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► Biology

Chapter 6
Energy and life



Med learn

❖ Introduction

- The living cell is a miniature chemical factory where thousands of reactions occur, such as:
 - Cellular respiration extracts energy stored in sugars and other fuels then cells apply this energy to perform work
 - A single celled marine organisms called **dinoflagellates** convert the energy stored in certain organic molecules to light, in a process called **bioluminescence**

❖ 6.2: [The free-energy change of a reaction tells us whether or not the reaction occurs spontaneously]

• Free-Energy Change, ΔG

- Is energy that can do work when temperature and pressure are uniform as in living cell
 - It can be calculated for a chemical reaction by applying the following equation:
 - So it depends on (related to):
 - ΔH → change in system's **enthalpy** (change in total energy)
 - ΔS → change in system's **entropy**
 - T → absolute **temperature** in Kelvin (K)
 - It also depends (affected) on conditions such as **pH**, **temperature**, and **concentrations** of reactants and products
- $$\Delta G = \Delta H - T\Delta S$$
- Another way to calculate ΔG represents **the difference** between the free energy of the final state and the free energy of the initial state: $\Delta G = G_{\text{final state}} - G_{\text{initial state}}$
 - **Free energy** is the measure of the instability of the system is the free energy and it is the tendency to change to more stable state
 - Unstable systems (high G, greater work capacity) tend to change in such a way that they become **more stable** (low G, less work capacity)
 - **Equilibrium** is a state of maximum stability
 - At equilibrium **G is at its lowest possible value** in that system and then it can do no work
 - **Chemical equilibrium**: a state of reactions in which the forward and backward reactions occur at the same rate and there is no further net change in the relative concentration of products and reactants
 - We can classify reactions and processes into **Spontaneous & Non-spontaneous** according to ΔG charge

Spontaneous system

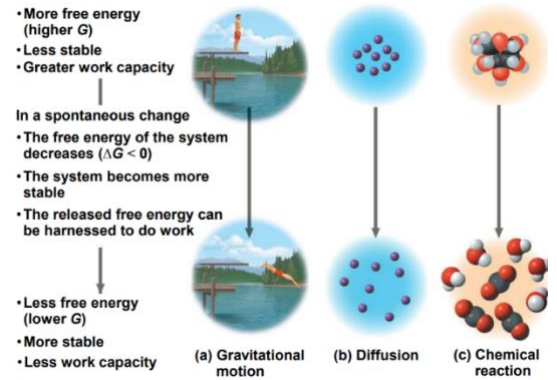
- ΔG is **negative** ($\Delta G < 0$)
- **Decreases** in the system's free energy
- **Increase** in system's stability
 - Moving **toward** equilibrium
- The released free energy can be harnessed to do work
- Occur without an input of energy

Non-spontaneous system

- ΔG is **positive** ($\Delta G > 0$)
- **Increase** in the system's free energy
- **Decrease** in system's stability
 - Moving **away** from equilibrium
 - Any change from the equilibrium position will have a **positive ΔG** and **will not be spontaneous**
- Occur with an input of energy

- For ΔG to be **negative** → **ΔH must be negative** (the system gives up enthalpy and H decreases) **OR $T\Delta S$ must be positive**

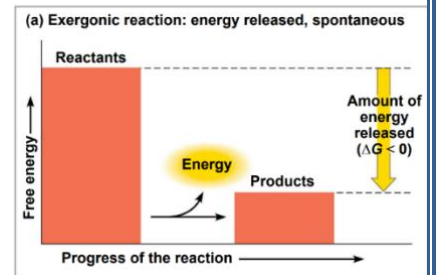
- Each of the following systems will **move toward greater stability**: The diver falls, the solution becomes uniformly colored (diffusion), and the glucose molecule is broken down into smaller molecules



- Reactions are classified into endergonic and exergonic based on their free energy changes (ΔG)

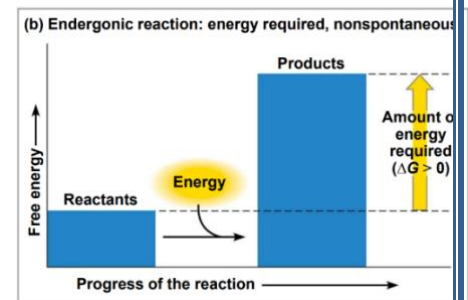
- An **exergonic reaction** (energy outward)

- Proceeds with a net **release** of free energy
- ΔG is **negative** \rightarrow **spontaneous**
- The magnitude of ΔG in a spontaneous process represents the **maximum work it can perform**
- The **greater the decrease in free energy (ΔG magnitude)**, the **greater the amount of work** that can be done (greater work capacity)

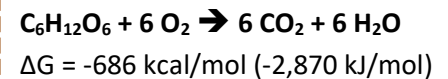


- An **endergonic reaction** (energy inward)

- Absorbs** free energy from its surroundings (**stores** free energy in molecules)
- ΔG is **positive** \rightarrow **non-spontaneous**
- The magnitude of ΔG in a non-spontaneous process represents **the amount of energy required to drive the reaction**



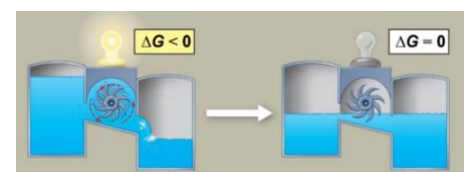
- If a chemical process is **exergonic (downhill)**, then the **reverse process** must be **endergonic (uphill)**
- A reversible process **cannot be downhill in both directions**
- If $\Delta G = -686$ kcal/mol for respiration, which converts glucose & O_2 to carbon dioxide and water, then the reverse process must be strongly endergonic, with $\Delta G = +686$ kcal/mol



NOTES:

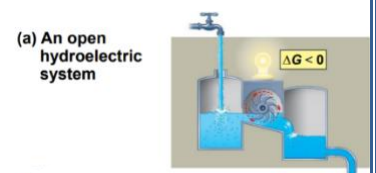
- ✓ Breaking bonds is **not the cause of releasing energy** (it **requires energy**), but energy is released because the products have **less free energy** than the reactants
- ✓ Energy stored in bonds = **potential energy** that can be released when new bonds are formed after the original bonds break, as long as **the products are of lower free energy than the reactants**

- In a closed/isolated system \rightarrow when a reaction reaches equilibrium (maximum stability) then **it can't do work**

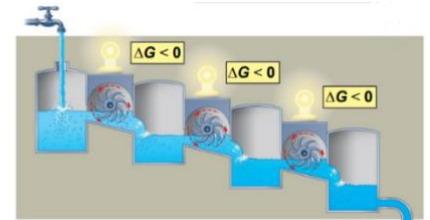


- A cell that has reached metabolic equilibrium **is dead**

- So living cells **are not in equilibrium**; they are **open systems** experiencing a constant flow of materials



- **catabolic pathway** → in the cell **releases** free energy in a **series** of reactions



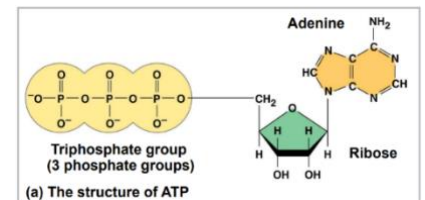
(b) A multistep open hydroelectric system

❖ 6.3: [ATP powers cellular work by coupling exergonic reactions to endergonic reactions]

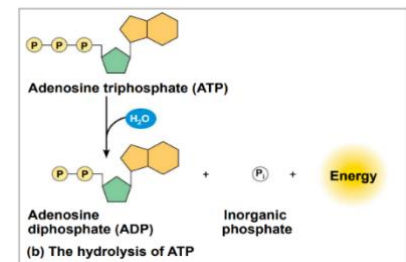
- The main 3 kinds of work in the cells:
 - **Chemical work** → pushing endergonic reactions (such as synthesis of polymers from monomers)
 - **Transport work** → pumping substances against the direction of spontaneous movement
 - **Mechanical work** → such as contraction of muscle cells, the beating of cilia and the movement of chromosomes during cellular reproduction
- To do work, cells manage energy resources by **energy coupling**, the use of an exergonic process to drive an endergonic one
- Most energy coupling in cells is mediated by **ATP**

◆ The Structure and Hydrolysis of ATP

- **ATP (Adenosine TriPhosphate)** is the cell's energy shuttle
- ATP is composed of:
 - **Ribose** (a sugar)
 - **Adenine** (a nitrogenous base)
 - **3 phosphate groups**
- ATP is also one of the nucleoside triphosphates used to make **RNA**

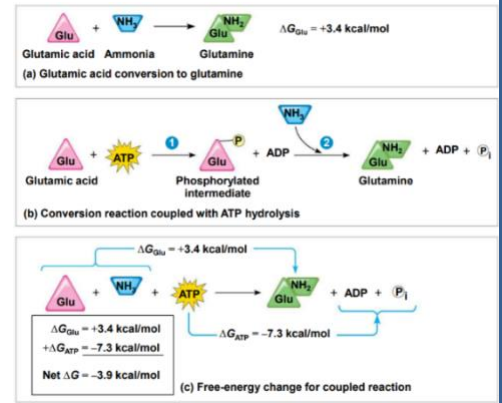
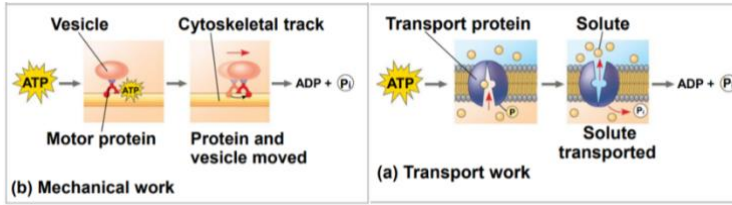


- Energy is released from ATP when the bond of the terminal phosphate is broken by **hydrolysis** (forming ADP + P_i)
 - This release of energy come from the chemical change to a state of lower free energy NOT from the phosphate bond itself
- ATP is useful to the cell because the energy released from it is somewhat **greater than most other molecules could deliver** Because of the instability of the region of the three phosphate groups (the tail) → due to the **negative charge** on each group that leads to **repulsive force** between them
 - The value (-7.3 kcal/mol) of free energy is measured under standard conditions
 - In the cell, conditions do not conform to standard conditions, primarily because reactant and product concentrations differ from 1 M
 - Hydrolysis of ATP under **cellular conditions**, released energy is about **-13 kcal/mol**, 78% greater than the energy released by ATP hydrolysis under standard conditions
- The **3** types of cellular work are powered by the **hydrolysis of ATP** (which is exergonic) → **driving an endergonic** reaction → and the overall coupled reactions are **exergonic**
- ATP drives endergonic reactions by **phosphorylation** (transferring a phosphate group to some other molecule, such as a reactant)
- **The molecule that receive the phosphate** is then called **phosphorylated intermediate** and is more reactive (less stable) than the original molecule

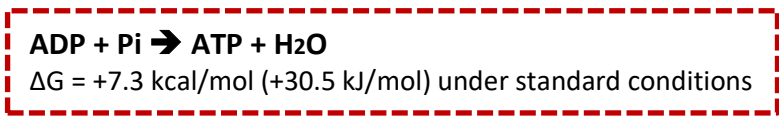
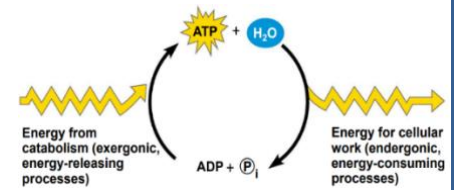


• **Example of energy coupling:**

- The conversion of glutamic acid into glutamine (endergonic) is coupled with ATP hydrolysis
- The hydrolysis of ATP leads to a **change** in a protein's shape & its ability to bind another molecule in transport & mechanical work (such as **motor proteins** walking along the cytoskeleton)

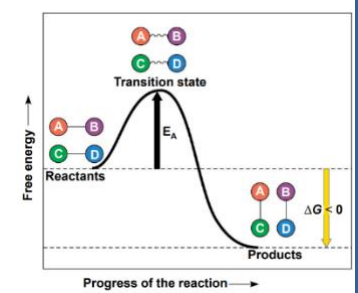
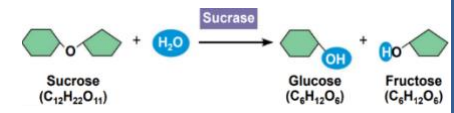


- ATP is a renewable resource that is regenerated by **addition of a phosphate** group to adenosine diphosphate (ADP)
- The energy to phosphorylate ADP comes from **catabolic reactions**
- **The ATP cycle:** is a revolving door through which energy passes during its transfer **from catabolic to anabolic pathways**



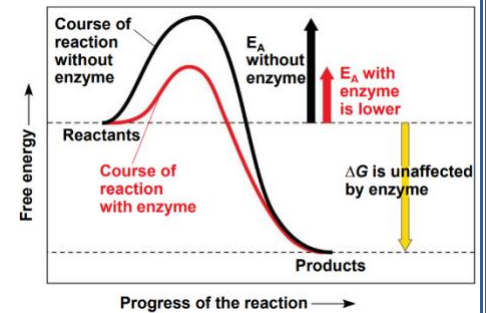
❖ **6.4: [Enzymes speed up metabolic reactions by lowering energy barriers]**

- A spontaneous chemical reaction occurs without any requirement for outside energy, but **it may occur so slowly**
- A **catalyst** is a chemical agent that speeds up a reaction without being consumed by the reaction
- An **enzyme** is a catalytic protein
 - For example, **sucrase** is an enzyme that catalyzes the hydrolysis of sucrose
- Without regulation by enzymes, chemical traffic through the pathways of metabolism would become terribly congested because many chemical reactions **would take such a long time**
- Every chemical reaction between molecules involves both bond breaking and bond forming
- **Activation energy (EA):** **initial energy needed to start a chemical reaction** (it is called also free energy of activation)
- Activation energy is often supplied in the form of **thermal energy** that the reactant molecules absorb from their surroundings → that **accelerates the reactant molecules**, so they **collide** more often and more forcefully
- When the molecules absorb enough energy for the bonds to break, the reactants reach an **unstable condition** known as the **transition state**
- The free-energy content of the reactant molecules is **increasing** → when they absorb energy equivalent to **EA**, they reach the **transition state** → so they are **activated**, and their bonds **can be broken** → as the atoms then settle into their new, more stable bonding arrangements and energy is released to the surroundings



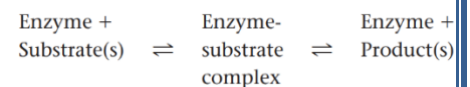
◆ How Enzymes Speed Up Reaction?

- enzymes or other catalysts speed up a specific reactions by **lowering the EA barrier** → enabling the reactant molecules to absorb enough energy to **reach the transition state** easier even at moderate temperatures
- Enzymes **do not affect** the change in free energy (ΔG)

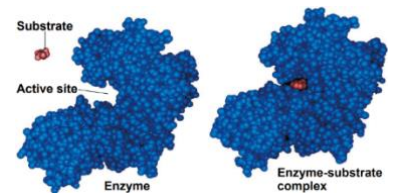


◆ Substrate Specificity of Enzymes

- Enzymes are **very specific** for the reactions they catalyze
 - The specificity of an enzyme results from its shape; enzymes are proteins and each protein has its **specific 3D shape** resulting from its **amino acid sequence**
- The reactant that an enzyme acts on is called → the **enzyme's substrate**
- The enzyme binds to its substrate, forming → an **enzyme-substrate complex**
- Then the activity of the enzyme **converts substrate to product**
- Most enzyme names end in **-ase**
- Active site:** The region (groove or pocket) on the surface where the substrate **binds** the enzyme

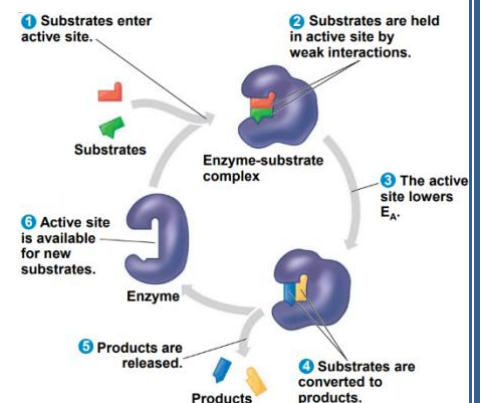


- The active site is formed by **only few amino acids**, and the rest of the protein molecule provide a framework that determines the shape of the active site
- The specificity of an enzyme is attributed to a **complementary fit between the shape of its active site and the shape of the substrate.**
- The active site itself is not a rigid receptacle for the substrate
- After the substrate enters the active site → the enzyme changes its shape slightly due to the interactions between the chemical groups on the substrate and amino acid of the active site → and the **tightening in binding** after the initial contact is called **induced fit** → that lead to bring the chemical groups of the active site in to position that **enhance the catalytic activity**



◆ Catalysis in the Enzyme's Active Site

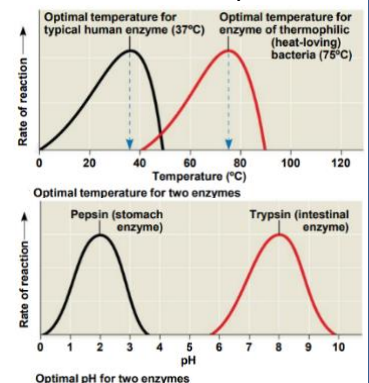
- In most enzymatic reactions, the substrate is held in the active site by **weak interactions**, such as **hydrogen bonds** and **ionic bonds**
- The **R groups** of a few of the amino acids that make up the active site **catalyze** the conversion of substrate to product
- Enzyme are extremely **fast** acting and emerge from reactions in their **original form (not changed)** → so a small amount of enzymes can have a huge effect because they are used repeatedly



NOTE

- ✓ Enzyme can catalyze either the forward or the reverse reaction, **depending on** which direction has **a negative ΔG** (The net effect is always in the direction of equilibrium)
- ✓ The initial binding between the substrate and active site **is always non-covalent**
- ✓ But sometimes **while catalyzing** the reaction there may be **covalent bonds** between them.

- **The active site can lower an EA barrier by:**
 1. Orienting substrates correctly
 2. Straining substrate bonds → reduces the amount of free energy that must be absorbed to achieve the transition state
 3. Providing a favorable microenvironment
 4. Covalently bonding to the substrate
- The rate of an enzyme-catalyzed reaction **depends on concentration of substrates**
 - The rate increases by the increase in the concentration because the more substrate molecules that are available, the more frequently they access the active sites of the enzyme molecules
- At some point in the reaction the concentration of substrate will be high enough that **all** enzyme molecules will have their **active sites engaged** → then the enzyme is **saturated**
 - When an enzyme is saturated, the only way to increase the rate of product formation is to **add more enzyme**
- An enzyme's activity can be affected by:
 - **General environmental factors**, such as temperature and pH
 - **Chemicals** that specifically influence the enzyme
- Each enzyme works better under some conditions than under other conditions, because these **optimal conditions** favor the most active shape for the enzyme
 - Each enzyme has an optimal temperature and PH values that they can function in, for example:
 - Temperature of **most human enzyme** is about **35°-40°C** and PH of most human enzymes is about **6-8**
 - The **thermophilic bacteria** that live in hot springs with optimal temperatures of **70°C or higher**
 - **Pepsin** a digestive enzyme in the human stomach works best at a **very low pH (such as 2)**
 - **Trypsin** a digestive enzyme residing in the human intestine **works best at pH=8**



- The rate of an enzymatic reaction increases with increasing temperature because substrates collide with active sites more frequently, until reaching the optimal temperature
- When the temperature becomes very high (above optimal) → the speed of the enzymatic reaction **drops sharply** → because the thermal agitation of the enzyme molecule disrupts the hydrogen bonds, ionic bonds, and other weak interactions that stabilize the active shape of the enzyme, and the protein molecule eventually denatures

◆ Cofactors

- **Cofactors:** are **non-protein** enzyme **helpers**, can be bound to the enzyme permanently and might be soluble and bind with the substrate to the enzyme
- Cofactors may be:
 - **Inorganic** → such as **metals** in ionic form: **zinc, iron, and copper**
 - **Organic** → and it is called **coenzyme**, such as: **vitamins**

◆ Enzyme Inhibitors

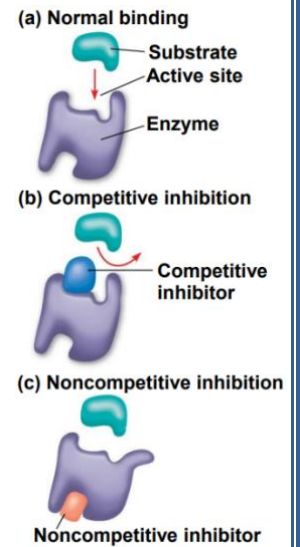
- Are certain chemicals selectively inhibit the action of specific enzymes
- Enzyme Inhibitors are 2 type:

1. Competitive inhibitors

- They bind **to active site** of the enzyme with weak interactions, and it mimics the substrate and compete it
- Reduce the productivity of enzymes **by blocking substrates from entering active sites** → the inhibition is **reversible**
- It can be overcome by **increasing the concentration of substrate** (active sites become available)

2. Non-competitive inhibitors

- They bind **to another part** of an enzyme, causing the enzyme to **change shape and making the active site less effective**
- Some examples of inhibitors are: **toxins, poisons** (such as serin), **pesticides**, and **antibiotics** (such as penicillin)

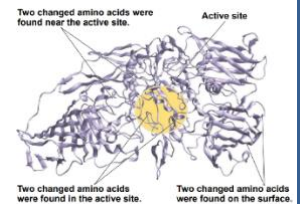


NOTES:

- ✓ If the inhibitor attaches to the enzyme by **covalent bonds** → the inhibition is **irreversible**
- ✓ If the inhibitors bind to the enzyme by **weak interactions** → the inhibition is **reversible**
- ✓ Enzyme inhibition is not always abnormal and harmful

◆ The Evolution of Enzymes

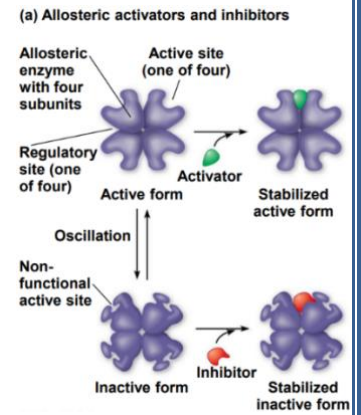
- Enzymes are proteins encoded by genes, and some **mutations** lead to changes in amino acid composition of an enzyme (particularly at the active site) → forming novel **enzyme activity** or altered **substrate specificity**
- Under environmental conditions where the new function is beneficial, natural selection would favor the mutated allele
 - For example, repeated mutation and selection on the **β-galactosidase** enzyme in E. coli resulted in a change of sugar substrate under lab conditions (become more specific)



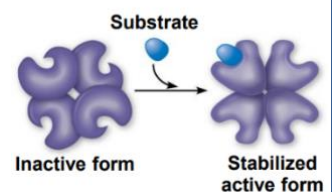
❖ 6.5: [Regulation of enzyme activity helps control metabolism]

- Chemical chaos would result if a cell's metabolic pathways were not tightly regulated
- **Cell regulate its metabolic pathways by:**
 - **Switching on or off the genes that encode specific enzymes**
 - **Regulating the activity of enzymes**
- **Allosteric regulation:** occurs when a regulatory molecule binds to a protein at one site and affects the protein's function at another site
 - Allosteric regulation may either **inhibit** or **stimulate** an enzyme's activity
- Most enzymes known to be allosterically regulated are constructed from two or more subunits, each composed of a polypeptide chain with its own active site

- The enzyme complex has active and inactive forms:
 - The binding of an activator stabilizes the **active form** of the enzyme
 - The binding of an inhibitor stabilizes the **inactive form** of the enzyme
- The subunits of an allosteric enzyme fit together in such a way that a **shape change in one subunit is transmitted to all others**
 - ✓ a **single** activator or inhibitor molecule that binds to one regulatory site (allosteric site) **will affect the active sites of all subunits**
- **ATP** binds to several catabolic enzymes allosterically, lowering their affinity for substrate and thus **inhibiting** their activity
- **ADP** functions as an **activator** of the same enzymes
- **Cooperativity**: is a form of allosteric regulation that can **amplify** enzyme activity
 - One substrate molecule primes an enzyme to act on additional substrate molecules more readily
 - Cooperativity is considered allosteric regulation because binding by a **substrate to one active site** affects catalysis in another active site
- **Hemoglobin** (not an enzyme) it carries O₂, classic studies of hemoglobin have elucidated the **principle of cooperativity**, as following:
 - ✓ Hemoglobin is made up of **four subunits**, each with an oxygen-binding site
 - ✓ The binding of an oxygen molecule to one binding site **increases** the affinity for oxygen of the remaining binding sites

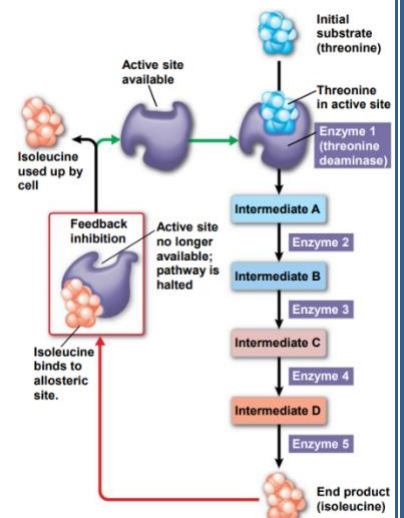


(b) Cooperativity: another type of allosteric activation



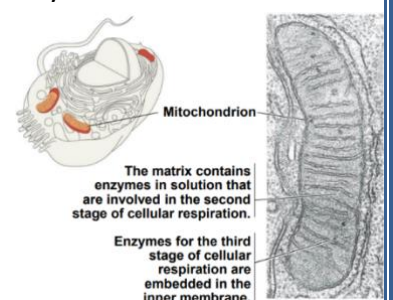
◆ Feedback Inhibition

- **Feedback Inhibition**: the **end product** of a metabolic pathway **shuts down** the pathway by binding to an enzyme that acts early in the pathway
- Feedback inhibition **prevents a cell from wasting chemical resources &** synthesizing more product than is needed
 - Synthesis of **isoleucine** from **threonine** is slowed down when isoleucine accumulates by allosterically inhibiting the enzyme for the first step of the pathway



◆ Localization of Enzymes Within the Cell

- Arrangement of Structures within the cell help bring order to metabolic pathways
- The arrangement of enzymes facilitates the sequence of reactions
- Some enzymes act as **structural components** of membranes
 - In eukaryotic cells, some enzymes reside in specific organelles; for example, **enzymes for cellular respiration are located in mitochondria**



Past Papers

1. A negative delta G for a chemical processes indicates:

- A. the reaction is exergonic
- B. the products of the chemical process store less energy than the reactants
- C. the reaction can happen spontaneously
- D. the reaction can proceed without an input of energy
- E. all of the above is correct

Answer: E

2. In a spontaneous change:

- A. The free energy of a system decrease
- B. The system becomes move stable
- C. The released free energy can be harnessed to do work
- D. Always move toward equilibrium
- E. All above are correct

Answer: E

3. In Exergonic reactions, energy is

- A. transformed into light
- B. used
- C. either released or used
- D. transformed into heat
- E. released

Answer: E

4. Enzymes catalyze chemical reactions by...

- A. adding heat to the system
- B. reacting with substrate to form new products
- C. increasing activation energy
- D. decreasing activation energy
- E. decreasing free energy

Answer: D

5. The active site of an enzyme is the region that..

- A. Binds to a noncompetitive inhibitor
- B. Binds to an allosteric inhibitor
- C. Binds to an allosteric activator
- D. Binds to a heme group
- E. Binds to substrate(s)

Answer: E

6. catabolic pathways...

- A. Provide the cell with energy, primarily in the form of ATP to work
- B. Are endergonic
- C. Combine molecules into more energy-rich molecules
- D. Are non-spontaneous
- E. Don't need enzyme catalyst

Answer: A

7. Which of the followings is FALSE about exergonic reactions?

- A. They are spontaneous
- B. They are energy releasing
- C. They have negative delta G
- D. They are mostly catabolic
- E. The products have higher total energy than reactants

Answer: E

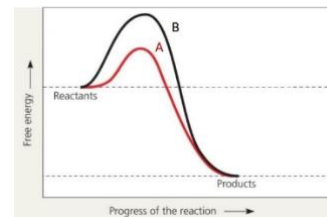
8. Coenzymes are usually...

- A. inorganic cofactors
- B. Organic cofactors
- C. Vitamins
- D. allosteric regulators
- E. both B and C are correct

Answer: E

9. Which of the following represents an un-catalyzed reaction?

- A. A
- B. B



Answer: B

10. The minimum amount of energy needed for a reaction is known as:

- A. Entropy
- B. Activation energy
- C. endothermic level
- D. Equilibrium point
- E. Free energy

Answer: B

11. Which of the following is not a product of hydrolysis of ATP?

- A. ADP
- B. Energy
- C. Pi (inorganic phosphate)
- D. Amino acids
- E. ADP and Pi

Answer: D

12. Reactant capable of interacting to form products in a chemical reaction must first overcome a thermodynamic barrier known as the reaction's:

- A. Entropy
- B. Activation energy
- C. Endothermic level
- D. Equilibrium point
- E. Free energy

Answer: B

13. The transfer of free energy from exergonic path ways to endergonic pathways is best called:

- A. Feedback inhibition
- B. ATP cycle
- C. Energy coupling
- D. Cooperatively
- E. None of the above

Answer: C

14. Which of the following is (are) true for anabolic pathways?

- A. They do not depend on enzymes
- B. They are usually highly spontaneous chemical reactions
- C. They consume energy to build up polymers from monomers
- D. They release energy as they degrade polymers to monomers
- E. They consume energy to decrease the entropy of the organism and its environment

Answer: C

15. Which term most precisely describes the cellular process of breaking down large molecules into smaller ones?

- A. Catalysis
- B. Metabolism
- C. Anabolism
- D. Dehydration
- E. Catabolism

Answer: E

16. Some bacteria are metabolically active in hot springs because:

- A. They are able to maintain a lower internal temperature
- B. High temperatures make catalysis unnecessary
- C. Their enzymes have high optimal temperatures
- D. Their enzymes are completely insensitive to temperature
- E. They use molecules other than proteins or RNAs as their main catalysts

Answer: C

17. Increasing the substrate concentration in an enzymatic reaction could overcome which of the following?

- A. Denaturization of the enzyme
- B. Allosteric inhibition
- C. Competitive inhibition
- D. Saturation of the enzyme activity
- E. Insufficient cofactors

Answer: C

18. The enzyme can speed the chemical reaction by:

- A. Speeding the movement of molecules
- B. Lowering the activation energy
- C. Increasing the number of substrate molecules
- D. All of the above
- E. None of the above

Answer: B

19. Why is ATP an important molecule in metabolism?

- A. Its hydrolysis provides an input of free energy for exergonic reactions.
- B. It provides energy coupling between exergonic and endergonic reactions
- C. Its terminal phosphate group contains a strong covalent bond that, when hydrolyzed, releases free energy.
- D. Its terminal phosphate bond has higher energy than the other two.
- E. It is one of the four building blocks for DNA synthesis

Answer: B

20. Which of the following is most similar in structure to ATP?

- A. A pentose sugar
- B. ADNA nucleotide
- C. An RNA nucleotide
- D. An amino acid with three phosphate groups attached
- E. A phospholipid

Answer: C

21. How does a non-competitive inhibitor decrease the rate of an enzyme reaction?

- A. By binding at the active site of the enzyme
- B. By changing the shape of the enzyme's active site
- C. By changing the free energy change of the reaction
- D. By acting as a coenzyme for the reaction
- E. By decreasing the activation energy of the reaction

Answer: B

22. The mechanism in which the end product of a metabolic path way inhibits an earlier step in the pathway is most precisely described as:

- A. Metabolic inhibition
- B. Feedback inhibition
- C. Allosteric inhibition
- D. Non-cooperative inhibition
- E. Reversible inhibition

Answer: B

23. In the cell, coupling reactions need the use of:

- A. Amino acids
- B. Light
- C. Sugars
- D. Fatty acids
- E. ATP

Answer: E

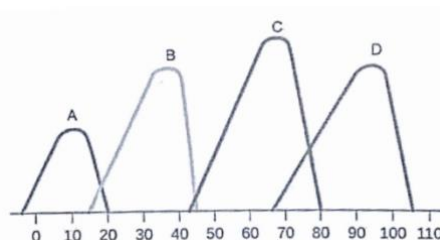
24. If an enzyme is added to a solution where its substrate and product are in equilibrium, what will occur?

- A. Additional product will be formed
- B. Additional substrate will be formed
- C. The reaction will change from endergonic to exergonic
- D. The free energy of the system will change
- E. Nothing; the reaction will stay at equilibrium

Answer: E

25. Which of the following curves represent optimal temperature of a human enzyme?

- A. A
- B. B
- C. C
- D. D
- E. None of the above



Answer: B

26. During a laboratory experiment, you discover that an enzyme-catalyzed reaction has a Delta G of -20 kcal/mol. If you double the amount of enzyme in the reaction, what will be the Delta G for the new reaction?

- A. 40 kcal/mol
- B. -20 kcal/mol
- C. 0 kcal/mol
- D. +20 kcal/mol
- E. +40 kcal/mol

Answer: B

27. Induced fit results from binding of _____ to an enzyme

- A. Vitamins
- B. Non-competitive inhibitor
- C. Specific substrate molecule
- D. b and c
- E. None of the above

Answer: C

28. If an enzyme in solution is saturated with substrate, the most effective way to obtain a faster yield of products is to:

- A. Add more of the enzyme
- B. Heat the solution to 90C
- C. Add more substrate
- D. Add an allosteric inhibitor
- E. Add a noncompetitive inhibitor

Answer: A

29. Allosteric inhibitors act as:

- A. Competitive inhibitors
- B. Coenzymes
- C. Non-competitive inhibitors
- D. Cofactors
- E. Either competitive or non-competitive inhibitors

Answer: C

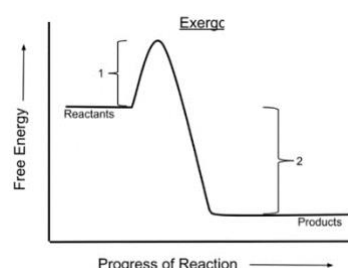
30. Allosteric enzyme regulation is usually associated with:

- A. Lack of cooperatively
- B. Feedback inhibition
- C. Activating activity
- D. An enzyme with more than one subunit
- E. The need for cofactors

Answer: D

31. This reaction could be an

- A. Endergonic
- B. Exergonic



Answer: B