Cell Communication and Cell Cycle

Exam Weight: 10–15%

IN THIS CHAPTER

Summary: This chapter teaches you what you need to know about cell communication, signal transduction pathway, feedback mechanisms, the cell cycle, mitosis, and cell cycle regulation.

Key Ideas

- Cells communicate by cell-to-cell contact or via chemical signals over distance in an organism.
- Signal transduction pathway starts with a signal followed by a transduction of the signal resulting in a cellular response.
- Feedback mechanisms are used to maintain homeostasis.
- There are four main stages in the cell cycle: G_1, S, G_2, and M.
- The stages of mitosis are prophase, metaphase, anaphase, telophase, and cytokinesis.
- Examples of cell division control mechanisms are growth factors, checkpoints, density-dependent inhibition, and cyclins/protein kinases.

Introduction

Cells use energy in many ways: for maintenance of homeostasis through feedback mechanisms, for communication with other cells, and for replication. In this chapter, we will discuss how cells communicate with one another via cell-to-cell contact or chemical signals with signal transduction pathways. Next, we will discuss how cells respond to their changing environments via negative and positive feedback pathways. After dissecting the cell cycle and the phases of mitosis, we will touch on cell cycle regulation.

Cell Communication

IST-3

Cells communicate by generating, transmitting, receiving, and responding to chemical signals.

The ability of a cell to communicate with its environment and with itself is key to maintaining homeostasis and surviving. This survival depends on receiving and processing information from outside the cell—information about changing environmental conditionals, availability of nutrients, or any other information vital to surviving. Cells have developed a variety of signaling mechanisms to accomplish the transmission of important biological information. For example, the presence of receptors that allow ion currents to flow in response to photons, which translate light into chemical messengers inside the retina of the eye.

Cell signaling involves a ligand, a signaling molecule, and a receptor protein to which the ligand binds. The receptor can be located on the cell membrane for hydrophilic ligands that can't cross the membrane, or it can be located *inside* the cell for hydrophobic ligands that are small enough to cross the membrane.

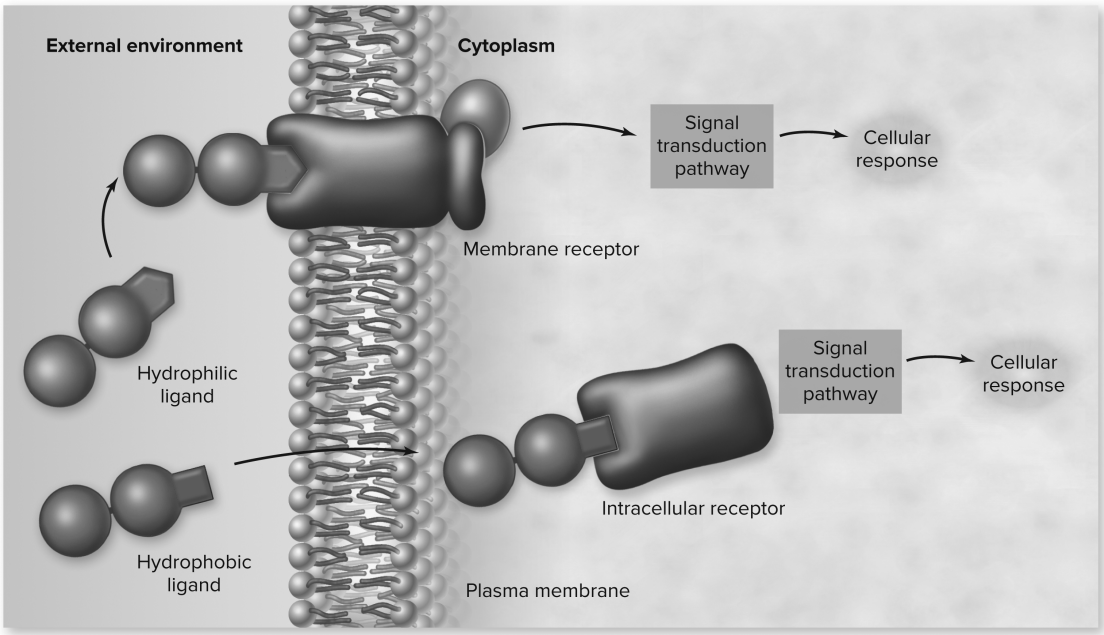

Figure 8.1 Overview of cell signaling. Cell signaling involves a signal molecule called a ligand, a receptor, and a signal transduction pathway that produces a cellular response. The location of the receptor can either be intracellular, for hydrophobic ligands that can cross the membrane, or in the plasma membrane, for hydrophilic ligands that cannot cross the membrane. (*Reproduced with permission from Raven P, Johnson G, Mason K, Losos J, Duncan T;* Biology, *12th ed. New York: McGraw Hill; 2020*)

Signaling

Cells communicate in a variety of ways, depending on the distance between the cells communicating.

KEY IDEA

1. *Direct cell-to-cell signaling* involves the direct physical contact between cells during communication. Gap junctions in animals and plasmodesmata in plants are tiny channels that directly connect to neighboring cells, which allow the cells to transfer signaling molecules that transmit their current state of homeostasis with one another.
2. *Paracrine signaling* involves cells close to one another but not in direct contact. A cell releases a short-lived signal into a localized area that will induce changes in a nearby cell. Paracrine signals can diffuse only over relatively short distances.

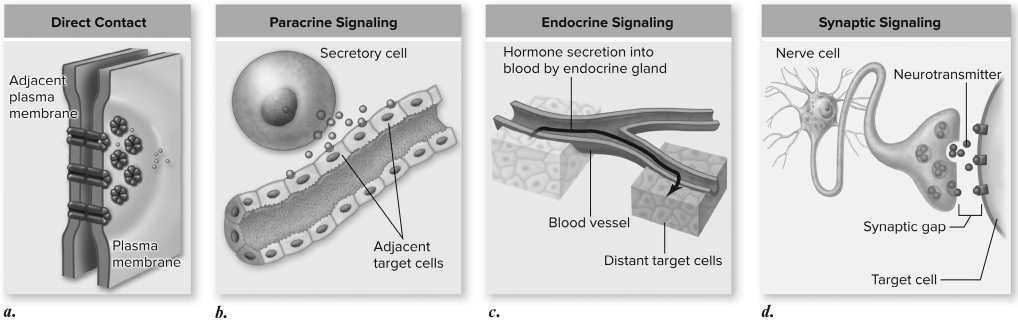

Figure 8.2 Four kinds of cell signaling. Cells communicate in several ways. ***a.*** Two cells in direct contact with each other may send signals across gap junctions. ***b.*** In paracrine signaling, secretions from one cell have an effect only on cells in the immediate area. ***c.*** In endocrine signaling, hormones are released into the organism's circulatory system, which carries them to the target cells. ***d.*** Chemical synapse signaling involves transmission of signal molecules, called neurotransmitters, from a neuron over a small synaptic gap to the target cell. (*Reproduced with permission from Raven P, Johnson G, Mason K, Losos J, Duncan T;* Biology, *12th ed. New York: McGraw Hill; 2020*)

3. *Endocrine signaling* involves cells far apart in which a longer-lasting signal, called a hormone, is released into the extracellular fluid and travels widely throughout the organisms to target cells. Protein hormones are large molecules that must bind to receptors on the cell membrane. Steroid hormones are lipid-soluble molecules that are able to pass through the cell membrane and attach to an intracellular receptor. One example of endocrine signaling involves the release of human growth hormone (HGH) from the pituitary gland into the bloodstream, which targets bone and muscle cells to trigger growth (See Figure 8.2 *a-d*).
4. *Synaptic signaling* involves a specialized nerve cell, a neuron, and its target cell. This association is called a chemical synapse and involves the release of neurotransmitters from the neuron into the synaptic gap to target the target cell.
5. *Autocrine signaling* occurs when a cell sends a signal to itself by secreting something that in turn binds to specific receptors on its own membrane. This plays an important role in cell development and immune system.

Signal Transduction Pathway

When a ligand binds to a receptor on a cell, the work has just begun for the cell. The cell relays the message through a series of reactions to elicit a cellular response known as the signal transduction pathway (Figure 8.1). The binding of the ligand to the receptor generally causes the receptor to change shape, resulting in an activation of an enzyme or binding of other molecules. This starts a signaling cascade that can amplify the signal through a series of reactions that leads to a cellular response, resulting in a change to a cell's behavior or characteristics.

Phosphorylation

The signal transduction pathway may require activating or inactivating proteins via the addition of a phosphate group in a process called phosphorylation.

The phosphorylation of proteins (addition of phosphate groups) is catalyzed by enzymes called **kinases**. There are many different types of kinases that target different proteins in the cell. The dephosphorylation of proteins (removal of phosphate groups) is catalyzed by enzymes called **phosphatases**. Many proteins are activated when phosphorylated and deactivated when dephosphorylated, which creates a pretty nifty way for cells to turn on and off various important cellular pathways (See Figure 8.3).

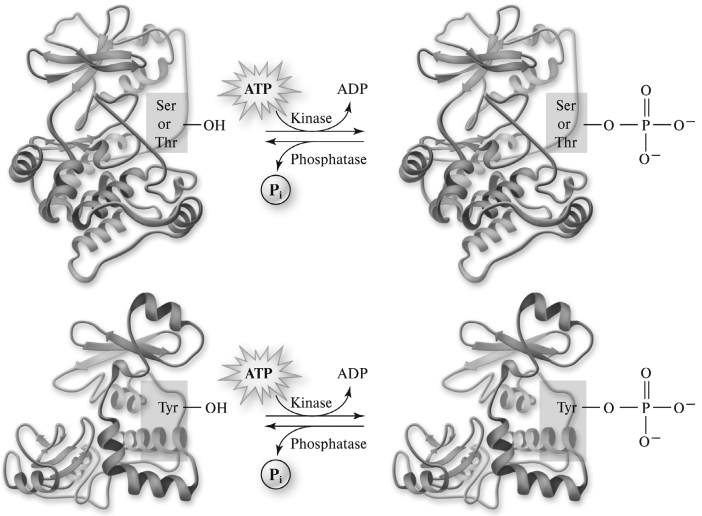

Figure 8.3 Phosphorylation of proteins. Many proteins are controlled by their phosphorylation state—that is, they are activated by phosphorylation and deactivated by dephosphorylation or the reverse. The enzymes that add phosphate groups are called kinases. These form two classes depending on the amino acid the phosphate is added to, either serine– threonine kinases or tyrosine kinases. The action of kinases is reversed by protein phosphatase enzymes. (*Reproduced with permission from Raven P, Johnson G, Mason K, Losos J, Duncan T;* Biology, *12th ed. New York: McGraw Hill; 2020*)

Secondary Messengers

While proteins are a main component of most signal transduction pathways, many other molecules play important roles in the process as secondary messengers, which are small, nonprotein molecules that pass messages along.

1. Calcium (Ca^{2+}): Calcium is widely used by cells as a secondary messenger. Some proteins have binding sites for Ca^{2+} and when calcium binds to the protein, the shape changes, leading to a change in function. One such example is the use of Ca^{2+} in muscle to start muscle contraction after receiving a signal from a neuron.
2. Cyclic AMP (cAMP): Cyclic adenosine monophosphate (cAMP) is involved in many signal cascade pathways. Protein hormones activate cAMP though a multistep process that begins with protein-hormone activation of relay proteins such as G-proteins. These proteins are able to directly activate a compound known as adenyl cyclase, which in turn produces cAMP (See Figure 8.4).

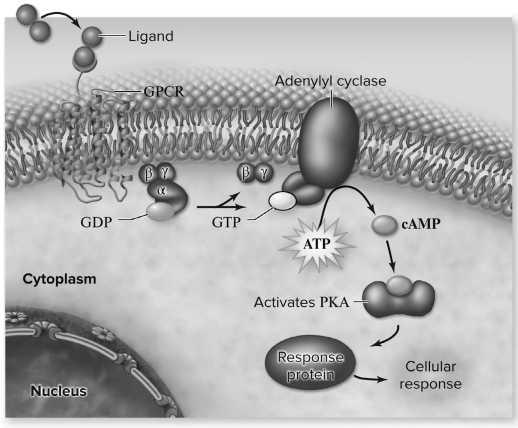

Figure 8.4 cAMP signaling pathway. Extracellular signal binds to a GPCR, activating a G protein. The G protein then activates the effector protein adenylyl cyclase, which catalyzes the conversion of ATP to cAMP. The cAMP then activates protein kinase A (PKA), which phosphorylates target proteins to cause a cellular response. (*Reproduced with permission from Raven P, Johnson G, Mason K, Losos J, Duncan T;* Biology, *12th ed. New York: McGraw Hill; 2020*)

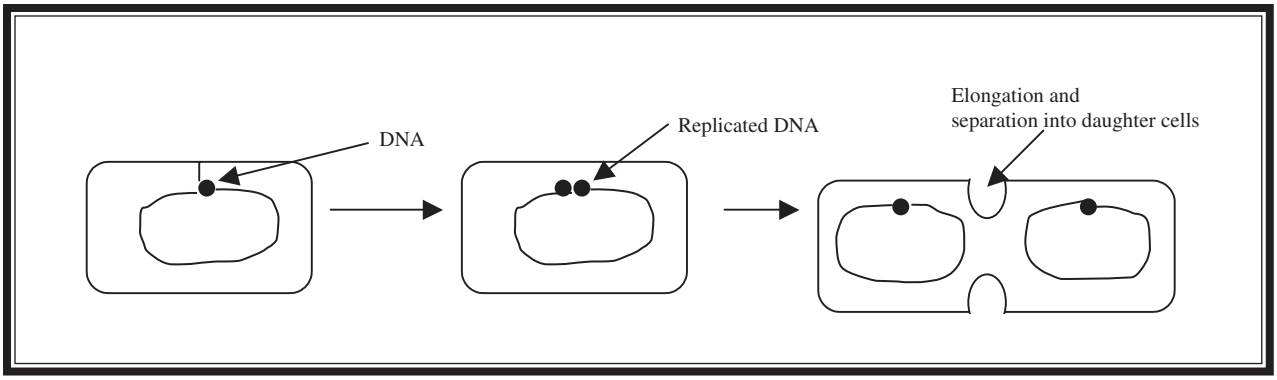

Figure 8.5 Binary fission.

Cell Division in Prokaryotes

Prokaryotes are simple single-celled organisms without a nucleus. Their genetic material is arranged in a single circular chromosome of DNA, which is anchored to the cell membrane. As in eukaryotes, the genetic material of prokaryotes is duplicated before division. However, instead of entering into a complex cycle for cell division, prokaryotes simply elongate until they are double their original size. At this point, the cell pinches in and separates into two identical daughter cells in a process known as **binary fission** (Figure 8.5).

The Cell Cycle

IST-1
Heritable information provides for continuity.

Eukaryotic cell reproduction is a bit more complicated. The cell cycle functions as the daily planner of growth and development for the eukaryotic cell. It tells the cell when and in what order it is going to do things, and consists of all the necessary steps required for the reproduction of a cell. It begins after the creation of the cell and concludes with the formation of two daughter cells through cell division. It then begins again for the two daughter cells that have just been formed. There are four main stages to the cell cycle, and they occur in the following sequence: **phases G_1**, **S**, **G_2**, and **M** (Figure 8.6). Phases G_1 and G_2 are growth stages; S is the part of the cell cycle during which the DNA is duplicated; and the M phase stands for mitosis, the cell division phase.

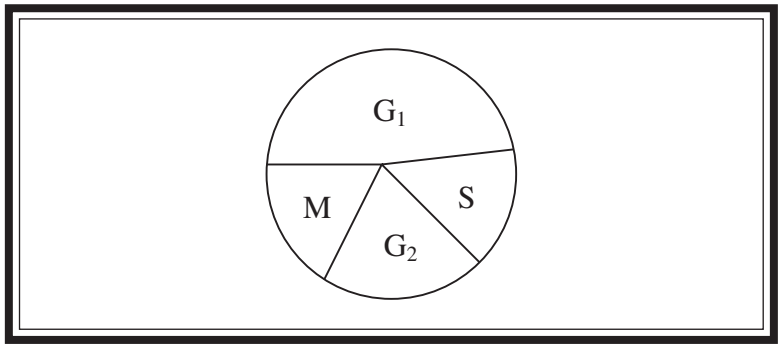

Figure 8.6 Pie chart showing the four main stages of the cell cycle.

KEY IDEA

Stages of the Cell Cycle

G_1 phase. During the first growth phase of the cell cycle, the cell prepares itself for the synthesis stage of the cycle, making sure that it has all the necessary raw materials for DNA synthesis.

S phase. The DNA is copied so that each daughter cell has a complete set of chromosomes at the conclusion of the cell cycle.

G_2 phase. During the second growth phase of the cycle, the cell prepares itself for mitosis (for producing body cells) and/or meiosis (for producing gametes), making sure that it has the raw materials necessary for the physical separation and formation of daughter cells.

M phase. Mitosis is the stage during which the cell separates into two new cells.

The first three stages of the cycle (G_1, S, and G_2) make up the portion of the cell cycle known as **interphase.** A cell spends approximately 90 percent of its cycle in this phase. The other 10 percent is spent in the final stage, mitosis.

The amount of time that a cell requires to complete a cycle varies by cell type. Some cells complete a full cycle in hours, while others can take days to finish. The rapidity with which cells replicate also varies. Skin cells are continually zipping along through the cell cycle, whereas nerve cells do not replicate—once they are damaged, they are lost for good. This is one reason why the death of nerve cells is such a problem—these cells cannot be repaired or regenerated through mitotic replication.

Mitosis

During mitosis, the fourth stage of the cell cycle, the cell actually takes the second copy of DNA made during the S phase and divides it equally between two cells. Single-cell eukaryotes undergo mitosis for the purpose of asexual reproduction. More complex multicellular eukaryotes use mitosis for other processes as well, such as growth and repair.

Mitosis consists of four major stages: prophase, metaphase, anaphase, and telophase. These stages are immediately followed by **cytokinesis**—the physical separation of the newly formed daughter cells. During interphase, chromosomes are invisible. The **chromatin**—the raw material that gives rise to the chromosomes—is long and thin during this phase. When the chromatin condenses to the point where the chromosome becomes visible through a microscope, the cell is said to have begun mitosis. The AP Biology exam is not going to ask you detailed questions about the different stages of mitosis; just have a *general* understanding of what happens during each step.

KEY IDEA

Mitosis

Prophase. Nucleus and nucleolus disappear; chromosomes appear as two identical, connected sister chromatids; mitotic spindle (made of microtubules) begins to form; centrioles move to opposite poles of the cell (plant cells do not have centrioles).

Metaphase. For metaphase, think middle. The sister chromatids line up along the middle of the cell, ready to split apart.

Anaphase. For anaphase, think apart. The split sister chromatids move via the microtubules to the opposing poles of the cell—the chromosomes are pulled to opposite poles by the spindle apparatus. After anaphase, each pole of the cell has a complete set of chromosomes.

Telophase. The nuclei for the newly split cells form; the nucleoli reappear, and the chromatin uncoils.

Cytokinesis. Newly formed daughter cells split apart. Animal cells are split by the formation of a cleavage furrow, and plant cells split by the formation of a cell plate (See Figure 8.7).

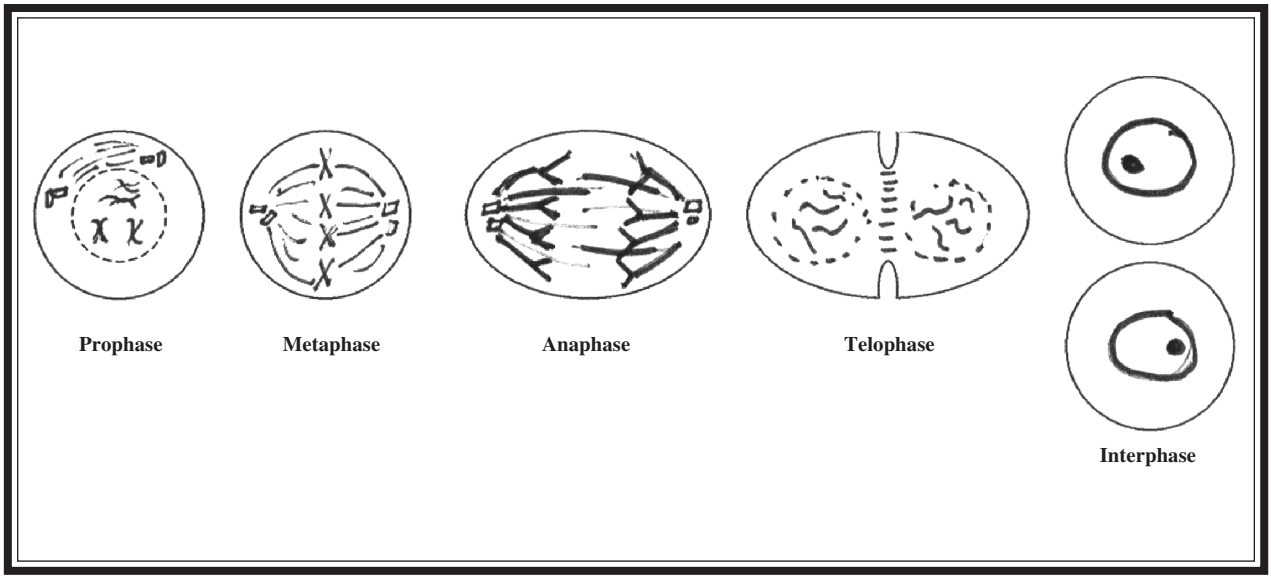

Figure 8.7 Pictorial representation of the stages of mitosis.

Here are the definitions for words you may need to know:

Cell plate: plant cell structure, constructed in the Golgi apparatus, composed of vesicles that fuse together along the middle of the cell, completing the separation process.

Cleavage furrow: groove formed (in animal cells) between the two daughter cells that pinches together to complete the separation of the two cells after mitosis.

Cytokinesis: the actual splitting of the newly formed daughter cells that completes each trip around the cell cycle—some consider it part of mitosis; others regard it as the step immediately following mitosis.

Mitotic spindle: apparatus constructed from microtubules that assists the cell in the physical separation of the chromosomes during mitosis.

Control of Cell Division

Sam (12th grader): "Control mechanisms are an important theme for this test. Be able to write about them."

Control of the cell cycle is important to normal cell growth. There are various ways in which the cell controls the process of cell division:

1. *Checkpoints.* There are checkpoints throughout the cell cycle where the cell verifies that there are enough nutrients and raw materials to progress to the next stage of the cycle. The G_1 checkpoint, for example, makes sure that the cell has enough raw materials to progress to and successfully complete the S phase.
2. *Density-dependent inhibition.* When a certain density of cells is reached, growth of the cells will slow or stop because there are not enough raw materials for the growth and survival of more cells. Cells that are halted by this inhibition enter a quiescent phase of the cell cycle known as G_0. Cancer cells can lose this inhibition and grow out of control.

3. *Growth factors.* Some cells will not divide if certain factors are absent. Growth factors, as their name indicates, assist in the growth of structures.
4. *Cyclins and protein kinases.* **Cyclin** is a protein that accumulates during G_1, S, and G_2 of the cell cycle. A **protein kinase** is a protein that controls other proteins through the addition of phosphate groups. Cyclin-dependent kinase (CDK) is present at all times throughout the cell cycle and binds with cyclin to form a complex known as MPF (maturation or mitosis promoting factor). Early in the cell cycle, because the cyclin concentration is low, the concentration of MPF is also low. As the concentration of cyclin reaches a certain threshold level, enough MPF is formed to push the cell into mitosis. As mitosis proceeds, the level of cyclin declines, decreasing the amount of MPF present and pulling the cell out of mitosis.

Apoptosis

Cells have the ability to undergo programmed cell death known as apoptosis, which is key to maintaining a proper balance of cells in the human body. Apoptosis removes cells during development, which is vital to the elimination of cancerous and virus-infected cells. If a cancerous cell is able to escape apoptosis, it will continue to divide and eventually create a tumor.

Feedback

ENE-3

Timing and coordination of biological mechanisms involved in growth, reproduction, and homeostasis depend on organisms responding to environmental cues.

How is the hormone secretion process of the body regulated? The two main types of regulation with which you should be familiar are negative feedback and positive feedback. **Negative feedback** occurs when a hormone acts to directly or indirectly inhibit further secretion of the hormone of interest. A good example of negative feedback involves insulin, which is secreted by the pancreas. When the blood glucose gets too high, the pancreas is stimulated to produce insulin, which causes cells to use more glucose. As a result of this activity, the blood glucose level declines, halting the production of insulin by the pancreas. **Positive feedback** occurs when a hormone acts to directly or indirectly cause increased secretion of the hormone. An example of this feedback mechanism is the LH surge that occurs prior to ovulation in females. Estrogen is released as a result of the action of FSH, and travels to the anterior pituitary to stimulate the release of LH, which acts on the ovaries to stimulate further secretion of estrogen.

Homeostasis

NYC teacher: "This could make a nice subquestion to an essay. Understand these relationships."

Homeostasis is the maintenance of balance. Hormones can work antagonistically to maintain homeostasis in the body. Two examples we will talk about are insulin/glucagon and calcitonin/PTH:

1. *Insulin/glucagon.* Both are hormones of the pancreas and have opposing effects on blood glucose. Let's say that you eat a nice sugary snack that pushes the blood glucose above its desired level. This results in the release of insulin from the pancreas to stimulate the uptake of glucose from the blood to the liver to be stored as glycogen. It also causes other cells of the body to take up glucose to be used for energy. Sometimes if you go a long time between meals, your blood glucose can dip *below* the desired level. This sets glucagon into action and causes its release from the pancreas. Glucagon acts on the liver to stimulate the removal of glycogen from storage to produce glucose to pump into the bloodstream. When the glucose level gets back to the appropriate level, glucagon

ENE-3

Timing and coordination of biological mechanisms involved in growth, reproduction, and homeostasis depend on organisms responding to environmental cues.

release ceases. This back-and-forth dance works to keep the glucose concentration in our bodies relatively stable over time.

2. *Calcitonin/PTH*. Like glucose, the body has a desired blood calcium (Ca^{2+}) level it tries to maintain. If it drops below this level, PTH is released by the parathyroid gland and works to increase the amount of Ca^{2+} in circulation in three major ways: it (a) releases Ca^{2+} from bones, (b) increases absorption of Ca^{2+} by the intestines, and (c) increases reabsorption of Ca^{2+} by the kidneys. If the blood Ca^{2+} level gets too high, the thyroid gland releases calcitonin, which pretty much performs the three *opposite* responses to PTH's work: it (a) puts Ca^{2+} *into* bone, (b) decreases absorption of Ca^{2+} by the intestines, and (c) decreases reabsorption of Ca^{2+} by the kidneys.