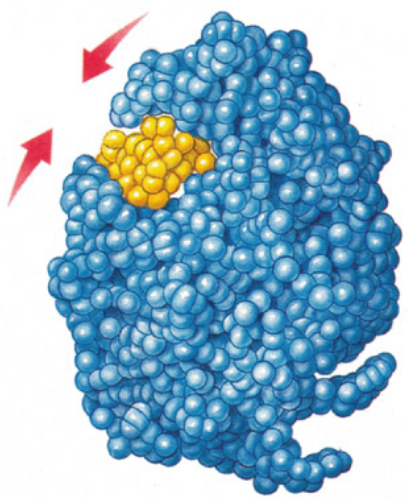
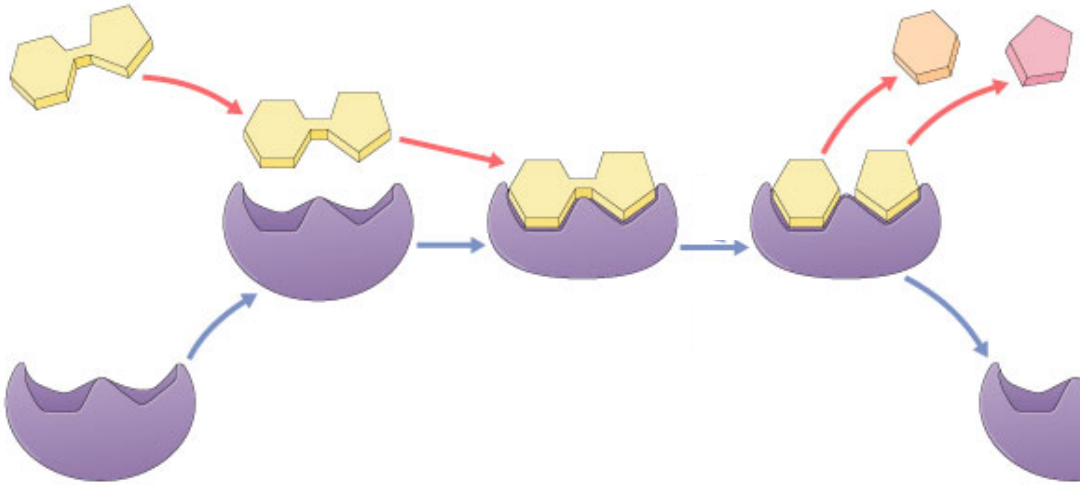


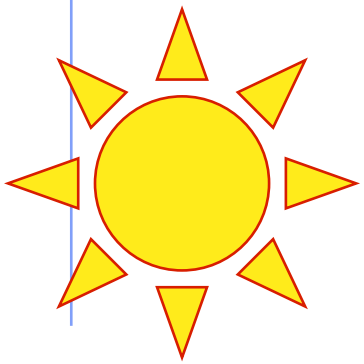
Chapter 6.

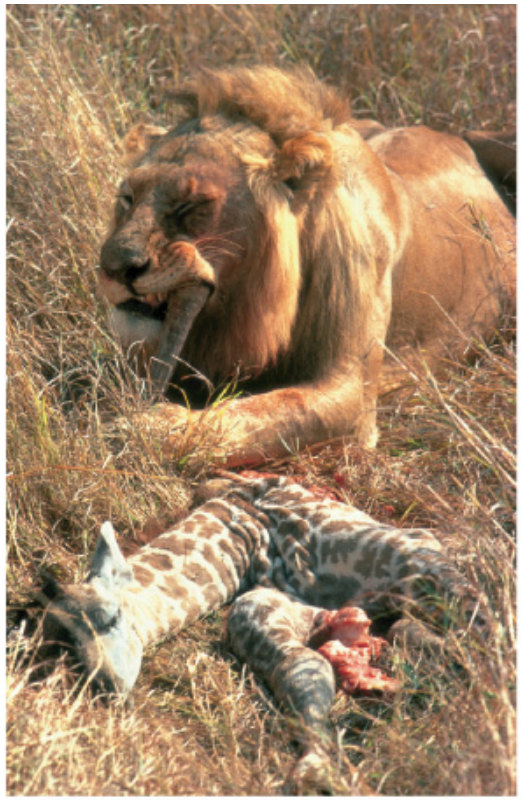
Metabolism & Enzymes



Flow of energy through life

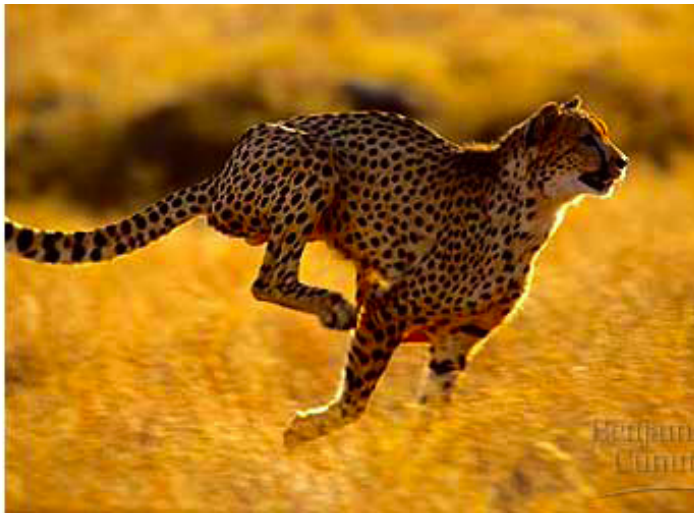
- Life is built on chemical reactions





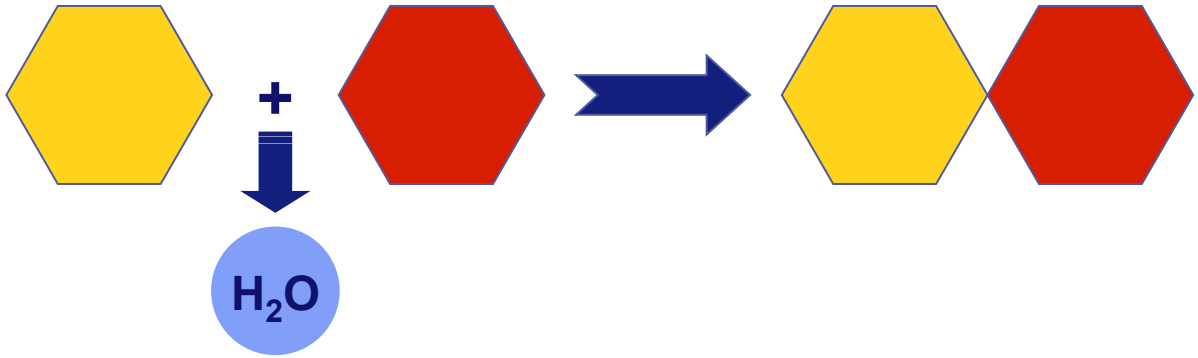
Chemical reactions of life

- **Metabolism**
  - forming bonds between molecules
    - dehydration synthesis
    - anabolic reactions
  - breaking bonds between molecules
    - hydrolysis
    - catabolic reactions

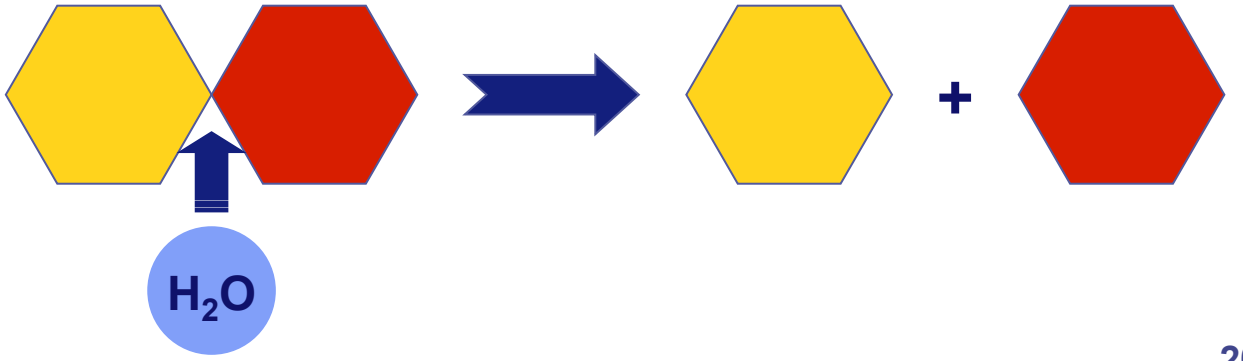


Examples

- dehydration synthesis

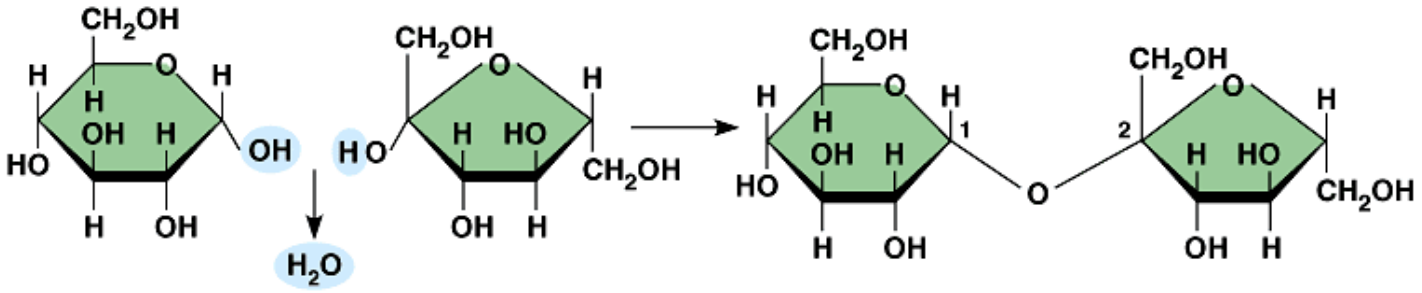


- hydrolysis

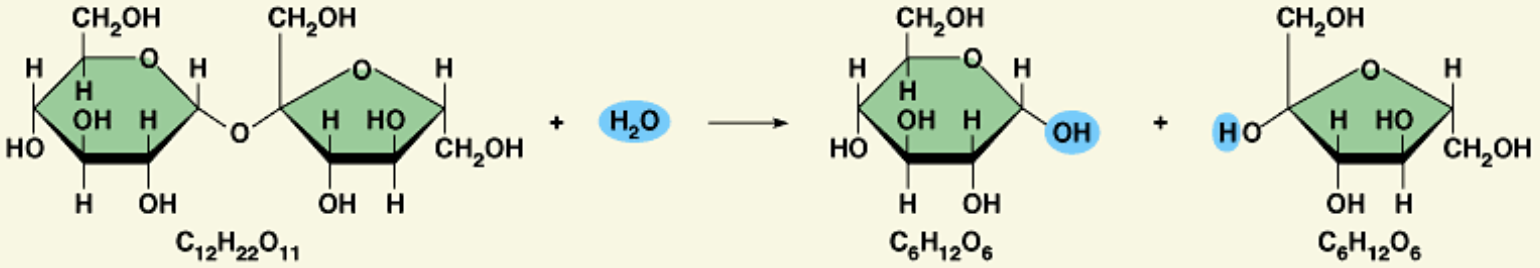


Examples

- dehydration synthesis

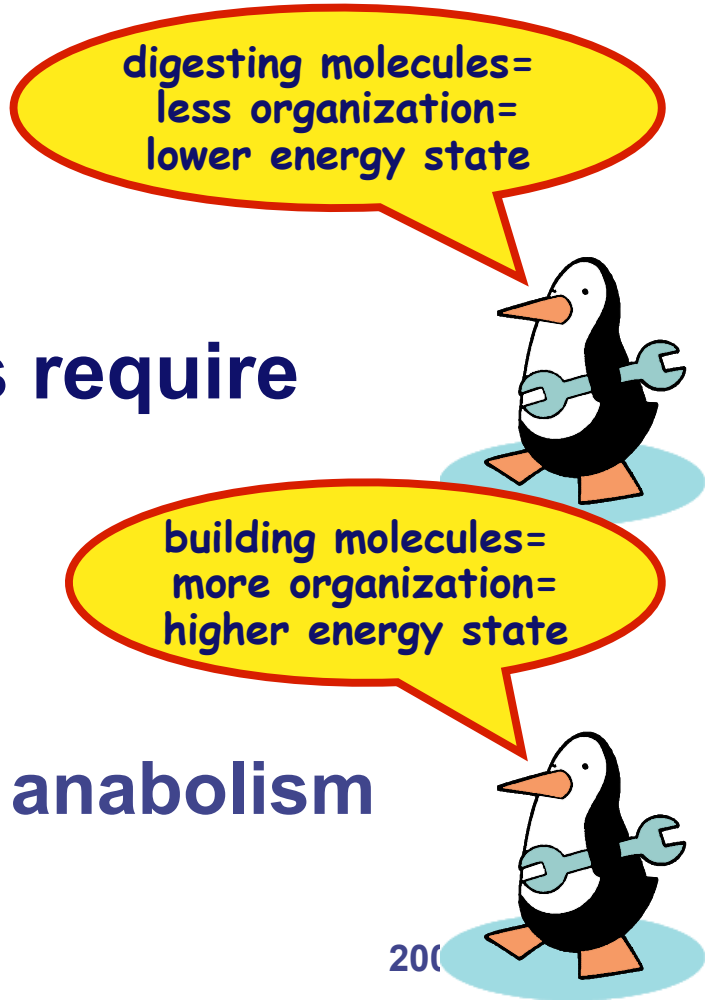


- hydrolysis



Chemical reactions & energy

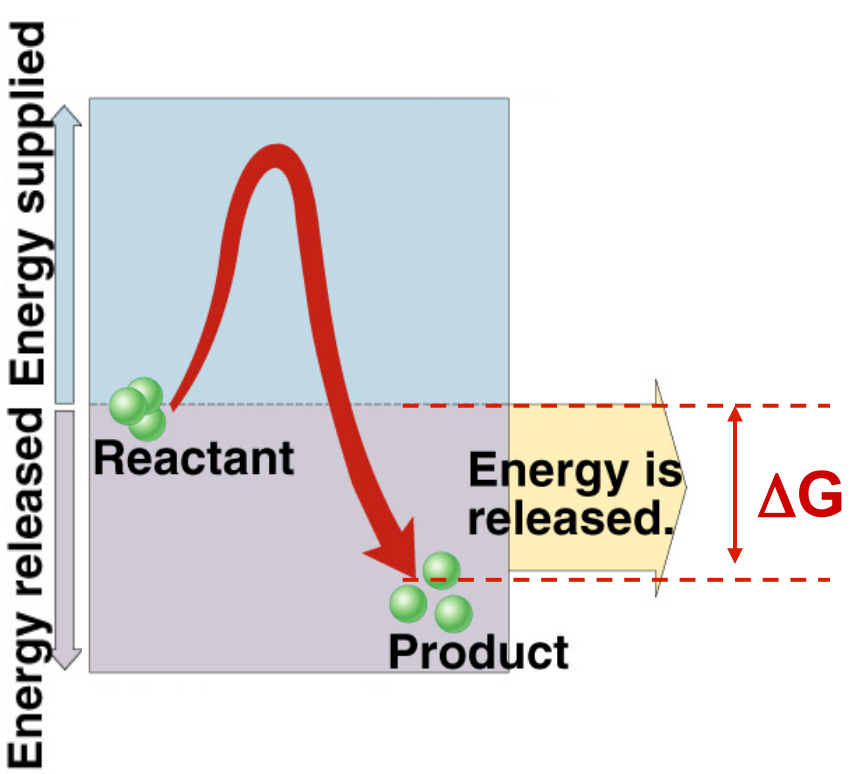
- Some chemical reactions release energy
  - exergonic
  - digesting polymers
  - hydrolysis = catabolism
- Some chemical reactions require input of energy
  - endergonic
  - building polymers
  - dehydration synthesis = anabolism



Endergonic vs. exergonic reactions

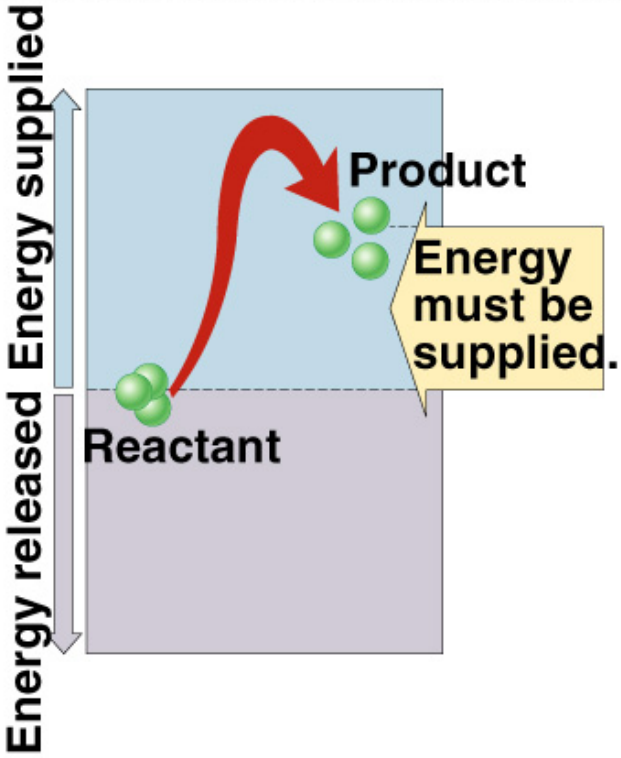
exergonic

energy released



endergonic

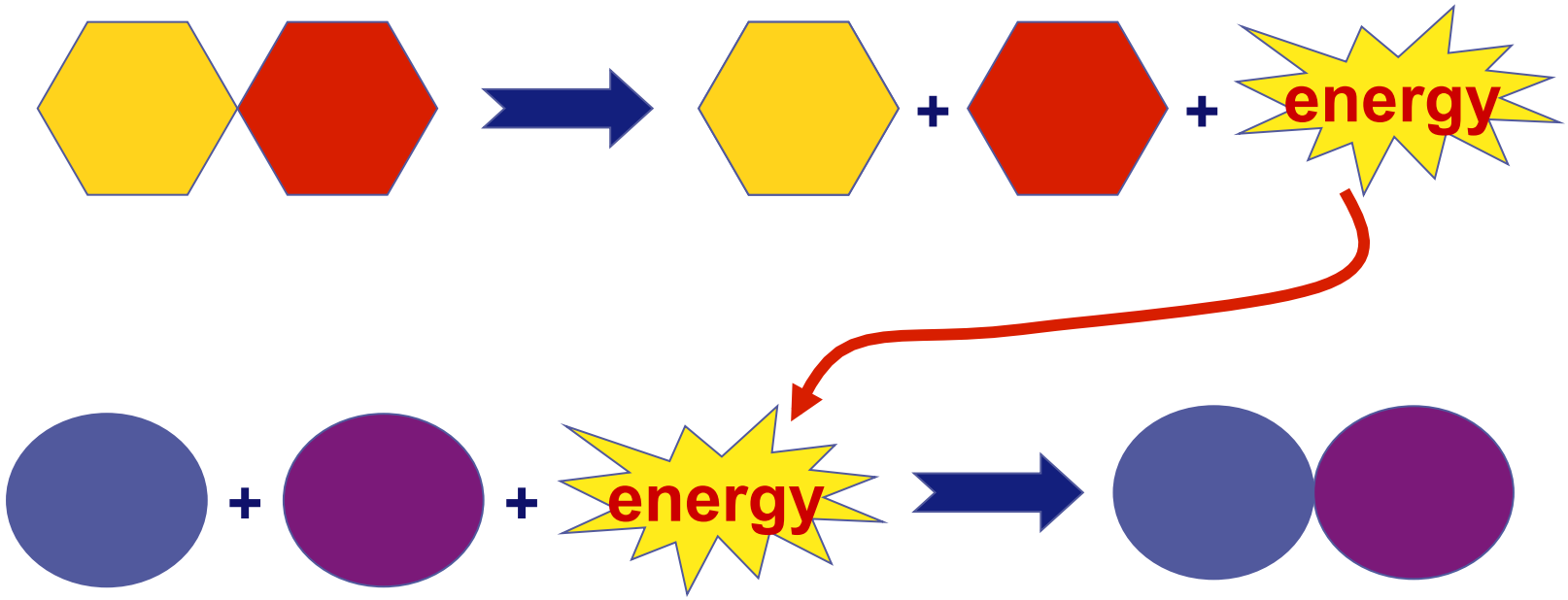
energy invested



ΔG = change in free energy = ability to do work

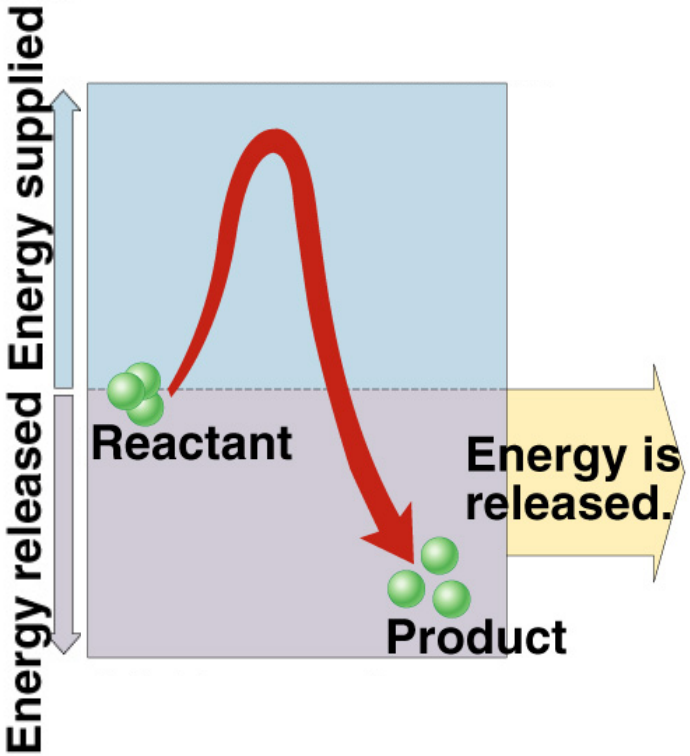
Energy & life

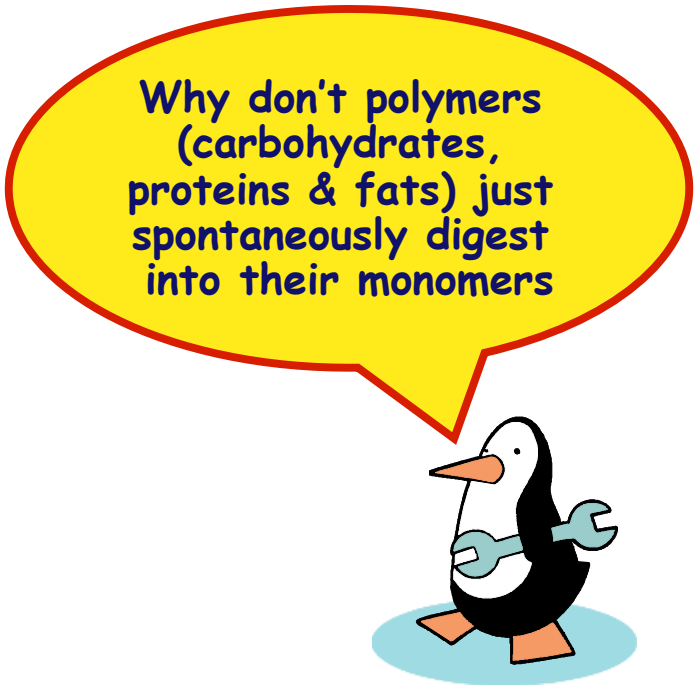
- Organisms require energy to live
  - where does that energy come from?
    - coupling exergonic reactions (releasing energy) with endergonic reactions (needing energy)



Spontaneous reactions?

- If reactions are "downhill", why don't they just happen spontaneously?
  - because covalent bonds are stable

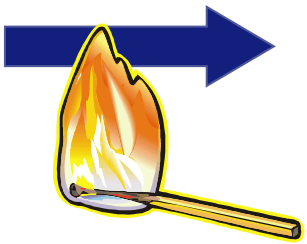




Activation energy

- Breaking down large molecules requires an initial input of energy
  - activation energy
  - large biomolecules are stable
  - must absorb energy to break bonds

cellulose

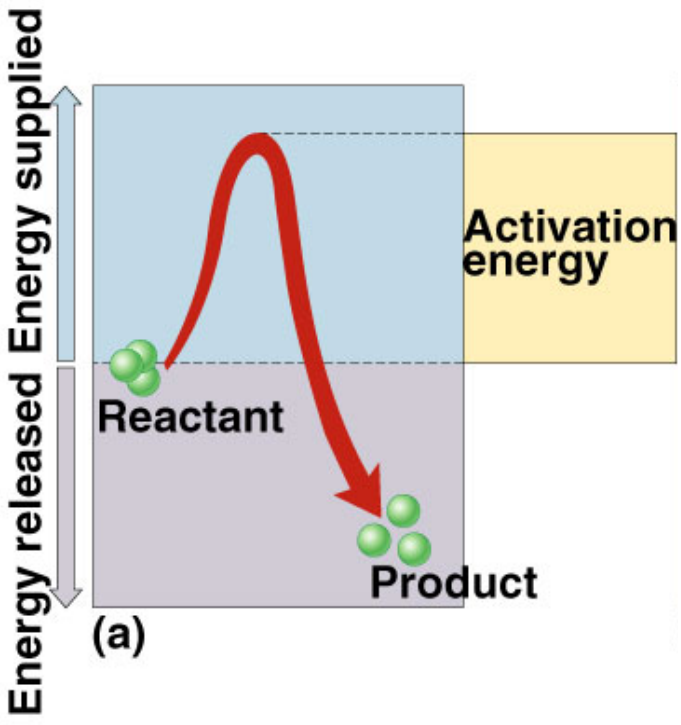


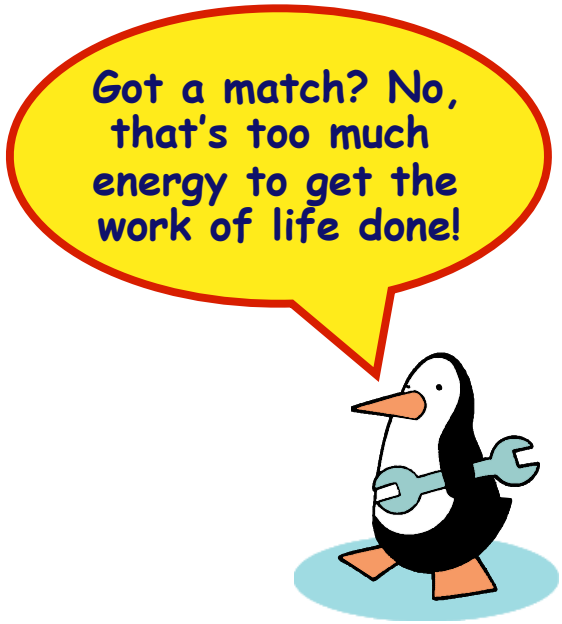
energy

$CO_2 + H_2O +$ heat

Activation energy

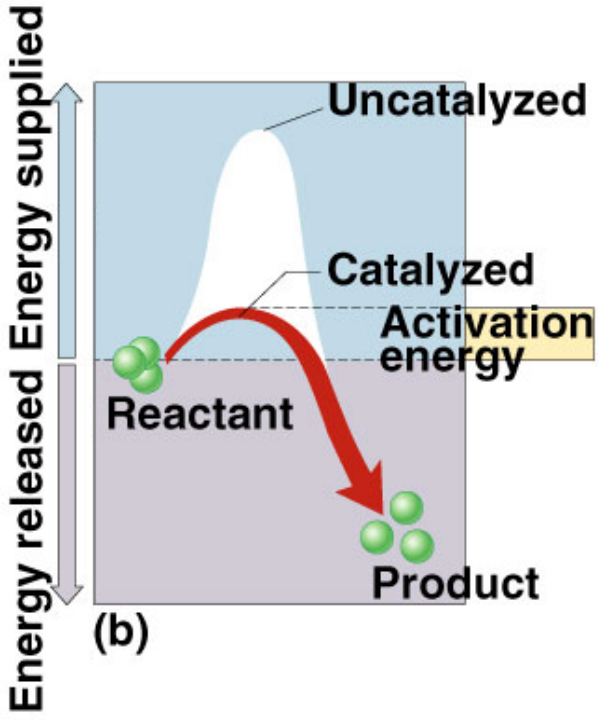
- the amount of energy needed to destabilize the bonds of a molecule
  - moves the reaction over an "energy hill"

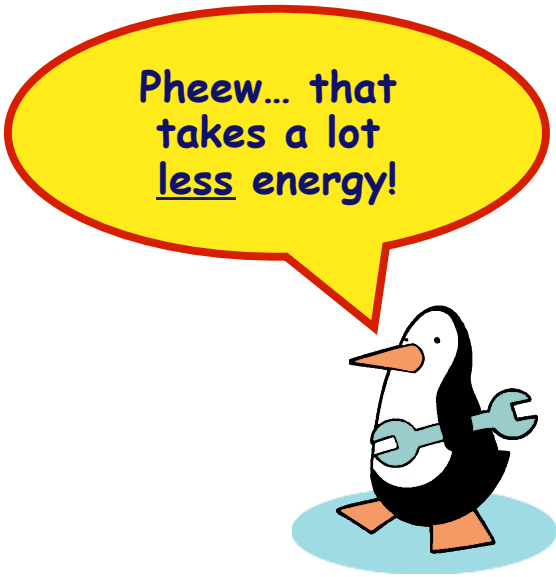




Reducing Activation energy

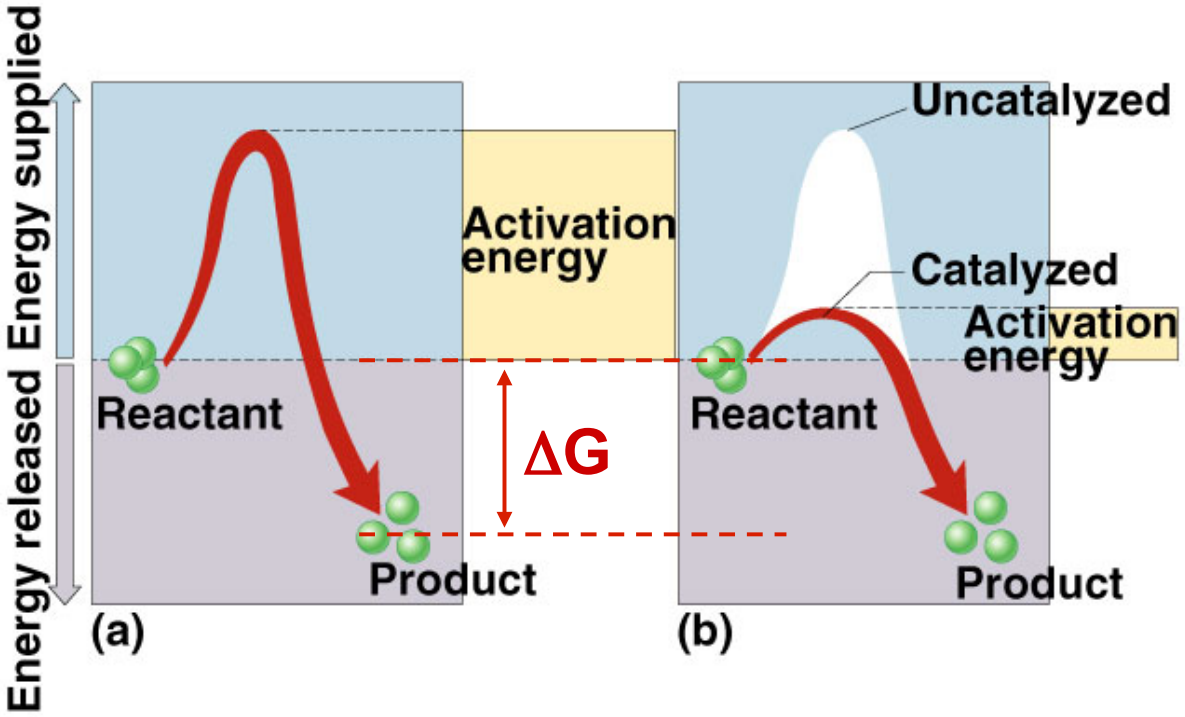
- **Catalysts**
  - reducing the amount of energy to start a reaction



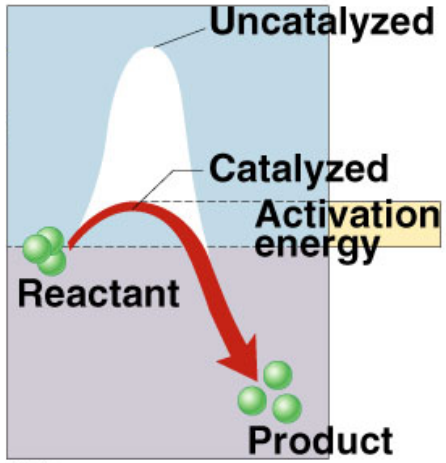


Catalysts

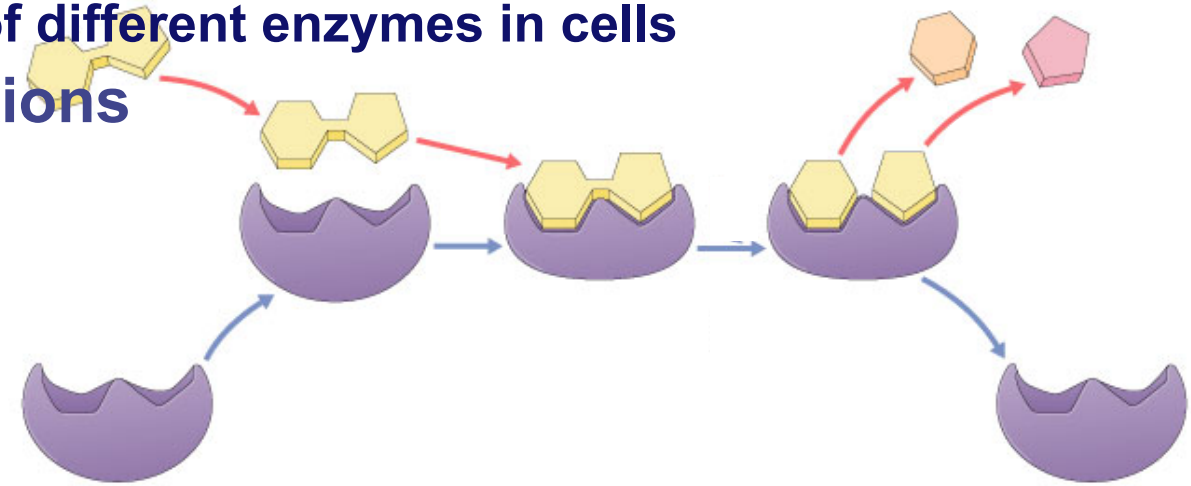
- So what's a cell to do to reduce activation energy?
  - get help! … chemical help… ENZYMES



Enzymes



- **Biological catalysts**
  - proteins (& RNA)
  - facilitate chemical reactions
    - increase rate of reaction without being consumed
    - reduce activation energy
    - don't change free energy (ΔG) released or required
  - required for most biological reactions
  - highly specific
    - thousands of different enzymes in cells
  - control reactions



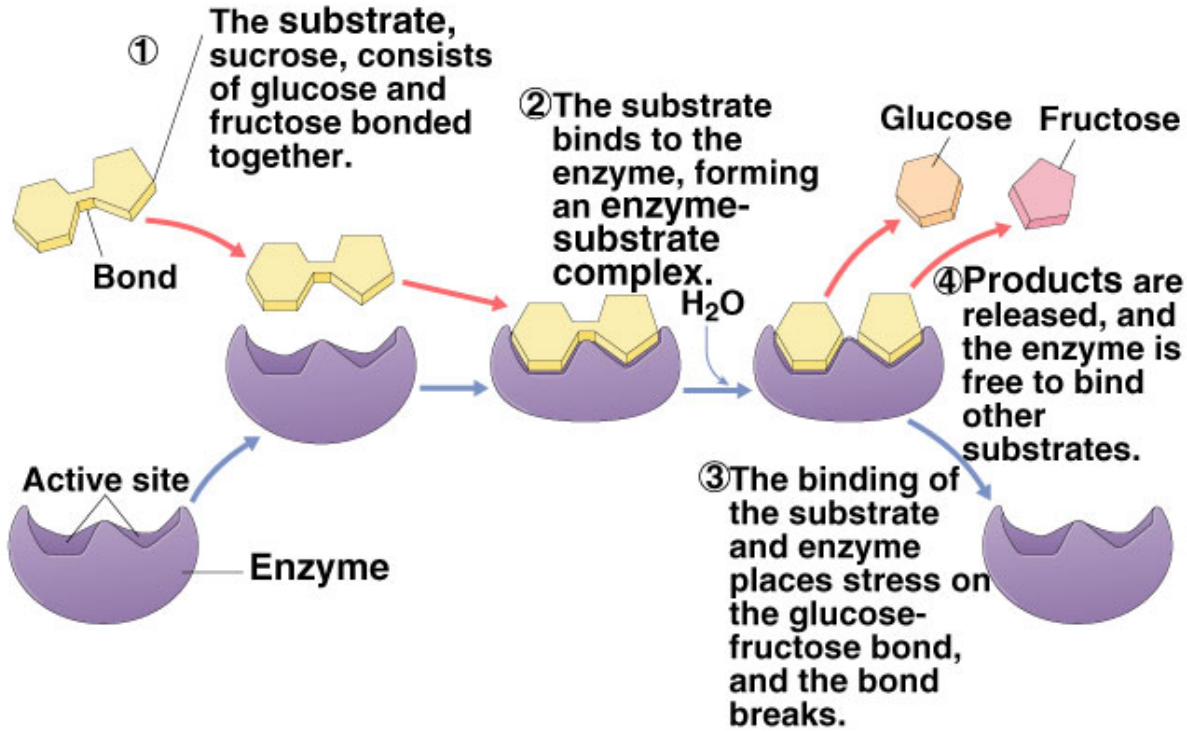
Enzymes & substrates

substrate

- reactant which binds to enzyme
- enzyme-substrate complex: temporary association

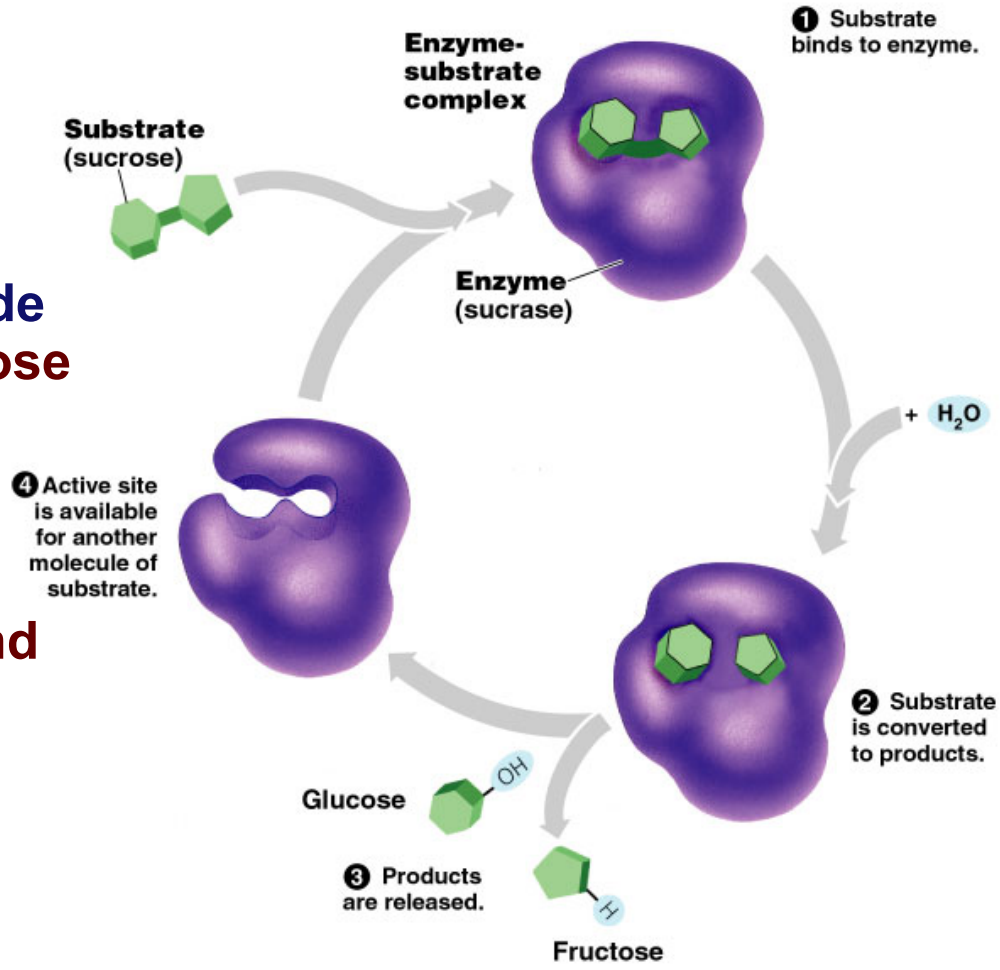
product

- end result of reaction

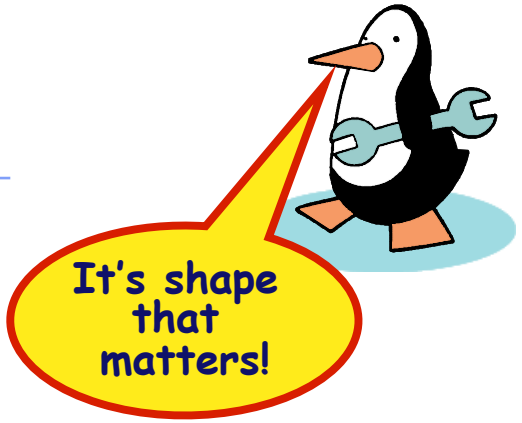


Enzymes & substrates

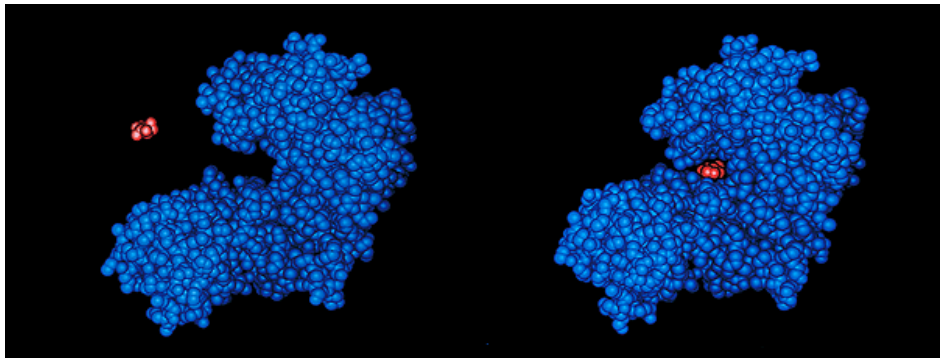
- Enzyme + substrates → products
  - sucrase
    - enzyme breaks down sucrose
    - binds to sucrose & breaks disaccharide into fructose & glucose
  - DNA polymerase
    - enzyme builds DNA
    - adds nucleotides to a growing DNA strand

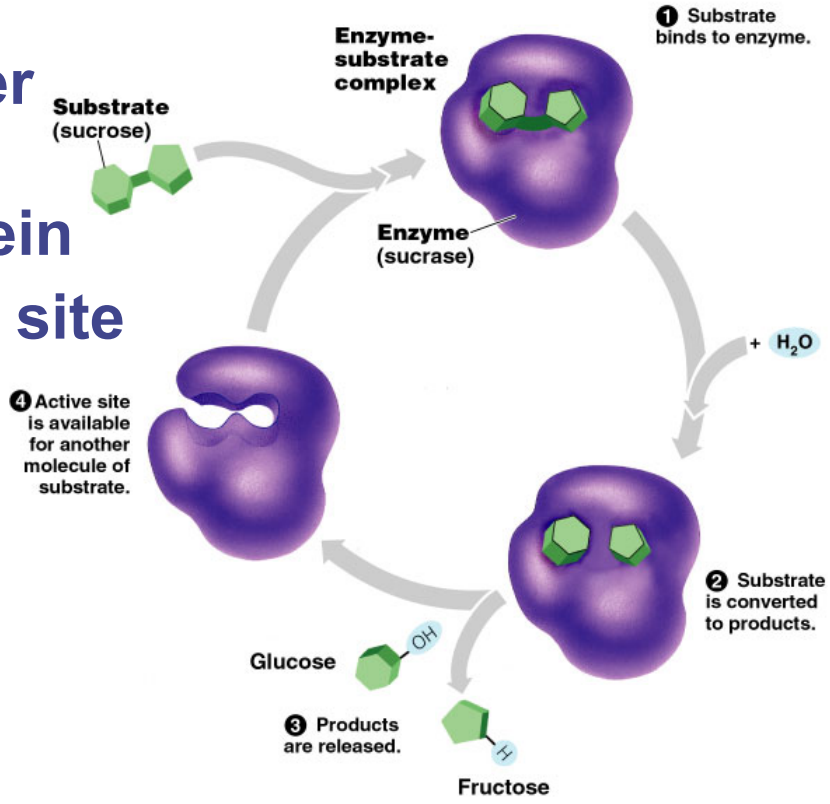


Lock and Key model



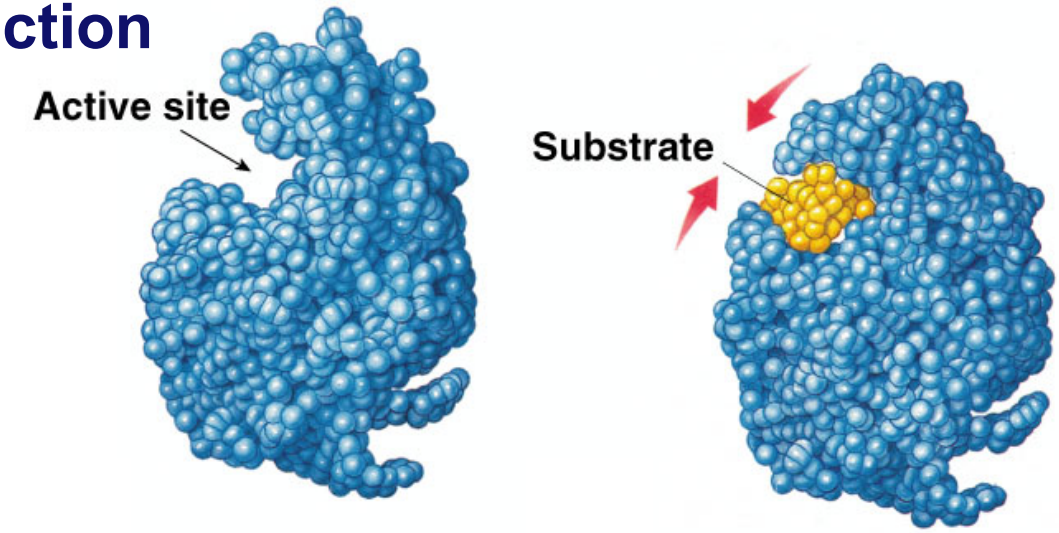
- Simplistic model of enzyme action
  - 3-D structure of enzyme fits substrate
- Active site
  - enzyme's catalytic center
  - pocket or groove on surface of globular protein
  - substrate fits into active site





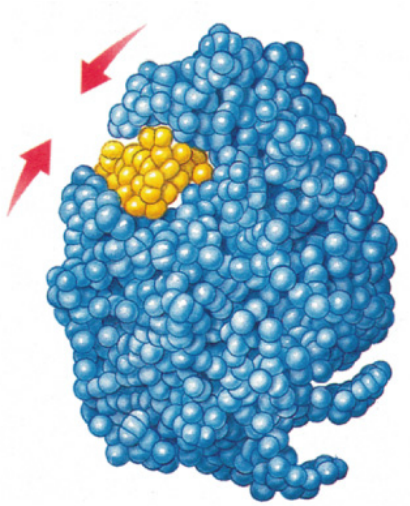
Induced fit model

- More accurate model of enzyme action
  - 3-D structure of enzyme fits substrate
  - as substrate binds, enzyme changes shape leading to a tighter fit
    - "conformational change"
    - bring chemical groups in position to catalyze reaction



How does it work?

- Variety of mechanisms to lower activation energy & speed up reaction
  - active site orients substrates in correct position for reaction
    - enzyme brings substrate closer together
  - active site binds substrate & puts stress on bonds that must be broken, making it easier to separate molecules



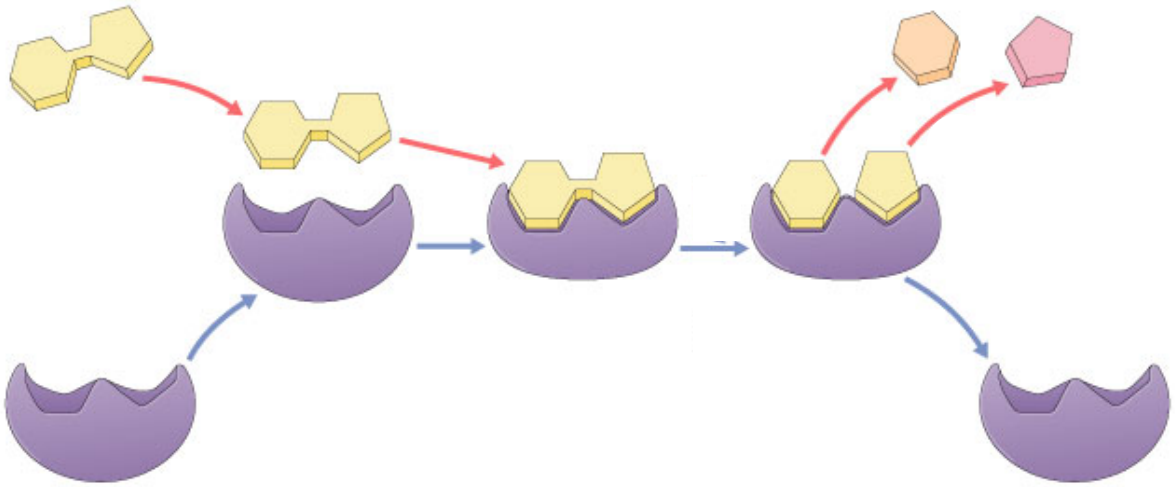
Properties of Enzymes

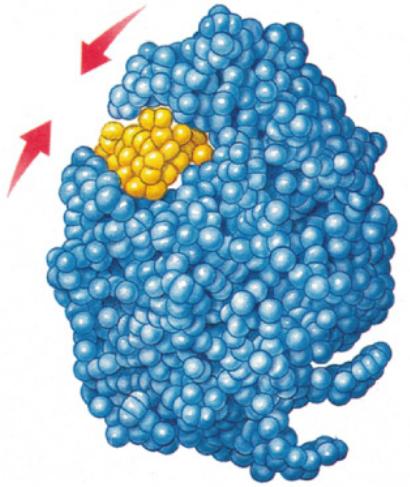
Specificity of enzymes

- Reaction specific
  - each enzyme is substrate-specific
    - due to fit between active site & substrate
      - substrates held in active site by weak interactions
        - H bonds
        - ionic bonds
  - enzymes named for reaction they catalyze
    - sucrase breaks down sucrose
    - proteases break down proteins
    - lipases break down lipids
    - DNA polymerase builds DNA
    - pepsin breaks down proteins (polypeptides)

Reusable

- Not consumed in reaction
  - single enzyme molecule can catalyze thousands or more reactions per second
  - enzymes unaffected by the reaction





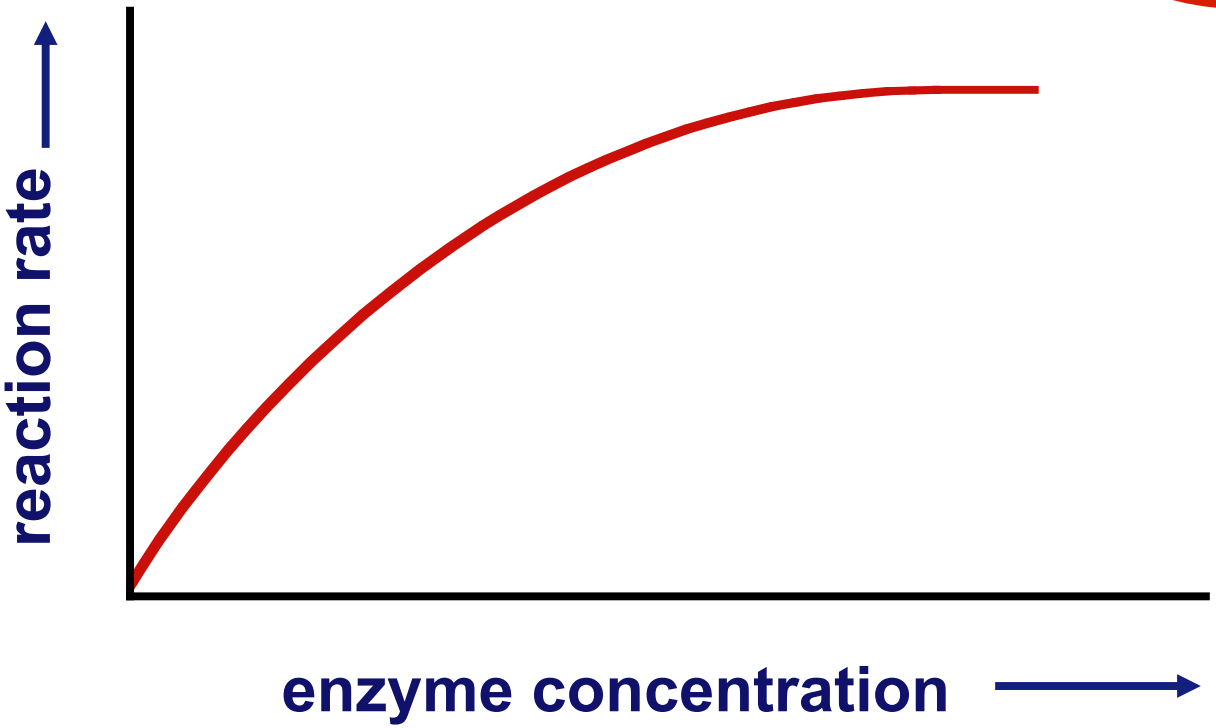
Factors that Affect Enzymes

Factors Affecting Enzymes

- Enzyme concentration
- Substrate concentration
- Temperature
- pH
- Salinity
- Activators
- Inhibitors

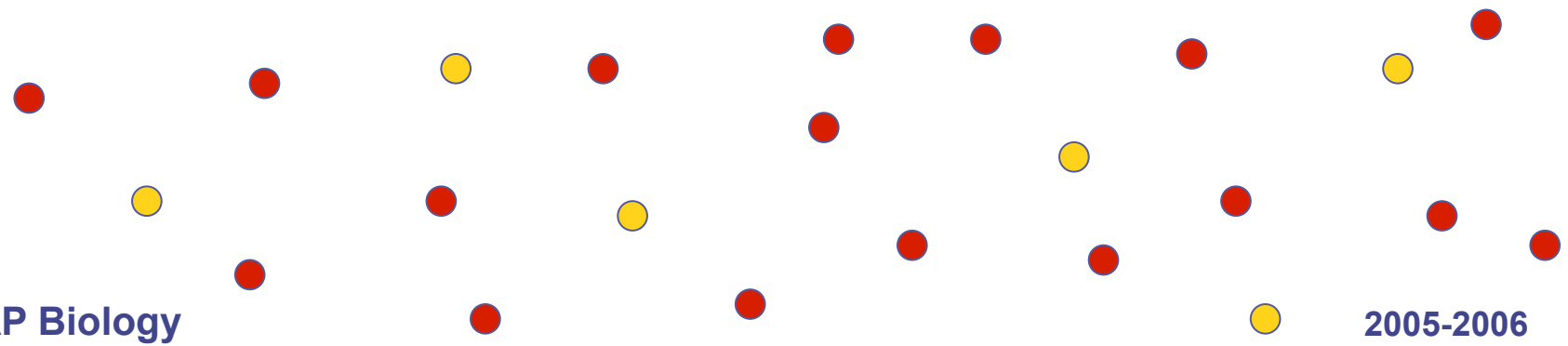
catalase

Enzyme concentration

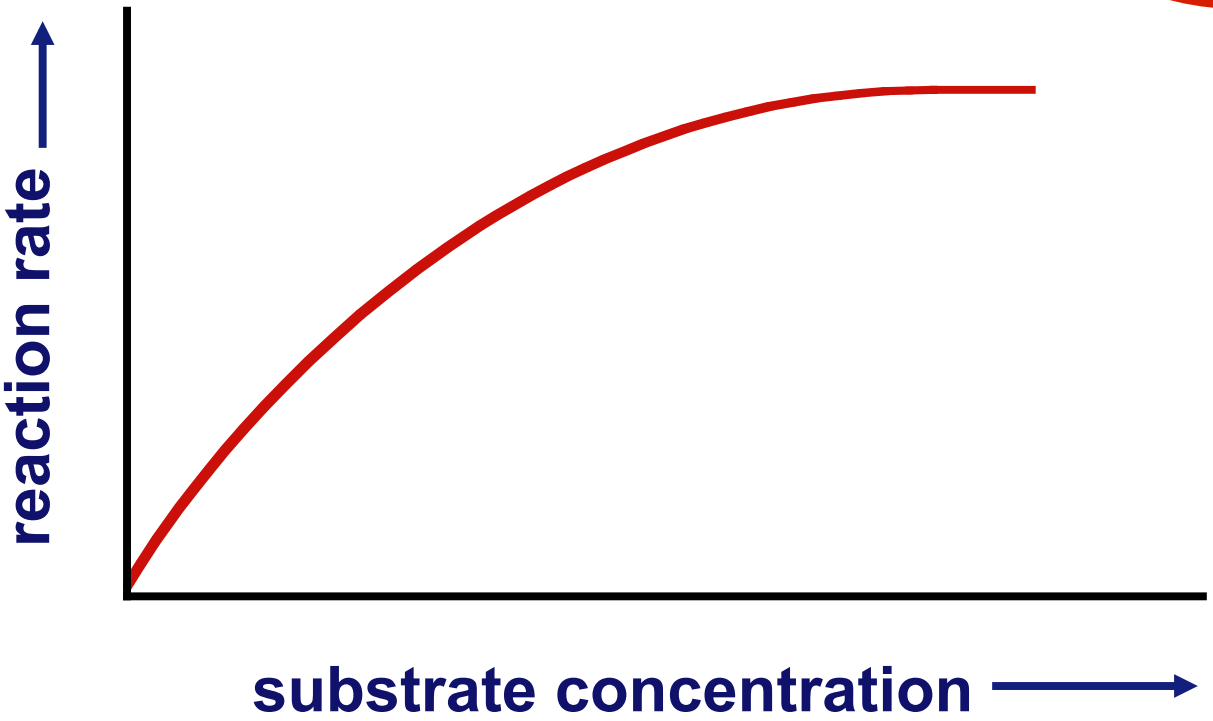


Enzyme concentration

- Effect on rates of enzyme activity
  - as ↑ enzyme = ↑ reaction rate
    - more enzymes = more frequently collide with substrate
  - reaction rate levels off
    - substrate becomes limiting factor
    - not all enzyme molecules can find substrate

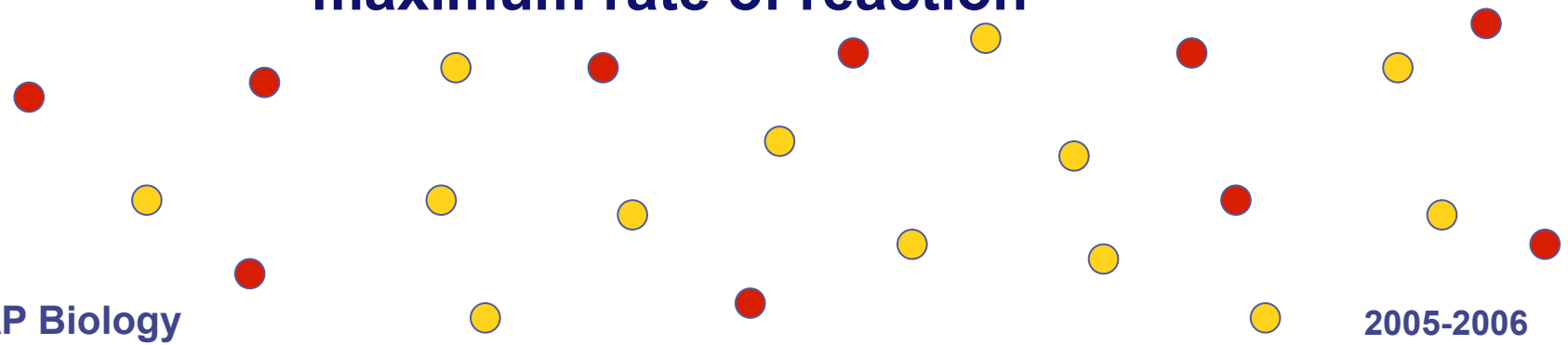


Substrate concentration

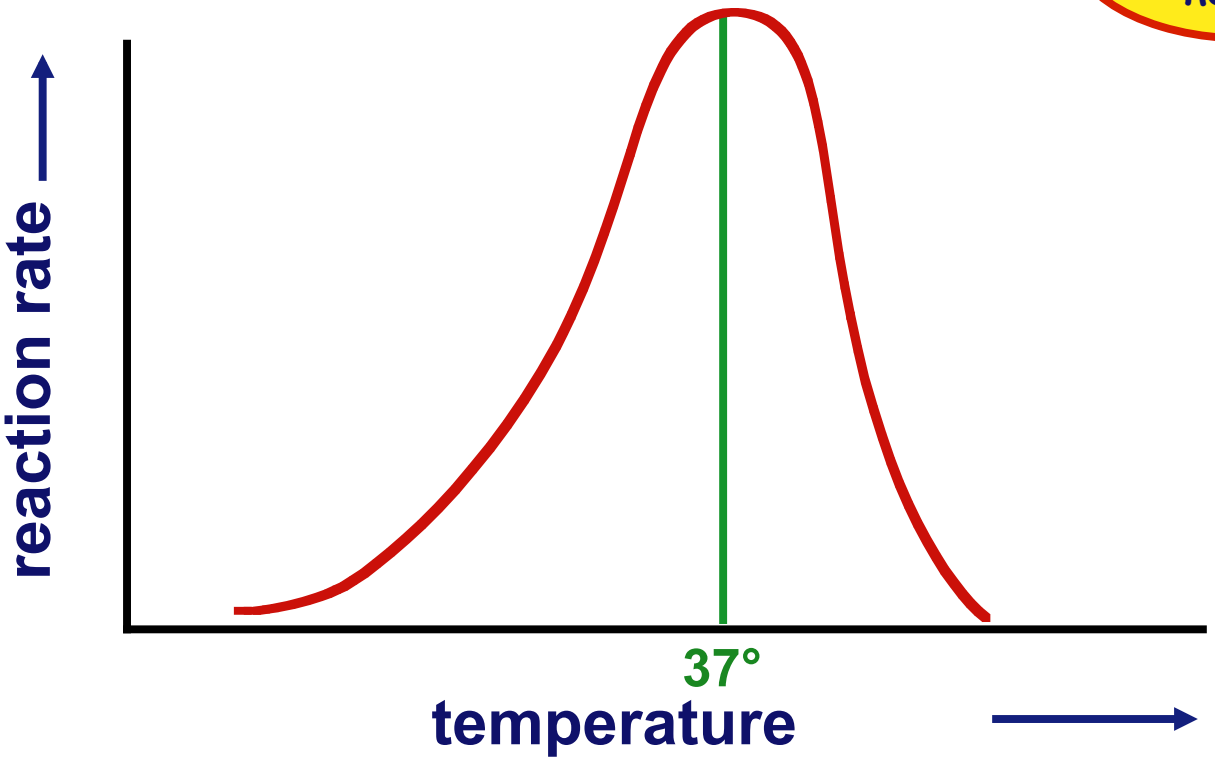


Substrate concentration

- Effect on rates of enzyme activity
  - as ↑ substrate = ↑ reaction rate
    - more substrate = more frequently collide with enzymes
  - reaction rate levels off
    - all enzymes have active site engaged
    - enzyme is saturated
    - maximum rate of reaction



Temperature

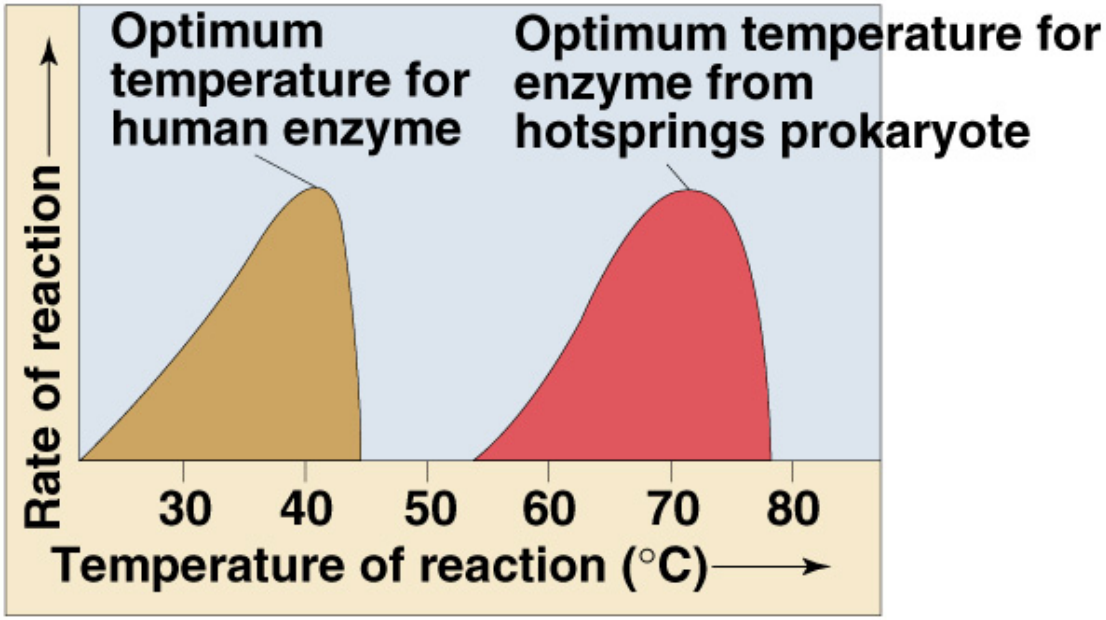


Temperature

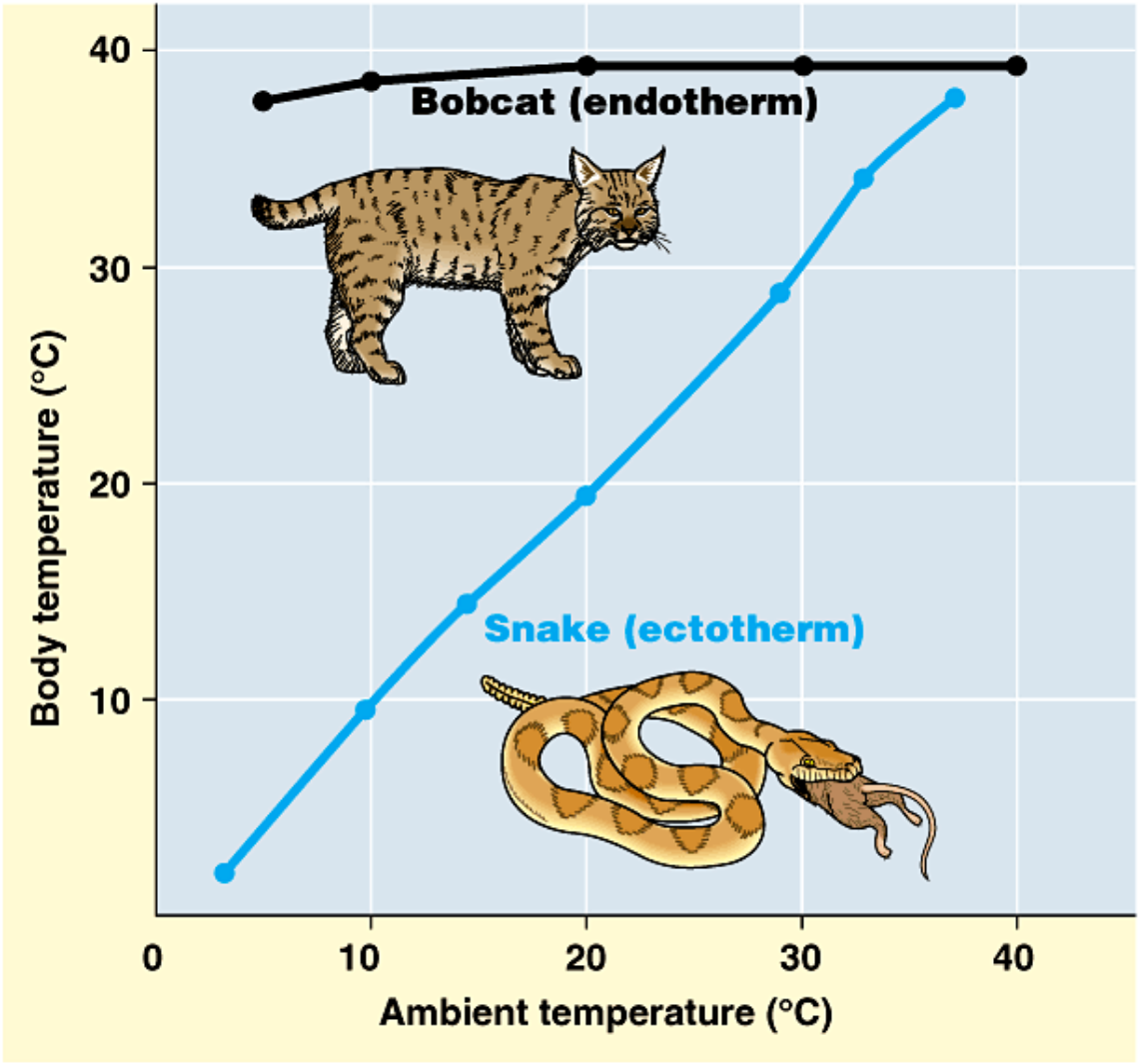
- Effect on rates of enzyme activity
  - Optimum T°
    - greatest number of molecular collisions
    - human enzymes = 35°- 40°C (body temp = 37°C)
  - Increase beyond optimum T°
    - increased agitation of molecules disrupts bonds
      - H, ionic = weak bonds
    - denaturation = lose 3D shape (3° structure)
  - Decrease T°
    - molecules move slower
    - decrease collisions

Enzymes and temperature

- Different enzymes functional in different organisms

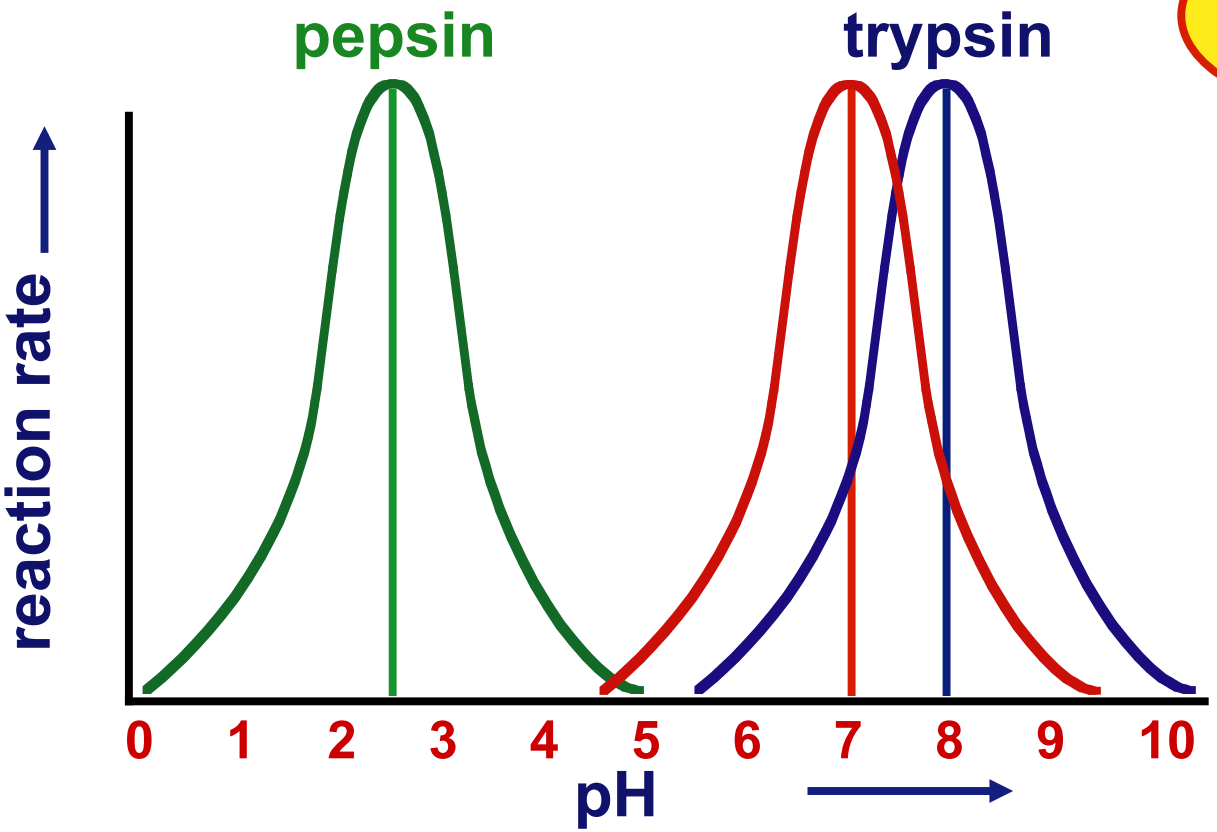


How do ectotherms do it?



pH

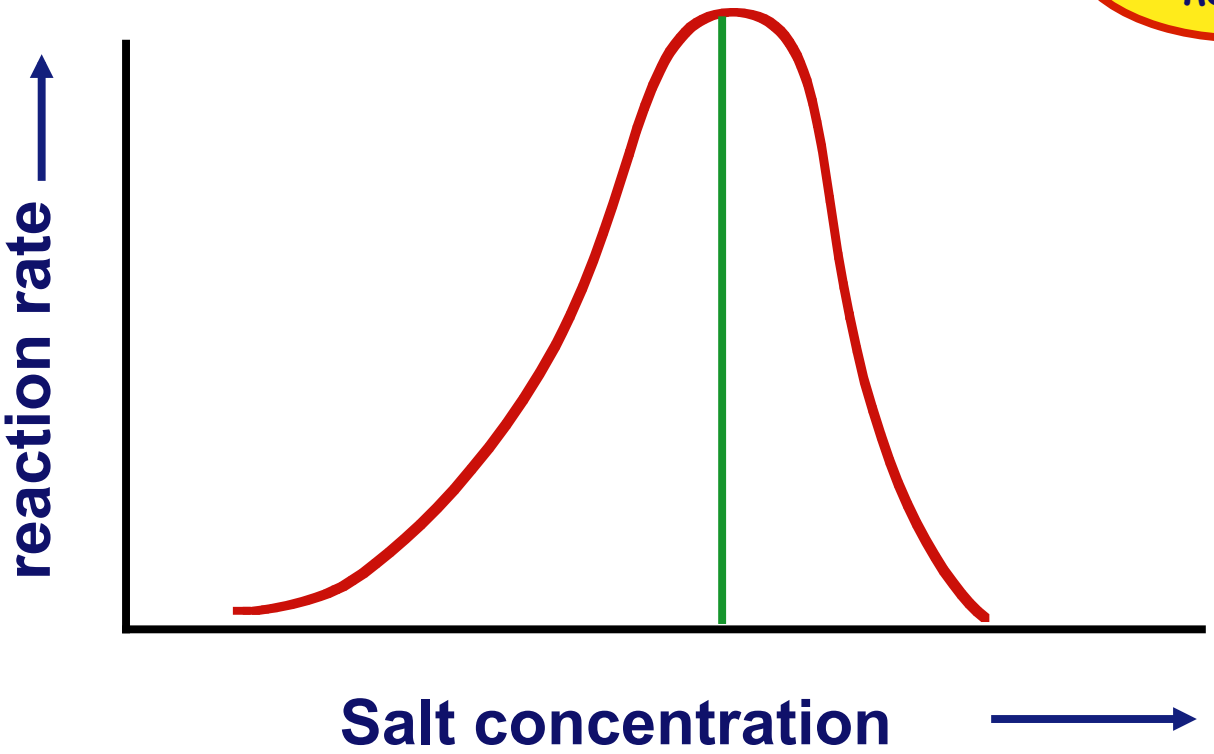

What's happening here?!


pepsin
trypsin
reaction rate
0
1
2
3
4
5
6
7
8
9
10
pH

pH

- Effect on rates of enzyme activity
  - protein shape (conformation)
    - attraction of charged amino acids
  - pH changes
    - changes charges (add or remove H^+)
    - disrupt bonds, disrupt 3D shape
      - affect 3° structure
  - most human enzymes = pH 6-8
    - depends on localized conditions
    - pepsin (stomach) = pH 3
    - trypsin (small intestines) = pH 8

Salinity

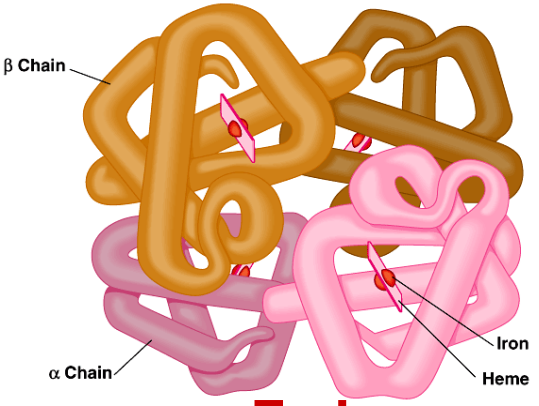


Salt concentration

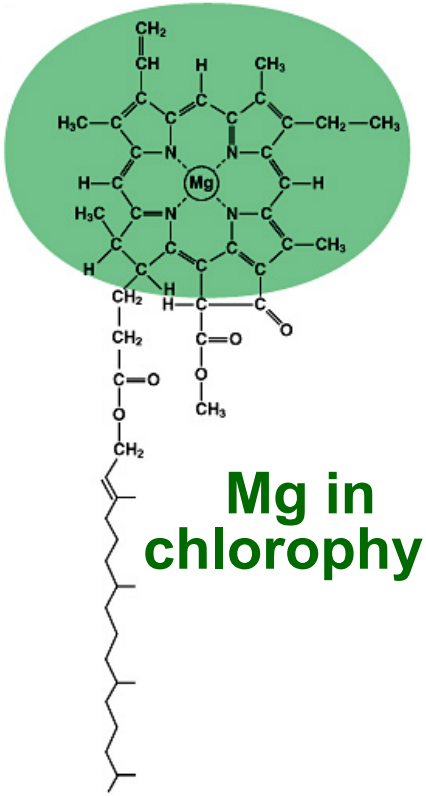
- Effect on rates of enzyme activity
  - protein shape (conformation)
    - depends on attraction of charged amino acids
  - salinity changes
    - change [inorganic ions]
    - changes charges (add + or –)
    - disrupt bonds, disrupt 3D shape
      - affect 3° structure
  - enzymes intolerant of extreme salinity
    - Dead Sea is called dead for a reason!

Activators

- Compounds which help enzymes
- Cofactors
  - non-protein, small inorganic compounds & ions
    - Mg, K, Ca, Zn, Fe, Cu
    - bound in enzyme molecule
- Coenzymes
  - non-protein, organic molecules
    - bind temporarily or permanently to enzyme near active site
  - many vitamins
    - NAD (niacin; B3)
    - FAD (riboflavin; B2)
    - Coenzyme A



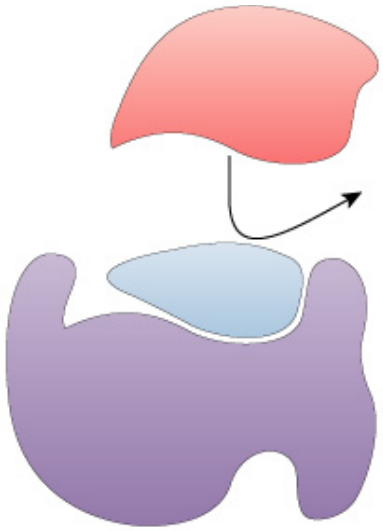
Fe in hemoglobin



Mg in chlorophyll

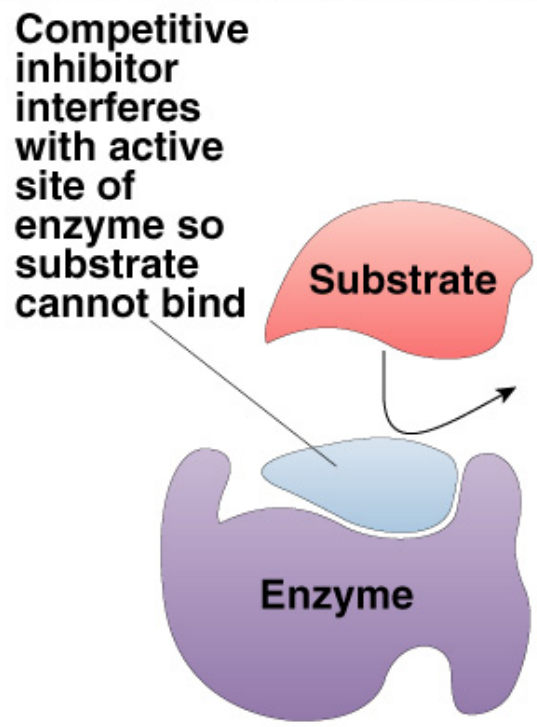
Inhibitors

- Regulation of enzyme activity
  - other molecules that affect enzyme activity
- Selective inhibition & activation
  - competitive inhibition
  - noncompetitive inhibition
  - irreversible inhibition
  - feedback inhibition



Competitive Inhibitor

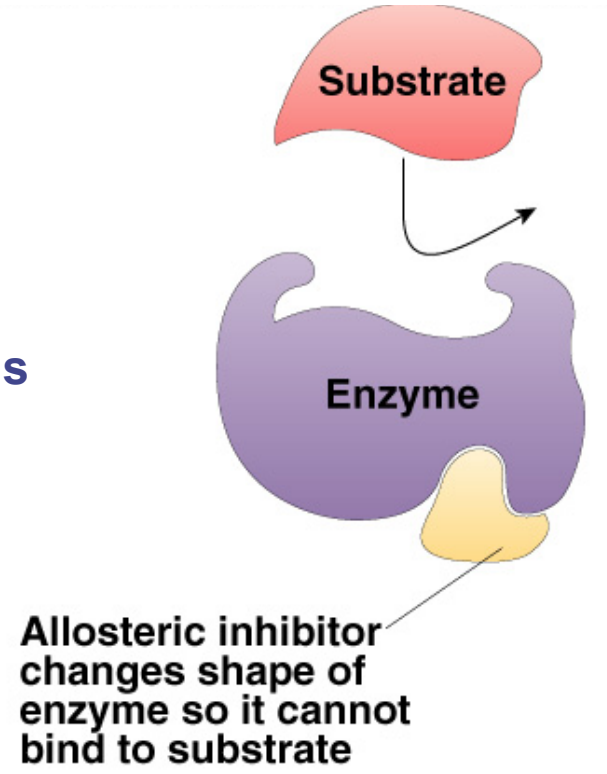
- **Effect**
  - inhibitor & substrate "compete" for active site
    - ex: penicillin blocks enzyme that bacteria use to build cell walls
    - ex: disulfiram (Antabuse) to overcome alcoholism
    - ex: methanol poisoning
  - overcome by increasing substrate concentration
    - saturate solution with substrate so it out-competes inhibitor for active site on enzyme



(a) Competitive inhibition

Non-Competitive Inhibitor

- **Effect**
  - inhibitor binds to site other than active site
    - allosteric site
    - called allosteric inhibitor
      - ex: some anti-cancer drugs inhibit enzymes involved in synthesis of nucleotides & therefore in building of DNA = stop DNA production, stop division of more cancer cells
      - ex: heavy metal poisoning
      - ex: cyanide poisoning
    - causes enzyme to change shape
      - conformational change
    - renders active site unreceptive



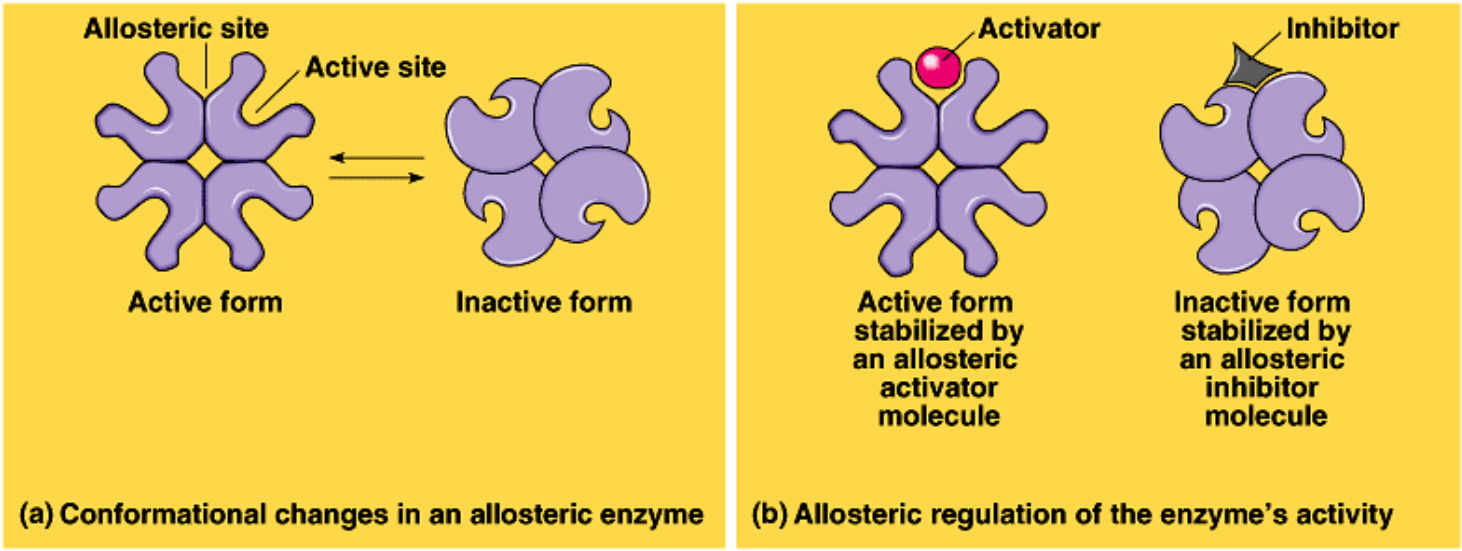
(b) Noncompetitive inhibition

Irreversible inhibition

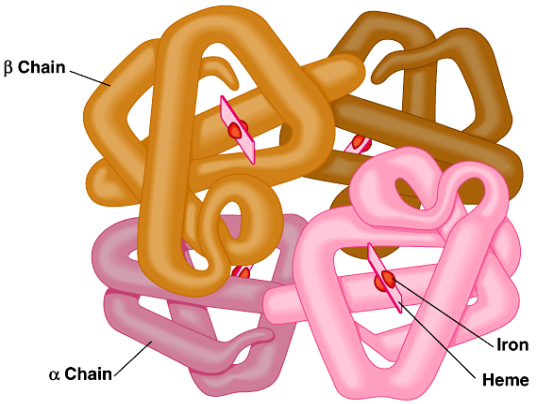
- Inhibitor permanently binds to enzyme
  - competitor
    - permanently binds to active site
  - allosteric
    - permanently changes shape of enzyme
    - ex: nerve gas, sarin, many insecticides (malathion, parathion…)
      - cholinesterase inhibitors
        doesn't breakdown the neurotransmitter, acetylcholine

Action of Allosteric control

- Inhibitors & activators
  - regulatory molecules attach to allosteric site causing conformational (shape) change
  - inhibitor keeps enzyme in inactive form
  - activator keeps enzyme in active form

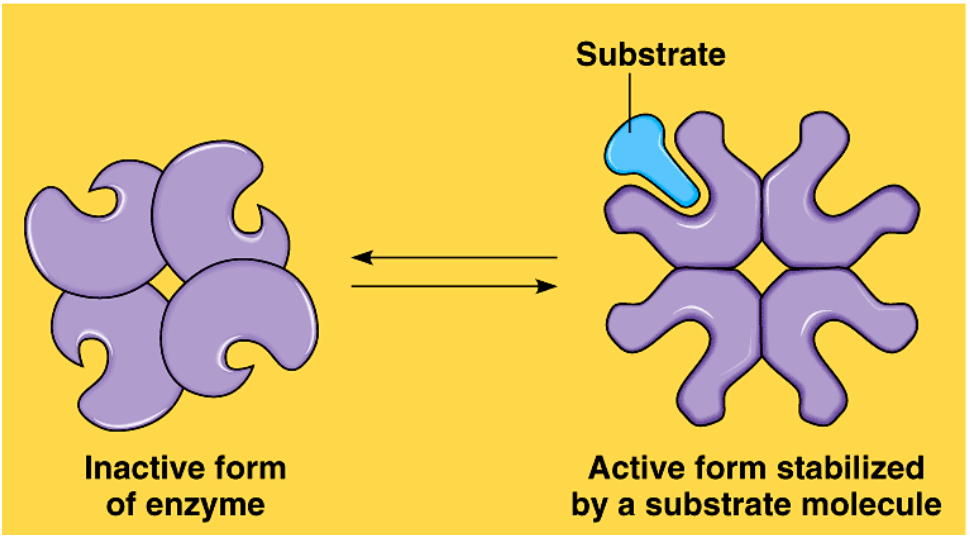


Cooperativity

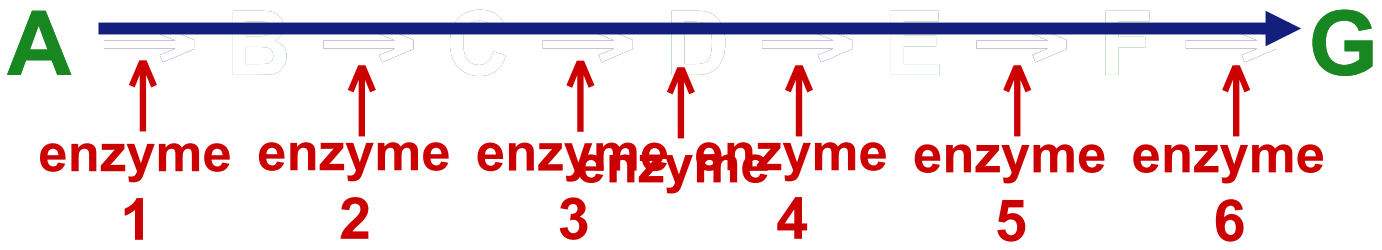


- Substrate acts as an activator
  - substrate causes conformational change in enzyme
    - induced fit
  - favors binding of substrate at 2nd site
  - makes enzyme more active & effective
    - ex: hemoglobin

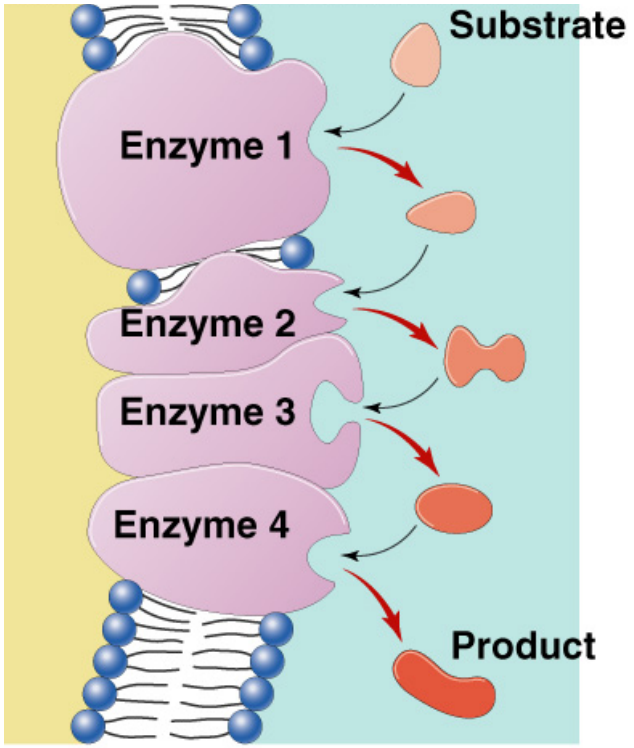
4 polypeptide chains:
- bind 4 O_2;
- 1st O_2 binds
- makes it easier for other 3 O_2 to bind



Metabolic pathways

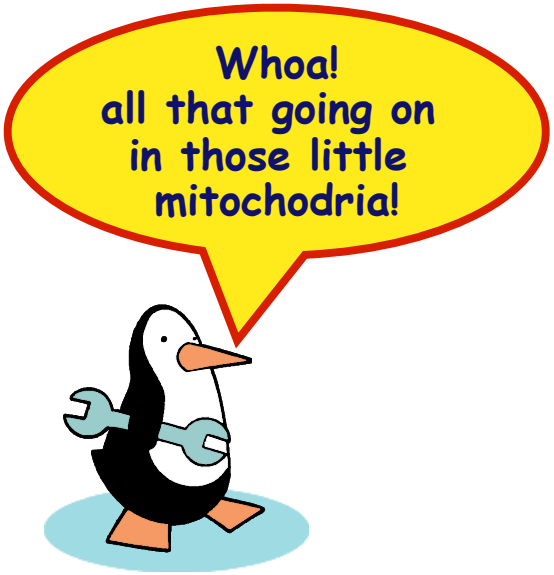


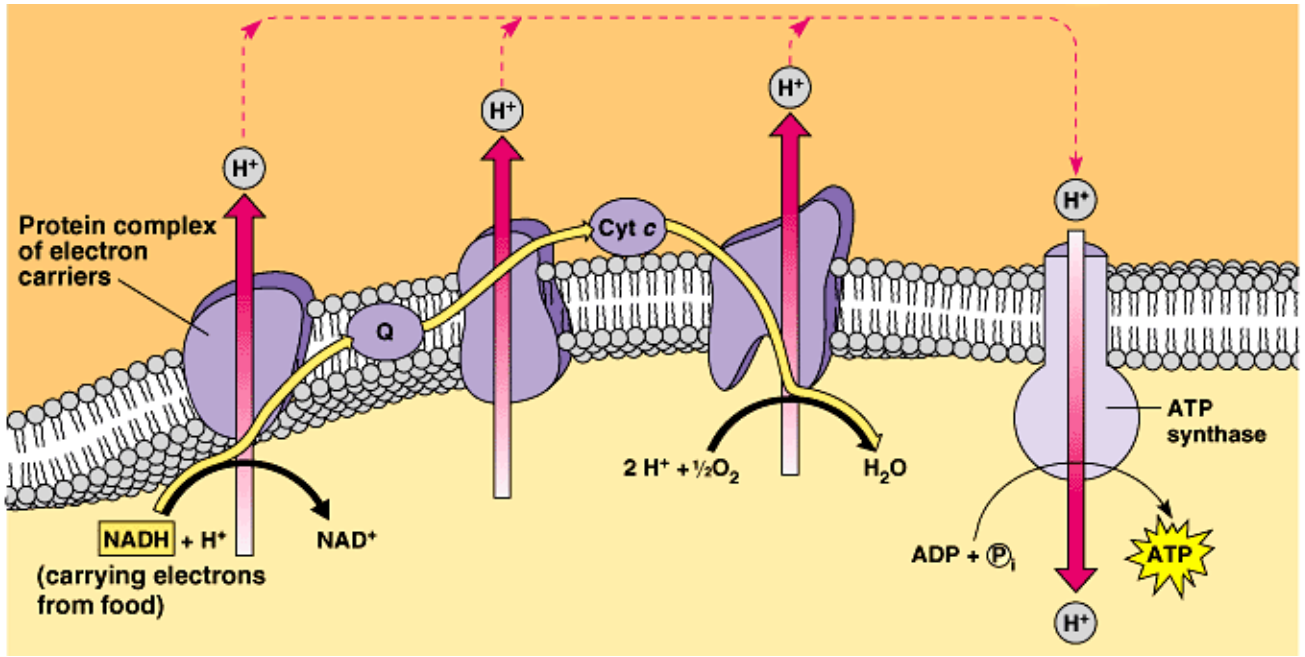
- Chemical reactions of life are organized in pathways
  - divide chemical reaction into many small steps
    - efficiency
    - control = regulation



Efficiency

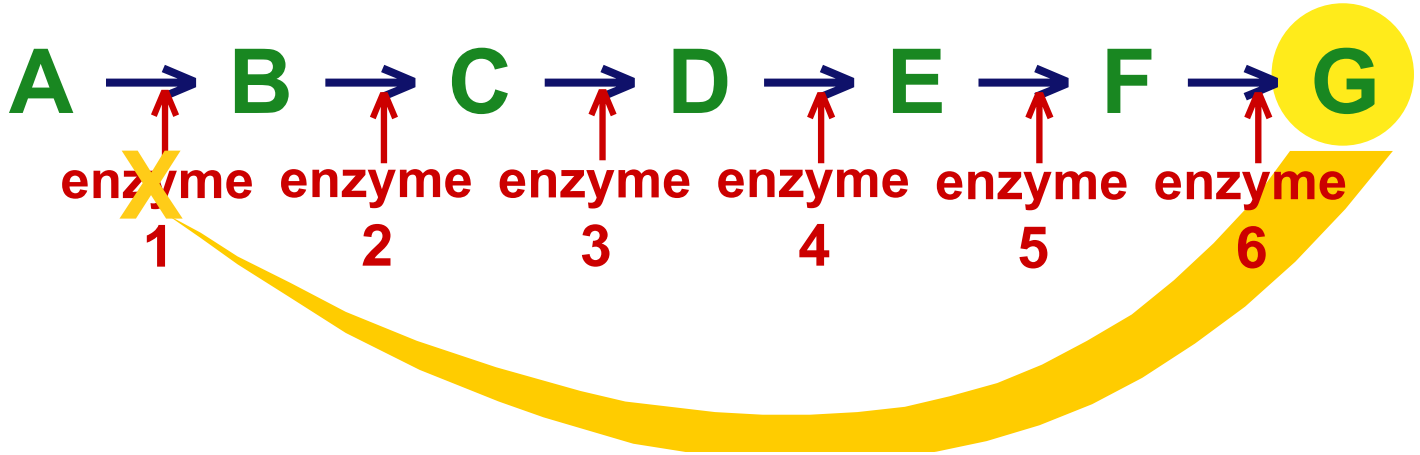
- Groups of enzymes organized
  - if enzymes are embedded in membrane they are arranged sequentially
- Link endergonic & exergonic reactions





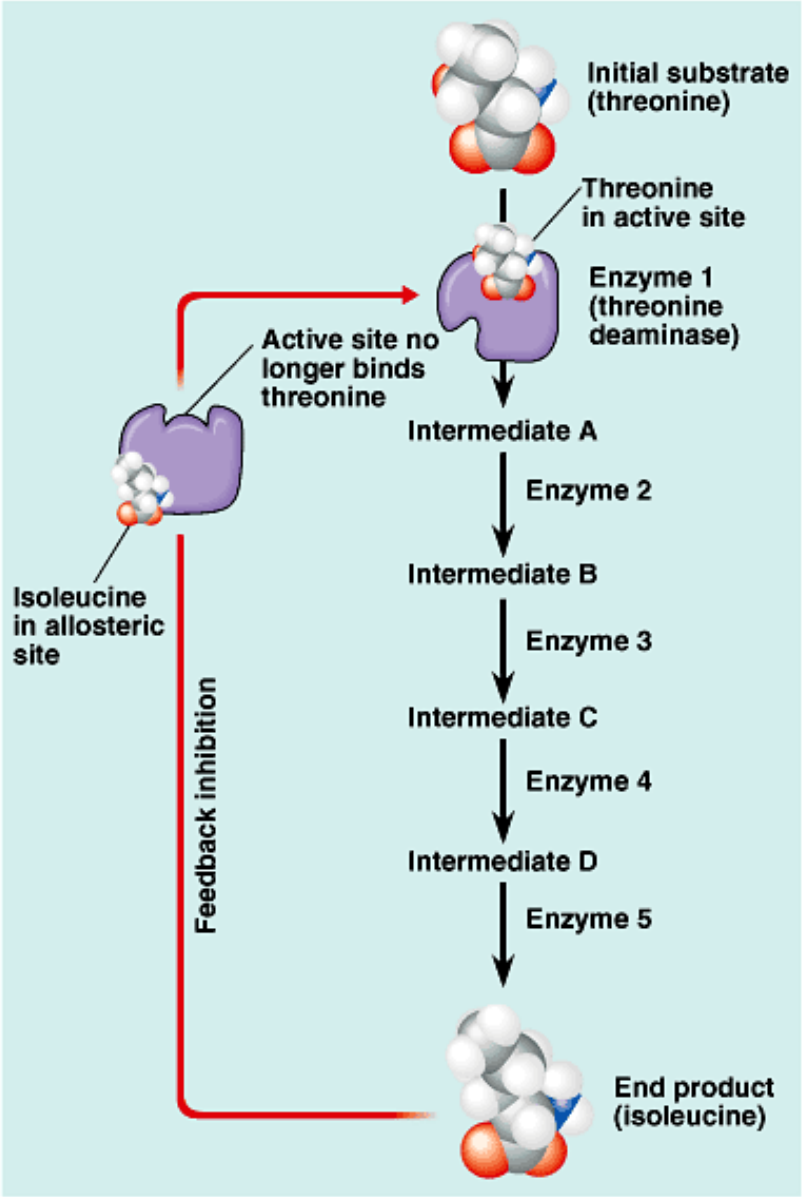
Feedback Inhibition

- **Regulation & coordination of production**
  - product is used by next step in pathway
  - final product is inhibitor of earlier step
    - allosteric inhibitor of earlier enzyme
    - feedback inhibition
  - no unnecessary accumulation of product



Feedback inhibition

- Example
  - synthesis of amino acid, isoleucine from amino acid, threonine



Any Questions??