Enzymes catalyze metabolic reactions that are crucial for life.

A computer model of the protein kinase AKT1.
RAC-alpha serine/threonine-protein kinase (AKT1) is an enzyme that modifies proteins by adding phosphate groups to them. All kinases add phosphate groups to other molecules.) AKT1 plays a critical role in programmed cell death in neurons. This computer model shows the AKT1 enzyme (white) interacting with an inhibitor molecule (gray, blue, and red) and a substrate peptide.
Ramón Andrade, 3Dciencia/Science Source.

Topics Covered in this Module
- The Role of Enzymes in Metabolism
- Enzyme Activity

Major Objectives of this Module
- Describe what a catalyst does.
- Explain the mechanisms by which enzymes lower the activation energy of reactions.
- Describe environmental factors that affect enzyme activity.
- Explain how cells regulate enzyme activity.
Many of the chemical reactions required for life could occur on their own, with no additional help. However, they would proceed at such a slow rate, in some cases years, that we would be long dead before the required product became available. Without enzymes, the human body could not digest food or turn it into cellular energy; plants could not create sugar from sunlight; and life as we know it would not exist. Enzymes speed up these chemical reactions and in doing so make life possible. How do enzymes perform this vital function?

**The Role of Enzymes in Metabolism**

Most chemical reactions in cells do not happen fast enough on their own to support life. They require catalysis, or acceleration of a chemical reaction by a catalyst that is not consumed by the reaction. Enzymes are biological catalysts that speed up chemical reactions inside cells. The word enzyme was first used by German physiologist Wilhelm Kühne in 1877 to describe the action of yeast leavening bread. Most enzymes are proteins, but enzymes can also be composed of RNA, in which case they are called ribozymes. Enzymes interact with specific molecules, allowing them to proceed down a specific biochemical pathway. For example, enzymes are necessary to produce a consistent and abundant supply of ATP, which provides the energy required by cells to sustain life. Enzymes also play a role in detoxifying toxic substances, as when alcohol dehydrogenase breaks down alcohol to facilitate its removal from the body. Their actions make all the difference between a reaction that happens fast enough to sustain life and one that does not. Why do chemical reactions need to be sped up? What is slowing them down?

**What do enzymes do?**

Enzymes facilitate the transformation of initial substances called substrates into different molecules called products. The names of enzymes indicate their specific functions. The suffix -ase indicates that a molecule is an enzyme, although some enzymes, such as the digestive enzyme pepsin, do not carry this suffix. The rest of the enzyme's name details its function. For example, a protease is an enzyme that degrades proteins; a lipase is an enzyme that breaks down lipids. Enzymes that build molecules are often called synthases. An isomerase, like ribose isomerase, is an enzyme that rearranges a molecule into its isomer. This naming convention makes it easier to recognize the nature of the reaction driven by the specific enzyme.

As substrates are transformed into products during a chemical reaction, they go through an intermediate transition state. The chemical reaction is at its highest energy at the transition state. The difference between the energy level of the substrate and the energy level of the transition state is called the activation energy (Figure 1). Activation energy is the energy needed to overcome the energy barrier of breaking and reforming bonds for a reaction to proceed.

The activation energy determines the number of molecules of product that can form via the transition state over a certain time period. Increasing the temperature increases the kinetic energy of the molecules, which allows the substrates to overcome the activation energy barrier more quickly. However, this strategy is not feasible in most cells because proteins denature and other cellular processes are disrupted when temperatures become too high. Cells need a different approach to overcome the activation energy barrier.
Enzymes facilitate chemical reactions by lowering the activation energy required for the reaction to occur. In effect, enzymes can take a reaction to completion but through a different path. This quality of lowering activation energy makes enzymes biological catalysts (Figure 1). Within living cells, almost all metabolic pathways rely on enzymes to transform substrates into products that the cell can use for biological activity.

Figure 1: Enzymes and activation energy.
During a chemical reaction, substrates (A + BC) reach a transition state (A—B—C) before they are transformed into products (AB + C). The activation energy is the energy required to reach the transition state. Compared to an uncatalyzed reaction (left), enzymes lower the activation energy by stabilizing the transition state into a more energetically favorable conformation (right).

Test Yourself
Why is it important to living things that chemical reactions have activation energies?

Every enzyme has an active site, a pocket where it binds its substrates. The active site is formed at the tertiary or quaternary level of protein structure and is where the chemical transformation of substrate to product occurs. Most enzymes act on a specific, preferred substrate, although some will act on multiple substrates that are similar to each other. When the substrate enters the active site of the enzyme, the substrate and the enzyme bind together to form an enzyme-substrate complex. The enzyme and substrate(s) interact through transient hydrogen bonding and ionic and hydrophobic interactions between the substrate and the R-groups of the enzyme's amino acids. These non-covalent bonds position the substrate(s) in ways that favor a specific chemical reaction to occur.

How do enzymes work?
There are two important things to remember about how enzymes work. First, the reaction does not permanently change the enzyme's chemistry or conformation. Although the enzyme facilitates the reaction that converts substrates into products, and while the enzyme will often change its shape, or conformation, during the reaction, it reverts to its original conformation once the reaction is completed (Figure 2).
During the catalytic cycle, an enzyme binds to a substrate to form an enzyme-substrate complex. After the reaction, the enzyme releases the product, after which the enzyme is ready for another substrate. Note that the enzyme is not changed or consumed by the reaction.

**Test Yourself**

Explain the catalytic cycle of an enzyme involved in a synthesis reaction.

Second, enzymes exhibit remarkable substrate specificity. Biologists used to think of enzymes as a static "lock" that fits the substrate "key." However, more recently, the *induced-fit* model of enzyme reactions has replaced the lock-and-key model. The induced-fit model builds on the same basic idea — that the enzyme is specific to one "correct" substrate — but it also takes into account that the enzyme changes its shape in response to the presence of the substrate. The specificity of the enzyme to the substrate allows cells to regulate metabolic reactions very closely. Often an enzyme that works on glucose will not bind any other sugar isomers, which allows the cell to regulate exactly which reactions are happening at any given time. However, enzymes can be "tricked" if a chemical has a region that can bind to the active site. This is how pharmaceutical drugs can be used to turn off enzymes that are overactive. The drug is similar enough to the substrate to bind to the active site but different enough that no reaction happens. As a result, the active site of the enzyme remains occupied by the drug, preventing the real substrate from binding and undergoing its chemical reaction. For example, the drug Lipitor® inhibits HMG-CoA reductase, a key enzyme in the production of cholesterol in the liver. Inhibition of HMG-CoA reductase by Lipitor prevents the enzyme from synthesizing cholesterol, resulting in lower levels of cholesterol in the blood, which ultimately reduces the risk of atherosclerosis and other cardiovascular diseases.
There are several ways by which enzymes can lower the activation energy of a reaction (Figure 3). The active site of the enzyme can position its substrates into an orientation that favors the breaking and/or forming of chemical bonds. Alternatively, the enzyme can apply torque on its substrates, providing mechanical stress on chemical bonds to make them more likely to break. The active site may have a chemical microenvironment, such as a different local pH or charge environment, that is more energetically favorable to the transition state. Finally, the enzyme may transfer or accept protons, electrons or functional groups to help convert the substrates into the products.

Figure 3: Understanding how enzymes lower activation energy.
Activation energy is the energy needed to start a reaction. Enzymes lower activation energy, which makes it easier for the substrates to reach their transition states.

Some enzymes require substances known as cofactors in order to be biologically functional catalysts. Cofactors are typically involved in the transfer of chemical groups between molecules, helping transform substrates into final products. Some cofactors are metal ions such as iron (Fe²⁺ and Fe³⁺), magnesium (Mg²⁺), and zinc (Zn²⁺), which are involved in electron transfer. In humans, these ions are often the minerals that are part of a healthy diet, and they are available naturally in many of the foods we eat. Coenzymes are small organic cofactors that bind to enzymes. Many of the vitamins that are essential for proper nutrition and bodily function are coenzymes (e.g., vitamin C). For example, coenzyme A interacts with acetyl groups in fatty acid synthesis and pyruvate oxidation pathways of cellular respiration. Coenzyme A plays such an important role in these reactions, among many others, that it is present in all living cells. Other common coenzymes include molecules such as ATP, NAD⁺, and NADP⁺; the latter two are essential in cellular respiration and photosynthesis, respectively. Both coenzymes and inorganic cofactors can bind tightly or transiently to the active site and help the enzyme-substrate complex form.
Enzyme Activity

Summary

Test Your Knowledge

PRIMARY LITERATURE

Growing new heart cells to treat damaged hearts
Conversion of mouse fibroblasts into cardiomyocytes using a direct reprogramming strategy.
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Structural basis for regulation of the Crk signaling protein by a proline switch.
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RNA-dependent DNA polymerase in virions of RNA tumour viruses.
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Enzyme Activity

Cells need to maintain homeostasis to live. Enzymes will not work above or below a specific temperature or pH. The cell needs to maintain the proper environment for the enzymes to help the cell carry out the metabolism it needs.

Each enzyme has an optimal temperature and pH level.

Enzymes lower activation energy of biochemical reactions, but the substrates still need to have enough kinetic energy to reach their transition state, allowing the reaction to occur. The temperature at which the enzyme works best is called the enzyme's **optimum temperature**. Lowering the temperature decreases kinetic energy, so fewer chemical reactions reach the necessary activation energy, even with an enzyme present.

Increasing the temperature increases the Brownian motion (random movement) of the substrate molecules, increasing the number of collisions between substrates and enzymes. Also, increased vibrations in the bonds of the substrates reduce their stability, making them more likely to break. Thus, raising temperature generally increases the reaction rate. However, if the temperature is too high, the increased kinetic energy can irreversibly denature the enzyme by breaking down some of the bonds that hold together the three-dimensional structure of the enzyme. Denatured enzymes are no longer able to catalyze biochemical reactions. This is one of the reasons an extremely high fever can be dangerous — the increased temperature over an extended period of time can denature human proteins. However, moderate fever is part of the body's adaptive immune response and can help increase the reaction rates of the body's defenses as well as cause the denaturation of pathogen proteins.

Not all enzymes have the same optimum temperature (Figure 4). Most human enzymes have an optimum temperature around 37°C (human body temperature). Many of our enzymes denature above 50°C. Such enzymes would be useless for bacteria that live in hot springs, where temperatures are regularly 70°C or higher. These bacteria use enzymes that function with much higher optimum temperatures. Other organisms, like plants and reptiles, experience a widely fluctuating range of cellular temperatures. Many of these organisms have evolved multiple variants of key enzymes that catalyze the same reaction at different optimum temperatures. The activity of most human enzymes dramatically drops if body temperature drops more than 10°C below normal, from 37°C to 26°C (i.e., dropping from a normal 98.6°F to 80.6°F), causing great risk to life functions. The reason for this drastic drop in human enzyme activity at cooler temperatures is reduced molecular motion, leading to reduced collisions between enzymes and substrates and reduced thermal agitation of substrate bonds.

Enzymes are also sensitive to changes in pH (Figure 4). Each enzyme has an optimal pH at which it functions most effectively. For example, stomach enzymes function at a very low pH where food breakdown takes place, while other enzymes in the body function best at a more neutral pH. If the pH is below an enzyme's optimum, the enzyme becomes inappropriately protonated, which can change the shape of its active site as well as its interactions with the substrates. As a result, when the pH is suboptimal it is more difficult for the enzyme-substrate complex to form. Likewise, if the pH is too high, the enzyme becomes inappropriately deprotonated, which will have similar effects on the enzyme's conformation. In addition, extreme pH can
Enzymes function best at their optimum pH and temperature. Increasing temperature above the optimum value will denature the enzyme. However, with low temperatures the rates of reaction are also low, due to fewer molecular collisions. As temperature increases, the rate of reaction increases until it reaches optimum temperature. Likewise, as the pH of the environment moves away from the optimum value, the enzyme becomes less functional and eventually denatures.

**Test Yourself**

List three characteristics that all enzymes have in common.

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Substrate concentration affects the rate of catalysis. Adding more substrate to an enzyme-catalyzed reaction should speed up the rate of the reaction. This is true when the concentration of substrate is low, but above a certain concentration, all of the enzyme's active sites become occupied with substrate molecules, and the reaction reaches saturation. At this point, adding more substrate will not speed up the rate of reaction; instead, more enzyme molecules are required for the reaction speed to increase further. This maximum rate of reaction for an enzyme is called $V_{max}$. A high $V_{max}$ value indicates an efficient enzyme. The constant $K_m$ is a measure of how well the enzyme is able to bind to the substrate. A low $K_m$ value indicates the enzyme has a better affinity for its substrate. $K_m$ is defined as the substrate concentration at which the reaction rate is half of $V_{max}$ (Figure 5).
Adding more substrate increases the reaction rate until the enzyme reaches the saturation point, at which point the reaction approaches the maximum rate, $V_{\text{max}}$. $K_m$ is the substrate concentration at half maximum velocity ($V_{\text{max}}/2$).

**Certain compounds affect enzyme activity.**

Enzymes catalyze almost all of the chemical reactions required for life, but only some of them are active at any given time. A cell regulates enzymes by turning them off or on. Some enzymes begin in the "on" position and are active until something specifically inhibits them. Others begin in the "off" position until something activates them. The regulation mechanisms used by the cell are reversible, which means that a cell can turn enzymes on or off as needed. Poisons such as nerve gas and drugs such as antibiotics can cause the irreversible inhibition of enzymes.

As an example of enzyme regulation, consider an enzymatic pathway that continues until the cell has accumulated enough product molecules. At this point, the pathway should stop because further reactions will waste substrate molecules that can be used for other purposes in the cell. How does the cell turn off enzymatic pathways when there are enough products? In feedback inhibition, the products of an enzymatic pathway bind to and inhibit enzymes in the pathway. Since many enzymes are parts of long, multi-step pathways, feedback inhibition often involves the product inhibiting an enzyme near the very beginning of the pathway, so that there are fewer intermediates produced that are already committed to the pathway.

Feedback inhibition tells us what is inhibiting the enzyme, but it does not tell us how the enzyme is being inhibited. In competitive inhibition, inhibitor molecules that are similar to the substrate bind to the enzyme's active site but do not react. Because the active site is occupied by the inhibitor, the enzyme cannot bind any substrates to catalyze the reaction. As a result, inhibitor molecules compete with substrate molecules for the active site and overall reduce the rate of the reaction catalyzed by the enzyme. Allosteric inhibition, also known as non-competitive inhibition, involves inhibitors that do not bind to the active site. Instead, allosteric inhibitors bind to an allosteric site separate from the active site. The binding of an allosteric inhibitor to an enzyme changes the conformation of the enzyme so that the active site is no longer able to bind to the substrate. Allosteric inhibition turns enzymes off; conversely, allosteric activation turns enzymes on. Enzymes regulated by an allosteric activator are inactive until the allosteric activator binds to the allosteric site. Before the allosteric activator binds, the active site is inaccessible to the substrate. Upon binding the allosteric activator, the...
Enzyme regulation occurs in many different forms, including competitive inhibition, allosteric inhibition and allosteric activation. A competitive inhibitor binds to and blocks the active site so that the substrate cannot bind. Allosteric inhibitors bind to allosteric sites separate from the active site and change the conformation of the enzyme so that the active site can no longer bind the substrate. Allosteric activators bind to allosteric sites of inactive enzymes and change the conformation of the enzyme to expose the active site for binding to the substrate.

**Figure 6: Regulation of enzymes.**

Enzyme regulation occurs in many different forms, including competitive inhibition, allosteric inhibition and allosteric activation. A competitive inhibitor binds to and blocks the active site so that the substrate cannot bind. Allosteric inhibitors bind to allosteric sites separate from the active site and change the conformation of the enzyme so that the active site can no longer bind the substrate. Allosteric activators bind to allosteric sites of inactive enzymes and change the conformation of the enzyme to expose the active site for binding to the substrate.

Scientists are still uncovering the different strategies that cells use to regulate enzymes. Some enzymes are regulated by covalent modification, the addition or removal of chemical groups such as methyl (–CH$_3$) and acetyl (–COCH$_3$) groups. In particular, phosphate (–PO$_4^{3-}$) groups regulate enzyme function by binding to the protein, causing a conformational change, thereby turning the enzyme on or off.

Kinases are enzymes that add phosphate groups to other enzymes or non-catalytic substrates. Enzymes involved in sending signals within the cell are often activated when the kinase adds a phosphate group to another enzyme in the pathway. A cascade of kinases, in which a kinase activates another kinase, which activates another kinase, and so on, can lead to a variety of cellular responses.

Enzymes can also be regulated by proteolytic cleavage, in which the removal of part of the enzyme activates the enzyme. The pancreas produces digestive enzymes in an inactive form. The small intestines produce other enzymes that cleave away parts of the inactive pancreatic enzymes to activate them. This ensures that the pancreatic enzymes do not digest proteins while still in the pancreas but are able to digest food molecules once they have been secreted into the small intestines.

Cells also use substrate concentration to regulate enzyme function. Some enzymes are composed of multiple subunits — they have a quaternary level of protein structure. When a substrate binds to one active site, conformational changes occur in the active sites of the other subunits that favor further substrate binding. This type of positive regulation in enzymes is
called cooperativity. Similar to allosteric regulation, cooperativity involves conformational changes in the enzyme subunits, turning the enzyme complex on or off or enhancing the rate of the reaction.

Test Yourself

List and define at least five ways in which enzyme activity can be regulated.

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BIOSKILL

Enzyme Kinetics

Explore Figure 7 to see how different inhibitors affect enzyme kinetics.

Figure 7: How do inhibitors affect enzyme kinetics?

Competitive inhibitors increase $K_m$ but do not alter $V_{max}$. Allosteric inhibitors decrease $V_{max}$ but do not alter $K_m$.

Current research.

Enzyme research has a number of everyday applications. For example, enzymes are often important targets of pharmaceuticals, as described earlier with Lipitor’s ability to inhibit HMG-CoA reductase in the treatment of high cholesterol. Other pharmaceuticals that target the enzyme reverse transcriptase are an important part of anti-retroviral therapy in the treatment of HIV. Reverse transcriptase is an enzyme that HIV uses to produce a DNA copy of its RNA genome to infect host cells. The discovery of reverse
transcriptase was so important to human health that it led to the Nobel Prize in Physiology or Medicine in 1975 for Howard Temin, Renato Dulbecco and David Baltimore.

Enzymes are also playing an important role in the development of biofuels as a more sustainable fuel source. Through the process of photosynthesis, plants capture energy from the Sun and store it in their cells in chemical form (e.g., sugars). The energy can be released by burning the plant material, but enzymatic digestion of the plant materials is a more effective way to process this stored energy. One particularly useful application would be the ability to process plant materials that are currently considered waste products in agriculture, such as cornstalks and cobs. Although humans do not have the enzymes to break the bonds in plant cellulose, a large polysaccharide in plant cell walls that contains stored energy in its bonds, other organisms, like fungi and bacteria, have such enzymes. Pete Heinzelman and colleagues at the University of Oklahoma are working on improving the efficiency of these fungal enzymes in order to produce biofuels from agricultural wastes. One challenge is that the cellulose is bound up with lignin in plant cell walls. Clint Chapple and colleagues at Purdue University are modifying plants to have decreased lignin content so cellulose is more readily available for the enzymes. If biofuel production becomes sufficiently efficient and economically and environmentally sustainable, it will likely become an important source of sustainable energy.
Principles of Biology

11 Enzymes

### Summary

**OBJECTIVE** Describe what a catalyst does.
A catalyst is a substance that speeds up a chemical reaction without being consumed by the reaction. Catalysts achieve this by lowering the activation energy of the reaction. By definition, enzymes are macromolecule-based catalysts that speed up biological reactions. Enzymes are generally reusable but only bind to specific substrates.

**OBJECTIVE** Explain the mechanisms by which enzymes lower the activation energy of reactions.
Enzymes lower activation energy through various means, including positioning substrates together in the proper orientation, applying torque on the substrates, providing the proper charge or pH microenvironment, and adding or removing functional groups on the substrates. In each of these methods, the enzyme functions to stabilize the transition state between the substrates as they are transformed into products.

**OBJECTIVE** Describe environmental factors that affect enzyme activity.
Most enzymes have a narrow range of temperature and pH at which they function optimally. At temperatures below the optimal temperature, there is insufficient kinetic energy for the substrate molecules and the enzyme to collide into each other. At temperatures above the optimal temperature, the bonds holding the enzyme together can be disrupted, resulting in denaturation, or permanent inactivation of the enzyme. A pH outside of the optimal range of the enzyme can result in excessive protonation or deprotonation of the enzyme, changing its conformation and its ability to bind substrates. In addition, extreme pH can denature enzymes.

**OBJECTIVE** Explain how cells regulate enzyme activity.
Enzyme activity can be regulated by binding of inhibitors to the active site (competitive inhibition) or an allosteric site (non-competitive inhibition and allosteric inhibition/activation). In feedback inhibition, the end product of a multi-step enzymatic pathway inhibits enzymes early in the pathway. Covalent modification of enzymes, such as phosphorylation, is a way to rapidly switch an enzyme on or off. Finally, in cooperativity, the binding of substrate to one subunit of a multi-subunit enzyme complex promotes the binding of additional substrate molecules to the other subunits.

### Key Terms

**activation energy**
The energy required to initiate a chemical reaction; also defined as the energy required to overcome the energy barrier to a chemical reaction.

**active site**
A location on an enzyme at which a substrate binds.

**allosteric activation**
Binding of a molecule to a site other than the active site in a way that promotes the binding of a substrate to the enzyme’s active site.

**allosteric inhibition**
Binding of a molecule to a site other than the active site in a way that inhibits the binding of a substrate to the enzyme’s active site; also called non-competitive inhibition.

**catalyst**
A substance that speeds up a chemical reaction without itself being consumed in the reaction.

**coenzyme**
An organic molecule that acts as a cofactor for an enzyme.

**cofactor**
A non-protein substance bound to and essential to the activity of a protein, particularly an enzyme.

**competitive inhibition**
Binding of a non-substrate molecule to an enzyme's active site, thus inhibiting the binding of the substrate to the active site.

**conformation**
The spatial arrangement or shape of a macromolecule, such as a protein or nucleic acid.

**cooperativity**
Describes the phenomenon in which one substrate molecule binds to an active site of a multi-subunit enzyme and thereby increases the affinity of other active sites for additional substrate molecules; a positive regulation of enzyme activity.

**enzyme**
A biological macromolecule that serves as a catalyst in biochemical reactions.

**enzyme-substrate complex**
The combination of an enzyme with its substrate(s) bound to the active site.

**feedback inhibition**
A process in which excess products work to inhibit the biochemical pathways that make those products by binding to and inhibiting enzymes early in the pathway, thus shutting down further product formation.

**induced fit**
A model of enzyme action in which substrate binding to the active site causes a temporary conformational change in the enzyme's shape, inducing further interactions between the substrate and the active site.

**isozyme**
An enzyme that catalyzes the same reaction as another enzyme but at a different optimum temperature.

**non-competitive inhibition**
Binding of a molecule to a site other than the active site in a way that inhibits the binding of a substrate to the enzyme's active site; also called allosteric inhibition.

**optimum temperature**
The temperature at which an enzyme functions at maximum efficiency.

**product**
The result(s) of a chemical reaction.

**ribozyme**
An RNA molecule that catalyzes a biochemical reaction.

**substrate**
Any reactant in a biochemical process; usually something that is acted upon by an enzyme.

**transition state**
The unstable intermediate condition of a substrate in a biochemical reaction after which the reaction will proceed to forming products.
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Test Your Knowledge

1. Which of the following is **NOT** a mechanism by which enzymes can lower activation energy barriers?
   - increasing the kinetic energy of the substrate
   - providing a microenvironment that makes it easier for the transition state to be formed
   - bringing substrates in close proximity and appropriate orientation
   - putting stress on the structure of the substrate
   - adding or removing units to the substrate

2. How do enzymes increase the rates of chemical reactions?
   - Enzymes make the product energetically more favorable than the substrate.
   - Enzymes provide the energy needed to overcome the activation energy barrier.
   - Enzymes provide a lower-energy pathway to form the transition state.
   - Enzymes serve as the substrates for chemical reactions.
   - All answers are correct.

3. Which of the following types of bonds are **NOT** commonly used to stabilize an enzyme-substrate complex?
   - hydrogen bonds
   - van der Waals forces
   - ionic bonds
   - covalent bonds
   - hydrophobic forces

4. Why do enzymes work poorly at suboptimal pH levels?
   - The substrates do not have enough kinetic energy.
   - All enzymes function best at pH 7.
   - The pH of the environment can alter the chemistry of the active site, affecting the non-covalent bonds that stabilize the enzyme-substrate complex.
   - None of the answers are correct.
   - All answers are correct.

5. How can kinases regulate enzyme activity?
   - They are allosteric activators.
   - They provide energy for the reaction.
   - They can add phosphate groups to enzymes, typically activating them.
   - They block the active site and inhibit the enzyme.
   - They decrease the rate of the reaction.
PRIMARY LITERATURE

Growing new heart cells to treat damaged hearts
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