In section 7.1, you saw how developments in technology helped curious researchers develop the cell theory. Since Robert Hooke made his first observations of cells, microscopes have continued to improve. These improvements have allowed scientists to explore the world of the cell in much greater detail. In this section, you will learn how advances in computer and optical technology have made possible enormous progress in cell biology.

**Light Microscopes**

The earliest microscopes were simple microscopes. They used only one lens, which was similar to a magnifying glass. Because visible light was used to view objects, the simple microscopes were a type of light microscope.

In 1595, a Dutch maker of reading glasses, Zacharias Janssen (1580–c. 1638), designed a microscope that used two lenses to produce a large image. In doing so, he created the first compound microscope. This type of microscope, shown in Figure 7.8, uses two or more lenses placed one on top of the other. Compound microscopes that are used to view objects illuminated by visible light are called compound light microscopes.

The quality of the lenses in Robert Hooke's compound light microscope was poor. As a result he could see little detail. (Van Leeuwenhoek's simple microscope, on the other hand, was far superior to compound microscopes of the time. How he obtained such good results is still a mystery.) During the 1800s, methods for producing better-quality lenses had paved the way for creation of the modern compound microscope. You use compound light microscopes in science class. These microscopes are commonly used to study prepared slides of stained cells as well as living cells. (See Figure 7.10A on the next page.)

**Electron Microscopes**

Many objects that are too small to be seen with a light microscope can be viewed with an electron microscope. Using this type of microscope, specimens are illuminated with a beam of electrons instead of a beam of light. A photograph of an image from an electron microscope is called an electron micrograph. Electron microscopes are extremely powerful, some magnifying images up to 1.2 million times.
The transmission electron microscope (TEM) is one of two main types of electron microscopes. German scientists built the first TEM in 1931. Canadian scientists improved on its design in 1938. The TEM works much like a slide projector, as shown in Figure 7.9. A beam of electrons is transmitted through a specimen to produce a two-dimensional image magnified 10,000× to 100,000× (see Figure 7.10B).

The scanning electron microscope (SEM) was also designed by German scientists in the 1930s. The SEM sweeps a beam of electrons over an object to create a three-dimensional image. These microscopes can be used to view the shapes of specimens in realistic detail (see Figure 7.10C). Although the SEM can reach a magnification of 300,000×, most specimens are easier to view at magnifications less than 10,000×.

![Image of nerve cell stained for light microscopy](A)

![Image of cross-section of nerve cell](B)

![Image of nerve cell with SEM](C)

![Image of nerve cell with TEM](D)

![Image of atomic structure with SEM](E)

**Figure 7.10** A Using compound light microscopes, researchers can view some of the structures within cells. The nerve cell shown here was stained for light microscopy. The other micrographs of nerve cells (B–D) have been coloured. B To view objects with the TEM, specimens are thinly sliced and placed under a vacuum to remove moisture and other interfering particles. Electrons are directed through ultrathin specimens to view internal structures and details. The TEM can magnify images over 1 million times. C Tiny details are visible under the SEM, but only the surface of an object can be observed. D As described on page 268, the confocal laser scanning microscope produces three-dimensional images of cells and their components. E The scanning tunnelling microscope, described on page 268, produces an image of the atomic structure of the cell surface.
Confocal Laser Scanning Microscope

Czech researchers invented the confocal laser scanning microscope (CLSM) in the 1960s. This microscope was introduced elsewhere in the 1980s. The CLSM makes it possible to study specimens that are too thick to be viewed using a compound light microscope. It is not necessary to cut the specimens. Instead, a laser beam is first directed at one plane, then another, and so on. This process creates a series of two-dimensional images. In this way, the CLSM produces optical “slices” of a three-dimensional object, such as those shown in Figure 7.11. The images are “stitched” together using computer software. Using a CLSM is much like studying a whole loaf of bread by examining several slices.

Scanning Tunnelling Microscope

In Unit 1 you saw that it is possible to obtain an image of atoms on an object’s surface. The scanning tunnelling microscope (STM) allows scientists to do this. The STM revolutionized microscopy in the mid-1980s. Because it has more magnifying power than an electron microscope, an STM lets researchers produce images of molecules such as DNA.

To use this microscope, a very fine metal probe is brought near the specimen. Electrons flow between the tip of the probe and atoms on the specimen’s surface. As the probe follows surface contours on the specimen, this information is interpreted by a computer. The computer creates a three-dimensional image, like the one shown in Figure 7.10E on page 267.

In the next investigation you will learn how microscopes are used in cell research.

Many modern microscopes, including electron microscopes, CLSMs, and STMs, are integrated with computers. In many cases, the computer can save the microscope image and display it on a monitor. Researchers can then retrieve, manipulate, and study the image long after it was created. It is also much easier and faster to use a computer to operate the microscope indirectly and adjust the position of a specimen than to do these painstaking tasks by hand. Computers allow researchers to obtain more precise and better-quality images.

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How would you like to try out a magnifying microscope, scanning electron microscope, confocal microscope, and more? Go to the web site above to find out where to go next. Use the virtual tools at the site to view specimens under the microscope. What kinds of specimens can be viewed with each type of microscope? What did you learn from the images? Did the site help you learn more about how microscopes are used? Write a short paragraph evaluating the site’s usefulness.
Microscopes and Cell Research

Think About It

Thousands of scientists use microscopes daily to make new discoveries about cells. Their research improves our health and basic knowledge about biology. What are these scientists learning? How are their discoveries made?

What to Do

1. With a partner, identify an area of cell research that interests you. The research area you choose should apply the use of microscopes in some way. You can use the Internet to search for different types of research, or select one from the list below. Here are some sample topics in cell research:
   - how cells divide
   - how viruses and bacteria infect cells
   - diagnosis of viral and bacterial infection
   - how genes affect a cell’s activities
   - how cancer cells grow and spread

2. Use the library and, if possible, the Internet to gather more information about this research area.

3. As you complete your research, keep a record of all books, web sites, and other resources you used. Include a comment regarding the quality of each resource.

Analyze

1. What question(s) does the research address?
2. (a) How do the researchers use microscopes? (b) What were their observations?
3. What is being learned from this research? How is the new knowledge being applied?
4. Compile your research and list of references in a one- to two-page document. If possible, share your findings by e-mailing your document as an attachment to your classmates.

Skill Focus

- For tips on researching and organizing information, turn to Skill Focus 6.

Math Connect

“Resolution” refers to the ability to distinguish between two points. The smallest distance the unaided human eye can resolve is about 0.2 mm, about the width of a human hair. The scanning tunneling microscope has a maximum “magnification” of 200,000,000x. Calculate the size of the smallest thing your eye can resolve through one of these powerful microscopes.

Chapter 7 The Basis of Life • MHR 269
The Power of Microscopes

When scientists discovered cells, they were eager to learn more about how cells function. Much of what they learned about cell functions came from observations using the microscope. Even at high magnification, however, many cells are difficult to see clearly. Stains and dyes make cells easier to see by marking specific substances.

Question

How do different types of microscopy techniques enhance our observations?

Safety Precautions

- Avoid getting methylene blue stain on your skin or in your eyes.
- Handle microscope slides and cover slips with care so they do not break.
- Dispose of your materials according to your teacher’s directions.
- Be careful when using sharp objects such as tweezers.

Apparatus

tweezers
2 microscope slides
medicine dropper
2 cover slips
magnifying glass
compound light microscope

Materials

onion
water
protective gloves
methylene blue solution
filter paper

Procedure

1 You will examine onion cells at differing levels of magnification, both with and without stain. Predict what you will see at different magnifications and with and without stain. Which technique do you think will allow you to see the most detail in the cells?

2 Copy the data/analysis table shown here into your notebook. You will be making drawings in the table, so be sure it is large enough to give you plenty of room.

3 Use the tweezers to carefully peel away a thin layer of onion skin. Place the section on a microscope slide.

4 Using a medicine dropper, add a drop of water. Then carefully place the cover slip on the slide.

5 Observe the specimen with a magnifying glass. Draw what you see.

6 Observe the specimen under the microscope at low power. Draw what you see.

7 Increase the magnification to medium power. Draw what you see.

Skill Focus

- For tips on making scientific drawings, turn to Skill Focus 9.
- For tips on using a microscope, turn to Skill Focus 10.

<table>
<thead>
<tr>
<th>Magnification level</th>
<th>Magnification of objective lens (microscope only)</th>
<th>Total magnification (ocular x objective) (microscope only)</th>
<th>No stain</th>
<th>Stained with methylene blue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Magnifying glass</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Microscope at low power</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Microscope at medium power</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Microscope at high power</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


When scientists discovered cells, they were eager to learn more about how cells function. Much of what they learned about cell functions came from observations using the microscope. Even at high magnification, however, many cells are difficult to see clearly. Stains and dyes make cells easier to see by marking specific substances.
8 Increase the magnification to high power. Draw what you see.

9 Now, prepare another specimen, following the instructions in steps 3 and 4. While wearing protective gloves, use another medicine dropper to add one drop of methylene blue stain to one edge of the cover slip. CAUTION: Avoid getting methylene blue on your skin or in your eye. If you get methylene blue on your skin or in your eye, inform your teacher and rinse the affected area with water. The eye should be rinsed for at least 15 min — methylene blue is an irritant.

10 Hold a small piece of filter paper next to the cover slip away from the drop of stain. This will draw the methylene blue through the specimen.

11 Examine the stained specimen as you did with the unstained one, repeating steps 6 and 7. When you study the specimen under the microscope, look for a well-stained area with cells that have blue edges.

12 Some of the structures you see in the cells may be familiar to you. Later in this chapter, you will review many of their names and functions. In your notebook, list the structures that you recognize. Make a note of some questions you have about these structures and their functions.

13 Wash your hands when you have finished the investigation and cleaned your work area.

**Analyze**

1. How did the images of the cells change with increasing magnification?
2. How was the methylene blue stain useful for observing the cells?
3. What new details emerged as you examined the cells in different ways?
4. What do the details you observed suggest about the cells' activities?

**Did You Know?**

Many bacteria are transparent. Such cells must be stained to examine them under the microscope. The Gram stain, developed by Danish scientist Hans Christian Gram (1853–1938), not only stains bacteria, but also allows researchers to distinguish between different kinds of bacteria. The Gram stain procedure stains one group (Gram-positive bacteria) purple, and another (Gram-negative bacteria) red. The difference in the colour the cells stain is due to differences in the chemical structure of their cell walls. The Gram stain is helpful in trying to determine what type of bacteria has contaminated a food or water supply, or made someone sick.
Neha Datta attended Western Canada High School in Calgary, Alberta. Along with other science students across Canada, she has participated in local science fairs and has represented Calgary twice at the Canada-Wide Science Fair. At age 17, she entered the 2002 Intel International Science Fair. Her project involved tracking mammalian neural stem cell expansion. Much research is currently being done into the regeneration mechanisms employed by the central nervous system. Scientists hope that one day it will be possible to repair damage and restore function in cells affected by Parkinson's disease, multiple sclerosis, and other such conditions.

A large supply of neural stem cells (NSC) is required for research and treatment. Neha researched methods for expanding neural stem cells that have been specially grown for research purposes. In her study, she was able to establish optimal growing conditions.

Neha has always enjoyed science and hopes to continue to learn and have fun with science throughout her career.

**A Molecular World**

Cells are tiny hubs of molecular activity. It is not surprising that much of the progress in cell research has come from discoveries made at the level of molecules. For example, we now know that genes direct the activities of our cells. Genes are sections of long molecules called DNA. DNA is found in the nucleus of every cell. Genetic research shows that changes in the DNA can result in disease by causing cells to function improperly. Sickle cell anemia, for example, is a blood disease caused by a change in a gene. The change in the gene causes the body to make deformed red blood cells, which clog the blood vessels.

In order to study changes in our genes, many scientists rely on gene sequencing. DNA is constructed of thousands to millions of molecular subunits. Each subunit contains one of four kinds of bases: adenine (A), cytosine (C), guanine (G), and thymine (T). The order of bases is different in every gene.

**Gene sequencing** involves mapping the order of all of a gene's bases. Often, scientists compare gene sequences from two or more sources to look for differences or similarities between the gene sequences. Not all differences between gene sequences indicate that one gene is "faulty." Many are just normal variations.

The Human Genome Project (HGP) is an international project to sequence all 30 000 to 40 000 human genes and learn more about them. Scientists have completed the sequence. The genes of organisms commonly used in research, such as yeast, mice, fruit flies, and the worm *Caenorhabditis elegans*, have also been mapped. Now that scientists know these sequences, they can learn the genes' functions more quickly. The sequences can also be used to develop methods for diagnosing and treating genetic disorders.
Cancer — Is It All in the Genes?

Cancer is the second leading cause of death in North America. Heart disease is the number one killer. Most cancers are caused by damage to genes. Some kinds of gene damage introduce mutations (changes in the sequence of bases). Mutations increase a person's chance of developing cancer. Figure 7.14 shows a mutation that results in tumours in rats. Such mutations cause cells to grow and divide uncontrollably, forming a tumour.

As shown in Figure 7.15 on the next page, normal cells are prevented from growing too close together. Cancer cells, however, grow without any restrictions. One of the ways researchers learn more about cancer-causing genes is by determining their sequences. Information about a given gene's sequence helps researchers to learn how the gene affects cell activity.

Figure 7.13. Shown here are the gene sequences, or order of bases, in a normal gene (left) and the mutated version of this gene (right). The mutated gene differs from the normal gene by one base.

Living or Not?

At the beginning of this chapter you learned that all living organisms share some key characteristics. For example, they require energy, produce waste, and reproduce. How would you classify a structure that exhibits only some of the characteristics of life?

A virus is a non-cellular structure made up of a stretch of genetic material enclosed in a protein coat. When a virus infects a cell, it takes over the host cell's reproductive machinery and causes the host cell to produce more viruses.

The prion is another sub-cellular structure that can reproduce in living tissue. A prion is a protein that converts from its normal form into a harmful particle. Prions cause several deadly diseases, including Bovine Spongiform Encephalopathy (BSE) or "mad cow disease." Like a virus, a prion does not have any independent life functions, and therefore is not considered a functional unit of life.

Figure 7.14. This illustration shows the shapes of four different types of virus particles. Viruses are responsible for many human diseases including polio and the common cold. Viruses can also infect plants and bacteria.
DidYouKnow?

When scientists study human cells in the laboratory, they use cells that people have donated for research purposes. One well-studied line of cells, called HeLa cells, is named for their donor, Henrietta Lacks. In 1951, 31-year-old Ms. Lacks was diagnosed with cancer of the cervix. Researchers from Johns Hopkins University in the United States collected some of Ms. Lacks's cancerous cervical cells. The scientists then grew the cells in cell culture. Although Ms. Lacks died from cervical cancer only eight months after her diagnosis, her cells live on in the laboratory. HeLa cells have made possible important successes in cancer research. Research on HeLa cells has also generated much basic knowledge about the biology of cells.

Culturing Cells in the Laboratory

Cell culture is another valuable technique in cancer and cell research. In cell culture, isolated cells are placed in test tubes, petri dishes, or special flasks (see Figure 7.15). The cells are supplied with all the nutrients they need for growth. The generations of cells that result from growth and division in each culture are called cell lines. These cell lines provide cells for research. Many cell lines have been cultured from a variety of cancers. Cancer cells can grow indefinitely in the laboratory, whereas normal cells can live outside the body for only a limited time.

Stem Cells

What if doctors could grow organs in the lab for patients who needed new hearts and kidneys? What if doctors could grow new nerves for people paralyzed by spinal cord injury? Are stem cells the key to these dreams? Stem cells are “blank slate” cells that divide to produce all other types of specialized cells. Stem cells differ from the other cells in your body, which can divide to produce only cells like themselves. For example, skin cells can produce other skin cells, but they cannot produce liver cells. As far as scientists know, some of your cells, such as mature nerve cells, can never divide or be replaced if they are damaged. Most of the rapidly dividing cells of a one-week-old embryo are stem cells. As shown in the diagram on the next page, stem cells divide to become the multitude of cell types in the body. After they mature into specialized cells, most cells lose the ability to produce cell types other than their own. Adults retain a limited number of stem cells, which supply new cells to replace those that are worn-out or damaged. Most adult stem cells are located in the bone marrow, where new blood cells are produced.

By taking advantage of stem cells' ability to develop into other cell types, scientists are looking to develop treatments and cures for a variety of diseases. Scientists also hope to grow tissues or organs for transplants. Adult stem cells cannot give rise to all cell types of the body. As a result, adult stem cells cannot be applied in as many ways as embryonic stem cells can. In the next investigation you will research more about stem cells.
Exploring Stem Cell Research

Think About It

Stem cells could potentially be used in the treatment of Parkinson's disease, Alzheimer's disease, diabetes, and spinal cord injury. Human stem cells cultured in the laboratory could be grown into tissues and organs for transplants. Drug development and testing using stem cells could lead to more rapid development of new medicines. The study of stem cells is also helping scientists to understand more about how developing cells become specialized. However, many people argue that stem cell research is unethical. Some people are especially concerned that stem cell research devalues human life. There may also be safety concerns with stem cell treatments. What can we learn from stem cell research? How could it change the treatment of disease and injury? What are the pros and cons of using stem cells?

Procedure

1. Using the Internet or the library, do some preliminary investigation on stem cell research. How are stem cells being collected and used?

2. There are many applications for stem cells in research and medicine. Identify one application and investigate it more thoroughly. Keep a record of the resources you used and note which sources were most useful.

3. Find out why some people view the use of stem cells in research and medicine as unethical, in terms of the application you are investigating.

Skill Focus

- For tips on researching and organizing information, turn to Skill Focus 6.

Analyze

1. Respond to the following questions about the area of research you examined:
   - Where do the stem cells come from?
   - How are the stem cells being used?
   - What are the possible benefits of the research?
   - What are the risks and ethical concerns involved?

2. Organize the information that you have gathered in a poster to present to your class. Write a paragraph or two summarizing what you found out. Include a list of pros and cons in your analysis of the costs and benefits of stem cell research. Also include a flowchart that illustrates how the stem cells are used or how the research is done.

Word Connect

Why do you think biologists have given the name "stem" to stem cells? How are stem cells like the stem of a plant? Draw a Venn diagram to show the similarities and differences between the stem of a plant and stem cells.
Healthy Cells, Healthy People

Your body contains hundreds of different kinds of cells that perform hundreds of specialized functions. What would happen if some of your cells stopped functioning properly? Chances are, you would get sick. The kind of health problem you developed would depend on which cells stopped functioning properly and the reason for their failure.

Rudolf Virchow was the first scientist to see a link between malfunctioning cells and most illnesses. He thought the best way to understand disease was to study the activity of the infected or damaged cells. In Virchow’s time, researchers were still piecing together the basics of cell function and tissue function. Since then, scientists have made great advances in understanding how cells work and how cell activity contributes to disease.

Section 7.2 Summary

In this section, you learned how developments in microscope technology have increased our knowledge of cells. Light microscopes and electron microscopes help researchers investigate cells in remarkable detail. The use of these tools has resulted in a better understanding of the structure and function of cells. You also learned about cell research as it relates to human health. Gene mapping, cancer research, and stem cell research are linked to the advances in our understanding of cells and the advances in microscope technology.

Check Your Understanding

1. What is the difference between a simple microscope and a compound microscope?
2. Compare how images are produced when using an electron microscope versus a light microscope.
3. Describe how and why staining techniques are used to study cells.
4. How do scientists grow cells in the laboratory?
5. (a) What is a gene sequence?
   (b) Why is it valuable to know a gene’s sequence?
6. Explain how stem cells differ from other kinds of cells.
7. Thinking Critically How do the SEM and CLSM differ in the way that they collect data and provide three-dimensional images?
8. Thinking Critically At first glance, research on the genes of yeast, flies, and worms may appear to have little to do with learning about human health. Explain why scientific discoveries made about these and other organisms’ genes might be important to medical researchers.
9. (a) Compare the technologies available to cell biologists today with the tools that were available to scientists such as Robert Hooke and Antony van Leeuwenhoek.
   (b) Explain, using one example, how the availability of tools influences the types of questions scientists can address in their research.