ that absorbs nutrients from digested food. This is an excellent example of form following function. People with celiac disease have an immune response to gluten, which is a protein found in wheat, barley, and rye. The immune response damages microvilli, and thus, afflicted individuals cannot absorb nutrients. This leads to malnutrition, cramping, and diarrhea. Patients suffering from celiac disease must follow a gluten-free diet.

Microvilli, shown here as they appear on cells lining the small intestine, increase the surface area available for absorption. These microvilli are only found on the area of the plasma membrane that faces the cavity from which substances will be absorbed. (credit "micrograph": modification of work by Louisa

Howard)

## **The Cytoplasm**

The cytoplasm is the entire region of a cell between the plasma membrane and the nuclear envelope (a structure to be discussed shortly). It is made up of organelles suspended in the gel-like cytosol, the cytoskeleton, and various chemicals ( [\[link\]](#)). Even though the cytoplasm consists of 70 to 80 percent water, it has a semi-solid consistency, which comes from the proteins within it. However, proteins are not the only organic molecules found in the cytoplasm. Glucose and other simple sugars, polysaccharides, amino acids, nucleic acids, fatty acids, and derivatives of glycerol are found there, too. Ions of sodium, potassium,

calcium, and many other elements are also dissolved in the cytoplasm. Many metabolic reactions, including protein synthesis, take place in the cytoplasm.

## **The Nucleus**

Typically, the nucleus is the most prominent organelle in a cell ( [link](#)). The nucleus (plural = nuclei) houses the cell's DNA and directs the synthesis of ribosomes and proteins. Let's look at it in more detail ( [link](#)).

The nucleus stores chromatin (DNA plus proteins) in a gel-like substance called the nucleoplasm. The nucleolus is a condensed region of chromatin where ribosome synthesis occurs. The boundary of the nucleus is called the nuclear envelope. It consists of two phospholipid bilayers: an outer membrane and an inner membrane. The nuclear membrane is continuous with the endoplasmic reticulum. Nuclear pores allow substances to enter and exit

the nucleus.

### **The Nuclear Envelope**

The nuclear envelope is a double-membrane structure that constitutes the outermost portion of the nucleus ( [link](#)). Both the inner and outer membranes of the nuclear envelope are phospholipid bilayers.

The nuclear envelope is punctuated with pores that control the passage of ions, molecules, and RNA between the nucleoplasm and cytoplasm. The nucleoplasm is the semi-solid fluid inside the nucleus, where we find the chromatin and the nucleolus.

### **Chromatin and Chromosomes**

To understand chromatin, it is helpful to first consider chromosomes. Chromosomes are structures within the nucleus that are made up of DNA, the hereditary material. You may remember that in prokaryotes, DNA is organized into a single circular chromosome. In eukaryotes, chromosomes are linear structures. Every eukaryotic species has a specific

number of chromosomes in the nuclei of its body's cells. For example, in humans, the chromosome number is 46, while in fruit flies, it is eight. Chromosomes are only visible and distinguishable from one another when the cell is getting ready to divide. When the cell is in the growth and maintenance phases of its life cycle, proteins are attached to chromosomes, and they resemble an unwound, jumbled bunch of threads. These unwound protein-chromosome complexes are called chromatin ([link](#)); chromatin describes the material that makes up the chromosomes both when condensed and decondensed.

(a) This image shows various levels of the organization of chromatin (DNA and protein). (b) This image shows paired chromosomes. (credit b: modification of work by NIH; scale-bar

data from Matt Russell)

## **The Nucleolus**

We already know that the nucleus directs the synthesis of ribosomes, but how does it do this? Some chromosomes have sections of DNA that encode ribosomal RNA. A darkly staining area within the nucleus called the nucleolus (plural = nucleoli) aggregates the ribosomal RNA with associated proteins to assemble the ribosomal subunits that are then transported out through the pores in the nuclear envelope to the cytoplasm.

## **Ribosomes**

Ribosomes are the cellular structures responsible for protein synthesis. When viewed through an electron microscope, ribosomes appear either as clusters (polyribosomes) or single, tiny dots that float freely in the cytoplasm. They may be attached to the cytoplasmic side of the plasma membrane or the cytoplasmic side of the endoplasmic reticulum and the outer

membrane of the nuclear envelope ( [link](#)). Electron microscopy has shown us that ribosomes, which are large complexes of protein and RNA, consist of two subunits, aptly called large and small ( [link](#)). Ribosomes receive their “orders” for protein synthesis from the nucleus where the DNA is transcribed into messenger RNA (mRNA). The mRNA travels to the ribosomes, which translate the code provided by the sequence of the nitrogenous bases in the mRNA into a specific order of amino acids in a protein. Amino acids are the building blocks of proteins.

Ribosomes are made up of a large subunit (top) and a small subunit (bottom). During protein synthesis, ribosomes assemble amino acids into

proteins.

Because proteins synthesis is an essential function of all cells (including enzymes, hormones, antibodies, pigments, structural components, and surface receptors), ribosomes are found in practically every cell. Ribosomes are particularly abundant in cells that synthesize large amounts of protein. For example, the pancreas is responsible for creating several digestive enzymes and the cells that produce these enzymes contain many ribosomes. Thus, we see another example of form following function.

## **Mitochondria**

Mitochondria (singular = mitochondrion) are often called the “powerhouses” or “energy factories” of a cell because they are responsible for making adenosine triphosphate (ATP), the cell’s main energy-carrying molecule. ATP represents the short-term stored energy of the cell. Cellular respiration is the process of making ATP using the chemical energy found in glucose and other nutrients. In mitochondria, this process uses oxygen and produces carbon dioxide as a waste product. In fact, the carbon dioxide that you exhale with every breath comes from the cellular reactions that produce carbon dioxide as a byproduct.

In keeping with our theme of form following function, it is important to point out that muscle cells have a very high concentration of mitochondria that produce ATP. Your muscle cells need a lot of energy to keep your body moving. When your cells don’t get enough oxygen,

they do not make a lot of ATP. Instead, the small amount of ATP they make in the absence of oxygen is accompanied by the production of lactic acid.

Mitochondria are oval-shaped, double membrane organelles ([link](#)) that have their own ribosomes and DNA. Each membrane is a phospholipid bilayer embedded with proteins. The inner layer has folds called cristae. The area surrounded by the folds is called the mitochondrial matrix. The cristae and the matrix have different roles in cellular respiration.

This electron micrograph shows a mitochondrion as viewed with a transmission electron microscope. This organelle has an outer membrane and an inner membrane. The inner membrane contains folds, called cristae, which increase its surface area. The space between the two membranes is called the intermembrane space, and the space inside the inner membrane is called the mitochondrial matrix. ATP synthesis takes place on the inner membrane. (credit: modification of work by Matthew Britton; scale-bar data from Matt

Russell)

## **Peroxisomes**

Peroxisomes are small, round organelles enclosed by single membranes. They carry out oxidation reactions that break down fatty acids and amino acids. They also detoxify many poisons that may enter the body. (Many of these oxidation reactions release hydrogen peroxide,  $H_2O_2$ , which would be damaging to cells; however, when these reactions are confined to peroxisomes, enzymes safely break down the  $H_2O_2$  into oxygen and water.) For example, alcohol is detoxified by peroxisomes in liver cells. Glyoxysomes, which are specialized peroxisomes in plants, are responsible for converting stored fats into sugars.

## **Vesicles and Vacuoles**

Vesicles and vacuoles are membrane-bound sacs that function in storage and transport. Other than the fact that vacuoles are somewhat larger than vesicles, there is a very subtle distinction between them: The membranes of vesicles can fuse with either the plasma membrane or other membrane systems within the cell. Additionally, some agents such as enzymes within plant

vacuoles break down macromolecules. The membrane of a vacuole does not fuse with the membranes of other cellular components.

## **Animal Cells versus Plant Cells**

At this point, you know that each eukaryotic cell has a plasma membrane, cytoplasm, a nucleus, ribosomes, mitochondria, peroxisomes, and in some, vacuoles, but there are some striking differences between animal and plant cells. While both animal and plant cells have microtubule organizing centers (MTOCs), animal cells also have centrioles associated with the MTOC: a complex called the centrosome. Animal cells each have a centrosome and lysosomes, whereas plant cells do not. Plant cells have a cell wall, chloroplasts and other specialized plastids, and a large central vacuole, whereas animal cells do not.

### **The Centrosome**

The centrosome is a microtubule-organizing center found near the nuclei of animal cells. It contains a pair of centrioles, two structures that lie perpendicular to each other ( [link](#)). Each centriole is a cylinder of nine triplets of microtubules.

The centrosome consists of two centrioles that lie at right angles to each other. Each centriole is a cylinder made up of nine triplets of microtubules. Nontubulin proteins (indicated by the green lines) hold the microtubule triplets

together.

The centrosome (the organelle where all microtubules originate) replicates itself before a cell divides, and the centrioles appear to have some role in pulling the duplicated chromosomes to opposite ends of the dividing cell. However, the exact function of the centrioles in cell division isn't clear, because cells that have had the centrosome removed can still divide, and plant cells, which lack centrosomes, are capable of cell division.

### **Lysosomes**

Animal cells have another set of organelles not found in plant cells: lysosomes. The lysosomes are the cell's "garbage disposal." In plant cells, the digestive processes take place in vacuoles. Enzymes within the lysosomes aid the breakdown of proteins, polysaccharides, lipids, nucleic acids, and even worn-out organelles. These enzymes are active at a much lower pH than that of the cytoplasm. Therefore, the pH within lysosomes is more acidic than the pH of the cytoplasm. Many reactions that take place in the cytoplasm could not occur at a low pH, so again, the advantage of compartmentalizing the eukaryotic cell into organelles is apparent.

## **The Cell Wall**

If you examine [\[link\]](#)<sup>b</sup>, the diagram of a plant cell, you will see a structure external to the plasma membrane called the cell wall. The cell wall is a rigid covering that protects the cell, provides structural support, and gives shape to the cell. Fungal and protistan cells also have cell walls. While the chief component of prokaryotic cell walls is peptidoglycan, the major organic molecule in the plant cell wall is cellulose ( [\[link\]](#)), a polysaccharide made up of glucose units. Have you ever noticed that when you bite into a raw vegetable, like celery, it crunches? That's because you are tearing the rigid cell walls of the celery cells with your teeth.

Cellulose is a long chain of  $\beta$ -glucose molecules connected by a 1-4 linkage. The dashed lines at each end of the figure indicate a series of many more glucose units. The size of the page makes it impossible to portray an entire cellulose

molecule.

## **Chloroplasts**

Like the mitochondria, chloroplasts have their own DNA and ribosomes, but chloroplasts have an entirely different function. Chloroplasts are plant cell organelles that carry out photosynthesis. Photosynthesis is the series of reactions that use carbon dioxide, water, and light energy to make glucose and oxygen. This is a major difference between plants and

animals; plants (autotrophs) are able to make their own food, like sugars, while animals (heterotrophs) must ingest their food.

Like mitochondria, chloroplasts have outer and inner membranes, but within the space enclosed by a chloroplast's inner membrane is a set of interconnected and stacked fluid-filled membrane sacs called thylakoids ([link](#)). Each stack of thylakoids is called a granum (plural = grana). The fluid enclosed by the inner membrane that surrounds the grana is called the stroma.

The chloroplast has an outer membrane, an inner membrane, and membrane structures called thylakoids that are stacked into grana. The space inside the thylakoid membranes is called the thylakoid space. The light harvesting reactions take place in the thylakoid membranes, and the synthesis of sugar takes place in the fluid inside the inner membrane, which is called the stroma. Chloroplasts also have their own genome, which is contained on a single circular

chromosome.

The chloroplasts contain a green pigment called chlorophyll, which captures the light energy that drives the reactions of photosynthesis. Like plant cells, photosynthetic protists also have chloroplasts. Some bacteria perform photosynthesis, but their chlorophyll is not relegated to an organelle.

### Evolution Connection

**Endosymbiosis** We have mentioned that both mitochondria and chloroplasts contain DNA and ribosomes. Have you wondered why? Strong evidence points to endosymbiosis as the explanation.

Symbiosis is a relationship in which organisms from two separate species depend on each other for their survival. Endosymbiosis (endo- = "within") is a mutually beneficial relationship in which one organism lives inside the other. Endosymbiotic relationships abound in nature. We have already mentioned that microbes that produce vitamin K live inside the human gut. This relationship is beneficial for us because we are unable to

synthesize vitamin K. It is also beneficial for the microbes because they are protected from other organisms and from drying out, and they receive abundant food from the environment of the large intestine.

Scientists have long noticed that bacteria, mitochondria, and chloroplasts are similar in size. We also know that bacteria have DNA and ribosomes, just as mitochondria and chloroplasts do. Scientists believe that host cells and bacteria formed an endosymbiotic relationship when the host cells ingested both aerobic and autotrophic bacteria (cyanobacteria) but did not destroy them. Through many millions of years of evolution, these ingested bacteria became more specialized in their functions, with the aerobic bacteria becoming mitochondria and the autotrophic bacteria becoming chloroplasts.

### **The Central Vacuole**

Previously, we mentioned vacuoles as essential components of plant cells. If you look at [\[link\]](#), you will see that plant cells each have a large central vacuole that occupies most of the area of the cell. The central vacuole plays a key role in regulating the cell's concentration of water in changing environmental conditions. Have you ever noticed that if you forget to water a plant for a few days, it wilts? That's because as the water concentration in the soil becomes lower than the water concentration in the plant, water moves out of the central vacuoles and cytoplasm. As the central vacuole shrinks, it leaves the cell wall unsupported. This loss of support to the cell walls of plant cells results in the wilted appearance of the plant.

The central vacuole also supports the expansion of the cell. When the central vacuole holds more water, the cell gets larger without having to invest a lot of energy in synthesizing new cytoplasm.

### **Section Summary**

Like a prokaryotic cell, a eukaryotic cell has a plasma membrane, cytoplasm, and ribosomes, but a eukaryotic cell is typically larger than a prokaryotic cell, has a true nucleus (meaning its DNA is surrounded by a membrane), and has other membrane-bound organelles that allow for compartmentalization of functions. The plasma membrane is a phospholipid bilayer embedded with proteins. The nucleus's nucleolus is the site of ribosome assembly. Ribosomes are either found in the cytoplasm or attached to the cytoplasmic side of the plasma membrane or endoplasmic reticulum. They perform protein synthesis. Mitochondria participate in cellular respiration; they are responsible for the majority of ATP produced in the cell. Peroxisomes hydrolyze fatty acids, amino acids, and some toxins. Vesicles and vacuoles are storage and transport compartments. In plant cells, vacuoles also help break down macromolecules.

Animal cells also have a centrosome and lysosomes. The centrosome has two bodies perpendicular to each other, the centrioles, and has an unknown purpose in cell division. Lysosomes are the digestive organelles of animal cells.

Plant cells and plant-like cells each have a cell wall, chloroplasts, and a central vacuole. The plant cell wall, whose primary component is cellulose, protects the cell, provides structural support, and gives shape to the cell. Photosynthesis takes place in chloroplasts. The central vacuole can expand without having to produce more cytoplasm.

## Art Connections

[\[link\]](#) If the nucleolus were not able to carry out its function, what other cellular organelles would be affected?

[\[link\]](#) Free ribosomes and rough endoplasmic reticulum (which contains ribosomes) would not be able to form.

## Review Questions

Which of the following is surrounded by two phospholipid bilayers?

- a. the ribosomes
- b. the vesicles
- c. the cytoplasm
- d. the nucleoplasm

D

Peroxisomes got their name because hydrogen peroxide is:

- a. used in their detoxification reactions
- b. produced during their oxidation reactions
- c. incorporated into their membranes
- d. a cofactor for the organelles' enzymes

B

In plant cells, the function of the lysosomes is carried out by \_\_\_\_\_.

- a. vacuoles
- b. peroxisomes
- c. ribosomes
- d. nuclei

A

Which of the following is found both in eukaryotic and prokaryotic cells?

- a. nucleus
- b. mitochondrion
- c. vacuole
- d. ribosomes

D

## Free Response

You already know that ribosomes are abundant in red blood cells. In what other cells of the body would you find them in great abundance? Why?

Ribosomes are abundant in muscle cells as well because muscle cells are constructed of the proteins made by the ribosomes.

What are the structural and functional similarities and differences between mitochondria and chloroplasts?

Both are similar in that they are enveloped in a double membrane, both have an intermembrane space, and both make ATP. Both mitochondria and chloroplasts have DNA, and mitochondria have inner folds called cristae and a matrix, while chloroplasts have chlorophyll and accessory pigments in the thylakoids that form stacks (grana) and a stroma.

## **Glossary**

cell wall

rigid cell covering made of various molecules that protects the cell, provides structural support, and gives shape to the cell

central vacuole

large plant cell organelle that regulates the cell's storage compartment, holds water, and plays a significant role in cell growth as the site of macromolecule degradation

centrosome

region in animal cells made of two centrioles

chlorophyll

green pigment that captures the light energy that drives the light reactions of photosynthesis

chloroplast

plant cell organelle that carries out photosynthesis

chromatin

protein-DNA complex that serves as the building material of chromosomes

chromosome

structure within the nucleus that is made up of chromatin that contains DNA, the hereditary material

cytoplasm

entire region between the plasma membrane and the nuclear envelope, consisting of organelles suspended in the gel-like cytosol, the cytoskeleton, and various chemicals

cytosol

gel-like material of the cytoplasm in which cell structures are suspended

eukaryotic cell

cell that has a membrane-bound nucleus and several other membrane-bound compartments or sacs

lysosome

organelle in an animal cell that functions as the cell's digestive component; it breaks down proteins, polysaccharides, lipids, nucleic acids, and even worn-out organelles

mitochondria

(singular = mitochondrion) cellular organelles responsible for carrying out cellular respiration, resulting in the production of ATP, the cell's main energy-carrying molecule

nuclear envelope

double-membrane structure that constitutes the outermost portion of the nucleus

nucleolus

darkly staining body within the nucleus that is responsible for assembling the subunits of the ribosomes

nucleoplasm

semi-solid fluid inside the nucleus that contains the chromatin and nucleolus

nucleus

cell organelle that houses the cell's DNA and directs the synthesis of ribosomes and proteins

organelle

compartment or sac within a cell

peroxisome

small, round organelle that contains hydrogen peroxide, oxidizes fatty acids and amino acids, and detoxifies many poisons

plasma membrane

phospholipid bilayer with embedded (integral) or attached (peripheral) proteins, and separates the internal content of the cell from its surrounding environment

ribosome

cellular structure that carries out protein synthesis

vacuole

membrane-bound sac, somewhat larger than a vesicle, which functions in cellular storage and transport

vesicle

small, membrane-bound sac that functions in cellular storage and transport; its membrane is capable of fusing with the plasma membrane and the membranes of the endoplasmic reticulum and Golgi apparatus

The Cytoskeleton

By the end of this section, you will be able to:

- Describe the cytoskeleton
- Compare the roles of microfilaments, intermediate filaments, and microtubules
- Compare and contrast cilia and flagella
- Summarize the differences among the components of prokaryotic cells, animal cells, and plant cells

If you were to remove all the organelles from a cell, would the plasma membrane and the cytoplasm be the only components left? No. Within the cytoplasm, there would still be ions and organic molecules, plus a network of protein fibers that help maintain the shape of the cell, secure some organelles in specific positions, allow cytoplasm and vesicles to move within the cell, and enable cells within multicellular organisms to move. Collectively, this network of protein fibers is known as the cytoskeleton. There are three types of fibers within the cytoskeleton: microfilaments, intermediate filaments, and microtubules ([\[link\]](#)). Here, we will examine each.

Microfilaments thicken the cortex around the inner edge of a cell; like rubber bands, they resist tension. Microtubules are found in the interior of the cell where they maintain cell shape by resisting compressive forces. Intermediate filaments are found throughout the cell

and hold organelles in place.

## **Microfilaments**

Of the three types of protein fibers in the cytoskeleton, microfilaments are the narrowest. They function in cellular movement, have a diameter of about 7 nm, and are made of two intertwined strands of a globular protein called actin ([\[link\]](#)). For this reason, microfilaments are also known as actin filaments.

Microfilaments are made of two intertwined strands of

actin.

Actin is powered by ATP to assemble its filamentous form, which serves as a track for the movement of a motor protein called myosin. This enables actin to engage in cellular events requiring motion, such as cell division in animal cells and cytoplasmic streaming, which is the circular movement of the cell cytoplasm in plant cells. Actin and myosin are plentiful in muscle cells. When your actin and myosin filaments slide past each other, your muscles contract.

Microfilaments also provide some rigidity and shape to the cell. They can depolymerize (disassemble) and reform quickly, thus enabling a cell to change its shape and move. White blood cells (your body's infection-fighting cells) make good use of this ability. They can move to the site of an infection and phagocytize the pathogen.

Link to Learning

To see an example of a white blood cell in action, watch a short time-lapse video of the cell capturing two bacteria. It engulfs one and then moves on to the other.

Connections between Cells and Cellular Activities

By the end of this section, you will be able to:

- Describe the extracellular matrix
- List examples of the ways that plant cells and animal cells communicate with adjacent cells
- Summarize the roles of tight junctions, desmosomes, gap junctions, and plasmodesmata

You already know that a group of similar cells working together is called a tissue. As you might expect, if cells are to work together, they must communicate with each other, just as you need to communicate with others if you work on a group project. Let's take a look at how cells communicate with each other.

## **Extracellular Matrix of Animal Cells**

Most animal cells release materials into the extracellular space. The primary components of these materials are proteins, and the most abundant protein is collagen. Collagen fibers are interwoven with carbohydrate-containing protein molecules called proteoglycans. Collectively, these materials are called the extracellular matrix ([link](#)). Not only does the extracellular matrix hold the cells together to form a tissue, but it also allows the cells within the tissue to communicate with each other. How can this happen?

The extracellular matrix consists of a network of proteins and

carbohydrates.

Cells have protein receptors on the extracellular surfaces of their plasma membranes. When a molecule within the matrix binds to the receptor, it changes the molecular structure of the receptor. The receptor, in turn, changes the conformation of the microfilaments positioned just inside the plasma membrane. These conformational changes induce chemical signals inside the cell that reach the nucleus and turn "on" or "off" the transcription of specific sections of DNA, which affects the production of associated proteins, thus changing the activities within the cell.

Blood clotting provides an example of the role of the extracellular matrix in cell communication. When the cells lining a blood vessel are damaged, they display a protein receptor called tissue factor. When tissue factor binds with another factor in the extracellular matrix, it causes platelets to adhere to the wall of the damaged blood vessel, stimulates the adjacent smooth muscle cells in the blood vessel to contract (thus constricting the blood vessel), and initiates a series of steps that stimulate the platelets to produce clotting factors.

## **Intercellular Junctions**

Cells can also communicate with each other via direct contact, referred to as intercellular junctions. There are some differences in the ways that plant and animal cells do this. Plasmodesmata are junctions between plant cells, whereas animal cell contacts include tight junctions, gap junctions, and desmosomes.

### **Plasmodesmata**

In general, long stretches of the plasma membranes of neighboring plant cells cannot touch one another because they are separated by the cell wall that surrounds each cell ([link](#)**b**). How then, can a plant transfer water and other soil nutrients from its roots, through its stems, and to its leaves? Such transport uses the vascular tissues (xylem and phloem) primarily. There also exist structural modifications called plasmodesmata (singular = plasmodesma), numerous channels that pass between cell walls of adjacent plant cells, connect their cytoplasm, and enable materials to be transported from cell to cell, and thus throughout the plant ([link](#)).

A plasmodesma is a channel between the cell walls of two adjacent plant cells. Plasmodesmata allow materials to pass from the cytoplasm of one plant cell to the cytoplasm

of an adjacent cell.

### **Tight Junctions**

A tight junction is a watertight seal between two adjacent animal cells ([link](#)). The cells are held tightly against each other by proteins (predominantly two proteins called claudins and occludins).

Tight junctions form watertight connections between adjacent animal cells. Proteins create tight junction adherence. (credit: modification of work by Mariana Ruiz

Villareal)

This tight adherence prevents materials from leaking between the cells; tight junctions are typically found in epithelial tissues that line internal organs and cavities, and comprise most of the skin. For example, the tight junctions of the epithelial cells lining your urinary bladder prevent urine from leaking out into the extracellular space.

### **Desmosomes**

Also found only in animal cells are desmosomes, which act like spot welds between adjacent epithelial cells ([link](#)). Short proteins called cadherins in the plasma membrane connect to intermediate filaments to create desmosomes. The cadherins join two adjacent cells together and maintain the cells in a sheet-like formation in organs and tissues that stretch, like the skin, heart, and muscles.

A desmosome forms a very strong spot weld between cells. It is created by the linkage of cadherins and intermediate filaments. (credit: modification of work by Mariana Ruiz

Villareal)

### **Gap Junctions**

Gap junctions in animal cells are like plasmodesmata in plant cells in that they are channels between adjacent cells that allow for the transport of ions, nutrients, and other substances that enable cells to communicate ([link](#)). Structurally, however, gap junctions and plasmodesmata differ.

A gap junction is a protein-lined pore that allows water and small molecules to pass between adjacent animal cells. (credit: modification of work by Mariana Ruiz

Villareal)

Gap junctions develop when a set of six proteins (called connexins) in the plasma membrane arrange themselves in an elongated donut-like configuration called a connexon. When the pores (“doughnut holes”) of connexons in adjacent animal cells align, a channel between the two cells forms. Gap junctions are particularly important in cardiac muscle: The electrical

signal for the muscle to contract is passed efficiently through gap junctions, allowing the heart muscle cells to contract in tandem.

Link to Learning

To conduct a virtual microscopy lab and review the parts of a cell, work through the steps of this [interactive assignment](#).

## Section Summary

Animal cells communicate via their extracellular matrices and are connected to each other via tight junctions, desmosomes, and gap junctions. Plant cells are connected and communicate with each other via plasmodesmata.

When protein receptors on the surface of the plasma membrane of an animal cell bind to a substance in the extracellular matrix, a chain of reactions begins that changes activities taking place within the cell. Plasmodesmata are channels between adjacent plant cells, while gap junctions are channels between adjacent animal cells. However, their structures are quite different. A tight junction is a watertight seal between two adjacent cells, while a desmosome acts like a spot weld.

## Review Questions

Which of the following are found only in plant cells?

- gap junctions
- desmosomes
- plasmodesmata
- tight junctions

C

The key components of desmosomes are cadherins and \_\_\_\_\_.

- actin
- microfilaments
- intermediate filaments
- microtubules

C

## Free Response

How does the structure of a plasmodesma differ from that of a gap junction?

They differ because plant cell walls are rigid. Plasmodesmata, which a plant cell needs for transportation and communication, are able to allow movement of really large molecules. Gap junctions are necessary in animal cells for transportation and communication.

Explain how the extracellular matrix functions.

The extracellular matrix functions in support and attachment for animal tissues. It also functions in the healing and growth of the tissue.

## Glossary

desmosome

linkages between adjacent epithelial cells that form when cadherins in the plasma membrane attach to intermediate filaments

extracellular matrix

material (primarily collagen, glycoproteins, and proteoglycans) secreted from animal cells that provides mechanical protection and anchoring for the cells in the tissue

gap junction

channel between two adjacent animal cells that allows ions, nutrients, and low molecular weight substances to pass between cells, enabling the cells to communicate

plasmodesma

(plural = plasmodesmata) channel that passes between the cell walls of adjacent plant cells, connects their cytoplasm, and allows materials to be transported from cell to cell

tight junction

firm seal between two adjacent animal cells created by protein adherence

Introduction

class="introduction" class="summary" title="Sections Summary" class="art-exercise" title="Art Connections" class="multiple-choice" title="Multiple Choice" class="free-response" title="Free Response" Despite its seeming hustle and bustle, Grand Central Station functions with a high level of organization: People and objects move from one location to another, they cross or are contained within certain boundaries, and they provide a constant flow as part of larger activity. Analogously, a plasma membrane's functions involve movement within the cell and across boundaries in the process of intracellular and intercellular activities. (credit: modification of work by Randy

Le'Moine)

The plasma membrane, which is also called the cell membrane, has many functions, but the most basic one is to define the borders of the cell and keep the cell functional. The plasma membrane is selectively permeable. This means that the membrane allows some materials to freely enter or leave the cell, while other materials cannot move freely, but require the use of a specialized structure, and occasionally, even energy investment for crossing.

#### Components and Structure

By the end of this section, you will be able to:

- Understand the fluid mosaic model of cell membranes
- Describe the functions of phospholipids, proteins, and carbohydrates in membranes
- Discuss membrane fluidity

A cell's plasma membrane defines the cell, outlines its borders, and determines the nature of its interaction with its environment (see [\[link\]](#) for a summary). Cells exclude some substances, take in others, and excrete still others, all in controlled quantities. The plasma membrane must be very flexible to allow certain cells, such as red blood cells and white blood cells, to change shape as they pass through narrow capillaries. These are the more obvious functions of a plasma membrane. In addition, the surface of the plasma membrane carries markers that allow cells to recognize one another, which is vital for tissue and organ formation during early development, and which later plays a role in the “self” versus “non-self” distinction of the immune response.

Among the most sophisticated functions of the plasma membrane is the ability to transmit signals by means of complex, integral proteins known as receptors. These proteins act both as receivers of extracellular inputs and as activators of intracellular processes. These membrane receptors provide extracellular attachment sites for effectors like hormones and growth factors, and they activate intracellular response cascades when their effectors are bound. Occasionally, receptors are hijacked by viruses (HIV, human immunodeficiency virus, is one example) that use them to gain entry into cells, and at times, the genes encoding receptors become mutated, causing the process of signal transduction to malfunction with disastrous consequences.

### **Fluid Mosaic Model**

The existence of the plasma membrane was identified in the 1890s, and its chemical components were identified in 1915. The principal components identified at that time were lipids and proteins. The first widely accepted model of the plasma membrane's structure was proposed in 1935 by Hugh Davson and James Danielli; it was based on the “railroad track” appearance of the plasma membrane in early electron micrographs. They theorized that the structure of the plasma membrane resembles a sandwich, with protein being analogous to the bread, and lipids being analogous to the filling. In the 1950s, advances in microscopy, notably transmission electron microscopy (TEM), allowed researchers to see that the core of the plasma membrane consisted of a double, rather than a single, layer. A new model that better explains both the microscopic observations and the function of that plasma membrane was proposed by S.J. Singer and Garth L. Nicolson in 1972.

The explanation proposed by Singer and Nicolson is called the fluid mosaic model. The model has evolved somewhat over time, but it still best accounts for the structure and functions of the plasma membrane as we now understand them. The fluid mosaic model describes the structure of the plasma membrane as a mosaic of components—including phospholipids, cholesterol, proteins, and carbohydrates—that gives the membrane a fluid character. Plasma membranes range from 5 to 10 nm in thickness. For comparison, human red blood cells, visible via light microscopy, are approximately 8  $\mu\text{m}$  wide, or approximately 1,000 times wider than a plasma membrane. The membrane does look a bit like a sandwich ([\[link\]](#)).

The fluid mosaic model of the plasma membrane describes the plasma membrane as a fluid combination of phospholipids, cholesterol, and proteins. Carbohydrates attached to lipids (glycolipids) and to proteins (glycoproteins) extend from the outward-facing surface of the membrane.

The principal components of a plasma membrane are lipids (phospholipids and cholesterol), proteins, and carbohydrates attached to some of the lipids and some of the proteins. A phospholipid is a molecule consisting of glycerol, two fatty acids, and a phosphate-linked head group. Cholesterol, another lipid composed of four fused carbon rings, is found alongside the phospholipids in the core of the membrane. The proportions of proteins, lipids, and carbohydrates in the plasma membrane vary with cell type, but for a typical human cell, protein accounts for about 50 percent of the composition by mass, lipids (of all types) account for about 40 percent of the composition by mass, with the remaining 10 percent of the composition by mass being carbohydrates. However, the concentration of proteins and lipids varies with different cell membranes. For example, myelin, an outgrowth of the membrane of specialized cells that insulates the axons of the peripheral nerves, contains only 18 percent protein and 76 percent lipid. The mitochondrial inner membrane contains 76 percent protein and only 24 percent lipid. The plasma membrane of human red blood cells is 30 percent lipid. Carbohydrates are present only on the exterior surface of the plasma membrane and are attached to proteins, forming glycoproteins, or attached to lipids, forming glycolipids.

## Phospholipids

The main fabric of the membrane is composed of amphiphilic, phospholipid molecules. The hydrophilic or “water-loving” areas of these molecules (which look like a collection of balls in an artist’s rendition of the model) ([link](#)) are in contact with the aqueous fluid both inside and outside the cell. Hydrophobic, or water-hating molecules, tend to be non-polar. They interact with other non-polar molecules in chemical reactions, but generally do not interact with polar molecules. When placed in water, hydrophobic molecules tend to form a ball or cluster. The hydrophilic regions of the phospholipids tend to form hydrogen bonds with water and other polar molecules on both the exterior and interior of the cell. Thus, the membrane surfaces that face the interior and exterior of the cell are hydrophilic. In contrast, the interior of the cell membrane is hydrophobic and will not interact with water. Therefore, phospholipids form an excellent two-layer cell membrane that separates fluid within the cell from the fluid outside of the cell.

A phospholipid molecule ([link](#)) consists of a three-carbon glycerol backbone with two fatty acid molecules attached to carbons 1 and 2, and a phosphate-containing group attached to the third carbon. This arrangement gives the overall molecule an area described as its head (the phosphate-containing group), which has a polar character or negative charge, and an area called the tail (the fatty acids), which has no charge. The head can form hydrogen bonds, but the tail cannot. A molecule with this arrangement of a positively or negatively charged area and an uncharged, or non-polar, area is referred to as amphiphilic or “dual-loving.”

This phospholipid molecule is composed of a hydrophilic head and two hydrophobic tails. The hydrophilic head group consists of a phosphate-containing group attached to a glycerol molecule. The hydrophobic tails, each containing either a saturated or an unsaturated fatty

acid, are long hydrocarbon chains.

This characteristic is vital to the structure of a plasma membrane because, in water, phospholipids tend to become arranged with their hydrophobic tails facing each other and their hydrophilic heads facing out. In this way, they form a lipid bilayer—a barrier composed of a double layer of phospholipids that separates the water and other materials on one side of the barrier from the water and other materials on the other side. In fact, phospholipids heated

in an aqueous solution tend to spontaneously form small spheres or droplets (called micelles or liposomes), with their hydrophilic heads forming the exterior and their hydrophobic tails on the inside ([link](#)).

In an aqueous solution, phospholipids tend to arrange themselves with their polar heads facing outward and their hydrophobic tails facing inward. (credit: modification of work by

Mariana Ruiz Villareal)

## **Proteins**

Proteins make up the second major component of plasma membranes. Integral proteins (some specialized types are called integrins) are, as their name suggests, integrated completely into the membrane structure, and their hydrophobic membrane-spanning regions interact with the hydrophobic region of the the phospholipid bilayer ([link](#)). Single-pass integral membrane proteins usually have a hydrophobic transmembrane segment that consists of 20–25 amino acids. Some span only part of the membrane—associating with a single layer—while others stretch from one side of the membrane to the other, and are exposed on either side. Some complex proteins are composed of up to 12 segments of a single protein, which are extensively folded and embedded in the membrane ([link](#)). This type of protein has a hydrophilic region or regions, and one or several mildly hydrophobic regions. This arrangement of regions of the protein tends to orient the protein alongside the phospholipids, with the hydrophobic region of the protein adjacent to the tails of the phospholipids and the hydrophilic region or regions of the protein protruding from the membrane and in contact with the cytosol or extracellular fluid.

Integral membranes proteins may have one or more alpha-helices that span the membrane (examples 1 and 2), or they may have beta-sheets that span the membrane (example 3).

(credit: “Foobar”/Wikimedia Commons)

Peripheral proteins are found on the exterior and interior surfaces of membranes, attached either to integral proteins or to phospholipids. Peripheral proteins, along with integral proteins, may serve as enzymes, as structural attachments for the fibers of the cytoskeleton, or as part of the cell’s recognition sites. These are sometimes referred to as “cell-specific” proteins. The body recognizes its own proteins and attacks foreign proteins associated with invasive pathogens.

## **Carbohydrates**

Carbohydrates are the third major component of plasma membranes. They are always found on the exterior surface of cells and are bound either to proteins (forming glycoproteins) or to lipids (forming glycolipids) ([link](#)). These carbohydrate chains may consist of 2–60 monosaccharide units and can be either straight or branched. Along with peripheral proteins, carbohydrates form specialized sites on the cell surface that allow cells to recognize each other. These sites have unique patterns that allow the cell to be recognized, much the way that the facial features unique to each person allow him or her to be recognized. This recognition function is very important to cells, as it allows the immune system to differentiate between body cells (called “self”) and foreign cells or tissues (called “non-self”). Similar types of glycoproteins and glycolipids are found on the surfaces of viruses and may change frequently, preventing immune cells from recognizing and attacking them.

These carbohydrates on the exterior surface of the cell—the carbohydrate components of both glycoproteins and glycolipids—are collectively referred to as the glycocalyx (meaning “sugar coating”). The glycocalyx is highly hydrophilic and attracts large amounts of water to the surface of the cell. This aids in the interaction of the cell with its watery environment and in the cell’s ability to obtain substances dissolved in the water. As discussed above, the glycocalyx is also important for cell identification, self/non-self determination, and embryonic development, and is used in cell-cell attachments to form tissues.

## Evolution Connection

**How Viruses Infect Specific Organs** Glycoprotein and glycolipid patterns on the surfaces of cells give many viruses an opportunity for infection. HIV and hepatitis viruses infect only specific organs or cells in the human body. HIV is able to penetrate the plasma membranes of a subtype of lymphocytes called T-helper cells, as well as some monocytes and central nervous system cells. The hepatitis virus attacks liver cells.

These viruses are able to invade these cells, because the cells have binding sites on their surfaces that are specific to and compatible with certain viruses ([link](#)). Other recognition sites on the virus's surface interact with the human immune system, prompting the body to produce antibodies. Antibodies are made in response to the antigens or proteins associated with invasive pathogens, or in response to foreign cells, such as might occur with an organ transplant. These same sites serve as places for antibodies to attach and either destroy or inhibit the activity of the virus. Unfortunately, these recognition sites on HIV change at a rapid rate because of mutations, making the production of an effective vaccine against the virus very difficult, as the virus evolves and adapts. A person infected with HIV will quickly develop different populations, or variants, of the virus that are distinguished by differences in these recognition sites. This rapid change of surface markers decreases the effectiveness of the person's immune system in attacking the virus, because the antibodies will not recognize the new variations of the surface patterns. In the case of HIV, the problem is compounded by the fact that the virus specifically infects and destroys cells involved in the immune response, further incapacitating the host.

HIV binds to the CD4 receptor, a glycoprotein on the surfaces of T cells. (credit:

modification of work by NIH, NIAID)

## Membrane Fluidity

The mosaic characteristic of the membrane, described in the fluid mosaic model, helps to illustrate its nature. The integral proteins and lipids exist in the membrane as separate but loosely attached molecules. These resemble the separate, multicolored tiles of a mosaic picture, and they float, moving somewhat with respect to one another. The membrane is not

like a balloon, however, that can expand and contract; rather, it is fairly rigid and can burst if penetrated or if a cell takes in too much water. However, because of its mosaic nature, a very fine needle can easily penetrate a plasma membrane without causing it to burst, and the membrane will flow and self-seal when the needle is extracted.

The mosaic characteristics of the membrane explain some but not all of its fluidity. There are two other factors that help maintain this fluid characteristic. One factor is the nature of the phospholipids themselves. In their saturated form, the fatty acids in phospholipid tails are saturated with bound hydrogen atoms. There are no double bonds between adjacent carbon atoms. This results in tails that are relatively straight. In contrast, unsaturated fatty acids do not contain a maximal number of hydrogen atoms, but they do contain some double bonds between adjacent carbon atoms; a double bond results in a bend in the string of carbons of approximately 30 degrees ([\[link\]](#)).

Thus, if saturated fatty acids, with their straight tails, are compressed by decreasing temperatures, they press in on each other, making a dense and fairly rigid membrane. If unsaturated fatty acids are compressed, the “kinks” in their tails elbow adjacent phospholipid molecules away, maintaining some space between the phospholipid molecules. This “elbow room” helps to maintain fluidity in the membrane at temperatures at which membranes with saturated fatty acid tails in their phospholipids would “freeze” or solidify. The relative fluidity of the membrane is particularly important in a cold environment. A cold environment tends to compress membranes composed largely of saturated fatty acids, making them less fluid and more susceptible to rupturing. Many organisms (fish are one example) are capable of adapting to cold environments by changing the proportion of unsaturated fatty acids in their membranes in response to the lowering of the temperature.

Link to Learning

Visit this [site](#) to see animations of the fluidity and mosaic quality of membranes.

Animals have an additional membrane constituent that assists in maintaining fluidity. Cholesterol, which lies alongside the phospholipids in the membrane, tends to dampen the effects of temperature on the membrane. Thus, this lipid functions as a buffer, preventing lower temperatures from inhibiting fluidity and preventing increased temperatures from increasing fluidity too much. Thus, cholesterol extends, in both directions, the range of temperature in which the membrane is appropriately fluid and consequently functional. Cholesterol also serves other functions, such as organizing clusters of transmembrane proteins into lipid rafts.

### **The Components and Functions of the Plasma Membrane**

<b>Component</b>	<b>Location</b>
Phospholipid	Main fabric of the membrane

## The Components and Functions of the Plasma Membrane

Component	Location
Cholesterol	Attached between phospholipids and between the two phospholipid layers
Integral proteins (for example, integrins)	Embedded within the phospholipid layer(s). May or may not penetrate through both layers
Peripheral proteins	On the inner or outer surface of the phospholipid bilayer; not embedded within the phospholipids
Carbohydrates (components of glycoproteins and glycolipids)	Generally attached to proteins on the outside membrane layer
Career Connection	

**Immunologist** The variations in peripheral proteins and carbohydrates that affect a cell's recognition sites are of prime interest in immunology. These changes are taken into consideration in vaccine development. Many infectious diseases, such as smallpox, polio, diphtheria, and tetanus, were conquered by the use of vaccines.

Immunologists are the physicians and scientists who research and develop vaccines, as well as treat and study allergies or other immune problems. Some immunologists study and treat autoimmune problems (diseases in which a person's immune system attacks his or her own cells or tissues, such as lupus) and immunodeficiencies, whether acquired (such as acquired immunodeficiency syndrome, or AIDS) or hereditary (such as severe combined immunodeficiency, or SCID). Immunologists are called in to help treat organ transplantation patients, who must have their immune systems suppressed so that their bodies will not reject a transplanted organ. Some immunologists work to understand natural immunity and the effects of a person's environment on it. Others work on questions about how the immune system affects diseases such as cancer. In the past, the importance of having a healthy immune system in preventing cancer was not at all understood.

To work as an immunologist, a PhD or MD is required. In addition, immunologists undertake at least 2–3 years of training in an accredited program and must pass an examination given by the American Board of Allergy and Immunology. Immunologists must possess knowledge of the functions of the human body as they relate to issues beyond immunization, and knowledge of pharmacology and medical technology, such as medications, therapies, test materials, and surgical procedures.

### Section Summary

The modern understanding of the plasma membrane is referred to as the fluid mosaic model. The plasma membrane is composed of a bilayer of phospholipids, with their hydrophobic, fatty acid tails in contact with each other. The landscape of the membrane is studded with proteins, some of which span the membrane. Some of these proteins serve to transport materials into or out of the cell. Carbohydrates are attached to some of the proteins and lipids on the outward-facing surface of the membrane, forming complexes that function to identify the cell to other cells. The fluid nature of the membrane is due to temperature, the configuration of the fatty acid tails (some kinked by double bonds), the presence of cholesterol embedded in the membrane, and the mosaic nature of the proteins and protein-carbohydrate combinations, which are not firmly fixed in place. Plasma membranes enclose

and define the borders of cells, but rather than being a static bag, they are dynamic and constantly in flux.

## Review Questions

Which plasma membrane component can be either found on its surface or embedded in the membrane structure?

- a. protein
- b. cholesterol
- c. carbohydrate
- d. phospholipid

A

Which characteristic of a phospholipid contributes to the fluidity of the membrane?

- a. its head
- b. cholesterol
- c. a saturated fatty acid tail
- d. double bonds in the fatty acid tail

D

What is the primary function of carbohydrates attached to the exterior of cell membranes?

- a. identification of the cell
- b. flexibility of the membrane
- c. strengthening the membrane
- d. channels through membrane

A

## Free Response

Why is it advantageous for the cell membrane to be fluid in nature?

The fluid characteristic of the cell membrane allows greater flexibility to the cell than it would if the membrane were rigid. It also allows the motion of membrane components, required for some types of membrane transport.

Why do phospholipids tend to spontaneously orient themselves into something resembling a membrane?

The hydrophobic, nonpolar regions must align with each other in order for the structure to have minimal potential energy and, consequently, higher stability. The fatty acid tails of the phospholipids cannot mix with water, but the phosphate “head” of the molecule can. Thus, the head orients to water, and the tail to other lipids.

## Glossary

### amphiphilic

molecule possessing a polar or charged area and a nonpolar or uncharged area capable of interacting with both hydrophilic and hydrophobic environments

### fluid mosaic model

describes the structure of the plasma membrane as a mosaic of components including phospholipids, cholesterol, proteins, glycoproteins, and glycolipids (sugar chains attached to proteins or lipids, respectively), resulting in a fluid character (fluidity)

### glycolipid

combination of carbohydrates and lipids

### glycoprotein

combination of carbohydrates and proteins

### hydrophilic

molecule with the ability to bond with water; “water-loving”

### hydrophobic

molecule that does not have the ability to bond with water; “water-hating”

### integral protein

protein integrated into the membrane structure that interacts extensively with the hydrocarbon chains of membrane lipids and often spans the membrane; these proteins can be removed only by the disruption of the membrane by detergents

### peripheral protein

protein found at the surface of a plasma membrane either on its exterior or interior side; these proteins can be removed (washed off of the membrane) by a high-salt wash

### Passive Transport

By the end of this section, you will be able to:

- Explain why and how passive transport occurs
- Understand the processes of osmosis and diffusion
- Define tonicity and describe its relevance to passive transport

Plasma membranes must allow certain substances to enter and leave a cell, and prevent some harmful materials from entering and some essential materials from leaving. In other words, plasma membranes are selectively permeable—they allow some substances to pass through, but not others. If they were to lose this selectivity, the cell would no longer be able to sustain itself, and it would be destroyed. Some cells require larger amounts of specific substances than do other cells; they must have a way of obtaining these materials from extracellular fluids. This may happen passively, as certain materials move back and forth, or the cell may have special mechanisms that facilitate transport. Some materials are so important to a cell that it spends some of its energy, hydrolyzing adenosine

triphosphate (ATP), to obtain these materials. Red blood cells use some of their energy doing just that. All cells spend the majority of their energy to maintain an imbalance of sodium and potassium ions between the interior and exterior of the cell.

The most direct forms of membrane transport are passive. Passive transport is a naturally occurring phenomenon and does not require the cell to exert any of its energy to accomplish the movement. In passive transport, substances move from an area of higher concentration to an area of lower concentration. A physical space in which there is a range of concentrations of a single substance is said to have a concentration gradient.

### **Selective Permeability**

Plasma membranes are asymmetric: the interior of the membrane is not identical to the exterior of the membrane. In fact, there is a considerable difference between the array of phospholipids and proteins between the two leaflets that form a membrane. On the interior of the membrane, some proteins serve to anchor the membrane to fibers of the cytoskeleton. There are peripheral proteins on the exterior of the membrane that bind elements of the extracellular matrix. Carbohydrates, attached to lipids or proteins, are also found on the exterior surface of the plasma membrane. These carbohydrate complexes help the cell bind substances that the cell needs in the extracellular fluid. This adds considerably to the selective nature of plasma membranes ([link](#)).

The exterior surface of the plasma membrane is not identical to the interior surface of the same

membrane.

Recall that plasma membranes are amphiphilic: They have hydrophilic and hydrophobic regions. This characteristic helps the movement of some materials through the membrane and hinders the movement of others. Lipid-soluble material with a low molecular weight can easily slip through the hydrophobic lipid core of the membrane. Substances such as the fat-soluble vitamins A, D, E, and K readily pass through the plasma membranes in the digestive tract and other tissues. Fat-soluble drugs and hormones also gain easy entry into cells and are readily transported into the body's tissues and organs. Molecules of oxygen and carbon dioxide have no charge and so pass through membranes by simple diffusion.

Polar substances present problems for the membrane. While some polar molecules connect easily with the outside of a cell, they cannot readily pass through the lipid core of the plasma membrane. Additionally, while small ions could easily slip through the spaces in the mosaic of the membrane, their charge prevents them from doing so. Ions such as sodium, potassium, calcium, and chloride must have special means of penetrating plasma membranes. Simple

sugars and amino acids also need help with transport across plasma membranes, achieved by various transmembrane proteins (channels).

## **Diffusion**

Diffusion is a passive process of transport. A single substance tends to move from an area of high concentration to an area of low concentration until the concentration is equal across a space. You are familiar with diffusion of substances through the air. For example, think about someone opening a bottle of ammonia in a room filled with people. The ammonia gas is at its highest concentration in the bottle; its lowest concentration is at the edges of the room. The ammonia vapor will diffuse, or spread away, from the bottle, and gradually, more and more people will smell the ammonia as it spreads. Materials move within the cell's cytosol by diffusion, and certain materials move through the plasma membrane by diffusion ([link](#)). Diffusion expends no energy. On the contrary, concentration gradients are a form of potential energy, dissipated as the gradient is eliminated.

Diffusion through a permeable membrane moves a substance from an area of high concentration (extracellular fluid, in this case) down its concentration gradient (into the cytoplasm). (credit: modification of work by Mariana Ruiz

Villareal)

Each separate substance in a medium, such as the extracellular fluid, has its own concentration gradient, independent of the concentration gradients of other materials. In addition, each substance will diffuse according to that gradient. Within a system, there will be different rates of diffusion of the different substances in the medium.

### **Factors That Affect Diffusion**

Molecules move constantly in a random manner, at a rate that depends on their mass, their environment, and the amount of thermal energy they possess, which in turn is a function of temperature. This movement accounts for the diffusion of molecules through whatever medium in which they are localized. A substance will tend to move into any space available to it until it is evenly distributed throughout it. After a substance has diffused completely through a space, removing its concentration gradient, molecules will still move around in the space, but there will be no *net* movement of the number of molecules from one area to another. This lack of a concentration gradient in which there is no net movement of a

substance is known as dynamic equilibrium. While diffusion will go forward in the presence of a concentration gradient of a substance, several factors affect the rate of diffusion.

- **Extent of the concentration gradient:** The greater the difference in concentration, the more rapid the diffusion. The closer the distribution of the material gets to equilibrium, the slower the rate of diffusion becomes.
- **Mass of the molecules diffusing:** Heavier molecules move more slowly; therefore, they diffuse more slowly. The reverse is true for lighter molecules.
- **Temperature:** Higher temperatures increase the energy and therefore the movement of the molecules, increasing the rate of diffusion. Lower temperatures decrease the energy of the molecules, thus decreasing the rate of diffusion.
- **Solvent density:** As the density of a solvent increases, the rate of diffusion decreases. The molecules slow down because they have a more difficult time getting through the denser medium. If the medium is less dense, diffusion increases. Because cells primarily use diffusion to move materials within the cytoplasm, any increase in the cytoplasm's density will inhibit the movement of the materials. An example of this is a person experiencing dehydration. As the body's cells lose water, the rate of diffusion decreases in the cytoplasm, and the cells' functions deteriorate. Neurons tend to be very sensitive to this effect. Dehydration frequently leads to unconsciousness and possibly coma because of the decrease in diffusion rate within the cells.
- **Solubility:** As discussed earlier, nonpolar or lipid-soluble materials pass through plasma membranes more easily than polar materials, allowing a faster rate of diffusion.
- **Surface area and thickness of the plasma membrane:** Increased surface area increases the rate of diffusion, whereas a thicker membrane reduces it.
- **Distance travelled:** The greater the distance that a substance must travel, the slower the rate of diffusion. This places an upper limitation on cell size. A large, spherical cell will die because nutrients or waste cannot reach or leave the center of the cell, respectively. Therefore, cells must either be small in size, as in the case of many prokaryotes, or be flattened, as with many single-celled eukaryotes.

A variation of diffusion is the process of filtration. In filtration, material moves according to its concentration gradient through a membrane; sometimes the rate of diffusion is enhanced by pressure, causing the substances to filter more rapidly. This occurs in the kidney, where blood pressure forces large amounts of water and accompanying dissolved substances, or solutes, out of the blood and into the renal tubules. The rate of diffusion in this instance is almost totally dependent on pressure. One of the effects of high blood pressure is the appearance of protein in the urine, which is "squeezed through" by the abnormally high pressure.

## **Facilitated transport**

In facilitated transport, also called facilitated diffusion, materials diffuse across the plasma membrane with the help of membrane proteins. A concentration gradient exists that would allow these materials to diffuse into the cell without expending cellular energy. However, these materials are ions or polar molecules that are repelled by the hydrophobic parts of the cell membrane. Facilitated transport proteins shield these materials from the repulsive force of the membrane, allowing them to diffuse into the cell.

The material being transported is first attached to protein or glycoprotein receptors on the exterior surface of the plasma membrane. This allows the material that is needed by the cell to be removed from the extracellular fluid. The substances are then passed to specific integral proteins that facilitate their passage. Some of these integral proteins are collections of beta pleated sheets that form a pore or channel through the phospholipid bilayer. Others are carrier proteins which bind with the substance and aid its diffusion through the membrane.

## **Channels**

The integral proteins involved in facilitated transport are collectively referred to as transport proteins, and they function as either channels for the material or carriers. In both cases, they are transmembrane proteins. Channels are specific for the substance that is being transported. Channel proteins have hydrophilic domains exposed to the intracellular and extracellular fluids; they additionally have a hydrophilic channel through their core that provides a hydrated opening through the membrane layers ([link](#)). Passage through the channel allows polar compounds to avoid the nonpolar central layer of the plasma membrane that would otherwise slow or prevent their entry into the cell. Aquaporins are channel proteins that allow water to pass through the membrane at a very high rate.

Facilitated transport moves substances down their concentration gradients. They may cross the plasma membrane with the aid of channel proteins. (credit: modification of work by

Mariana Ruiz Villareal)

Channel proteins are either open at all times or they are “gated,” which controls the opening of the channel. The attachment of a particular ion to the channel protein may control the opening, or other mechanisms or substances may be involved. In some tissues, sodium and chloride ions pass freely through open channels, whereas in other tissues a gate must be opened to allow passage. An example of this occurs in the kidney, where both forms of channels are found in different parts of the renal tubules. Cells involved in the transmission of electrical impulses, such as nerve and muscle cells, have gated channels for sodium, potassium, and calcium in their membranes. Opening and closing of these channels changes the relative concentrations on opposing sides of the membrane of these ions, resulting in the

facilitation of electrical transmission along membranes (in the case of nerve cells) or in muscle contraction (in the case of muscle cells).

### **Carrier Proteins**

Another type of protein embedded in the plasma membrane is a carrier protein. This aptly named protein binds a substance and, in doing so, triggers a change of its own shape, moving the bound molecule from the outside of the cell to its interior ([link](#)); depending on the gradient, the material may move in the opposite direction. Carrier proteins are typically specific for a single substance. This selectivity adds to the overall selectivity of the plasma membrane. The exact mechanism for the change of shape is poorly understood. Proteins can change shape when their hydrogen bonds are affected, but this may not fully explain this mechanism. Each carrier protein is specific to one substance, and there are a finite number of these proteins in any membrane. This can cause problems in transporting enough of the material for the cell to function properly. When all of the proteins are bound to their ligands, they are saturated and the rate of transport is at its maximum. Increasing the concentration gradient at this point will not result in an increased rate of transport.

Some substances are able to move down their concentration gradient across the plasma membrane with the aid of carrier proteins. Carrier proteins change shape as they move molecules across the membrane. (credit: modification of work by Mariana Ruiz

Villareal)

An example of this process occurs in the kidney. Glucose, water, salts, ions, and amino acids needed by the body are filtered in one part of the kidney. This filtrate, which includes glucose, is then reabsorbed in another part of the kidney. Because there are only a finite number of carrier proteins for glucose, if more glucose is present than the proteins can handle, the excess is not transported and it is excreted from the body in the urine. In a diabetic individual, this is described as “spilling glucose into the urine.” A different group of carrier proteins called glucose transport proteins, or GLUTs, are involved in transporting glucose and other hexose sugars through plasma membranes within the body.

Channel and carrier proteins transport material at different rates. Channel proteins transport much more quickly than do carrier proteins. Channel proteins facilitate diffusion at a rate of tens of millions of molecules per second, whereas carrier proteins work at a rate of a thousand to a million molecules per second.

## **Osmosis**

Osmosis is the movement of water through a semipermeable membrane according to the concentration gradient of water across the membrane, which is inversely proportional to the concentration of solutes. While diffusion transports material across membranes and within cells, osmosis transports *only water* across a membrane and the membrane limits the diffusion of solutes in the water. Not surprisingly, the aquaporins that facilitate water movement play a large role in osmosis, most prominently in red blood cells and the membranes of kidney tubules.

### **Mechanism**

Osmosis is a special case of diffusion. Water, like other substances, moves from an area of high concentration to one of low concentration. An obvious question is what makes water move at all? Imagine a beaker with a semipermeable membrane separating the two sides or halves ([link](#)). On both sides of the membrane the water level is the same, but there are different concentrations of a dissolved substance, or solute, that cannot cross the membrane (otherwise the concentrations on each side would be balanced by the solute crossing the membrane). If the volume of the solution on both sides of the membrane is the same, but the concentrations of solute are different, then there are different amounts of water, the solvent, on either side of the membrane.

In osmosis, water always moves from an area of higher water concentration to one of lower concentration. In the diagram shown, the solute cannot pass through the selectively

permeable membrane, but the water can.

To illustrate this, imagine two full glasses of water. One has a single teaspoon of sugar in it, whereas the second one contains one-quarter cup of sugar. If the total volume of the solutions in both cups is the same, which cup contains more water? Because the large amount of sugar in the second cup takes up much more space than the teaspoon of sugar in the first cup, the first cup has more water in it.

Returning to the beaker example, recall that it has a mixture of solutes on either side of the membrane. A principle of diffusion is that the molecules move around and will spread evenly throughout the medium if they can. However, only the material capable of getting through the

membrane will diffuse through it. In this example, the solute cannot diffuse through the membrane, but the water can. Water has a concentration gradient in this system. Thus, water will diffuse down its concentration gradient, crossing the membrane to the side where it is less concentrated. This diffusion of water through the membrane—osmosis—will continue until the concentration gradient of water goes to zero or until the hydrostatic pressure of the water balances the osmotic pressure. Osmosis proceeds constantly in living systems.

## **Tonicity**

Tonicity describes how an extracellular solution can change the volume of a cell by affecting osmosis. A solution's tonicity often directly correlates with the osmolarity of the solution. Osmolarity describes the total solute concentration of the solution. A solution with low osmolarity has a greater number of water molecules relative to the number of solute particles; a solution with high osmolarity has fewer water molecules with respect to solute particles. In a situation in which solutions of two different osmolarities are separated by a membrane permeable to water, though not to the solute, water will move from the side of the membrane with lower osmolarity (and more water) to the side with higher osmolarity (and less water). This effect makes sense if you remember that the solute cannot move across the membrane, and thus the only component in the system that can move—the water—moves along its own concentration gradient. An important distinction that concerns living systems is that osmolarity measures the number of particles (which may be molecules) in a solution. Therefore, a solution that is cloudy with cells may have a lower osmolarity than a solution that is clear, if the second solution contains more dissolved molecules than there are cells.

## **Hypotonic Solutions**

Three terms—hypotonic, isotonic, and hypertonic—are used to relate the osmolarity of a cell to the osmolarity of the extracellular fluid that contains the cells. In a hypotonic situation, the extracellular fluid has lower osmolarity than the fluid inside the cell, and water enters the cell. (In living systems, the point of reference is always the cytoplasm, so the prefix *hypo-* means that the extracellular fluid has a lower concentration of solutes, or a lower osmolarity, than the cell cytoplasm.) It also means that the extracellular fluid has a higher concentration of water in the solution than does the cell. In this situation, water will follow its concentration gradient and enter the cell.

## **Hypertonic Solutions**

As for a hypertonic solution, the prefix *hyper-* refers to the extracellular fluid having a higher osmolarity than the cell's cytoplasm; therefore, the fluid contains less water than the cell does. Because the cell has a relatively higher concentration of water, water will leave the cell.

## **Isotonic Solutions**

In an isotonic solution, the extracellular fluid has the same osmolarity as the cell. If the osmolarity of the cell matches that of the extracellular fluid, there will be no net movement of water into or out of the cell, although water will still move in and out. Blood cells and plant cells in hypertonic, isotonic, and hypotonic solutions take on characteristic appearances ([link](#)).

Art Connection

Osmotic pressure changes the shape of red blood cells in hypertonic, isotonic, and hypotonic

solutions. (credit: Mariana Ruiz Villareal)

A doctor injects a patient with what the doctor thinks is an isotonic saline solution. The patient dies, and an autopsy reveals that many red blood cells have been destroyed. Do you think the solution the doctor injected was really isotonic?

Link to Learning

For a video illustrating the process of diffusion in solutions, visit this [site](#).

## **Tonicity in Living Systems**

In a hypotonic environment, water enters a cell, and the cell swells. In an isotonic condition, the relative concentrations of solute and solvent are equal on both sides of the membrane. There is no net water movement; therefore, there is no change in the size of the cell. In a hypertonic solution, water leaves a cell and the cell shrinks. If either the hypo- or hyper-condition goes to excess, the cell's functions become compromised, and the cell may be destroyed.

A red blood cell will burst, or lyse, when it swells beyond the plasma membrane's capability to expand. Remember, the membrane resembles a mosaic, with discrete spaces between the molecules composing it. If the cell swells, and the spaces between the lipids and proteins become too large, the cell will break apart.

In contrast, when excessive amounts of water leave a red blood cell, the cell shrinks, or crenates. This has the effect of concentrating the solutes left in the cell, making the cytosol denser and interfering with diffusion within the cell. The cell's ability to function will be compromised and may also result in the death of the cell.

Various living things have ways of controlling the effects of osmosis—a mechanism called osmoregulation. Some organisms, such as plants, fungi, bacteria, and some protists, have cell walls that surround the plasma membrane and prevent cell lysis in a hypotonic solution. The plasma membrane can only expand to the limit of the cell wall, so the cell will not lyse. In fact, the cytoplasm in plants is always slightly hypertonic to the cellular environment, and water will always enter a cell if water is available. This inflow of water produces turgor pressure, which stiffens the cell walls of the plant ([link](#)). In nonwoody plants, turgor pressure supports the plant. Conversely, if the plant is not watered, the extracellular fluid will become hypertonic, causing water to leave the cell. In this condition, the cell does not shrink because the cell wall is not flexible. However, the cell membrane detaches from the wall and constricts the cytoplasm. This is called plasmolysis. Plants lose turgor pressure in this condition and wilt ([link](#)).

The turgor pressure within a plant cell depends on the tonicity of the solution that it is bathed in. (credit: modification of work by Mariana Ruiz

Villareal) Without adequate water, the plant on the left has lost turgor pressure, visible in its wilting; the turgor pressure is restored by watering it (right). (credit: Victor M. Vicente

Selvas)

Tonicity is a concern for all living things. For example, paramecia and amoebas, which are protists that lack cell walls, have contractile vacuoles. This vesicle collects excess water from the cell and pumps it out, keeping the cell from lysing as it takes on water from its environment ([link](#)).

A paramecium's contractile vacuole, here visualized using bright field light microscopy at 480x magnification, continuously pumps water out of the organism's body to keep it from

bursting in a hypotonic medium. (credit: modification of work by NIH; scale-bar data from

Matt Russell)

Many marine invertebrates have internal salt levels matched to their environments, making them isotonic with the water in which they live. Fish, however, must spend approximately five percent of their metabolic energy maintaining osmotic homeostasis. Freshwater fish live in an environment that is hypotonic to their cells. These fish actively take in salt through their gills and excrete diluted urine to rid themselves of excess water. Saltwater fish live in the reverse environment, which is hypertonic to their cells, and they secrete salt through their gills and excrete highly concentrated urine.

In vertebrates, the kidneys regulate the amount of water in the body. Osmoreceptors are specialized cells in the brain that monitor the concentration of solutes in the blood. If the levels of solutes increase beyond a certain range, a hormone is released that retards water loss through the kidney and dilutes the blood to safer levels. Animals also have high concentrations of albumin, which is produced by the liver, in their blood. This protein is too large to pass easily through plasma membranes and is a major factor in controlling the osmotic pressures applied to tissues.

## **Section Summary**

The passive forms of transport, diffusion and osmosis, move materials of small molecular weight across membranes. Substances diffuse from areas of high concentration to areas of lower concentration, and this process continues until the substance is evenly distributed in a system. In solutions containing more than one substance, each type of molecule diffuses according to its own concentration gradient, independent of the diffusion of other substances. Many factors can affect the rate of diffusion, including concentration gradient, size of the particles that are diffusing, temperature of the system, and so on.

In living systems, diffusion of substances into and out of cells is mediated by the plasma membrane. Some materials diffuse readily through the membrane, but others are hindered, and their passage is made possible by specialized proteins, such as channels and transporters.

The chemistry of living things occurs in aqueous solutions, and balancing the concentrations of those solutions is an ongoing problem. In living systems, diffusion of some substances would be slow or difficult without membrane proteins that facilitate transport.

### Art Connections

[\[link\]](#) A doctor injects a patient with what the doctor thinks is an isotonic saline solution. The patient dies, and an autopsy reveals that many red blood cells have been destroyed. Do you think the solution the doctor injected was really isotonic?

[\[link\]](#) No, it must have been hypotonic as a hypotonic solution would cause water to enter the cells, thereby making them burst.

### Review Questions

Water moves via osmosis \_\_\_\_\_.

- throughout the cytoplasm
- from an area with a high concentration of other solutes to a lower one
- from an area with a high concentration of water to one of lower concentration
- from an area with a low concentration of water to one of higher concentration

C

The principal force driving movement in diffusion is the \_\_\_\_\_.

- temperature
- particle size
- concentration gradient
- membrane surface area

C

What problem is faced by organisms that live in fresh water?

- Their bodies tend to take in too much water.
- They have no way of controlling their tonicity.
- Only salt water poses problems for animals that live in it.
- Their bodies tend to lose too much water to their environment.

A

### Free Response

Discuss why the following affect the rate of diffusion: molecular size, temperature, solution density, and the distance that must be traveled.

Heavy molecules move more slowly than lighter ones. It takes more energy in the medium to move them along. Increasing or decreasing temperature increases or decreases the energy in

the medium, affecting molecular movement. The denser a solution is, the harder it is for molecules to move through it, causing diffusion to slow down due to friction. Living cells require a steady supply of nutrients and a steady rate of waste removal. If the distance these substances need to travel is too great, diffusion cannot move nutrients and waste materials efficiently to sustain life.

Why does water move through a membrane?

Water moves through a membrane in osmosis because there is a concentration gradient across the membrane of solute and solvent. The solute cannot effectively move to balance the concentration on both sides of the membrane, so water moves to achieve this balance.

Both of the regular intravenous solutions administered in medicine, normal saline and lactated Ringer's solution, are isotonic. Why is this important?

Injection of isotonic solutions ensures that there will be no perturbation of the osmotic balance, and no water taken from tissues or added to them from the blood.

## **Glossary**

aquaporin

channel protein that allows water through the membrane at a very high rate

carrier protein

membrane protein that moves a substance across the plasma membrane by changing its own shape

channel protein

membrane protein that allows a substance to pass through its hollow core across the plasma membrane

concentration gradient

area of high concentration adjacent to an area of low concentration

diffusion

passive process of transport of low-molecular weight material according to its concentration gradient

facilitated transport

process by which material moves down a concentration gradient (from high to low concentration) using integral membrane proteins

hypertonic

situation in which extracellular fluid has a higher osmolarity than the fluid inside the cell, resulting in water moving out of the cell

hypotonic

situation in which extracellular fluid has a lower osmolarity than the fluid inside the cell, resulting in water moving into the cell

isotonic

situation in which the extracellular fluid has the same osmolarity as the fluid inside the cell, resulting in no net movement of water into or out of the cell

osmolarity

total amount of substances dissolved in a specific amount of solution

osmosis

transport of water through a semipermeable membrane according to the concentration gradient of water across the membrane that results from the presence of solute that cannot pass through the membrane

passive transport

method of transporting material through a membrane that does not require energy

plasmolysis

detaching of the cell membrane from the cell wall and constriction of the cell membrane when a plant cell is in a hypertonic solution

selectively permeable

characteristic of a membrane that allows some substances through but not others

solute

substance dissolved in a liquid to form a solution

tonicity

amount of solute in a solution

transport protein

membrane protein that facilitates passage of a substance across a membrane by binding it

Active Transport

By the end of this section, you will be able to:

- Understand how electrochemical gradients affect ions
- Distinguish between primary active transport and secondary active transport

Active transport mechanisms require the use of the cell's energy, usually in the form of adenosine triphosphate (ATP). If a substance must move into the cell against its concentration gradient—that is, if the concentration of the substance inside the cell is greater than its concentration in the extracellular fluid (and vice versa)—the cell must use energy to move the substance. Some active transport mechanisms move small-molecular weight materials, such as ions, through the membrane. Other mechanisms transport much larger molecules.

## Electrochemical Gradient

We have discussed simple concentration gradients—differential concentrations of a substance across a space or a membrane—but in living systems, gradients are more complex. Because ions move into and out of cells and because cells contain proteins that do not move across the membrane and are mostly negatively charged, there is also an electrical gradient, a difference of charge, across the plasma membrane. The interior of living cells is electrically negative with respect to the extracellular fluid in which they are bathed, and at the same time, cells have higher concentrations of potassium ( $K^+$ ) and lower concentrations of sodium ( $Na^+$ ) than does the extracellular fluid. So in a living cell, the concentration gradient of  $Na^+$  tends to drive it into the cell, and the electrical gradient of  $Na^+$  (a positive ion) also tends to drive it

inward to the negatively charged interior. The situation is more complex, however, for other elements such as potassium. The electrical gradient of  $K^+$ , a positive ion, also tends to drive it into the cell, but the concentration gradient of  $K^+$  tends to drive  $K^+$  *out* of the cell ([link](#)). The combined gradient of concentration and electrical charge that affects an ion is called its electrochemical gradient.

#### Art Connection

Electrochemical gradients arise from the combined effects of concentration gradients and electrical gradients. (credit: “Synaptitude”/Wikimedia Commons)

Injection of a potassium solution into a person’s blood is lethal; this is used in capital punishment and euthanasia. Why do you think a potassium solution injection is lethal?

#### **Moving Against a Gradient**

To move substances against a concentration or electrochemical gradient, the cell must use energy. This energy is harvested from ATP generated through the cell’s metabolism. Active transport mechanisms, collectively called pumps, work against electrochemical gradients. Small substances constantly pass through plasma membranes. Active transport maintains

concentrations of ions and other substances needed by living cells in the face of these passive movements. Much of a cell's supply of metabolic energy may be spent maintaining these processes. (Most of a red blood cell's metabolic energy is used to maintain the imbalance between exterior and interior sodium and potassium levels required by the cell.) Because active transport mechanisms depend on a cell's metabolism for energy, they are sensitive to many metabolic poisons that interfere with the supply of ATP.

Two mechanisms exist for the transport of small-molecular weight material and small molecules. Primary active transport moves ions across a membrane and creates a difference in charge across that membrane, which is directly dependent on ATP. Secondary active transport describes the movement of material that is due to the electrochemical gradient established by primary active transport that does not directly require ATP.

### **Carrier Proteins for Active Transport**

An important membrane adaption for active transport is the presence of specific carrier proteins or pumps to facilitate movement: there are three types of these proteins or transporters ([link](#)). A uniporter carries one specific ion or molecule. A symporter carries two different ions or molecules, both in the same direction. An antiporter also carries two different ions or molecules, but in different directions. All of these transporters can also transport small, uncharged organic molecules like glucose. These three types of carrier proteins are also found in facilitated diffusion, but they do not require ATP to work in that process. Some examples of pumps for active transport are  $\text{Na}^+\text{-K}^+$  ATPase, which carries sodium and potassium ions, and  $\text{H}^+\text{-K}^+$  ATPase, which carries hydrogen and potassium ions. Both of these are antiporter carrier proteins. Two other carrier proteins are  $\text{Ca}^{2+}$  ATPase and  $\text{H}^+$  ATPase, which carry only calcium and only hydrogen ions, respectively. Both are pumps.

A uniporter carries one molecule or ion. A symporter carries two different molecules or ions, both in the same direction. An antiporter also carries two different molecules or ions, but in different directions. (credit: modification of work by "Lupask"/Wikimedia)

Commons)

### **Primary Active Transport**

The primary active transport that functions with the active transport of sodium and potassium allows secondary active transport to occur. The second transport method is still considered active because it depends on the use of energy as does primary transport ([link](#)).

Primary active transport moves ions across a membrane, creating an electrochemical gradient (electrogenic transport). (credit: modification of work by Mariana Ruiz Villareal)

One of the most important pumps in animal cells is the sodium-potassium pump ( $\text{Na}^+$ - $\text{K}^+$  ATPase), which maintains the electrochemical gradient (and the correct concentrations of  $\text{Na}^+$  and  $\text{K}^+$ ) in living cells. The sodium-potassium pump moves  $\text{K}^+$  into the cell while moving  $\text{Na}^+$  out at the same time, at a ratio of three  $\text{Na}^+$  for every two  $\text{K}^+$  ions moved in. The  $\text{Na}^+$ - $\text{K}^+$  ATPase exists in two forms, depending on its orientation to the interior or exterior of the cell and its affinity for either sodium or potassium ions. The process consists of the following six steps.

1. With the enzyme oriented towards the interior of the cell, the carrier has a high affinity for sodium ions. Three ions bind to the protein.
2. ATP is hydrolyzed by the protein carrier and a low-energy phosphate group attaches to it.
3. As a result, the carrier changes shape and re-orientates itself towards the exterior of the membrane. The protein's affinity for sodium decreases and the three sodium ions leave the carrier.
4. The shape change increases the carrier's affinity for potassium ions, and two such ions attach to the protein. Subsequently, the low-energy phosphate group detaches from the carrier.
5. With the phosphate group removed and potassium ions attached, the carrier protein repositions itself towards the interior of the cell.
6. The carrier protein, in its new configuration, has a decreased affinity for potassium, and the two ions are released into the cytoplasm. The protein now has a higher affinity for sodium ions, and the process starts again.

Several things have happened as a result of this process. At this point, there are more sodium ions outside of the cell than inside and more potassium ions inside than out. For every three ions of sodium that move out, two ions of potassium move in. This results in the interior being slightly more negative relative to the exterior. This difference in charge is important in creating the conditions necessary for the secondary process. The sodium-potassium pump is, therefore, an electrogenic pump (a pump that creates a charge imbalance), creating an electrical imbalance across the membrane and contributing to the membrane potential.

Link to Learning

Watch this [video](#) to see a simulation of active transport in a sodium-potassium ATPase.

### **Secondary Active Transport (Co-transport)**

Secondary active transport brings sodium ions, and possibly other compounds, into the cell. As sodium ion concentrations build outside of the plasma membrane because of the action of the primary active transport process, an electrochemical gradient is created. If a channel protein exists and is open, the sodium ions will be pulled through the membrane. This movement is used to transport other substances that can attach themselves to the transport protein through the membrane ([link](#)). Many amino acids, as well as glucose, enter a cell this way. This secondary process is also used to store high-energy hydrogen ions in the mitochondria of plant and animal cells for the production of ATP. The potential energy that accumulates in the stored hydrogen ions is translated into kinetic energy as the ions surge through the channel protein ATP synthase, and that energy is used to convert ADP into ATP.

Art Connection

An electrochemical gradient, created by primary active transport, can move other substances against their concentration gradients, a process called co-transport or secondary active transport. (credit: modification of work by Mariana Ruiz Villareal)

If the pH outside the cell decreases, would you expect the amount of amino acids transported into the cell to increase or decrease?

### **Section Summary**

The combined gradient that affects an ion includes its concentration gradient and its electrical gradient. A positive ion, for example, might tend to diffuse into a new area, down its concentration gradient, but if it is diffusing into an area of net positive charge, its diffusion will be hampered by its electrical gradient. When dealing with ions in aqueous solutions, a combination of the electrochemical and concentration gradients, rather than just the concentration gradient alone, must be considered. Living cells need certain substances that exist inside the cell in concentrations greater than they exist in the extracellular space.

Moving substances up their electrochemical gradients requires energy from the cell. Active transport uses energy stored in ATP to fuel this transport. Active transport of small molecular-sized materials uses integral proteins in the cell membrane to move the materials: These proteins are analogous to pumps. Some pumps, which carry out primary active transport, couple directly with ATP to drive their action. In co-transport (or secondary active transport), energy from primary transport can be used to move another substance into the cell and up its concentration gradient.

## Art Connections

[\[link\]](#) Injection of a potassium solution into a person's blood is lethal; this is used in capital punishment and euthanasia. Why do you think a potassium solution injection is lethal?

[\[link\]](#) Cells typically have a high concentration of potassium in the cytoplasm and are bathed in a high concentration of sodium. Injection of potassium dissipates this electrochemical gradient. In heart muscle, the sodium/potassium potential is responsible for transmitting the signal that causes the muscle to contract. When this potential is dissipated, the signal can't be transmitted, and the heart stops beating. Potassium injections are also used to stop the heart from beating during surgery.

[\[link\]](#) If the pH outside the cell decreases, would you expect the amount of amino acids transported into the cell to increase or decrease?

[\[link\]](#) A decrease in pH means an increase in positively charged  $H^+$  ions, and an increase in the electrical gradient across the membrane. The transport of amino acids into the cell will increase.

## Review Questions

Active transport must function continuously because \_\_\_\_\_.

- plasma membranes wear out
- not all membranes are amphiphilic
- facilitated transport opposes active transport
- diffusion is constantly moving solutes in opposite directions

D

How does the sodium-potassium pump make the interior of the cell negatively charged?

- by expelling anions
- by pulling in anions
- by expelling more cations than are taken in
- by taking in and expelling an equal number of cations

C

What is the combination of an electrical gradient and a concentration gradient called?

- potential gradient

- b. electrical potential
- c. concentration potential
- d. electrochemical gradient

D

## Free Response

Where does the cell get energy for active transport processes?

The cell harvests energy from ATP produced by its own metabolism to power active transport processes, such as the activity of pumps.

How does the sodium-potassium pump contribute to the net negative charge of the interior of the cell?

The sodium-potassium pump forces out three (positive)  $\text{Na}^+$  ions for every two (positive)  $\text{K}^+$  ions it pumps in, thus the cell loses a positive charge at every cycle of the pump.

## Glossary

active transport

method of transporting material that requires energy

antiporter

transporter that carries two ions or small molecules in different directions

electrochemical gradient

gradient produced by the combined forces of an electrical gradient and a chemical gradient

electrogenic pump

pump that creates a charge imbalance

primary active transport

active transport that moves ions or small molecules across a membrane and may create a difference in charge across that membrane

pump

active transport mechanism that works against electrochemical gradients

secondary active transport

movement of material that is due to the electrochemical gradient established by primary active transport

symporter

transporter that carries two different ions or small molecules, both in the same direction

transporter

specific carrier proteins or pumps that facilitate movement

uniporter

transporter that carries one specific ion or molecule

Bulk Transport

By the end of this section, you will be able to:

- Describe endocytosis, including phagocytosis, pinocytosis, and receptor-mediated endocytosis
- Understand the process of exocytosis

In addition to moving small ions and molecules through the membrane, cells also need to remove and take in larger molecules and particles (see [\[link\]](#) for examples). Some cells are even capable of engulfing entire unicellular microorganisms. You might have correctly hypothesized that the uptake and release of large particles by the cell requires energy. A large particle, however, cannot pass through the membrane, even with energy supplied by the cell.

## **Endocytosis**

Endocytosis is a type of active transport that moves particles, such as large molecules, parts of cells, and even whole cells, into a cell. There are different variations of endocytosis, but all share a common characteristic: The plasma membrane of the cell invaginates, forming a pocket around the target particle. The pocket pinches off, resulting in the particle being contained in a newly created intracellular vesicle formed from the plasma membrane.

## **Phagocytosis**

Phagocytosis (the condition of “cell eating”) is the process by which large particles, such as cells or relatively large particles, are taken in by a cell. For example, when microorganisms invade the human body, a type of white blood cell called a neutrophil will remove the invaders through this process, surrounding and engulfing the microorganism, which is then destroyed by the neutrophil ([\[link\]](#)).

In phagocytosis, the cell membrane surrounds the particle and engulfs it. (credit: Mariana

Ruiz Villareal)

In preparation for phagocytosis, a portion of the inward-facing surface of the plasma membrane becomes coated with a protein called clathrin, which stabilizes this section of the

membrane. The coated portion of the membrane then extends from the body of the cell and surrounds the particle, eventually enclosing it. Once the vesicle containing the particle is enclosed within the cell, the clathrin disengages from the membrane and the vesicle merges with a lysosome for the breakdown of the material in the newly formed compartment (endosome). When accessible nutrients from the degradation of the vesicular contents have been extracted, the newly formed endosome merges with the plasma membrane and releases its contents into the extracellular fluid. The endosomal membrane again becomes part of the plasma membrane.

### **Pinocytosis**

A variation of endocytosis is called pinocytosis. This literally means “cell drinking” and was named at a time when the assumption was that the cell was purposefully taking in extracellular fluid. In reality, this is a process that takes in molecules, including water, which the cell needs from the extracellular fluid. Pinocytosis results in a much smaller vesicle than does phagocytosis, and the vesicle does not need to merge with a lysosome ([link](#)).

In pinocytosis, the cell membrane invaginates, surrounds a small volume of fluid, and pinches

off. (credit: Mariana Ruiz Villareal)

A variation of pinocytosis is called potocytosis. This process uses a coating protein, called caveolin, on the cytoplasmic side of the plasma membrane, which performs a similar function to clathrin. The cavities in the plasma membrane that form the vacuoles have membrane receptors and lipid rafts in addition to caveolin. The vacuoles or vesicles formed in caveolae (singular caveola) are smaller than those in pinocytosis. Potocytosis is used to bring small molecules into the cell and to transport these molecules through the cell for their release on the other side of the cell, a process called transcytosis.

### **Receptor-mediated Endocytosis**

A targeted variation of endocytosis employs receptor proteins in the plasma membrane that have a specific binding affinity for certain substances ([link](#)).

In receptor-mediated endocytosis, uptake of substances by the cell is targeted to a single type of substance that binds to the receptor on the external surface of the cell membrane. (credit:

modification of work by Mariana Ruiz

Villareal)

In receptor-mediated endocytosis, as in phagocytosis, clathrin is attached to the cytoplasmic side of the plasma membrane. If uptake of a compound is dependent on receptor-mediated endocytosis and the process is ineffective, the material will not be removed from the tissue fluids or blood. Instead, it will stay in those fluids and increase in concentration. Some human diseases are caused by the failure of receptor-mediated endocytosis. For example, the form of cholesterol termed low-density lipoprotein or LDL (also referred to as “bad” cholesterol) is removed from the blood by receptor-mediated endocytosis. In the human genetic disease familial hypercholesterolemia, the LDL receptors are defective or missing entirely. People with this condition have life-threatening levels of cholesterol in their blood, because their cells cannot clear LDL particles from their blood.

Although receptor-mediated endocytosis is designed to bring specific substances that are normally found in the extracellular fluid into the cell, other substances may gain entry into the cell at the same site. Flu viruses, diphtheria, and cholera toxin all have sites that cross-react with normal receptor-binding sites and gain entry into cells.

Link to Learning

See receptor-mediated endocytosis in action, and click on different [parts](#) for a focused animation.

## **Exocytosis**

The reverse process of moving material into a cell is the process of exocytosis. Exocytosis is the opposite of the processes discussed above in that its purpose is to expel material from the

cell into the extracellular fluid. Waste material is enveloped in a membrane and fuses with the interior of the plasma membrane. This fusion opens the membranous envelope on the exterior of the cell, and the waste material is expelled into the extracellular space ([link](#)). Other examples of cells releasing molecules via exocytosis include the secretion of proteins of the extracellular matrix and secretion of neurotransmitters into the synaptic cleft by synaptic vesicles.

In exocytosis, vesicles containing substances fuse with the plasma membrane. The contents are then released to the exterior of the cell. (credit: modification of work by Mariana Ruiz

Villareal)

### **Methods of Transport, Energy Requirements, and Types of Material Transported**

<b>Transport Method</b>	<b>Active/Passive</b>	<b>Material Transported</b>
Diffusion	Passive	Small-molecular weight material
Osmosis	Passive	Water
Facilitated transport/diffusion	Passive	Sodium, potassium, calcium, glucose
Primary active transport	Active	Sodium, potassium, calcium
Secondary active transport	Active	Amino acids, lactose
Phagocytosis	Active	Large macromolecules, whole cells, or cellular structures
Pinocytosis and potocytosis	Active	Small molecules (liquids/water)
Receptor-mediated endocytosis	Active	Large quantities of macromolecules

### **Section Summary**

Active transport methods require the direct use of ATP to fuel the transport. Large particles, such as macromolecules, parts of cells, or whole cells, can be engulfed by other cells in a process called phagocytosis. In phagocytosis, a portion of the membrane invaginates and flows around the particle, eventually pinching off and leaving the particle entirely enclosed by an envelope of plasma membrane. Vesicle contents are broken down by the cell, with the particles either used as food or dispatched. Pinocytosis is a similar process on a smaller scale. The plasma membrane invaginates and pinches off, producing a small envelope of fluid from

outside the cell. Pinocytosis imports substances that the cell needs from the extracellular fluid. The cell expels waste in a similar but reverse manner: it pushes a membranous vacuole to the plasma membrane, allowing the vacuole to fuse with the membrane and incorporate itself into the membrane structure, releasing its contents to the exterior.

## Review Questions

What happens to the membrane of a vesicle after exocytosis?

- It leaves the cell.
- It is disassembled by the cell.
- It fuses with and becomes part of the plasma membrane.
- It is used again in another exocytosis event.

C

Which transport mechanism can bring whole cells into a cell?

- pinocytosis
- phagocytosis
- facilitated transport
- primary active transport

B

In what important way does receptor-mediated endocytosis differ from phagocytosis?

- It transports only small amounts of fluid.
- It does not involve the pinching off of membrane.
- It brings in only a specifically targeted substance.
- It brings substances into the cell, while phagocytosis removes substances.

C

## Free Response

Why is it important that there are different types of proteins in plasma membranes for the transport of materials into and out of a cell?

The proteins allow a cell to select what compound will be transported, meeting the needs of the cell and not bringing in anything else.

Why do ions have a difficult time getting through plasma membranes despite their small size?

Ions are charged, and consequently, they are hydrophilic and cannot associate with the lipid portion of the membrane. Ions must be transported by carrier proteins or ion channels.

## Glossary

caveolin

protein that coats the cytoplasmic side of the plasma membrane and participates in the process of liquid update by potocytosis

clathrin

protein that coats the inward-facing surface of the plasma membrane and assists in the formation of specialized structures, like coated pits, for phagocytosis

endocytosis

type of active transport that moves substances, including fluids and particles, into a cell

exocytosis

process of passing bulk material out of a cell

pinocytosis

a variation of endocytosis that imports macromolecules that the cell needs from the extracellular fluid

potocytosis

variation of pinocytosis that uses a different coating protein (caveolin) on the cytoplasmic side of the plasma membrane

receptor-mediated endocytosis

variation of endocytosis that involves the use of specific binding proteins in the plasma membrane for specific molecules or particles, and clathrin-coated pits that become clathrin-coated vesicles

Introduction

class="introduction" class="summary" title="Sections Summary" class="art-exercise" title="Art Connections" class="multiple-choice" title="Multiple Choice" class="free-response" title="Free Response" A hummingbird needs energy to maintain prolonged periods of flight. The bird obtains its energy from taking in food and transforming the nutrients into energy through a series of biochemical reactions. The flight muscles in birds are extremely

efficient in energy production. (credit: modification of work by Cory

Zanker)

Virtually every task performed by living organisms requires energy. Energy is needed to perform heavy labor and exercise, but humans also use a great deal of energy while thinking, and even during sleep. In fact, the living cells of every organism constantly use energy. Nutrients and other molecules are imported, metabolized (broken down) and possibly synthesized into new molecules, modified if needed, transported around the cell, and may be distributed to the entire organism. For example, the large proteins that make up muscles are actively built from smaller molecules. Complex carbohydrates are broken down into simple sugars that the cell uses for energy. Just as energy is required to both build and demolish a building, energy is required for both the synthesis and breakdown of molecules. Additionally, signaling molecules such as hormones and neurotransmitters are transported between cells. Pathogenic bacteria and viruses are ingested and broken down by cells. Cells must also export waste and toxins to stay healthy, and many cells must swim or move surrounding materials via the beating motion of cellular appendages like cilia and flagella.

The cellular processes listed above require a steady supply of energy. From where, and in what form, does this energy come? How do living cells obtain energy, and

how do they use it? This chapter will discuss different forms of energy and the physical laws that govern energy transfer. This chapter will also describe how cells use energy and replenish it, and how chemical reactions in the cell are performed with great efficiency.

### The Laws of Thermodynamics

By the end of this section, you will be able to:

- Discuss the concept of entropy
- Explain the first and second laws of thermodynamics

Thermodynamics refers to the study of energy and energy transfer involving physical matter. The matter and its environment relevant to a particular case of energy transfer are classified as a system, and everything outside of that system is called the surroundings. For instance, when heating a pot of water on the stove, the system includes the stove, the pot, and the water. Energy is transferred within the system (between the stove, pot, and water). There are two types of systems: open and closed. An open system is one in which energy can be transferred between the system and its surroundings. The stovetop system is open because heat can be lost into the air. A closed system is one that cannot transfer energy to its surroundings.

Biological organisms are open systems. Energy is exchanged between them and their surroundings, as they consume energy-storing molecules and release energy to the environment by doing work. Like all things in the physical world, energy is subject to the laws of physics. The laws of thermodynamics govern the transfer of energy in and among all systems in the universe.

### The First Law of Thermodynamics

The first law of thermodynamics deals with the total amount of energy in the universe. It states that this total amount of energy is constant. In other words, there has always been, and always will be, exactly the same amount of energy in the universe. Energy exists in many different forms. According to the first law of thermodynamics, energy may be transferred from place to place or transformed into different forms, but it cannot be created or destroyed. The transfers and transformations of energy take place around us all the time. Light bulbs transform electrical energy into light energy. Gas stoves transform chemical energy from natural gas into heat energy. Plants perform one of the most biologically useful energy transformations on earth: that of converting the energy of sunlight into the chemical energy stored within organic molecules ([\[link\]](#)). Some examples of energy transformations are shown in [\[link\]](#).

The challenge for all living organisms is to obtain energy from their surroundings in forms that they can transfer or transform into usable energy to do work. Living cells have evolved to meet this challenge very well. Chemical energy stored within organic molecules such as sugars and fats is transformed through a series of cellular chemical reactions into energy within molecules of ATP. Energy in ATP molecules is easily accessible to do work. Examples of the types of work that cells need to do include building complex molecules,

transporting materials, powering the beating motion of cilia or flagella, contracting muscle fibers to create movement, and reproduction.

Shown are two examples of energy being transferred from one system to another and transformed from one form to another. Humans can convert the chemical energy in food, like this ice cream cone, into kinetic energy (the energy of movement to ride a bicycle). Plants can convert electromagnetic radiation (light energy) from the sun into chemical energy. (credit “ice cream”: modification of work by D. Sharon Pruitt; credit “kids on bikes”: modification of work by Michelle Rikken-Ransom; credit “leaf”: modification of work by Cory

Zanker)

## **The Second Law of Thermodynamics**

A living cell’s primary tasks of obtaining, transforming, and using energy to do work may seem simple. However, the second law of thermodynamics explains why these tasks are harder than they appear. None of the energy transfers we’ve discussed, along with all energy transfers and transformations in the universe, is completely efficient. In every energy transfer, some amount of energy is lost in a form that is unusable. In most cases, this form is heat energy. Thermodynamically, heat energy is defined as the energy transferred from one system to another that is not doing work. For example, when an airplane flies through the air, some of the energy of the flying plane is lost as heat energy due to friction with the surrounding air. This friction actually heats the air by temporarily increasing the speed of air molecules. Likewise, some energy is lost as heat energy during cellular metabolic reactions. This is good for warm-blooded creatures like us, because heat energy helps to maintain our body temperature. Strictly speaking, no energy transfer is completely efficient, because some energy is lost in an unusable form.

An important concept in physical systems is that of order and disorder (also known as randomness). The more energy that is lost by a system to its surroundings, the less ordered and more random the system is. Scientists refer to the measure of randomness or disorder within a system as entropy. High entropy means high disorder and low energy ([\[link\]](#)). To better understand entropy, think of a student’s bedroom. If no energy or work were put into it, the room would quickly become messy. It would exist in a very disordered state, one of high entropy. Energy must be put into the system, in the form of the student doing work and

putting everything away, in order to bring the room back to a state of cleanliness and order. This state is one of low entropy. Similarly, a car or house must be constantly maintained with work in order to keep it in an ordered state. Left alone, the entropy of the house or car gradually increases through rust and degradation. Molecules and chemical reactions have varying amounts of entropy as well. For example, as chemical reactions reach a state of equilibrium, entropy increases, and as molecules at a high concentration in one place diffuse and spread out, entropy also increases.

### Scientific Connection

**Transfer of Energy and the Resulting Entropy** Set up a simple experiment to understand how energy is transferred and how a change in entropy results.

1. Take a block of ice. This is water in solid form, so it has a high structural order. This means that the molecules cannot move very much and are in a fixed position. The temperature of the ice is  $0^{\circ}\text{C}$ . As a result, the entropy of the system is low.
2. Allow the ice to melt at room temperature. What is the state of molecules in the liquid water now? How did the energy transfer take place? Is the entropy of the system higher or lower? Why?
3. Heat the water to its boiling point. What happens to the entropy of the system when the water is heated?

All physical systems can be thought of in this way: Living things are highly ordered, requiring constant energy input to be maintained in a state of low entropy. As living systems take in energy-storing molecules and transform them through chemical reactions, they lose some amount of usable energy in the process, because no reaction is completely efficient. They also produce waste and by-products that aren't useful energy sources. This process increases the entropy of the system's surroundings. Since all energy transfers result in the loss of some usable energy, the second law of thermodynamics states that every energy transfer or transformation increases the entropy of the universe. Even though living things are highly ordered and maintain a state of low entropy, the entropy of the universe in total is constantly increasing due to the loss of usable energy with each energy transfer that occurs. Essentially, living things are in a continuous uphill battle against this constant increase in universal entropy.

Entropy is a measure of randomness or disorder in a system. Gases have higher entropy than liquids, and liquids have higher entropy than

solids.

## Section Summary

In studying energy, scientists use the term “system” to refer to the matter and its environment involved in energy transfers. Everything outside of the system is called the surroundings. Single cells are biological systems. Systems can be thought of as having a certain amount of order. It takes energy to make a system more ordered. The more ordered a system is, the lower its entropy. Entropy is a measure of the disorder of a system. As a system becomes more disordered, the lower its energy and the higher its entropy become.

A series of laws, called the laws of thermodynamics, describe the properties and processes of energy transfer. The first law states that the total amount of energy in the universe is constant. This means that energy can't be created or destroyed, only transferred or transformed. The second law of thermodynamics states that every energy transfer involves some loss of energy in an unusable form, such as heat energy, resulting in a more disordered system. In other words, no energy transfer is completely efficient and tends toward disorder.

## Review Questions

Which of the following is not an example of an energy transformation?

- a. Turning on a light switch
- b. Solar panels at work
- c. Formation of static electricity
- d. None of the above

A

Label each of the following systems as high or low entropy: i. the instant that a perfume bottle is sprayed compared with 30 seconds later, ii. an old 1950s car compared with a brand new car, and iii. a living cell compared with a dead cell.

- a. i. low, ii. high, iii. low
- b. i. low, ii. high, iii. high
- c. i. high, ii. low, iii. high
- d. i. high, ii. low, iii. Low

A

## Free Response

Imagine an elaborate ant farm with tunnels and passageways through the sand where ants live in a large community. Now imagine that an earthquake shook the ground and demolished the ant farm. In which of these two scenarios, before or after the earthquake, was the ant farm system in a state of higher or lower entropy?

The ant farm had lower entropy before the earthquake because it was a highly ordered system. After the earthquake, the system became much more disordered and had higher entropy.

Energy transfers take place constantly in everyday activities. Think of two scenarios: cooking on a stove and driving. Explain how the second law of thermodynamics applies to these two scenarios.

While cooking, food is heating up on the stove, but not all of the heat goes to cooking the food, some of it is lost as heat energy to the surrounding air, increasing entropy. While driving, cars burn gasoline to run the engine and move the car. This reaction is not completely efficient, as some energy during this process is lost as heat energy, which is why the hood and the components underneath it heat up while the engine is turned on. The tires also heat up because of friction with the pavement, which is additional energy loss. This energy transfer, like all others, also increases entropy.

## Glossary

entropy (S)

measure of randomness or disorder within a system

heat

energy energy transferred from one system to another that is not work  
(energy of the motion of molecules or particles)

thermodynamics

study of energy and energy transfer involving physical matter

Potential, Kinetic, Free, and Activation Energy

By the end of this section, you will be able to:

- Define “energy”
- Explain the difference between kinetic and potential energy
- Discuss the concepts of free energy and activation energy
- Describe endergonic and exergonic reactions

Energy is defined as the ability to do work. As you've learned, energy exists in different forms. For example, electrical energy, light energy, and heat energy are all different types of energy. While these are all familiar types of energy that one can see or feel, there is another type of energy that is much less tangible. This energy is associated with something as simple as an object held above the ground. In order to appreciate the way energy flows into and out of biological systems, it is important to understand more about the different types of energy that exist in the physical world.

## Types of Energy

When an object is in motion, there is energy associated with that object. In the example of an airplane in flight, there is a great deal of energy associated with the motion of the airplane. This is because moving objects are capable of enacting a change, or doing work. Think of a wrecking ball. Even a slow-moving wrecking ball can do a great deal of damage to other objects. However, a wrecking ball that is not in motion is incapable of performing work. Energy associated with objects in motion is called kinetic energy. A speeding bullet, a walking person, the rapid movement of molecules in the air (which produces heat), and electromagnetic radiation like light all have kinetic energy.

Now what if that same motionless wrecking ball is lifted two stories above a car with a crane? If the suspended wrecking ball is unmoving, is there energy associated with it? The answer is yes. The suspended wrecking ball has energy associated with it that is fundamentally different from the kinetic energy of objects in motion. This form of energy results from the fact that there is the *potential* for the wrecking ball to do work. If it is released, indeed it would do work. Because this type of energy refers to the potential to do work, it is called potential energy. Objects transfer their energy between kinetic and potential in the following way: As the wrecking ball hangs motionless, it has 0 kinetic and 100 percent potential energy. Once it is released, its kinetic energy begins to increase because it builds speed due to gravity. At the same time, as it nears the ground, it loses potential energy. Somewhere mid-fall it has 50 percent kinetic and 50 percent potential energy. Just before it hits the ground, the ball has nearly lost its potential energy and has near-maximal kinetic energy. Other examples of potential energy include the energy of water held behind a dam ([link](#)), or a person about to skydive out of an airplane.

Water behind a dam has potential energy. Moving water, such as in a waterfall or a rapidly flowing river, has kinetic energy. (credit "dam": modification of work by "Pascal"/Flickr;

credit “waterfall”: modification of work by Frank

Gualtieri)

Potential energy is not only associated with the location of matter (such as a child sitting on a tree branch), but also with the structure of matter. A spring on the ground has potential energy if it is compressed; so does a rubber band that is pulled taut. The very existence of living cells relies heavily on structural potential energy. On a chemical level, the bonds that hold the atoms of molecules together have potential energy. Remember that anabolic cellular pathways require energy to synthesize complex molecules from simpler ones, and catabolic pathways release energy when complex molecules are broken down. The fact that energy can be released by the breakdown of certain chemical bonds implies that those bonds have potential energy. In fact, there is potential energy stored within the bonds of all the food molecules we eat, which is eventually harnessed for use. This is because these bonds can release energy when broken. The type of potential energy that exists within chemical bonds, and is released when those bonds are broken, is called chemical energy ([link](#)). Chemical energy is responsible for providing living cells with energy from food. The release of energy is brought about by breaking the molecular bonds within fuel molecules.

The molecules in gasoline (octane, the chemical formula shown) contain chemical energy within the chemical bonds. This energy is transformed into kinetic energy that allows a car to

race on a racetrack. (credit “car”: modification of work by Russell

Trow)  
Link to Learning

Visit this [site](#) and select “A simple pendulum” on the menu (under “Harmonic Motion”) to see the shifting kinetic (K) and potential energy (U) of a pendulum in motion.

## Free Energy

After learning that chemical reactions release energy when energy-storing bonds are broken, an important next question is how is the energy associated with chemical reactions quantified and expressed? How can the energy released from one reaction be compared to that of another reaction? A measurement of free energy is used to quantitate these energy transfers. Free energy is called Gibbs free energy (abbreviated with the letter G) after Josiah Willard Gibbs, the scientist who developed the measurement. Recall that according to the second law of thermodynamics, all energy transfers involve the loss of some amount of energy in an unusable form such as heat, resulting in entropy. Gibbs free energy specifically refers to the energy associated with a chemical reaction that is available after entropy is accounted for. In other words, Gibbs free energy is usable energy, or energy that is available to do work.

Every chemical reaction involves a change in free energy, called delta G ( $\Delta G$ ). The change in free energy can be calculated for any system that undergoes such a change, such as a chemical reaction. To calculate  $\Delta G$ , subtract the amount of energy lost to entropy (denoted as  $\Delta S$ ) from the total energy change of the system. This total energy change in the system is called enthalpy and is denoted as  $\Delta H$ . The formula for calculating  $\Delta G$  is as follows, where the symbol T refers to absolute temperature in Kelvin (degrees Celsius + 273):

$$\Delta G = \Delta H - T\Delta S$$

The standard free energy change of a chemical reaction is expressed as an amount of energy per mole of the reaction product (either in kilojoules or kilocalories, kJ/mol or kcal/mol; 1 kJ = 0.239 kcal) under standard pH, temperature, and pressure conditions. Standard pH, temperature, and pressure conditions are generally calculated at pH 7.0 in biological systems, 25 degrees Celsius, and 100 kilopascals (1 atm pressure), respectively. It is important to note that cellular conditions vary considerably from these standard conditions, and so standard calculated  $\Delta G$  values for biological reactions will be different inside the cell.

### **Endergonic Reactions and Exergonic Reactions**

If energy is released during a chemical reaction, then the resulting value from the above equation will be a negative number. In other words, reactions that release energy have a  $\Delta G < 0$ . A negative  $\Delta G$  also means that the products of the reaction have less free energy than the reactants, because they gave off some free energy during the reaction. Reactions that have a negative  $\Delta G$  and consequently release free energy are called exergonic reactions.

Think: *ex*ergonic means energy is *ex*iting the system. These reactions are also referred to as spontaneous reactions, because they can occur without the addition of energy into the system. Understanding which chemical reactions are spontaneous and release free energy is extremely useful for biologists, because these reactions can be harnessed to perform work inside the cell. An important distinction must be drawn between the term spontaneous and the idea of a chemical reaction that occurs immediately. Contrary to the everyday use of the term, a spontaneous reaction is not one that suddenly or quickly occurs. The rusting of iron is an example of a spontaneous reaction that occurs slowly, little by little, over time.

If a chemical reaction requires an input of energy rather than releasing energy, then the  $\Delta G$  for that reaction will be a positive value. In this case, the products have more free energy than the reactants. Thus, the products of these reactions can be thought of as energy-storing molecules. These chemical reactions are called endergonic reactions, and they are non-spontaneous. An endergonic reaction will not take place on its own without the addition of free energy.

Let's revisit the example of the synthesis and breakdown of the food molecule, glucose. Remember that the building of complex molecules, such as sugars, from simpler ones is an anabolic process and requires energy. Therefore, the chemical reactions involved in anabolic processes are endergonic reactions. On the other hand, the catabolic process of breaking sugar down into simpler molecules releases energy in a series of exergonic reactions. Like the example of rust above, the breakdown of sugar involves spontaneous reactions, but these reactions don't occur instantaneously. [\[link\]](#) shows some other examples of endergonic and exergonic reactions. Later sections will provide more information about what else is required to make even spontaneous reactions happen more efficiently.

#### **Art Connection**

Shown are some examples of endergonic processes (ones that require energy) and exergonic processes (ones that release energy). These include (a) a compost pile decomposing, (b) a chick hatching from a fertilized egg, (c) sand art being destroyed, and (d) a ball rolling down a hill. (credit a: modification of work by Natalie Maynor; credit b: modification of work by

USDA; credit c: modification of work by “Athlex”/Flickr; credit d: modification of work by

Harry Malsch)

Look at each of the processes shown, and decide if it is endergonic or exergonic. In each case, does enthalpy increase or decrease, and does entropy increase or decrease?

An important concept in the study of metabolism and energy is that of chemical equilibrium. Most chemical reactions are reversible. They can proceed in both directions, releasing energy into their environment in one direction, and absorbing it from the environment in the other direction ([link](#)). The same is true for the chemical reactions involved in cell metabolism, such as the breaking down and building up of proteins into and from individual amino acids, respectively. Reactants within a closed system will undergo chemical reactions in both directions until a state of equilibrium is reached. This state of equilibrium is one of the lowest possible free energy and a state of maximal entropy. Energy must be put into the system to push the reactants and products away from a state of equilibrium. Either reactants or products must be added, removed, or changed. If a cell were a closed system, its chemical reactions would reach equilibrium, and it would die because there would be insufficient free energy left to perform the work needed to maintain life. In a living cell, chemical reactions are constantly moving towards equilibrium, but never reach it. This is because a living cell is an open system. Materials pass in and out, the cell recycles the products of certain chemical reactions into other reactions, and chemical equilibrium is never reached. In this way, living organisms are in a constant energy-requiring, uphill battle against equilibrium and entropy. This constant supply of energy ultimately comes from sunlight, which is used to produce nutrients in the process of photosynthesis.

Exergonic and endergonic reactions result in changes in Gibbs free energy. Exergonic reactions release energy; endergonic reactions require energy to

proceed.

## Activation Energy

There is another important concept that must be considered regarding endergonic and exergonic reactions. Even exergonic reactions require a small amount of energy input to get going before they can proceed with their energy-releasing steps. These reactions have a net release of energy, but still require some energy in the beginning. This small amount of energy input necessary for all chemical reactions to occur is called the activation energy (or free energy of activation) and is abbreviated  $E_A$  ([link](#)).

Why would an energy-releasing, negative  $\Delta G$  reaction actually require some energy to proceed? The reason lies in the steps that take place during a chemical reaction. During chemical reactions, certain chemical bonds are broken and new ones are formed. For example, when a glucose molecule is broken down, bonds between the carbon atoms of the molecule are broken. Since these are energy-storing bonds, they release energy when broken. However, to get them into a state that allows the bonds to break, the molecule must be somewhat contorted. A small energy input is required to achieve this contorted state. This contorted state is called the transition state, and it is a high-energy, unstable state. For this reason, reactant molecules don't last long in their transition state, but very quickly proceed to

the next steps of the chemical reaction. Free energy diagrams illustrate the energy profiles for a given reaction. Whether the reaction is exergonic or endergonic determines whether the products in the diagram will exist at a lower or higher energy state than both the reactants and the products. However, regardless of this measure, the transition state of the reaction exists at a higher energy state than the reactants, and thus,  $E_A$  is always positive.

### Link to Learning

Watch an animation of the move from free energy to transition state at [this](#) site.

Where does the activation energy required by chemical reactants come from? The source of the activation energy needed to push reactions forward is typically heat energy from the surroundings. Heat energy (the total bond energy of reactants or products in a chemical reaction) speeds up the motion of molecules, increasing the frequency and force with which they collide; it also moves atoms and bonds within the molecule slightly, helping them reach their transition state. For this reason, heating up a system will cause chemical reactants within that system to react more frequently. Increasing the pressure on a system has the same effect. Once reactants have absorbed enough heat energy from their surroundings to reach the transition state, the reaction will proceed.

The activation energy of a particular reaction determines the rate at which it will proceed. The higher the activation energy, the slower the chemical reaction will be. The example of iron rusting illustrates an inherently slow reaction. This reaction occurs slowly over time because of its high  $E_A$ . Additionally, the burning of many fuels, which is strongly exergonic, will take place at a negligible rate unless their activation energy is overcome by sufficient heat from a spark. Once they begin to burn, however, the chemical reactions release enough heat to continue the burning process, supplying the activation energy for surrounding fuel molecules. Like these reactions outside of cells, the activation energy for most cellular reactions is too high for heat energy to overcome at efficient rates. In other words, in order for important cellular reactions to occur at appreciable rates (number of reactions per unit time), their activation energies must be lowered ([link](#)); this is referred to as catalysis. This is a very good thing as far as living cells are concerned. Important macromolecules, such as proteins, DNA, and RNA, store considerable energy, and their breakdown is exergonic. If cellular temperatures alone provided enough heat energy for these exergonic reactions to overcome their activation barriers, the essential components of a cell would disintegrate.

### Art Connection

Activation energy is the energy required for a reaction to proceed, and it is lower if the reaction is catalyzed. The horizontal axis of this diagram describes the sequence of events in

time.

If no activation energy were required to break down sucrose (table sugar), would you be able to store it in a sugar bowl?

## Section Summary

Energy comes in many different forms. Objects in motion do physical work, and kinetic energy is the energy of objects in motion. Objects that are not in motion may have the potential to do work, and thus, have potential energy. Molecules also have potential energy because the breaking of molecular bonds has the potential to release energy. Living cells depend on the harvesting of potential energy from molecular bonds to perform work. Free energy is a measure of energy that is available to do work. The free energy of a system changes during energy transfers such as chemical reactions, and this change is referred to as  $\Delta G$ .

The  $\Delta G$  of a reaction can be negative or positive, meaning that the reaction releases energy or consumes energy, respectively. A reaction with a negative  $\Delta G$  that gives off energy is called an exergonic reaction. One with a positive  $\Delta G$  that requires energy input is called an endergonic reaction. Exergonic reactions are said to be spontaneous, because their products have less energy than their reactants. The products of endergonic reactions have a higher energy state than the reactants, and so these are nonspontaneous reactions. However, all reactions (including spontaneous  $-\Delta G$  reactions) require an initial input of energy in order to reach the transition state, at which they'll proceed. This initial input of energy is called the activation energy.

## Art Connections

[\[link\]](#) Look at each of the processes shown, and decide if it is endergonic or exergonic. In each case, does enthalpy increase or decrease, and does entropy increase or decrease?

[\[link\]](#) A compost pile decomposing is an exergonic process; enthalpy increases (energy is released) and entropy increases (large molecules are broken down into smaller ones). A baby

developing from a fertilized egg is an endergonic process; enthalpy decreases (energy is absorbed) and entropy decreases. Sand art being destroyed is an exergonic process; there is no change in enthalpy, but entropy increases. A ball rolling downhill is an exergonic process; enthalpy decreases (energy is released), but there is no change in entropy.

[\[link\]](#) If no activation energy were required to break down sucrose (table sugar), would you be able to store it in a sugar bowl?

[\[link\]](#) No. We can store chemical energy because of the need to overcome the barrier to its breakdown.

## Review Questions

Consider a pendulum swinging. Which type(s) of energy is/are associated with the pendulum in the following instances: i. the moment at which it completes one cycle, just before it begins to fall back towards the other end, ii. the moment that it is in the middle between the two ends, iii. just before it reaches the end of one cycle (just before instant i.).

- i. potential and kinetic, ii. potential and kinetic, iii. kinetic
- i. potential, ii. potential and kinetic, iii. potential and kinetic
- i. potential, ii. kinetic, iii. potential and kinetic
- i. potential and kinetic, ii. kinetic iii. kinetic

C

Which of the following comparisons or contrasts between endergonic and exergonic reactions is false?

- Endergonic reactions have a positive  $\Delta G$  and exergonic reactions have a negative  $\Delta G$
- Endergonic reactions consume energy and exergonic reactions release energy
- Both endergonic and exergonic reactions require a small amount of energy to overcome an activation barrier
- Endergonic reactions take place slowly and exergonic reactions take place quickly

D

Which of the following is the best way to judge the relative activation energies between two given chemical reactions?

- Compare the  $\Delta G$  values between the two reactions
- Compare their reaction rates
- Compare their ideal environmental conditions
- Compare the spontaneity between the two reactions

B

## Free Response

Explain in your own words the difference between a spontaneous reaction and one that occurs instantaneously, and what causes this difference.

A spontaneous reaction is one that has a negative  $\Delta G$  and thus releases energy. However, a spontaneous reaction need not occur quickly or suddenly like an instantaneous reaction. It may occur over long periods due to a large energy of activation, which prevents the reaction from occurring quickly.

Describe the position of the transition state on a vertical energy scale, from low to high, relative to the position of the reactants and products, for both endergonic and exergonic reactions.

The transition state is always higher in energy than the reactants and the products of a reaction (therefore, above), regardless of whether the reaction is endergonic or exergonic.

## Glossary

activation energy

energy necessary for reactions to occur

chemical energy

potential energy in chemical bonds that is released when those bonds are broken

endergonic

describes chemical reactions that require energy input

enthalpy

total energy of a system

exergonic

describes chemical reactions that release free energy

free energy

Gibbs free energy is the usable energy, or energy that is available to do work.

heat energy

total bond energy of reactants or products in a chemical reaction

kinetic energy

type of energy associated with objects or particles in motion

potential energy

type of energy that has the potential to do work; stored energy

transition state

high-energy, unstable state (an intermediate form between the substrate and the product) occurring during a chemical reaction

ATP: Adenosine Triphosphate

By the end of this section, you will be able to:

- Explain the role of ATP as the cellular energy currency
- Describe how energy is released through hydrolysis of ATP

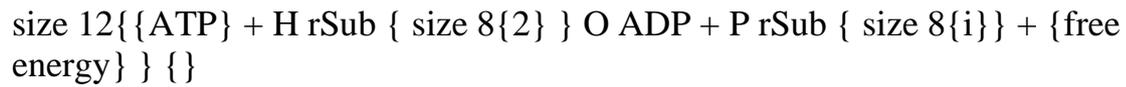
Even exergonic, energy-releasing reactions require a small amount of activation energy in order to proceed. However, consider endergonic reactions, which require much more energy input, because their products have more free energy than their

reactants. Within the cell, where does energy to power such reactions come from? The answer lies with an energy-supplying molecule called adenosine triphosphate, or ATP. ATP is a small, relatively simple molecule ([\[link\]](#)), but within some of its bonds, it contains the potential for a quick burst of energy that can be harnessed to perform cellular work. This molecule can be thought of as the primary energy currency of cells in much the same way that money is the currency that people exchange for things they need. ATP is used to power the majority of energy-requiring cellular reactions.

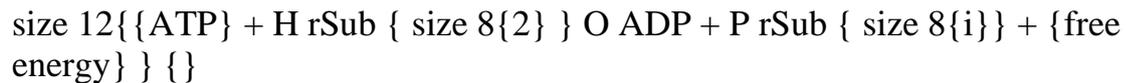
ATP is the primary energy currency of the cell. It has an adenosine backbone with three

phosphate groups attached.

As its name suggests, adenosine triphosphate is comprised of adenosine bound to three phosphate groups ([\[link\]](#)). Adenosine is a nucleoside consisting of the nitrogenous base adenine and a five-carbon sugar, ribose. The three phosphate groups, in order of closest to furthest from the ribose sugar, are labeled alpha, beta, and gamma. Together, these chemical groups constitute an energy powerhouse. However, not all bonds within this molecule exist in a particularly high-energy state. Both bonds that link the phosphates are equally high-energy bonds (phosphoanhydride bonds) that, when broken, release sufficient energy to power a variety of cellular reactions and processes. These high-energy bonds are the bonds between the second and third (or beta and gamma) phosphate groups and between the first and second phosphate groups. The reason that these bonds are considered “high-energy” is because the products of such bond breaking—adenosine diphosphate (ADP) and one inorganic phosphate group ( $P_i$ )—have considerably lower free energy than the reactants: ATP and a water molecule. Because this reaction takes place with the use of a water molecule, it is considered a hydrolysis reaction. In other words, ATP is hydrolyzed into ADP in the following reaction:



Like most chemical reactions, the hydrolysis of ATP to ADP is reversible. The reverse reaction regenerates ATP from ADP + P<sub>i</sub>. Indeed, cells rely on the regeneration of ATP just as people rely on the regeneration of spent money through some sort of income. Since ATP hydrolysis releases energy, ATP regeneration must require an input of free energy. The formation of ATP is expressed in this equation:



Two prominent questions remain with regard to the use of ATP as an energy source. Exactly how much free energy is released with the hydrolysis of ATP, and how is that free energy used to do cellular work? The calculated  $\Delta G$  for the hydrolysis of one mole of ATP into ADP and P<sub>i</sub> is  $-7.3$  kcal/mole ( $-30.5$  kJ/mol). Since this calculation is true under standard conditions, it would be expected that a different value exists under cellular conditions. In fact, the  $\Delta G$  for the hydrolysis of one mole of ATP in a living cell is almost double the value at standard conditions:  $-14$  kcal/mol ( $-57$  kJ/mol).

ATP is a highly unstable molecule. Unless quickly used to perform work, ATP spontaneously dissociates into ADP + P<sub>i</sub>, and the free energy released during this process is lost as heat. The second question posed above, that is, how the energy released by ATP hydrolysis is used to perform work inside the cell, depends on a strategy called energy coupling. Cells couple the exergonic reaction of ATP hydrolysis with endergonic reactions, allowing them to proceed. One example of energy coupling using ATP involves a transmembrane ion pump that is extremely important for cellular function. This sodium-potassium pump (Na<sup>+</sup>/K<sup>+</sup> pump) drives sodium out of the cell and potassium into the cell ([link](#)). A large percentage of a cell's ATP is spent powering this pump, because cellular processes bring a great deal of sodium into the cell and potassium out of the cell. The pump works constantly to stabilize cellular concentrations of sodium and potassium. In order for the pump to turn one cycle (exporting three Na<sup>+</sup> ions and importing two K<sup>+</sup> ions), one molecule of ATP must be hydrolyzed. When ATP is hydrolyzed, its gamma phosphate doesn't simply float away, but is actually transferred onto the pump protein. This process of a phosphate group binding to a molecule is called phosphorylation. As with most cases of ATP hydrolysis, a phosphate from ATP is transferred onto another molecule. In a phosphorylated state, the Na<sup>+</sup>/K<sup>+</sup> pump has more free energy and is triggered to undergo a conformational change. This change allows it to release Na<sup>+</sup> to the outside of the cell. It then binds extracellular K<sup>+</sup>, which, through another conformational change, causes the phosphate to detach from the pump. This release of phosphate triggers the K<sup>+</sup> to be released to the inside of the cell. Essentially, the energy released from the hydrolysis of ATP is

coupled with the energy required to power the pump and transport  $\text{Na}^+$  and  $\text{K}^+$  ions. ATP performs cellular work using this basic form of energy coupling through phosphorylation.

#### Art Connection

The sodium-potassium pump is an example of energy coupling. The energy derived from exergonic ATP hydrolysis is used to pump sodium and potassium

ions across the cell membrane.

The hydrolysis of one ATP molecule releases 7.3 kcal/mol of energy ( $\Delta G = -7.3$  kcal/mol of energy). If it takes 2.1 kcal/mol of energy to move one  $\text{Na}^+$  across the membrane ( $\Delta G = +2.1$  kcal/mol of energy), how many sodium ions could be moved by the hydrolysis of one ATP molecule?

Often during cellular metabolic reactions, such as the synthesis and breakdown of nutrients, certain molecules must be altered slightly in their conformation to become substrates for the next step in the reaction series. One example is during the very first steps of cellular respiration, when a molecule of the sugar glucose is broken down in the process of glycolysis. In the first step of this process, ATP is required for the phosphorylation of glucose, creating a high-energy but unstable intermediate. This phosphorylation reaction powers a conformational change that allows the phosphorylated glucose molecule to be converted to the phosphorylated sugar fructose. Fructose is a necessary intermediate for glycolysis to move forward. Here, the exergonic reaction of ATP hydrolysis is coupled with the endergonic reaction of converting glucose into a phosphorylated intermediate in the pathway. Once again, the energy released by breaking a phosphate bond within ATP was used for the phosphorylation of another molecule, creating an unstable intermediate and powering an important conformational change.

Link to Learning

See an interactive animation of the ATP-producing glycolysis process at this [site](#).

## Section Summary

ATP is the primary energy-supplying molecule for living cells. ATP is made up of a nucleotide, a five-carbon sugar, and three phosphate groups. The bonds that connect the phosphates (phosphoanhydride bonds) have high-energy content. The energy released from the hydrolysis of ATP into ADP + P<sub>i</sub> is used to perform cellular work. Cells use ATP to perform work by coupling the exergonic reaction of ATP hydrolysis with endergonic reactions. ATP donates its phosphate group to another molecule via a process known as phosphorylation. The phosphorylated molecule is at a higher-energy state and is less stable than its unphosphorylated form, and this added energy from the addition of the phosphate allows the molecule to undergo its endergonic reaction.

## Art Connections

[\[link\]](#) The hydrolysis of one ATP molecule releases 7.3 kcal/mol of energy ( $\Delta G = -7.3$  kcal/mol of energy). If it takes 2.1 kcal/mol of energy to move one Na<sup>+</sup> across the membrane ( $\Delta G = +2.1$  kcal/mol of energy), how many sodium ions could be moved by the hydrolysis of one ATP molecule?

[\[link\]](#) Three sodium ions could be moved by the hydrolysis of one ATP molecule. The  $\Delta G$  of the coupled reaction must be negative. Movement of three sodium ions across the membrane will take 6.3 kcal of energy ( $2.1 \text{ kcal} \times 3 \text{ Na}^+ \text{ ions} = 6.3 \text{ kcal}$ ). Hydrolysis of ATP provides 7.3 kcal of energy, more than enough to power this reaction. Movement of four sodium ions across the membrane, however, would require 8.4 kcal of energy, more than one ATP molecule can provide.

## Review Questions

The energy released by the hydrolysis of ATP is

- primarily stored between the alpha and beta phosphates
- equal to  $-57$  kcal/mol
- harnessed as heat energy by the cell to perform work
- providing energy to coupled reactions

D

Which of the following molecules is likely to have the most potential energy?

- a. sucrose
- b. ATP
- c. glucose
- d. ADP

A

## Free Response

Do you think that the  $E_A$  for ATP hydrolysis is relatively low or high? Explain your reasoning.

The activation energy for hydrolysis is very low. Not only is ATP hydrolysis an exergonic process with a large  $-\Delta G$ , but ATP is also a very unstable molecule that rapidly breaks down into  $ADP + P_i$  if not utilized quickly. This suggests a very low  $E_A$  since it hydrolyzes so quickly.

## Glossary

ATP

adenosine triphosphate, the cell's energy currency  
phosphoanhydride bond

bond that connects phosphates in an ATP molecule

Enzymes

By the end of this section, you will be able to:

- Describe the role of enzymes in metabolic pathways
- Explain how enzymes function as molecular catalysts
- Discuss enzyme regulation by various factors

A substance that helps a chemical reaction to occur is a catalyst, and the special molecules that catalyze biochemical reactions are called enzymes. Almost all enzymes are proteins, made up of chains of amino acids, and they perform the critical task of lowering the activation energies of chemical reactions inside the cell. Enzymes do this by binding to the reactant molecules, and holding them in such a way as to make the chemical bond-breaking and bond-forming processes take place more readily. It is important to remember that enzymes don't change the  $\Delta G$  of a reaction. In other words, they don't change whether a reaction is exergonic (spontaneous) or endergonic. This is because they don't change the free energy of the reactants or products. They only reduce the activation energy required to reach the transition state ([\[link\]](#)).

Enzymes lower the activation energy of the reaction but do not change the free energy of the

reaction.

### **Enzyme Active Site and Substrate Specificity**

The chemical reactants to which an enzyme binds are the enzyme's substrates. There may be one or more substrates, depending on the particular chemical reaction. In some reactions, a single-reactant substrate is broken down into multiple products. In others, two substrates may come together to create one larger molecule. Two reactants might also enter a reaction, both become modified, and leave the reaction as two products. The location within the enzyme where the substrate binds is called the enzyme's active site. The active site is where the "action" happens, so to speak. Since enzymes are proteins, there is a unique combination of amino acid residues (also called side chains, or R groups) within the active site. Each residue is characterized by different properties. Residues can be large or small, weakly acidic or basic, hydrophilic or hydrophobic, positively or negatively charged, or neutral. The unique combination of amino acid residues, their positions, sequences, structures, and properties, creates a very specific chemical environment within the active site. This specific environment is suited to bind, albeit briefly, to a specific chemical substrate (or substrates). Due to this jigsaw puzzle-like match between an enzyme and its substrates (which adapts to find the best fit between the transition state and the active site), enzymes are known for their specificity. The "best fit" results from the shape and the amino acid functional group's attraction to the substrate. There is a specifically matched enzyme for each substrate and, thus, for each chemical reaction; however, there is flexibility as well.

The fact that active sites are so perfectly suited to provide specific environmental conditions also means that they are subject to influences by the local environment. It is true that increasing the environmental temperature generally increases reaction rates, enzyme-catalyzed or otherwise. However, increasing or decreasing the temperature outside of an optimal range can affect chemical bonds within the active site in such a way that they are less well suited to bind substrates. High temperatures will eventually cause enzymes, like other biological molecules, to denature, a process that changes the natural properties of a substance. Likewise, the pH of the local environment can also affect enzyme function. Active site amino acid residues have their own acidic or basic properties that are optimal for catalysis. These residues are sensitive to changes in pH that can impair the way substrate molecules bind.

Enzymes are suited to function best within a certain pH range, and, as with temperature, extreme pH values (acidic or basic) of the environment can cause enzymes to denature.

### **Induced Fit and Enzyme Function**

For many years, scientists thought that enzyme-substrate binding took place in a simple “lock-and-key” fashion. This model asserted that the enzyme and substrate fit together perfectly in one instantaneous step. However, current research supports a more refined view called induced fit ([link](#)). The induced-fit model expands upon the lock-and-key model by describing a more dynamic interaction between enzyme and substrate. As the enzyme and substrate come together, their interaction causes a mild shift in the enzyme’s structure that confirms an ideal binding arrangement between the enzyme and the transition state of the substrate. This ideal binding maximizes the enzyme’s ability to catalyze its reaction.

Link to Learning

View an animation of induced fit at [this website](#).

When an enzyme binds its substrate, an enzyme-substrate complex is formed. This complex lowers the activation energy of the reaction and promotes its rapid progression in one of many ways. On a basic level, enzymes promote chemical reactions that involve more than one substrate by bringing the substrates together in an optimal orientation. The appropriate region (atoms and bonds) of one molecule is juxtaposed to the appropriate region of the other molecule with which it must react. Another way in which enzymes promote the reaction of their substrates is by creating an optimal environment within the active site for the reaction to occur. Certain chemical reactions might proceed best in a slightly acidic or non-polar environment. The chemical properties that emerge from the particular arrangement of amino acid residues within an active site create the perfect environment for an enzyme’s specific substrates to react.

You’ve learned that the activation energy required for many reactions includes the energy involved in manipulating or slightly contorting chemical bonds so that they can easily break and allow others to reform. Enzymatic action can aid this process. The enzyme-substrate complex can lower the activation energy by contorting substrate molecules in such a way as to facilitate bond-breaking, helping to reach the transition state. Finally, enzymes can also lower activation energies by taking part in the chemical reaction itself. The amino acid residues can provide certain ions or chemical groups that actually form covalent bonds with substrate molecules as a necessary step of the reaction process. In these cases, it is important to remember that the enzyme will always return to its original state at the completion of the reaction. One of the hallmark properties of enzymes is that they remain ultimately unchanged by the reactions they catalyze. After an enzyme is done catalyzing a reaction, it releases its product(s).

According to the induced-fit model, both enzyme and substrate undergo dynamic conformational changes upon binding. The enzyme contorts the substrate into its transition state, thereby increasing the rate of the

reaction.

## **Control of Metabolism Through Enzyme Regulation**

It would seem ideal to have a scenario in which all of the enzymes encoded in an organism's genome existed in abundant supply and functioned optimally under all cellular conditions, in all cells, at all times. In reality, this is far from the case. A variety of mechanisms ensure that this does not happen. Cellular needs and conditions vary from cell to cell, and change within individual cells over time. The required enzymes and energetic demands of stomach cells are different from those of fat storage cells, skin cells, blood cells, and nerve cells. Furthermore, a digestive cell works much harder to process and break down nutrients during the time that closely follows a meal compared with many hours after a meal. As these cellular demands and conditions vary, so do the amounts and functionality of different enzymes.

Since the rates of biochemical reactions are controlled by activation energy, and enzymes lower and determine activation energies for chemical reactions, the relative amounts and functioning of the variety of enzymes within a cell ultimately determine which reactions will proceed and at which rates. This determination is tightly controlled. In certain cellular environments, enzyme activity is partly controlled by environmental factors, like pH and temperature. There are other mechanisms through which cells control the activity of enzymes and determine the rates at which various biochemical reactions will occur.

## Regulation of Enzymes by Molecules

Enzymes can be regulated in ways that either promote or reduce their activity. There are many different kinds of molecules that inhibit or promote enzyme function, and various mechanisms exist for doing so. In some cases of enzyme inhibition, for example, an inhibitor molecule is similar enough to a substrate that it can bind to the active site and simply block the substrate from binding. When this happens, the enzyme is inhibited through competitive inhibition, because an inhibitor molecule competes with the substrate for active site binding ([link](#)). On the other hand, in noncompetitive inhibition, an inhibitor molecule binds to the enzyme in a location other than an allosteric site and still manages to block substrate binding to the active site.

Competitive and noncompetitive inhibition affect the rate of reaction differently. Competitive inhibitors affect the initial rate but do not affect the maximal rate, whereas noncompetitive

inhibitors affect the maximal rate.

Some inhibitor molecules bind to enzymes in a location where their binding induces a conformational change that reduces the affinity of the enzyme for its substrate. This type of inhibition is called allosteric inhibition ([link](#)). Most allosterically regulated enzymes are made up of more than one polypeptide, meaning that they have more than one protein subunit. When an allosteric inhibitor binds to an enzyme, all active sites on the protein subunits are changed slightly such that they bind their substrates with less efficiency. There are allosteric activators as well as inhibitors. Allosteric activators bind to locations on an enzyme away from the active site, inducing a conformational change that increases the affinity of the enzyme's active site(s) for its substrate(s).

Allosteric inhibitors modify the active site of the enzyme so that substrate binding is reduced or prevented. In contrast, allosteric activators modify the active site of the enzyme so that the

affinity for the substrate

increases.

Everyday Connection

Have you ever wondered how pharmaceutical drugs are developed? (credit: Deborah

Austin)

Drug Discovery by Looking for Inhibitors of Key Enzymes in Specific Pathways Enzymes are key components of metabolic pathways. Understanding how enzymes work and how they can be regulated is a key principle behind the development of many of the pharmaceutical drugs ([link](#)) on the market today. Biologists working in this field collaborate with other scientists, usually chemists, to design drugs.

Consider statins for example—which is the name given to the class of drugs that reduces cholesterol levels. These compounds are essentially inhibitors of the enzyme HMG-CoA

reductase. HMG-CoA reductase is the enzyme that synthesizes cholesterol from lipids in the body. By inhibiting this enzyme, the levels of cholesterol synthesized in the body can be reduced. Similarly, acetaminophen, popularly marketed under the brand name Tylenol, is an inhibitor of the enzyme cyclooxygenase. While it is effective in providing relief from fever and inflammation (pain), its mechanism of action is still not completely understood.

How are drugs developed? One of the first challenges in drug development is identifying the specific molecule that the drug is intended to target. In the case of statins, HMG-CoA reductase is the drug target. Drug targets are identified through painstaking research in the laboratory. Identifying the target alone is not sufficient; scientists also need to know how the target acts inside the cell and which reactions go awry in the case of disease. Once the target and the pathway are identified, then the actual process of drug design begins. During this stage, chemists and biologists work together to design and synthesize molecules that can either block or activate a particular reaction. However, this is only the beginning: both if and when a drug prototype is successful in performing its function, then it must undergo many tests from in vitro experiments to clinical trials before it can get FDA approval to be on the market.

Many enzymes don't work optimally, or even at all, unless bound to other specific non-protein helper molecules, either temporarily through ionic or hydrogen bonds or permanently through stronger covalent bonds. Two types of helper molecules are cofactors and coenzymes. Binding to these molecules promotes optimal conformation and function for their respective enzymes. Cofactors are inorganic ions such as iron ( $\text{Fe}^{++}$ ) and magnesium ( $\text{Mg}^{++}$ ). One example of an enzyme that requires a metal ion as a cofactor is the enzyme that builds DNA molecules, DNA polymerase, which requires bound zinc ion ( $\text{Zn}^{++}$ ) to function. Coenzymes are organic helper molecules, with a basic atomic structure made up of carbon and hydrogen, which are required for enzyme action. The most common sources of coenzymes are dietary vitamins ([link](#)). Some vitamins are precursors to coenzymes and others act directly as coenzymes. Vitamin C is a coenzyme for multiple enzymes that take part in building the important connective tissue component, collagen. An important step in the breakdown of glucose to yield energy is catalysis by a multi-enzyme complex called pyruvate dehydrogenase. Pyruvate dehydrogenase is a complex of several enzymes that actually requires one cofactor (a magnesium ion) and five different organic coenzymes to catalyze its specific chemical reaction. Therefore, enzyme function is, in part, regulated by an abundance of various cofactors and coenzymes, which are supplied primarily by the diets of most organisms.

Vitamins are important coenzymes or precursors of coenzymes, and are required for enzymes to function properly. Multivitamin capsules usually contain mixtures of all the vitamins at

different percentages.

### **Enzyme Compartmentalization**

In eukaryotic cells, molecules such as enzymes are usually compartmentalized into different organelles. This allows for yet another level of regulation of enzyme activity. Enzymes required only for certain cellular processes can be housed separately along with their substrates, allowing for more efficient chemical reactions. Examples of this sort of enzyme regulation based on location and proximity include the enzymes involved in the latter stages of cellular respiration, which take place exclusively in the mitochondria, and the enzymes involved in the digestion of cellular debris and foreign materials, located within lysosomes.

### **Feedback Inhibition in Metabolic Pathways**

Molecules can regulate enzyme function in many ways. A major question remains, however: What are these molecules and where do they come from? Some are cofactors and coenzymes, ions, and organic molecules, as you've learned. What other molecules in the cell provide enzymatic regulation, such as allosteric modulation, and competitive and noncompetitive inhibition? The answer is that a wide variety of molecules can perform these roles. Some of these molecules include pharmaceutical and non-pharmaceutical drugs, toxins, and poisons from the environment. Perhaps the most relevant sources of enzyme regulatory molecules, with respect to cellular metabolism, are the products of the cellular metabolic reactions themselves. In a most efficient and elegant way, cells have evolved to use the products of their own reactions for feedback inhibition of enzyme activity. Feedback inhibition involves the use of a reaction product to regulate its own further production ([link](#)). The cell responds to the abundance of specific products by slowing down production during anabolic or

catabolic reactions. Such reaction products may inhibit the enzymes that catalyzed their production through the mechanisms described above.

Metabolic pathways are a series of reactions catalyzed by multiple enzymes. Feedback inhibition, where the end product of the pathway inhibits an upstream step, is an important regulatory mechanism in

cells.

The production of both amino acids and nucleotides is controlled through feedback inhibition. Additionally, ATP is an allosteric regulator of some of the enzymes involved in the catabolic breakdown of sugar, the process that produces ATP. In this way, when ATP is abundant, the cell can prevent its further production. Remember that ATP is an unstable molecule that can spontaneously dissociate into ADP. If too much ATP were present in a cell, much of it would go to waste. On the other hand, ADP serves as a positive allosteric regulator (an allosteric activator) for some of the same enzymes that are inhibited by ATP. Thus, when relative levels of ADP are high compared to ATP, the cell is triggered to produce more ATP through the catabolism of sugar.

## **Section Summary**

Enzymes are chemical catalysts that accelerate chemical reactions at physiological temperatures by lowering their activation energy. Enzymes are usually proteins consisting of one or more polypeptide chains. Enzymes have an active site that provides a unique chemical environment, made up of certain amino acid R groups (residues). This unique environment is

perfectly suited to convert particular chemical reactants for that enzyme, called substrates, into unstable intermediates called transition states. Enzymes and substrates are thought to bind with an induced fit, which means that enzymes undergo slight conformational adjustments upon substrate contact, leading to full, optimal binding. Enzymes bind to substrates and catalyze reactions in four different ways: bringing substrates together in an optimal orientation, compromising the bond structures of substrates so that bonds can be more easily broken, providing optimal environmental conditions for a reaction to occur, or participating directly in their chemical reaction by forming transient covalent bonds with the substrates.

Enzyme action must be regulated so that in a given cell at a given time, the desired reactions are being catalyzed and the undesired reactions are not. Enzymes are regulated by cellular conditions, such as temperature and pH. They are also regulated through their location within a cell, sometimes being compartmentalized so that they can only catalyze reactions under certain circumstances. Inhibition and activation of enzymes via other molecules are other important ways that enzymes are regulated. Inhibitors can act competitively, noncompetitively, or allosterically; noncompetitive inhibitors are usually allosteric. Activators can also enhance the function of enzymes allosterically. The most common method by which cells regulate the enzymes in metabolic pathways is through feedback inhibition. During feedback inhibition, the products of a metabolic pathway serve as inhibitors (usually allosteric) of one or more of the enzymes (usually the first committed enzyme of the pathway) involved in the pathway that produces them.

## Review Questions

Which of the following is not true about enzymes:

- They increase  $\Delta G$  of reactions
- They are usually made of amino acids
- They lower the activation energy of chemical reactions
- Each one is specific to the particular substrate(s) to which it binds

A

An allosteric inhibitor does which of the following?

- Binds to an enzyme away from the active site and changes the conformation of the active site, increasing its affinity for substrate binding
- Binds to the active site and blocks it from binding substrate
- Binds to an enzyme away from the active site and changes the conformation of the active site, decreasing its affinity for the substrate
- Binds directly to the active site and mimics the substrate

C

Which of the following analogies best describe the induced-fit model of enzyme-substrate binding?

- A hug between two people
- A key fitting into a lock

- c. A square peg fitting through the square hole and a round peg fitting through the round hole of a children's toy
- d. The fitting together of two jigsaw puzzle pieces.

A

## Free Response

With regard to enzymes, why are vitamins necessary for good health? Give examples.

Most vitamins and minerals act as coenzymes and cofactors for enzyme action. Many enzymes require the binding of certain cofactors or coenzymes to be able to catalyze their reactions. Since enzymes catalyze many important reactions, it is critical to obtain sufficient vitamins and minerals from the diet and from supplements. Vitamin C (ascorbic acid) is a coenzyme necessary for the action of enzymes that build collagen, an important protein component of connective tissue throughout the body. Magnesium ion ( $Mg^{++}$ ) is an important cofactor that is necessary for the enzyme pyruvate dehydrogenase to catalyze part of the pathway that breaks down sugar to produce energy. Vitamins cannot be produced in the human body and therefore must be obtained in the diet.

Explain in your own words how enzyme feedback inhibition benefits a cell.

Feedback inhibition allows cells to control the amounts of metabolic products produced. If there is too much of a particular product relative to what the cell's needs, feedback inhibition effectively causes the cell to decrease production of that particular product. In general, this reduces the production of superfluous products and conserves energy, maximizing energy efficiency.

## Glossary

active site

specific region of the enzyme to which the substrate binds

allosteric inhibition

inhibition by a binding event at a site different from the active site, which induces a conformational change and reduces the affinity of the enzyme for its substrate

coenzyme

small organic molecule, such as a vitamin or its derivative, which is required to enhance the activity of an enzyme

cofactor

inorganic ion, such as iron and magnesium ions, required for optimal regulation of enzyme activity

competitive inhibition

type of inhibition in which the inhibitor competes with the substrate molecule by binding to the active site of the enzyme

denature

process that changes the natural properties of a substance

feedback inhibition

effect of a product of a reaction sequence to decrease its further production by inhibiting the activity of the first enzyme in the pathway that produces it

induced fit

dynamic fit between the enzyme and its substrate, in which both components modify their structures to allow for ideal binding

substrate

molecule on which the enzyme acts

Introduction

class="introduction" class="summary" title="Sections Summary" class="art-exercise" title="Art Connections" class="multiple-choice" title="Multiple Choice" class="free-response" title="Free Response" This geothermal energy plant transforms thermal energy from deep in the ground into electrical energy, which can be easily used. (credit: modification of work by the U.S. Department of

Defense)

The electrical energy plant in [\[link\]](#) converts energy from one form to another form that can be more easily used. This type of generating plant starts with underground thermal energy (heat) and transforms it into electrical energy that will be transported to homes and factories. Like a generating plant, plants and animals also must take in energy from the environment and convert it into a form that their cells can use. Energy enters an organism's body in one form and is converted into another form that can fuel the organism's life functions. In the process of photosynthesis, plants and other photosynthetic producers take in energy in the form of light (solar energy) and convert it into chemical energy, glucose, which

stores this energy in its chemical bonds. Then, a series of metabolic pathways, collectively called cellular respiration, extracts the energy from the bonds in glucose and converts it into a form that all living things can use—both producers, such as plants, and consumers, such as animals.

### Oxidation of Pyruvate and the Citric Acid Cycle

By the end of this section, you will be able to:

- Explain how a circular pathway, such as the citric acid cycle, fundamentally differs from a linear pathway, such as glycolysis
- Describe how pyruvate, the product of glycolysis, is prepared for entry into the citric acid cycle

If oxygen is available, aerobic respiration will go forward. In eukaryotic cells, the pyruvate molecules produced at the end of glycolysis are transported into mitochondria, which are the sites of cellular respiration. There, pyruvate will be transformed into an acetyl group that will be picked up and activated by a carrier compound called coenzyme A (CoA). The resulting compound is called acetyl CoA. CoA is made from vitamin B5, pantothenic acid. Acetyl CoA can be used in a variety of ways by the cell, but its major function is to deliver the acetyl group derived from pyruvate to the next stage of the pathway in glucose catabolism.

### Breakdown of Pyruvate

In order for pyruvate, the product of glycolysis, to enter the next pathway, it must undergo several changes. The conversion is a three-step process ([link](#)).

Step 1. A carboxyl group is removed from pyruvate, releasing a molecule of carbon dioxide into the surrounding medium. The result of this step is a two-carbon hydroxyethyl group bound to the enzyme (pyruvate dehydrogenase). This is the first of the six carbons from the original glucose molecule to be removed. This step proceeds twice (remember: there are *two* pyruvate molecules produced at the end of glycolysis) for every molecule of glucose metabolized; thus, two of the six carbons will have been removed at the end of both steps.

Step 2. The hydroxyethyl group is oxidized to an acetyl group, and the electrons are picked up by  $\text{NAD}^+$ , forming NADH. The high-energy electrons from NADH will be used later to generate ATP.

Step 3. The enzyme-bound acetyl group is transferred to CoA, producing a molecule of acetyl CoA.

Upon entering the mitochondrial matrix, a multi-enzyme complex converts pyruvate into acetyl CoA. In the process, carbon dioxide is released and one molecule of NADH is

formed.

Note that during the second stage of glucose metabolism, whenever a carbon atom is removed, it is bound to two oxygen atoms, producing carbon dioxide, one of the major end products of cellular respiration.

## **Acetyl CoA to CO<sub>2</sub>**

In the presence of oxygen, acetyl CoA delivers its acetyl group to a four-carbon molecule, oxaloacetate, to form citrate, a six-carbon molecule with three carboxyl groups; this pathway will harvest the remainder of the extractable energy from what began as a glucose molecule. This single pathway is called by different names: the citric acid cycle (for the first intermediate formed—citric acid, or citrate—when acetate joins to the oxaloacetate), the TCA cycle (since citric acid or citrate and isocitrate are tricarboxylic acids), and the Krebs cycle, after Hans Krebs, who first identified the steps in the pathway in the 1930s in pigeon flight muscles.

## **Citric Acid Cycle**

Like the conversion of pyruvate to acetyl CoA, the citric acid cycle takes place in the matrix of mitochondria. Almost all of the enzymes of the citric acid cycle are soluble, with the single exception of the enzyme succinate dehydrogenase, which is embedded in the inner membrane of the mitochondrion. Unlike glycolysis, the citric acid cycle is a closed loop: The last part of the pathway regenerates the compound used in the first step. The eight steps of the cycle are a series of redox, dehydration, hydration, and decarboxylation reactions that produce two carbon dioxide molecules, one GTP/ATP, and reduced forms of NADH and FADH<sub>2</sub> ([link](#)). This is considered an aerobic pathway because the NADH and FADH<sub>2</sub> produced must transfer their electrons to the next pathway in the system, which will use oxygen. If this transfer does not occur, the oxidation steps of the citric acid cycle also do not occur. Note that the citric acid cycle produces very little ATP directly and does not directly consume oxygen.

In the citric acid cycle, the acetyl group from acetyl CoA is attached to a four-carbon oxaloacetate molecule to form a six-carbon citrate molecule. Through a series of steps, citrate is oxidized, releasing two carbon dioxide molecules for each acetyl group fed into the cycle. In the process, three  $\text{NAD}^+$  molecules are reduced to NADH, one FAD molecule is reduced to  $\text{FADH}_2$ , and one ATP or GTP (depending on the cell type) is produced (by substrate-level phosphorylation). Because the final product of the citric acid cycle is also the first reactant, the cycle runs continuously in the presence of sufficient reactants. (credit: modification of work by “Yikrazuul”/Wikimedia)

Commons)

### **Steps in the Citric Acid Cycle**

Step 1. Prior to the start of the first step, a transitional phase occurs during which pyruvic acid is converted to acetyl CoA. Then, the first step of the cycle begins: This is a condensation step, combining the two-carbon acetyl group with a four-carbon oxaloacetate molecule to form a six-carbon molecule of citrate. CoA is bound to a sulfhydryl group (-SH) and diffuses away to eventually combine with another acetyl group. This step is irreversible because it is highly exergonic. The rate of this reaction is controlled by negative feedback and the amount of ATP available. If ATP levels increase, the rate of this reaction decreases. If ATP is in short supply, the rate increases.

Step 2. In step two, citrate loses one water molecule and gains another as citrate is converted into its isomer, isocitrate.

Step 3. In step three, isocitrate is oxidized, producing a five-carbon molecule,  $\alpha$ -ketoglutarate, together with a molecule of  $\text{CO}_2$  and two electrons, which reduce  $\text{NAD}^+$  to NADH. This step is also regulated by negative feedback from ATP and NADH, and a positive effect of ADP.

Steps 3 and 4. Steps three and four are both oxidation and decarboxylation steps, which release electrons that reduce  $\text{NAD}^+$  to NADH and release carboxyl groups that form  $\text{CO}_2$  molecules.  $\alpha$ -Ketoglutarate is the product of step three, and a succinyl group is the product of step four. CoA binds the succinyl group to form succinyl CoA. The enzyme that catalyzes step four is regulated by feedback inhibition of ATP, succinyl CoA, and NADH.

Step 5. In step five, a phosphate group is substituted for coenzyme A, and a high-energy bond is formed. This energy is used in substrate-level phosphorylation (during the conversion of the succinyl group to succinate) to form either guanine triphosphate (GTP) or ATP. There are two forms of the enzyme, called isoenzymes, for this step, depending upon the type of animal tissue in which they are found. One form is found in tissues that use large amounts of ATP, such as heart and skeletal muscle. This form produces ATP. The second form of the enzyme is found in tissues that have a high number of anabolic pathways, such as liver. This form produces GTP. GTP is energetically equivalent to ATP; however, its use is more restricted. In particular, protein synthesis primarily uses GTP.

Step 6. Step six is a dehydration process that converts succinate into fumarate. Two hydrogen atoms are transferred to FAD, producing  $\text{FADH}_2$ . The energy contained in the electrons of these atoms is insufficient to reduce  $\text{NAD}^+$  but adequate to reduce FAD. Unlike NADH, this carrier remains attached to the enzyme and transfers the electrons to the electron transport chain directly. This process is made possible by the localization of the enzyme catalyzing this step inside the inner membrane of the mitochondrion.

Step 7. Water is added to fumarate during step seven, and malate is produced. The last step in the citric acid cycle regenerates oxaloacetate by oxidizing malate. Another molecule of NADH is produced in the process.

Link to Learning

Click through each step of the citric acid cycle [here](#).

### **Products of the Citric Acid Cycle**

Two carbon atoms come into the citric acid cycle from each acetyl group, representing four out of the six carbons of one glucose molecule. Two carbon dioxide molecules are released on each turn of the cycle; however, these do not necessarily contain the most recently added carbon atoms. The two acetyl carbon atoms will eventually be released on later turns of the cycle; thus, all six carbon atoms from the original glucose molecule are eventually incorporated into carbon dioxide. Each turn of the cycle forms three NADH molecules and

one FADH<sub>2</sub> molecule. These carriers will connect with the last portion of aerobic respiration to produce ATP molecules. One GTP or ATP is also made in each cycle. Several of the intermediate compounds in the citric acid cycle can be used in synthesizing non-essential amino acids; therefore, the cycle is amphibolic (both catabolic and anabolic).

## Section Summary

In the presence of oxygen, pyruvate is transformed into an acetyl group attached to a carrier molecule of coenzyme A. The resulting acetyl CoA can enter several pathways, but most often, the acetyl group is delivered to the citric acid cycle for further catabolism. During the conversion of pyruvate into the acetyl group, a molecule of carbon dioxide and two high-energy electrons are removed. The carbon dioxide accounts for two (conversion of two pyruvate molecules) of the six carbons of the original glucose molecule. The electrons are picked up by NAD<sup>+</sup>, and the NADH carries the electrons to a later pathway for ATP production. At this point, the glucose molecule that originally entered cellular respiration has been completely oxidized. Chemical potential energy stored within the glucose molecule has been transferred to electron carriers or has been used to synthesize a few ATPs.

The citric acid cycle is a series of redox and decarboxylation reactions that remove high-energy electrons and carbon dioxide. The electrons temporarily stored in molecules of NADH and FADH<sub>2</sub> are used to generate ATP in a subsequent pathway. One molecule of either GTP or ATP is produced by substrate-level phosphorylation on each turn of the cycle. There is no comparison of the cyclic pathway with a linear one.

## Review Questions

What is removed from pyruvate during its conversion into an acetyl group?

- oxygen
- ATP
- B vitamin
- carbon dioxide

D

What do the electrons added to NAD<sup>+</sup> do?

- They become part of a fermentation pathway.
- They go to another pathway for ATP production.
- They energize the entry of the acetyl group into the citric acid cycle.
- They are converted to NADP.

B

GTP or ATP is produced during the conversion of \_\_\_\_\_.

- isocitrate into  $\alpha$ -ketoglutarate
- succinyl CoA into succinate
- fumarate into malate
- malate into oxaloacetate

B

How many NADH molecules are produced on each turn of the citric acid cycle?

- a. one
- b. two
- c. three
- d. four

C

### Free Response

What is the primary difference between a circular pathway and a linear pathway?

In a circular pathway, the final product of the reaction is also the initial reactant. The pathway is self-perpetuating, as long as any of the intermediates of the pathway are supplied. Circular pathways are able to accommodate multiple entry and exit points, thus being particularly well suited for amphibolic pathways. In a linear pathway, one trip through the pathway completes the pathway, and a second trip would be an independent event.

### Glossary

acetyl CoA

combination of an acetyl group derived from pyruvic acid and coenzyme A, which is made from pantothenic acid (a B-group vitamin)

citric acid cycle

(also, Krebs cycle) series of enzyme-catalyzed chemical reactions of central importance in all living cells

Krebs cycle

(also, citric acid cycle) alternate name for the citric acid cycle, named after Hans Krebs who first identified the steps in the pathway in the 1930s in pigeon flight muscles; see citric acid cycle

TCA cycle

(also, citric acid cycle) alternate name for the citric acid cycle, named after the group name for citric acid, tricarboxylic acid (TCA); see citric acid cycle

The Endomembrane System and Proteins

By the end of this section, you will be able to:

- List the components of the endomembrane system
- Recognize the relationship between the endomembrane system and its functions

The endomembrane system (endo = “within”) is a group of membranes and organelles ([\[link\]](#)) in eukaryotic cells that works together to modify, package, and transport lipids and proteins. It includes the nuclear envelope, lysosomes, and vesicles, which we’ve already mentioned, and the endoplasmic reticulum and

Golgi apparatus, which we will cover shortly. Although not technically *within* the cell, the plasma membrane is included in the endomembrane system because, as you will see, it interacts with the other endomembranous organelles. The endomembrane system does not include the membranes of either mitochondria or chloroplasts.

#### Art Connection

"Membrane and secretory proteins are synthesized in the rough endoplasmic reticulum (RER). The RER also sometimes modifies proteins. In this illustration, a (green) integral membrane protein in the ER is modified by attachment of a (purple) carbohydrate. Vesicles with the integral protein bud from the ER and fuse with the cis face of the Golgi apparatus. As the protein passes along the Golgi's cisternae, it is further modified by the addition of more carbohydrates. After its synthesis is complete, it exits as integral membrane protein of the vesicle that bud from the Golgi's trans face and when the vesicle fuses with the cell membrane the protein becomes integral portion of that cell membrane. (credit: modification of

work by Magnus Manske)

If a peripheral membrane protein were synthesized in the lumen (inside) of the ER, would it end up on the inside or outside of the plasma membrane?

### **The Endoplasmic Reticulum**

The endoplasmic reticulum (ER) ([link](#)) is a series of interconnected membranous sacs and tubules that collectively modifies proteins and synthesizes lipids. However, these two functions are performed in separate areas of the ER: the rough ER and the smooth ER, respectively.

The hollow portion of the ER tubules is called the lumen or cisternal space. The membrane of the ER, which is a phospholipid bilayer embedded with proteins, is continuous with the nuclear envelope.

### **Rough ER**

The rough endoplasmic reticulum (RER) is so named because the ribosomes attached to its cytoplasmic surface give it a studded appearance when viewed through an electron microscope ([link](#)).

This transmission electron micrograph shows the rough endoplasmic reticulum and other organelles in a pancreatic cell. (credit: modification of work by Louisa

Howard)

Ribosomes transfer their newly synthesized proteins into the lumen of the RER where they undergo structural modifications, such as folding or the acquisition of side chains. These modified proteins will be incorporated into cellular membranes—the membrane of the ER or those of other organelles—or secreted from the cell (such as protein hormones, enzymes). The RER also makes phospholipids for cellular membranes.

If the phospholipids or modified proteins are not destined to stay in the RER, they will reach their destinations via transport vesicles that bud from the RER's membrane ([link](#)).

Since the RER is engaged in modifying proteins (such as enzymes, for example) that will be secreted from the cell, you would be correct in assuming that the RER is abundant in cells that secrete proteins. This is the case with cells of the liver, for example.

### **Smooth ER**

The smooth endoplasmic reticulum (SER) is continuous with the RER but has few or no ribosomes on its cytoplasmic surface ([link](#)). Functions of the SER include synthesis of

carbohydrates, lipids, and steroid hormones; detoxification of medications and poisons; and storage of calcium ions.

In muscle cells, a specialized SER called the sarcoplasmic reticulum is responsible for storage of the calcium ions that are needed to trigger the coordinated contractions of the muscle cells.

Link to Learning

You can watch an excellent animation of the endomembrane system [here](#). At the end of the animation, there is a short self-assessment.

Career Connection

Cardiologist Heart disease is the leading cause of death in the United States. This is primarily due to our sedentary lifestyle and our high trans-fat diets.

Heart failure is just one of many disabling heart conditions. Heart failure does not mean that the heart has stopped working. Rather, it means that the heart can't pump with sufficient force to transport oxygenated blood to all the vital organs. Left untreated, heart failure can lead to kidney failure and failure of other organs.

The wall of the heart is composed of cardiac muscle tissue. Heart failure occurs when the endoplasmic reticula of cardiac muscle cells do not function properly. As a result, an insufficient number of calcium ions are available to trigger a sufficient contractile force.

Cardiologists (cardi- = "heart"; -ologist = "one who studies") are doctors who specialize in treating heart diseases, including heart failure. Cardiologists can make a diagnosis of heart failure via physical examination, results from an electrocardiogram (ECG, a test that measures the electrical activity of the heart), a chest X-ray to see whether the heart is enlarged, and other tests. If heart failure is diagnosed, the cardiologist will typically prescribe appropriate medications and recommend a reduction in table salt intake and a supervised exercise program.

## **The Golgi Apparatus**

We have already mentioned that vesicles can bud from the ER and transport their contents elsewhere, but where do the vesicles go? Before reaching their final destination, the lipids or proteins within the transport vesicles still need to be sorted, packaged, and tagged so that they wind up in the right place. Sorting, tagging, packaging, and distribution of lipids and proteins takes place in the Golgi apparatus (also called the Golgi body), a series of flattened membranes ([link](#)).

The Golgi apparatus in this white blood cell is visible as a stack of semicircular, flattened rings in the lower portion of the image. Several vesicles can be seen near the Golgi apparatus. (credit: modification of work by Louisa

Howard)

The receiving side of the Golgi apparatus is called the *cis* face. The opposite side is called the *trans* face. The transport vesicles that formed from the ER travel to the *cis* face, fuse with it, and empty their contents into the lumen of the Golgi apparatus. As the proteins and lipids travel through the Golgi, they undergo further modifications that allow them to be sorted. The most frequent modification is the addition of short chains of sugar molecules. These newly modified proteins and lipids are then tagged with phosphate groups or other small molecules so that they can be routed to their proper destinations.

Finally, the modified and tagged proteins are packaged into secretory vesicles that bud from the *trans* face of the Golgi. While some of these vesicles deposit their contents into other parts of the cell where they will be used, other secretory vesicles fuse with the plasma membrane and release their contents outside the cell.

In another example of form following function, cells that engage in a great deal of secretory activity (such as cells of the salivary glands that secrete digestive enzymes or cells of the immune system that secrete antibodies) have an abundance of Golgi.

In plant cells, the Golgi apparatus has the additional role of synthesizing polysaccharides, some of which are incorporated into the cell wall and some of which are used in other parts of the cell.

#### Career Connection

**Geneticist** Many diseases arise from genetic mutations that prevent the synthesis of critical proteins. One such disease is Lowe disease (also called oculocerebrorenal syndrome, because it affects the eyes, brain, and kidneys). In Lowe disease, there is a deficiency in an enzyme localized to the Golgi apparatus. Children with Lowe disease are born with cataracts,

typically develop kidney disease after the first year of life, and may have impaired mental abilities.

Lowe disease is a genetic disease caused by a mutation on the X chromosome. The X chromosome is one of the two human sex chromosomes, as these chromosomes determine a person's sex. Females possess two X chromosomes while males possess one X and one Y chromosome. In females, the genes on only one of the two X chromosomes are expressed. Therefore, females who carry the Lowe disease gene on one of their X chromosomes have a 50/50 chance of having the disease. However, males only have one X chromosome and the genes on this chromosome are always expressed. Therefore, males will always have Lowe disease if their X chromosome carries the Lowe disease gene. The location of the mutated gene, as well as the locations of many other mutations that cause genetic diseases, has now been identified. Through prenatal testing, a woman can find out if the fetus she is carrying may be afflicted with one of several genetic diseases.

Geneticists analyze the results of prenatal genetic tests and may counsel pregnant women on available options. They may also conduct genetic research that leads to new drugs or foods, or perform DNA analyses that are used in forensic investigations.

## **Lysosomes**

In addition to their role as the digestive component and organelle-recycling facility of animal cells, lysosomes are considered to be parts of the endomembrane system. Lysosomes also use their hydrolytic enzymes to destroy pathogens (disease-causing organisms) that might enter the cell. A good example of this occurs in a group of white blood cells called macrophages, which are part of your body's immune system. In a process known as phagocytosis or endocytosis, a section of the plasma membrane of the macrophage invaginates (folds in) and engulfs a pathogen. The invaginated section, with the pathogen inside, then pinches itself off from the plasma membrane and becomes a vesicle. The vesicle fuses with a lysosome. The lysosome's hydrolytic enzymes then destroy the pathogen ([\[link\]](#)).

A macrophage has engulfed (phagocytized) a potentially pathogenic bacterium and then fuses with a lysosomes within the cell to destroy the pathogen. Other organelles are present in the

cell but for simplicity are not shown.

## Section Summary

The endomembrane system includes the nuclear envelope, lysosomes, vesicles, the ER, and Golgi apparatus, as well as the plasma membrane. These cellular components work together to modify, package, tag, and transport proteins and lipids that form the membranes.

The RER modifies proteins and synthesizes phospholipids used in cell membranes. The SER synthesizes carbohydrates, lipids, and steroid hormones; engages in the detoxification of medications and poisons; and stores calcium ions. Sorting, tagging, packaging, and distribution of lipids and proteins take place in the Golgi apparatus. Lysosomes are created by the budding of the membranes of the RER and Golgi. Lysosomes digest macromolecules, recycle worn-out organelles, and destroy pathogens.

## Art Connections

[\[link\]](#) If a peripheral membrane protein were synthesized in the lumen (inside) of the ER, would it end up on the inside or outside of the plasma membrane?

[\[link\]](#) It would end up on the outside. After the vesicle passes through the Golgi apparatus and fuses with the plasma membrane, it turns inside out.

## Review Questions

Which of the following is not a component of the endomembrane system?

- a. mitochondrion
- b. Golgi apparatus

- c. endoplasmic reticulum
- d. lysosome

A

The process by which a cell engulfs a foreign particle is known as:

- a. endosymbiosis
- b. phagocytosis
- c. hydrolysis
- d. membrane synthesis

B

Which of the following is most likely to have the greatest concentration of smooth endoplasmic reticulum?

- a. a cell that secretes enzymes
- b. a cell that destroys pathogens
- c. a cell that makes steroid hormones
- d. a cell that engages in photosynthesis

C

Which of the following sequences correctly lists in order the steps involved in the incorporation of a proteinaceous molecule within a cell?

- a. synthesis of the protein on the ribosome; modification in the Golgi apparatus; packaging in the endoplasmic reticulum; tagging in the vesicle
- b. synthesis of the protein on the lysosome; tagging in the Golgi; packaging in the vesicle; distribution in the endoplasmic reticulum
- c. synthesis of the protein on the ribosome; modification in the endoplasmic reticulum; tagging in the Golgi; distribution via the vesicle
- d. synthesis of the protein on the lysosome; packaging in the vesicle; distribution via the Golgi; tagging in the endoplasmic reticulum

C

### **Free Response**

In the context of cell biology, what do we mean by form follows function? What are at least two examples of this concept?

“Form follows function” refers to the idea that the function of a body part dictates the form of that body part. As an example, compare your arm to a bat’s wing. While the bones of the two correspond, the parts serve different functions in each organism and their forms have adapted to follow that function.

In your opinion, is the nuclear membrane part of the endomembrane system? Why or why not? Defend your answer.

Since the external surface of the nuclear membrane is continuous with the rough endoplasmic reticulum, which is part of the endomembrane system, then it is correct to say that it is part of the system.

## Glossary

endomembrane system

group of organelles and membranes in eukaryotic cells that work together modifying, packaging, and transporting lipids and proteins

endoplasmic reticulum (ER)

series of interconnected membranous structures within eukaryotic cells that collectively modify proteins and synthesize lipids

Golgi apparatus

eukaryotic organelle made up of a series of stacked membranes that sorts, tags, and packages lipids and proteins for distribution

rough endoplasmic reticulum (RER)

region of the endoplasmic reticulum that is studded with ribosomes and engages in protein modification and phospholipid synthesis

smooth endoplasmic reticulum (SER)

region of the endoplasmic reticulum that has few or no ribosomes on its cytoplasmic surface and synthesizes carbohydrates, lipids, and steroid hormones; detoxifies certain chemicals (like pesticides, preservatives, medications, and environmental pollutants), and stores calcium ions

Oxidative Phosphorylation

By the end of this section, you will be able to:

- Describe how electrons move through the electron transport chain and what happens to their energy levels
- Explain how a proton ( $H^+$ ) gradient is established and maintained by the electron transport chain

You have just read about two pathways in glucose catabolism—glycolysis and the citric acid cycle—that generate ATP. Most of the ATP generated during the aerobic catabolism of glucose, however, is not generated directly from these pathways. Rather, it is derived from a process that begins with moving electrons through a series of electron transporters that undergo redox reactions. This causes hydrogen ions to accumulate within the matrix space. Therefore, a concentration gradient forms in which hydrogen ions diffuse out of the matrix space by passing through ATP synthase. The current of hydrogen ions powers the catalytic action of ATP synthase, which phosphorylates ADP, producing ATP.

## Electron Transport Chain

The electron transport chain ([link](#)) is the last component of aerobic respiration and is the only part of glucose metabolism that uses atmospheric oxygen. Oxygen continuously diffuses into plants; in animals, it enters the body through the respiratory system. Electron transport is

a series of redox reactions that resemble a relay race or bucket brigade in that electrons are passed rapidly from one component to the next, to the endpoint of the chain where the electrons reduce molecular oxygen, producing water. There are four complexes composed of proteins, labeled I through IV in [\[link\]](#), and the aggregation of these four complexes, together with associated mobile, accessory electron carriers, is called the electron transport chain. The electron transport chain is present in multiple copies in the inner mitochondrial membrane of eukaryotes and the plasma membrane of prokaryotes.

The electron transport chain is a series of electron transporters embedded in the inner mitochondrial membrane that shuttles electrons from NADH and FADH<sub>2</sub> to molecular oxygen. In the process, protons are pumped from the mitochondrial matrix to the intermembrane space, and oxygen is reduced to form

water.

### **Complex I**

To start, two electrons are carried to the first complex aboard NADH. This complex, labeled I, is composed of flavin mononucleotide (FMN) and an iron-sulfur (Fe-S)-containing protein. FMN, which is derived from vitamin B<sub>2</sub>, also called riboflavin, is one of several prosthetic groups or co-factors in the electron transport chain. A prosthetic group is a non-protein molecule required for the activity of a protein. Prosthetic groups are organic or inorganic, non-peptide molecules bound to a protein that facilitate its function; prosthetic groups include co-enzymes, which are the prosthetic groups of enzymes. The enzyme in complex I is NADH dehydrogenase and is a very large protein, containing 45 amino acid chains. Complex I can pump four hydrogen ions across the membrane from the matrix into the intermembrane space, and it is in this way that the hydrogen ion gradient is established and maintained between the two compartments separated by the inner mitochondrial membrane.

### **Q and Complex II**

Complex II directly receives FADH<sub>2</sub>, which does not pass through complex I. The compound connecting the first and second complexes to the third is ubiquinone (Q). The Q molecule is lipid soluble and freely moves through the hydrophobic core of the membrane. Once it is

reduced, (QH<sub>2</sub>), ubiquinone delivers its electrons to the next complex in the electron transport chain. Q receives the electrons derived from NADH from complex I and the electrons derived from FADH<sub>2</sub> from complex II, including succinate dehydrogenase. This enzyme and FADH<sub>2</sub> form a small complex that delivers electrons directly to the electron transport chain, bypassing the first complex. Since these electrons bypass and thus do not energize the proton pump in the first complex, fewer ATP molecules are made from the FADH<sub>2</sub> electrons. The number of ATP molecules ultimately obtained is directly proportional to the number of protons pumped across the inner mitochondrial membrane.

### **Complex III**

The third complex is composed of cytochrome b, another Fe-S protein, Rieske center (2Fe-2S center), and cytochrome c proteins; this complex is also called cytochrome oxidoreductase. Cytochrome proteins have a prosthetic group of heme. The heme molecule is similar to the heme in hemoglobin, but it carries electrons, not oxygen. As a result, the iron ion at its core is reduced and oxidized as it passes the electrons, fluctuating between different oxidation states: Fe<sup>++</sup> (reduced) and Fe<sup>+++</sup> (oxidized). The heme molecules in the cytochromes have slightly different characteristics due to the effects of the different proteins binding them, giving slightly different characteristics to each complex. Complex III pumps protons through the membrane and passes its electrons to cytochrome c for transport to the fourth complex of proteins and enzymes (cytochrome c is the acceptor of electrons from Q; however, whereas Q carries pairs of electrons, cytochrome c can accept only one at a time).

### **Complex IV**

The fourth complex is composed of cytochrome proteins c, a, and a<sub>3</sub>. This complex contains two heme groups (one in each of the two cytochromes, a, and a<sub>3</sub>) and three copper ions (a pair of Cu<sub>A</sub> and one Cu<sub>B</sub> in cytochrome a<sub>3</sub>). The cytochromes hold an oxygen molecule very tightly between the iron and copper ions until the oxygen is completely reduced. The reduced oxygen then picks up two hydrogen ions from the surrounding medium to make water (H<sub>2</sub>O). The removal of the hydrogen ions from the system contributes to the ion gradient used in the process of chemiosmosis.

### **Chemiosmosis**

In chemiosmosis, the free energy from the series of redox reactions just described is used to pump hydrogen ions (protons) across the membrane. The uneven distribution of H<sup>+</sup> ions across the membrane establishes both concentration and electrical gradients (thus, an electrochemical gradient), owing to the hydrogen ions' positive charge and their aggregation on one side of the membrane.

If the membrane were open to diffusion by the hydrogen ions, the ions would tend to diffuse back across into the matrix, driven by their electrochemical gradient. Recall that many ions cannot diffuse through the nonpolar regions of phospholipid membranes without the aid of ion channels. Similarly, hydrogen ions in the matrix space can only pass through the inner mitochondrial membrane through an integral membrane protein called ATP synthase ([link](#)). This complex protein acts as a tiny generator, turned by the force of the hydrogen ions diffusing through it, down their electrochemical gradient. The turning of parts of this molecular machine facilitates the addition of a phosphate to ADP, forming ATP, using the potential energy of the hydrogen ion gradient.

### Art Connection

ATP synthase is a complex, molecular machine that uses a proton ( $H^+$ ) gradient to form ATP from ADP and inorganic phosphate ( $P_i$ ). (Credit: modification of work by Klaus

Hoffmeier)

Dinitrophenol (DNP) is an uncoupler that makes the inner mitochondrial membrane leaky to protons. It was used until 1938 as a weight-loss drug. What effect would you expect DNP to have on the change in pH across the inner mitochondrial membrane? Why do you think this might be an effective weight-loss drug?

Chemiosmosis ([link](#)) is used to generate 90 percent of the ATP made during aerobic glucose catabolism; it is also the method used in the light reactions of photosynthesis to harness the energy of sunlight in the process of photophosphorylation. Recall that the production of ATP using the process of chemiosmosis in mitochondria is called oxidative phosphorylation. The overall result of these reactions is the production of ATP from the energy of the electrons removed from hydrogen atoms. These atoms were originally part of a glucose molecule. At the end of the pathway, the electrons are used to reduce an oxygen molecule to oxygen ions. The extra electrons on the oxygen attract hydrogen ions (protons) from the surrounding medium, and water is formed.

Art Connection

In oxidative phosphorylation, the pH gradient formed by the electron transport chain is used

by ATP synthase to form ATP.

Cyanide inhibits cytochrome c oxidase, a component of the electron transport chain. If cyanide poisoning occurs, would you expect the pH of the intermembrane space to increase or decrease? What effect would cyanide have on ATP synthesis?

### **ATP Yield**

The number of ATP molecules generated from the catabolism of glucose varies. For example, the number of hydrogen ions that the electron transport chain complexes can pump through the membrane varies between species. Another source of variance stems from the shuttle of electrons across the membranes of the mitochondria. (The NADH generated from glycolysis cannot easily enter mitochondria.) Thus, electrons are picked up on the inside of mitochondria by either  $\text{NAD}^+$  or  $\text{FAD}^+$ . As you have learned earlier, these  $\text{FAD}^+$  molecules can transport fewer ions; consequently, fewer ATP molecules are generated when  $\text{FAD}^+$  acts as a carrier.  $\text{NAD}^+$  is used as the electron transporter in the liver and  $\text{FAD}^+$  acts in the brain.

Another factor that affects the yield of ATP molecules generated from glucose is the fact that intermediate compounds in these pathways are used for other purposes. Glucose catabolism connects with the pathways that build or break down all other biochemical compounds in cells, and the result is somewhat messier than the ideal situations described thus far. For example, sugars other than glucose are fed into the glycolytic pathway for energy extraction. Moreover, the five-carbon sugars that form nucleic acids are made from intermediates in glycolysis. Certain nonessential amino acids can be made from intermediates of both glycolysis and the citric acid cycle. Lipids, such as cholesterol and triglycerides, are also made from intermediates in these pathways, and both amino acids and triglycerides are broken down for energy through these pathways. Overall, in living systems, these pathways of glucose catabolism extract about 34 percent of the energy contained in glucose.

## Section Summary

The electron transport chain is the portion of aerobic respiration that uses free oxygen as the final electron acceptor of the electrons removed from the intermediate compounds in glucose catabolism. The electron transport chain is composed of four large, multiprotein complexes embedded in the inner mitochondrial membrane and two small diffusible electron carriers shuttling electrons between them. The electrons are passed through a series of redox reactions, with a small amount of free energy used at three points to transport hydrogen ions across a membrane. This process contributes to the gradient used in chemiosmosis. The electrons passing through the electron transport chain gradually lose energy. High-energy electrons donated to the chain by either NADH or FADH<sub>2</sub> complete the chain, as low-energy electrons reduce oxygen molecules and form water. The level of free energy of the electrons drops from about 60 kcal/mol in NADH or 45 kcal/mol in FADH<sub>2</sub> to about 0 kcal/mol in water. The end products of the electron transport chain are water and ATP. A number of intermediate compounds of the citric acid cycle can be diverted into the anabolism of other biochemical molecules, such as nonessential amino acids, sugars, and lipids. These same molecules can serve as energy sources for the glucose pathways.

## Art Connections

[\[link\]](#) Dinitrophenol (DNP) is an uncoupler that makes the inner mitochondrial membrane leaky to protons. It was used until 1938 as a weight-loss drug. What effect would you expect DNP to have on the change in pH across the inner mitochondrial membrane? Why do you think this might be an effective weight-loss drug?

[\[link\]](#) After DNP poisoning, the electron transport chain can no longer form a proton gradient, and ATP synthase can no longer make ATP. DNP is an effective diet drug because it uncouples ATP synthesis; in other words, after taking it, a person obtains less energy out of the food he or she eats. Interestingly, one of the worst side effects of this drug is hyperthermia, or overheating of the body. Since ATP cannot be formed, the energy from electron transport is lost as heat.

[\[link\]](#) Cyanide inhibits cytochrome c oxidase, a component of the electron transport chain. If cyanide poisoning occurs, would you expect the pH of the intermembrane space to increase or decrease? What effect would cyanide have on ATP synthesis?

[\[link\]](#) After cyanide poisoning, the electron transport chain can no longer pump electrons into the intermembrane space. The pH of the intermembrane space would increase, the pH gradient would decrease, and ATP synthesis would stop.

## Review Questions

What compound receives electrons from NADH?

- FMN
- ubiquinone
- cytochrome c<sub>1</sub>
- oxygen

A

Chemiosmosis involves \_\_\_\_\_.

- a. the movement of electrons across the cell membrane
- b. the movement of hydrogen atoms across a mitochondrial membrane
- c. the movement of hydrogen ions across a mitochondrial membrane
- d. the movement of glucose through the cell membrane

C

## Free Response

How do the roles of ubiquinone and cytochrome c differ from the other components of the electron transport chain?

Q and cytochrome c are transport molecules. Their function does not result directly in ATP synthesis in that they are not pumps. Moreover, Q is the only component of the electron transport chain that is not a protein. Ubiquinone and cytochrome c are small, mobile, electron carriers, whereas the other components of the electron transport chain are large complexes anchored in the inner mitochondrial membrane.

What accounts for the different number of ATP molecules that are formed through cellular respiration?

Few tissues except muscle produce the maximum possible amount of ATP from nutrients. The intermediates are used to produce needed amino acids, fatty acids, cholesterol, and sugars for nucleic acids. When NADH is transported from the cytoplasm to the mitochondria, an active transport mechanism is used, which decreases the amount of ATP that can be made. The electron transport chain differs in composition between species, so different organisms will make different amounts of ATP using their electron transport chains.

## Glossary

ATP synthase

(also, F<sub>1</sub>F<sub>0</sub> ATP synthase) membrane-embedded protein complex that adds a phosphate to ADP with energy from protons diffusing through it

prosthetic group

(also, prosthetic cofactor) molecule bound to a protein that facilitates the function of the protein

ubiquinone

soluble electron transporter in the electron transport chain that connects the first or second complex to the third

Connections of Carbohydrate, Protein, and Lipid Metabolic Pathways

By the end of this section, you will be able to:

- Discuss the ways in which carbohydrate metabolic pathways, glycolysis, and the citric acid cycle interrelate with protein and lipid metabolic pathways
- Explain why metabolic pathways are not considered closed systems

You have learned about the catabolism of glucose, which provides energy to living cells. But living things consume more than glucose for food. How does a turkey sandwich end up as ATP in your cells? This happens because all of the catabolic pathways for carbohydrates, proteins, and lipids eventually connect into glycolysis and the citric acid cycle pathways (see [\[link\]](#)). Metabolic pathways should be thought of as porous—that is, substances enter from other pathways, and intermediates leave for other pathways. These pathways are not closed systems. Many of the substrates, intermediates, and products in a particular pathway are reactants in other pathways.

### **Connections of Other Sugars to Glucose Metabolism**

Glycogen, a polymer of glucose, is an energy storage molecule in animals. When there is adequate ATP present, excess glucose is shunted into glycogen for storage. Glycogen is made and stored in both liver and muscle. The glycogen will be hydrolyzed into glucose monomers (G-1-P) if blood sugar levels drop. The presence of glycogen as a source of glucose allows ATP to be produced for a longer period of time during exercise. Glycogen is broken down into G-1-P and converted into G-6-P in both muscle and liver cells, and this product enters the glycolytic pathway.

Sucrose is a disaccharide with a molecule of glucose and a molecule of fructose bonded together with a glycosidic linkage. Fructose is one of the three dietary monosaccharides, along with glucose and galactose (which is part of the milk sugar, the disaccharide lactose), which are absorbed directly into the bloodstream during digestion. The catabolism of both fructose and galactose produces the same number of ATP molecules as glucose.

### **Connections of Proteins to Glucose Metabolism**

Proteins are hydrolyzed by a variety of enzymes in cells. Most of the time, the amino acids are recycled into the synthesis of new proteins. If there are excess amino acids, however, or if the body is in a state of starvation, some amino acids will be shunted into the pathways of glucose catabolism ([\[link\]](#)). Each amino acid must have its amino group removed prior to entry into these pathways. The amino group is converted into ammonia. In mammals, the liver synthesizes urea from two ammonia molecules and a carbon dioxide molecule. Thus, urea is the principal waste product in mammals produced from the nitrogen originating in amino acids, and it leaves the body in urine.

The carbon skeletons of certain amino acids (indicated in boxes) derived from proteins can feed into the citric acid cycle. (credit: modification of work by Mikael

Hägström)

### **Connections of Lipid and Glucose Metabolisms**

The lipids that are connected to the glucose pathways are cholesterol and triglycerides. Cholesterol is a lipid that contributes to cell membrane flexibility and is a precursor of steroid hormones. The synthesis of cholesterol starts with acetyl groups and proceeds in only one direction. The process cannot be reversed.

Triglycerides are a form of long-term energy storage in animals. Triglycerides are made of glycerol and three fatty acids. Animals can make most of the fatty acids they need. Triglycerides can be both made and broken down through parts of the glucose catabolism pathways. Glycerol can be phosphorylated to glycerol-3-phosphate, which continues through glycolysis. Fatty acids are catabolized in a process called beta-oxidation that takes place in the matrix of the mitochondria and converts their fatty acid chains into two carbon units of acetyl groups. The acetyl groups are picked up by CoA to form acetyl CoA that proceeds into the citric acid cycle.

Glycogen from the liver and muscles, hydrolyzed into glucose-1-phosphate, together with fats and proteins, can feed into the catabolic pathways for

carbohydrates.

Evolution Connection

**Pathways of Photosynthesis and Cellular Metabolism**The processes of photosynthesis and cellular metabolism consist of several very complex pathways. It is generally thought that the first cells arose in an aqueous environment—a “soup” of nutrients—probably on the surface of some porous clays. If these cells reproduced successfully and their numbers climbed steadily, it follows that the cells would begin to deplete the nutrients from the medium in which they lived as they shifted the nutrients into the components of their own bodies. This hypothetical situation would have resulted in natural selection favoring those organisms that could exist by using the nutrients that remained in their environment and by manipulating these nutrients into materials upon which they could survive. Selection would favor those organisms that could extract maximal value from the nutrients to which they had access.

An early form of photosynthesis developed that harnessed the sun’s energy using water as a source of hydrogen atoms, but this pathway did not produce free oxygen (anoxygenic photosynthesis). (Early photosynthesis did not produce free oxygen because it did not use water as the source of hydrogen ions; instead, it used materials like hydrogen sulfide and consequently produced sulfur). It is thought that glycolysis could take advantage of the simple sugars being produced, but these reactions were unable to fully extract the energy stored in the carbohydrates. The development of glycolysis probably predated the evolution of photosynthesis, as it was well suited to extract energy from materials spontaneously accumulating in the “primeval soup.” A later form of photosynthesis used water as a source of electrons and hydrogen, and generated free oxygen. Over time, the atmosphere became

oxygenated, but not before the oxygen released oxidized metals in the ocean and created a “rust” layer in the sediment, permitting the dating of the rise of the first oxygenic photosynthesizers. Living things adapted to exploit this new atmosphere that allowed aerobic respiration as we know it to evolve. When the full process of oxygenic photosynthesis developed and the atmosphere became oxygenated, cells were finally able to use the oxygen expelled by photosynthesis to extract considerably more energy from the sugar molecules using the citric acid cycle and oxidative phosphorylation.

## Section Summary

The breakdown and synthesis of carbohydrates, proteins, and lipids connect with the pathways of glucose catabolism. The simple sugars are galactose, fructose, glycogen, and pentose. These are catabolized during glycolysis. The amino acids from proteins connect with glucose catabolism through pyruvate, acetyl CoA, and components of the citric acid cycle. Cholesterol synthesis starts with acetyl groups, and the components of triglycerides come from glycerol-3-phosphate from glycolysis and acetyl groups produced in the mitochondria from pyruvate.

## Review Questions

A major connection for sugars in glycolysis is \_\_\_\_\_.

- glucose-6-phosphate
- fructose-1,6-bisphosphate
- dihydroxyacetone phosphate
- phosphoenolpyruvate

A

Beta-oxidation is \_\_\_\_\_.

- the breakdown of sugars
- the assembly of sugars
- the breakdown of fatty acids
- the removal of amino groups from amino acids

C

## Free Response

Would you describe metabolic pathways as inherently wasteful or inherently economical, and why?

They are very economical. The substrates, intermediates, and products move between pathways and do so in response to finely tuned feedback inhibition loops that keep metabolism balanced overall. Intermediates in one pathway may occur in another, and they can move from one pathway to another fluidly in response to the needs of the cell.

## Regulation of Cellular Respiration

By the end of this section, you will be able to:

- Describe how feedback inhibition would affect the production of an intermediate or product in a pathway
- Identify the mechanism that controls the rate of the transport of electrons through the electron transport chain

Cellular respiration must be regulated in order to provide balanced amounts of energy in the form of ATP. The cell also must generate a number of intermediate compounds that are used in the anabolism and catabolism of macromolecules. Without controls, metabolic reactions would quickly come to a stand still as the forward and backward reactions reached a state of equilibrium. Resources would be used inappropriately. A cell does not need the maximum amount of ATP that it can make all the time: At times, the cell needs to shunt some of the intermediates to pathways for amino acid, protein, glycogen, lipid, and nucleic acid production. In short, the cell needs to control its metabolism.

### **Regulatory Mechanisms**

A variety of mechanisms is used to control cellular respiration. Some type of control exists at each stage of glucose metabolism. Access of glucose to the cell can be regulated using the GLUT proteins that transport glucose ([link](#)). Different forms of the GLUT protein control passage of glucose into the cells of specific tissues.

GLUT4 is a glucose transporter that is stored in vesicles. A cascade of events that occurs upon insulin binding to a receptor in the plasma membrane causes GLUT4-containing

vesicles to fuse with the plasma membrane so that glucose may be transported into the

cell.

Some reactions are controlled by having two different enzymes—one each for the two directions of a reversible reaction. Reactions that are catalyzed by only one enzyme can go to equilibrium, stalling the reaction. In contrast, if two different enzymes (each specific for a given direction) are necessary for a reversible reaction, the opportunity to control the rate of the reaction increases, and equilibrium is not reached.

A number of enzymes involved in each of the pathways—in particular, the enzyme catalyzing the first committed reaction of the pathway—are controlled by attachment of a molecule to an allosteric site on the protein. The molecules most commonly used in this capacity are the nucleotides ATP, ADP, AMP,  $\text{NAD}^+$ , and NADH. These regulators, allosteric effectors, may increase or decrease enzyme activity, depending on the prevailing conditions. The allosteric effector alters the steric structure of the enzyme, usually affecting the configuration of the active site. This alteration of the protein's (the enzyme's) structure either increases or decreases its affinity for its substrate, with the effect of increasing or decreasing the rate of the reaction. The attachment signals to the enzyme. This binding can increase or decrease the enzyme's activity, providing feedback. This feedback type of control is effective as long as the chemical affecting it is attached to the enzyme. Once the overall concentration of the chemical decreases, it will diffuse away from the protein, and the control is relaxed.

## **Control of Catabolic Pathways**

Enzymes, proteins, electron carriers, and pumps that play roles in glycolysis, the citric acid cycle, and the electron transport chain tend to catalyze non-reversible reactions. In other words, if the initial reaction takes place, the pathway is committed to proceeding with the remaining reactions. Whether a particular enzyme activity is released depends upon the energy needs of the cell (as reflected by the levels of ATP, ADP, and AMP).

## Glycolysis

The control of glycolysis begins with the first enzyme in the pathway, hexokinase ([link](#)). This enzyme catalyzes the phosphorylation of glucose, which helps to prepare the compound for cleavage in a later step. The presence of the negatively charged phosphate in the molecule also prevents the sugar from leaving the cell. When hexokinase is inhibited, glucose diffuses out of the cell and does not become a substrate for the respiration pathways in that tissue. The product of the hexokinase reaction is glucose-6-phosphate, which accumulates when a later enzyme, phosphofructokinase, is inhibited.

The glycolysis pathway is primarily regulated at the three key enzymatic steps (1, 2, and 7) as indicated. Note that the first two steps that are regulated occur early in the pathway and involve hydrolysis of ATP.

Phosphofructokinase is the main enzyme controlled in glycolysis. High levels of ATP, citrate, or a lower, more acidic pH decrease the enzyme's activity. An increase in citrate

concentration can occur because of a blockage in the citric acid cycle. Fermentation, with its production of organic acids like lactic acid, frequently accounts for the increased acidity in a cell; however, the products of fermentation do not typically accumulate in cells.

The last step in glycolysis is catalyzed by pyruvate kinase. The pyruvate produced can proceed to be catabolized or converted into the amino acid alanine. If no more energy is needed and alanine is in adequate supply, the enzyme is inhibited. The enzyme's activity is increased when fructose-1,6-bisphosphate levels increase. (Recall that fructose-1,6-bisphosphate is an intermediate in the first half of glycolysis.) The regulation of pyruvate kinase involves phosphorylation by a kinase (pyruvate kinase kinase), resulting in a less-active enzyme. Dephosphorylation by a phosphatase reactivates it. Pyruvate kinase is also regulated by ATP (a negative allosteric effect).

If more energy is needed, more pyruvate will be converted into acetyl CoA through the action of pyruvate dehydrogenase. If either acetyl groups or NADH accumulate, there is less need for the reaction and the rate decreases. Pyruvate dehydrogenase is also regulated by phosphorylation: A kinase phosphorylates it to form an inactive enzyme, and a phosphatase reactivates it. The kinase and the phosphatase are also regulated.

### **Citric Acid Cycle**

The citric acid cycle is controlled through the enzymes that catalyze the reactions that make the first two molecules of NADH ([link](#)). These enzymes are isocitrate dehydrogenase and  $\alpha$ -ketoglutarate dehydrogenase. When adequate ATP and NADH levels are available, the rates of these reactions decrease. When more ATP is needed, as reflected in rising ADP levels, the rate increases.  $\alpha$ -Ketoglutarate dehydrogenase will also be affected by the levels of succinyl CoA—a subsequent intermediate in the cycle—causing a decrease in activity. A decrease in the rate of operation of the pathway at this point is not necessarily negative, as the increased levels of the  $\alpha$ -ketoglutarate not used by the citric acid cycle can be used by the cell for amino acid (glutamate) synthesis.

### **Electron Transport Chain**

Specific enzymes of the electron transport chain are unaffected by feedback inhibition, but the rate of electron transport through the pathway is affected by the levels of ADP and ATP. Greater ATP consumption by a cell is indicated by a buildup of ADP. As ATP usage decreases, the concentration of ADP decreases, and now, ATP begins to build up in the cell. This change in the relative concentration of ADP to ATP triggers the cell to slow down the electron transport chain.

Link to Learning

Visit this [site](#) to see an animation of the electron transport chain and ATP synthesis.

For a summary of feedback controls in cellular respiration, see [\[link\]](#).

### Summary of Feedback Controls in Cellular Respiration

Pathway	Enzyme affected	Elevated levels of effector	Effect on pathway activity
glycolysis	hexokinase	glucose-6-phosphate	decrease
	phosphofruktokinase	low-energy charge (ATP, AMP), fructose-6-phosphate via fructose-2,6-bisphosphate	increase
		high-energy charge (ATP, AMP), citrate, acidic pH	decrease
	pyruvate kinase	fructose-1,6-bisphosphate	increase
pyruvate to acetyl CoA conversion	pyruvate dehydrogenase	ADP, pyruvate	increase
		acetyl CoA, ATP, NADH	decrease
citric acid cycle	isocitrate dehydrogenase	ADP	increase
		ATP, NADH	decrease
	$\alpha$ -ketoglutarate dehydrogenase	Calcium ions, ADP	increase
		ATP, NADH, succinyl CoA	decrease
electron transport chain		ADP	increase
		ATP	decrease

### Section Summary

Cellular respiration is controlled by a variety of means. The entry of glucose into a cell is controlled by the transport proteins that aid glucose passage through the cell membrane. Most of the control of the respiration processes is accomplished through the control of specific enzymes in the pathways. This is a type of negative feedback, turning the enzymes off. The enzymes respond most often to the levels of the available nucleosides ATP, ADP, AMP,  $\text{NAD}^+$ , and FAD. Other intermediates of the pathway also affect certain enzymes in the systems.

### Review Questions

The effect of high levels of ADP is to \_\_\_\_\_.

- increase the activity of the enzyme
- decrease the activity of the enzyme
- have no effect on the activity of the enzyme
- slow down the pathway

A

The control of which enzyme exerts the most control on glycolysis?

- a. hexokinase
- b. phosphofructokinase
- c. glucose-6-phosphatase
- d. aldolase

B

### Free Response

How does citrate from the citric acid cycle affect glycolysis?

Citrate can inhibit phosphofructokinase by feedback regulation.

Why might negative feedback mechanisms be more common than positive feedback mechanisms in living cells?

Negative feedback mechanisms actually control a process; it can turn it off, whereas positive feedback accelerates the process, allowing the cell no control over it. Negative feedback naturally maintains homeostasis, whereas positive feedback drives the system away from equilibrium.

### Glossary

GLUT protein

integral membrane protein that transports glucose

Metabolism without Oxygen

By the end of this section, you will be able to:

- Discuss the fundamental difference between anaerobic cellular respiration and fermentation
- Describe the type of fermentation that readily occurs in animal cells and the conditions that initiate that fermentation

In aerobic respiration, the final electron acceptor is an oxygen molecule,  $O_2$ . If aerobic respiration occurs, then ATP will be produced using the energy of high-energy electrons carried by NADH or  $FADH_2$  to the electron transport chain. If aerobic respiration does not occur, NADH must be reoxidized to  $NAD^+$  for reuse as an electron carrier for the glycolytic pathway to continue. How is this done? Some living systems use an organic molecule as the final electron acceptor. Processes that use an organic molecule to regenerate  $NAD^+$  from NADH are collectively referred to as fermentation. In contrast, some living systems use an inorganic molecule as a final electron acceptor. Both methods are called anaerobic

cellular respiration in which organisms convert energy for their use in the absence of oxygen.

### **Anaerobic Cellular Respiration**

Certain prokaryotes, including some species of bacteria and Archaea, use anaerobic respiration. For example, the group of Archaea called methanogens reduces carbon dioxide to methane to oxidize NADH. These microorganisms are found in soil and in the digestive tracts of ruminants, such as cows and sheep. Similarly, sulfate-reducing bacteria and Archaea, most of which are anaerobic ( [link](#)), reduce sulfate to hydrogen sulfide to regenerate  $\text{NAD}^+$  from NADH.

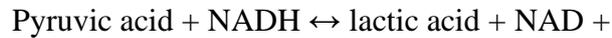
The green color seen in these coastal waters is from an eruption of hydrogen sulfide-producing bacteria. These anaerobic, sulfate-reducing bacteria release hydrogen sulfide gas as they decompose algae in the water. (credit: modification of work by NASA/Jeff Schmaltz, MODIS Land Rapid Response Team at NASA GSFC, Visible Earth Catalog of NASA

images)  
Link to Learning

Visit this [site](#) to see anaerobic cellular respiration in action.

### **Lactic Acid Fermentation**

The fermentation method used by animals and certain bacteria, like those in yogurt, is lactic acid fermentation ([link](#)). This type of fermentation is used routinely in mammalian red blood cells and in skeletal muscle that has an insufficient oxygen supply to allow aerobic respiration to continue (that is, in muscles used to the point of fatigue). In muscles, lactic acid accumulation must be removed by the blood circulation and the lactate brought to the liver for further metabolism. The chemical reactions of lactic acid fermentation are the following:



The enzyme used in this reaction is lactate dehydrogenase (LDH). The reaction can proceed in either direction, but the reaction from left to right is inhibited by acidic conditions. Such lactic acid accumulation was once believed to cause muscle stiffness, fatigue, and soreness, although more recent research disputes this hypothesis. Once the lactic acid has been removed from the muscle and circulated to the liver, it can be reconverted into pyruvic acid and further catabolized for energy.

#### Art Connection

Lactic acid fermentation is common in muscle cells that have run out of

oxygen.

Tremetol, a metabolic poison found in the white snake root plant, prevents the metabolism of lactate. When cows eat this plant, it is concentrated in the milk they produce. Humans who consume the milk become ill. Symptoms of this disease, which include vomiting, abdominal pain, and tremors, become worse after exercise. Why do you think this is the case?

#### Alcohol Fermentation

Another familiar fermentation process is alcohol fermentation ([link](#)) that produces ethanol, an alcohol. The first chemical reaction of alcohol fermentation is the following (CO<sub>2</sub> does not participate in the second reaction):



The first reaction is catalyzed by pyruvate decarboxylase, a cytoplasmic enzyme, with a coenzyme of thiamine pyrophosphate (TPP, derived from vitamin B<sub>1</sub> and also called thiamine). A carboxyl group is removed from pyruvic acid, releasing carbon dioxide as a gas. The loss of carbon dioxide reduces the size of the molecule by one carbon, making acetaldehyde. The second reaction is catalyzed by alcohol dehydrogenase to oxidize NADH to NAD<sup>+</sup> and reduce acetaldehyde to ethanol. The fermentation of pyruvic acid by yeast produces the ethanol found in alcoholic beverages. Ethanol tolerance of yeast is variable, ranging from about 5 percent to 21 percent, depending on the yeast strain and environmental conditions.

Fermentation of grape juice into wine produces CO<sub>2</sub> as a byproduct. Fermentation tanks have valves so that the pressure inside the tanks created by the carbon dioxide produced can be

released.

### **Other Types of Fermentation**

Other fermentation methods occur in bacteria. Many prokaryotes are facultatively anaerobic. This means that they can switch between aerobic respiration and fermentation, depending on the availability of oxygen. Certain prokaryotes, like *Clostridia*, are obligate anaerobes. Obligate anaerobes live and grow in the absence of molecular oxygen. Oxygen is a poison to these microorganisms and kills them on exposure. It should be noted that all forms of fermentation, except lactic acid fermentation, produce gas. The production of particular types of gas is used as an indicator of the fermentation of specific carbohydrates, which plays a role in the laboratory identification of the bacteria. Various methods of fermentation are used by assorted organisms to ensure an adequate supply of NAD<sup>+</sup> for the sixth step in glycolysis. Without these pathways, that step would not occur and no ATP would be harvested from the breakdown of glucose.

### **Section Summary**

If NADH cannot be oxidized through aerobic respiration, another electron acceptor is used. Most organisms will use some form of fermentation to accomplish the regeneration of NAD<sup>+</sup>,

ensuring the continuation of glycolysis. The regeneration of  $\text{NAD}^+$  in fermentation is not accompanied by ATP production; therefore, the potential of NADH to produce ATP using an electron transport chain is not utilized.

## Art Connections

[\[link\]](#) Tremetol, a metabolic poison found in the white snake root plant, prevents the metabolism of lactate. When cows eat this plant, it is concentrated in the milk they produce. Humans who consume the milk become ill. Symptoms of this disease, which include vomiting, abdominal pain, and tremors, become worse after exercise. Why do you think this is the case?

[\[link\]](#) The illness is caused by lactate accumulation. Lactate levels rise after exercise, making the symptoms worse. Milk sickness is rare today, but was common in the Midwestern United States in the early 1800s.

## Review Questions

Which of the following fermentation methods can occur in animal skeletal muscles?

- lactic acid fermentation
- alcohol fermentation
- mixed acid fermentation
- propionic fermentation

A

## Free Response

What is the primary difference between fermentation and anaerobic respiration?

Fermentation uses glycolysis only. Anaerobic respiration uses all three parts of cellular respiration, including the parts in the mitochondria like the citric acid cycle and electron transport; it also uses a different final electron acceptor instead of oxygen gas.

## Glossary

anaerobic cellular respiration

process in which organisms convert energy for their use in the absence of oxygen

fermentation

process of regenerating  $\text{NAD}^+$  with either an inorganic or organic compound serving as the final electron acceptor, occurs in the absence; occurs in the absence of oxygen

ntroduction

class="introduction" class="summary" title="Sections Summary" class="art-exercise"

title="Art Connections" class="multiple-choice" title="Multiple Choice" class="free-

response" title="Free Response"Have you ever become separated from a friend while in a

crowd? If so, you know the challenge of searching for someone when surrounded by thousands of other people. If you and your friend have cell phones, your chances of finding each other are good. A cell phone's ability to send and receive messages makes it an ideal communication device. (credit: modification of work by Vincent and Bella

Productions)

Imagine what life would be like if you and the people around you could not communicate. You would not be able to express your wishes to others, nor could you ask questions to find out more about your environment. Social organization is dependent on communication between the individuals that comprise that society; without communication, society would fall apart.

As with people, it is vital for individual cells to be able to interact with their environment. This is true whether a cell is growing by itself in a pond or is one of many cells that form a larger organism. In order to properly respond to external stimuli, cells have developed complex mechanisms of communication that can receive a message, transfer the information across the plasma membrane, and then produce changes within the cell in response to the message.

In multicellular organisms, cells send and receive chemical messages constantly to coordinate the actions of distant organs, tissues, and cells. The ability to send

messages quickly and efficiently enables cells to coordinate and fine-tune their functions.

While the necessity for cellular communication in larger organisms seems obvious, even single-celled organisms communicate with each other. Yeast cells signal each other to aid mating. Some forms of bacteria coordinate their actions in order to form large complexes called biofilms or to organize the production of toxins to remove competing organisms. The ability of cells to communicate through chemical signals originated in single cells and was essential for the evolution of multicellular organisms. The efficient and error-free function of communication systems is vital for all life as we know it.

### Signaling Molecules and Cellular Receptors

By the end of this section, you will be able to:

- Describe four types of signaling found in multicellular organisms
- Compare internal receptors with cell-surface receptors
- Recognize the relationship between a ligand's structure and its mechanism of action

There are two kinds of communication in the world of living cells. Communication between cells is called intercellular signaling, and communication within a cell is called intracellular signaling. An easy way to remember the distinction is by understanding the Latin origin of the prefixes: inter- means "between" (for example, intersecting lines are those that cross each other) and intra- means "inside" (like intravenous).

Chemical signals are released by signaling cells in the form of small, usually volatile or soluble molecules called ligands. A ligand is a molecule that binds another specific molecule, in some cases, delivering a signal in the process. Ligands can thus be thought of as signaling molecules. Ligands interact with proteins in target cells, which are cells that are affected by chemical signals; these proteins are also called receptors. Ligands and receptors exist in several varieties; however, a specific ligand will have a specific receptor that typically binds only that ligand.

### Forms of Signaling

There are four categories of chemical signaling found in multicellular organisms: paracrine signaling, endocrine signaling, autocrine signaling, and direct signaling across gap junctions ([link](#)). The main difference between the different categories of signaling is the distance that the signal travels through the organism to reach the target cell. Not all cells are affected by the same signals.

In chemical signaling, a cell may target itself (autocrine signaling), a cell connected by gap junctions, a nearby cell (paracrine signaling), or a distant cell (endocrine signaling). Paracrine

signaling acts on nearby cells, endocrine signaling uses the circulatory system to transport ligands, and autocrine signaling acts on the signaling cell. Signaling via gap junctions involves signaling molecules moving directly between adjacent

cells.

### **Paracrine Signaling**

Signals that act locally between cells that are close together are called paracrine signals. Paracrine signals move by diffusion through the extracellular matrix. These types of signals usually elicit quick responses that last only a short amount of time. In order to keep the response localized, paracrine ligand molecules are normally quickly degraded by enzymes or removed by neighboring cells. Removing the signals will reestablish the concentration gradient for the signal, allowing them to quickly diffuse through the intracellular space if released again.

One example of paracrine signaling is the transfer of signals across synapses between nerve cells. A nerve cell consists of a cell body, several short, branched extensions called dendrites that receive stimuli, and a long extension called an axon, which transmits signals to other nerve cells or muscle cells. The junction between nerve cells where signal transmission occurs is called a synapse. A synaptic signal is a chemical signal that travels between nerve cells. Signals within the nerve cells are propagated by fast-moving electrical impulses. When these impulses reach the end of the axon, the signal continues on to a dendrite of the next cell by the release of chemical ligands called neurotransmitters by the presynaptic cell (the cell emitting the signal). The neurotransmitters are transported across the very small distances between nerve cells, which are called chemical synapses ([link](#)). The small distance between nerve cells allows the signal to travel quickly; this enables an immediate response, such as, Take your hand off the stove!

When the neurotransmitter binds the receptor on the surface of the postsynaptic cell, the electrochemical potential of the target cell changes, and the next electrical impulse is launched. The neurotransmitters that are released into the chemical synapse are degraded quickly or get reabsorbed by the presynaptic cell so that the recipient nerve cell can recover quickly and be prepared to respond rapidly to the next synaptic signal.

The distance between the presynaptic cell and the postsynaptic cell—called the synaptic gap—is very small and allows for rapid diffusion of the neurotransmitter. Enzymes in the synaptic cleft degrade some types of neurotransmitters to terminate the

signal.

## **Endocrine Signaling**

Signals from distant cells are called endocrine signals, and they originate from endocrine cells. (In the body, many endocrine cells are located in endocrine glands, such as the thyroid gland, the hypothalamus, and the pituitary gland.) These types of signals usually produce a slower response but have a longer-lasting effect. The ligands released in endocrine signaling are called hormones, signaling molecules that are produced in one part of the body but affect other body regions some distance away.

Hormones travel the large distances between endocrine cells and their target cells via the bloodstream, which is a relatively slow way to move throughout the body. Because of their form of transport, hormones get diluted and are present in low concentrations when they act on their target cells. This is different from paracrine signaling, in which local concentrations of ligands can be very high.

## **Autocrine Signaling**

Autocrine signals are produced by signaling cells that can also bind to the ligand that is released. This means the signaling cell and the target cell can be the same or a similar cell (the prefix *auto-* means self, a reminder that the signaling cell sends a signal to itself). This type of signaling often occurs during the early development of an organism to ensure that cells develop into the correct tissues and take on the proper function. Autocrine signaling also regulates pain sensation and inflammatory responses. Further, if a cell is infected with a virus, the cell can signal itself to undergo programmed cell death, killing the virus in the process. In some cases, neighboring cells of the same type are also influenced by the released

ligand. In embryological development, this process of stimulating a group of neighboring cells may help to direct the differentiation of identical cells into the same cell type, thus ensuring the proper developmental outcome.

### **Direct Signaling Across Gap Junctions**

Gap junctions in animals and plasmodesmata in plants are connections between the plasma membranes of neighboring cells. These water-filled channels allow small signaling molecules, called intracellular mediators, to diffuse between the two cells. Small molecules, such as calcium ions ( $\text{Ca}^{2+}$ ), are able to move between cells, but large molecules like proteins and DNA cannot fit through the channels. The specificity of the channels ensures that the cells remain independent but can quickly and easily transmit signals. The transfer of signaling molecules communicates the current state of the cell that is directly next to the target cell; this allows a group of cells to coordinate their response to a signal that only one of them may have received. In plants, plasmodesmata are ubiquitous, making the entire plant into a giant, communication network.

### **Types of Receptors**

Receptors are protein molecules in the target cell or on its surface that bind ligand. There are two types of receptors, internal receptors and cell-surface receptors.

#### **Internal receptors**

Internal receptors, also known as intracellular or cytoplasmic receptors, are found in the cytoplasm of the cell and respond to hydrophobic ligand molecules that are able to travel across the plasma membrane. Once inside the cell, many of these molecules bind to proteins that act as regulators of mRNA synthesis (transcription) to mediate gene expression. Gene expression is the cellular process of transforming the information in a cell's DNA into a sequence of amino acids, which ultimately forms a protein. When the ligand binds to the internal receptor, a conformational change is triggered that exposes a DNA-binding site on the protein. The ligand-receptor complex moves into the nucleus, then binds to specific regulatory regions of the chromosomal DNA and promotes the initiation of transcription ([link](#)). Transcription is the process of copying the information in a cell's DNA into a special form of RNA called messenger RNA (mRNA); the cell uses information in the mRNA (which moves out into the cytoplasm and associates with ribosomes) to link specific amino acids in the correct order, producing a protein. Internal receptors can directly influence gene expression without having to pass the signal on to other receptors or messengers.

Hydrophobic signaling molecules typically diffuse across the plasma membrane and interact with intracellular receptors in the cytoplasm. Many intracellular receptors are transcription

factors that interact with DNA in the nucleus and regulate gene

expression.

### **Cell-Surface Receptors**

Cell-surface receptors, also known as transmembrane receptors, are cell surface, membrane-anchored (integral) proteins that bind to external ligand molecules. This type of receptor spans the plasma membrane and performs signal transduction, in which an extracellular signal is converted into an intercellular signal. Ligands that interact with cell-surface receptors do not have to enter the cell that they affect. Cell-surface receptors are also called cell-specific proteins or markers because they are specific to individual cell types.

Because cell-surface receptor proteins are fundamental to normal cell functioning, it should come as no surprise that a malfunction in any one of these proteins could have severe consequences. Errors in the protein structures of certain receptor molecules have been shown to play a role in hypertension (high blood pressure), asthma, heart disease, and cancer.

Each cell-surface receptor has three main components: an external ligand-binding domain, a hydrophobic membrane-spanning region, and an intracellular domain inside the cell. The ligand-binding domain is also called the extracellular domain. The size and extent of each of these domains vary widely, depending on the type of receptor.

### **Evolution Connection**

**How Viruses Recognize a Host** Unlike living cells, many viruses do not have a plasma membrane or any of the structures necessary to sustain life. Some viruses are simply composed of an inert protein shell containing DNA or RNA. To reproduce, viruses must invade a living cell, which serves as a host, and then take over the host's cellular apparatus. But how does a virus recognize its host?

Viruses often bind to cell-surface receptors on the host cell. For example, the virus that causes human influenza (flu) binds specifically to receptors on membranes of cells of the respiratory system. Chemical differences in the cell-surface receptors among hosts mean that

a virus that infects a specific species (for example, humans) cannot infect another species (for example, chickens).

However, viruses have very small amounts of DNA or RNA compared to humans, and, as a result, viral reproduction can occur rapidly. Viral reproduction invariably produces errors that can lead to changes in newly produced viruses; these changes mean that the viral proteins that interact with cell-surface receptors may evolve in such a way that they can bind to receptors in a new host. Such changes happen randomly and quite often in the reproductive cycle of a virus, but the changes only matter if a virus with new binding properties comes into contact with a suitable host. In the case of influenza, this situation can occur in settings where animals and people are in close contact, such as poultry and swine farms.<sup>1</sup> Once a virus jumps to a new host, it can spread quickly. Scientists watch newly appearing viruses (called emerging viruses) closely in the hope that such monitoring can reduce the likelihood of global viral epidemics.

Cell-surface receptors are involved in most of the signaling in multicellular organisms. There are three general categories of cell-surface receptors: ion channel-linked receptors, G-protein-linked receptors, and enzyme-linked receptors.

Ion channel-linked receptors bind a ligand and open a channel through the membrane that allows specific ions to pass through. To form a channel, this type of cell-surface receptor has an extensive membrane-spanning region. In order to interact with the phospholipid fatty acid tails that form the center of the plasma membrane, many of the amino acids in the membrane-spanning region are hydrophobic in nature. Conversely, the amino acids that line the inside of the channel are hydrophilic to allow for the passage of water or ions. When a ligand binds to the extracellular region of the channel, there is a conformational change in the proteins structure that allows ions such as sodium, calcium, magnesium, and hydrogen to pass through ([link](#)).

Gated ion channels form a pore through the plasma membrane that opens when the signaling molecule binds. The open pore then allows ions to flow into or out of the

cell.

G-protein-linked receptors bind a ligand and activate a membrane protein called a G-protein. The activated G-protein then interacts with either an ion channel or an enzyme in the membrane ([link](#)). All G-protein-linked receptors have seven transmembrane domains, but each receptor has its own specific extracellular domain and G-protein-binding site.

Cell signaling using G-protein-linked receptors occurs as a cyclic series of events. Before the ligand binds, the inactive G-protein can bind to a newly revealed site on the receptor specific for its binding. Once the ligand binds to the receptor, the resultant shape change activates the G-protein, which releases GDP and picks up GTP. The subunits of the G-protein then split into the  $\alpha$  subunit and the  $\beta\gamma$  subunit. One or both of these G-protein fragments may be able to activate other proteins as a result. After a while, the GTP on the active  $\alpha$  subunit of the G-protein is hydrolyzed to GDP and the  $\beta\gamma$  subunit is deactivated. The subunits reassociate to form the inactive G-protein and the cycle begins anew.

Heterotrimeric G proteins have three subunits:  $\alpha$ ,  $\beta$ , and  $\gamma$ . When a signaling molecule binds to a G-protein-coupled receptor in the plasma membrane, a GDP molecule associated with the  $\alpha$  subunit is exchanged for GTP. The  $\beta$  and  $\gamma$  subunits dissociate from the  $\alpha$  subunit, and a cellular response is triggered either by the  $\alpha$  subunit or the dissociated  $\beta\gamma$  pair. Hydrolysis of GTP to GDP terminates the

signal.

G-protein-linked receptors have been extensively studied and much has been learned about their roles in maintaining health. Bacteria that are pathogenic to humans can release poisons that interrupt specific G-protein-linked receptor function, leading to illnesses such as pertussis, botulism, and cholera. In cholera ([link](#)), for example, the water-borne bacterium *Vibrio cholerae* produces a toxin, cholera toxin, that binds to cells lining the small intestine. The toxin then enters these intestinal cells, where it modifies a G-protein that controls the opening of a chloride channel and causes it to remain continuously active, resulting in large losses of fluids from the body and potentially fatal dehydration as a result.

Transmitted primarily through contaminated drinking water, cholera is a major cause of death in the developing world and in areas where natural disasters interrupt the availability of clean water. The cholera bacterium, *Vibrio cholerae*, creates a toxin that modifies G-protein-mediated cell signaling pathways in the intestines. Modern sanitation eliminates the threat of cholera outbreaks, such as the one that swept through New York City in 1866. This poster from that era shows how, at that time, the way that the disease was transmitted was not understood. (credit: New York City Sanitary

Commission)

Enzyme-linked receptors are cell-surface receptors with intracellular domains that are associated with an enzyme. In some cases, the intracellular domain of the receptor itself is an enzyme. Other enzyme-linked receptors have a small intracellular domain that interacts directly with an enzyme. The enzyme-linked receptors normally have large extracellular and intracellular domains, but the membrane-spanning region consists of a single alpha-helical region of the peptide strand. When a ligand binds to the extracellular domain, a signal is transferred through the membrane, activating the enzyme. Activation of the enzyme sets off a chain of events within the cell that eventually leads to a response. One example of this type of enzyme-linked receptor is the tyrosine kinase receptor ([\[link\]](#)). A kinase is an enzyme that transfers phosphate groups from ATP to another protein. The tyrosine kinase receptor transfers phosphate groups to tyrosine molecules (tyrosine residues). First, signaling molecules bind to the extracellular domain of two nearby tyrosine kinase receptors. The two neighboring receptors then bond together, or dimerize. Phosphates are then added to tyrosine residues on the intracellular domain of the receptors (phosphorylation). The phosphorylated residues can then transmit the signal to the next messenger within the cytoplasm.

#### Art Connection

A receptor tyrosine kinase is an enzyme-linked receptor with a single transmembrane region, and extracellular and intracellular domains. Binding of a signaling molecule to the extracellular domain causes the receptor to dimerize. Tyrosine residues on the intracellular domain are then autophosphorylated, triggering a downstream cellular response. The signal is

terminated by a phosphatase that removes the phosphates from the phosphotyrosine

residues.

HER2 is a receptor tyrosine kinase. In 30 percent of human breast cancers, HER2 is permanently activated, resulting in unregulated cell division. Lapatinib, a drug used to treat breast cancer, inhibits HER2 receptor tyrosine kinase autophosphorylation (the process by which the receptor adds phosphates onto itself), thus reducing tumor growth by 50 percent. Besides autophosphorylation, which of the following steps would be inhibited by Lapatinib?

- a. Signaling molecule binding, dimerization, and the downstream cellular response
- b. Dimerization, and the downstream cellular response
- c. The downstream cellular response
- d. Phosphatase activity, dimerization, and the downstream cellular response

## Signaling Molecules

Produced by signaling cells and the subsequent binding to receptors in target cells, ligands act as chemical signals that travel to the target cells to coordinate responses. The types of molecules that serve as ligands are incredibly varied and range from small proteins to small ions like calcium ( $\text{Ca}^{2+}$ ).

### Small Hydrophobic Ligands

Small hydrophobic ligands can directly diffuse through the plasma membrane and interact with internal receptors. Important members of this class of ligands are the steroid hormones. Steroids are lipids that have a hydrocarbon skeleton with four fused rings; different steroids have different functional groups attached to the carbon skeleton. Steroid hormones include the female sex hormone, estradiol, which is a type of estrogen; the male sex hormone, testosterone; and cholesterol, which is an important structural component of biological membranes and a precursor of steroid hormones ([link](#)). Other hydrophobic hormones include thyroid hormones and vitamin D. In order to be soluble in blood, hydrophobic ligands must bind to carrier proteins while they are being transported through the bloodstream.

Steroid hormones have similar chemical structures to their precursor, cholesterol. Because these molecules are small and hydrophobic, they can diffuse directly across the plasma

membrane into the cell, where they interact with internal

receptors.

### **Water-Soluble Ligands**

Water-soluble ligands are polar and therefore cannot pass through the plasma membrane unaided; sometimes, they are too large to pass through the membrane at all. Instead, most water-soluble ligands bind to the extracellular domain of cell-surface receptors. This group of ligands is quite diverse and includes small molecules, peptides, and proteins.

### **Other Ligands**

Nitric oxide (NO) is a gas that also acts as a ligand. It is able to diffuse directly across the plasma membrane, and one of its roles is to interact with receptors in smooth muscle and induce relaxation of the tissue. NO has a very short half-life and therefore only functions over short distances. Nitroglycerin, a treatment for heart disease, acts by triggering the release of NO, which causes blood vessels to dilate (expand), thus restoring blood flow to the heart. NO has become better known recently because the pathway that it affects is targeted by prescription medications for erectile dysfunction, such as Viagra (erection involves dilated blood vessels).

### **Section Summary**

Cells communicate by both inter- and intracellular signaling. Signaling cells secrete ligands that bind to target cells and initiate a chain of events within the target cell. The four categories of signaling in multicellular organisms are paracrine signaling, endocrine signaling, autocrine signaling, and direct signaling across gap junctions. Paracrine signaling takes place over short distances. Endocrine signals are carried long distances through the bloodstream by hormones, and autocrine signals are received by the same cell that sent the signal or other nearby cells of the same kind. Gap junctions allow small molecules, including signaling molecules, to flow between neighboring cells.

Internal receptors are found in the cell cytoplasm. Here, they bind ligand molecules that cross the plasma membrane; these receptor-ligand complexes move to the nucleus and interact directly with cellular DNA. Cell-surface receptors transmit a signal from outside the cell to

the cytoplasm. Ion channel-linked receptors, when bound to their ligands, form a pore through the plasma membrane through which certain ions can pass. G-protein-linked receptors interact with a G-protein on the cytoplasmic side of the plasma membrane, promoting the exchange of bound GDP for GTP and interacting with other enzymes or ion channels to transmit a signal. Enzyme-linked receptors transmit a signal from outside the cell to an intracellular domain of a membrane-bound enzyme. Ligand binding causes activation of the enzyme. Small hydrophobic ligands (like steroids) are able to penetrate the plasma membrane and bind to internal receptors. Water-soluble hydrophilic ligands are unable to pass through the membrane; instead, they bind to cell-surface receptors, which transmit the signal to the inside of the cell.

## Art Connections

[\[link\]](#) HER2 is a receptor tyrosine kinase. In 30 percent of human breast cancers, HER2 is permanently activated, resulting in unregulated cell division. Lapatinib, a drug used to treat breast cancer, inhibits HER2 receptor tyrosine kinase autophosphorylation (the process by which the receptor adds phosphates onto itself), thus reducing tumor growth by 50 percent. Besides autophosphorylation, which of the following steps would be inhibited by Lapatinib?

- Signaling molecule binding, dimerization, and the downstream cellular response.
- Dimerization, and the downstream cellular response.
- The downstream cellular response.
- Phosphatase activity, dimerization, and the downstream cellular response.

[\[link\]](#) C. The downstream cellular response would be inhibited.

## Review Questions

What property prevents the ligands of cell-surface receptors from entering the cell?

- The molecules bind to the extracellular domain.
- The molecules are hydrophilic and cannot penetrate the hydrophobic interior of the plasma membrane.
- The molecules are attached to transport proteins that deliver them through the bloodstream to target cells.
- The ligands are able to penetrate the membrane and directly influence gene expression upon receptor binding.

B

The secretion of hormones by the pituitary gland is an example of \_\_\_\_\_.

- autocrine signaling
- paracrine signaling
- endocrine signaling
- direct signaling across gap junctions

C

Why are ion channels necessary to transport ions into or out of a cell?

- a. Ions are too large to diffuse through the membrane.
- b. Ions are charged particles and cannot diffuse through the hydrophobic interior of the membrane.
- c. Ions do not need ion channels to move through the membrane.
- d. Ions bind to carrier proteins in the bloodstream, which must be removed before transport into the cell.

B

Endocrine signals are transmitted more slowly than paracrine signals because \_\_\_\_\_.

- a. the ligands are transported through the bloodstream and travel greater distances
- b. the target and signaling cells are close together
- c. the ligands are degraded rapidly
- d. the ligands don't bind to carrier proteins during transport

A

### **Free Response**

What is the difference between intracellular signaling and intercellular signaling?

Intracellular signaling occurs within a cell, and intercellular signaling occurs between cells.

How are the effects of paracrine signaling limited to an area near the signaling cells?

The secreted ligands are quickly removed by degradation or reabsorption into the cell so that they cannot travel far.

What are the differences between internal receptors and cell-surface receptors?

Internal receptors are located inside the cell, and their ligands enter the cell to bind the receptor. The complex formed by the internal receptor and the ligand then enters the nucleus and directly affects protein production by binding to the chromosomal DNA and initiating the making of mRNA that codes for proteins. Cell-surface receptors, however, are embedded in the plasma membrane, and their ligands do not enter the cell. Binding of the ligand to the cell-surface receptor initiates a cell signaling cascade and does not directly influence the making of proteins; however, it may involve the activation of intracellular proteins.

Cells grown in the laboratory are mixed with a dye molecule that is unable to pass through the plasma membrane. If a ligand is added to the cells, observations show that the dye enters the cells. What type of receptor did the ligand bind to on the cell surface?

An ion channel receptor opened up a pore in the membrane, which allowed the ionic dye to move into the cell.

### **Footnotes**

- [1](#) A. B. Sigalov, The School of Nature. IV. Learning from Viruses, *Self/Nonsel* 1, no. 4 (2010): 282-298. Y. Cao, X. Koh, L. Dong, X. Du, A. Wu, X. Ding, H. Deng, Y. Shu, J. Chen, T. Jiang, Rapid Estimation of Binding Activity of Influenza Virus Hemagglutinin to Human and Avian Receptors, *PLoS One* 6, no. 4 (2011): e18664.

## Glossary

autocrine signal

signal that is sent and received by the same or similar nearby cells

cell-surface receptor

cell-surface protein that transmits a signal from the exterior of the cell to the interior, even though the ligand does not enter the cell

chemical synapse

small space between axon terminals and dendrites of nerve cells where neurotransmitters function

endocrine cell

cell that releases ligands involved in endocrine signaling (hormones)

endocrine signal

long-distance signal that is delivered by ligands (hormones) traveling through an organisms circulatory system from the signaling cell to the target cell

enzyme-linked receptor

cell-surface receptor with intracellular domains that are associated with membrane-bound enzymes

extracellular domain

region of a cell-surface receptor that is located on the cell surface

G-protein-linked receptor

cell-surface receptor that activates membrane-bound G-proteins to transmit a signal from the receptor to nearby membrane components

intercellular signaling

communication between cells

internal receptor

(also, intracellular receptor) receptor protein that is located in the cytosol of a cell and binds to ligands that pass through the plasma membrane

intracellular mediator

(also, second messenger) small molecule that transmits signals within a cell

intracellular signaling

communication within cells

ion channel-linked receptor

cell-surface receptor that forms a plasma membrane channel, which opens when a ligand binds to the extracellular domain (ligand-gated channels)

ligand

molecule produced by a signaling cell that binds with a specific receptor, delivering a signal in the process

neurotransmitter

chemical ligand that carries a signal from one nerve cell to the next

paracrine signal

signal between nearby cells that is delivered by ligands traveling in the liquid medium in the space between the cells

receptor

protein in or on a target cell that bind to ligands

signaling cell

cell that releases signal molecules that allow communication with another cell

synaptic signal

chemical signal (neurotransmitter) that travels between nerve cells

target cell

cell that has a receptor for a signal or ligand from a signaling cell

Propagation of the Signal

By the end of this section, you will be able to:

- Explain how the binding of a ligand initiates signal transduction throughout a cell
- Recognize the role of phosphorylation in the transmission of intracellular signals
- Evaluate the role of second messengers in signal transmission

Once a ligand binds to a receptor, the signal is transmitted through the membrane and into the cytoplasm. Continuation of a signal in this manner is called signal transduction. Signal transduction only occurs with cell-surface receptors because internal receptors are able to interact directly with DNA in the nucleus to initiate protein synthesis.

When a ligand binds to its receptor, conformational changes occur that affect the receptor's intracellular domain. Conformational changes of the extracellular domain upon ligand binding can propagate through the membrane region of the receptor and lead to activation of the intracellular domain or its associated proteins. In some cases, binding of the ligand causes dimerization of the receptor, which means that two receptors bind to each other to form a stable complex called a dimer. A dimer is a chemical compound formed when two molecules (often identical) join together. The binding of the receptors in this manner enables their intracellular domains to come into close contact and activate each other.

### **Binding Initiates a Signaling Pathway**

After the ligand binds to the cell-surface receptor, the activation of the receptor's intracellular components sets off a chain of events that is called a signaling pathway or a signaling cascade. In a signaling pathway, second messengers, enzymes, and activated proteins interact with specific proteins, which are in turn activated in a chain reaction that eventually leads to a change in the cell's environment ([\[link\]](#)). The events in the cascade occur in a series, much

like a current flows in a river. Interactions that occur before a certain point are defined as upstream events, and events after that point are called downstream events.

#### Art Connection

The epidermal growth factor (EGF) receptor (EGFR) is a receptor tyrosine kinase involved in the regulation of cell growth, wound healing, and tissue repair. When EGF binds to the EGFR, a cascade of downstream events causes the cell to grow and divide. If EGFR is activated at inappropriate times, uncontrolled cell growth (cancer) may

occur.

In certain cancers, the GTPase activity of the RAS G-protein is inhibited. This means that the RAS protein can no longer hydrolyze GTP into GDP. What effect would this have on downstream cellular events?

Signaling pathways can get very complicated very quickly because most cellular proteins can affect different downstream events, depending on the conditions within the cell. A single pathway can branch off toward different endpoints based on the interplay between two or more signaling pathways, and the same ligands are often used to initiate different signals in different cell types. This variation in response is due to differences in protein expression in different cell types. Another complicating element is signal integration of the pathways, in which signals from two or more different cell-surface receptors merge to activate the same response in the cell. This process can ensure that multiple external requirements are met before a cell commits to a specific response.

The effects of extracellular signals can also be amplified by enzymatic cascades. At the initiation of the signal, a single ligand binds to a single receptor. However, activation of a receptor-linked enzyme can activate many copies of a component of the signaling cascade, which amplifies the signal.

### **Methods of Intracellular Signaling**

The induction of a signaling pathway depends on the modification of a cellular component by an enzyme. There are numerous enzymatic modifications that can occur, and they are recognized in turn by the next component downstream. The following are some of the more common events in intracellular signaling.

Link to Learning

Observe an animation of cell signaling at this [site](#).

### **Phosphorylation**

One of the most common chemical modifications that occurs in signaling pathways is the addition of a phosphate group ( $\text{PO}_4^{-3}$ ) to a molecule such as a protein in a process called phosphorylation. The phosphate can be added to a nucleotide such as GMP to form GDP or GTP. Phosphates are also often added to serine, threonine, and tyrosine residues of proteins, where they replace the hydroxyl group of the amino acid ([link](#)). The transfer of the phosphate is catalyzed by an enzyme called a kinase. Various kinases are named for the substrate they phosphorylate. Phosphorylation of serine and threonine residues often activates enzymes. Phosphorylation of tyrosine residues can either affect the activity of an enzyme or create a binding site that interacts with downstream components in the signaling cascade. Phosphorylation may activate or inactivate enzymes, and the reversal of phosphorylation, dephosphorylation by a phosphatase, will reverse the effect.

In protein phosphorylation, a phosphate group ( $\text{PO}_4^{-3}$ ) is added to residues of the amino acids

serine, threonine, and tyrosine.

### **Second Messengers**

Second messengers are small molecules that propagate a signal after it has been initiated by the binding of the signaling molecule to the receptor. These molecules help to spread a signal through the cytoplasm by altering the behavior of certain cellular proteins.

Calcium ion is a widely used second messenger. The free concentration of calcium ions ( $\text{Ca}^{2+}$ ) within a cell is very low because ion pumps in the plasma membrane continuously use

adenosine-5'-triphosphate (ATP) to remove it. For signaling purposes,  $\text{Ca}^{2+}$  is stored in cytoplasmic vesicles, such as the endoplasmic reticulum, or accessed from outside the cell. When signaling occurs, ligand-gated calcium ion channels allow the higher levels of  $\text{Ca}^{2+}$  that are present outside the cell (or in intracellular storage compartments) to flow into the cytoplasm, which raises the concentration of cytoplasmic  $\text{Ca}^{2+}$ . The response to the increase in  $\text{Ca}^{2+}$  varies, depending on the cell type involved. For example, in the  $\beta$ -cells of the pancreas,  $\text{Ca}^{2+}$  signaling leads to the release of insulin, and in muscle cells, an increase in  $\text{Ca}^{2+}$  leads to muscle contractions.

Another second messenger utilized in many different cell types is cyclic AMP (cAMP). Cyclic AMP is synthesized by the enzyme adenylyl cyclase from ATP ([link](#)). The main role of cAMP in cells is to bind to and activate an enzyme called cAMP-dependent kinase (A-kinase). A-kinase regulates many vital metabolic pathways: It phosphorylates serine and threonine residues of its target proteins, activating them in the process. A-kinase is found in many different types of cells, and the target proteins in each kind of cell are different. Differences give rise to the variation of the responses to cAMP in different cells.

This diagram shows the mechanism for the formation of cyclic AMP (cAMP). cAMP serves as a second messenger to activate or inactivate proteins within the cell. Termination of the signal occurs when an enzyme called phosphodiesterase converts cAMP into

AMP.

Present in small concentrations in the plasma membrane, inositol phospholipids are lipids that can also be converted into second messengers. Because these molecules are membrane components, they are located near membrane-bound receptors and can easily interact with them. Phosphatidylinositol (PI) is the main phospholipid that plays a role in cellular

signaling. Enzymes known as kinases phosphorylate PI to form PI-phosphate (PIP) and PI-bisphosphate (PIP<sub>2</sub>).

The enzyme phospholipase C cleaves PIP<sub>2</sub> to form diacylglycerol (DAG) and inositol triphosphate (IP<sub>3</sub>) ([link](#)). These products of the cleavage of PIP<sub>2</sub> serve as second messengers. Diacylglycerol (DAG) remains in the plasma membrane and activates protein kinase C (PKC), which then phosphorylates serine and threonine residues in its target proteins. IP<sub>3</sub> diffuses into the cytoplasm and binds to ligand-gated calcium channels in the endoplasmic reticulum to release Ca<sup>2+</sup> that continues the signal cascade.

The enzyme phospholipase C breaks down PIP<sub>2</sub> into IP<sub>3</sub> and DAG, both of which serve as

second messengers.

## Section Summary

Ligand binding to the receptor allows for signal transduction through the cell. The chain of events that conveys the signal through the cell is called a signaling pathway or cascade. Signaling pathways are often very complex because of the interplay between different proteins. A major component of cell signaling cascades is the phosphorylation of molecules by enzymes known as kinases. Phosphorylation adds a phosphate group to serine, threonine, and tyrosine residues in a protein, changing their shapes, and activating or inactivating the protein. Small molecules like nucleotides can also be phosphorylated. Second messengers are small, non-protein molecules that are used to transmit a signal within a cell. Some examples of second messengers are calcium ions (Ca<sup>2+</sup>), cyclic AMP (cAMP), diacylglycerol (DAG), and inositol triphosphate (IP<sub>3</sub>).

## Art Connections

[\[link\]](#) In certain cancers, the GTPase activity of the RAS G-protein is inhibited. This means that the RAS protein can no longer hydrolyze GTP into GDP. What effect would this have on downstream cellular events?

[\[link\]](#) ERK would become permanently activated, resulting in cell proliferation, migration, adhesion, and the growth of new blood vessels. Apoptosis would be inhibited.

## Review Questions

Where do DAG and IP<sub>3</sub> originate?

- They are formed by phosphorylation of cAMP.
- They are ligands expressed by signaling cells.
- They are hormones that diffuse through the plasma membrane to stimulate protein production.
- They are the cleavage products of the inositol phospholipid, PIP<sub>2</sub>.

D

What property enables the residues of the amino acids serine, threonine, and tyrosine to be phosphorylated?

- They are polar.
- They are non-polar.
- They contain a hydroxyl group.
- They occur more frequently in the amino acid sequence of signaling proteins.

C

## Free Response

The same second messengers are used in many different cells, but the response to second messengers is different in each cell. How is this possible?

Different cells produce different proteins, including cell-surface receptors and signaling pathway components. Therefore, they respond to different ligands, and the second messengers activate different pathways. Signal integration can also change the end result of signaling.

What would happen if the intracellular domain of a cell-surface receptor was switched with the domain from another receptor?

The binding of the ligand to the extracellular domain would activate the pathway normally activated by the receptor donating the intracellular domain.

## Glossary

cyclic AMP (cAMP)

second messenger that is derived from ATP

cyclic AMP-dependent kinase

(also, protein kinase A, or PKA) kinase that is activated by binding to cAMP

diacylglycerol (DAG)

cleavage product of PIP<sub>2</sub> that is used for signaling within the plasma membrane

dimer

chemical compound formed when two molecules join together

dimerization

(of receptor proteins) interaction of two receptor proteins to form a functional complex called a dimer

inositol phospholipid

lipid present at small concentrations in the plasma membrane that is converted into a second messenger; it has inositol (a carbohydrate) as its hydrophilic head group

inositol triphosphate (IP<sub>3</sub>)

cleavage product of PIP<sub>2</sub> that is used for signaling within the cell

kinase

enzyme that catalyzes the transfer of a phosphate group from ATP to another molecule

second messenger

small, non-protein molecule that propagates a signal within the cell after activation of a receptor causes its release

signal integration

interaction of signals from two or more different cell-surface receptors that merge to activate the same response in the cell

signal transduction

propagation of the signal through the cytoplasm (and sometimes also the nucleus) of the cell

signaling pathway

(also signaling cascade) chain of events that occurs in the cytoplasm of the cell to propagate the signal from the plasma membrane to produce a response

Response to the Signal

By the end of this section, you will be able to:

- Describe how signaling pathways direct protein expression, cellular metabolism, and cell growth
- Identify the function of PKC in signal transduction pathways
- Recognize the role of apoptosis in the development and maintenance of a healthy organism

Inside the cell, ligands bind to their internal receptors, allowing them to directly affect the cell's DNA and protein-producing machinery. Using signal transduction pathways, receptors in the plasma membrane produce a variety of effects on the cell. The results of signaling pathways are extremely varied and depend on the type

of cell involved as well as the external and internal conditions. A small sampling of responses is described below.

## Gene Expression

Some signal transduction pathways regulate the transcription of RNA. Others regulate the translation of proteins from mRNA. An example of a protein that regulates translation in the nucleus is the MAP kinase ERK. ERK is activated in a phosphorylation cascade when epidermal growth factor (EGF) binds the EGF receptor (see [link](#)). Upon phosphorylation, ERK enters the nucleus and activates a protein kinase that, in turn, regulates protein translation ([link](#)).

ERK is a MAP kinase that activates translation when it is phosphorylated. ERK phosphorylates MNK1, which in turn phosphorylates eIF-4E, an elongation initiation factor that, with other initiation factors, is associated with mRNA. When eIF-4E becomes phosphorylated, the mRNA unfolds, allowing protein synthesis in the nucleus to begin. (See [link](#) for the phosphorylation pathway that activates

ERK.)

The second kind of protein with which PKC can interact is a protein that acts as an inhibitor. An inhibitor is a molecule that binds to a protein and prevents it from functioning or reduces its function. In this case, the inhibitor is a protein called I $\kappa$ -B, which binds to the regulatory protein NF- $\kappa$ B. (The symbol  $\kappa$  represents the Greek letter kappa.) When I $\kappa$ -B is bound to NF- $\kappa$ B, the complex cannot enter the nucleus of the cell, but when I $\kappa$ -B is phosphorylated by PKC, it can no longer bind NF- $\kappa$ B, and NF- $\kappa$ B (a transcription factor) can enter the nucleus and initiate RNA transcription. In this case, the effect of phosphorylation is to inactivate an inhibitor and thereby activate the process of transcription.

## Increase in Cellular Metabolism

The result of another signaling pathway affects muscle cells. The activation of  $\beta$ -adrenergic receptors in muscle cells by adrenaline leads to an increase in cyclic AMP (cAMP) inside the cell. Also known as epinephrine, adrenaline is a hormone (produced by the adrenal gland

attached to the kidney) that readies the body for short-term emergencies. Cyclic AMP activates PKA (protein kinase A), which in turn phosphorylates two enzymes. The first enzyme promotes the degradation of glycogen by activating intermediate glycogen phosphorylase kinase (GPK) that in turn activates glycogen phosphorylase (GP) that catabolizes glycogen into glucose. (Recall that your body converts excess glucose to glycogen for short-term storage. When energy is needed, glycogen is quickly reconverted to glucose.) Phosphorylation of the second enzyme, glycogen synthase (GS), inhibits its ability to form glycogen from glucose. In this manner, a muscle cell obtains a ready pool of glucose by activating its formation via glycogen degradation and by inhibiting the use of glucose to form glycogen, thus preventing a futile cycle of glycogen degradation and synthesis. The glucose is then available for use by the muscle cell in response to a sudden surge of adrenaline—the “fight or flight” reflex.

## Cell Growth

Cell signaling pathways also play a major role in cell division. Cells do not normally divide unless they are stimulated by signals from other cells. The ligands that promote cell growth are called growth factors. Most growth factors bind to cell-surface receptors that are linked to tyrosine kinases. These cell-surface receptors are called receptor tyrosine kinases (RTKs). Activation of RTKs initiates a signaling pathway that includes a G-protein called RAS, which activates the MAP kinase pathway described earlier. The enzyme MAP kinase then stimulates the expression of proteins that interact with other cellular components to initiate cell division.

### Career Connection

**Cancer Biologist** Cancer biologists study the molecular origins of cancer with the goal of developing new prevention methods and treatment strategies that will inhibit the growth of tumors without harming the normal cells of the body. As mentioned earlier, signaling pathways control cell growth. These signaling pathways are controlled by signaling proteins, which are, in turn, expressed by genes. Mutations in these genes can result in malfunctioning signaling proteins. This prevents the cell from regulating its cell cycle, triggering unrestricted cell division and cancer. The genes that regulate the signaling proteins are one type of oncogene which is a gene that has the potential to cause cancer. The gene encoding RAS is an oncogene that was originally discovered when mutations in the RAS protein were linked to cancer. Further studies have indicated that 30 percent of cancer cells have a mutation in the RAS gene that leads to uncontrolled growth. If left unchecked, uncontrolled cell division can lead tumor formation and metastasis, the growth of cancer cells in new locations in the body.

Cancer biologists have been able to identify many other oncogenes that contribute to the development of cancer. For example, HER2 is a cell-surface receptor that is present in excessive amounts in 20 percent of human breast cancers. Cancer biologists realized that gene duplication led to HER2 overexpression in 25 percent of breast cancer patients and developed a drug called Herceptin (trastuzumab). Herceptin is a monoclonal antibody that targets HER2 for removal by the immune system. Herceptin therapy helps to control signaling through HER2. The use of Herceptin in combination with chemotherapy has helped to increase the overall survival rate of patients with metastatic breast cancer.

More information on cancer biology research can be found at the National Cancer Institute website (<http://www.cancer.gov/cancertopics/understandingcancer/targetedtherapies>).

## Cell Death

When a cell is damaged, superfluous, or potentially dangerous to an organism, a cell can initiate a mechanism to trigger programmed cell death, or apoptosis. Apoptosis allows a cell to die in a controlled manner that prevents the release of potentially damaging molecules from inside the cell. There are many internal checkpoints that monitor a cell's health; if abnormalities are observed, a cell can spontaneously initiate the process of apoptosis. However, in some cases, such as a viral infection or uncontrolled cell division due to cancer, the cell's normal checks and balances fail. External signaling can also initiate apoptosis. For example, most normal animal cells have receptors that interact with the extracellular matrix, a network of glycoproteins that provides structural support for cells in an organism. The binding of cellular receptors to the extracellular matrix initiates a signaling cascade within the cell. However, if the cell moves away from the extracellular matrix, the signaling ceases, and the cell undergoes apoptosis. This system keeps cells from traveling through the body and proliferating out of control, as happens with tumor cells that metastasize.

Another example of external signaling that leads to apoptosis occurs in T-cell development. T-cells are immune cells that bind to foreign macromolecules and particles, and target them for destruction by the immune system. Normally, T-cells do not target "self" proteins (those of their own organism), a process that can lead to autoimmune diseases. In order to develop the ability to discriminate between self and non-self, immature T-cells undergo screening to determine whether they bind to so-called self proteins. If the T-cell receptor binds to self proteins, the cell initiates apoptosis to remove the potentially dangerous cell.

Apoptosis is also essential for normal embryological development. In vertebrates, for example, early stages of development include the formation of web-like tissue between individual fingers and toes ([link](#)). During the course of normal development, these unneeded cells must be eliminated, enabling fully separated fingers and toes to form. A cell signaling mechanism triggers apoptosis, which destroys the cells between the developing digits.

The histological section of a foot of a 15-day-old mouse embryo, visualized using light microscopy, reveals areas of tissue between the toes, which apoptosis will eliminate before the mouse reaches its full gestational age at 27 days. (credit: modification of work by Michal

Mañas)

## Termination of the Signal Cascade

The aberrant signaling often seen in tumor cells is proof that the termination of a signal at the appropriate time can be just as important as the initiation of a signal. One method of stopping

a specific signal is to degrade the ligand or remove it so that it can no longer access its receptor. One reason that hydrophobic hormones like estrogen and testosterone trigger long-lasting events is because they bind carrier proteins. These proteins allow the insoluble molecules to be soluble in blood, but they also protect the hormones from degradation by circulating enzymes.

Inside the cell, many different enzymes reverse the cellular modifications that result from signaling cascades. For example, phosphatases are enzymes that remove the phosphate group attached to proteins by kinases in a process called dephosphorylation. Cyclic AMP (cAMP) is degraded into AMP by phosphodiesterase, and the release of calcium stores is reversed by the  $\text{Ca}^{2+}$  pumps that are located in the external and internal membranes of the cell.

## Section Summary

The initiation of a signaling pathway is a response to external stimuli. This response can take many different forms, including protein synthesis, a change in the cell's metabolism, cell growth, or even cell death. Many pathways influence the cell by initiating gene expression, and the methods utilized are quite numerous. Some pathways activate enzymes that interact with DNA transcription factors. Others modify proteins and induce them to change their location in the cell. Depending on the status of the organism, cells can respond by storing energy as glycogen or fat, or making it available in the form of glucose. A signal transduction pathway allows muscle cells to respond to immediate requirements for energy in the form of glucose. Cell growth is almost always stimulated by external signals called growth factors. Uncontrolled cell growth leads to cancer, and mutations in the genes encoding protein components of signaling pathways are often found in tumor cells. Programmed cell death, or apoptosis, is important for removing damaged or unnecessary cells. The use of cellular signaling to organize the dismantling of a cell ensures that harmful molecules from the cytoplasm are not released into the spaces between cells, as they are in uncontrolled death, necrosis. Apoptosis also ensures the efficient recycling of the components of the dead cell. Termination of the cellular signaling cascade is very important so that the response to a signal is appropriate in both timing and intensity. Degradation of signaling molecules and dephosphorylation of phosphorylated intermediates of the pathway by phosphatases are two ways to terminate signals within the cell.

## Review Questions

What is the function of a phosphatase?

- A phosphatase removes phosphorylated amino acids from proteins.
- A phosphatase removes the phosphate group from phosphorylated amino acid residues in a protein.
- A phosphatase phosphorylates serine, threonine, and tyrosine residues.
- A phosphatase degrades second messengers in the cell.

B

How does NF- $\kappa$ B induce gene expression?

- A small, hydrophobic ligand binds to NF- $\kappa$ B, activating it.

- b. Phosphorylation of the inhibitor I $\kappa$ -B dissociates the complex between it and NF- $\kappa$ B, and allows NF- $\kappa$ B to enter the nucleus and stimulate transcription.
- c. NF- $\kappa$ B is phosphorylated and is then free to enter the nucleus and bind DNA.
- d. NF- $\kappa$ B is a kinase that phosphorylates a transcription factor that binds DNA and promotes protein production.

B

Apoptosis can occur in a cell when the cell is \_\_\_\_\_.

- a. damaged
- b. no longer needed
- c. infected by a virus
- d. all of the above

D

What is the effect of an inhibitor binding an enzyme?

- a. The enzyme is degraded.
- b. The enzyme is activated.
- c. The enzyme is inactivated.
- d. The complex is transported out of the cell.

C

### Free Response

What is a possible result of a mutation in a kinase that controls a pathway that stimulates cell growth?

If a kinase is mutated so that it is always activated, it will continuously signal through the pathway and lead to uncontrolled growth and possibly cancer. If a kinase is mutated so that it cannot function, the cell will not respond to ligand binding.

How does the extracellular matrix control the growth of cells?

Receptors on the cell surface must be in contact with the extracellular matrix in order to receive positive signals that allow the cell to live. If the receptors are not activated by binding, the cell will undergo apoptosis. This ensures that cells are in the correct place in the body and helps to prevent invasive cell growth as occurs in metastasis in cancer.

### Glossary

apoptosis

programmed cell death

growth factor

ligand that binds to cell-surface receptors and stimulates cell growth

inhibitor

molecule that binds to a protein (usually an enzyme) and keeps it from functioning

phosphatase

enzyme that removes the phosphate group from a molecule that has been previously phosphorylated

phosphodiesterase

enzyme that degrades cAMP, producing AMP, to terminate signaling

Signaling in Single-Celled Organisms

By the end of this section, you will be able to:

- Describe how single-celled yeasts use cell signaling to communicate with one another
- Relate the role of quorum sensing to the ability of some bacteria to form biofilms

Within-cell signaling allows bacteria to respond to environmental cues, such as nutrient levels, some single-celled organisms also release molecules to signal to each other.

### **Signaling in Yeast**

Yeasts are eukaryotes (fungi), and the components and processes found in yeast signals are similar to those of cell-surface receptor signals in multicellular organisms. Budding yeasts ([link](#)) are able to participate in a process that is similar to sexual reproduction that entails two haploid cells (cells with one-half the normal number of chromosomes) combining to form a diploid cell (a cell with two sets of each chromosome, which is what normal body cells contain). In order to find another haploid yeast cell that is prepared to mate, budding yeasts secrete a signaling molecule called mating factor. When mating factor binds to cell-surface receptors in other yeast cells that are nearby, they stop their normal growth cycles and initiate a cell signaling cascade that includes protein kinases and GTP-binding proteins that are similar to G-proteins.

Budding *Saccharomyces cerevisiae* yeast cells can communicate by releasing a signaling molecule called mating factor. In this micrograph, they are visualized using differential

interference contrast microscopy, a light microscopy technique that enhances the contrast of

the sample.

## Signaling in Bacteria

Signaling in bacteria enables bacteria to monitor extracellular conditions, ensure that there are sufficient amounts of nutrients, and ensure that hazardous situations are avoided. There are circumstances, however, when bacteria communicate with each other.

The first evidence of bacterial communication was observed in a bacterium that has a symbiotic relationship with Hawaiian bobtail squid. When the population density of the bacteria reaches a certain level, specific gene expression is initiated, and the bacteria produce bioluminescent proteins that emit light. Because the number of cells present in the environment (cell density) is the determining factor for signaling, bacterial signaling was named quorum sensing. In politics and business, a quorum is the minimum number of members required to be present to vote on an issue.

Quorum sensing uses autoinducers as signaling molecules. Autoinducers are signaling molecules secreted by bacteria to communicate with other bacteria of the same kind. The secreted autoinducers can be small, hydrophobic molecules such as acyl-homoserine lactone, (AHL) or larger peptide-based molecules; each type of molecule has a different mode of action. When AHL enters target bacteria, it binds to transcription factors, which then switch gene expression on or off ([link](#)). The peptide autoinducers stimulate more complicated signaling pathways that include bacterial kinases. The changes in bacteria following exposure to autoinducers can be quite extensive. The pathogenic bacterium *Pseudomonas aeruginosa* has 616 different genes that respond to autoinducers.

Art Connection

Autoinducers are small molecules or proteins produced by bacteria that regulate gene

expression.

Which of the following statements about quorum sensing is false?

- a. Autoinducer must bind to receptor to turn on transcription of genes responsible for the production of more autoinducer.
- b. The receptor stays in the bacterial cell, but the autoinducer diffuses out.
- c. Autoinducer can only act on a different cell: it cannot act on the cell in which it is made.
- d. Autoinducer turns on genes that enable the bacteria to form a biofilm.

Some species of bacteria that use quorum sensing form biofilms, complex colonies of bacteria (often containing several species) that exchange chemical signals to coordinate the release of toxins that will attack the host. Bacterial biofilms ([link](#)) can sometimes be found on medical equipment; when biofilms invade implants such as hip or knee replacements or heart pacemakers, they can cause life-threatening infections.

#### Art Connection

Cell-cell communication enables these (a) *Staphylococcus aureus* bacteria to work together to form a biofilm inside a hospital patient's catheter, seen here via scanning electron microscopy. *S. aureus* is the main cause of hospital-acquired infections. (b) Hawaiian bobtail squid have a symbiotic relationship with the bioluminescent bacteria *Vibrio fischeri*. The luminescence makes it difficult to see the squid from below because it effectively eliminates its shadow. In return for camouflage, the squid provides food for the bacteria. Free-living *V. fischeri* do not produce luciferase, the enzyme responsible for luminescence, but *V. fischeri* living in a symbiotic relationship with the squid do. Quorum sensing determines whether the bacteria should produce the luciferase enzyme. (credit a: modifications of work by CDC/Janice Carr; credit b: modifications of work by

Cliff1066/Flickr)

What advantage might biofilm production confer on the *S. aureus* inside the catheter?

Research on the details of quorum sensing has led to advances in growing bacteria for industrial purposes. Recent discoveries suggest that it may be possible to exploit bacterial signaling pathways to control bacterial growth; this process could replace or supplement antibiotics that are no longer effective in certain situations.

Link to Learning

Watch geneticist Bonnie Bassler discuss her [discovery](#) of quorum sensing in biofilm bacteria in squid.

Evolution Connection

**Cellular Communication in Yeasts**The first life on our planet consisted of single-celled prokaryotic organisms that had limited interaction with each other. While some external signaling occurs between different species of single-celled organisms, the majority of signaling within bacteria and yeasts concerns only other members of the same species. The evolution of cellular communication is an absolute necessity for the development of multicellular organisms, and this innovation is thought to have required approximately 2.5 billion years to appear in early life forms.

Yeasts are single-celled eukaryotes, and therefore have a nucleus and organelles characteristic of more complex life forms. Comparisons of the genomes of yeasts, nematode worms, fruit flies, and humans illustrate the evolution of increasingly complex signaling systems that allow for the efficient inner workings that keep humans and other complex life forms functioning correctly.

Kinases are a major component of cellular communication, and studies of these enzymes illustrate the evolutionary connectivity of different species. Yeasts have 130 types of kinases. More complex organisms such as nematode worms and fruit flies have 454 and 239 kinases, respectively. Of the 130 kinase types in yeast, 97 belong to the 55 subfamilies of kinases that are found in other eukaryotic organisms. The only obvious deficiency seen in yeasts is the complete absence of tyrosine kinases. It is hypothesized that phosphorylation of tyrosine residues is needed to control the more sophisticated functions of development, differentiation, and cellular communication used in multicellular organisms.

Because yeasts contain many of the same classes of signaling proteins as humans, these organisms are ideal for studying signaling cascades. Yeasts multiply quickly and are much simpler organisms than humans or other multicellular animals. Therefore, the signaling cascades are also simpler and easier to study, although they contain similar counterparts to human signaling.<sup>1</sup>

Link to Learning

Watch this collection of interview clips with biofilm researchers in “What Are Bacterial Biofilms?”

### Introduction

class="introduction" class="summary" title="Sections Summary" class="art-exercise" title="Art Connections" class="multiple-choice" title="Multiple Choice" class="free-response" title="Free Response" A sea urchin begins life as a single cell that (a) divides to form two cells, visible by scanning electron microscopy. After four rounds of cell division, (b) there are 16 cells, as seen in this SEM image. After many rounds of cell division, the individual develops into a complex, multicellular organism, as seen in this (c) mature sea urchin. (credit a: modification of work by Evelyn Spiegel, Louisa Howard; credit b: modification of work by Evelyn Spiegel, Louisa Howard; credit c: modification of work by

Marco Busdraghi; scale-bar data from Matt Russell)

A human, as well as every sexually reproducing organism, begins life as a fertilized egg (embryo) or zygote. Trillions of cell divisions subsequently occur in a controlled manner to produce a complex, multicellular human. In other words, that original single cell is the ancestor of every other cell in the body. Once a being is fully grown, cell reproduction is still necessary to repair or regenerate tissues. For example, new blood and skin cells are constantly being produced. All multicellular organisms use cell division for growth and the maintenance and repair of cells and tissues. Cell division is tightly regulated, and the occasional failure of regulation can have life-threatening consequences. Single-celled organisms use cell division as their method of reproduction.

### Cell Division

By the end of this section, you will be able to:

- Describe the structure of prokaryotic and eukaryotic genomes
- Distinguish between chromosomes, genes, and traits
- Describe the mechanisms of chromosome compaction

The continuity of life from one cell to another has its foundation in the reproduction of cells by way of the cell cycle. The cell cycle is an orderly sequence of events that describes the stages of a cell's life from the division of a single parent cell to the production of two new daughter cells. The mechanisms involved in the cell cycle are highly regulated.

## Genomic DNA

Before discussing the steps a cell must undertake to replicate, a deeper understanding of the structure and function of a cell's genetic information is necessary. A cell's DNA, packaged as a double-stranded DNA molecule, is called its genome. In prokaryotes, the genome is composed of a single, double-stranded DNA molecule in the form of a loop or circle ([\[link\]](#)). The region in the cell containing this genetic material is called a nucleoid. Some prokaryotes also have smaller loops of DNA called plasmids that are not essential for normal growth. Bacteria can exchange these plasmids with other bacteria, sometimes receiving beneficial new genes that the recipient can add to their chromosomal DNA. Antibiotic resistance is one trait that often spreads through a bacterial colony through plasmid exchange.

Prokaryotes, including bacteria and archaea, have a single, circular chromosome located in a

central region called the nucleoid.

In eukaryotes, the genome consists of several double-stranded linear DNA molecules ([\[link\]](#)). Each species of eukaryotes has a characteristic number of chromosomes in the nuclei of its cells. Human body cells have 46 chromosomes, while human gametes (sperm or eggs) have 23 chromosomes each. A typical body cell, or somatic cell, contains two matched sets of chromosomes, a configuration known as diploid. The letter  $n$  is used to represent a single set of chromosomes; therefore, a diploid organism is designated  $2n$ . Human cells that contain

one set of chromosomes are called gametes, or sex cells; these are eggs and sperm, and are designated *n*, or haploid.

There are 23 pairs of homologous chromosomes in a female human somatic cell. The condensed chromosomes are viewed within the nucleus (top), removed from a cell in mitosis and spread out on a slide (right), and artificially arranged according to length (left); an arrangement like this is called a karyotype. In this image, the chromosomes were exposed to fluorescent stains for differentiation of the different chromosomes. A method of staining called “chromosome painting” employs fluorescent dyes that highlight chromosomes in different colors. (credit: National Human Genome

Project/NIH)

Matched pairs of chromosomes in a diploid organism are called homologous (“same knowledge”) chromosomes. Homologous chromosomes are the same length and have specific nucleotide segments called genes in exactly the same location, or locus. Genes, the functional units of chromosomes, determine specific characteristics by coding for specific proteins. Traits are the variations of those characteristics. For example, hair color is a characteristic with traits that are blonde, brown, or black.

Each copy of a homologous pair of chromosomes originates from a different parent; therefore, the genes themselves are not identical. The variation of individuals within a species is due to the specific combination of the genes inherited from both parents. Even a slightly altered sequence of nucleotides within a gene can result in an alternative trait. For example, there are three possible gene sequences on the human chromosome that code for blood type: sequence A, sequence B, and sequence O. Because all diploid human cells have two copies of the chromosome that determines blood type, the blood type (the trait) is determined by which two versions of the marker gene are inherited. It is possible to have two copies of the same gene sequence on both homologous chromosomes, with one on each (for example, AA, BB, or OO), or two different sequences, such as AB.

Minor variations of traits, such as blood type, eye color, and handedness, contribute to the natural variation found within a species. However, if the entire DNA sequence from any pair of human homologous chromosomes is compared, the difference is less than one percent. The

sex chromosomes, X and Y, are the single exception to the rule of homologous chromosome uniformity: Other than a small amount of homology that is necessary to accurately produce gametes, the genes found on the X and Y chromosomes are different.

## **Eukaryotic Chromosomal Structure and Compaction**

If the DNA from all 46 chromosomes in a human cell nucleus was laid out end to end, it would measure approximately two meters; however, its diameter would be only 2 nm. Considering that the size of a typical human cell is about 10  $\mu\text{m}$  (100,000 cells lined up to equal one meter), DNA must be tightly packaged to fit in the cell's nucleus. At the same time, it must also be readily accessible for the genes to be expressed. During some stages of the cell cycle, the long strands of DNA are condensed into compact chromosomes. There are a number of ways that chromosomes are compacted.

In the first level of compaction, short stretches of the DNA double helix wrap around a core of eight histone proteins at regular intervals along the entire length of the chromosome ([link](#)). The DNA-histone complex is called chromatin. The beadlike, histone DNA complex is called a nucleosome, and DNA connecting the nucleosomes is called linker DNA. A DNA molecule in this form is about seven times shorter than the double helix without the histones, and the beads are about 10 nm in diameter, in contrast with the 2-nm diameter of a DNA double helix. The next level of compaction occurs as the nucleosomes and the linker DNA between them are coiled into a 30-nm chromatin fiber. This coiling further shortens the chromosome so that it is now about 50 times shorter than the extended form. In the third level of packing, a variety of fibrous proteins is used to pack the chromatin. These fibrous proteins also ensure that each chromosome in a non-dividing cell occupies a particular area of the nucleus that does not overlap with that of any other chromosome (see the top image in [link](#)).

Double-stranded DNA wraps around histone proteins to form nucleosomes that have the appearance of "beads on a string." The nucleosomes are coiled into a 30-nm chromatin fiber. When a cell undergoes mitosis, the chromosomes condense even

further.

DNA replicates in the S phase of interphase. After replication, the chromosomes are composed of two linked sister chromatids. When fully compact, the pairs of identically packed chromosomes are bound to each other by cohesin proteins. The connection between the sister chromatids is closest in a region called the centromere. The conjoined sister chromatids, with a diameter of about 1  $\mu\text{m}$ , are visible under a light microscope. The centromeric region is highly condensed and thus will appear as a constricted area.

Link to Learning

This animation illustrates the different levels of chromosome packing.

### The Cell Cycle

By the end of this section, you will be able to:

- Describe the three stages of interphase
- Discuss the behavior of chromosomes during karyokinesis
- Explain how the cytoplasmic content is divided during cytokinesis
- Define the quiescent  $G_0$  phase

The cell cycle is an ordered series of events involving cell growth and cell division that produces two new daughter cells. Cells on the path to cell division proceed through a series of precisely timed and carefully regulated stages of growth, DNA replication, and division that produces two identical (clone) cells. The cell cycle has two major phases: interphase and the mitotic phase ([link](#)). During interphase, the cell grows and DNA is replicated. During the mitotic phase, the replicated DNA and cytoplasmic contents are separated, and the cell divides.

The cell cycle consists of interphase and the mitotic phase. During interphase, the cell grows and the nuclear DNA is duplicated. Interphase is followed by the mitotic phase. During the mitotic phase, the duplicated chromosomes are segregated and distributed into daughter