Section 2.3
Enzymes

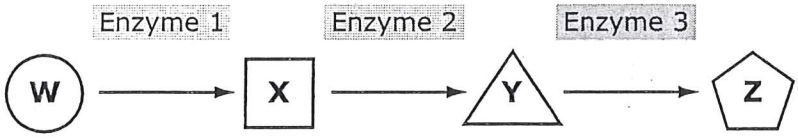
Section Overview

Life as we know it could not exist without enzymes. Enzymes help cells metabolize to produce energy used in activities such as synthesizing bones and muscles. Enzymes are proteins that are created by protein synthesis (which you learned about in the previous section). Simply put, they are catalysts that help chemical reactions in the body progress efficiently.

In this section you will learn all there is to know about enzymes—but were afraid to ask! Factors affecting enzyme action such as concentration, temperature, pH, and inhibitors and cofactors will be studied. Finally, the importance of the thyroid gland and thyroxin to metabolism in the body is explored. Phrases such as activation energy, metabolic pathway, substrates, and competitive inhibitors should be part of your vocabulary once you've completed this section.

Don't forget to do the guided practices!

Metabolic Pathway



Lesson 2.3A
Enzyme Metabolism

Overview

When you think of all the activities an organism must constantly perform in order to stay alive, you might think of eating, breathing, blood circulation, excretion, and movement. However, it's also important to think about what is happening at the cellular level. Cells must continuously metabolize to produce the energy that keeps an organism alive. Depending on the type of cell, other activities might include synthesis (producing bone, muscle, and other types of tissue), breakdown (e.g., digestion), communication (e.g., neurons, hormones, etc.), and so on. These diverse biochemical reactions have something in common. They must occur at a very fast rate, and they require **enzymes** to maintain that rate. In short, life as we know it could not exist without enzymes!

Enzymes are proteins that are created by protein synthesis (transcription and translation), which you have already studied. Although the precise number of different proteins coded for by DNA is unknown, estimates range up to 150,000. If we accept the estimate that half of these proteins are enzymes, then there are up to 75,000 different enzymes in the human body.

In this lesson you will examine the function of enzymes in biochemical reactions, how enzymes interact with reactants to assist in the formation of products, and why enzymes are so vital to cellular processes.

Resource List

- *Inquiry Into Life*
- *Biology 12 Provincial Exam Preparation package*
- *Biology 12 Web site*
  http://www.openschool.bc.ca/courses/biology/bi12/mod2.html

Enzymes and Metabolism

Biochemical reactions are chemical reactions that occur in living organisms. These reactions begin with one or more reactants, and then convert these reactants to products. The many chemical reactions that occur in cells are collectively termed **metabolism**.

A typical chemical reaction might be described as:

$A + B = C + D$

where A and B are reactants, and C and D are products.

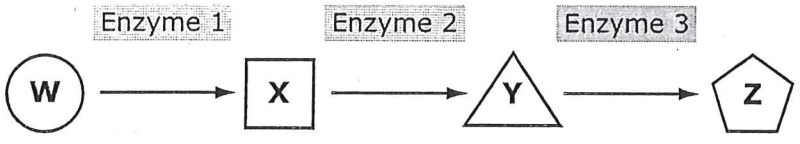
However, reactions in cells are often more complex and occur as part of a **metabolic pathway**—a series of conversions in which the product of one reaction becomes the reactant in the next reaction:

$A \rightarrow B \rightarrow C \rightarrow D \rightarrow E \rightarrow F$

Note that B, C, D, and E are both reactants and products. For example, in the reaction A → B, A is the reactant and B is the product. Next, in B → C, B becomes a reactant and C is a product, and so on.

Cellular metabolism must occur rapidly in order to sustain the life of an organism. This is why metabolic pathways, such as the one above, require enzymes. **Enzymes** are proteins that act as catalysts. They speed up chemical reactions without being used up in those reactions. The molecules that react with enzymes are called **substrates** (substrate is another word for reactant). Enzymes are specific—each enzyme will only form a complex with a certain substrate. That is why different enzymes are used in different steps of a metabolic pathway.

Metabolic Pathway



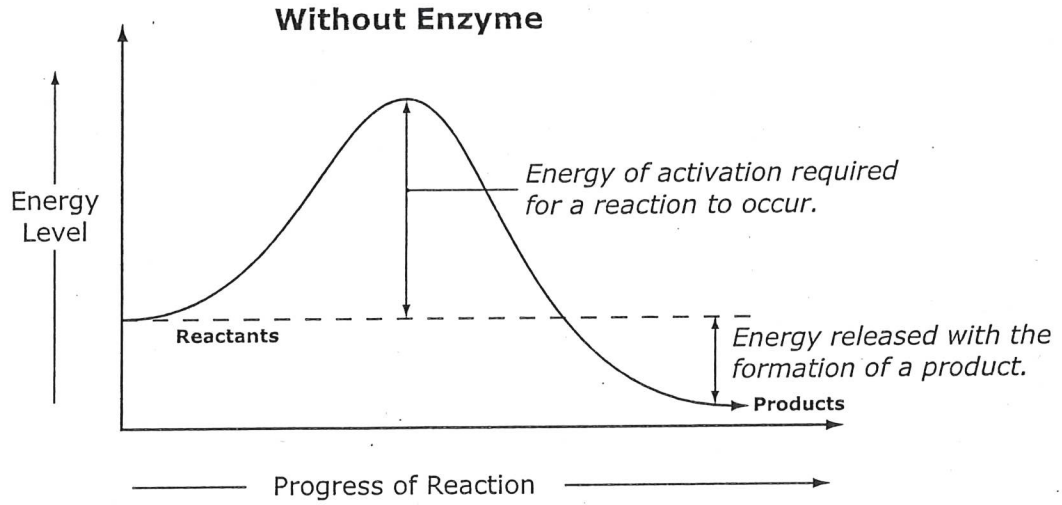
In your *Inquiry Into Life* textbook, read the information on metabolic pathways and enzymes before you proceed.

If you have access to the Internet, go to the *Biology 12 Web site* Lesson 2.3A Enzyme Metabolism to watch the animated clipped entitled "Feedback Inhibition of Biochemical Pathways."

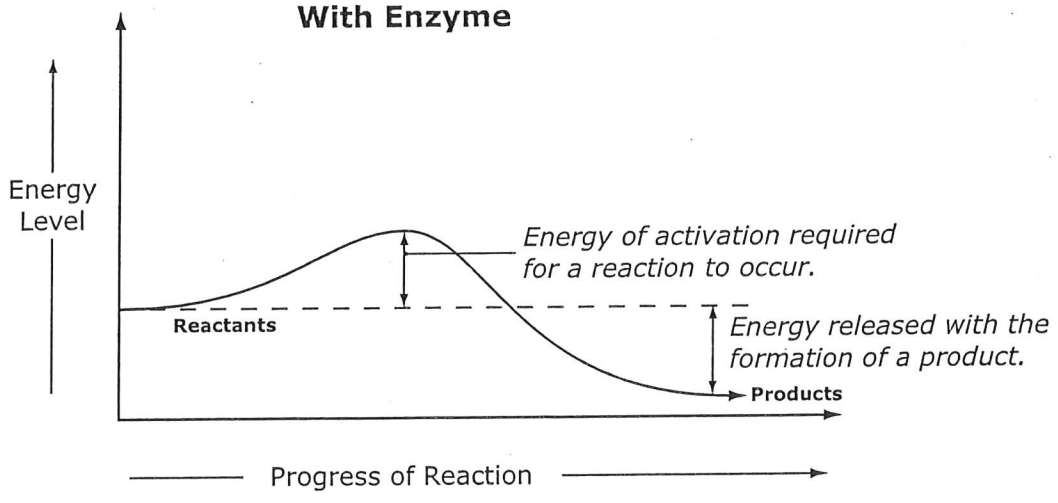
Energy of Activation

Chemical reactions cannot occur unless molecules have enough energy to react with each other. This required energy is termed energy of activation, or simply **activation energy**. Enzymes lower the energy of activation in a reaction, allowing it to proceed at a lower than usual energy level.

Graph X



Graph Y



In Graph X, no enzyme is present, and the conversion of substrate to product requires a higher Ea (energy of activation) before it can occur. Graph Y shows the same reaction when an enzyme is present. Note that Ea is much smaller when an enzyme facilitates a reaction.

It is also important to note that the product of a reaction is the same whether an enzyme is present or not. However, depending on reaction conditions, more products may result, or the rate of the reaction may be altered. This will be the focus of a future lesson.

If you have access to the Internet, go to the *Biology 12 Web site* Lesson 2.3A Enzyme Metabolism to review what you've learned and work through the Mader Essential Study Partner Cells—Metabolism content.

Guided Practice 2.3A 2
Make It Right!

Let's check to make sure you understand all this enzyme terminology!

Fill in the blanks using the definitions from the following Word bank. Not all terms will be used. Next, identify and correct any false statements.

Word Bank

- metabolism
- reactants
- metabolic pathway
- activation energy
- enzyme
- substrates
- products

1. A _____ is a series of chemical reactions in which the product formed in one step becomes the reactant in the next step.

2. Reactants are also called _____, and are converted to _____, in a chemical reaction.

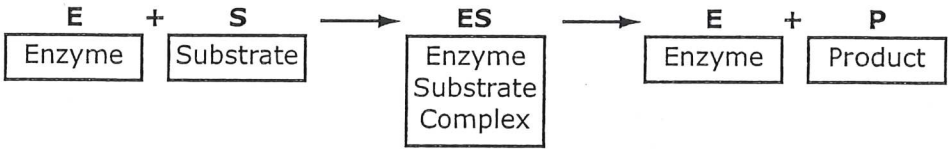
3. A(n) _____, is a substance that speeds up a chemical reaction and is used up to form a product.

4. Enzymes raise the _____, of a chemical reaction.

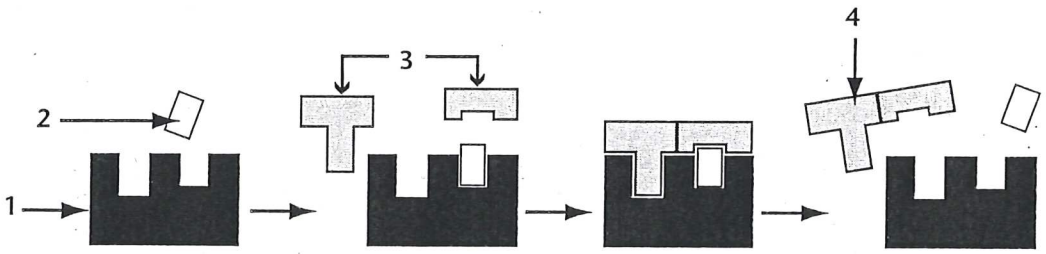
How Enzymes Work

Enzymes are catalysts for thousands of different biochemical reactions in the human body. Because each enzyme is specific to a certain substrate, there are many different enzymes. Although each enzyme is involved in a different reaction, all enzymes function in the same way.

Each enzyme contains an **active site** to which a particular substrate can bond to form an **enzyme-substrate complex**, an intermediate step between reactants and products.



This equation is demonstrated in the following diagram.



The structure labeled 1 is an enzyme, 2 is a cofactor (more on these shortly!). Label 3 represents substrate, and 4 is the product formed by the reaction.

Note that the enzyme remains intact and is not used up. After the reaction is complete, the enzyme is available to react again. For this reason, small amounts of enzyme are often all that is required, and these small amounts can have large effects.

Refer to your *Inquiry Into Life* textbook and study the diagram on enzymatic action. Note the following important points:

- formation of a temporary enzyme-substrate complex during reactions
- enzymes catalyze both synthesis and decomposition reactions
- enzymes are not changed or used up in reactions

In addition to the enzymatic action diagram in your *Inquiry Into Life* textbook, use your favorite search engine to find an animation of enzyme action if you have access to a computer and the Internet. Try using the search terms "enzyme animation." Watching a diagram come to life can often help clarify difficult concepts, such as enzyme action!

Check your understanding of enzymatic action by going to the *Biology 12 Web site* Lesson 2.3A Enzyme Metabolism and access Mader online by selecting the Cells → Metabolism → Enzymes → 1.99 (Metabolic pathway). Once there, try dragging the labels to their correct locations on the diagram.

Induced Fit Model

Enzyme and substrate fit together in much the same way as a lock and key, except that the enzyme actually changes itself slightly in order to fit with its substrate. Because of this slight alteration, we use the term **induced fit model** to better describe how the enzyme and substrate interact.

Go to your *Inquiry Into Life* textbook and look for an illustration of the induced fit model.

If you have access to a computer and the Internet, go to the *Biology 12 Web site* Lesson 2.3A Enzyme Metabolism and watch a narrated animation: Navigate to Cells—Metabolism. Pay attention to the way the enzyme changes shape to induce a better fit with its substrate.

The active site on an enzyme is restored to its original shape after a product is released. Because enzymes are not used up in the reactions they catalyze, cells generally only require a small amount of a given enzyme.

Enzyme names often end in -ase and are named for their particular substrate (e.g., lipase acts upon lipids, nuclease upon nucleic acids, lactase on the sugar lactose, etc.). This does not always hold true, however. The digestive enzymes trypsin and pepsin do not follow this naming convention.

If you have access to the Internet, and if you feel you need more practice, go to the *Biology 12 Web site* Lesson 2.3A Enzyme Metabolism and find the online provincial exam preparation resource. Choose "Cell processes and applications" to generate a practice quiz. You can answer only those questions that apply to what you've learned so far, and you will receive immediate feedback. The questions are taken from past exams, so they give a good sense of what to expect when you write the provincial exam.

Guided Practice 2.3A 3
Enzyme Self Quiz

Select the best answers for the following questions.

1. Which of the following is NOT a part of the theory of how an enzyme functions?

   A. The shape of the enzyme is permanently changed by the chemical reaction.

   B. The shape of the active site facilitates a reaction.

   C. Each enzyme catalyzes only one reaction.

   D. The enzyme lowers the activation energy required for the reaction.

2. The amount of energy required to start a chemical reaction is called:

   A. Reaction energy

   B. Initiation energy

   C. Activation energy

   D. Conversion energy

3. Enzymes catalyze reactions by:

   A. Lowering the energy of activation

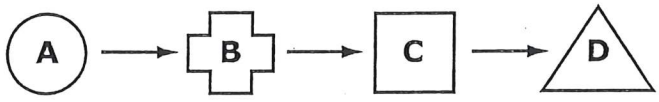
   B. Bringing the reactants together

   C. Increasing reaction rate

   D. All of the above

Use the following diagram to answer questions 4 and 5.

Metabolic Pathway



4. In the this diagram, B represents a(n):

   A. Enzyme

   B. Reactant

   C. Product

   D. Both b and c are correct

5. Assuming each step in this pathway is catalyzed by an enzyme, which of the statements is true?

   A. A, B, and C are products

   B. Each reaction requires its own enzyme

   C. B, C, and D are substrates

   D. None of the above

Guided Practice 2.3A 4

Written Response

Explain the lock and key analogy. How does this concept relate to the theory of induced fit?

There is no assignment for this lesson. The section assignment at the end of Lesson 2.3.C will address the content of all three lessons in Section 2.3.

Summary

Completing this lesson has helped you to:

- define enzyme and describe the role enzymes play in cellular chemical reactions
- understand the parts of metabolic pathways
- use the induced fit model to explain enzyme-substrate interactions

Lesson 2.3B
Factors Affecting Enzyme Action

Overview

There are at least 2000 enzymes in the human body and each one is involved in a different biochemical reaction. Enzymes are essential to life because biochemical reactions cannot occur without them, so it is important to understand some of the factors that affect enzyme activity reaction rates.

In this lesson you will look at the effect on reaction rates of substrate and **enzyme concentration**, temperature, pH, inhibitors, and **cofactors**. Each of these factors can be introduced, removed, or altered to influence the rate of an enzymatic reaction.

Resource List

- *Inquiry Into Life*
- *Biology 12 Provincial Exam Preparation package*
- *Biology 12 Web site*
  http://www.openschool.bc.ca/courses/biology/bi12/mod2.html

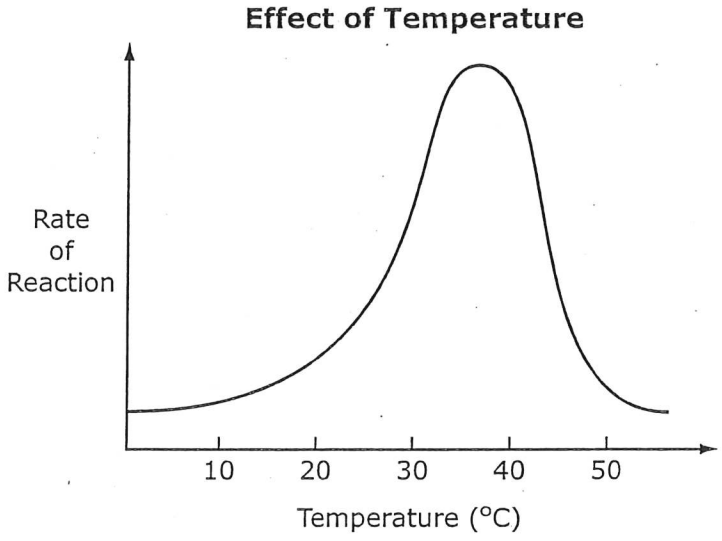
Factors Affecting Enzyme Action

Recall that reaction rate is the speed at which substrate is converted to product, and that biochemical reactions occur along metabolic pathways. These pathways are comprised of a specific sequence of steps that, in total, are more energy-efficient than one large reaction. Each reaction requires a specific enzyme. The more ideal the conditions for an enzyme, the more effectively it can catalyze the reaction to which it is so loyal, and the more quickly the entire pathway can proceed towards a final product.

As you work through this lesson, refer to "Factors affecting enzymatic speed" in the chapter titled "Metabolism: Energy and Enzymes" in your *Inquiry Into Life* textbook.

Temperature

Each enzyme functions most effectively at its own optimum temperature. At this optimum temperature, the movement of molecules is rapid enough to allow the maximum number of collisions between enzyme and substrate. More collisions mean an increased rate of formation of enzyme-substrate complexes. If the temperature rises too high, the enzyme becomes **denatured** and the reaction rate decreases. Denaturation is damage that alters the active site of an enzyme so its substrate can no longer bind to it.

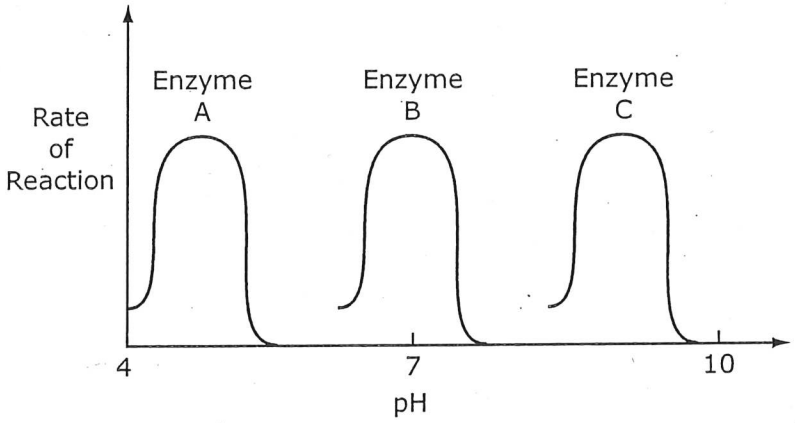


Note that the graph is not symmetrical because at lower temperatures, molecules move more slowly. Enzymes still function but not as effectively as they do at their optimum temperature. In the human body, this temperature is 37°C. At high temperatures, enzymes no longer work at all.

pH

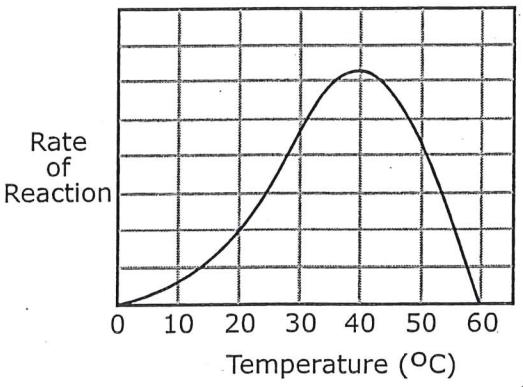
Enzymes also function best at an optimum pH. As with temperature, optimum **enzyme pH** varies with enzyme type and location. Recall that pH refers to the scale that indicates the acidity or alkalinity of a solution. Some enzymes, such as those involved in digestion in the stomach, function best in an acidic environment. Enzymes in the blood require a more neutral pH, and a basic pH is necessary to the activity of enzymes in the small intestine.

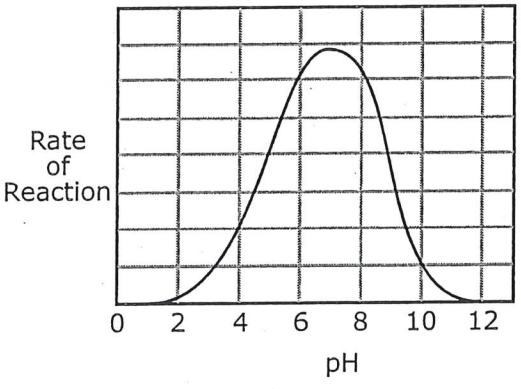
Effect of pH



This graph shows pH vs. the rate of reaction for three enzymes. The peaks of each curve represent the optimum pH for each enzyme. If pH is too low or too high for an enzyme, it will denature.

What is the optimum temperature and pH for the reaction shown?

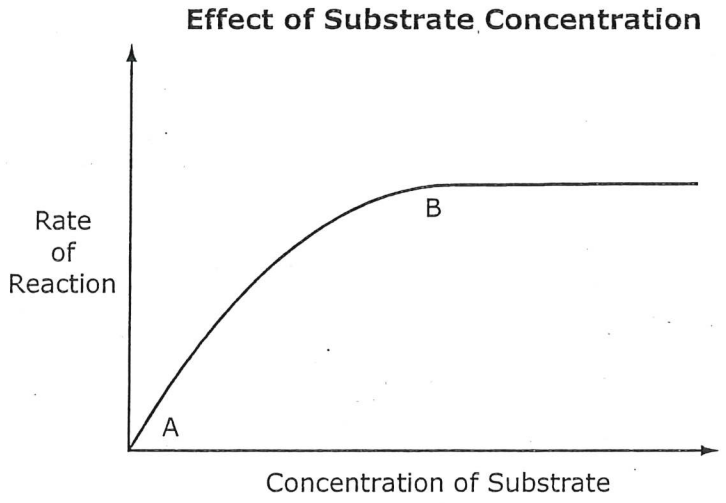




Answer: The reaction shown in these two graphs would proceed most rapidly at approximately 40°C and a pH of 7 (neutral).

Substrate and Enzyme Concentration

As **substrate concentration** increases, the rate of a reaction will also increase because substrate molecules take up more active sites. Once all available active sites are occupied, the reaction proceeds at its maximum rate (saturation point) and the graph levels off. Increased substrate concentration will have no effect on reaction rate.



Between points A and B on this graph, substrate concentration increases. The rate of reaction also increases to point B. B represents active site saturation—all the enzyme available is being used in the reaction, so the reaction cannot proceed any faster. If more enzyme is added, the rate of reaction would again increase.

Increasing **enzyme concentration** will also increase reaction rate. More active sites are available for bonding with substrate molecules, so the chance of collisions between enzyme and substrate is higher. The reaction rate will continue to increase as long as there is enough substrate available to form enzyme-substrate complexes.

Enzyme Inhibition

Enzyme inhibition occurs when the substrate is unable to bind to the active site of an enzyme. The enzyme is then prevented from catalyzing biochemical reactions in the body. Depending on the enzyme, the affects of inhibition will vary. The two main types of enzyme inhibition are competitive and non-competitive.

A **competitive inhibitor** (a molecule similar in shape to the actual substrate) binds to the enzyme active site. The inhibitor and the substrate have to compete for the active site. The substrate molecules cannot bind with the active site if the inhibitor has already done so, and vice-versa. Some examples of competitive inhibition include:

- In metabolic pathways, the pathway end product can bind with the first enzyme in the pathway. Since the products of one step in such a pathway become the reactants in the next step, this binding effectively blocks the pathway from proceeding. End product inhibition of metabolic pathways is almost always competitive.
- Some antibiotics work by occupying the active sites of enzymes. For example, an antibiotic interrupts the metabolic pathway that produces folic acid by competing for the active sites of one enzyme in the pathway.
- Many toxic substances act as inhibitors to enzymes involved in vital biochemical processes. Once the enzyme is inhibited the process cannot take place, and the results can include paralysis, coma, or death.

A **non-competitive inhibitor** is a molecule that binds to another site (not the active site) on the enzyme and inactivates the enzyme molecule. This type of inhibitor causes the enzyme to change shape, thus altering the active site and preventing the enzyme from forming bonds with its substrate.

Examples of non-competitive inhibitors include:

- **Heavy metal** ions (lead, mercury, silver, chromium, etc.) can affect the shape of enzymes, causing heavy metal poisoning (e.g., lead poisoning from lead-based paint).
- Nerve gases such as Sarin inhibit the active site of acetylcholinesterase, an enzyme vital to proper nerve response and functioning. Nerve gas poisoning can cause death.

If you have access to the Internet, go to the *Biology 12 Web site* Lesson 2.3B Factors Affecting Enzyme Action and access Mader Online for more on this topic.

You can also try a Reaction simulation on the *Biology 12 Web site* Lesson 2.3B Factors Affecting Enzyme Action. It allows step-by-step plotting of graphs of temperature and substrate concentration vs. rate of reaction. At each step in the reaction you will find a short explanation of what is happening.

Enzyme Cofactors

Just as enzymes can be inhibited, they can be helped by one of two **cofactors**:

- an inorganic ion (one that does not contain carbon)
- an organic, non-protein molecule called a **coenzyme**

One of these two helpers is required in order for enzymes to function correctly. Inorganic ions, called cofactors, include metals such as copper (Cu+2), Calcium (Ca+2) and Magnesium (Mg+2). The role of inorganic ions is to activate enzymes.

Organic, non-protein coenzymes assist the enzyme in its function. Coenzymes provide atoms, ions, or electrons to enzymatic reactions. **Vitamins** are common components of coenzymes, so that when we lack a vitamin in our diet, coenzymes (and therefore enzymes) may not function correctly. As a result, important chemical reactions in the body may be hindered.

Guided Practice 2.3B 2
Analyzing Reaction Rates

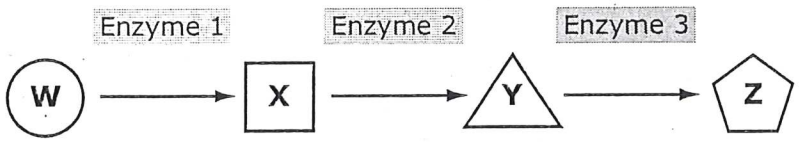
The following exercise will give you practice with interpreting graphs to determine the effect of certain conditions on the rates of chemical reactions. Enzymes play a role in all of these reactions.

Complete the explanation for each of the following scenarios:

1. Scenario: A competitive inhibitor for Enzyme 3 is added to the following metabolic pathway.

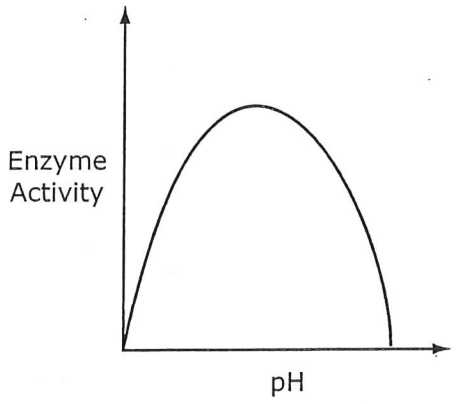
   Result: There would be _____ (less/more/no change) of Y produced; there would be _____ (less/more/no change) of Z produced.

Metabolic Pathway



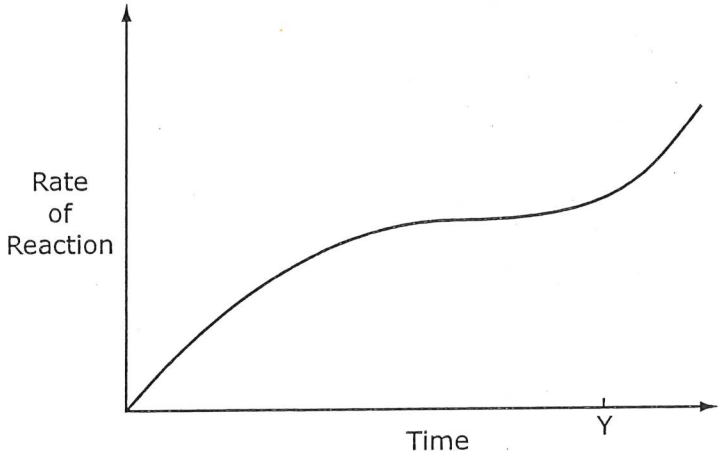
   Briefly explain why this result would occur. In your answer, be sure to consider the function of competitive inhibitors.

2. Scenario: Enzyme activity (rate of reaction) is for a given pH is shown in the following graph:



   Briefly describe what is shown in this graph.

3. Scenario: Use the following graph to answer the questions:



A. What could cause the change in the rate of reaction at point Y?

B. What would be the effect of adding more enzyme at point Y?

4. Complete the following chart to summarize the factors affecting enzyme action. For each factor, identify the effect of an increase and decrease on reaction rate. The first is completed as an example:

	Temperature (optimum = 37°C)	PH (optimum = 7)	Substrate concentration	Enzyme concentration	Inhibitor
Increase	Rx. Rate ↑ until optimum; if temperature rises too high, enzyme will be denatured				
Decrease					

Guided Practice 2.3B 3

Sample Questions on Enzymes

Try your hand at some provincial-exam-type questions on enzymes, and then check your answers before proceeding.

Select the best answers for the following questions.

1. What could be added to an enzyme-catalyzed reaction to decrease its rate?

   A. mercury ions

   B. substrate

   C. coenzymes

   D. enzymes

2. How are coenzymes involved in enzymatic reactions?

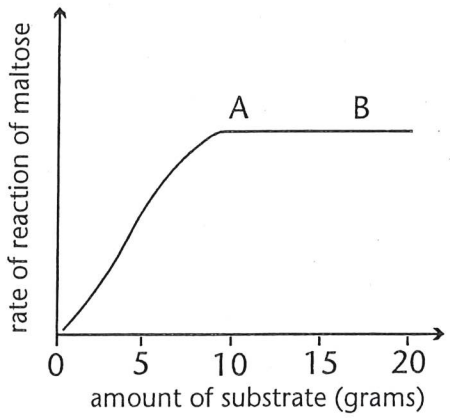
   A. they provide energy for the reaction

   B. they increase substrate concentration

   C. they provide atoms and/or electrons for the reaction

   D. they lower the activation energy required for a reaction

Use the following graph to answer question 3.



3. This graph shows the rate of a reaction involving maltase, an enzyme that digests maltose, which is a disaccharide. What accounts for the shape of the graph between A and B?

   A. there is not enough substrate

   B. a cofactor has been added

   C. enzyme concentration has decreased

   D. all the active sites are occupied

4. What is the role of lipase when it acts as a catalyst?

   A. it denatures lipids

   B. it increases the energy of activation required in the reaction

   C. it speeds up the reaction rate without being used up in the reaction

   D. it breaks down high-energy phosphate bonds

5. Coenzymes are best described as:

   A. heavy, inorganic, metallic ions

   B. able to accept/donate atoms to enzyme-mediated reactions

   C. atoms that disrupt the electron arrangement of enzymes

   D. providing energy for chemical reactions

Summary

Completing this lesson has helped you to:

- define enzyme and describe the role enzymes play in cellular chemical reactions
- understand the parts of metabolic pathways
- use the induced fit model to explain enzyme-substrate interactions
- identify factors influencing the rate of enzyme catalyzed reactions

Lesson 2.3C
Thyroxin

Overview

Proteins serve an enormous range of functions in the body. Two types of proteins in particular—enzymes and some hormones—are vitally important to processes such as **metabolism**. Enzymes, as you have learned, are catalysts. Their role is to speed up biochemical reactions. Hormones are chemical messengers or signals that influence the activity of glands or tissues at a different location from where they are produced. One way to look at the role of hormones in the body is to examine how just one gland fits into the larger picture of endocrine control.

This lesson introduces the **thyroid** gland as part of a larger process of regulation performed by the endocrine system. After this lesson, you will be able to identify the functions of the thyroid gland and the importance of **thyroxin** to metabolism in the body. You will also have a chance to apply this understanding to cases in which the thyroid malfunctions and causes metabolic abnormalities.

Although you will learn more about the endocrine system elsewhere in the Biology 12 course, this lesson provides a specific example of why proteins, including enzymes and protein hormones, are so crucial to continued health and proper body function.

Resource List

- *Inquiry Into Life*
- *Biology 12 Provincial Exam Preparation package*
- *Biology 12 Web site*
  http://www.openschool.bc.ca/courses/biology/bi12/mod2.html

The Action of Hormones

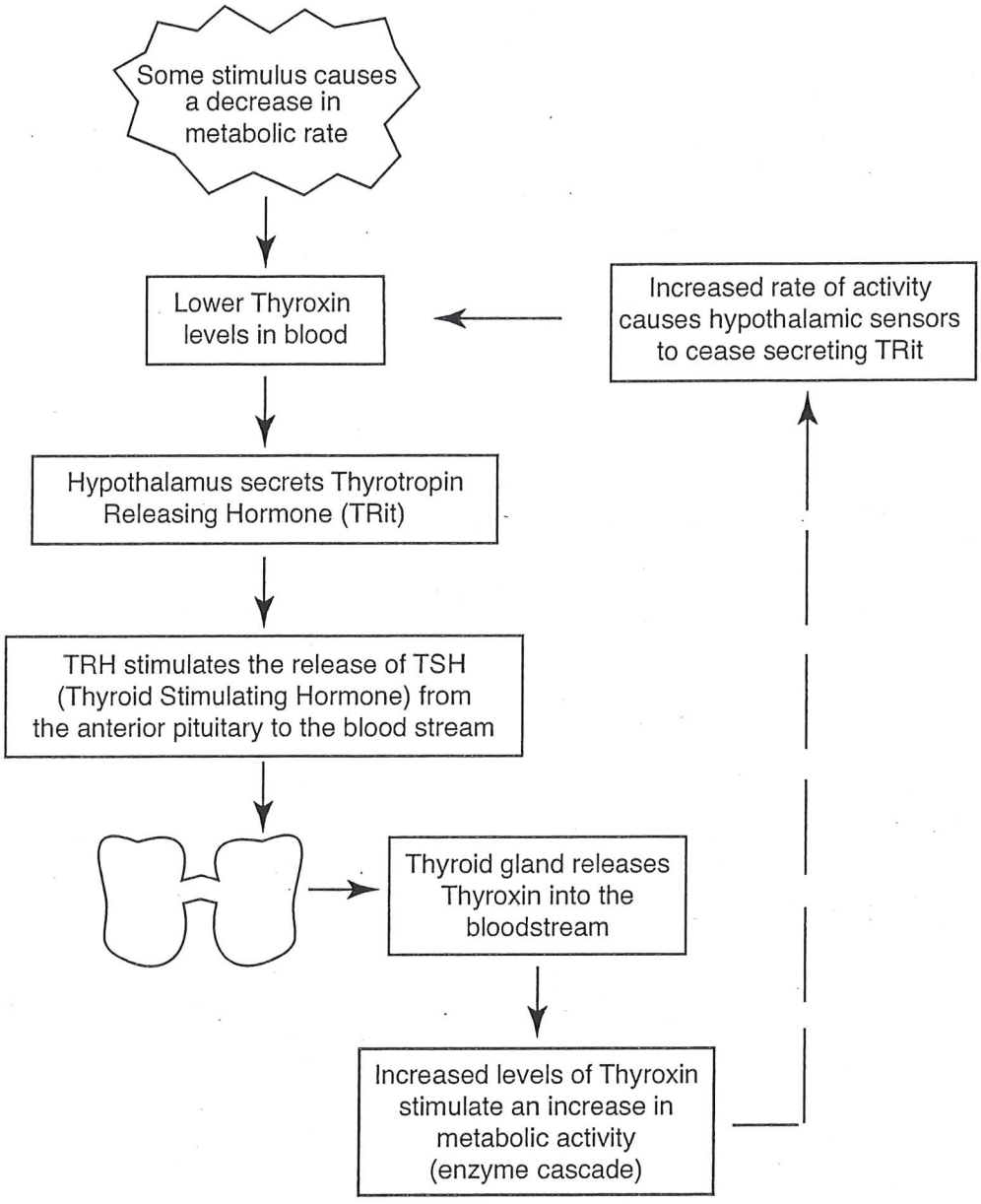
To begin, complete the reading assignment from the *Inquiry Into Life* textbook. It is a good idea to make your own notes to help you understand the relationship between the hypothalamus and anterior pituitary in the brain and the target gland in the body. In this case the target gland is the thyroid, which is wrapped around the upper trachea in the neck.

If you have access to a computer and the Internet, go to the *Biology 12 Web site* Lesson 2.3C Thyroxin to read the "Endocrine System-—Thyroid Gland" summary. Roll your mouse over the endocrine diagram. This demonstrates the way in which different endocrine organs interact to provide regulatory feedback and control hormone functions in the body.

The thyroid gland is part of an endocrine (hormonal) control system that also involves the hypothalamus, a part of the brain that controls the anterior pituitary gland. The anterior pituitary, in turn, secretes hormones that act upon the thyroid. The thyroid is considered a target gland. The thyroid is then stimulated to release its own hormones.

The following diagram summarizes the negative feedback mechanism that regulates hormone production.

Note that increasing levels of target gland hormones signal the hypothalamus and pituitary to stop releasing their own hormones. By responding to change (increased hormone levels) and reversing the process that causes change, these glands maintain stable conditions in the body.



Negative Feedback System for Regulation of Thyroxin

Rather than targeting a specific gland or tissue, the products of the thyroid gland (thyroxin and triiodothyronine, or T3) work to increase overall metabolic rate throughout the body. In short, thyroxin controls an organism's rate of metabolism (all biochemical processes in cells). The effects of increased cellular metabolism include:

- cells increase glucose breakdown (cellular respiration)
- cells release and use more energy
- production of complex molecules increases
- carbon dioxide production increases

Thyroxin is one of two hormones released by the thyroid; the molecule is nicknamed "T4" because it contains four iodine atoms. Iodine in an animal's diet is concentrated and stored in the thyroid gland. Without iodine, these hormones cannot be made.

Thyroxin is a **peptide hormone**. This means it works by indirectly activating an enzyme cascade (also known as a metabolic pathway) in which one enzymatic reaction triggers other reactions to begin.

Thyroid Abnormalities

In general, there are two categories of thyroid malfunction—either the gland produces too much hormone or it doesn't produce enough. The next part of this lesson focuses on how these situations create metabolic problems in affected individuals.

Hypothyroidism

Hypothyroidism refers to the underproduction of thyroid hormones. Since the function of these hormones is to increase cellular metabolism, any thyroid hormone deficiency will result in lower than normal metabolism. Affected individuals will likely be sluggish, may gain weight and feel cold due to lowered body temperature. When the thyroid is removed (for example, due to thyroid cancer), its function is replaced by lifelong medication. Hypothyroidism may be a temporary result of the trial and error process required to find the correct dose.

Hyperthyroidism

The opposite of hypothyroidism is hyperthyroidism, which is the overproduction of the thyroid hormones T3 and T4. Both hypothyroidism and hyperthyroidism can be detected with a simple blood test. This is sometimes performed on infants and young children who are not meeting growth projections. Hyperthyroidism is characterized by, among other symptoms, hyperactivity, inability to sleep, weight loss, and goiter.

Guided Practice 2.3C 2
Matching the Terms

Write the letter of the term in Column A beside the correct definition in Column B. Not all definitions will be used, and some may be used more than once.

Column A	Column B	
A. hyperthyroidism	1. underproduction of thyroid hormone	
B. iodine	2. one enzyme-mediated reaction triggers another	
C. thyroxin	3. bind to cell membrane to start an enzyme cascade	
D. metabolism	4. a chemical messenger; influences target glands/tissues	
E. hypothyroidism	5. required for thyroid hormone production	
F. thyroid	6. overproduction of thyroid hormone	
G. peptide hormone	7. source gland for thyroxin	
H. hormone	8. causes increased cellular metabolism	
I. enzyme cascade	9. biochemical reactions; rate is controlled by the thyroid gland	

Now do Section Assignment 2.3 Parts A, B, and C.

Summary

Completing this lesson has helped you to:

- identify the thyroid as the source endocrine gland for thyroxin
- relate the function of thyroxin to metabolism