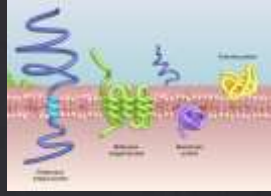
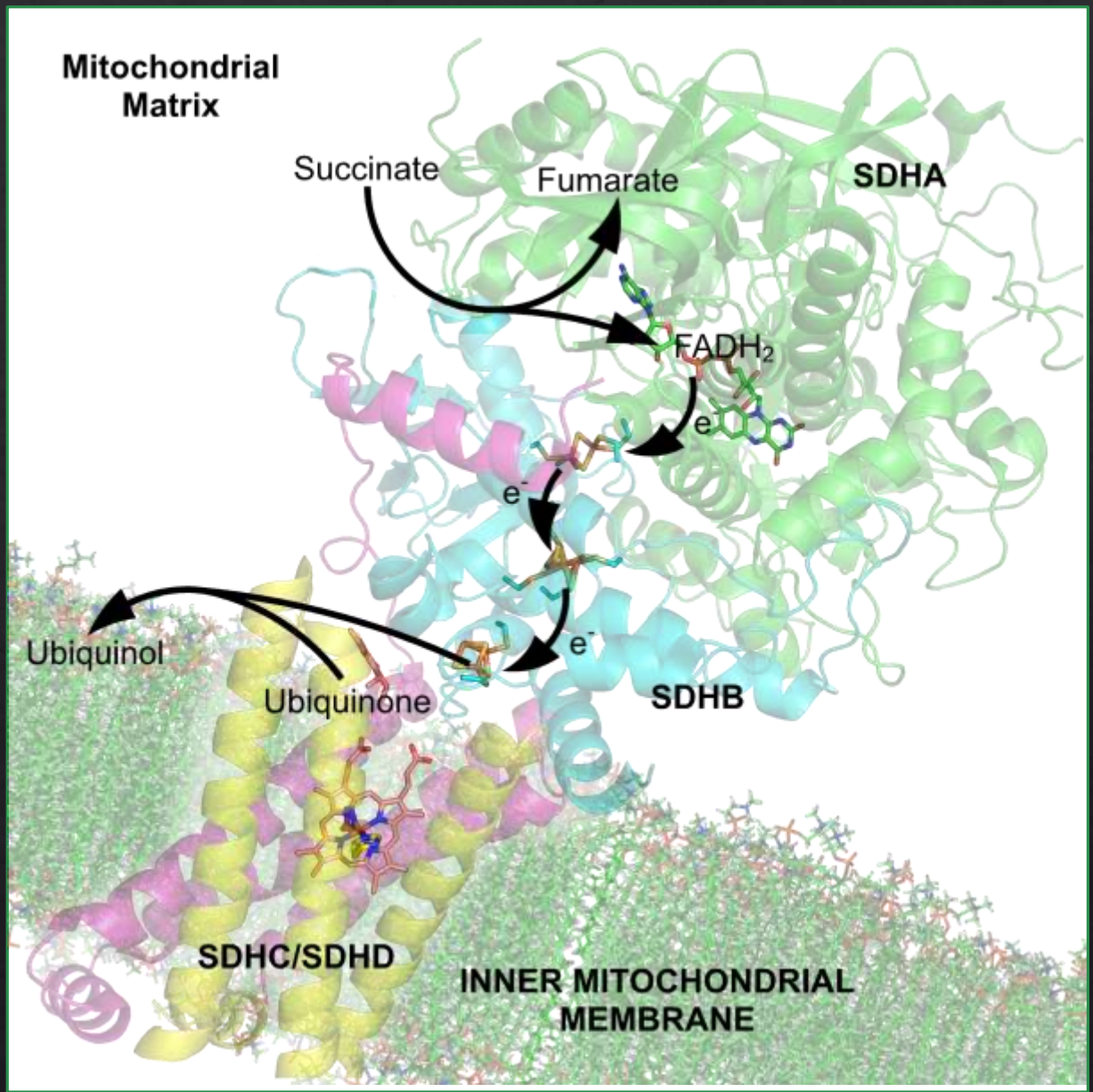
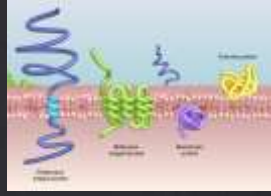
Protein function





Picture by Zephyris

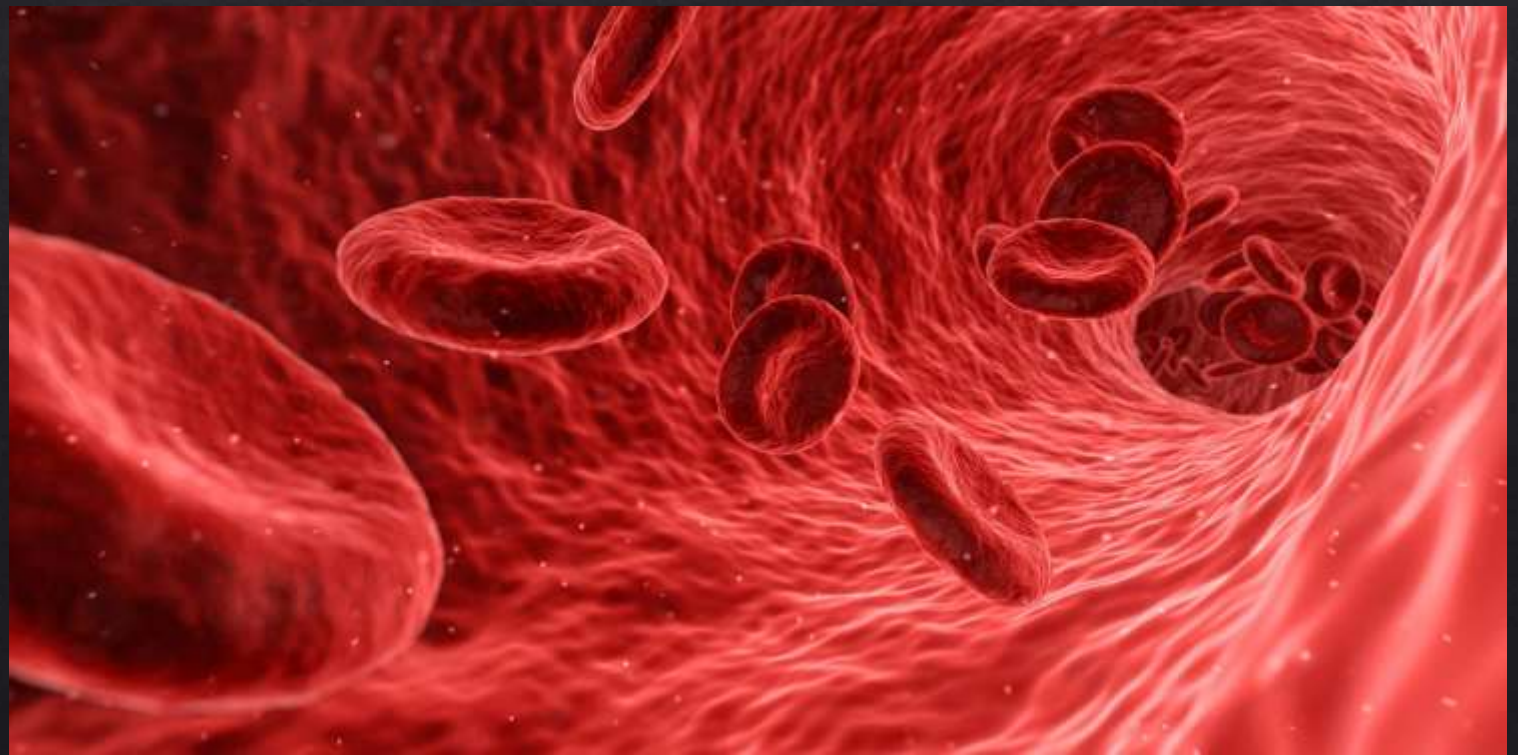


Protein function

Reversible binding ligand – binding site

Changes in conformation

Interaction might be regulated by other ligands or proteins

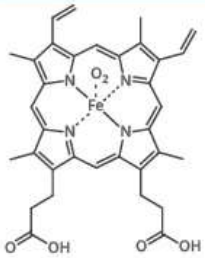


THE CHEMISTRY OF THE DIFFERENT COLOURS OF BLOOD

Red

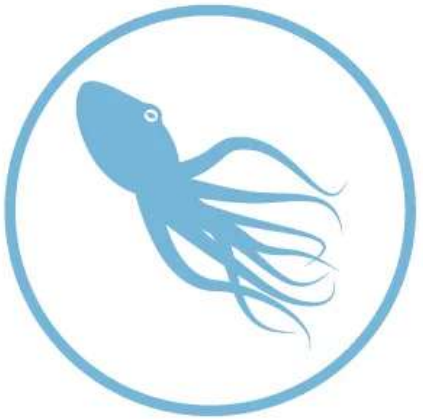
HUMANS AND THE MAJORITY OF OTHER VERTEBRATES

HAEMOGLOBIN



HAEM B
(oxygenated form)

Haemoglobin is a protein found in blood, built up from subunits containing 'haems'. These haems contain iron, and their structure gives blood its red colour when oxygenated. Deoxygenated blood is a deep red colour - not blue!



Blue

SPIDERS, CRUSTACEANS, SOME MOLLUSCS, OCTOPUSES & SQUID

HAEMOCYANIN

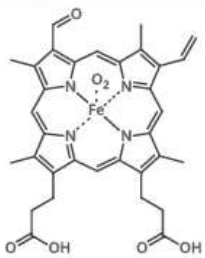
HAEMOCYANIN
(oxygenated form; R = histidine residues)

Unlike haemoglobin, which is bound to red blood cells, haemocyanin floats free in the blood. Haemocyanin contains copper instead of iron. When deoxygenated, the blood is colourless, but when oxygenated, it gives a blue colouration.

Green

SOME SEGMENTED WORMS, SOME LEECHES, & SOME MARINE WORMS

CHLOROCRUORIN



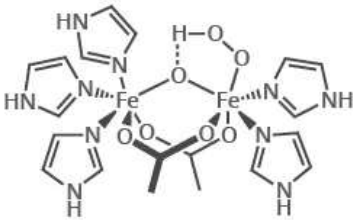
CHLOROCRUORIN
(oxygenated form)

Chemically similar to haemoglobin; the blood of some species contains both haemoglobin & chlorocruorin. Light green when deoxygenated, it is green when oxygenated, although when more concentrated it appears light red.

Violet

MARINE WORMS INCLUDING PEANUT WORMS, PENIS WORMS & BRACHIOPODS

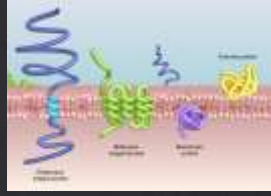
HAEMERYTHRIN



HAEMERYTHRIN
(oxygenated form)

Haemerythrin is only 1/4 as efficient at oxygen transport when compared to haemoglobin. In the deoxygenated state, haemerythtin is colourless, but it imparts a violet-pink colour when oxygenated.

The Heme group



Picture from Nelson&Cox

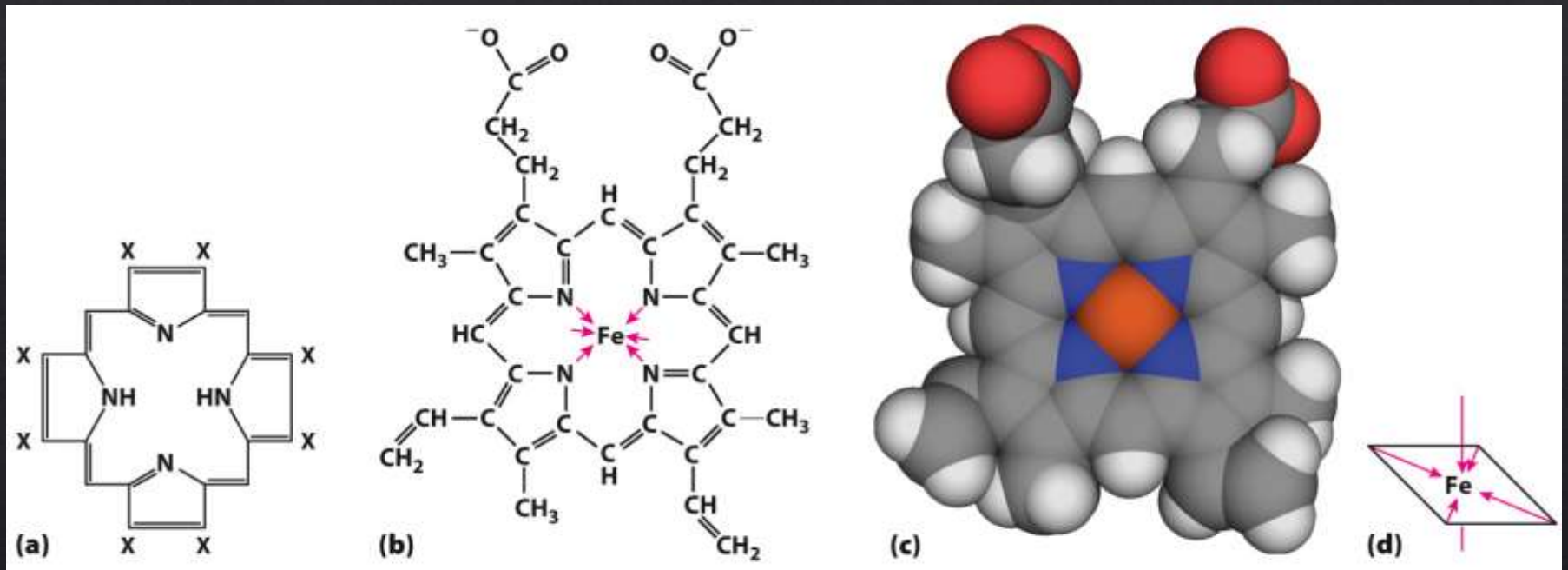
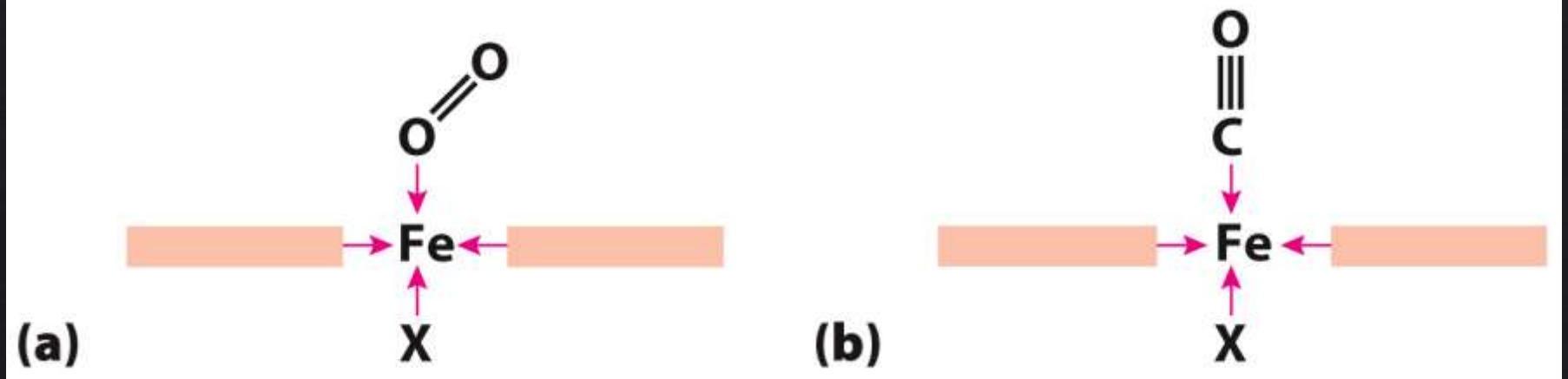
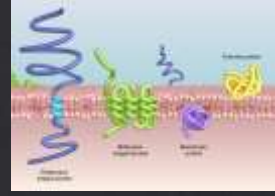


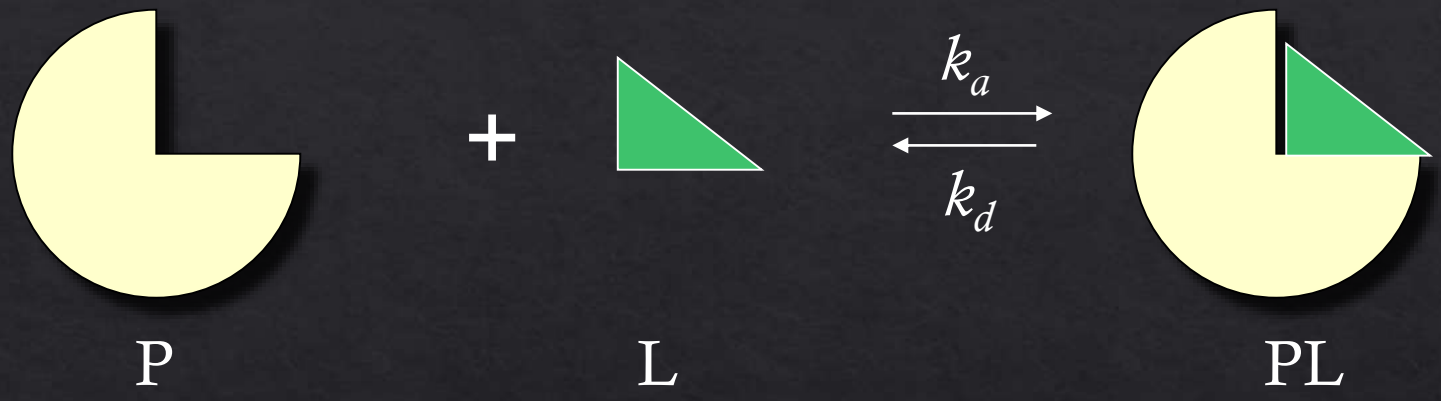
Figure 5-1



Reversible binding

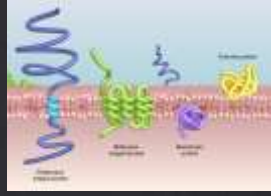


$$A + B \leftrightarrow AB$$



$$k_a[P][L] = k_d[PL]$$

Reversible binding



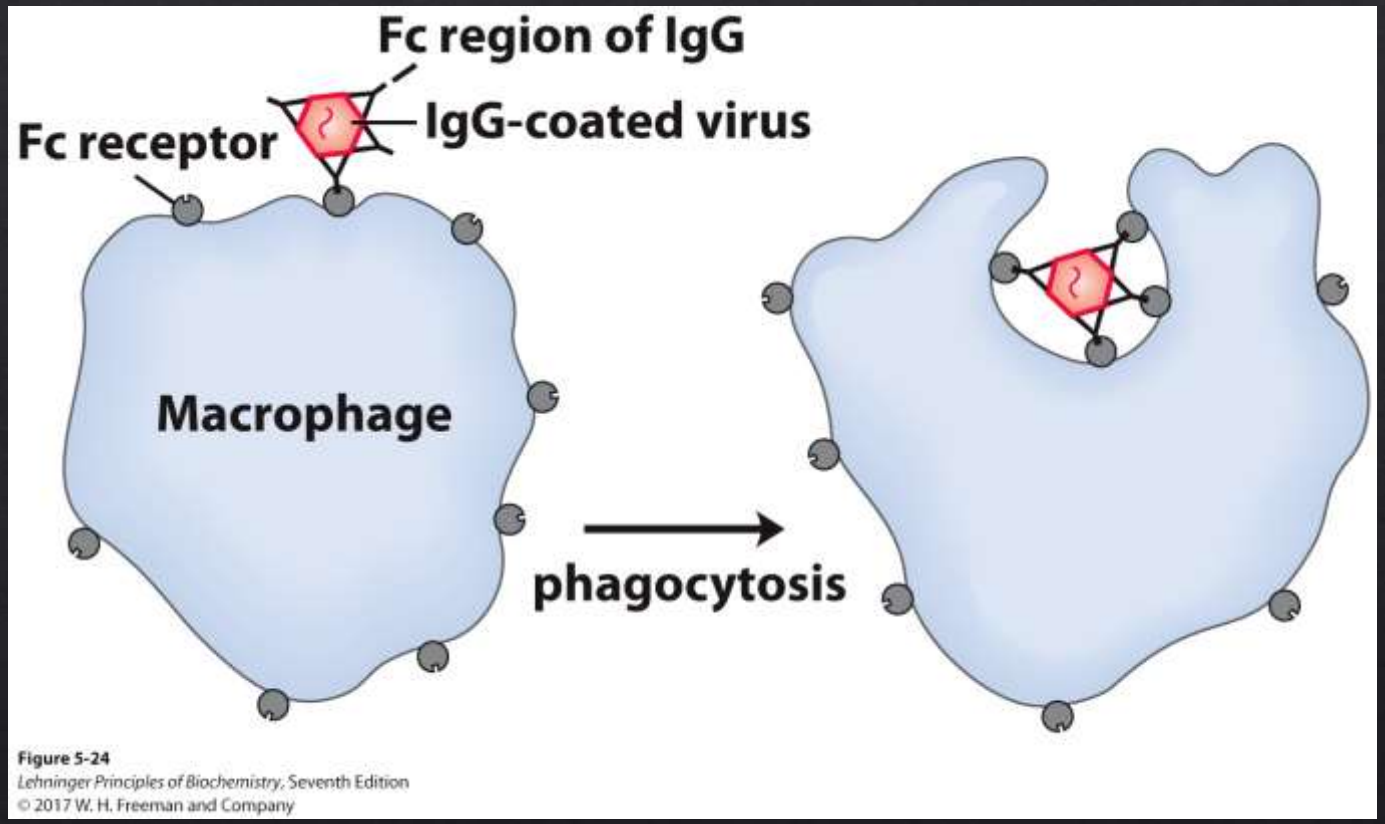


Figure 5-24
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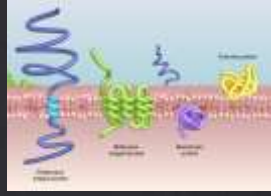
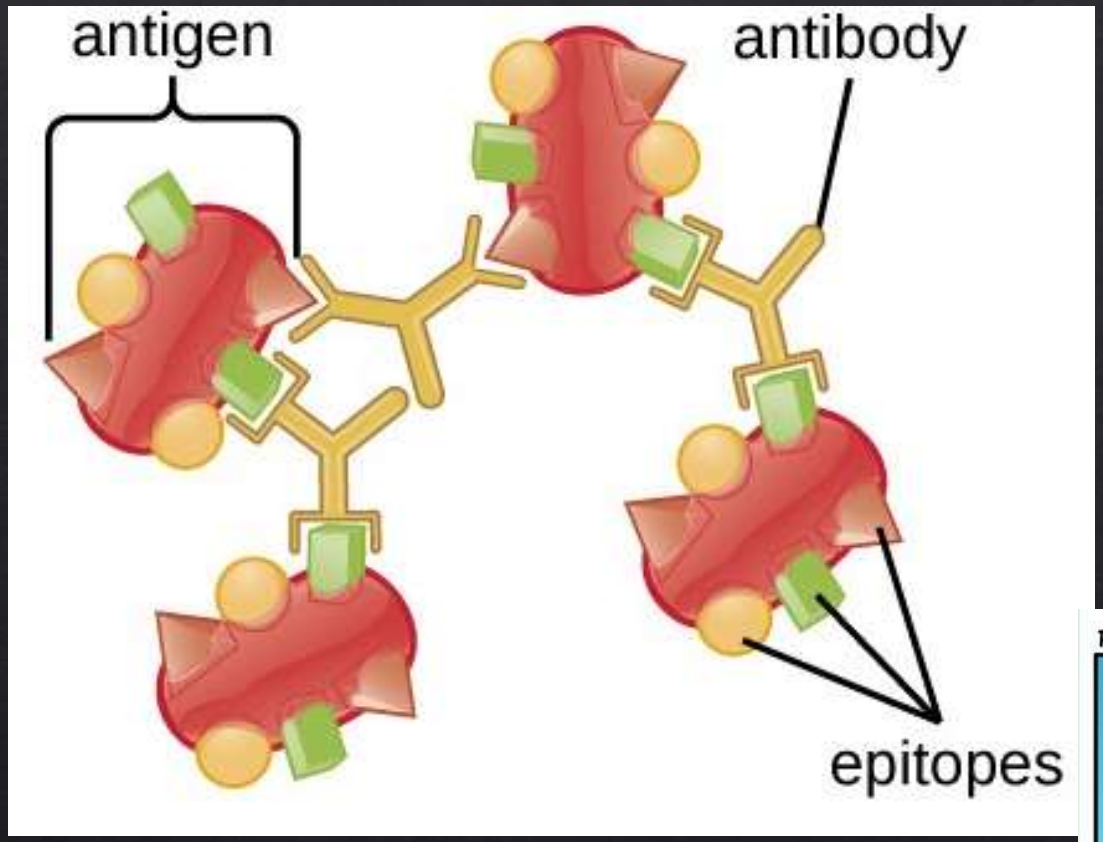
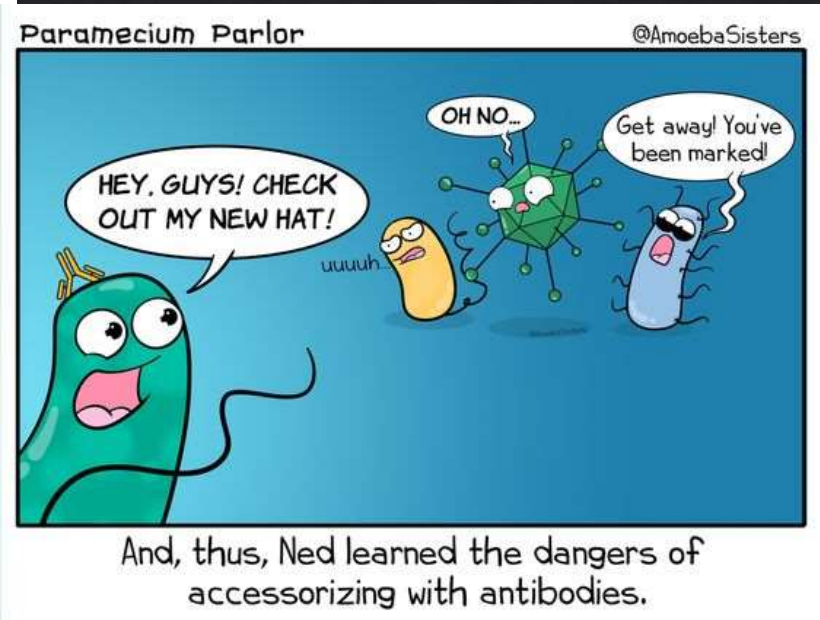
Reversible binding

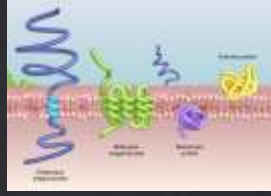


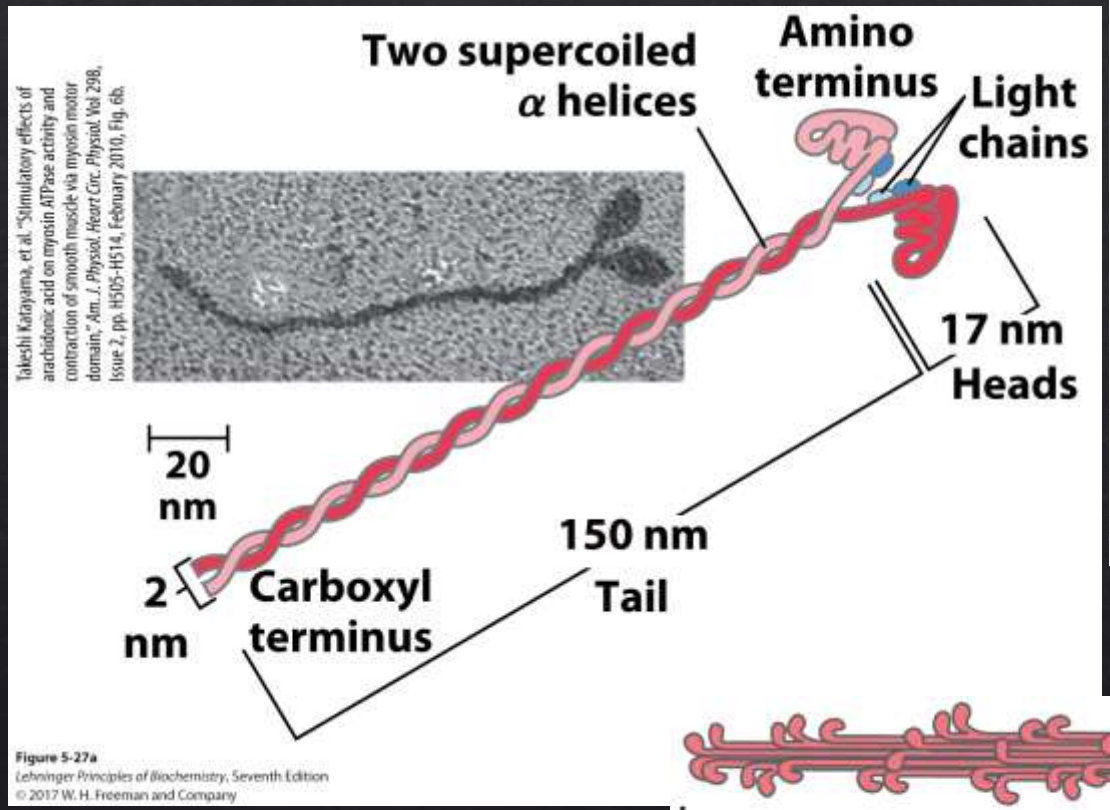


Picture from Lumen



Reversible binding





Takeshi Katayama, et al. "Stimulatory effects of arachidonic acid on myosin ATPase activity and contraction of smooth muscle via myosin motor domain," *Am. J. Physiol. Heart Circ. Physiol.* Vol 298, Issue 2, pp. H505-H514, February 2010, Fig. 6b.

Figure 5-27a
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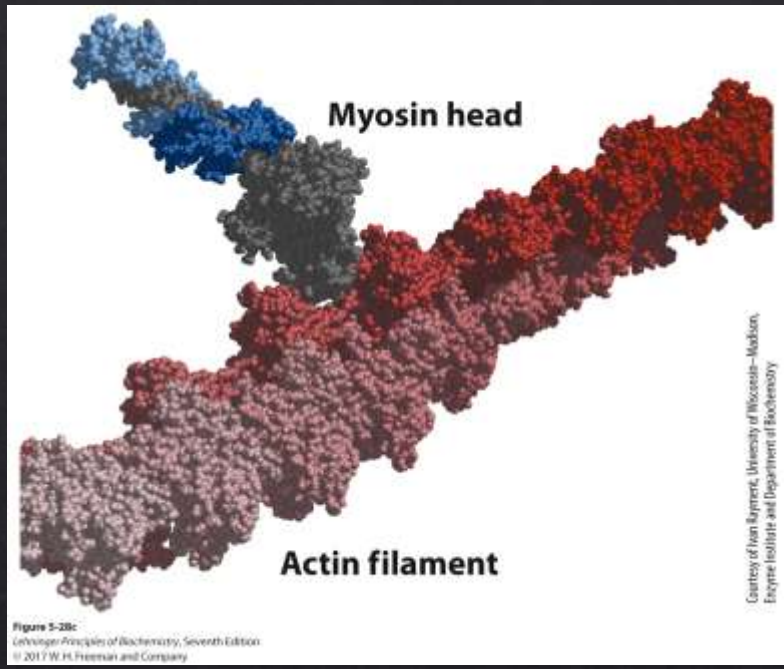

Courtesy of Ivan Rayment, University of Wisconsin–Madison, Enzyme Institute and Department of Biochemistry

Figure 5-28c
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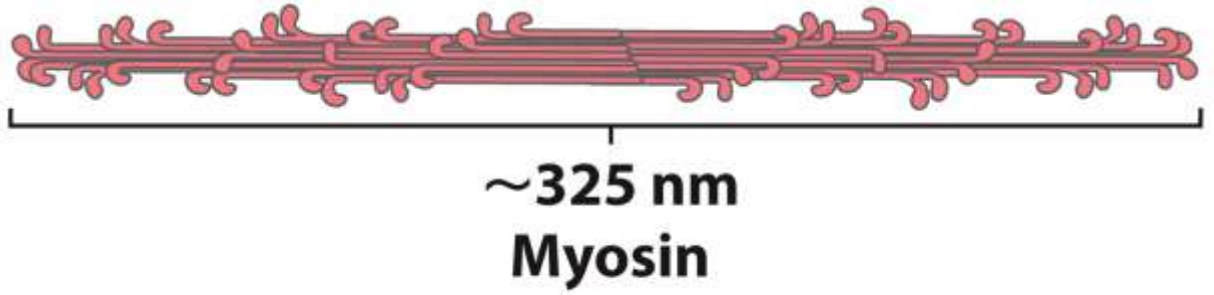

Figure 5-28a
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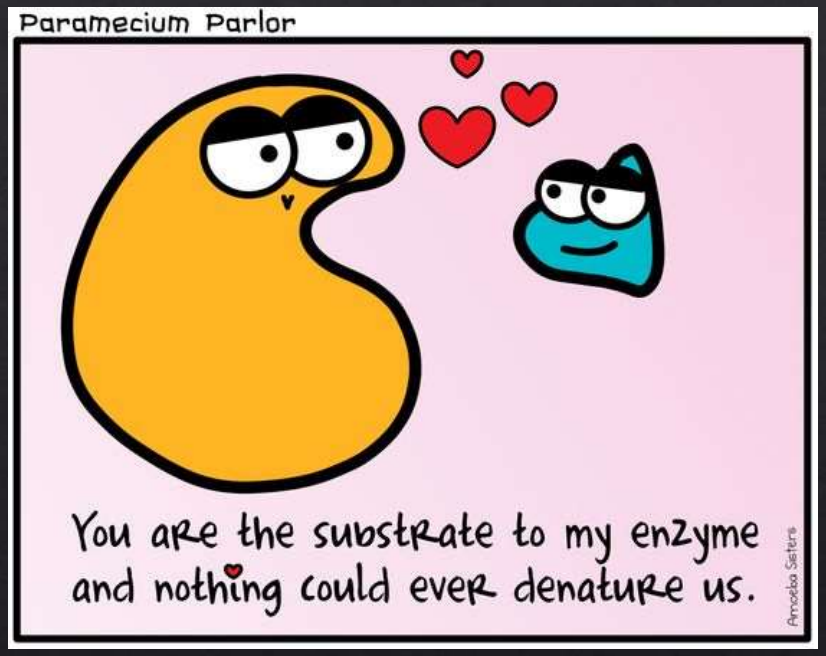
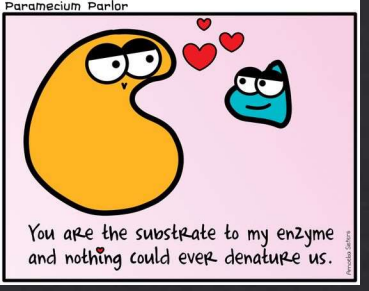
Enzymes

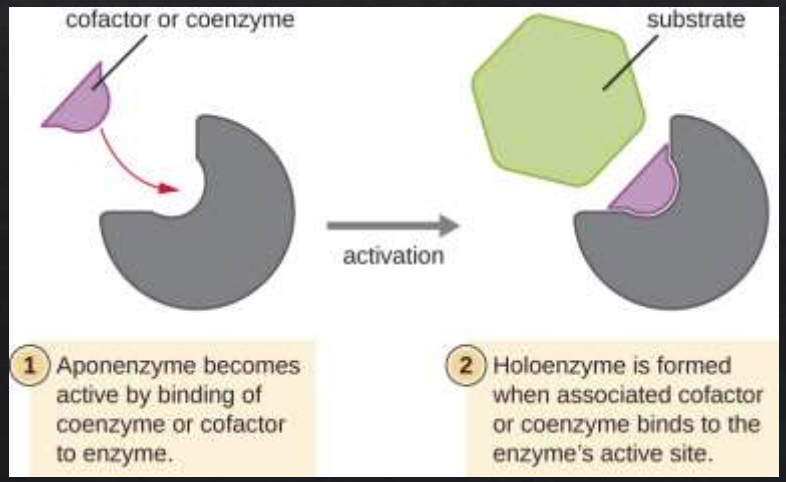
- Enzymes are catalysts.
  - increase reaction rates without being used up
- Most enzymes are globular proteins.
  - However, some RNA (ribozymes and ribosomal RNA) also catalyze reactions.
- The study of enzymatic processes is the oldest field of biochemistry, dating back to late 1700s.



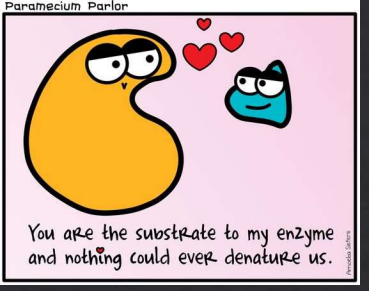


Enzymes

- Enzymes activity is connected to its composition and structure.
- Some enzymes require a:
  - Cofactor – one or more inorganic ions
  - Coenzyme – a complex organic or metalloorganic molecule



Picture from Libretext



Enzymes - names

TABLE 6-3 International Classification of Enzymes

Class no.	Class name	Type of reaction catalyzed
1	Oxidoreductases	Transfer of electrons (hydride ions or H atoms)
2	Transferases	Group transfer reactions
3	Hydrolases	Hydrolysis reactions (transfer of functional groups to water)
4	Lyases	Cleavage of C—C, C—O, C—N, or other bonds by elimination, leaving double bonds or rings, or addition of groups to double bonds
5	Isomerases	Transfer of groups within molecules to yield isomeric forms
6	Ligases	Formation of C—C, C—S, C—O, and C—N bonds by condensation reactions coupled to cleavage of ATP or similar cofactor

Table 6-3
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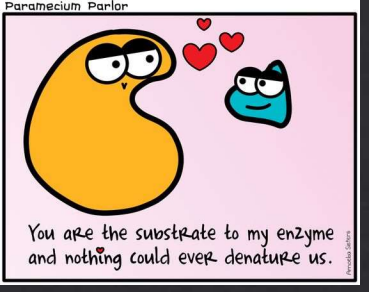
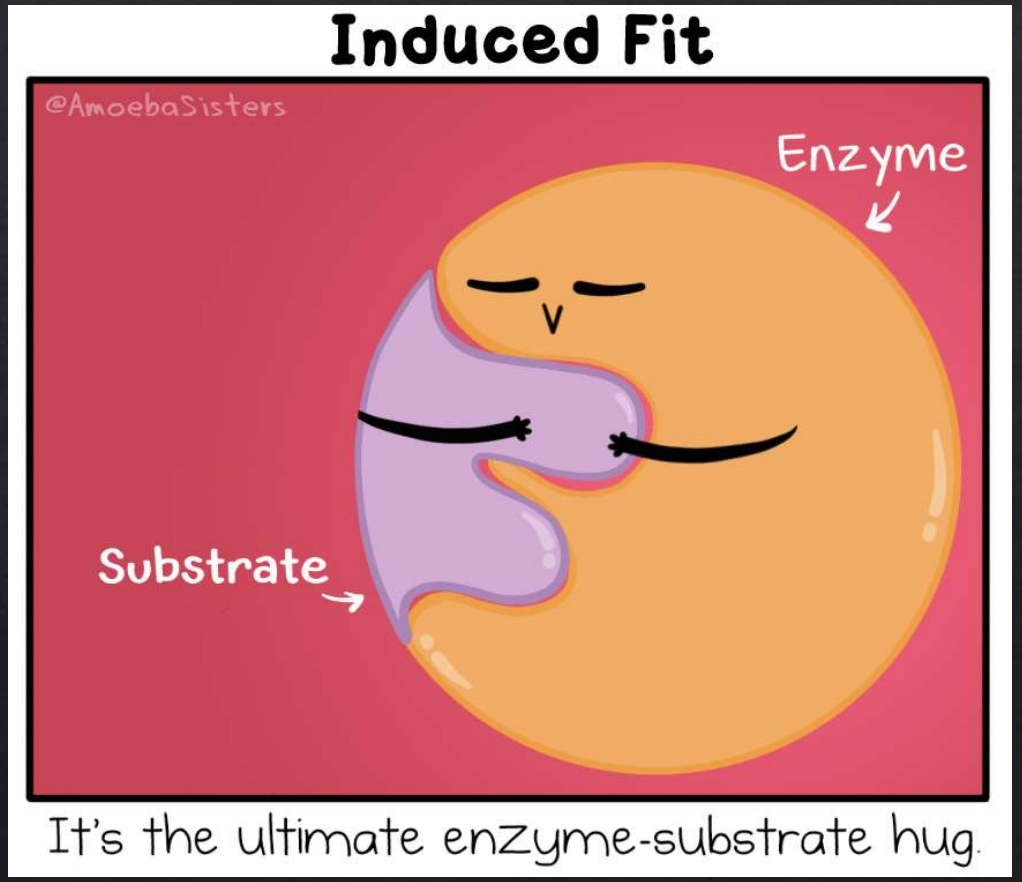
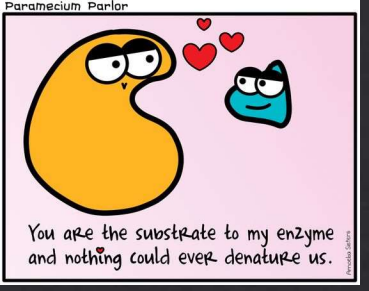
ATP + D-glucose → ADP + D-glucose 6-phosphate
ATP:D-hexose 6-phosphotransferase (2.7.1.1)



Enzymes – How they work

Enzymes provide a specific environment more favourable to the reaction that takes place within the active site thanks to the R groups present.





Enzymes – How they work

Enzymes decrease the activation energy though the creation of covalent and noncovalent bonds between the substrate and the binding site

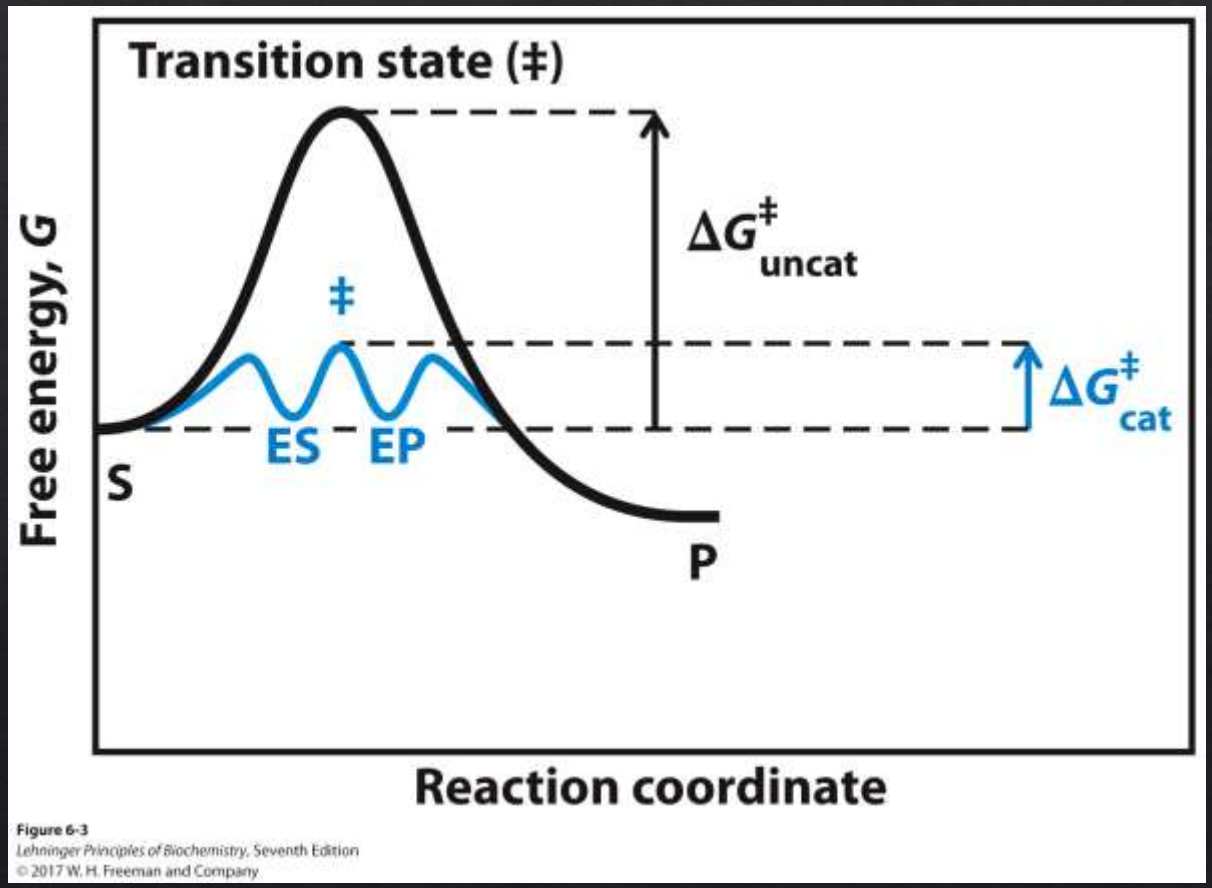


Figure 6-3
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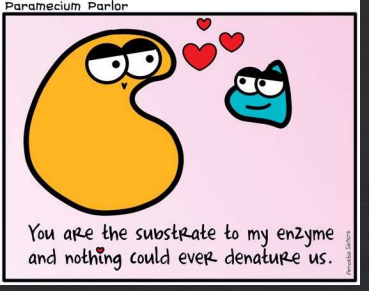

Enzymes – How they work

- Much of the energy required to lower the activation energy is derived from noncovalent bonds (binding energy).

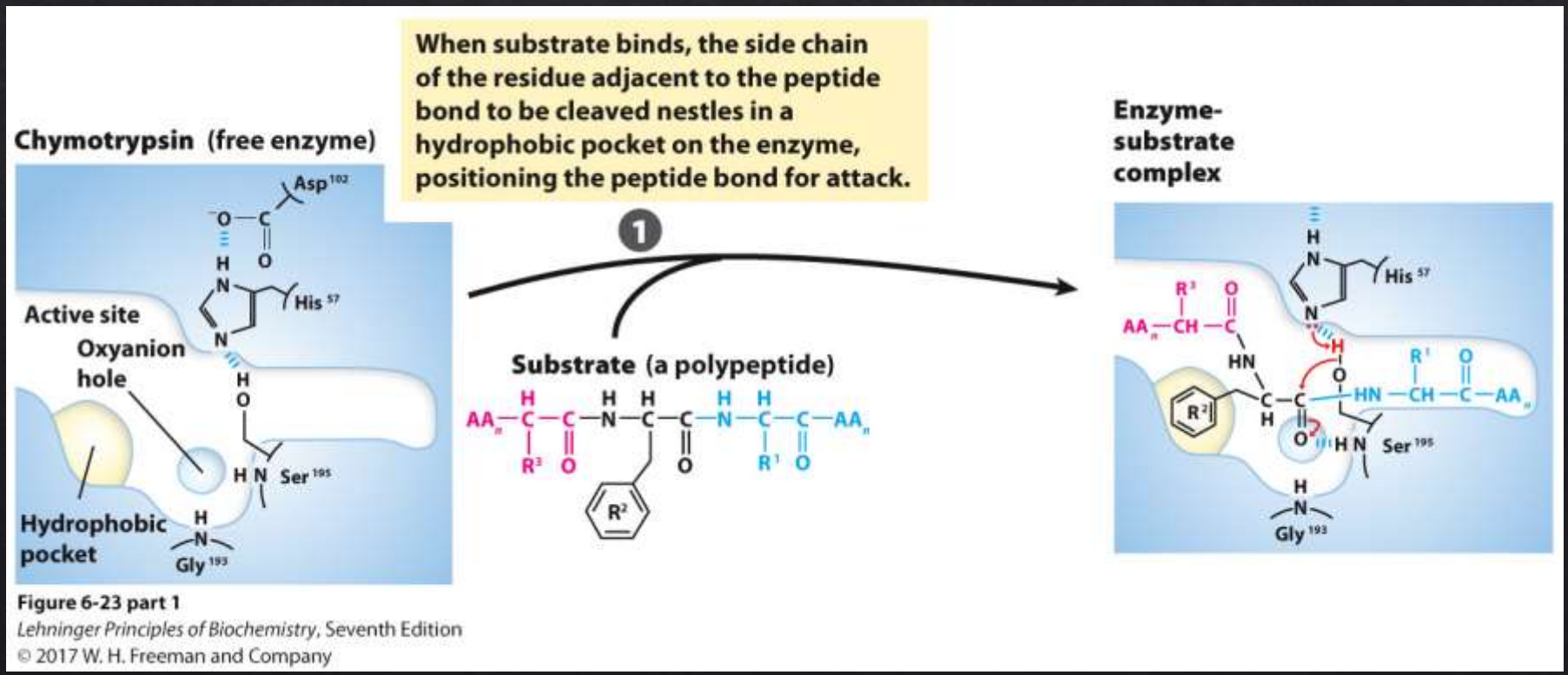

Figure 6-23 part 1
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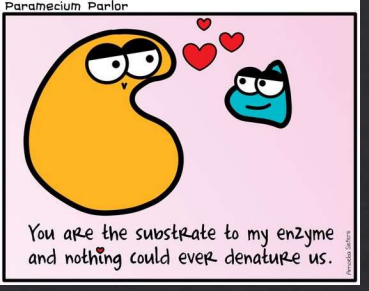

Enzymes – How they work

- Weak interactions are optimised in the transition state.

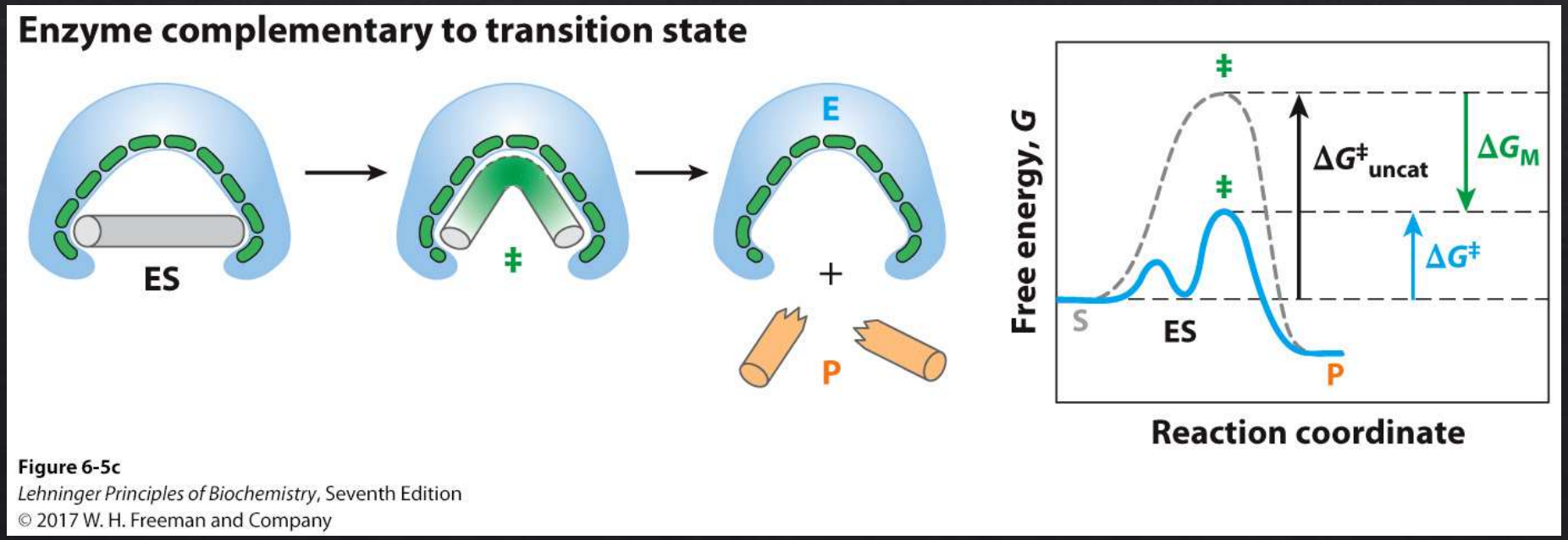

Figure 6-5c
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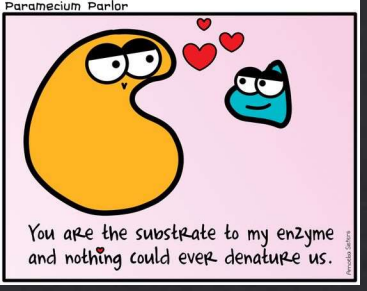
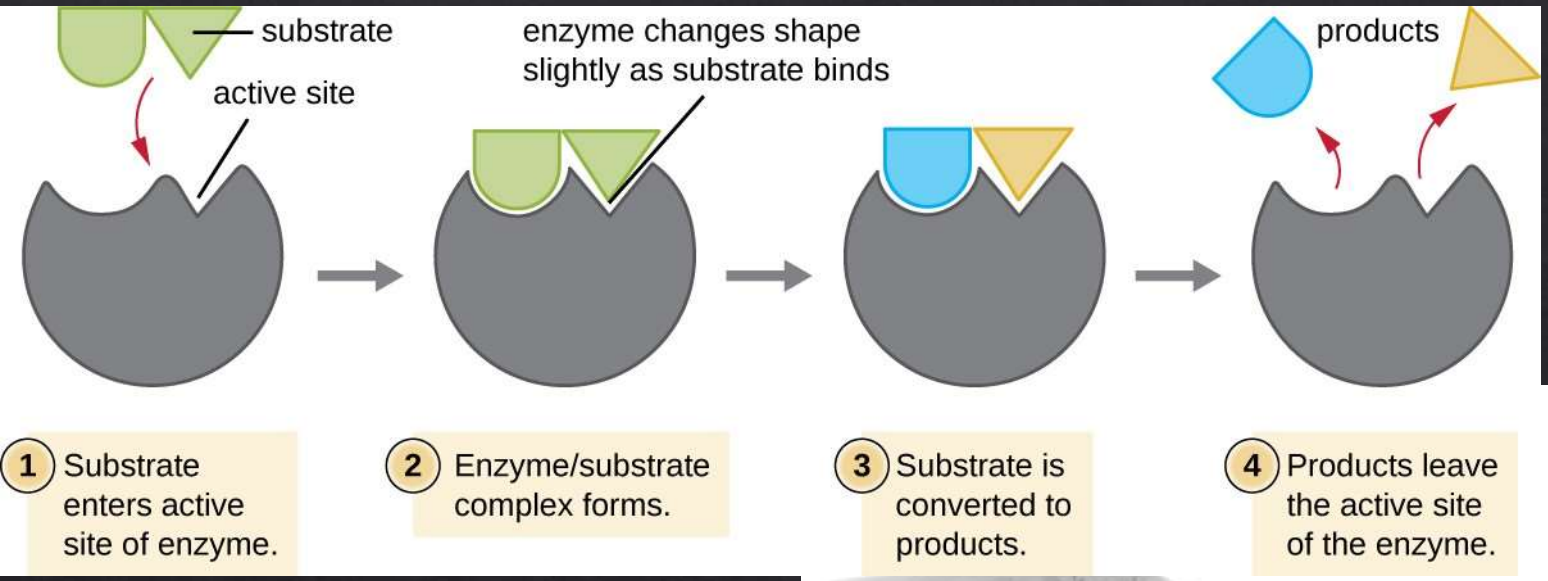
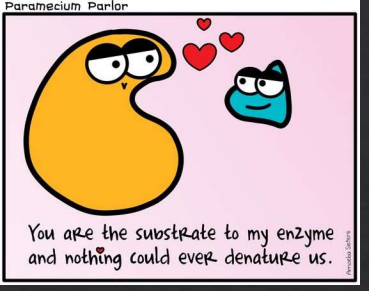


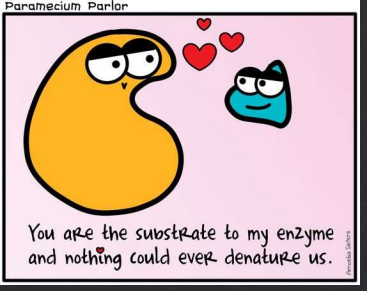
Enzymes – How they work



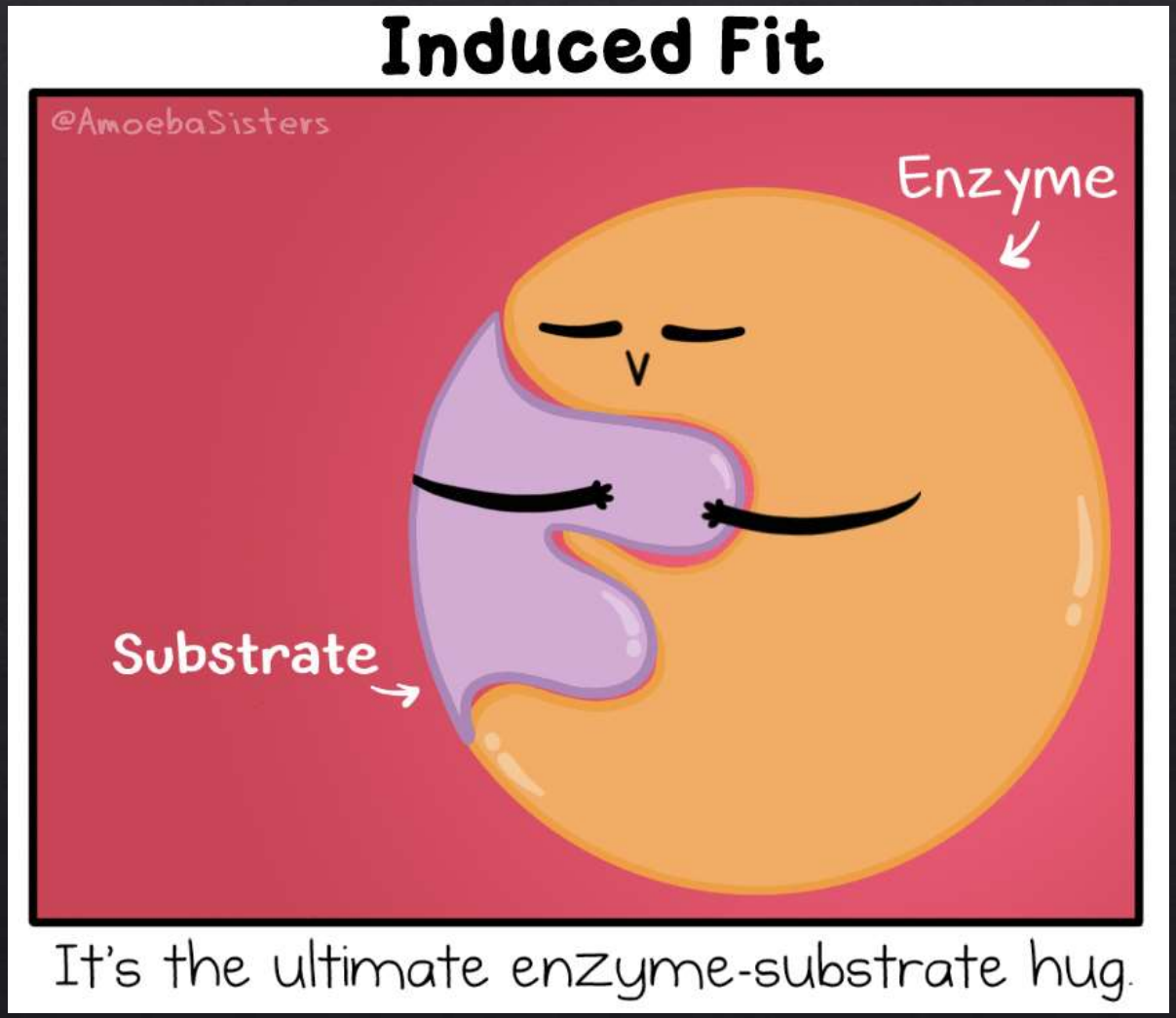
Picture from Libretext

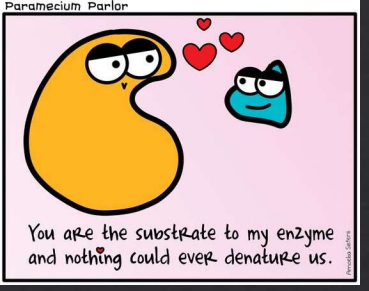


Enzymes – How they work



Enzymes – How they work

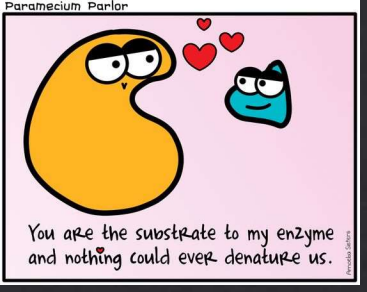




Catalytic mechanisms

Enzymes may use one or a combination of the following:

- acid-base catalysis: give and take protons
- covalent catalysis: change reaction paths
- metal ion catalysis: use redox cofactors, pK_a shifters



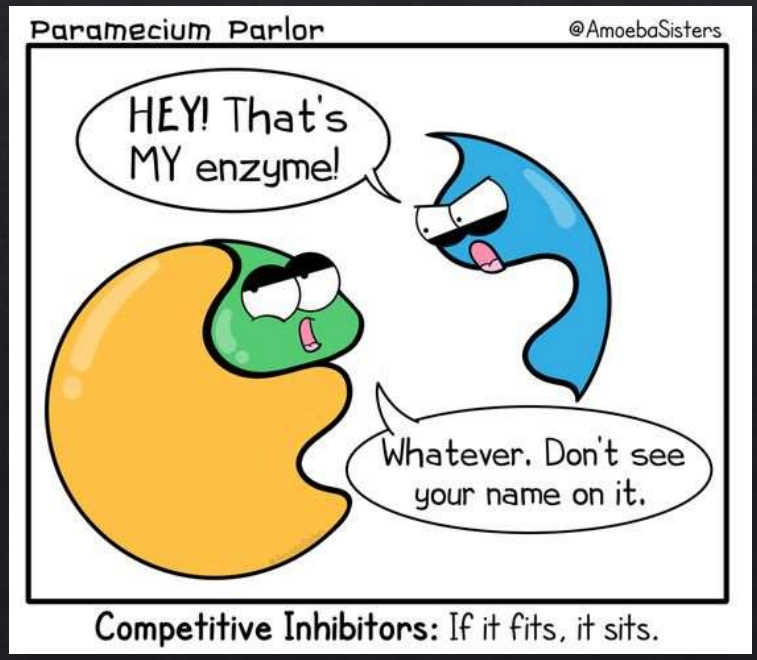
Enzymes regulation

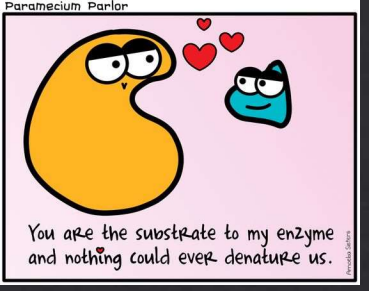
Metabolic pathways are regulated by regulatory enzymes that increase/decrease in response to signals.

- Allosteric enzymes: reversible, noncovalent binding of allosteric modulators/effectors
- Covalent modifications

Two other mechanisms:

- Binding with regulatory proteins
- Proteolitic cleavage of segments (irreversible!)

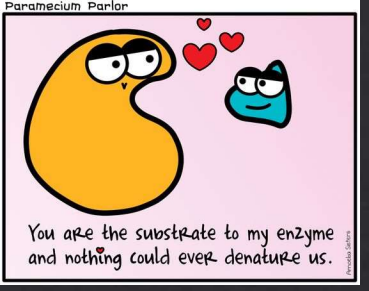




Enzymes regulation - Inhibitors

Inhibitors are compounds that decrease an enzyme's activity.

- Irreversible inhibitors (inactivators) react with the enzyme.
  - One inhibitor molecule can permanently shut off one enzyme molecule.
  - They are often powerful toxins but also may be used as drugs.
- Reversible inhibitors bind to and can dissociate from the enzyme.
  - They are often structural analogs of substrates or products.
  - They are often used as drugs to slow down a specific enzyme.
- Reversible inhibitor can bind to:
  - the free enzyme and prevent the binding of the substrate.
  - the enzyme-substrate complex and prevent the reaction.



Enzymes regulation – Allosteric enzymes

Allosteric regulation is connected to conformation changes induced by a modulator. It can be inhibitory or stimulatory. If the modulator is the substrate the enzyme is called homotropic, if different, it's called heterotropic.

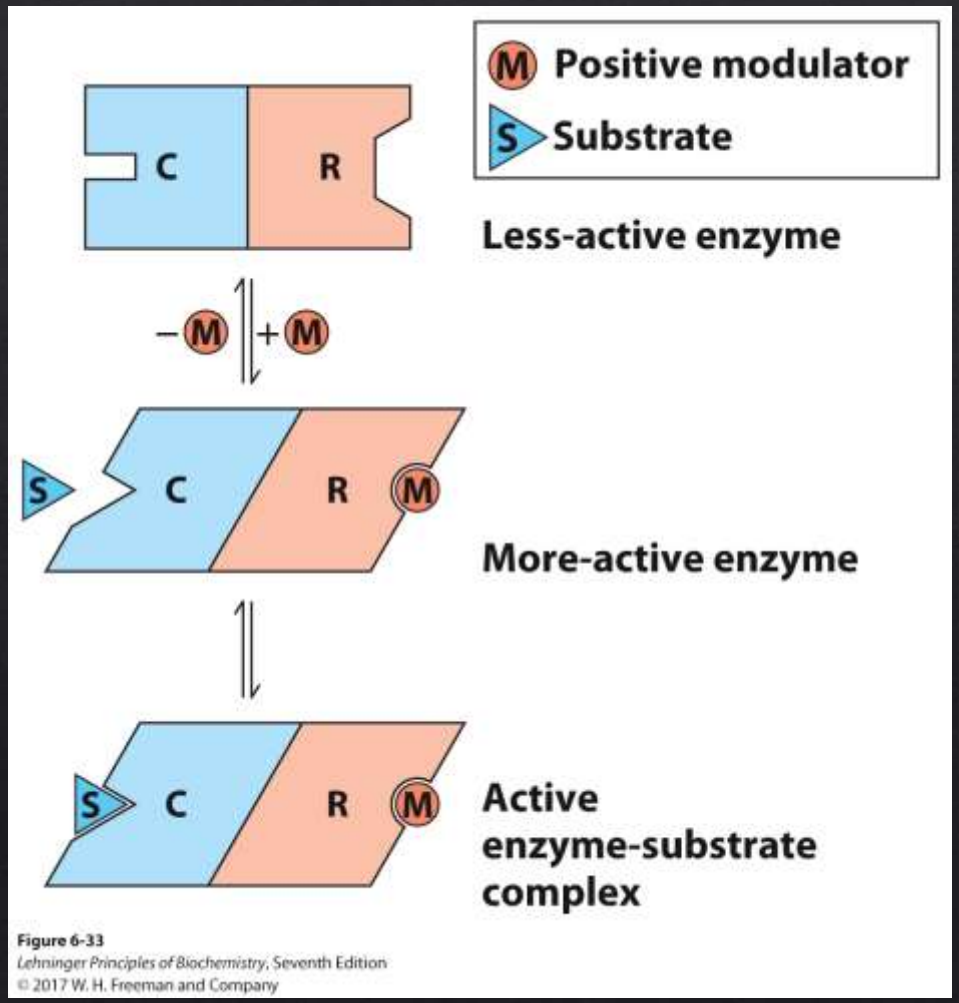


Figure 6-33
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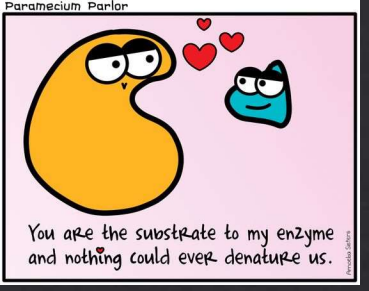
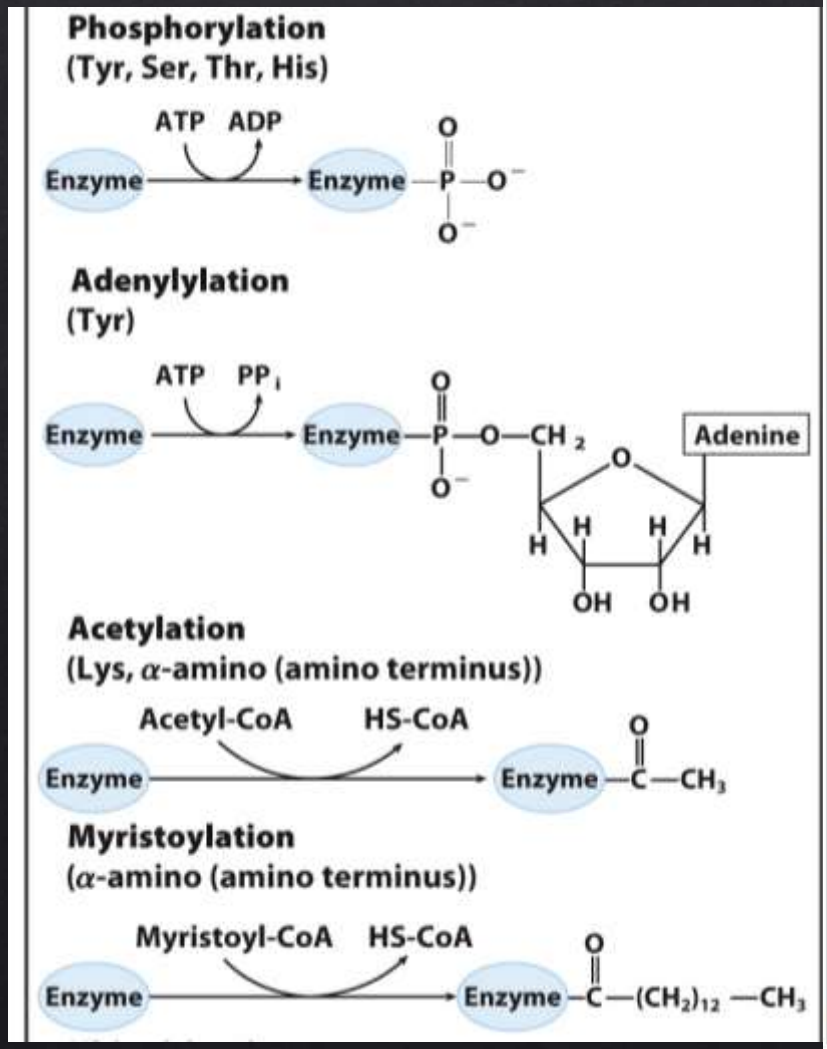
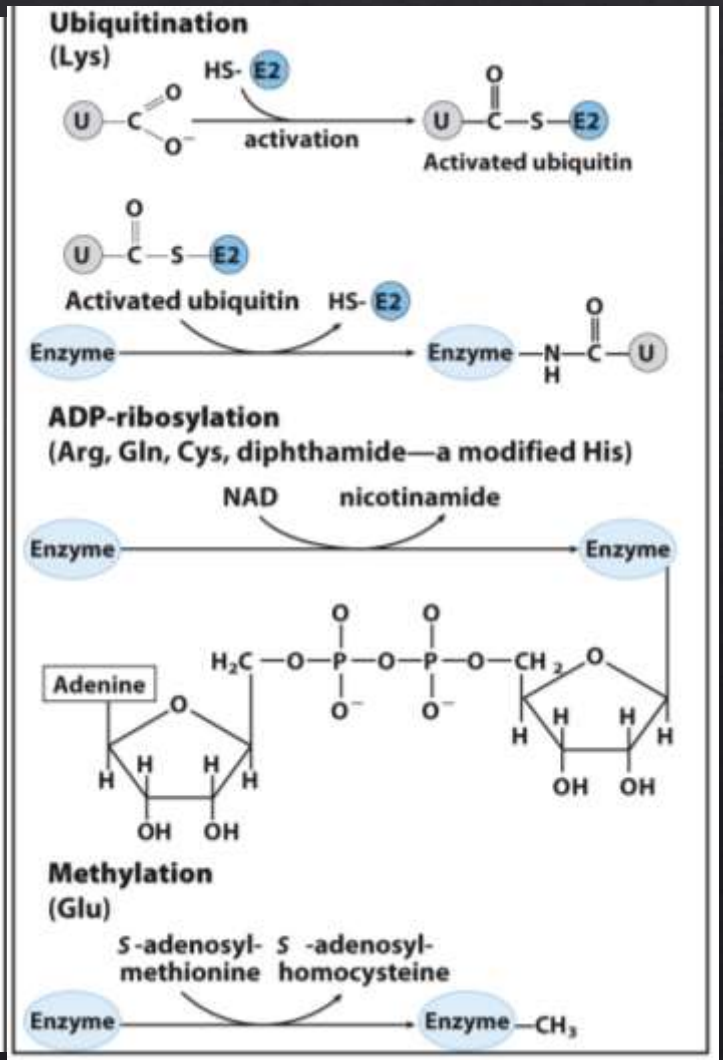
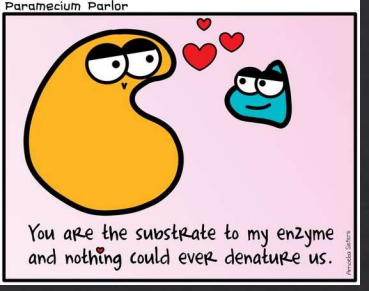


Enzymes regulation – Reversible Covalent Modification

Picture from Nelson&Cox

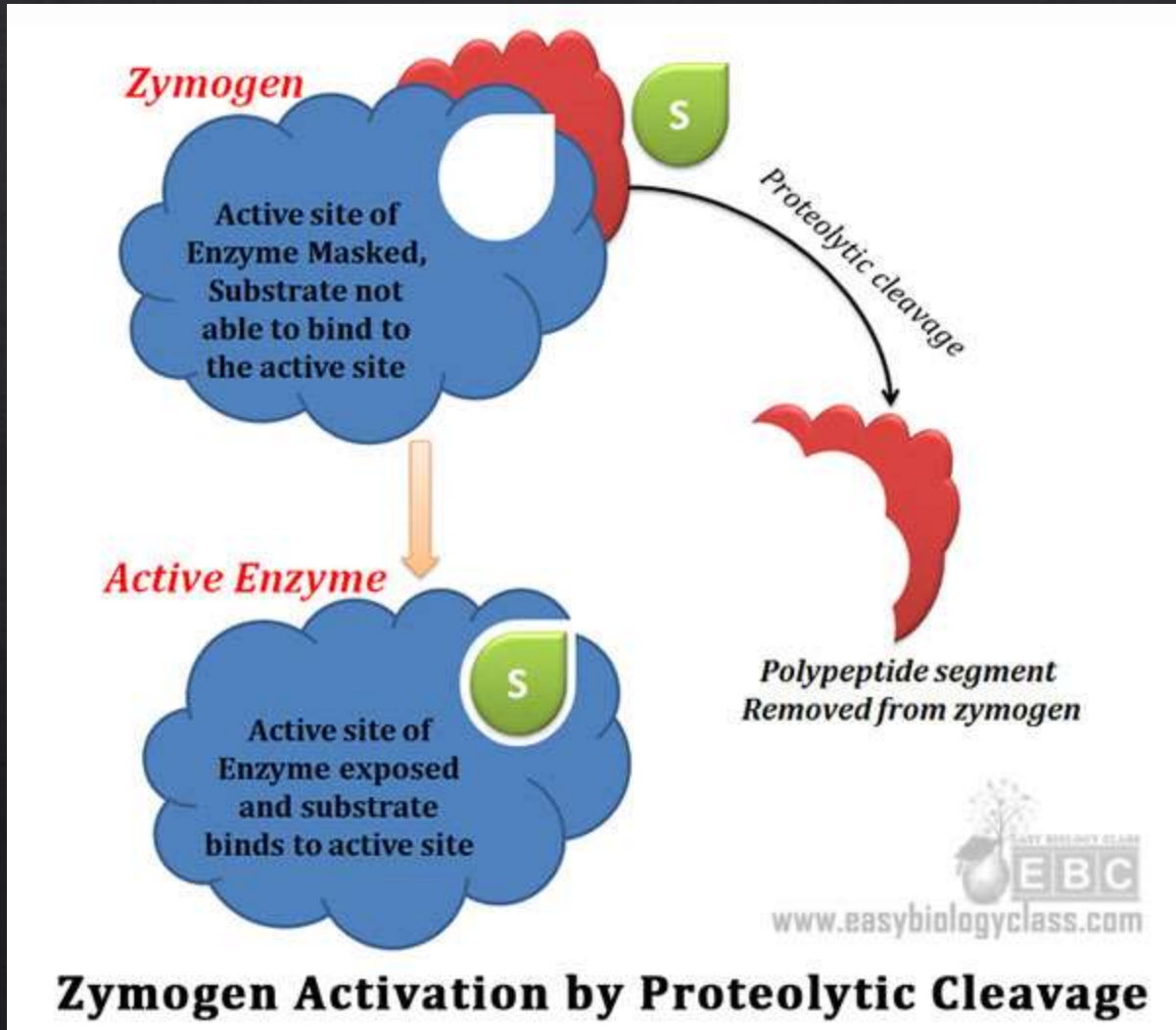


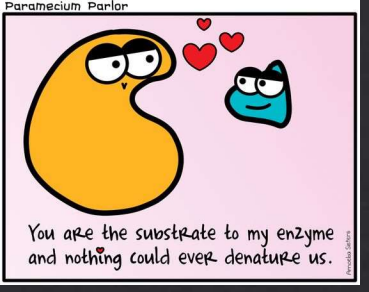




Enzymes regulation – Proteolytic cleavage

Specific cleavage causes conformational changes that expose the enzyme active site.
The process is irreversible, we need inhibitors





Regulatory cascade

These are mechanisms that allow an extremely sensitive response to a molecular signal.

They regulate a number of biological processes.

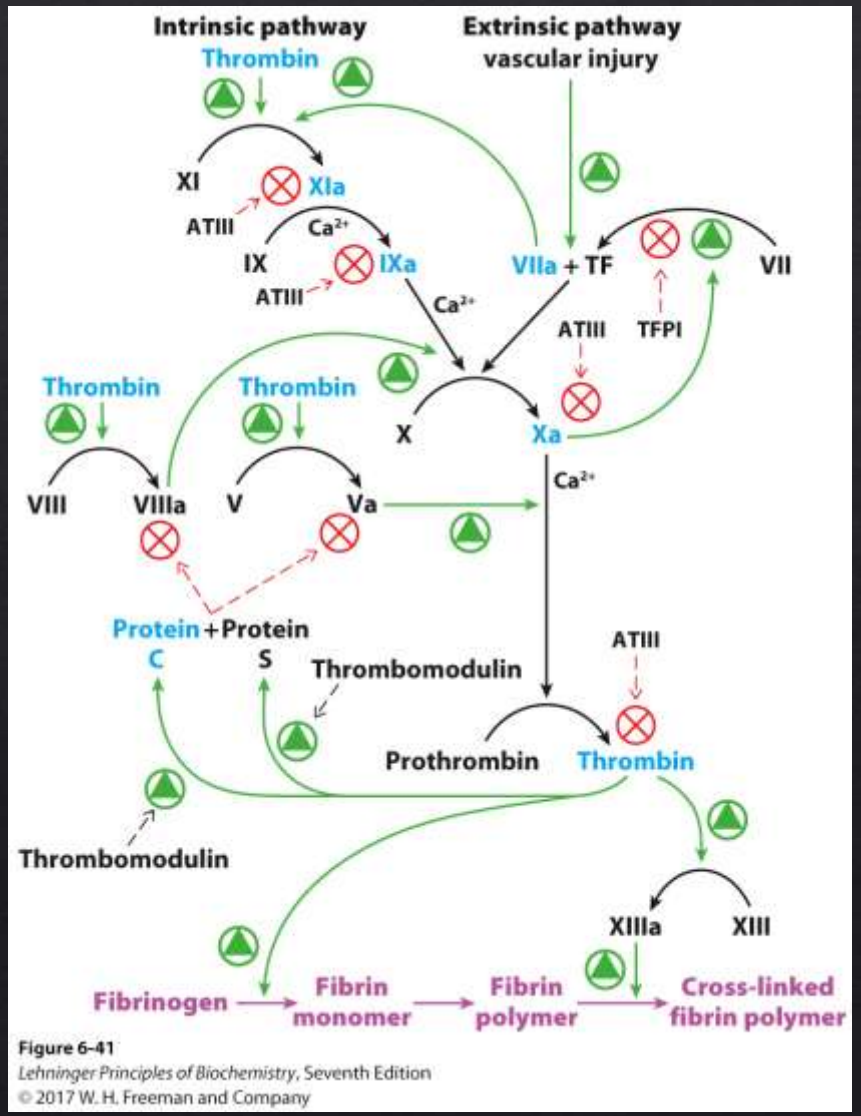


Figure 6-41
Lehninger Principles of Biochemistry, Seventh Edition