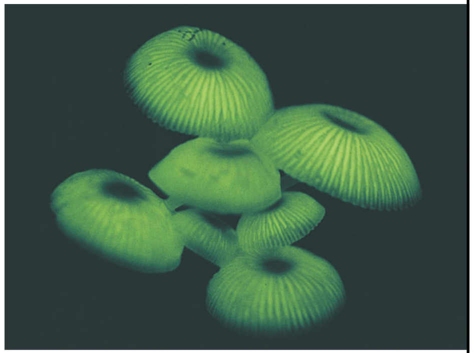
General Biology

Course No: BNG2003
Credits: 3.00

5. An Introduction into Cell Metabolism

Prof. Dr. Klaus Heese

- The Energy of Life
- The *living cell* is a miniature factory where thousands of reactions occur; it converts energy in many ways

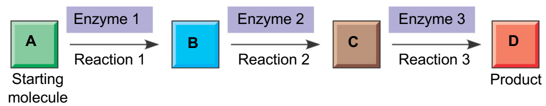


- Some organisms convert energy to light, as in bioluminescence or biofluorescence
- An organism's metabolism transforms matter and energy, subject to the laws of thermodynamics

- Metabolism
  - is the totality of an organism's chemical reactions
  - arises from interactions between molecules

Organization of the Chemistry of Life into Metabolic Pathways

- A metabolic pathway has many steps
  - that begin with a specific molecule and end with a product
  - that are each catalyzed by a specific enzyme



- Catabolic pathways
  - break down complex molecules into simpler compounds
  - release energy
- Anabolic pathways
  - build complicated molecules from simpler ones
  - consume energy

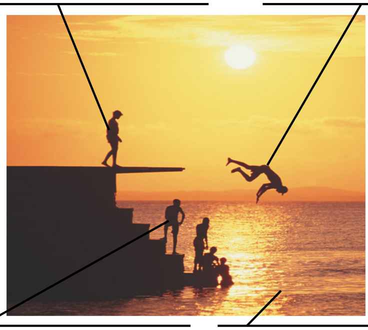
Forms of Energy

- **Energy**
  - is the capacity to cause change
  - exists in various forms, of which some can perform work
- Kinetic energy
  - is the energy associated with motion
- Potential energy
  - is stored in the location of matter
  - includes chemical energy stored in molecular structure

- Energy can be converted
  - from one form to another

On the platform, a diver has more potential energy.

Diving converts potential energy to kinetic energy.



Climbing up converts kinetic energy of muscle movement to potential energy.

In the water, a diver has less potential energy.

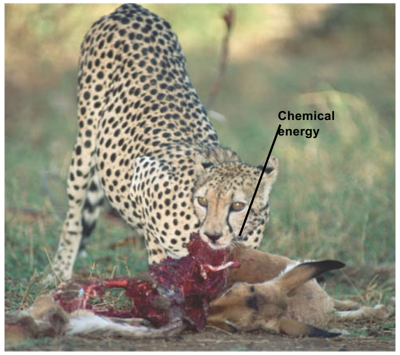
The Laws of Energy Transformation

- Thermodynamics
  - is the study of energy transformations

The First Law of Thermodynamics

- According to the first law of thermodynamics
  - Energy can be transferred and transformed
  - Energy cannot be created or destroyed

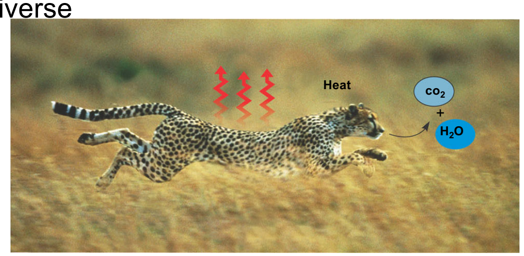
- **An example of energy conversion**



First law of thermodynamics: Energy can be transferred or transformed but neither created nor destroyed. For example, the chemical (potential) energy in food will be converted to the kinetic energy of the cheetah's movement.

The Second Law of Thermodynamics

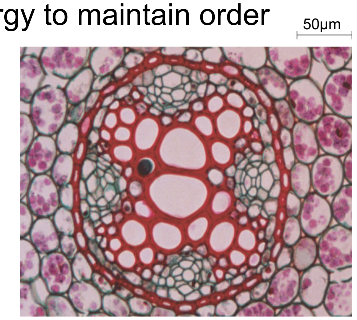
- According to the second law of thermodynamics
  - Spontaneous changes that do not require outside energy increase the entropy, or disorder, of the universe



Second law of thermodynamics: Every energy transfer or transformation increases the disorder (entropy) of the universe. For example, disorder is added to the cheetah's surroundings in the form of heat and the small molecules that are the by-products of metabolism.

Biological Order and Disorder

- *Living systems*
  - increase the entropy of the universe
  - use energy to maintain order



- The free-energy change of a reaction tells us whether the reaction occurs spontaneously

Gibbs Free-Energy Change, ΔG

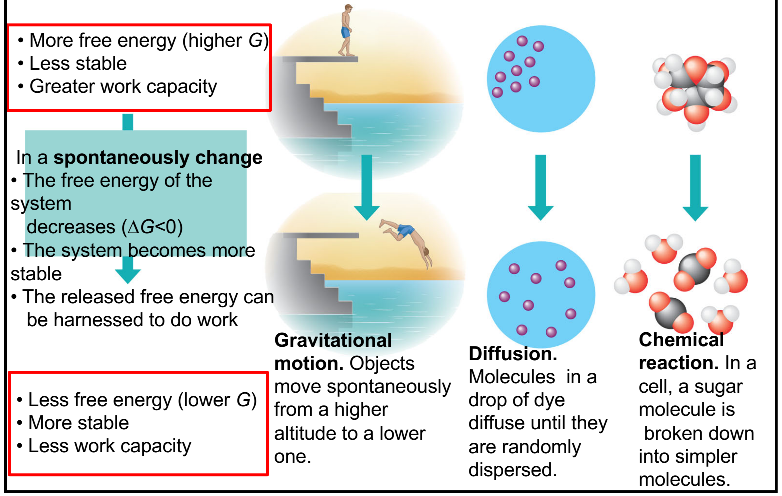
- A living system's free energy is energy that can do work under cellular conditions
- The change in free energy, ΔG during a biological process
  - is related directly to the enthalpy change (ΔH) and the change in entropy (ΔS)

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

Free Energy, Stability, and Equilibrium

- Organisms live at the expense of free energy
- during a spontaneous change
  - free energy decreases and the stability of a system increases

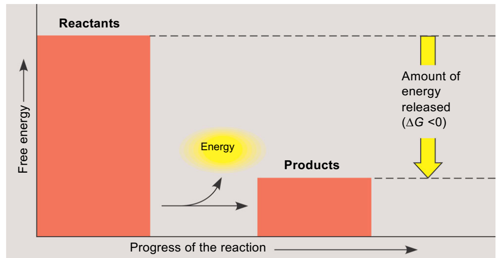
At maximum stability the system is at equilibrium



Free Energy and Metabolism

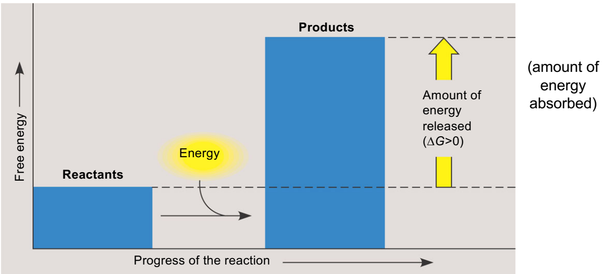
Exergonic and Endergonic Reactions in Metabolism

- An **exergonic** reaction
  - proceeds with a net release of free energy and is spontaneous



Exergonic reaction: energy released

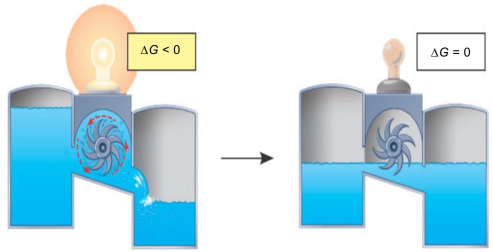
- An **endergonic** reaction
  - is one that absorbs free energy from its surroundings and is non-spontaneous



Endergonic reaction: energy required

Equilibrium and Metabolism

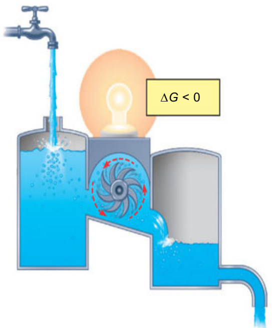
- reactions in a closed system
  - eventually reach equilibrium



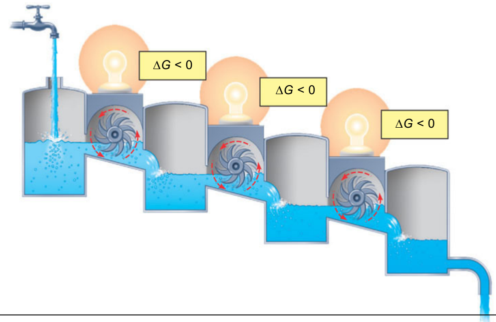
A closed hydroelectric system. Water flowing downhill turns a turbine that drives a generator providing electricity to a light bulb, but only until the system reaches equilibrium.

- Cells in our body
  - experience a constant flow of materials in and out, **preventing** metabolic pathways from reaching **equilibrium**

An open hydroelectric system. Flowing water keeps driving the generator because intake and outflow of water keep the system from reaching equilibrium.



- **An analogy for cellular respiration**

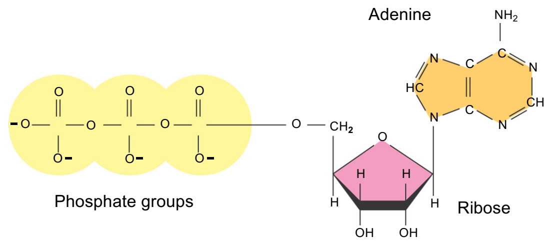


A multistep open hydroelectric system. Cellular respiration is analogous to this system: Glucose is broken down in a series of exergonic reactions that power the work of the cell. The product of each reaction becomes the reactant for the next, so no reaction reaches equilibrium.

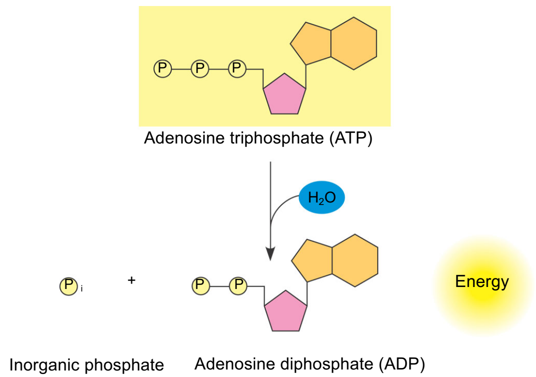
- **ATP powers cellular work** by coupling exergonic reactions to endergonic reactions
- A cell does three main kinds of work
  - Mechanical
  - Transport
  - Chemical
- Energy coupling
  - is a key feature in the way cells manage their energy resources to do this work

The Structure and Hydrolysis of ATP

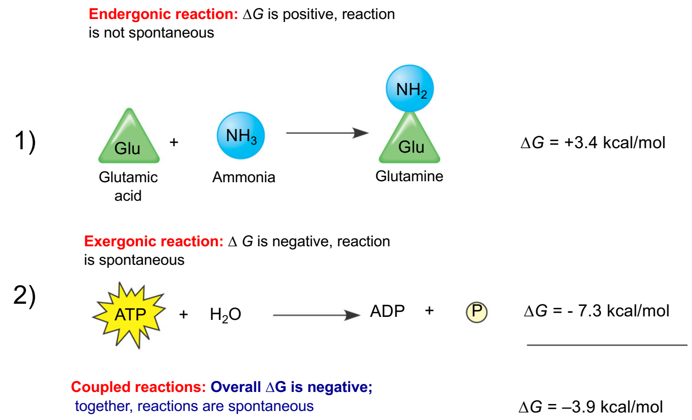
- ATP (adenosine triphosphate)
  - is the cell's energy shuttle ('currency')
  - provides energy for cellular functions



- Energy is released from ATP
  - when the terminal phosphate bond is broken



- ATP hydrolysis can be coupled to other reactions



(the 2nd reaction 'drives' the 1st reaction)

How ATP Performs Work

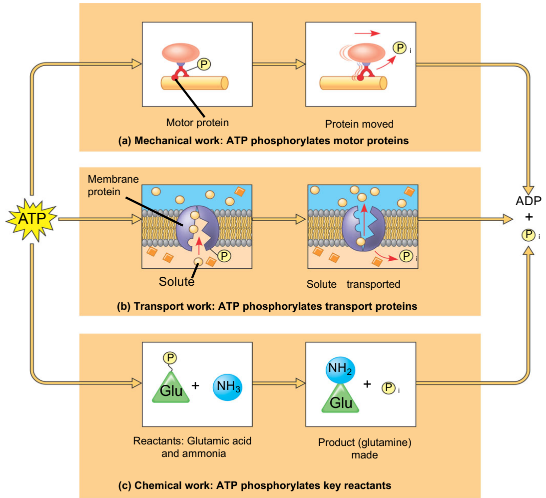
- ATP drives endergonic reactions
  - by phosphorylation, transferring a phosphate to other molecules

- The three types of cellular work are powered by the hydrolysis of ATP

Mechanical

Transport

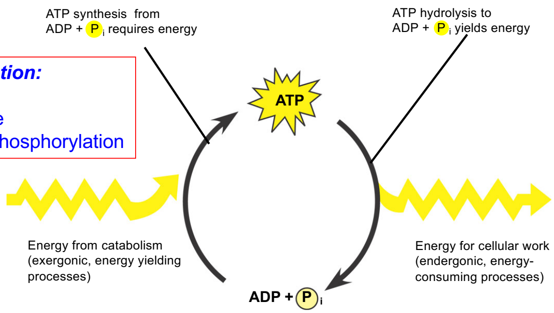
Chemical



The Regeneration of ATP

- Catabolic pathways
  - drive the regeneration of ATP from ADP and phosphate

Cell Respiration:
- Glycolysis
- Krebs Cycle
- Oxidative Phosphorylation



- **Enzymes**

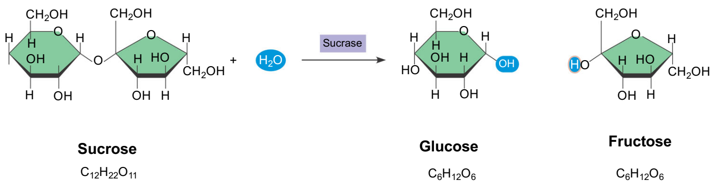
  speed up metabolic reactions by lowering energy barriers

- A catalyst is a chemical agent that speeds up a reaction without being consumed by the reaction
- An enzyme is a catalytic protein

The Activation Barrier

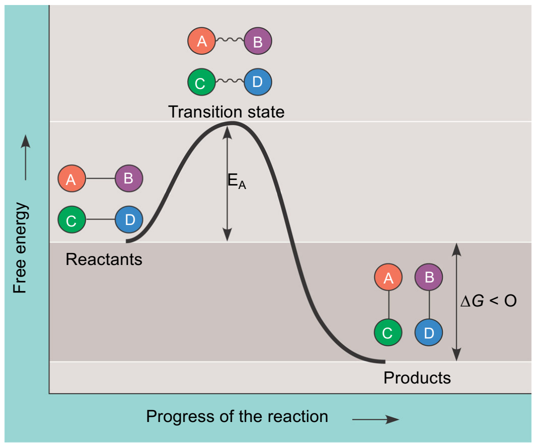
- Every chemical reaction between molecules involves both bond breaking and bond forming

- The hydrolysis is an example of a chemical reaction



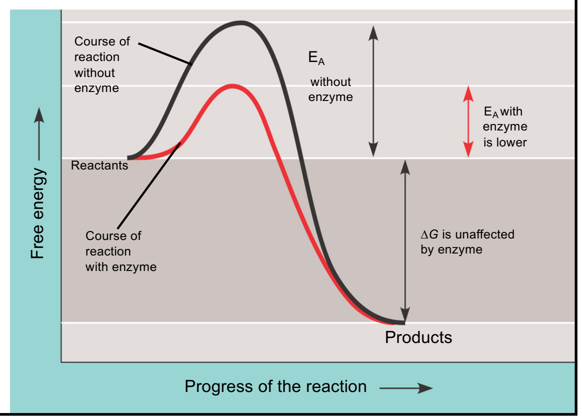
- The activation energy, E_A
  - is the initial amount of energy needed to start a chemical reaction
  - is often supplied in the form of heat from the surroundings in a system

- **The energy profile for an exergonic reaction**



Enzymes Lower the Reaction Activation Energy (E_A) Barrier

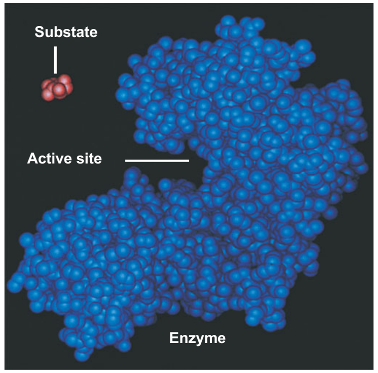
- An enzyme catalyzes reactions by lowering the E_A barrier
- The effect of enzymes on reaction rate



Substrate Specificity of Enzymes

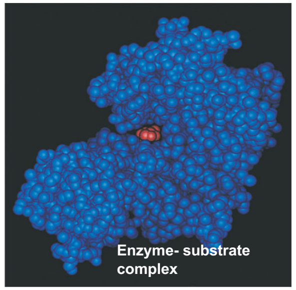
- The substrate
  - is the reactant an enzyme acts on
- The enzyme
  - binds to its substrate, forming an enzyme-substrate complex

- The active site
  - is the region on the enzyme where the substrate binds



Various models describe the enzyme-substrate reaction

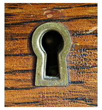
- Induced-Fit model of a substrate
  - brings chemical groups of the active site into positions that enhance their ability to catalyze the chemical reaction



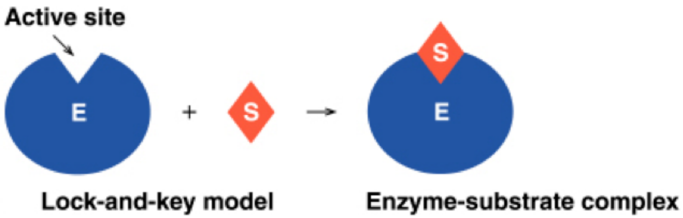
Conformation changes upon binding of a substrate

(other model: key-lock model)

Lock-and-Key Model

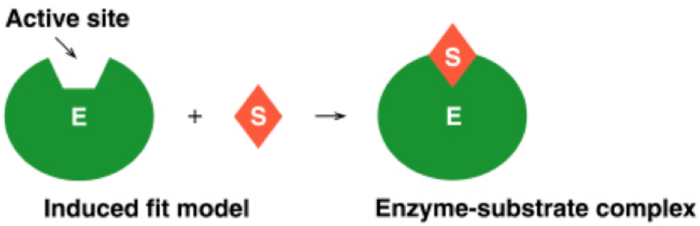


- In the **lock-and-key model** of enzyme ac
  - the active site has a rigid shape
  - only substrates with the matching shape can fit
  - the substrate is a key that fits the lock of the active site
- This is an older model, however, and does not work for all enzymes



Induced Fit Model

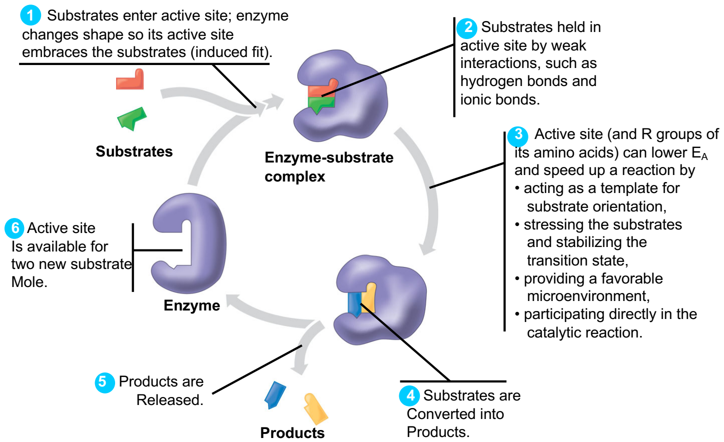
- In the **induced-fit model** of enzyme action:
  - the active site is flexible, not rigid
  - the shapes of the enzyme, active site, and substrate adjust to maximize the fit, which improves catalysis
  - there is a greater range of substrate specificity
- This model is more consistent with a wider range of enzymes



Catalysis in the Enzyme's Active Site

- In an enzymatic reaction
  - the substrate binds to the active site

- **The catalytic cycle of an enzyme** (conformation changes during the cycle)



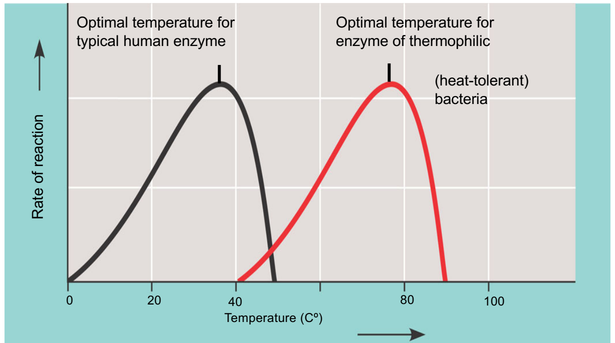
- The active site can lower an E_A barrier by
  - Orienting substrates correctly
  - Straining substrate bonds
  - Providing a favorable microenvironment
  - Covalently bonding to the substrate

Effects of Local Conditions on Enzyme Activity

- The activity of an enzyme is affected by general environmental factors

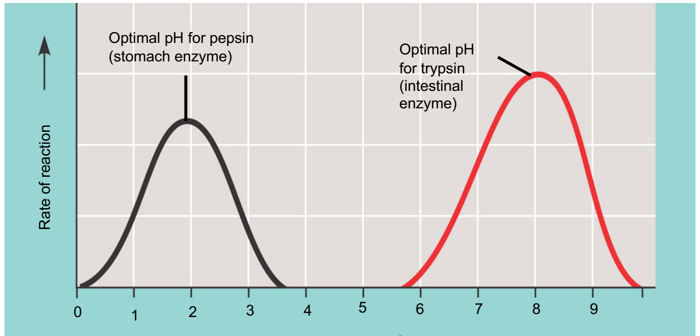
Effects of Temperature and pH

- Each enzyme has an optimal temperature in which it can function



(a) Optimal temperature for two enzymes

Each enzyme has an optimal pH in which it can function



(b) Optimal pH for two enzymes

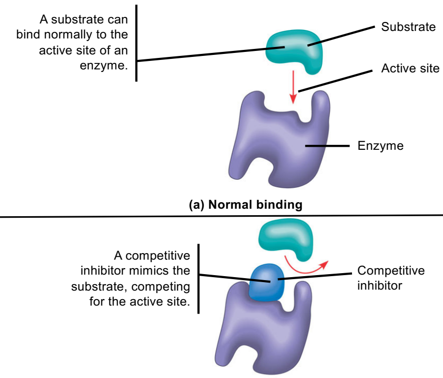
Cofactors

- Cofactors
  - are nonprotein enzyme helpers (e.g. ions)
- Coenzymes
  - are organic cofactors

Cofactors are not permanently bonded. Permanently bonded cofactors are called *prosthetic groups.*

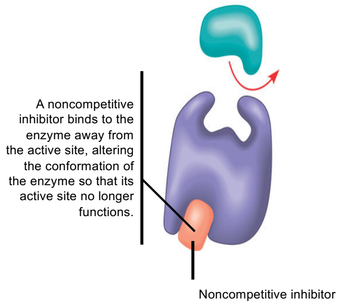
Enzyme Inhibitors

- Competitive inhibitors
  - Bind to the active site of an enzyme, competing with the substrate



(b) Competitive inhibition

- Noncompetitive inhibitors
  - bind to another part of an enzyme, changing the function



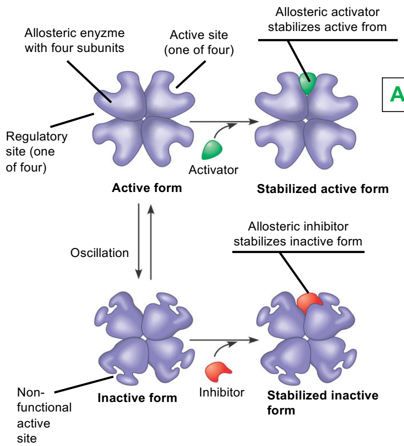
(c) Noncompetitive inhibition

- Regulation of enzyme activity helps control metabolism
- A cell's metabolic pathways
  - must be tightly regulated
- Allosteric regulation of enzymes
  - is the term used to describe any case in which a protein's function at one site is affected by binding of a regulatory molecule at another site

Allosteric Activation and Inhibition

- many enzymes are allosterically regulated

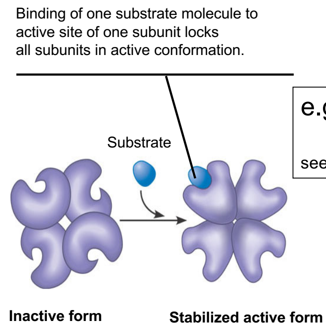
- Enzymes change shape when regulatory molecules bind to specific sites, affecting their function



Activator: e.g. Ca^{2+}

(a) Allosteric activators and inhibitors. In the cell, activators and inhibitors dissociate when at low concentrations. The enzyme can then oscillate again.

- Cooperativity is a form of allosteric regulation that can amplify enzyme activity



e.g. cAMP + PKA

see also G-protein signalling

(b) Cooperativity: another type of allosteric activation. Note that the inactive form shown on the left oscillates back and forth with the active fom when the active form is not stabilized by substrate.

Feedback Inhibition

- In feedback inhibition the end product of a metabolic pathway shuts down the pathway