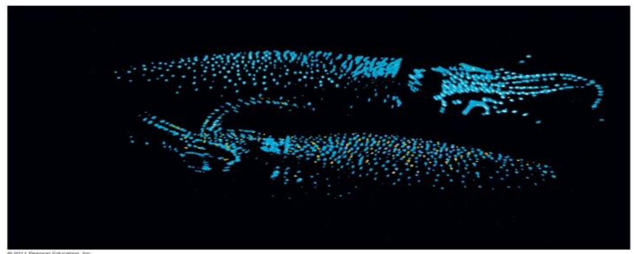
An introduction to metabolism

The living cell is (**a miniature chemical factory)** where thousands of reactions occur; which Make the cell extracts energy and applies energy to perform work. Some organisms even convert energy to light, as in bioluminescence.



Those reactions in the cells maybe spontaneous and may not, **HOW?!!!**

معلومات لازم تعرفوها مسبقا قبل البدء بالشرحَ:

- **Kinetic energy** is energy associated with motion
- **Heat (thermal energy)** is kinetic energy associated with random movement of atoms or molecules
- **Potential energy** is energy that matter possesses because of its location or structure
- **Chemical energy** is potential energy available for release in a chemical reaction
- Energy can be converted from one form to another

- **Catabolic pathways** release energy by breaking down complex molecules into simpler compounds
- Cellular respiration, the breakdown of glucose in the presence of oxygen, is an example of a pathway of catabolism

- **Anabolic pathways** consume energy to build complex molecules from simpler ones
- The synthesis of protein from amino acids is an example of anabolism
- **Bioenergetics** is the study of how organisms manage their energy resources

➢ ***CONCEPT 8.2:The free-energy change of a reaction tells us whether or not the reaction occurs spontaneously***

في هذا الجزء من الفصل، المعلومات الي لازم تفهموها:

1. Which reactions occur spontaneously.
2. Which reactions require some energy input from put side (needs energy to happen).

➢ Free energy change (ΔG)

A living system's **free energy** is energy that can do work when temperature and pressure are uniform, as in a living cell.

- But when reactions happens changes in the temperature or in the pressure or in both of them can occur. So, let's consider how we determine the free-energy change that occurs when the system changes-for example, during a chemical reaction.

The change in free energy ΔG, can be calculated for a chemical reaction by applying the following equation:

$$\Delta G = \Delta H - T\Delta S$$

ΔG= free energy change
ΔH= the change in the system enthalpy (total energy)
ΔS= the change in system entropy
T = the absolute temperature in Kelvin

The value of the ΔG will predict whether the reaction is energetically favorable (occur without energy input) or happens without help, so:

1. Negative ΔG (- ΔG) = Spontaneous reaction, **HOW**?!!
   Either → ***<u>ΔH must be negative</u>*** (the system gives up enthalpy and H decreases) or ***<u>TΔS must be positive</u>*** (the system gives up order and S increases) or ***<u>both</u>***.

In other words, every spontaneous process decreases the system's free energy.

2. Positive ΔG (+ΔG) = non-spontaneous reactions (they are never spontaneous)

- Free energy, stability, and equilibrium

Another way to think of ΔG is to realize that it represents the difference between the free energy of the final state and the free energy of the initial state:

$$\Delta G = G_{\text{final state}} - G_{\text{initial state}}$$

Thus, ΔG can be negative (spontaneous) only when the process involves loss of free energy during the change from initial to final state

1) ***Stability*** :

Because it has less free energy (spontaneous (-ΔG)), the system in its final state is less likely to change and it's therefore **more stable than it was previously**.

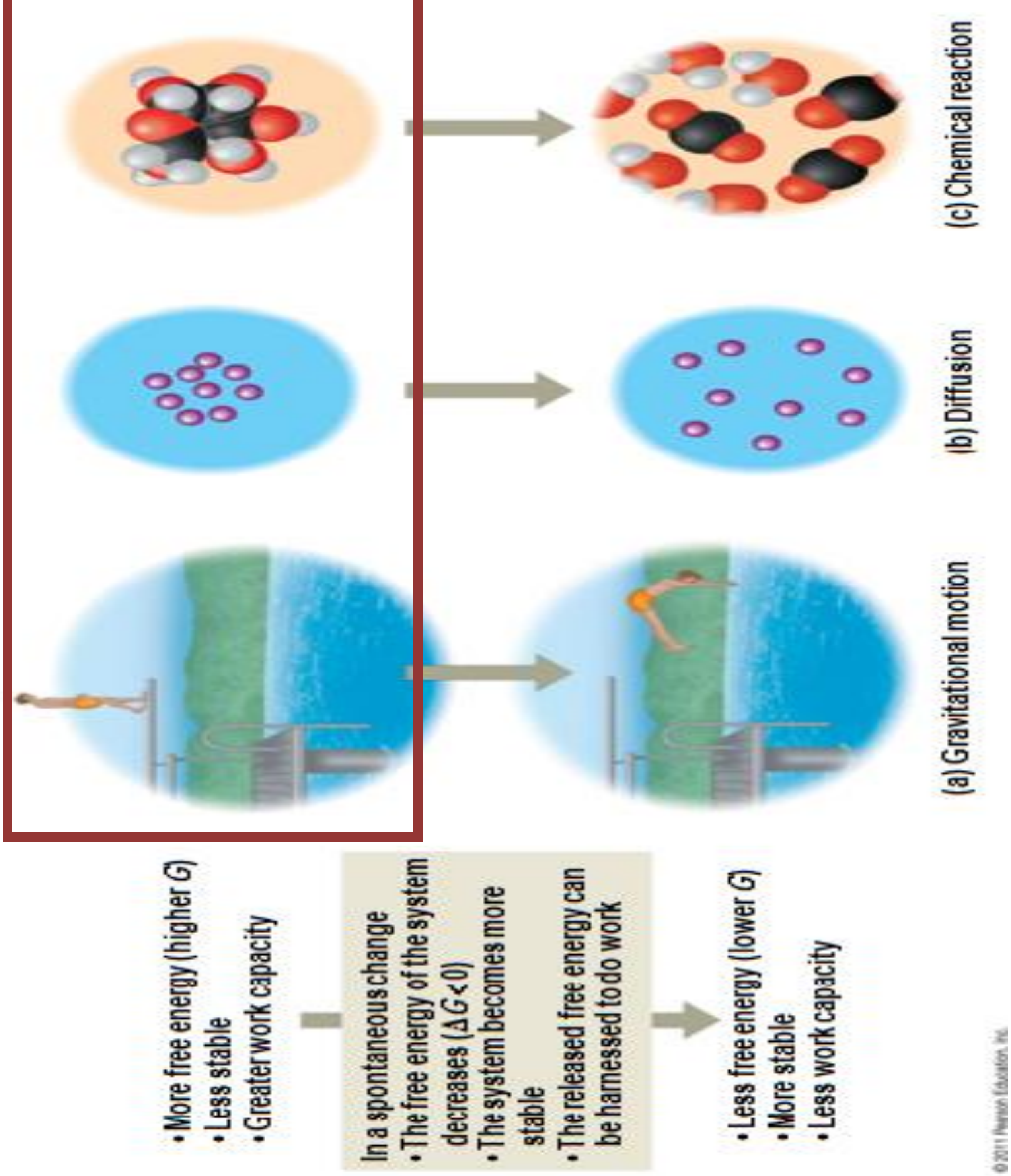
- (**Conclusion**: During a spontaneous change, free energy decreases and the stability of a system increases).

So, we can think of ***free energy*** as a measure of system's instability.

Note: instability = the systems tendency to change to a more stable state.

- For example:

Rich of free


(a) Gravitational motion
(b) Diffusion
(c) Chemical reaction
• More free energy (higher G)
• Less stable
• Greater work capacity
In a spontaneous change
• The free energy of the system decreases (ΔG<0)
• The system becomes more stable
• The released free energy can be harnessed to do work
• Less free energy (lower G)
• More stable
• Less work capacity

From the previous figure, unless something prevents it, each of these systems will move toward greater stability. The diver falls, the solution becomes uniformly colored, and the glucose molecule is broken down.

2) ***Equilibrium:***

1. It is the ***Maximum stability.***
2. The forward and backward reactions at equilibrium state occur at the same rate (reversible reactions). → Here there is no further net change in the relative concentration of products and reactants.
3. The free energy of reactants and products decreases when we move toward equilibrium, vice versa:

Note: free energy increases maybe by removing some of the products (and thus changing their concentration relative to that of the reactants).

4. G is at its lowest possible value at equilibrium state.
5. If ΔG is positive (never spontaneous systems) this means that the system is somehow moving away from equilibrium.
6. Because a system at equilibrium cannot spontaneously change, it can do no work. A process is spontaneous and can perform work only when it is **moving toward equilibrium**.

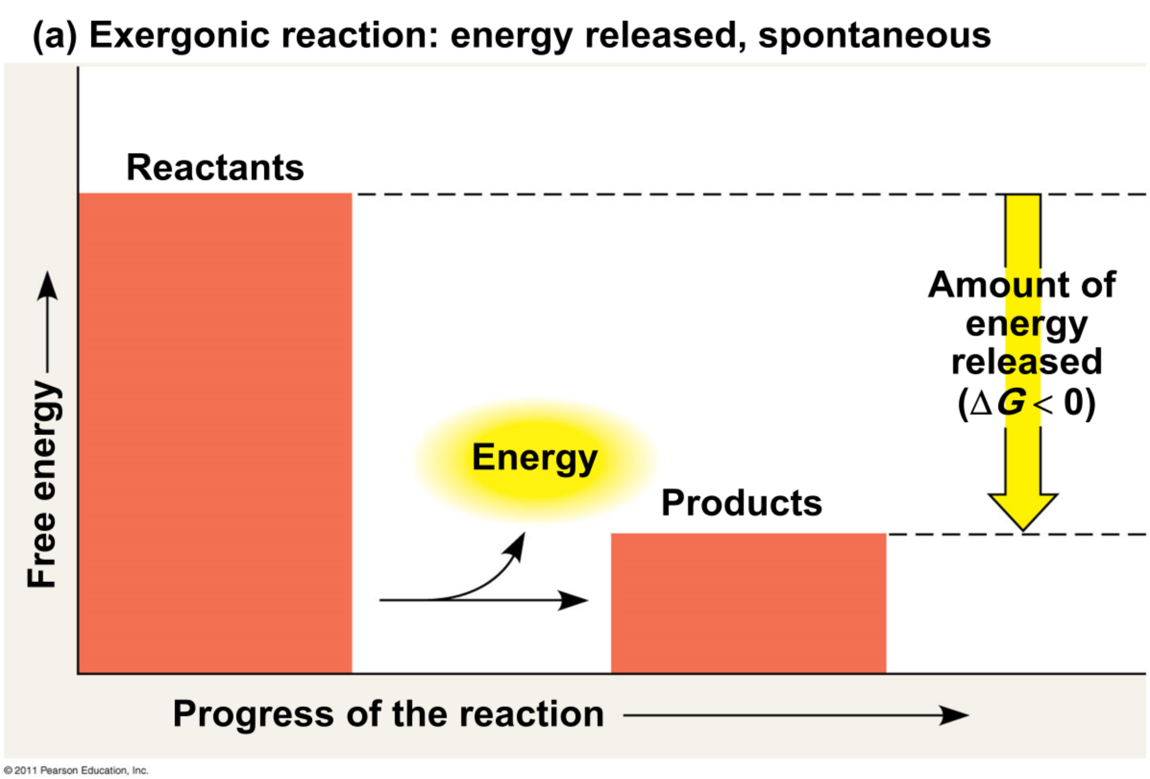
- Free energy and metabolism:

Reactions are classified depending on their **free-energy changes** in to 2 types:

1. Exer-gonic (downhill).
2. Ender-gonic (uphill).

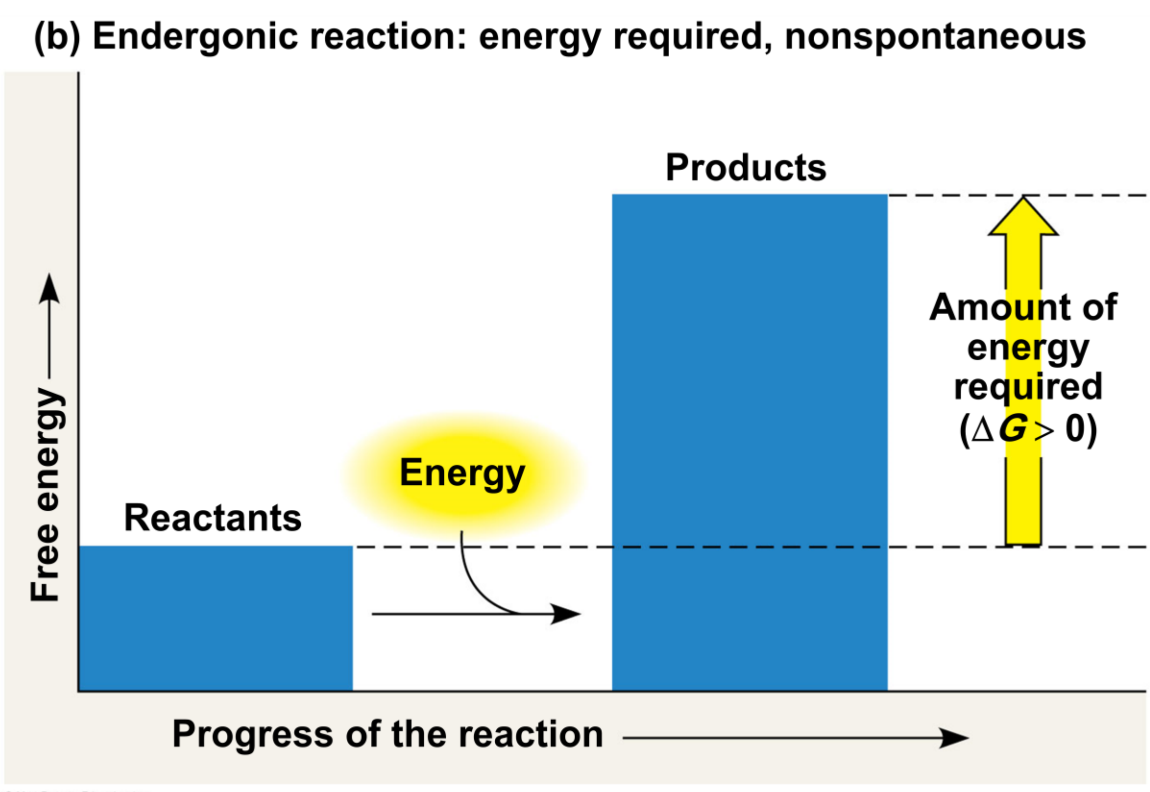
1. Exer-gonic reactions:

- They are energy ***<u>outward</u>*** reactions.
- It proceeds with a **<u>net release of free energy.</u>**
- Because of losing energy **G** increases. So, **ΔG** is negative (-ΔG).
- They are **<u>spontaneous</u>** reactions, because ΔG is negative.
- The magnitude of ΔG for an Exer-gonic reaction represents the maximum amount of work the reaction can perform. (Will be discussed later on). So, the greater the decrease in free energy, the greater the amount of work that can be done.
- Example: **cellular respiration.**



2. Ender-gonic reactions:

- They are energy ***inward*** reactions.
- It **absorbs** free energy from its surroundings.
- Stores free energy in molecules (**G increases**). So, ΔG is positive.
- They are ***non-spontaneous*** reactions, because ΔG is positive.
- The magnitude of ΔG is the quantity of energy required to drive the reaction.
- Example: **photosynthesis**.



في الجزء التالي من الشرح، سيتم طلاح مثال الكتاب وشرح المقصود بكل من التفاعلين السابقين من خلال المثال

المثال يتحدث عن التنفس الخلوي وعملية البناء الضوئي

We can use the overall reaction of cellular respiration as an example:

$C_6H_{12}O_6 + 6O_2 \rightarrow 6CO_2 + 6H_2O$

$\Delta G = -686$ kcal/mol (-2.870 kJ/mol)

Under standard conditions (1M of each reactant and product, 25◦C, pH 7), cellular respiration gives away 686 kcal of energy (available for work) for each mole (180g) of glucose broken down.

Note: because energy is <u>conserved,</u> the chemical products of respiration (**$6CO_2 + 6H_2O$**) **stores 686kcal less free energy per mole than the reactants. (This energy comes from the bonds between elements in the glucose molecules.)**

> Caution: the phrase "energy stored in bonds" is shorthand for the 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.

So, from above:

If a chemical process is Exer-gonic (downhill), releasing energy in **one direction**, then the reverse process must be ender-gonic (uphill), using energy. (a reversible process cannot be downhill in both directions.

So, if $\Delta G = -686$ kcal/mol for respiration, which converts glucose and oxygen to carbon dioxide and water, then the reverse process – the conversion of carbon dioxide and water in to glucose and oxygen – must be strongly ender-gonic, with $\Delta G = +686$ kcal/mol. So in simpler way:

product

Respiration: exer-gonic reaction **$C_6H_{12}O_6 + 6O_2 \rightarrow 6CO_2 + 6H_2O$ +*<u>686kcal</u>* (release energy)**

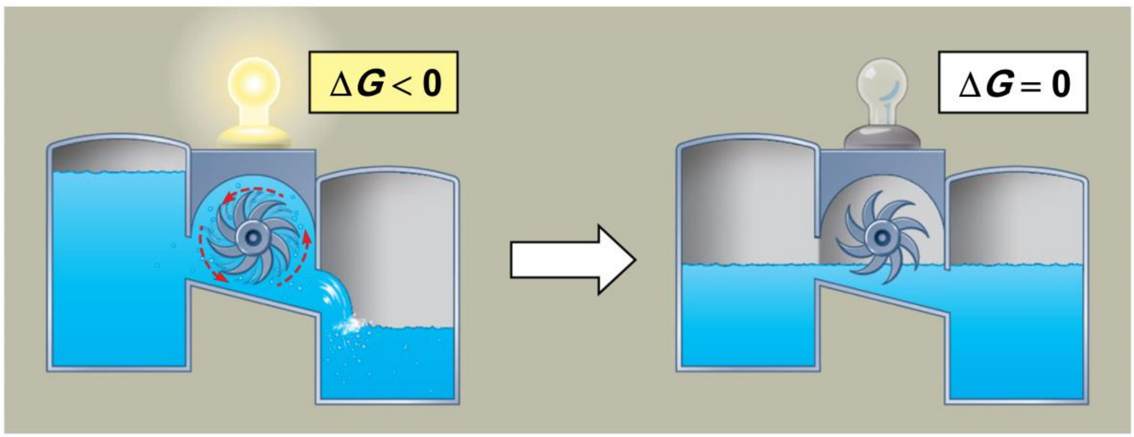
Photosynthesis: ender-gonic reaction **$6CO_2 + 6H_2O$ + *<u>686 kcal</u>* $\rightarrow C_6H_{12}O_6 + 6O_2$ (needs energy)**

From the light — reactant

- Equilibrium and metabolism:

1. In isolated systems:

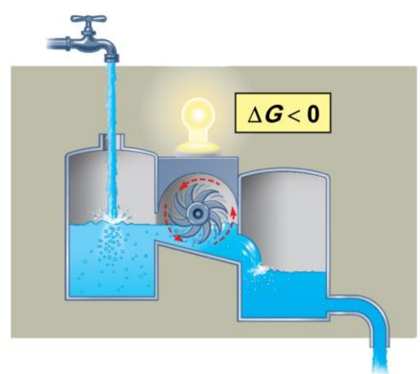
- Reactions eventually reach equilibrium, and can then do no work and at a minimum of G.



(a) An isolated hydroelectric system

2. In An open hydroelectric system:

- Never reaches equilibrium.
  - Cells are not in equilibrium; they are open systems experiencing a constant flow of materials, a defining feature of life is that metabolism is never at equilibrium. (A cell that has reached metabolic equilibrium is **dead).**



However, unlike this simple single step system, a catabolic pathway in a cell releases free energy in a series of reactions, and it's called:

3. Multistep open hydro-electronic systems:
    - The reactions are constantly "pulled" in one direction- that is, they are kept out of equilibrium.
    - Products of the first reaction does not accumulate, they become the reactant of the second reaction and so on.

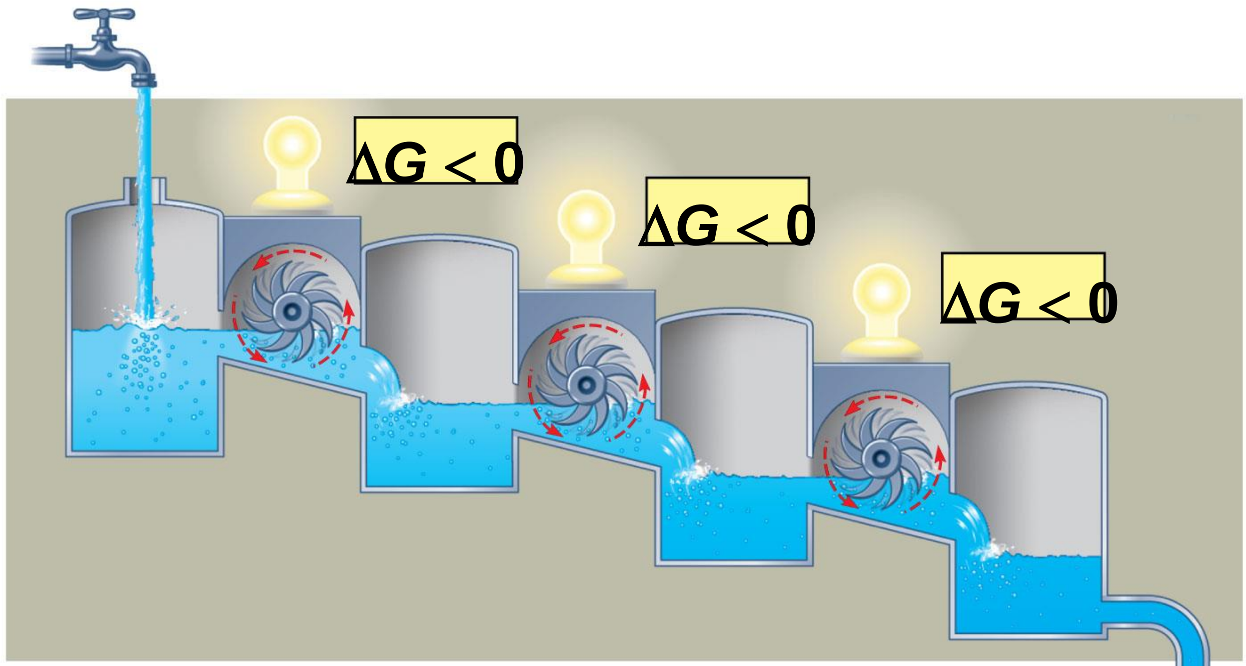
What the cells do in order to not reach equilibrium in their metabolic pathway?

1) Having a steady supply of glucose or other fuels and oxygen.
2) They are able to expel waste products to the surroundings.
3) It depends on the huge free energy difference between the reactants (hill) and products (downhill) end.

Concepts check 8.2:

1. Cellular respiration uses glucose and oxygen, which have high levels of free energy, and releases CO_2 and water, which have low levels of free energy. Is cellular respiration spontaneous or not? Is it Exer-gonic or ender-gonic? What happens to the energy released from glucose?
    - **Answer: cellular respiration is a spontaneous and exer-gonic process. The energy released from glucose is used to do work in the cell or is lost as heat.**
2. Make connections: as you saw in figure 7.20 on page 183, a key process in metabolism is the transport of hydrogen ions (H^+) across a membrane to create a concentration gradient. Other processes can result in an equal concentration of (H^+) to perform work in this system? How is the answer consistent with what is shown in regard to energy in figure 7.20?
    - **Answer: when the (H+) concentrations are the same, the system is at equilibrium and can do no work. Hydrogen ions can perform work only if their concentrations on the each side of a membrane differ - in other words, when a gradient is present. This is consistent with the figure 7.20, which shows that an energy input (provided by ATP-hydrolysis) is required to establish the concentration gradient (the H+ gradient) that can in tern perform work.**

3. What if? Some night-time partygoers wear glow-in-the-dark necklaces start glowing once they are "activated", which usually involves snapping the necklaces in a way that allows two chemicals to react and emit light in the form of chemiluminescence. Is the chemical reaction exer-gonic or ender-gonic? Explain your answer?
    - **Answer: the reaction is exer-gonic because it releases –energy- in this case, in the form of light.**



(c) A multistep open hydroelectric system

➢ ***<u>Concept 8.3: ATP powers cellular work by coupling exergonic reactions to endergonic reactions</u>***

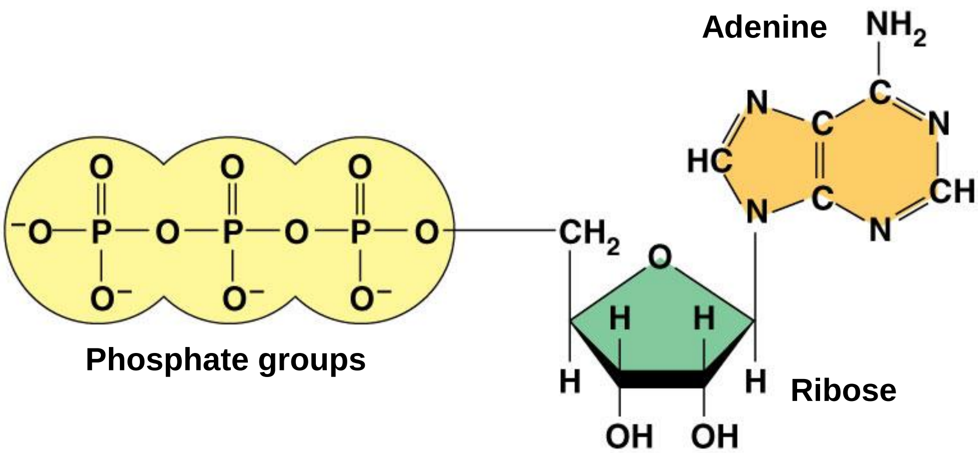
- The three main work of cells:
    1. Chemical: (synthesis of polymers from monomers).
    2. Transport: (the pumping of substances across membranes against the direction of spontaneous movement.
    3. Mechanical: (contraction of muscle cells, and the movement of chromosomes during cellular reproduction).

In order to do this work cells uses the ***<u>energy coupling</u>*** by using **ATP**.

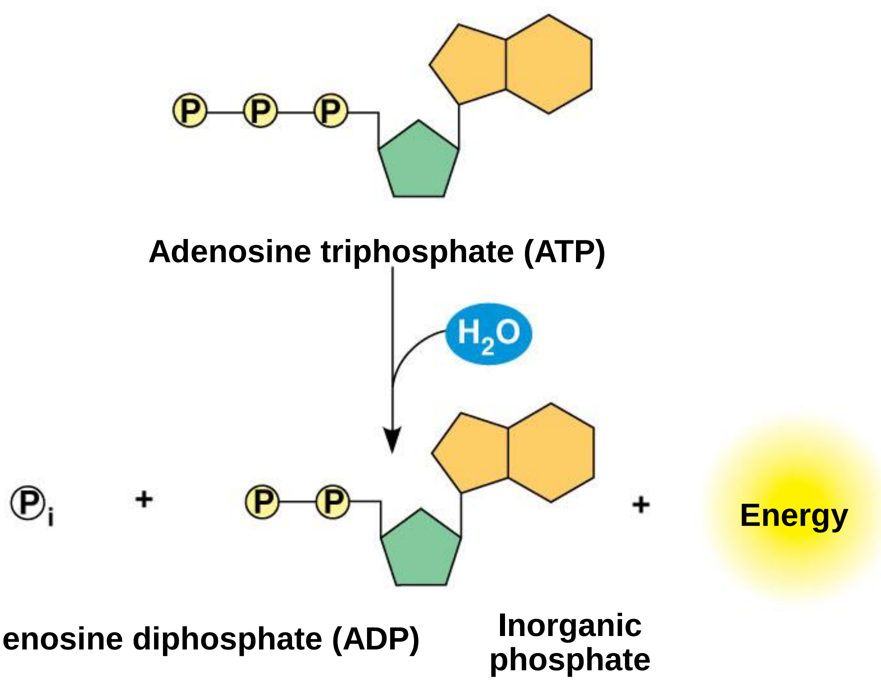
1) The structure and hydrolysis of ATP:

- ATP (adenosine triphosphate) is the cell's energy shuttle + **it is one of the nucleoside triphosphate used in make RNA.**
- ATP is composed of ribose (a sugar), adenine (a nitrogenous base), and three phosphate groups.

Hydrolysis of ATP:



(a) The structure of ATP

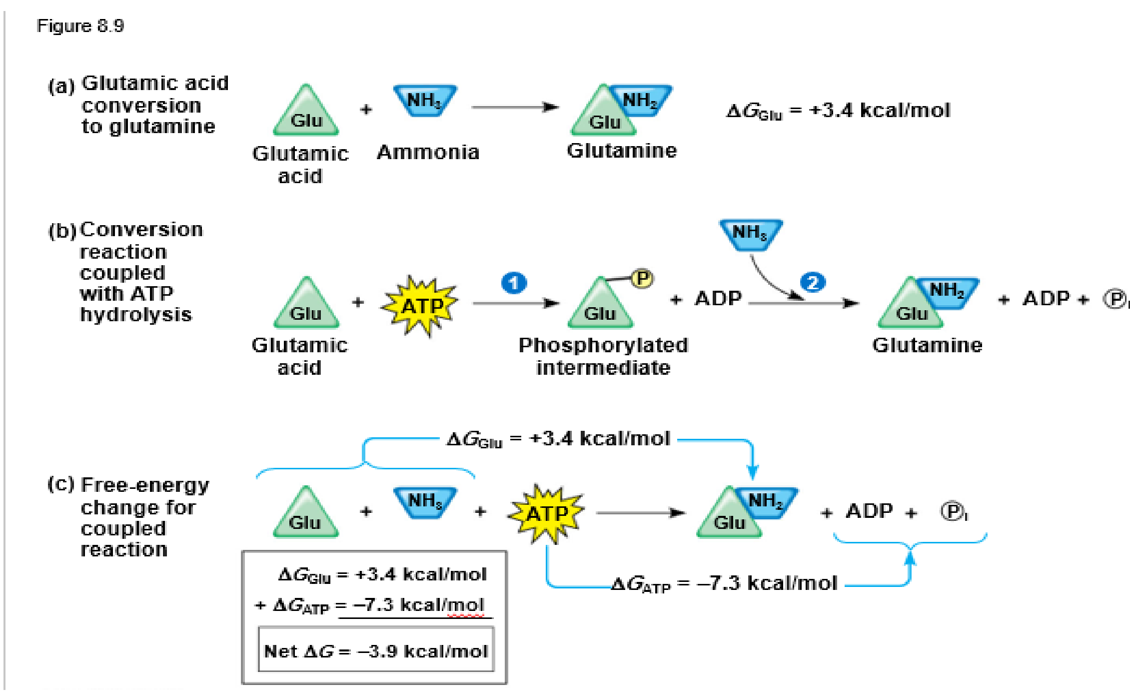


(b) The hydrolysis of ATP

- **Notes on the figure:**
  1. **The bonds between the phosphate groups of ATP can be broken by hydrolysis.**
  2. **we use <u>water</u> to break <u>the terminal phosphate bond.</u>**
  3. **The final out comes are <u>adenosine di-phosphate (ADP) + ENERGY + inorganic phosphate.</u>**
  4. **It is <u>exergonic (</u>releases 7.3 kcal of energy/mole of ATP).**
  5. **This release of energy comes from the chemical change to a state of lower free energy, not from the phosphate bonds themselves.**

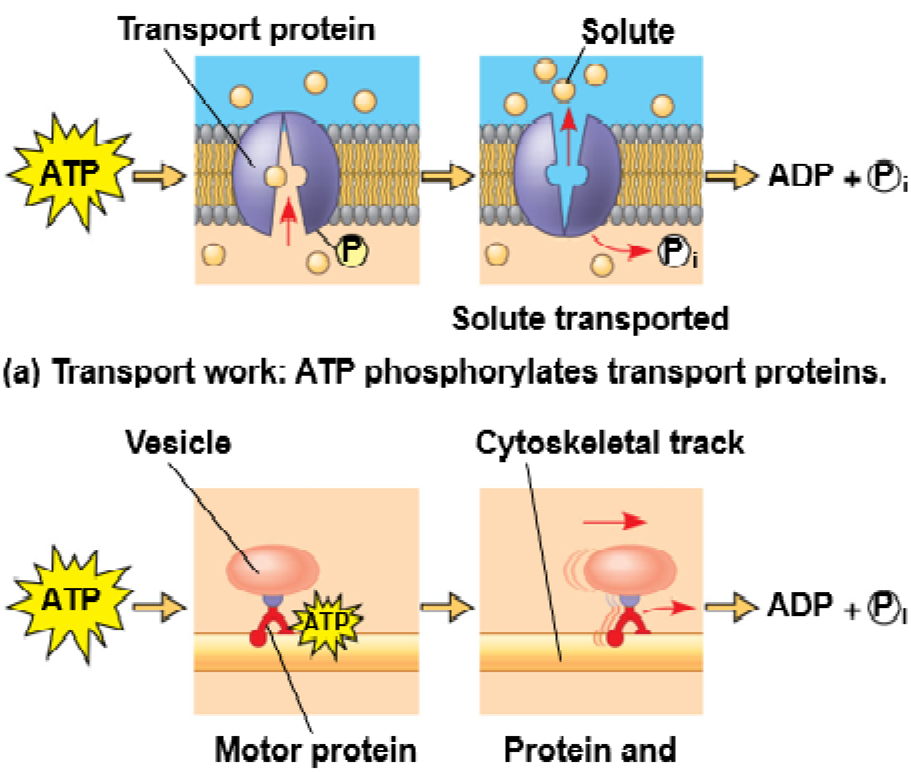
2) How the hydrolysis of ATP perform work?

- **The three types of cellular work (mechanical, transport, and chemical) are powered by the hydrolysis of ATP**
- **In the cell, the energy from the exergonic reaction of ATP hydrolysis can be used to drive an endergonic reaction**
- **Overall, the coupled reactions are exergonic.**



- ATP drives endergonic reactions by phosphorylation, transferring a phosphate group to some other molecule, such as a reactant
- The recipient molecule is now called a **phosphorylated intermediate.**

Figure 8.10

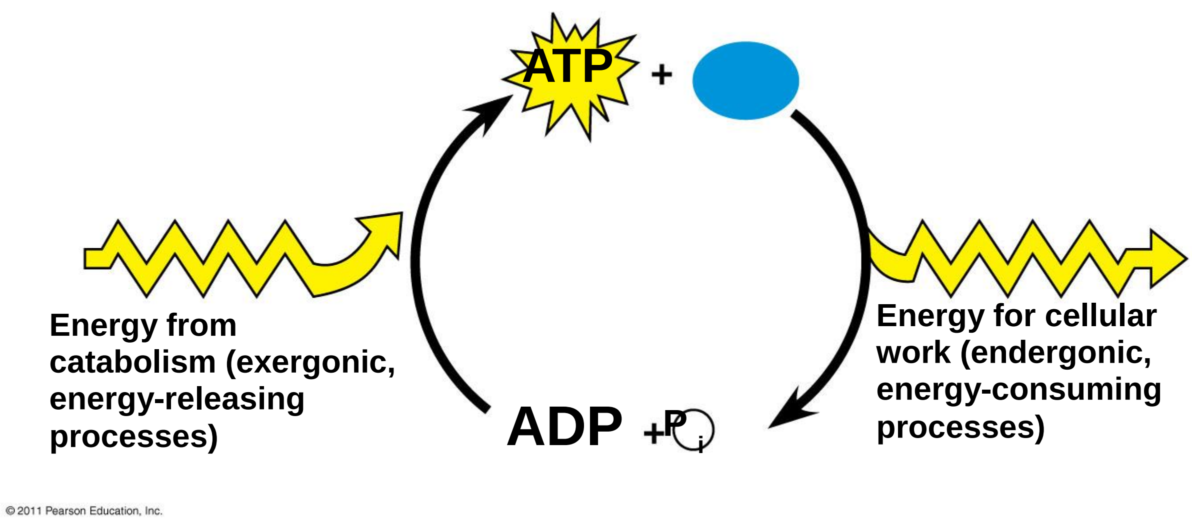


(a) Transport work: ATP phosphorylates transport proteins.

(b) Mechanical work: ATP binds noncovalently to motor proteins and then is hydrolyzed.

The re-generation of ATP:

- 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 in the cell
- The ATP cycle is a revolving door through which energy passes during its transfer from catabolic to anabolic pathways



CONCEPT CHECK 8.3:

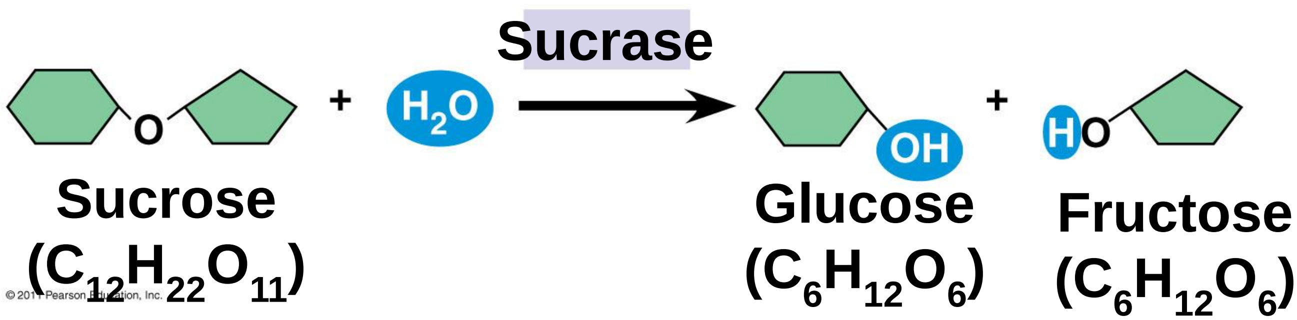
1) How does ATP typically transfer energy from exergonic reactions in the cell?
ATP usually transfer energy to endergonic processes phosphorylating (adding phosphate groups to) other molecules. (exergonic processes phosphorylate ADP to regenerate ATP).

2) CONSEPT CHECK 8.3 P.197 Q2.:
A set of coupled reactions can transform the first the first combination in to the second. Since this is an exergonic process overall, change in G is negative and the first combination must have more free energy.

3) Concept Check 8.3 p.197 Q3: active transport: the solute is being transported against its concentration gradient, which requires energy, provided by ATP hydrolysis.

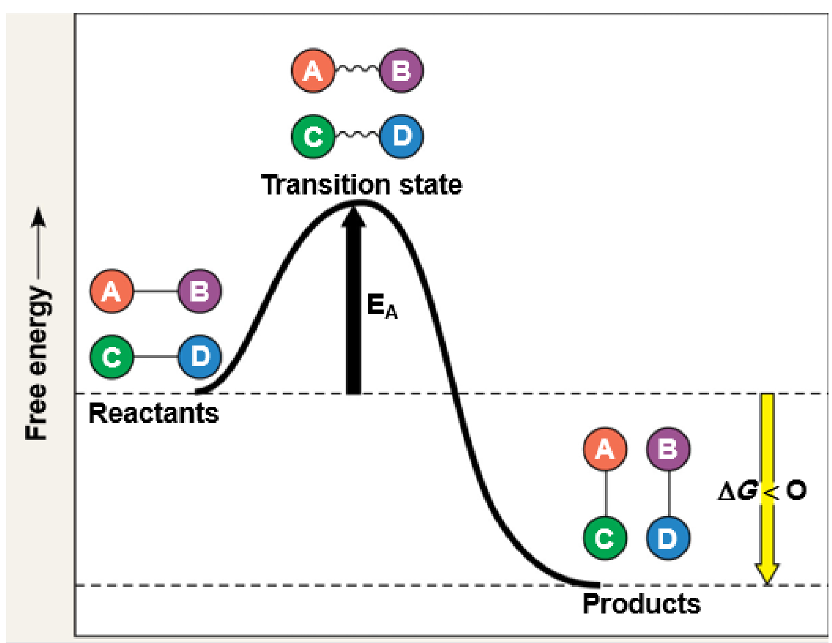
➢ ***Concept 8.4: enzymes speed up metabolic reactions by lowering energy barriers:***

- A **catalyst** is a chemical agent that speeds up a reaction without being consumed by the reaction.
- An **enzyme** is a catalytic protein.
- Hydrolysis of sucrose by the enzyme sucrase is an example of an enzyme-catalyzed reaction.



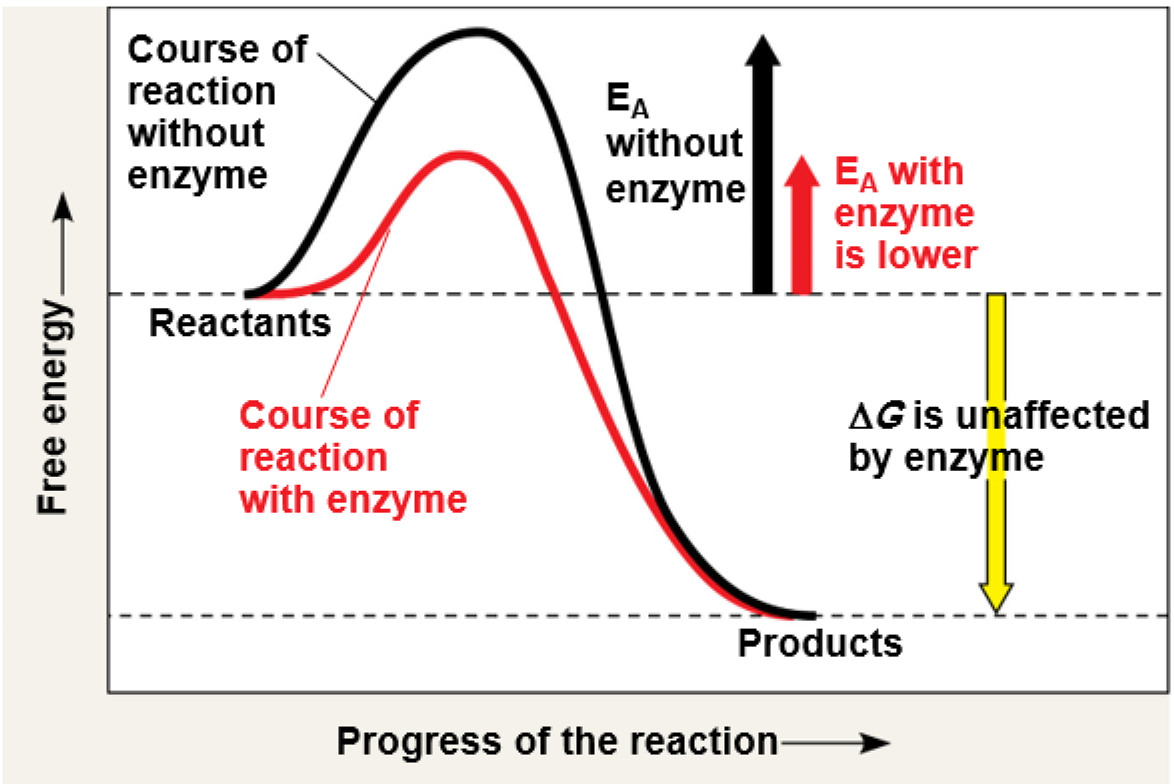
1) The activation energy barrier:

- Every chemical reaction between molecules involves bond breaking and bond forming.
- The initial energy needed to start a chemical reaction is called the free energy of activation, or **activation energy (E_A)**.
- Activation energy is often supplied in the form of thermal energy that the reactant molecules absorb from their surroundings.



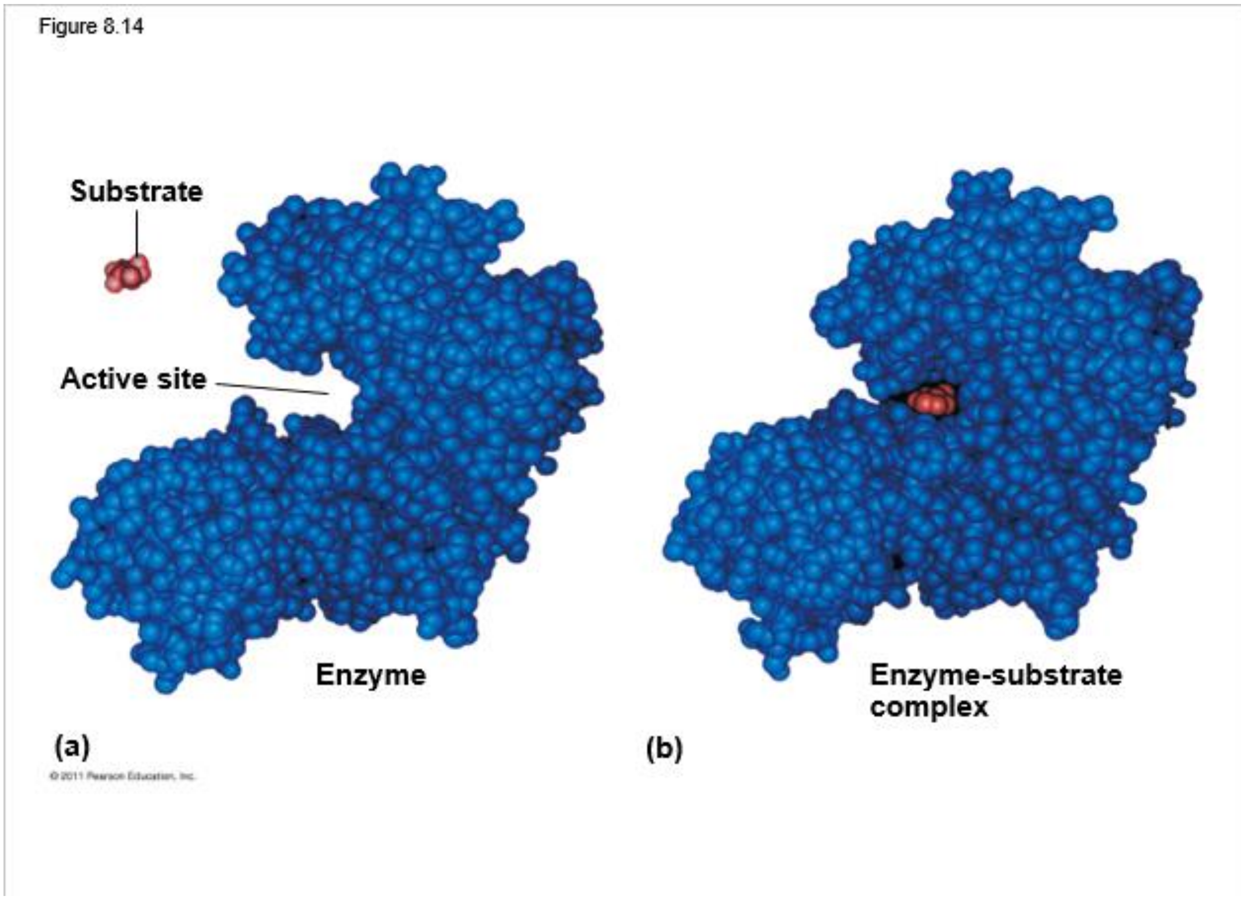
2) How enzymes lower the Ea barrier:

- Enzymes catalyze reactions by lowering the E_A barrier.
- Enzymes do not affect the change in free energy (ΔG); instead, they hasten reactions that would occur eventually.



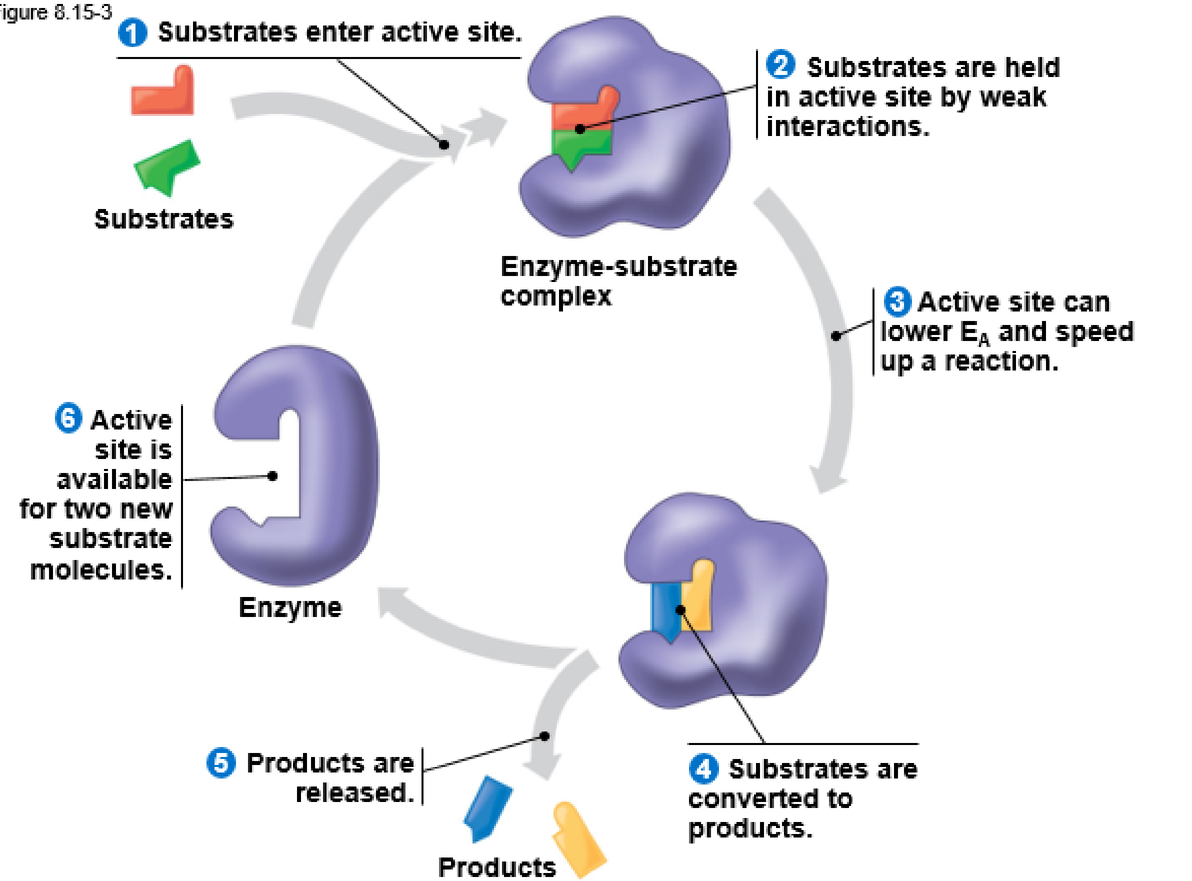
3) Substrate specificity of enzymes:

- **The reactant that an enzyme acts on is called the enzyme's substrate**
- **The enzyme binds to its substrate, forming an enzyme-substrate complex**
- **The active site is the region on the enzyme where the substrate binds**
- **Induced fit of a substrate brings chemical groups of the active site into positions that enhance their ability to catalyze the reaction**



4) Catalysis in the enzyme's activity site:
- In an enzymatic reaction, the substrate binds to the active site of the enzyme
- The active site can lower an E_A barrier by
    a. Orienting substrates correctly
    b. Straining substrate bonds
    c. Providing a favorable microenvironment
    d. Covalently bonding to the substrate

Figure 8.15-3



5) Effects of local conditions on enzyme activity:
   - An enzyme's activity can be affected by
   a. General environmental factors, such as temperature and pH
   b. Chemicals that specifically influence the enzyme
   c. Each enzyme has an optimal temperature in which it can function
   d. Each enzyme has an optimal pH in which it can function
   e. Optimal conditions favor the most active shape for the enzyme molecule

Figure 8.16

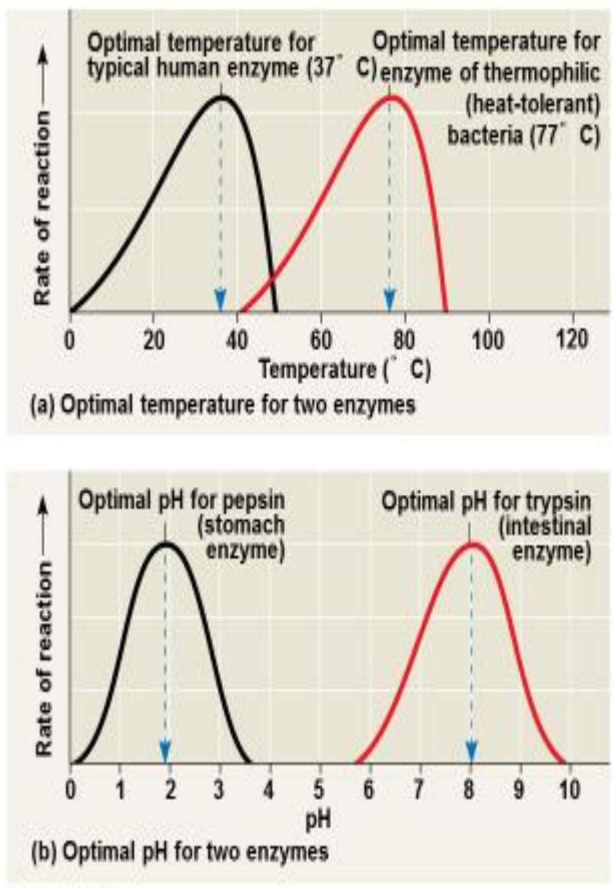


Figure 8.16a

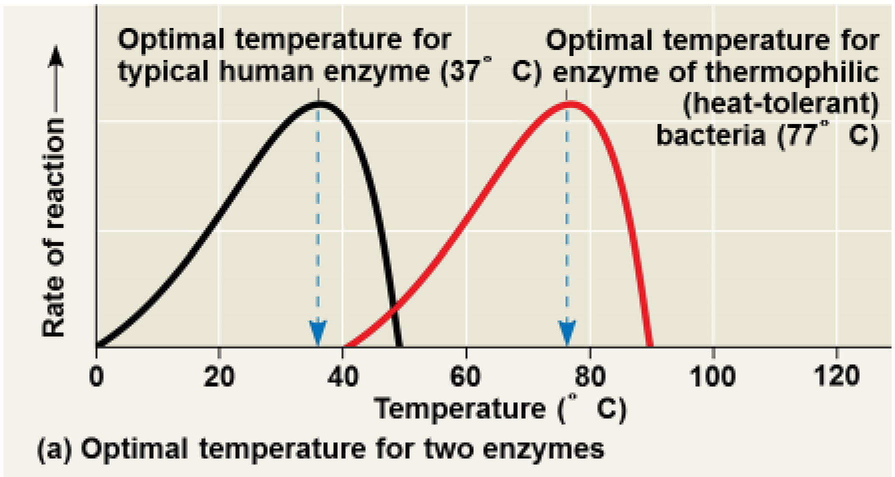
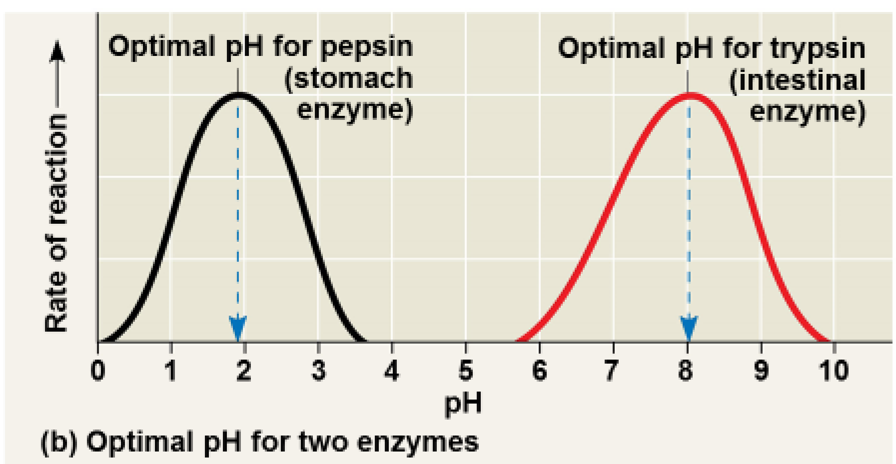


Figure 8.16b



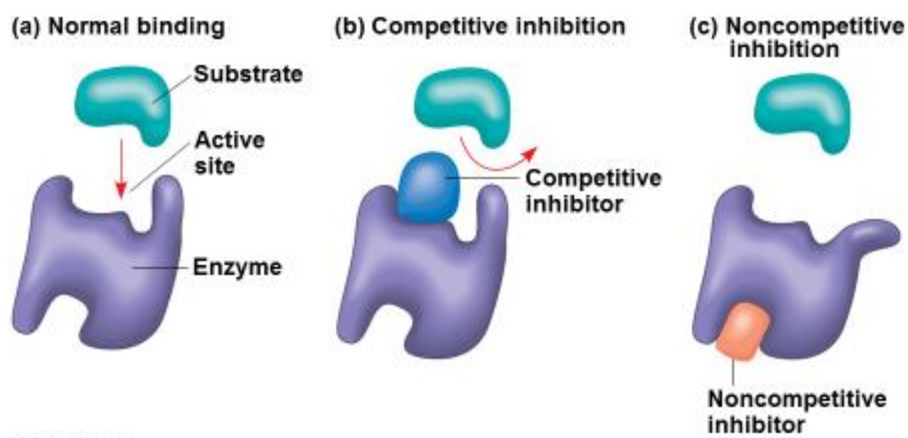
6) Cofactors:

- **Cofactors** are non-protein enzyme helpers
- Cofactors may be inorganic (such as a metal in ionic form) or organic
- An organic cofactor is called a **coenzyme**
- Coenzymes include vitamins

7) Enzymes inhibitors:

- **Competitive inhibitors** bind to the active site of an enzyme, competing with the substrate
- **Noncompetitive inhibitors** bind to another part of an enzyme, causing the enzyme to change shape and making the active site less effective
- Examples of inhibitors include toxins, poisons, pesticides, and antibiotics

Figure 8.17



Concept check 8.4: p.203

1) **Spontaneous reaction is a reaction that is exergonic. However, if it has a high activation energy that is rarely attained, the rate of reaction may be low.**
2) **Only the specific substrates will fit probably in to the active site of an enzyme, the part of the enzyme that carries out catalysis.**
3) **In the presence of malonate, increase the concentration of the normal substrate (succinate) and see whether the rate of reaction increase. If it does, malonate is competitive inhibitor.**
4) **If lactose wasn't present in the environment as a source of food and the fucose-containing disaccharide was available. Bacteria that could digest the latter would be better able to grow and multiply than those that could not.**

- **Concept 8.5: regulation of enzyme activity helps control metabolism:**

- Chemical chaos would result if a cell's metabolic pathways were not tightly regulated
- A cell does this by switching on or off the genes that encode specific enzymes or by regulating the activity of enzymes

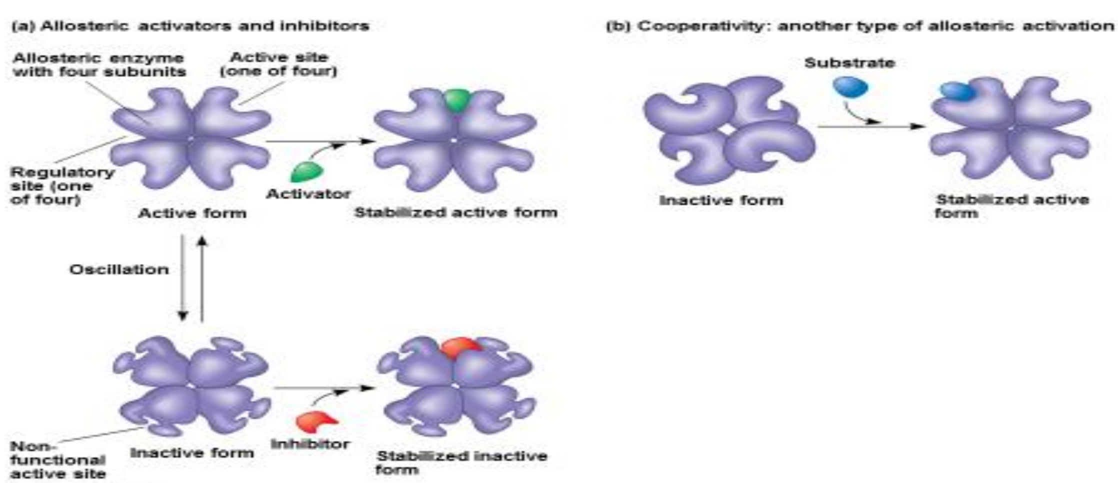
1) Allosteric regulation of enzymes:

- **Allosteric regulation may either inhibit or stimulate an enzyme's activity**
- **Allosteric regulation occurs when a regulatory molecule binds to a protein at one site and affects the protein's function at another site**

2) Allosteric inhibition and activation:

- **Most allosterically regulated enzymes are made from polypeptide subunits**
- **Each enzyme 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**

Figure 8.19

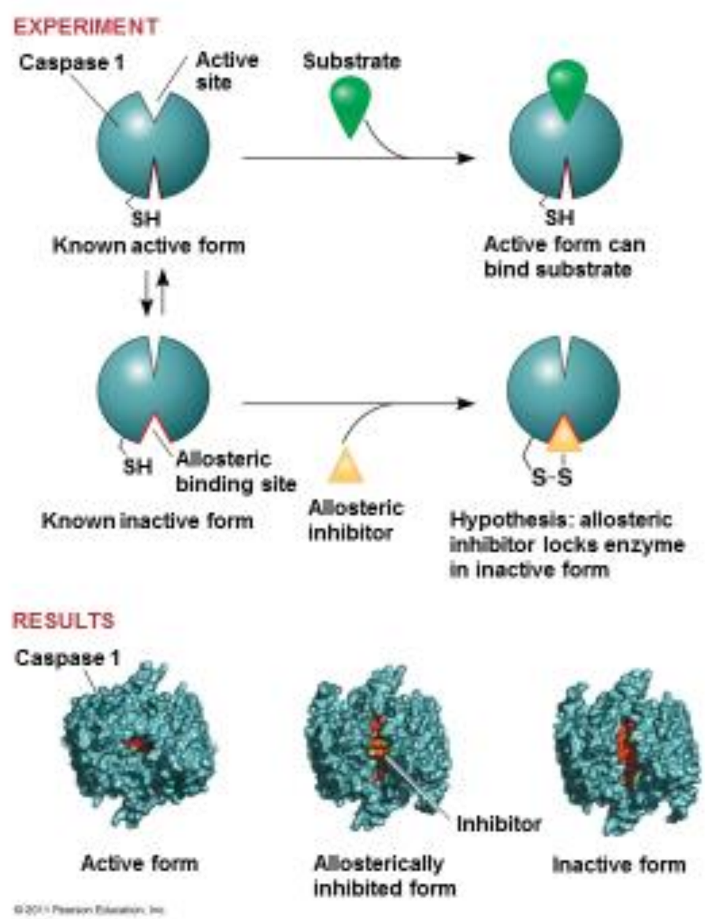


- **Cooperativity is a form of allosteric regulation that can amplify enzyme activity**
- **One substrate molecule primes an enzyme to act on additional substrate molecules more readily**
- **Cooperativity is allosteric because binding by a substrate to one active site affects catalysis in a different active site**

3) Identification of allosteric regulators:

- Allosteric regulators are attractive drug candidates for enzyme regulation because of their specificity
- Inhibition of proteolytic enzymes called *caspases* may help management of inappropriate inflammatory responses

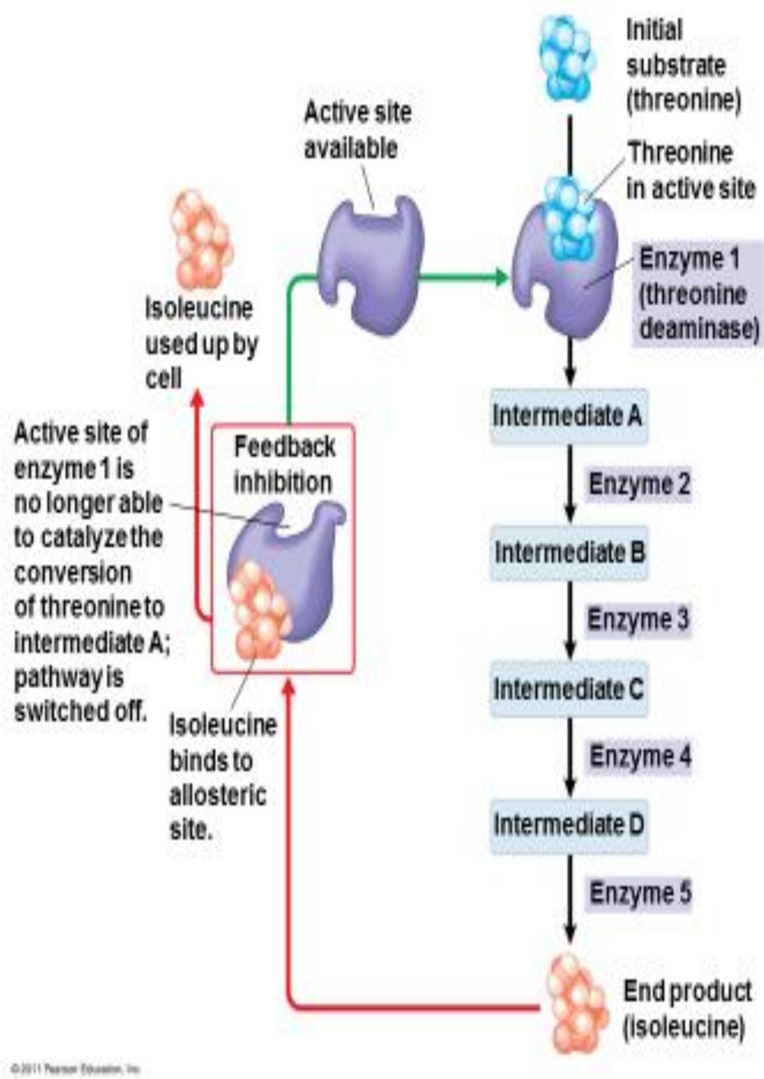
Figure 8.20



4) **Feedback inhibition:**

- **In feedback inhibition, the end product of a metabolic pathway shuts down the pathway**
- **Feedback inhibition prevents a cell from wasting chemical resources by synthesizing more product than is needed**

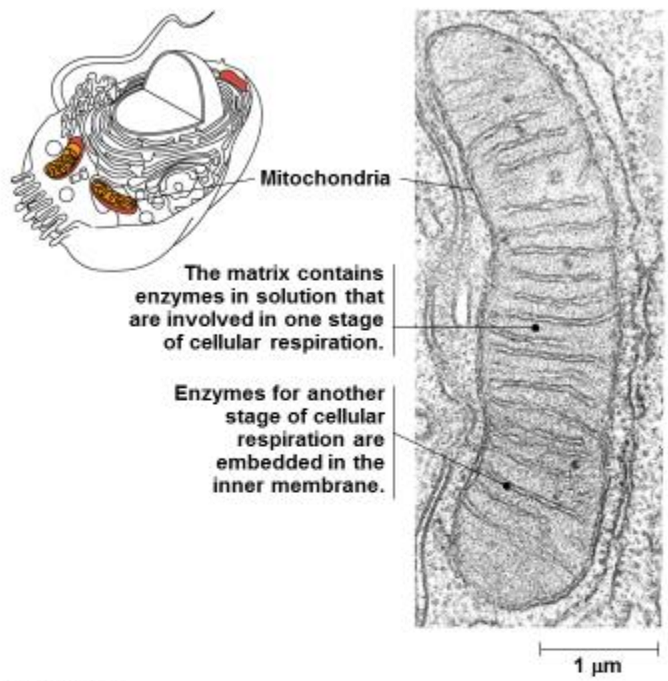
Figure 8.21



5) Specific localization of enzymes within the cell:

- **Structures within the cell help bring order to metabolic pathways**
- **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**

Figure 8.22



The end ☺

You can go to p.207-p.208 in the book and check the summary for each concept.