Week 2 Lectures 3&4
Enzymes

READING IN ALBERTS
Chapter 3: pp 91-93
Chapter 3: Figures 3-13, 3-14, 3-16
Chapter 4: pp 143-158, 91-94, 106-109

Consider the question posed on the next page
Given the complex, highly concentrated chemical mixture of macromolecules, inorganic and organic salts, metal ions etc, Why are random, uncontrolled chemical reactions NOT happening all of the time?

Artist/Scientist: David Goodsell

A small portion of cytoplasm is shown, including three types of filaments that make up the cytoskeleton: a microtubule (the largest), an intermediate filament (the knobby one) and two actin filaments (the smallest ones). The large blue molecules are ribosomes, busy in their task of synthesizing proteins.
Consider the following chemical reaction:

Sucrose + H₂O ----> glucose and fructose

*hydrolysis*

**Free energy of activation or activation energy:**
- the amount of energy required to cause a chemical reaction
- the amount of energy required to reach the *transition state*

**transition state:**
- unstable energized arrangement of atoms in which chemical bonds are in the process of being formed or broken
Most biological reactions occur rarely in the absence of a catalyst because the energy level of a molecule is not close to the energy of activation.

Notice that the large majority of the particles don't have enough energy to react when they collide. To enable them to react we either have to change the shape of the curve, or move the activation energy further to the left. Adding a catalyst has exactly this effect on activation energy. A catalyst provides an alternative route for the reaction. That alternative route has a lower activation energy.
The rate acceleration of 5 different enzymes
Connecting the DOTS:

The energy of most molecules is not even close to the activation energy required for an uncatalysed reaction

Therefore nothing much happens in the absence of a biological catalyst

The Genome specifies biological catalysts: Enzymes (protein catalysts) and Ribozymes (RNA catalysts)

Biological catalysts control the rate of biological reactions

The genome, internal environment and external environment control biological reactions by controlling the activity of the catalysts
Catalysis
http://www.chemguide.co.uk/physical/basicrates/catalyst.html#top

- catalysts work by providing an alternative route for the reaction with a lower activation energy
- a catalyst accomplishes this feat by combining transiently with the reactants in a way that promotes their entry into the reactive, transition state condition

**transition state:** substrate molecules must pass through a series of intermediate states of altered geometry and electron distribution before they form the ultimate products of the reaction

**activation energy:** the free energy (jiggling, vibrating, spinning) required to obtain the most unstable transition state
JARGON:

SUBSTRATE: the substance(s) on which an enzyme acts

ACTIVE SITE: a pocket or groove in the enzyme into which only particular substrates will fit

ENZYME-SUBSTRATE COMPLEX
Sucrose + H₂O ----> glucose and fructose

*hydrolysis*
Catalysts speed up the rate of a reaction

They are very specific and very powerful

Each enzyme typically catalyzes only one particular reaction

Enzymes permit cells to make or break bonds in a controlled way
How enzymes speed up reactions:

1. *Increase the local concentration* of substrate molecules at the catalytic site

2. *Holds all the appropriate atoms* in the correct orientation for the reaction that is to follow

3. Enzymes have a much higher affinity for the transition state of the substrates than they have for the stable form -- this tight binding *provides an alternative route for the reaction involving a lower activation energy*
**transition state:** substrate molecules must pass through a series of intermediate states of altered geometry and electron distribution before they form the ultimate products of the reaction

![Diagram of enzyme action](image)

(A) enzyme binds to two substrate molecules and orients them precisely to encourage a reaction to occur between them

(B) binding of substrate to enzyme rearranges electrons in the substrate, creating partial negative and positive charges that favor a reaction

(C) enzyme strains the bound substrate molecule, forcing it toward a transition state to favor a reaction

Figure 3–52. Molecular Biology of the Cell, 4th Edition.

**Enzymes can encourage catalysis in several ways**

a. Holding substrates together in a precise alignment

b. Charge stabilization of reaction intermediates

c. Altering bond angles in the substrate to increase the rate of a reaction
Addition of a DNA monomer unit to a DNA polymer is catalyzed by DNA polymerase.
**DNA polymerase**: enzyme that catalyzes the formation of a DNA polymer
active site of DNA polymerase showing mechanisms listed previously -- \textit{alignment of substrates}; \textit{charge stabilization (by the metal ions)}; bond "straining"
Catalysts affect the *kinetics* of a reaction, but have no effect on the overall free-energy change between substrate and product.

**Both endothermic and exothermic reactions require catalysts because activation energy is required typically for both types of reactions.**
For example:

The generation of a polymer from a monomer is an endothermic (uphill) reaction: absorbs free energy from its surroundings

The reverse reaction, the hydrolysis of a polymer to monomers, is an exothermic reaction: releases energy

Both types of reactions require enzymatic catalysis

This is why our DNA and protein polymers don’t fall apart on us!
Catalytic activities of Enzymes are often regulated by other molecules

Hypothetical enzyme in which a small molecule called ADP acts as an activator to increase the rate at which sugar molecules are broken down (oxidized)

Figure 4-40 Essential Cell Biology, 2/e. © 2004 Garland Science
The binding of a protein molecule (such as the enzyme depicted in the previous diagram) to another molecule (such as ADP) is highly selective and dependent on multiple weak non-covalent bonds (see next figure).

**Ligand:** a small molecule that binds to a specific site on a protein
Noncovalent bonds mediate protein-protein interactions and protein-ligand interactions
Binding sites allow a protein to interact with specific ligands