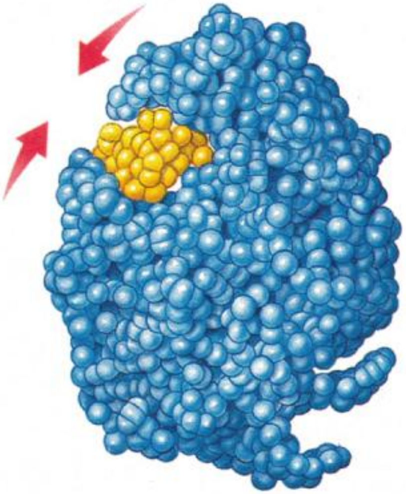
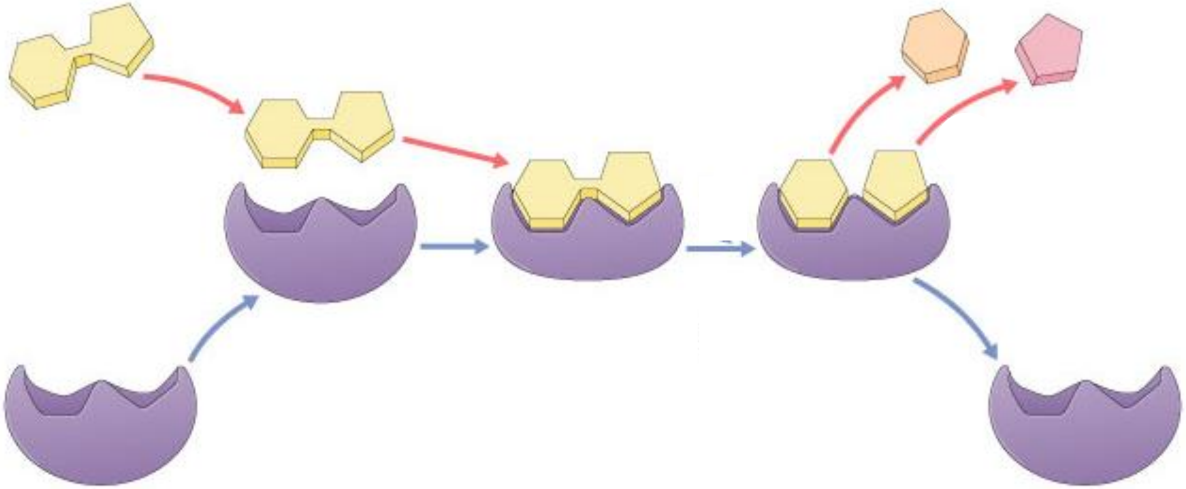
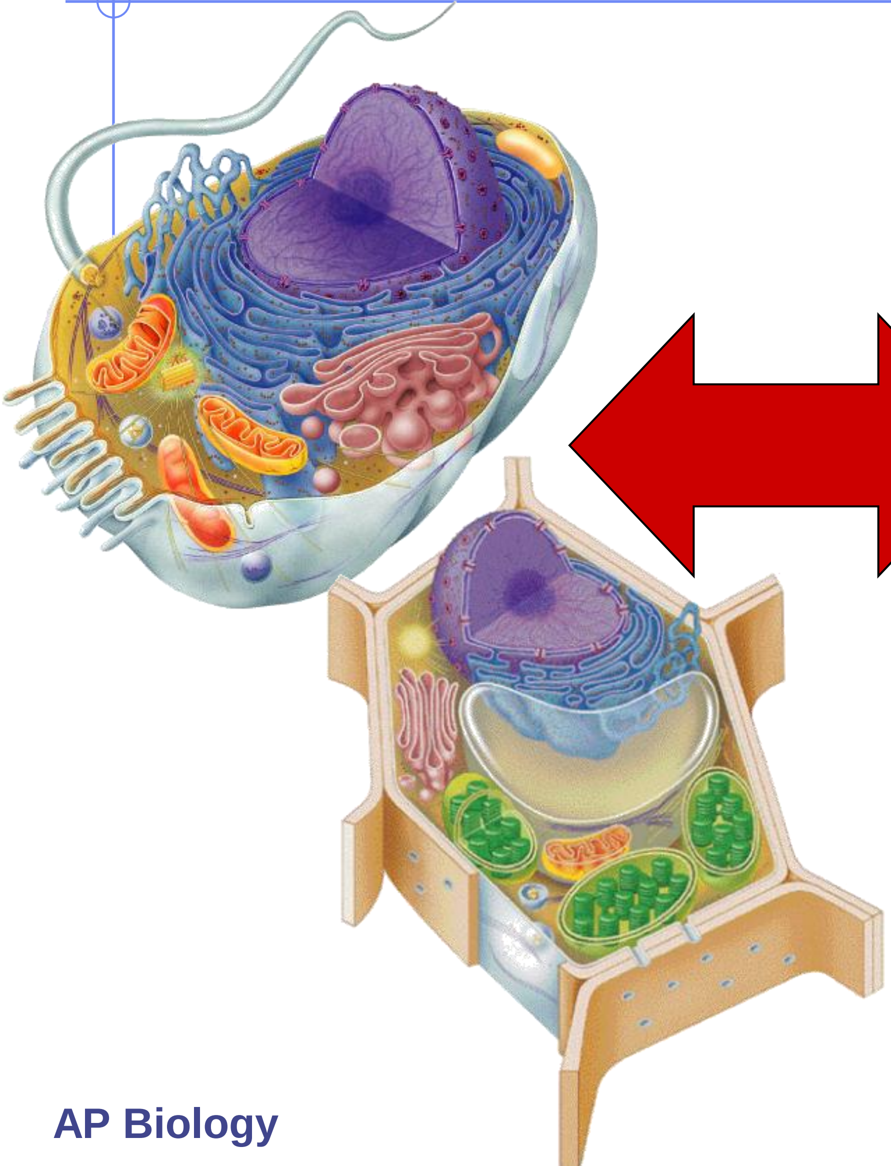
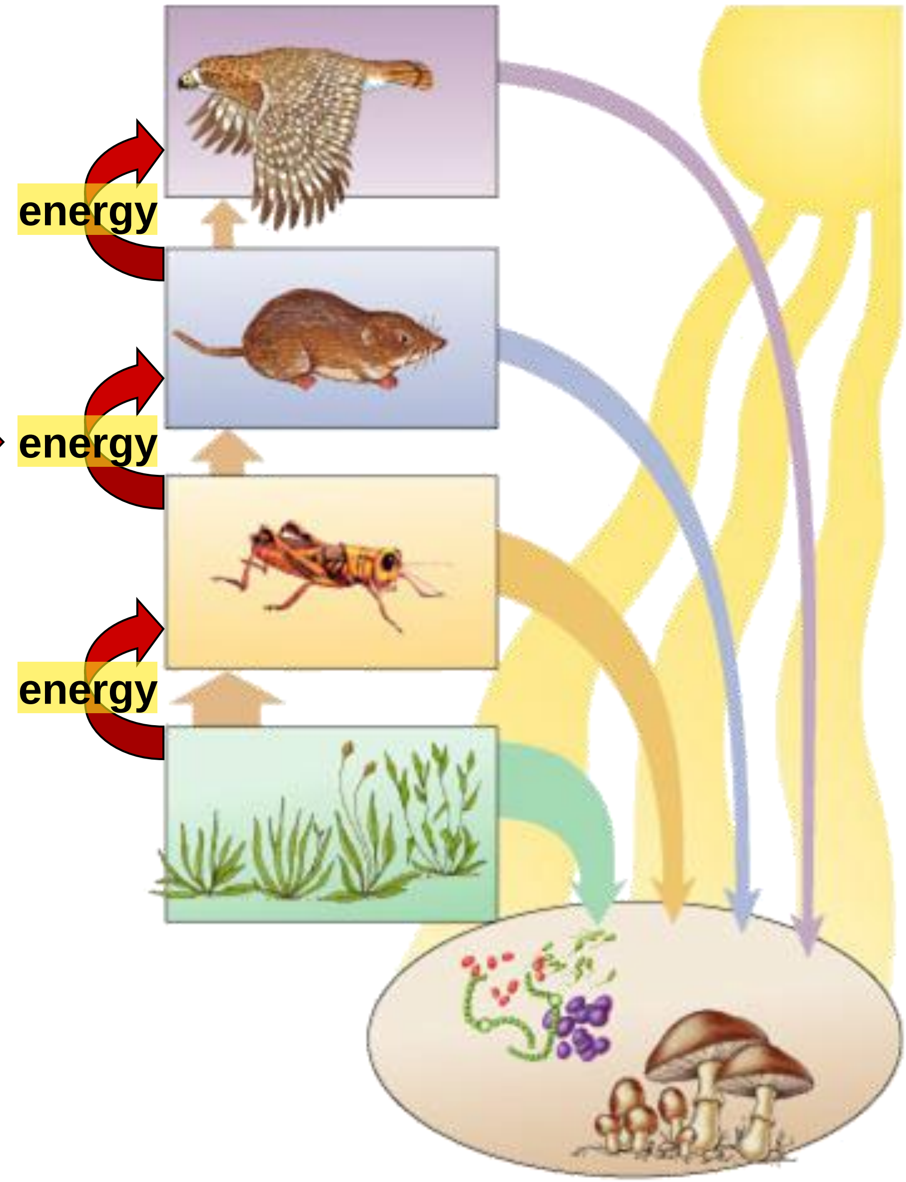


Metabolism & Enzymes



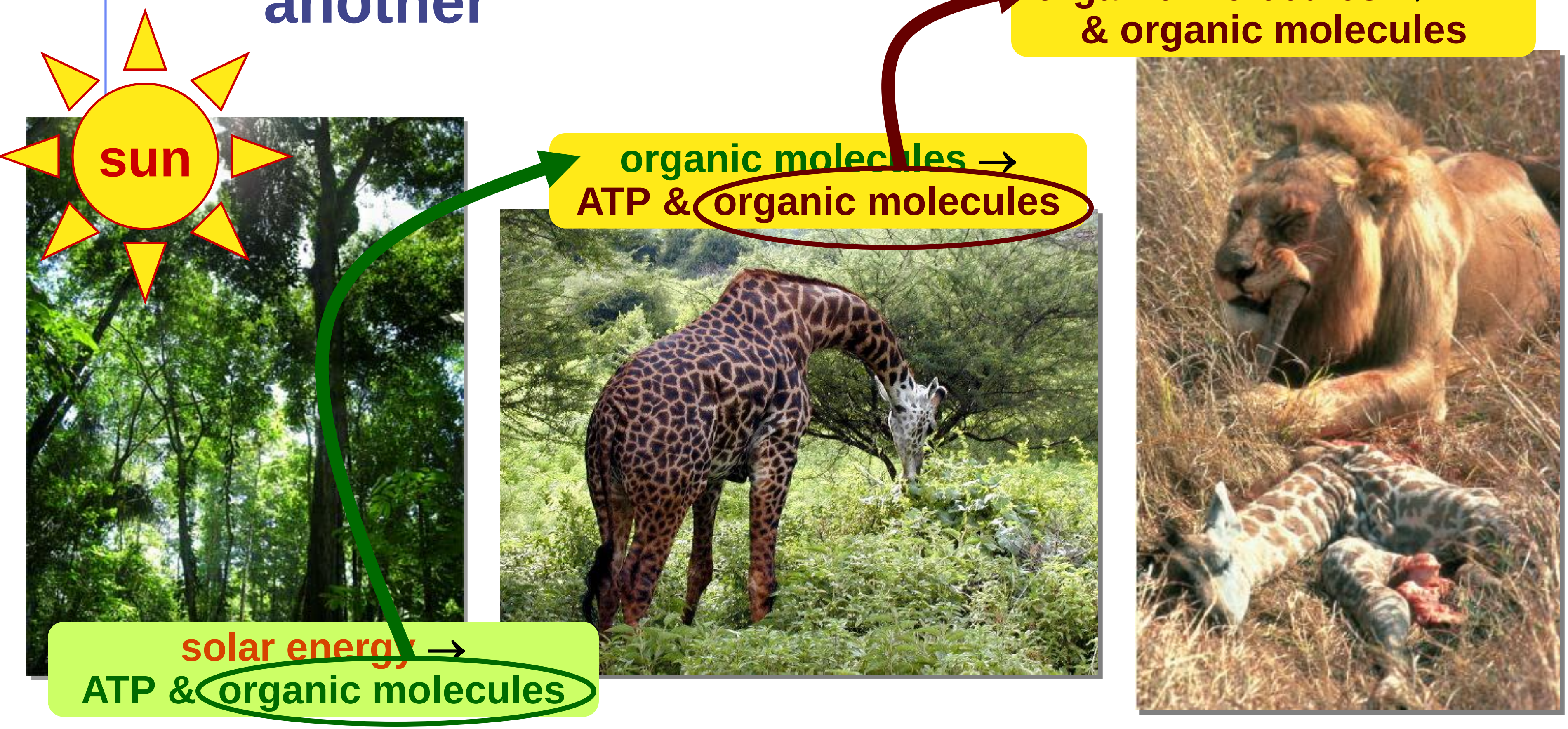
From food webs to the life of a cell





Flow of energy through life

- **Life is built on chemical reactions**
  - transforming energy from one form to another

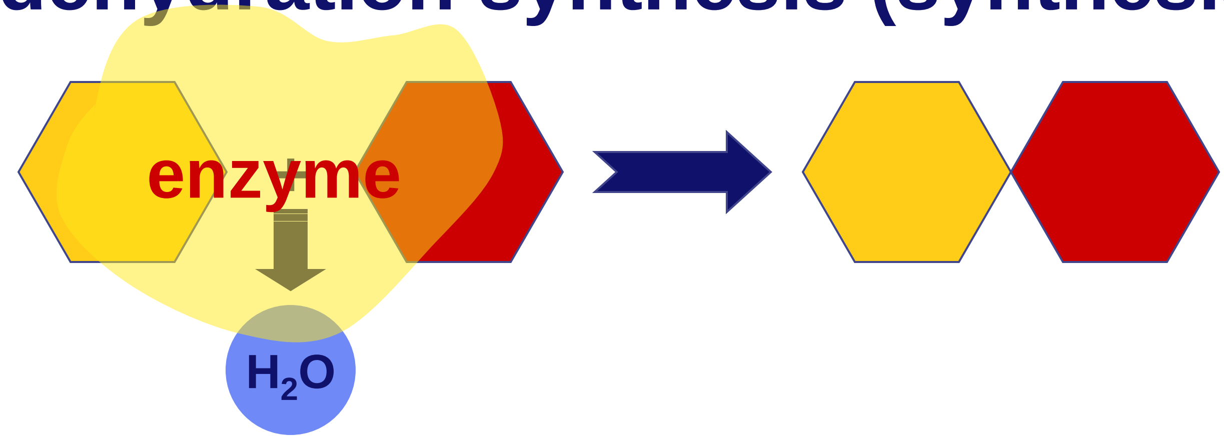


Metabolism

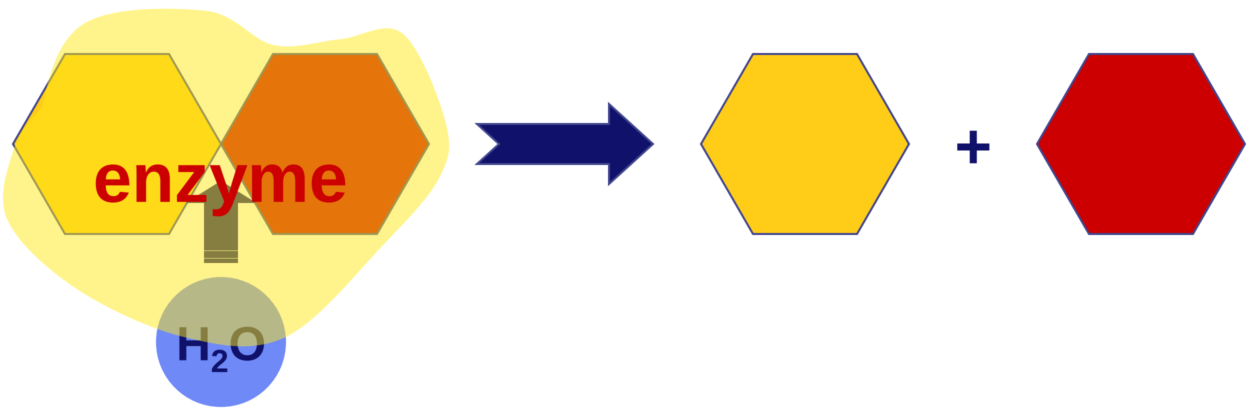
- Chemical reactions of life
  - <u>forming bonds</u> between molecules
    - dehydration synthesis
    - synthesis
    - <u>anabolic reactions</u>
  - <u>breaking bonds</u> between molecules
    - hydrolysis
    - digestion
    - <u>catabolic reactions</u>

Examples

- **dehydration synthesis (synthesis)**

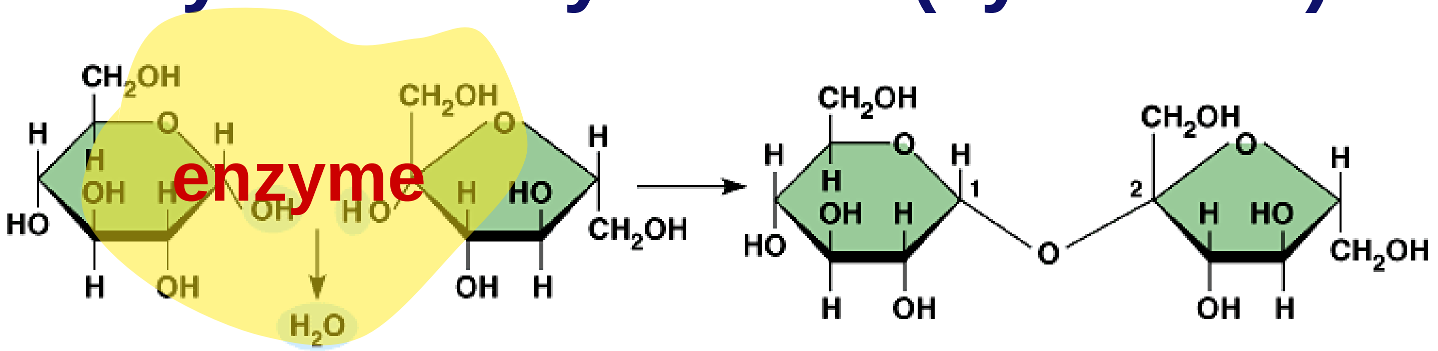


- **hydrolysis (digestion)**

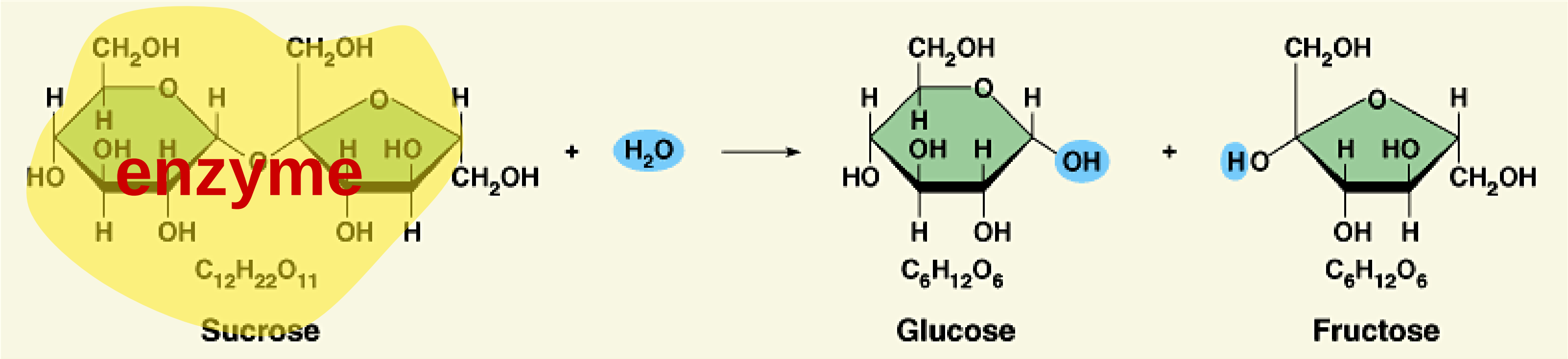


Examples

- dehydration synthesis (synthesis)

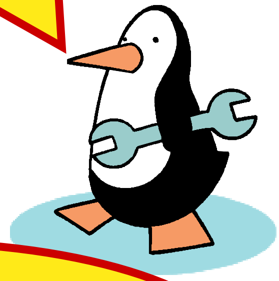


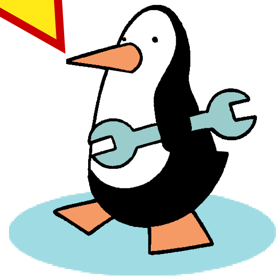
- hydrolysis (digestion)



Chemical reactions & energy

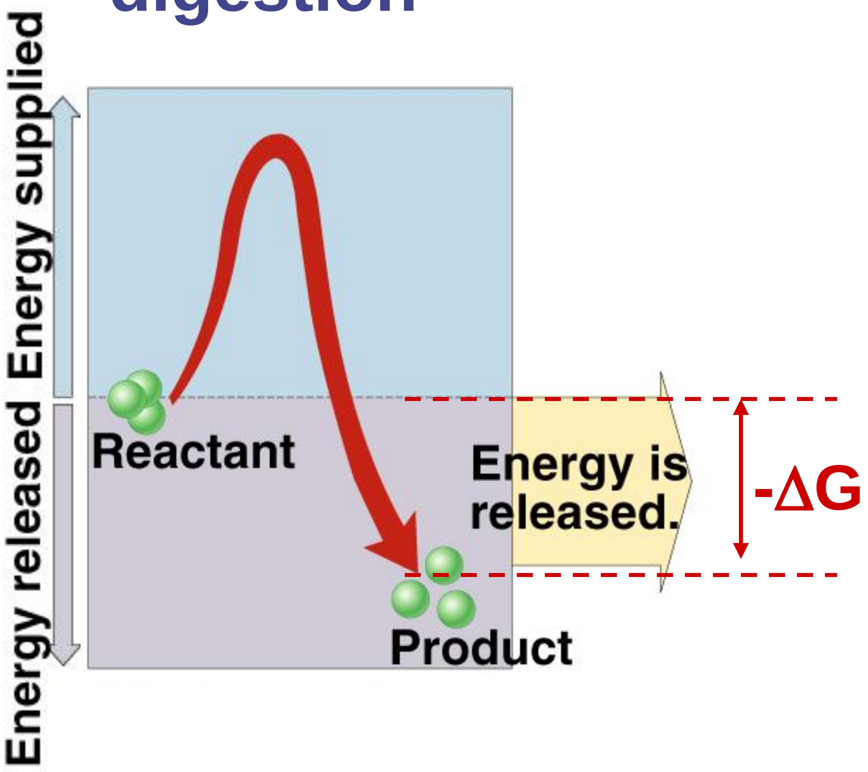
- Some chemical reactions **release energy**
  - **exergonic**
  - digesting polymers
  - hydrolysis = catabolism
- Some chemical reactions require **input of energy**
  - **endergonic**
  - building polymers
  - dehydration synthesis = anabolism



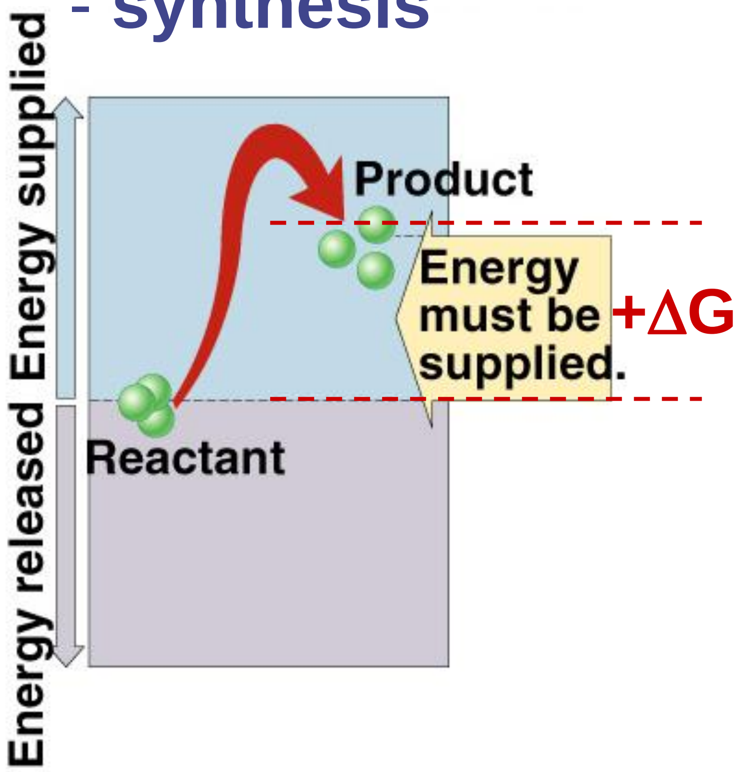


Endergonic vs. exergonic reactions

exergonic
- energy released
- digestion



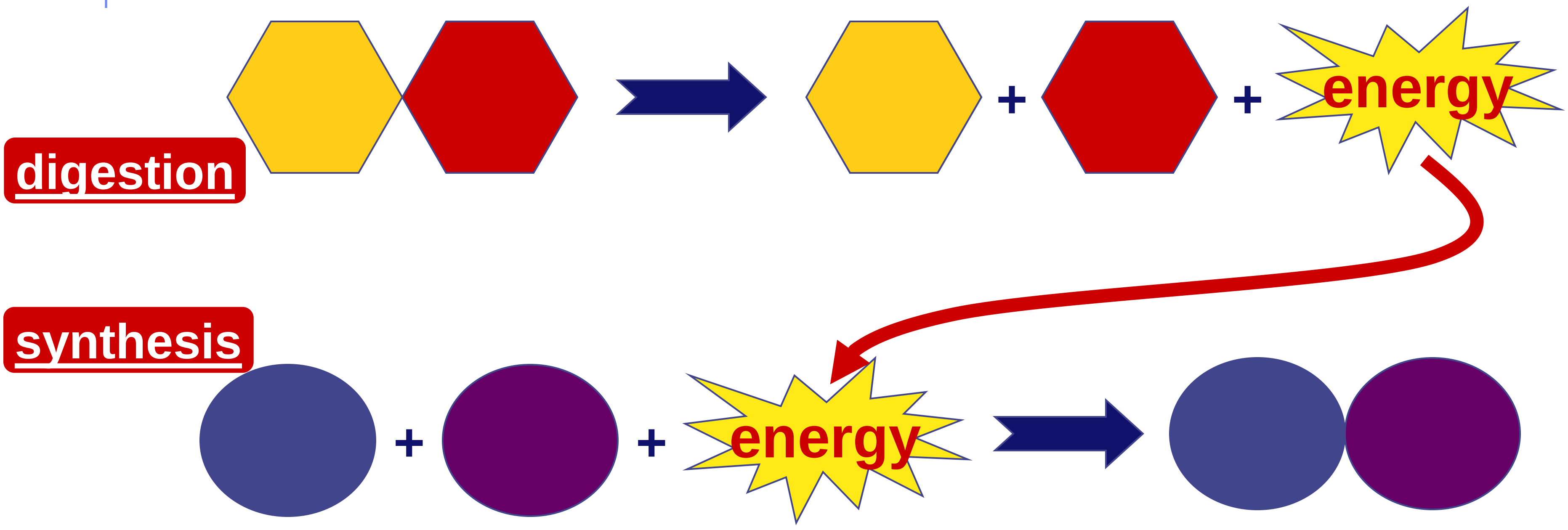
endergonic
- energy invested
- synthesis



ΔG = change in free energy = ability to do work

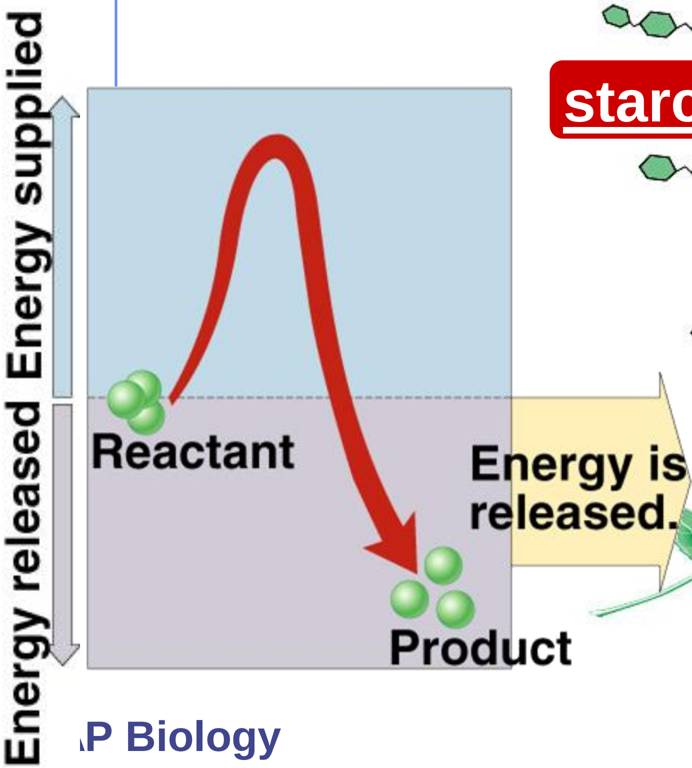
Energy & life

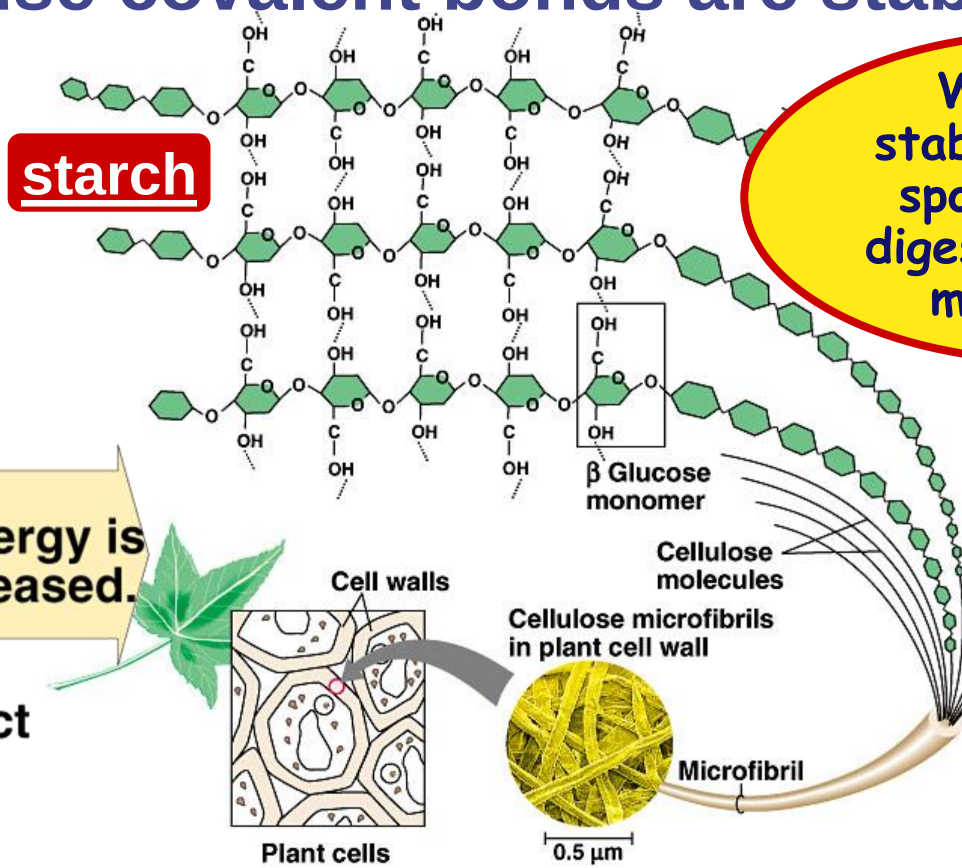
- **Organisms require energy to live**
  - **where does that energy come from?**
    - **coupling exergonic reactions (releasing energy) with endergonic reactions (needing energy)**

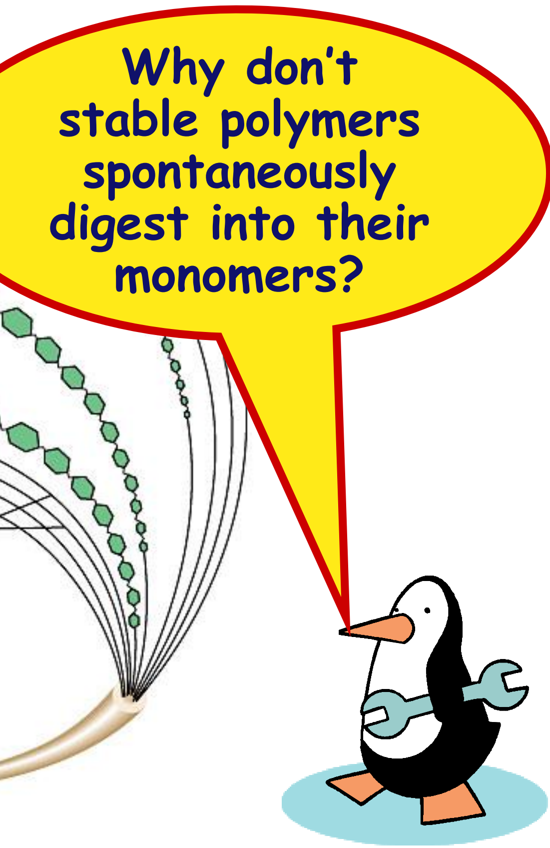


What drives reactions?

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

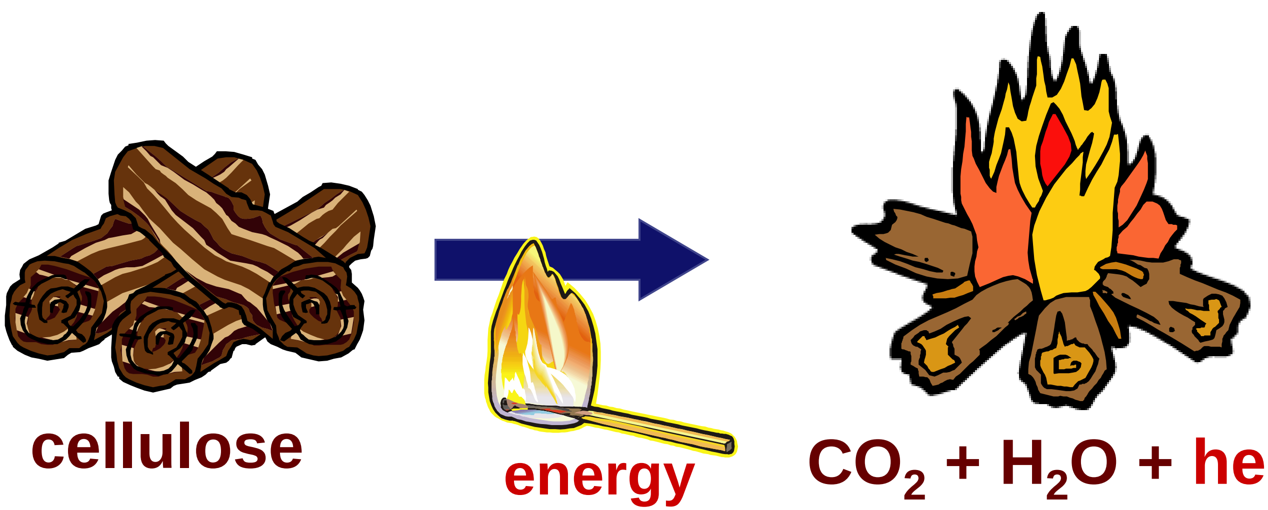






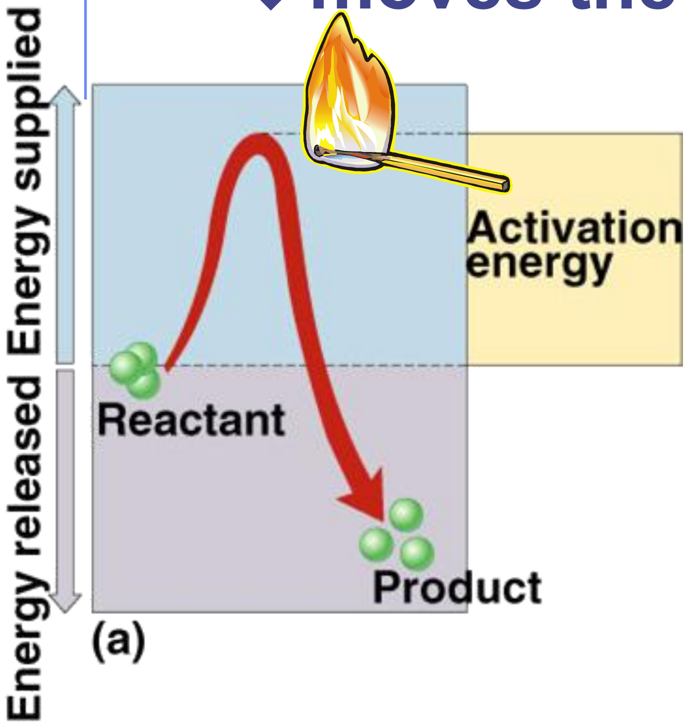
Activation energy

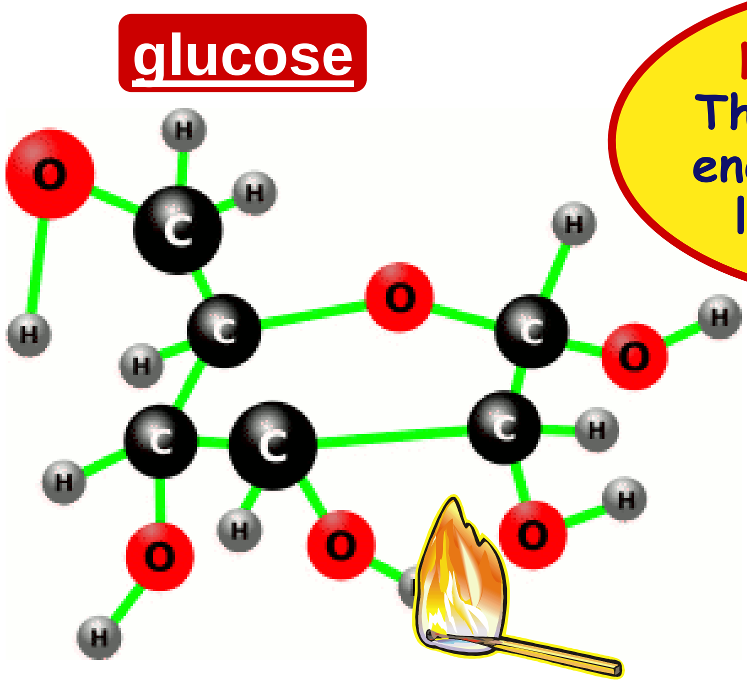
- **Breaking down large molecules requires an initial input of energy**
  - **<u>activation energy</u>**
  - **large biomolecules are stable**
  - **must absorb energy to break bonds**

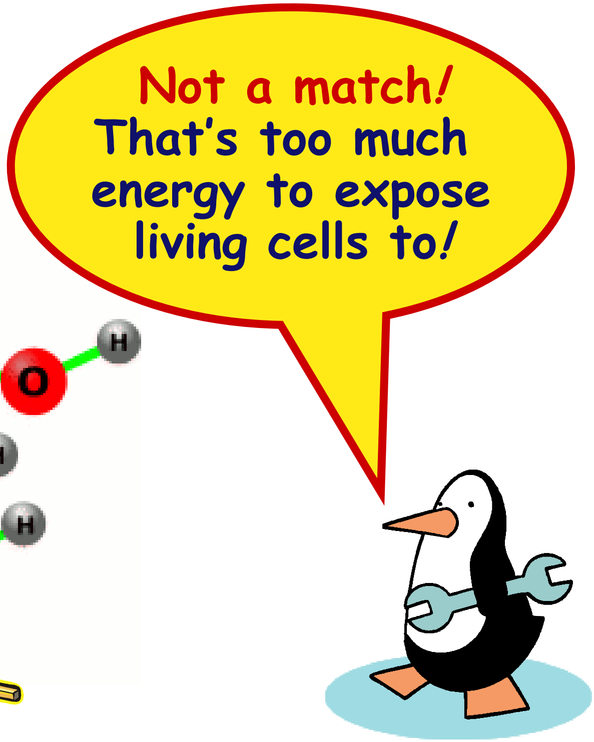


Too much activation energy for life

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

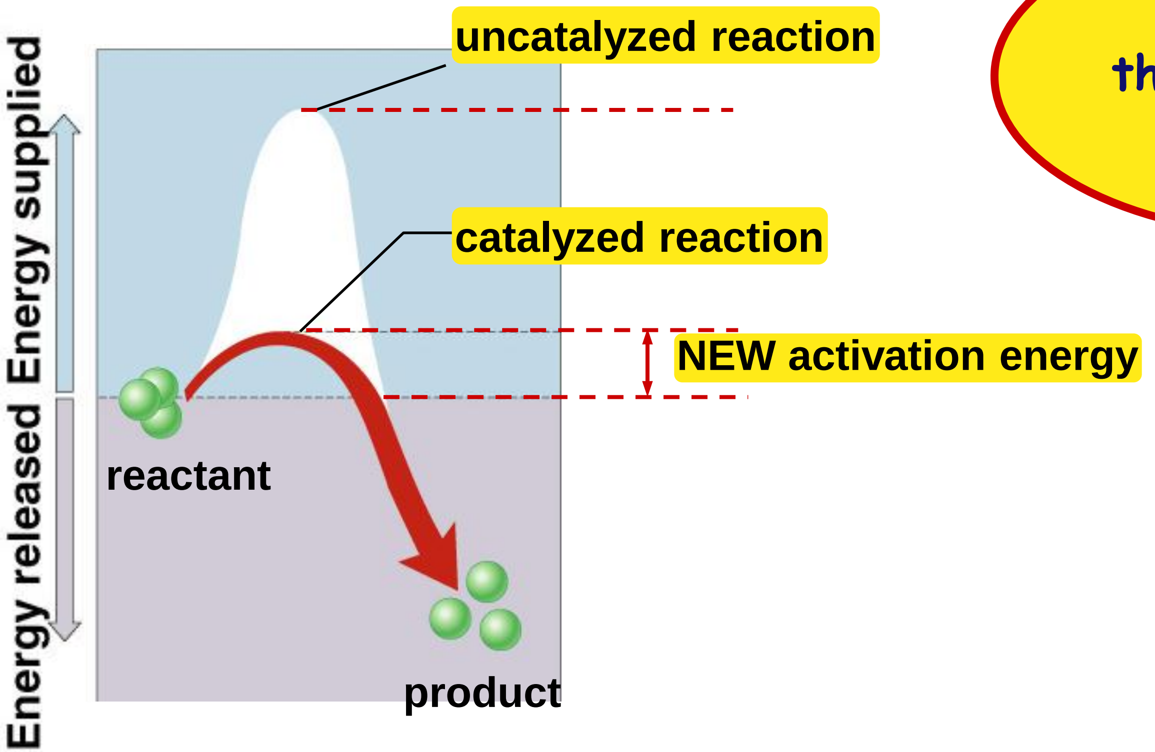


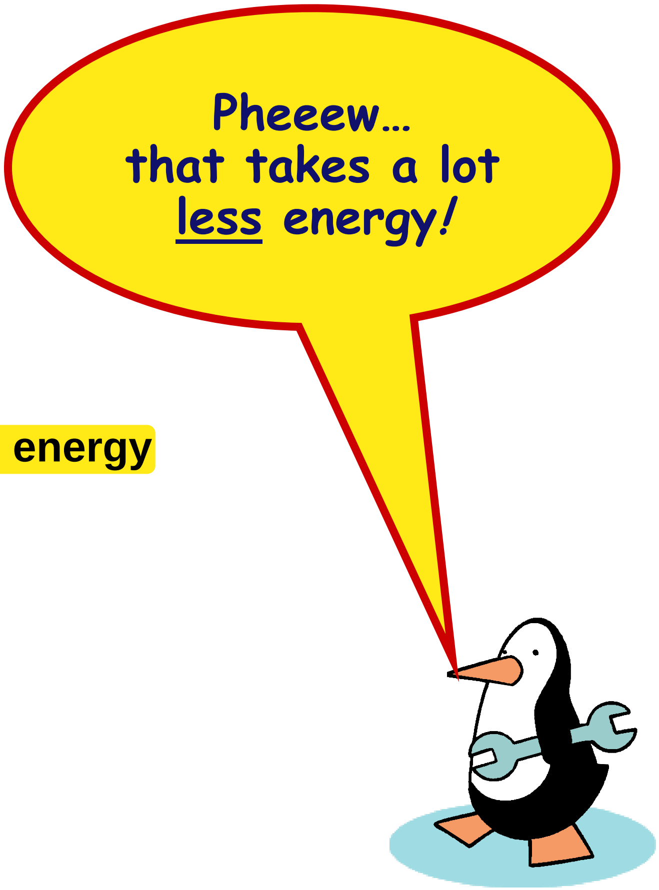




Reducing Activation energy

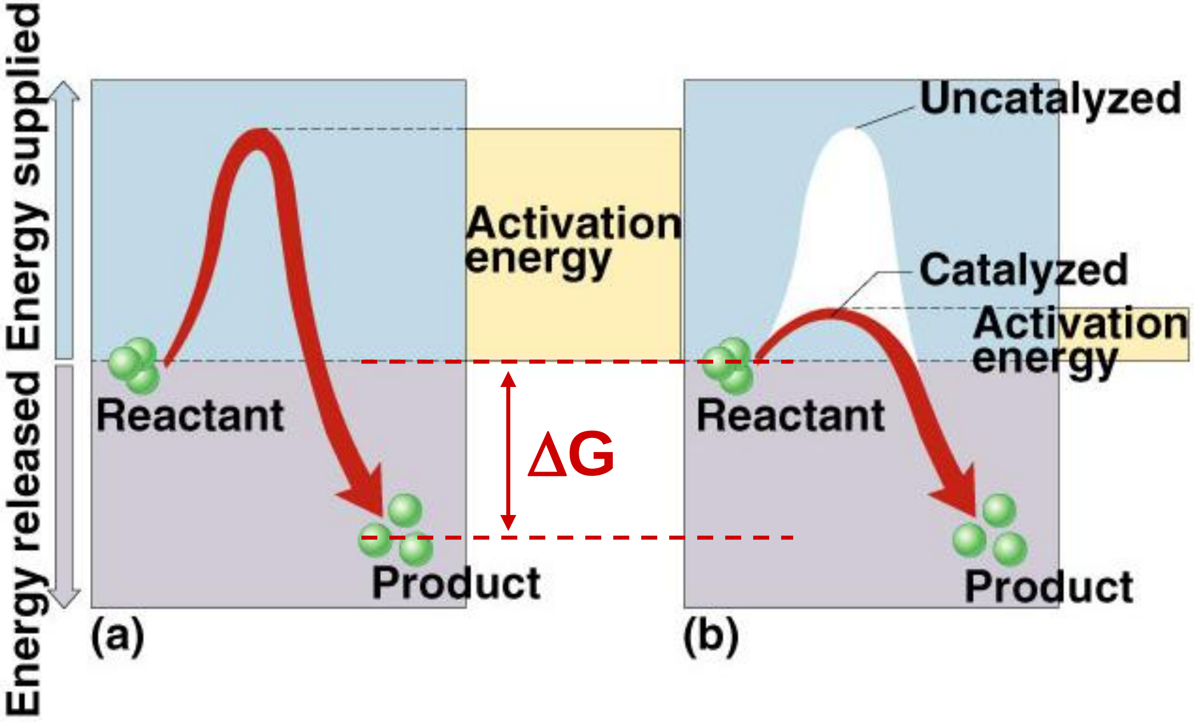
- **Catalysts**
  - reducing the amount of energy to start a reaction





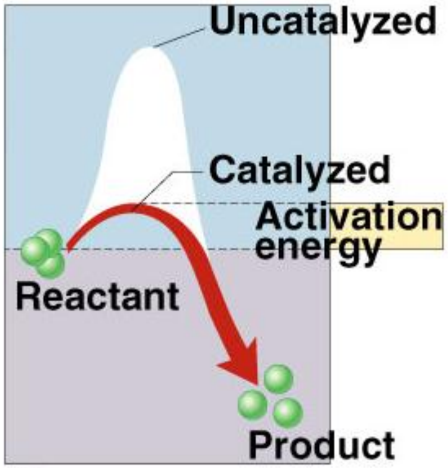
Catalysts

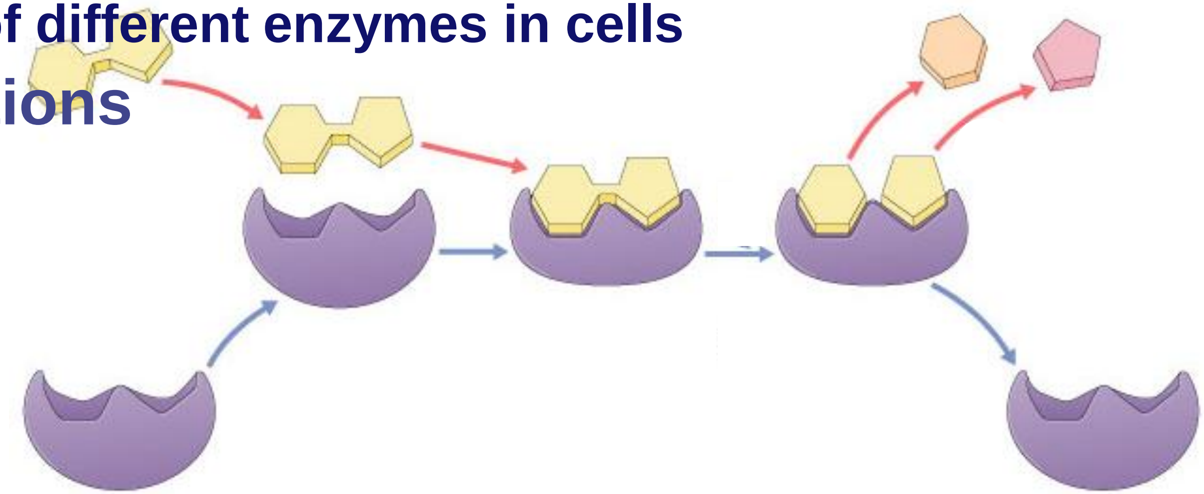
- So what's a cell got to do to reduce activation energy?
  - get help! … chemical help… ENZYMES



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 of life





Enzymes vocabulary

substrate

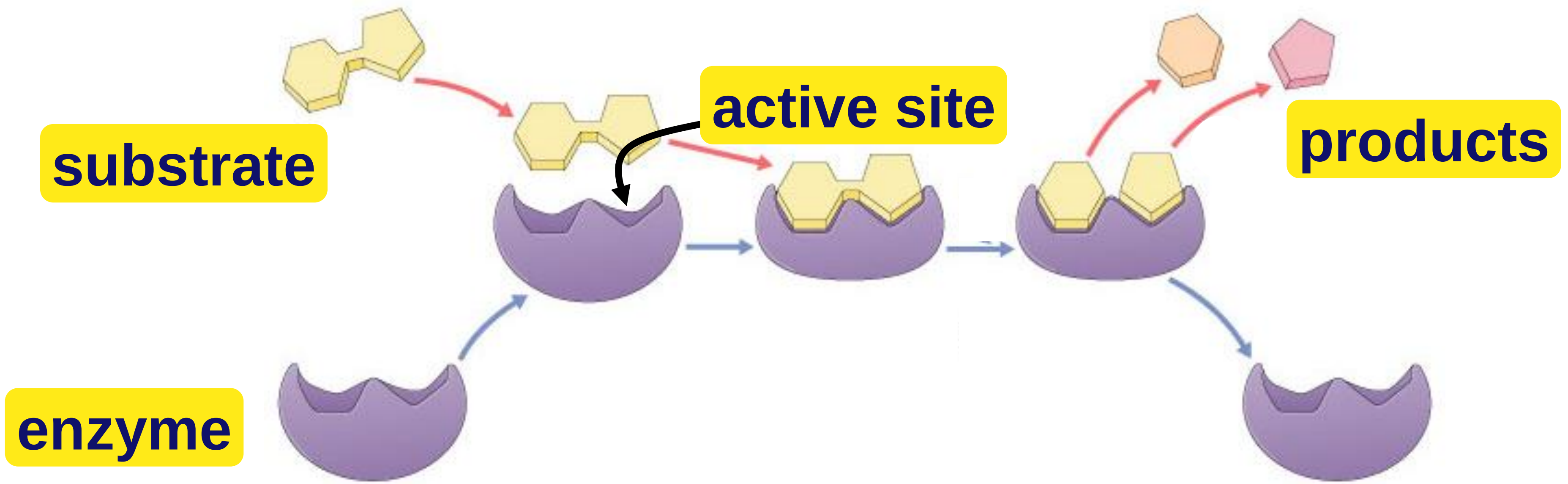
- reactant which binds to enzyme
- enzyme-substrate complex: temporary association

product

- end result of reaction

active site

- enzyme's catalytic site; substrate fits into active site

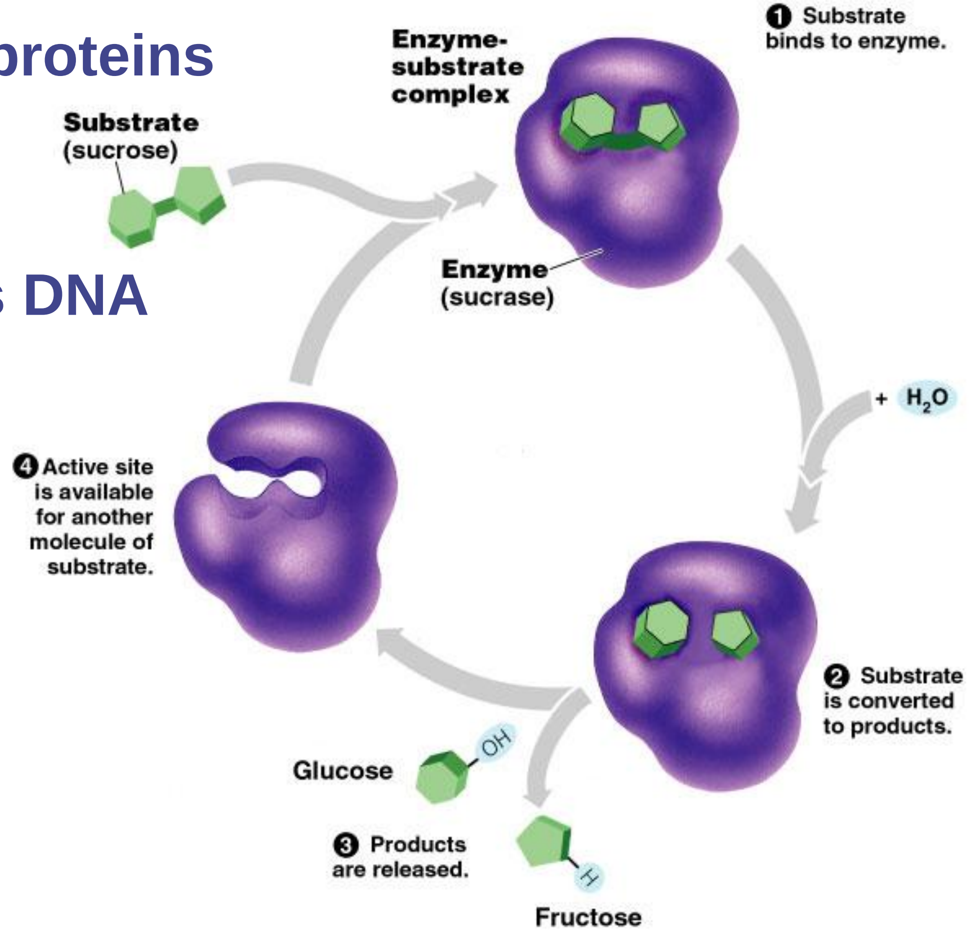


Properties of enzymes

- **Reaction specific**
  - each enzyme works with a specific substrate
    - chemical fit between active site & substrate
      - H bonds & ionic bonds
- **Not consumed in reaction**
  - single enzyme molecule can catalyze thousands or more reactions per second
    - enzymes unaffected by the reaction
- **Affected by cellular conditions**
  - any condition that affects protein structure
    - temperature, pH, salinity

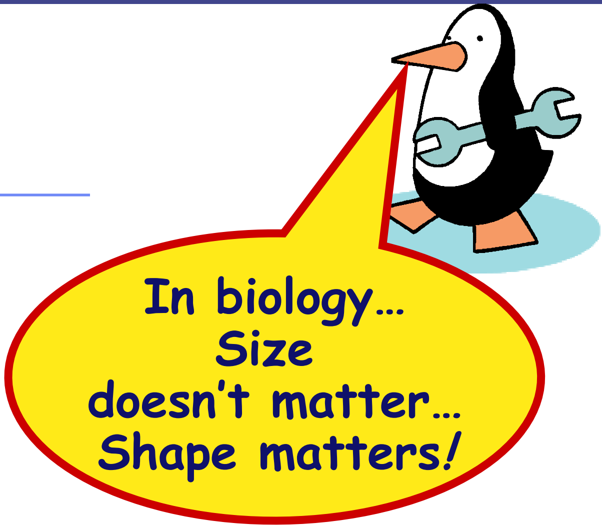
Naming conventions

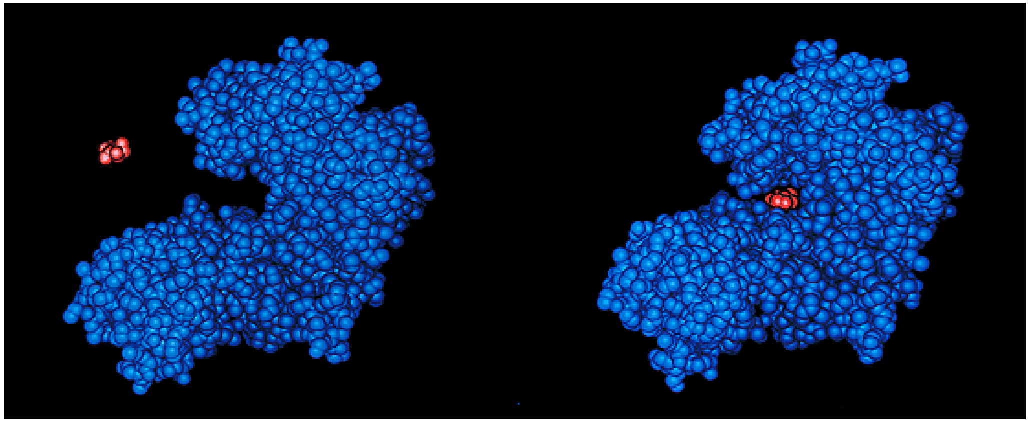
- Enzymes named for reaction they catalyze
  - sucrase breaks down sucrose
  - proteases break down proteins
  - lipases break down lipids
  - DNA polymerase builds DNA
    - adds nucleotides to DNA strand
  - pepsin breaks down proteins (polypeptides)

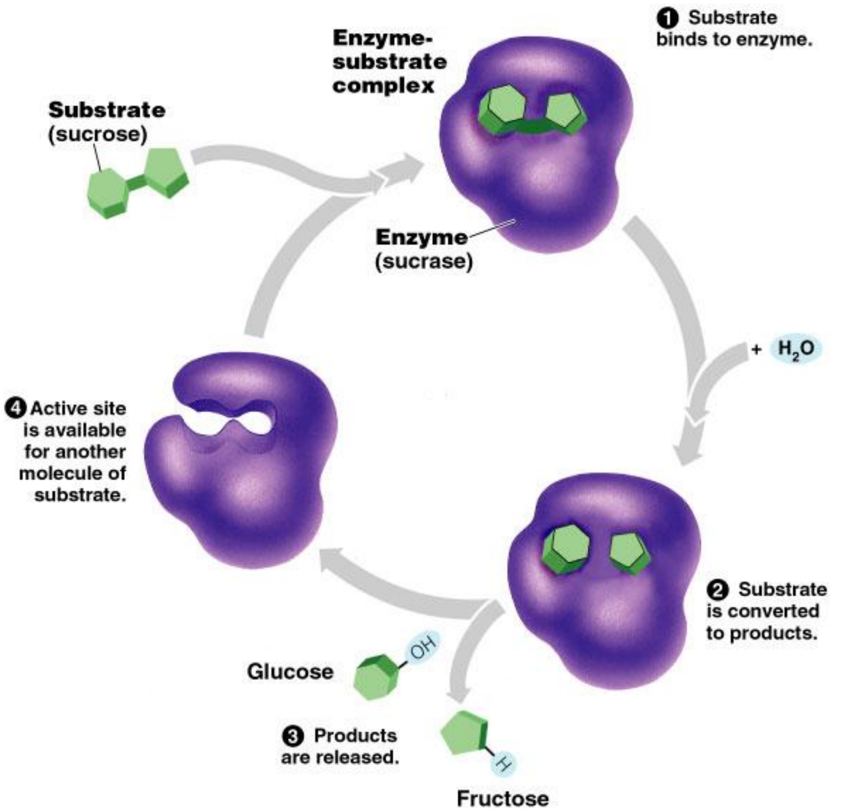


Lock and Key model

- Simplistic model of enzyme action
  - substrate fits into 3-D structure of enzyme' active site
    - H bonds between substrate & enzyme
  - like "key fits into lock"

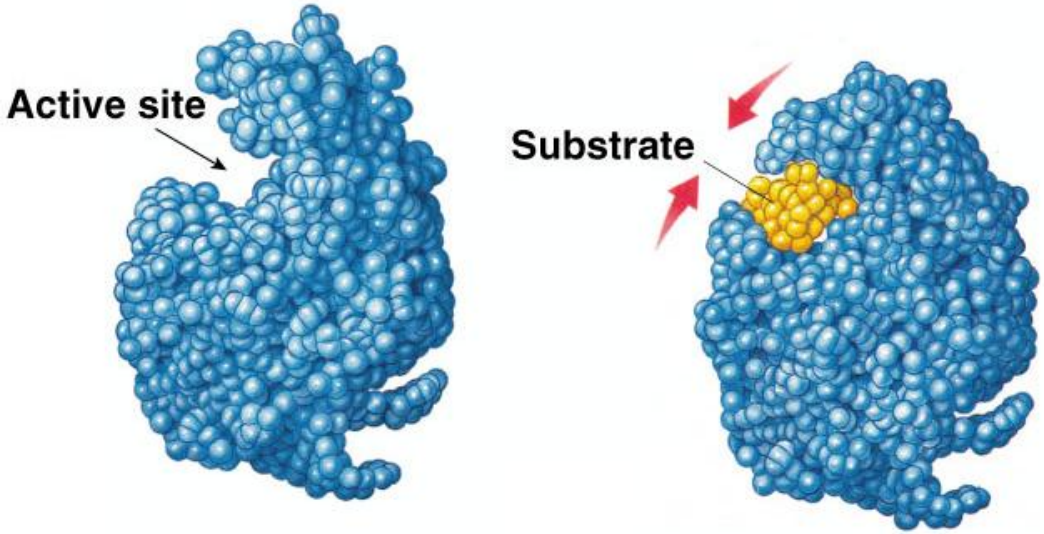






Induced fit model

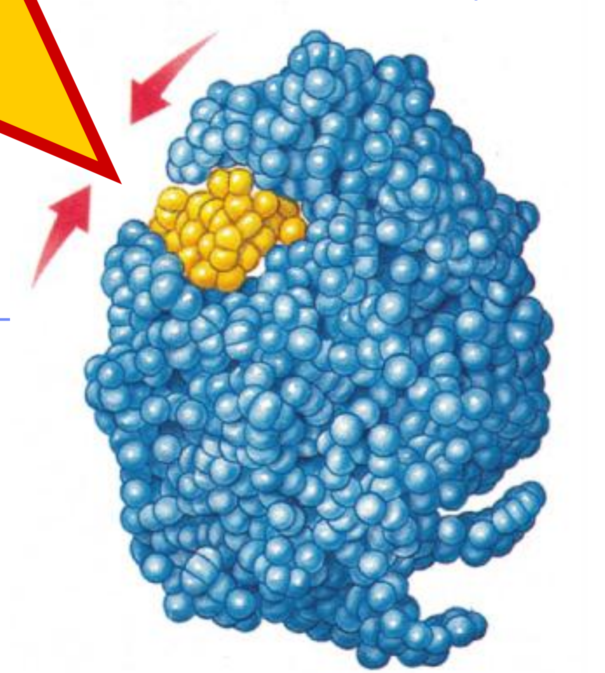
- More accurate model of enzyme action
  - 3-D structure of enzyme fits substrate
  - substrate binding cause enzyme to **change shape** leading to a tighter fit
    - "**conformational change**"
    - bring chemical groups in position to catalyze reaction

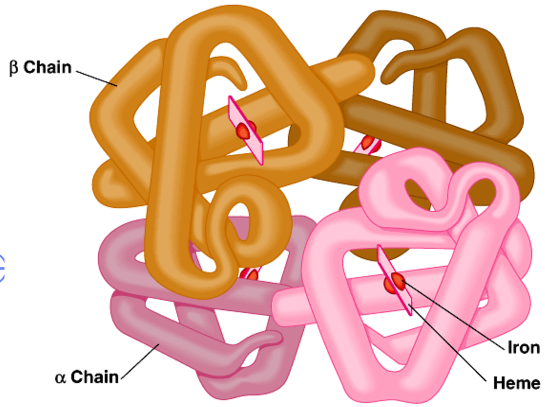


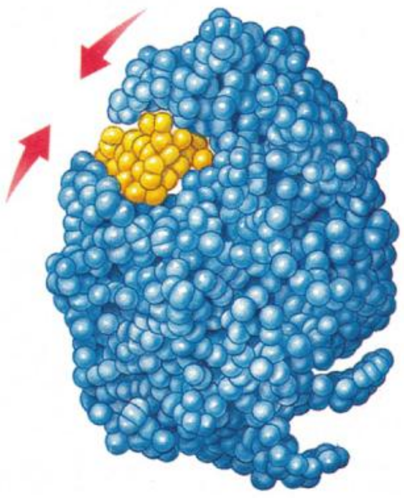
How does it work?

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

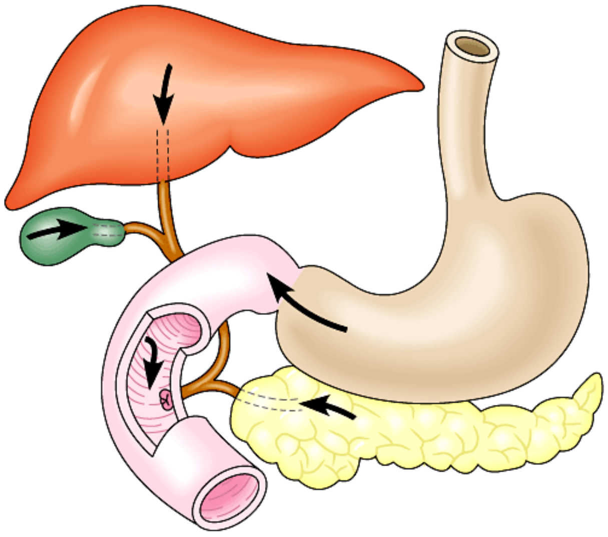
Got any Questions?*!*





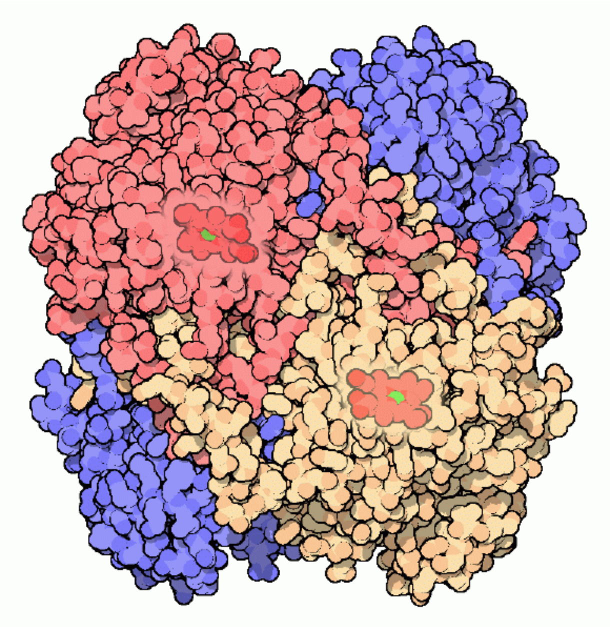


Factors that Affect Enzymes



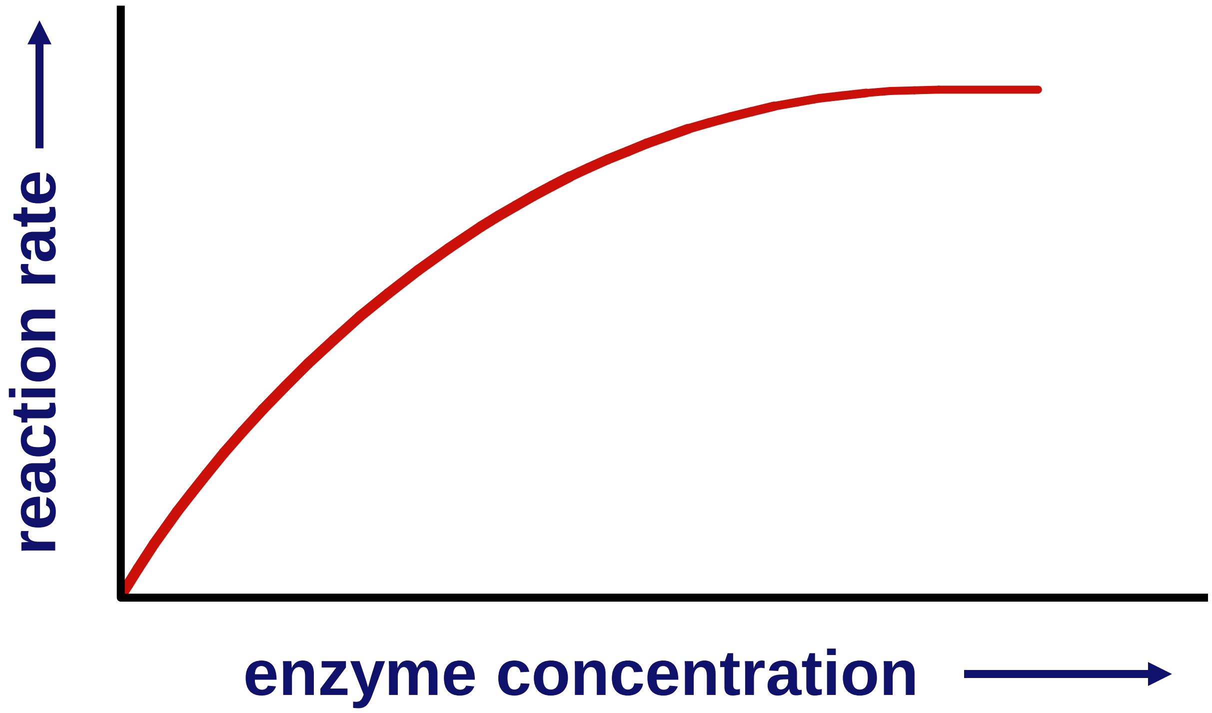
Factors Affecting Enzyme Function

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



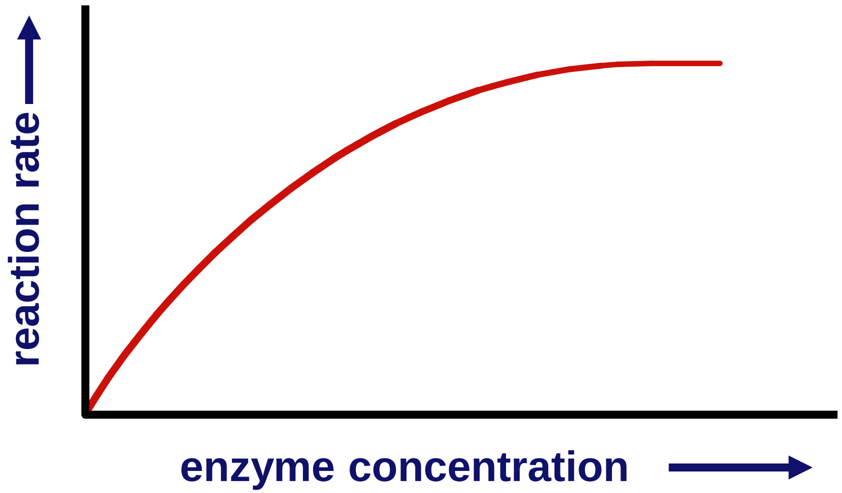
catalase

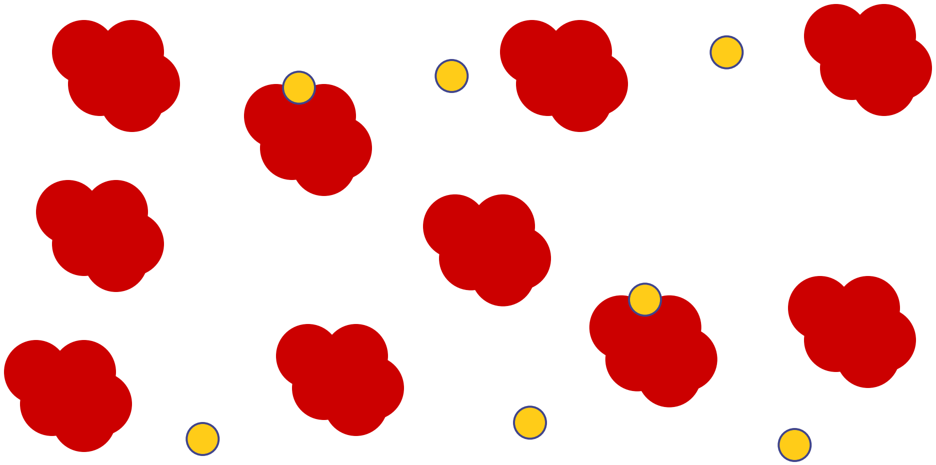
Enzyme concentration



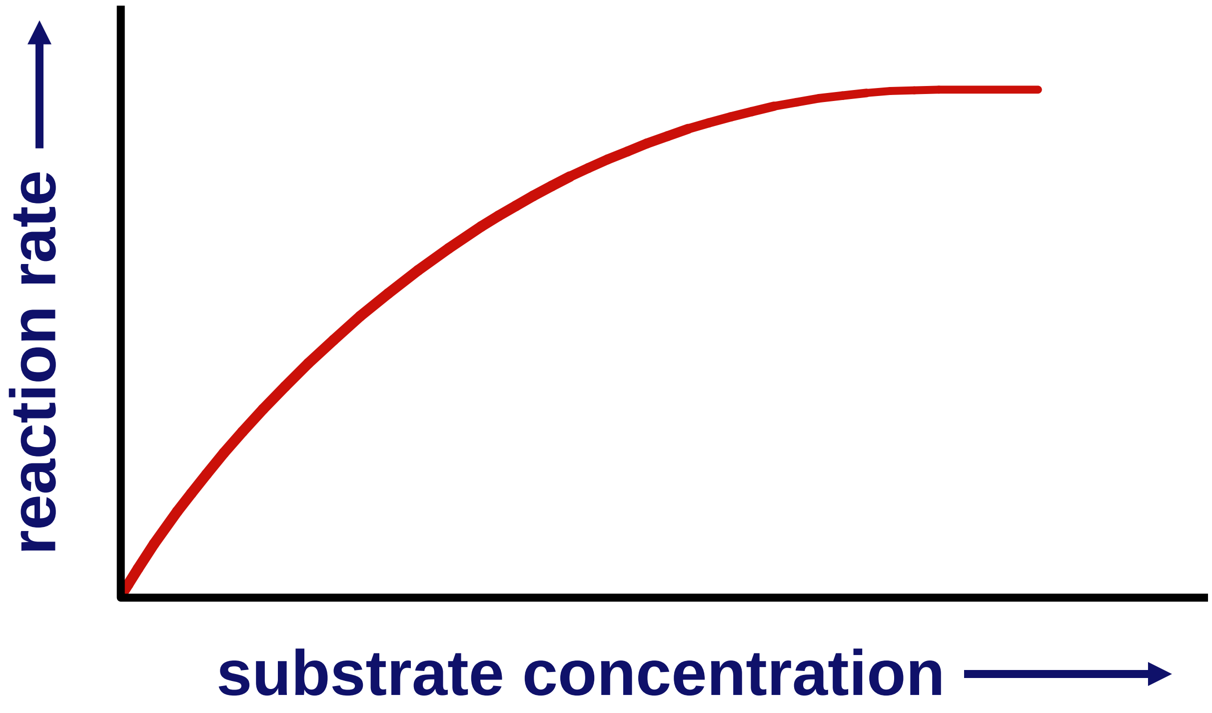
Factors affecting enzyme function

- **Enzyme concentration**
  - 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



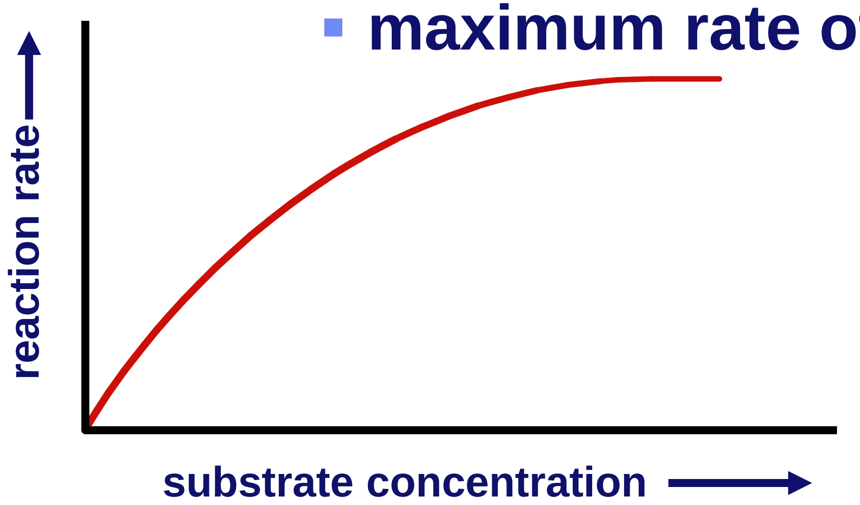


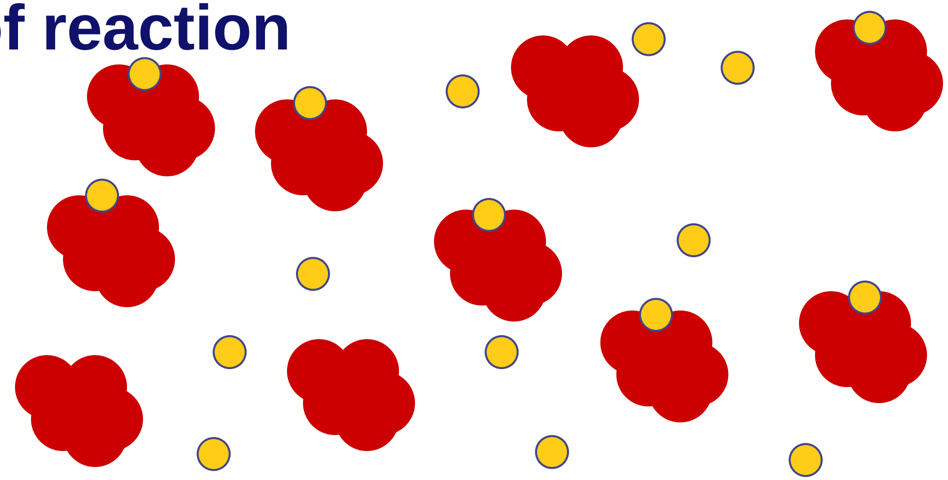
Substrate concentration



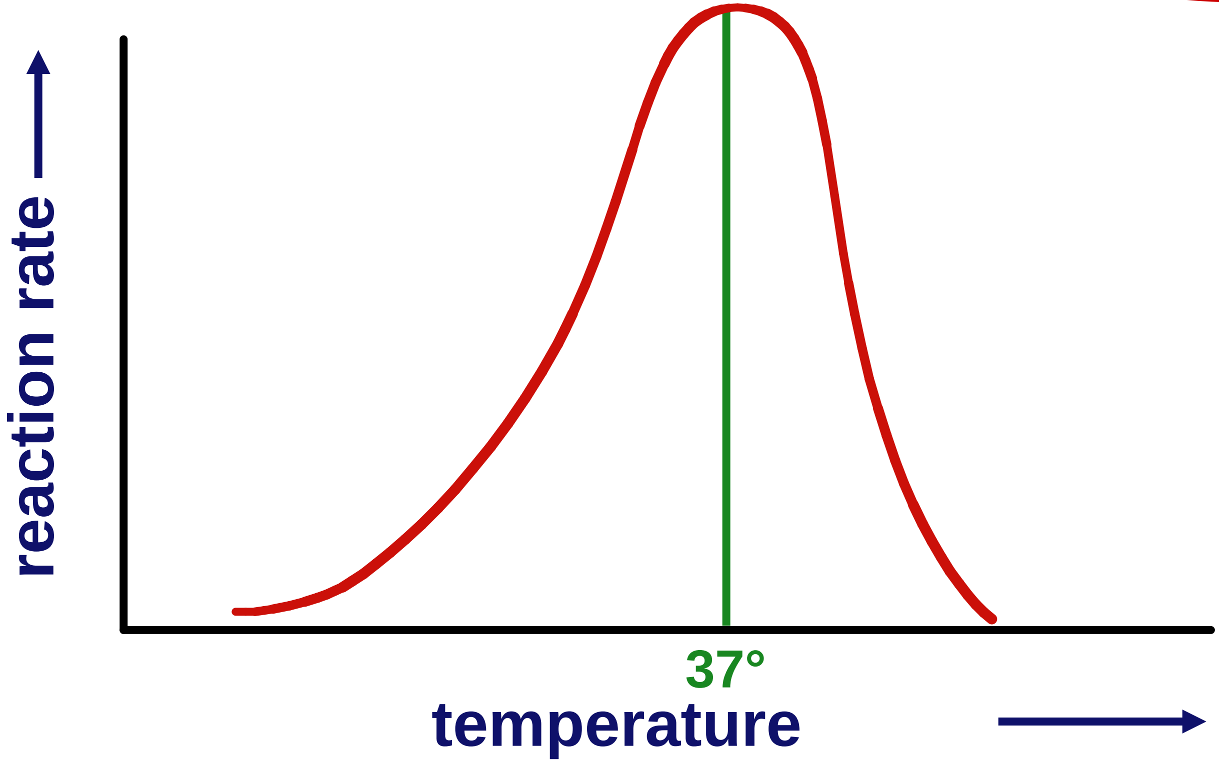
Factors affecting enzyme function

- **Substrate concentration**
  - **as ↑ substrate = ↑ reaction rate**
    - **more substrate = more frequently collide with enzyme**
  - **reaction rate levels off**
    - **all enzymes have active site engaged**
    - **enzyme is saturated**
    - **maximum rate of reaction**

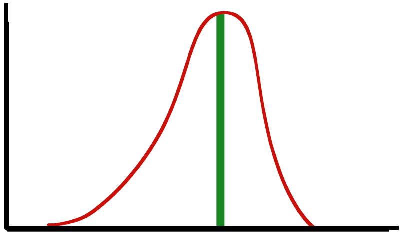




Temperature



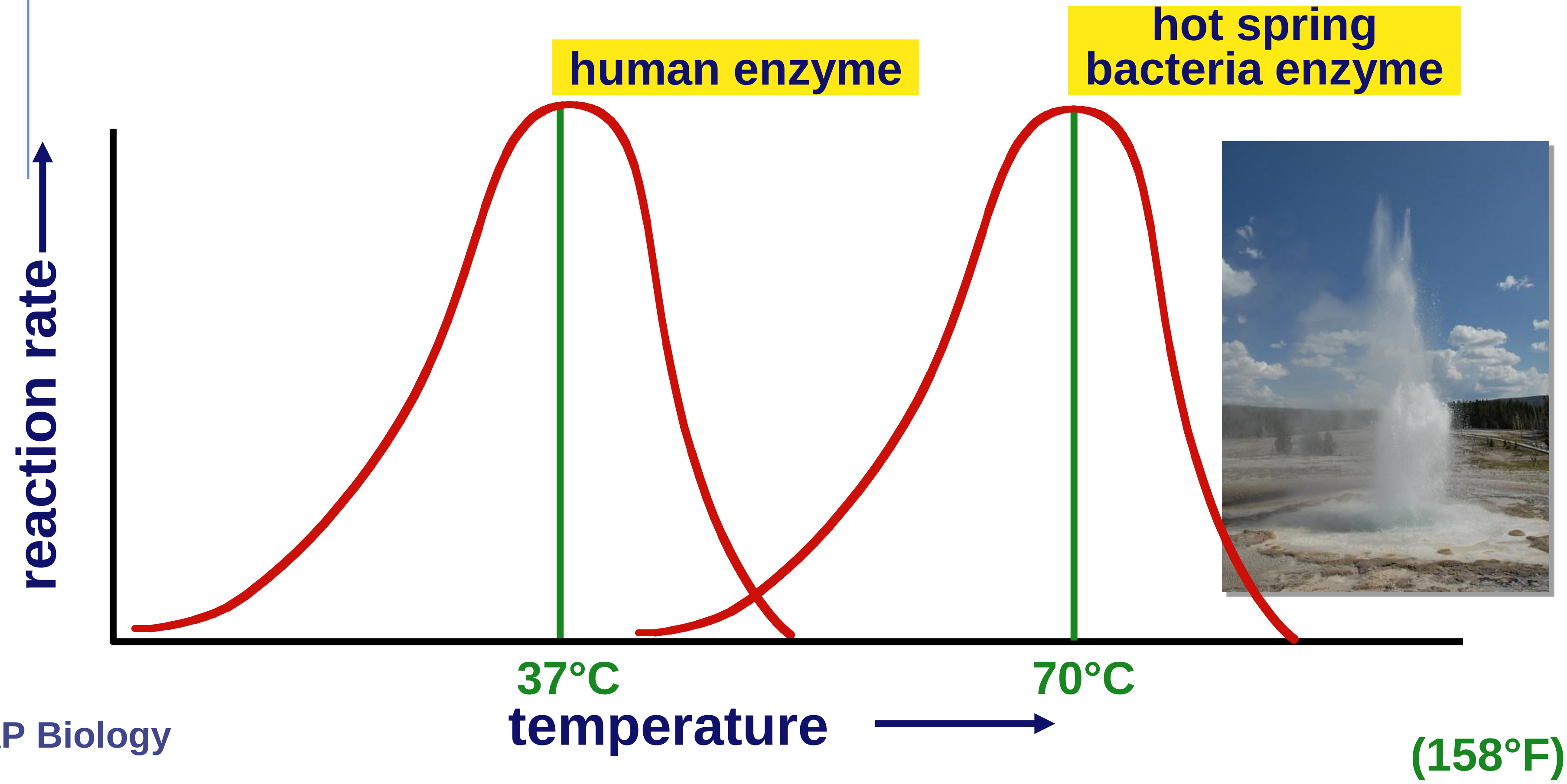
Factors affecting enzyme function



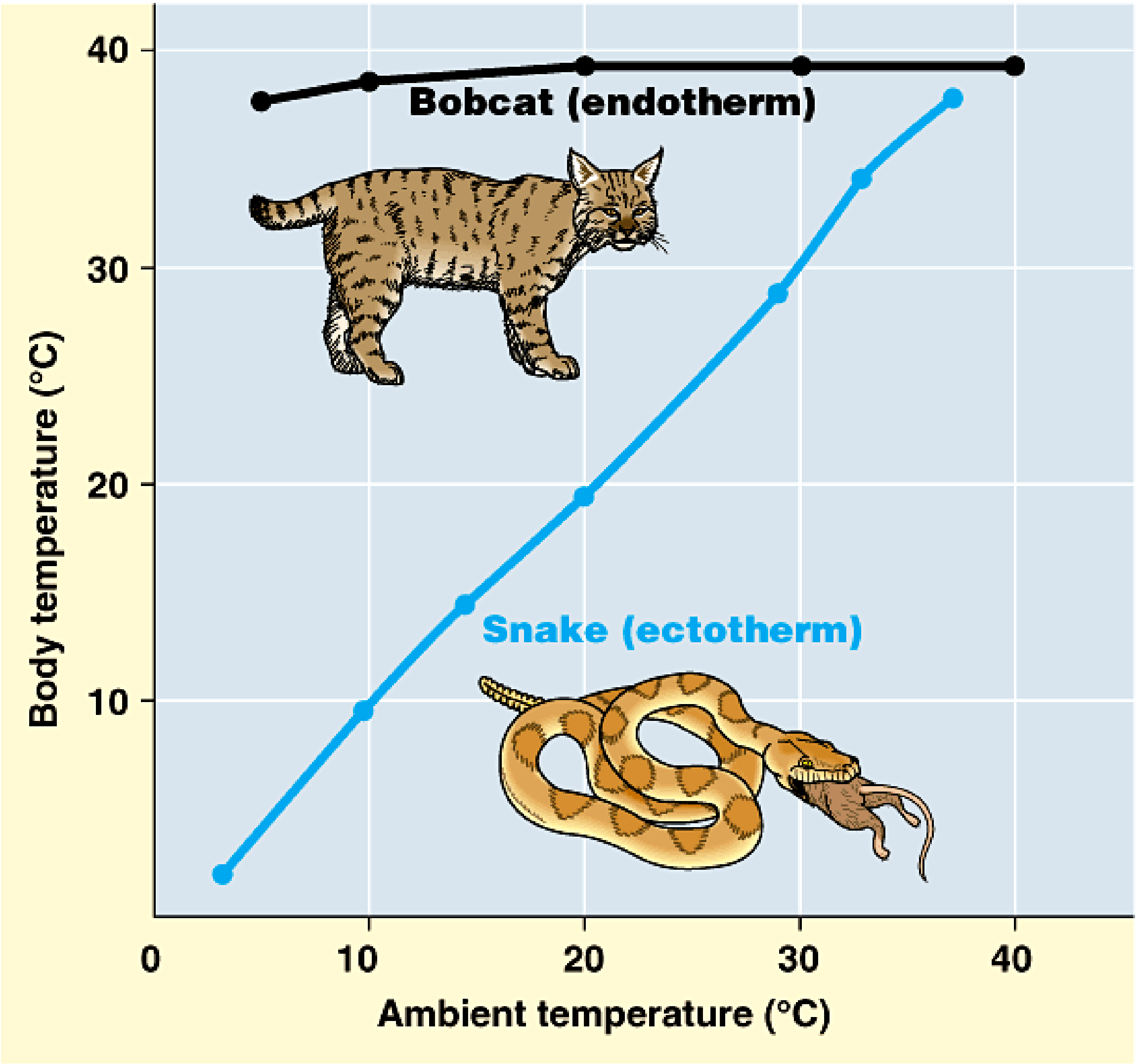
- **Temperature**
  - **Optimum T°**
    - **greatest number of molecular collisions**
    - **human enzymes = 35°- 40°C**
      - **body temp = 37°C**
  - **Heat: increase beyond optimum T°**
    - **increased energy level of molecules disrupts bonds in enzyme & between enzyme & substrate**
      - **H, ionic = weak bonds**
    - **denaturation = lose 3D shape (3° structure)**
  - **Cold: decrease T°**
    - **molecules move slower**
    - **decrease collisions between enzyme & substrate**

Enzymes and temperature

- Different enzymes function in different organisms in different environments

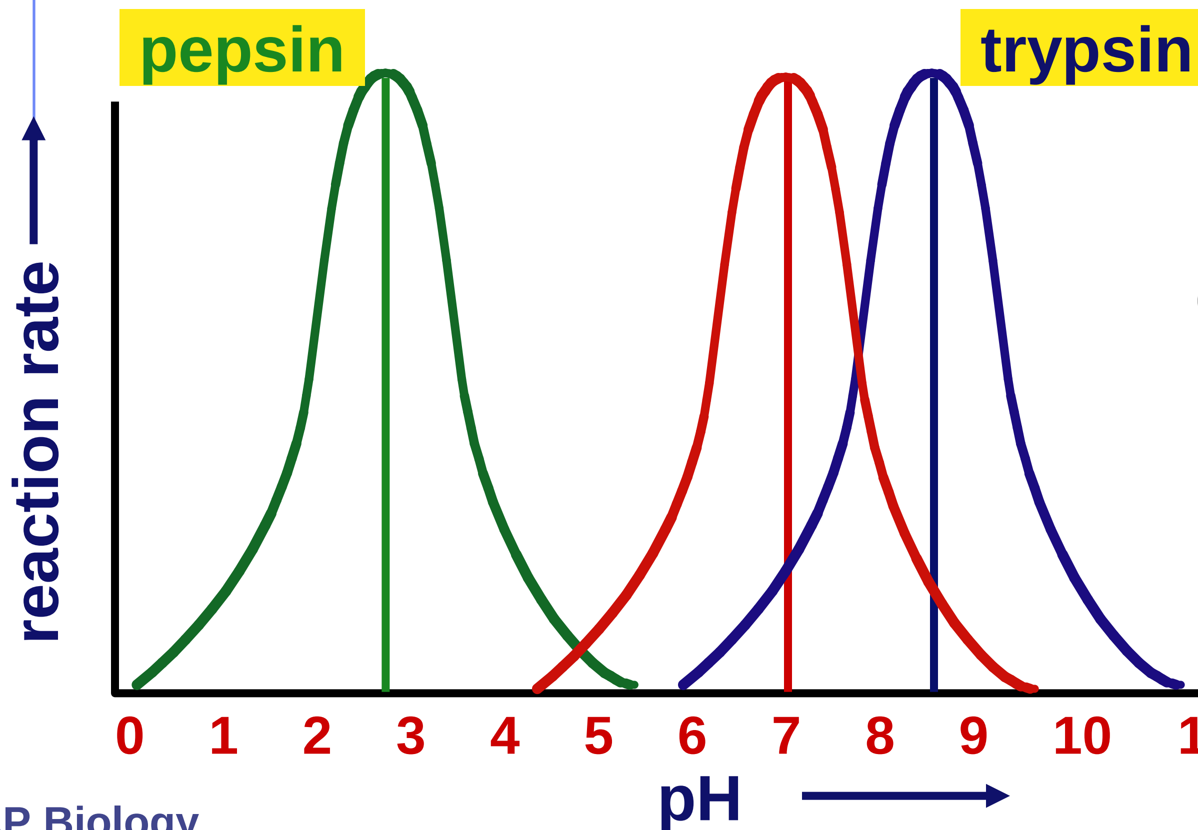


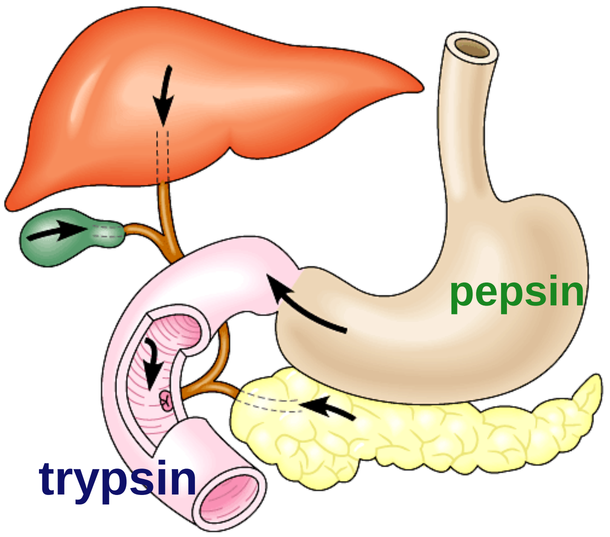
How do ectotherms do it?



pH

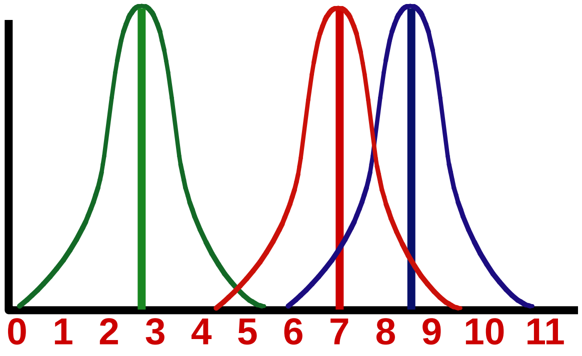

What's
happening here?!


pepsin
trypsin
reaction rate
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
pH

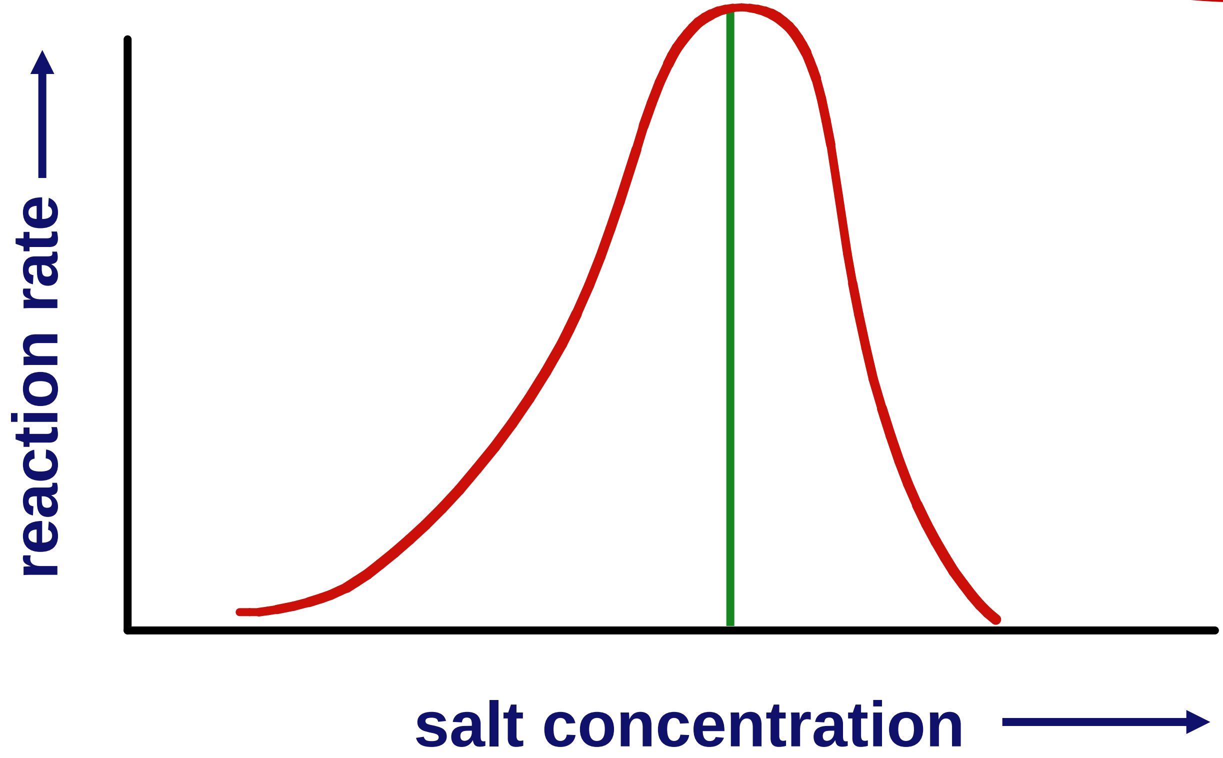

pepsin
trypsin

Factors affecting enzyme function

- pH
  - changes in pH
    - adds or remove H^+
    - disrupts bonds, disrupts 3D shape
      - disrupts attractions between charged amino acids
      - affect 2° & 3° structure
      - denatures protein
  - optimal pH?
    - most human enzymes = pH 6-8
      - depends on localized conditions
      - **pepsin** (stomach) = pH 2-3
      - **trypsin** (small intestines) = pH 8

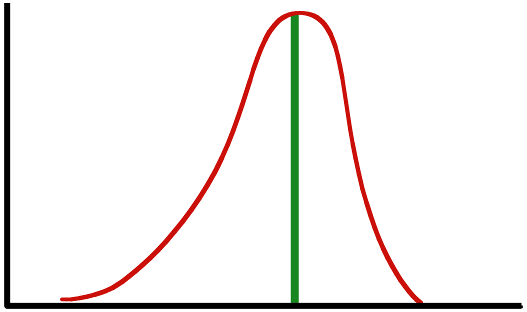


Salinity



Factors affecting enzyme function

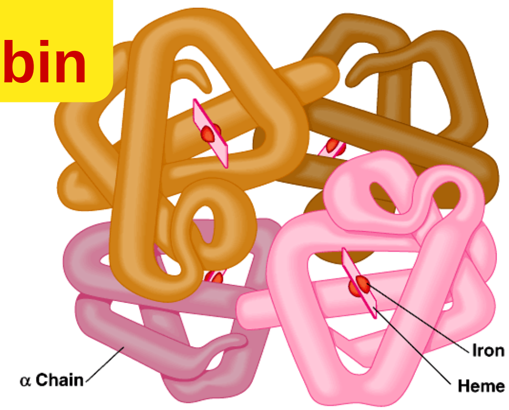
- **Salt concentration**
  - **changes in salinity**
    - **adds or removes cations (+) & anions (–)**
    - **disrupts bonds, disrupts 3D shape**
      - **disrupts attractions between charged amino acids**
      - **affect 2° & 3° structure**
      - **denatures protein**
  - **enzymes intolerant of extreme salinity**
    - **Dead Sea is called dead for a reason!**

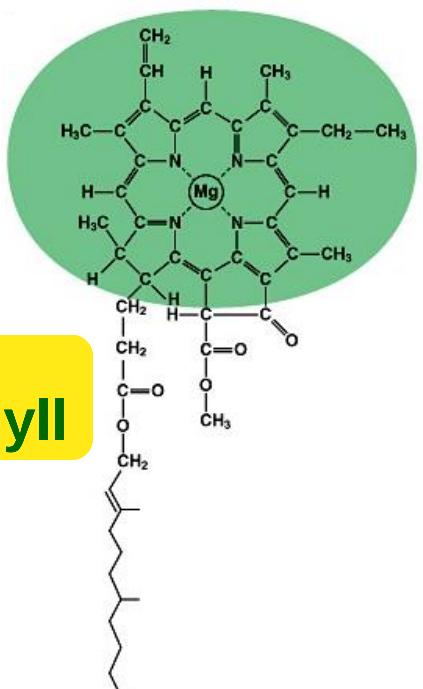


Compounds which help enzymes

- **Activators**
  - <u>cofactors</u>
    - non-protein, small <u>inorganic</u> compounds & ions
      - Mg, K, Ca, Zn, Fe, Cu
      - bound within enzyme molecule
  - <u>coenzymes</u>
    - non-protein, <u>organic</u> molecules
      - bind temporarily or permanently to enzyme near active site
    - many <u>vitamins</u>
      - NAD (niacin; B3)
      - FAD (riboflavin; B2)
      - Coenzyme A

Fe in hemoglobin

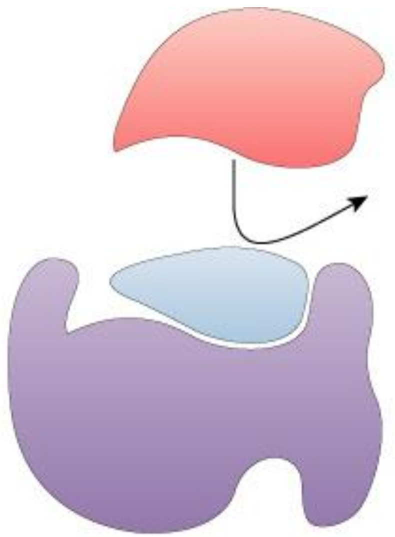




Mg in chlorophyll

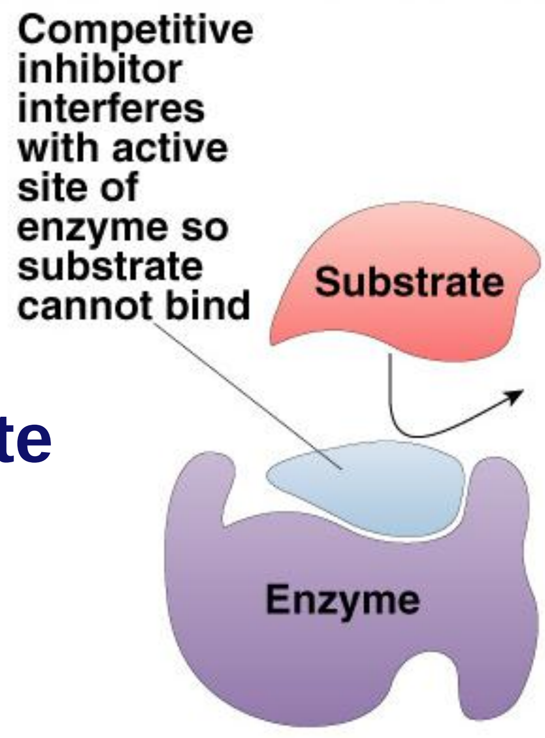
Compounds which regulate enzymes

- Inhibitors
  - molecules that reduce enzyme activity
  - competitive inhibition
  - noncompetitive inhibition
  - irreversible inhibition
  - feedback inhibition



Competitive Inhibitor

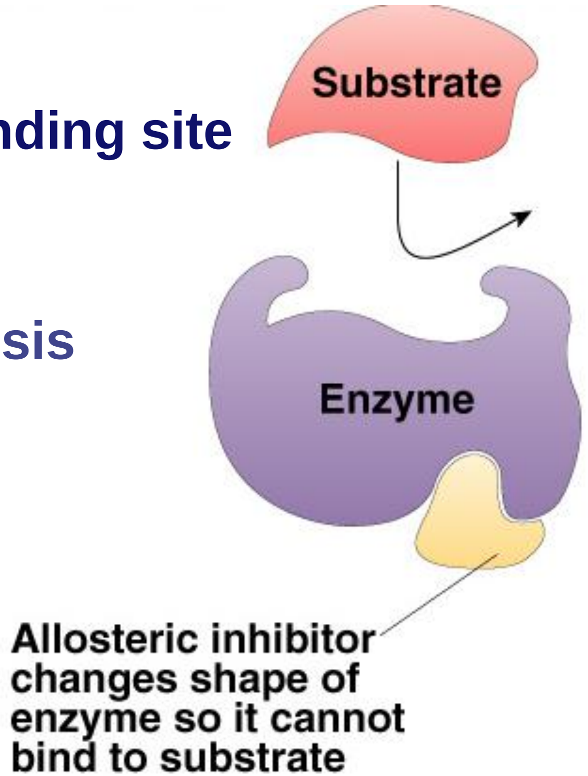
- Inhibitor & substrate "compete" for <u>active site</u>
  - <u>penicillin</u>
    blocks enzyme bacteria use to build cell walls
  - <u>disulfiram (Antabuse)</u>
    treats chronic alcoholism
    - blocks enzyme that breaks down alcohol
    - severe hangover & vomiting 5-10 minutes after drinking
- Overcome by <u>increasing</u> substrate concentration
  - saturate solution with substrate so it out-competes inhibitor for active site on enzyme



(a) Competitive inhibition

Non-Competitive Inhibitor

- Inhibitor binds to site other than active site
  - allosteric inhibitor binds to allosteric site
  - causes enzyme to change shape
    - conformational change
    - active site is no longer functional binding site
      - keeps enzyme inactive
  - some anti-cancer drugs inhibit enzymes involved in DNA synthesis
    - stop DNA production
    - stop division of more cancer cells
  - cyanide poisoning irreversible inhibitor of Cytochrome C, an enzyme in cellular respiration
    - stops production of ATP



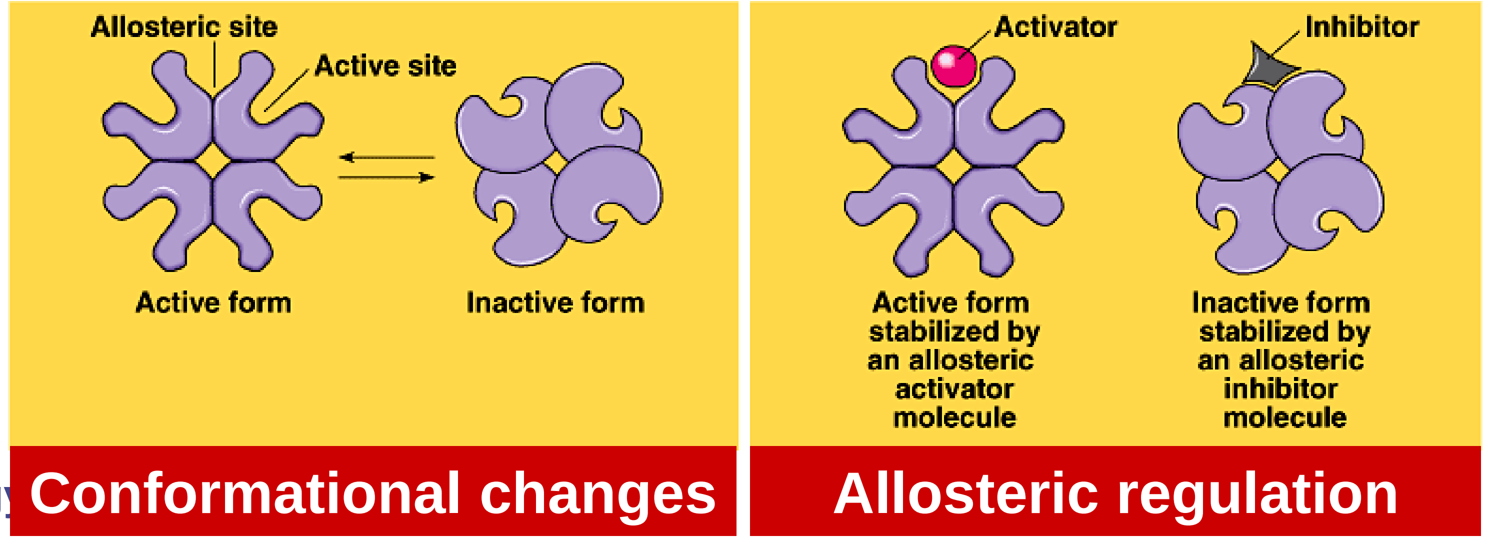
(b) Noncompetitive inhibition

Irreversible inhibition

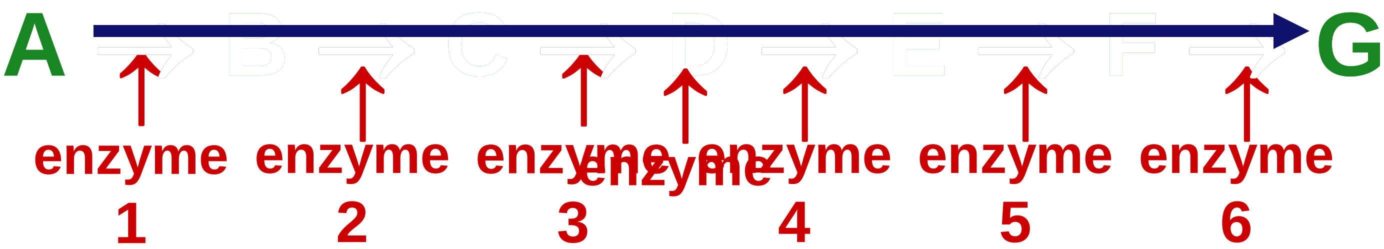
- Inhibitor permanently binds to enzyme
  - competitor
    - permanently binds to active site
  - allosteric
    - permanently binds to allosteric site
    - permanently changes shape of enzyme
    - nerve gas, sarin, many insecticides (malathion, parathion…)
      - cholinesterase inhibitors
      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

Allosteric regulation

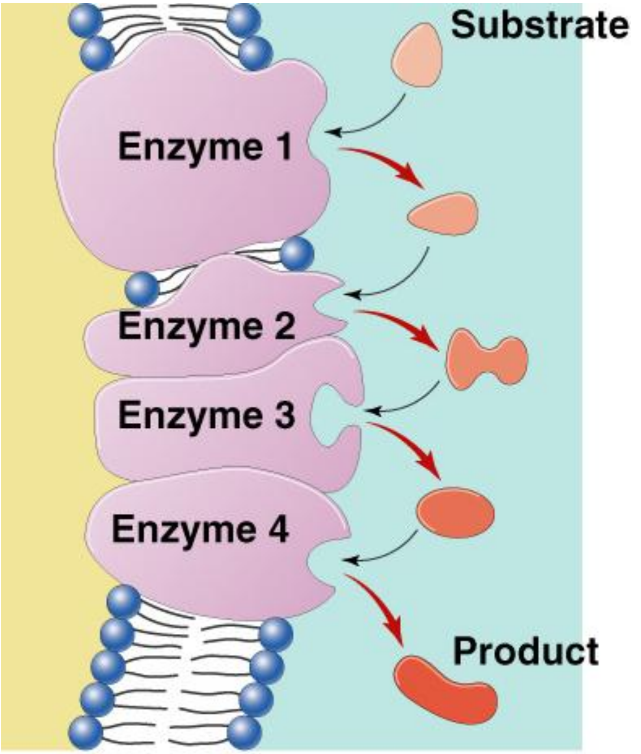
- Conformational changes by regulatory molecules
  - inhibitors
    - keeps enzyme in inactive form
  - activators
    - keeps enzyme in active form



Metabolic pathways

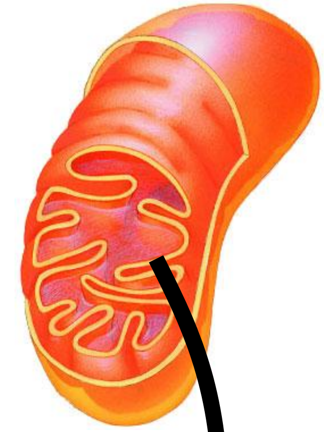


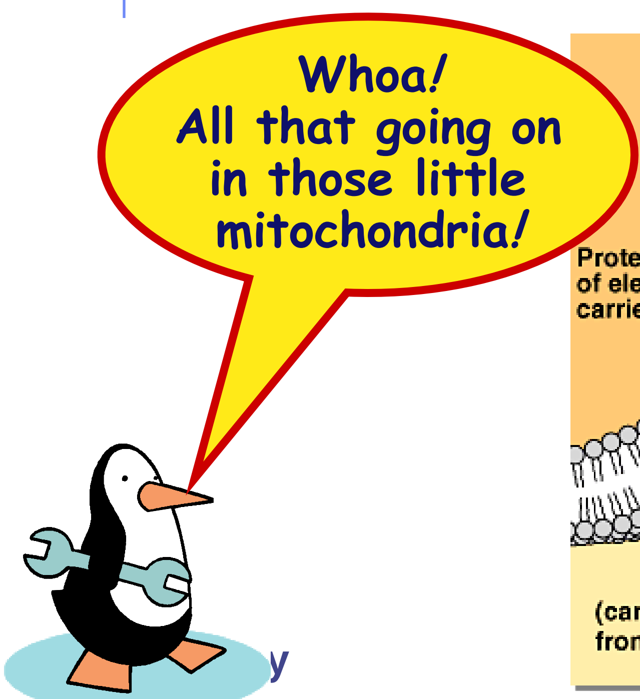
- Chemical reactions of life are organized in pathways
  - divide chemical reaction into many small steps
    - artifact of evolution
    - ↑ efficiency
      - intermediate branching points
    - ↑ control = regulation

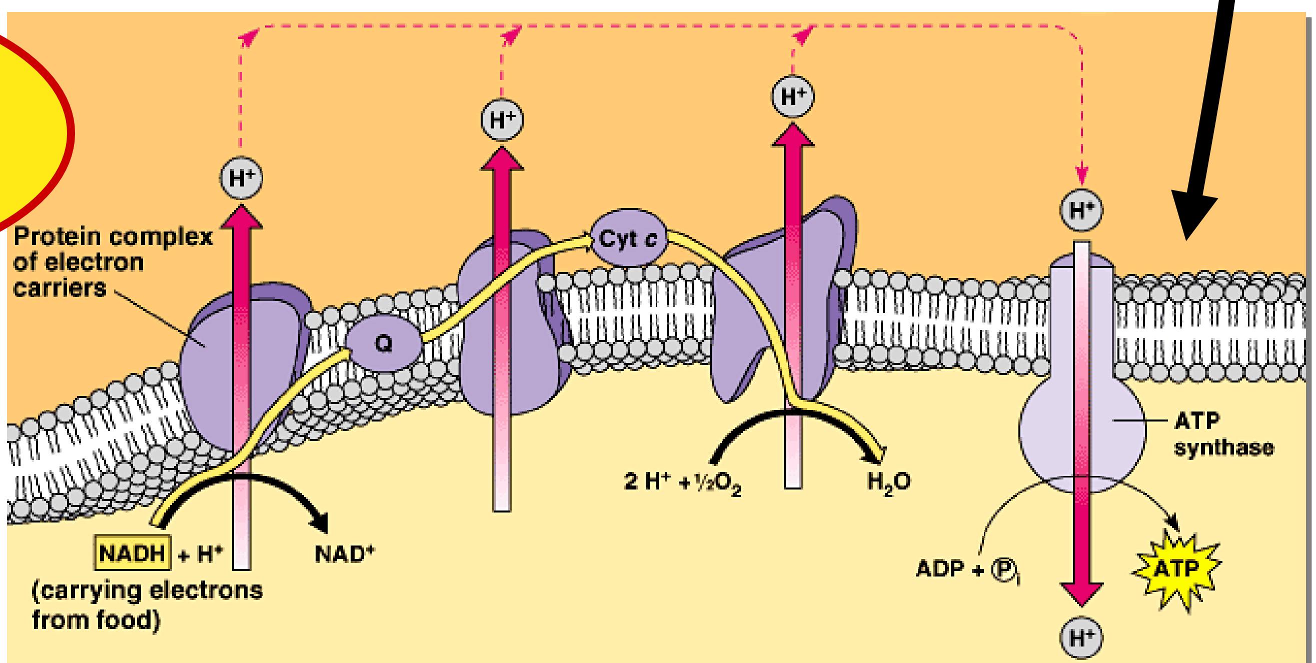


Efficiency

- **Organized groups of enzymes**
  - enzymes are embedded in membrane and arranged sequentially
- **Link <u>endergonic</u> & <u>exergonic</u> reactions**

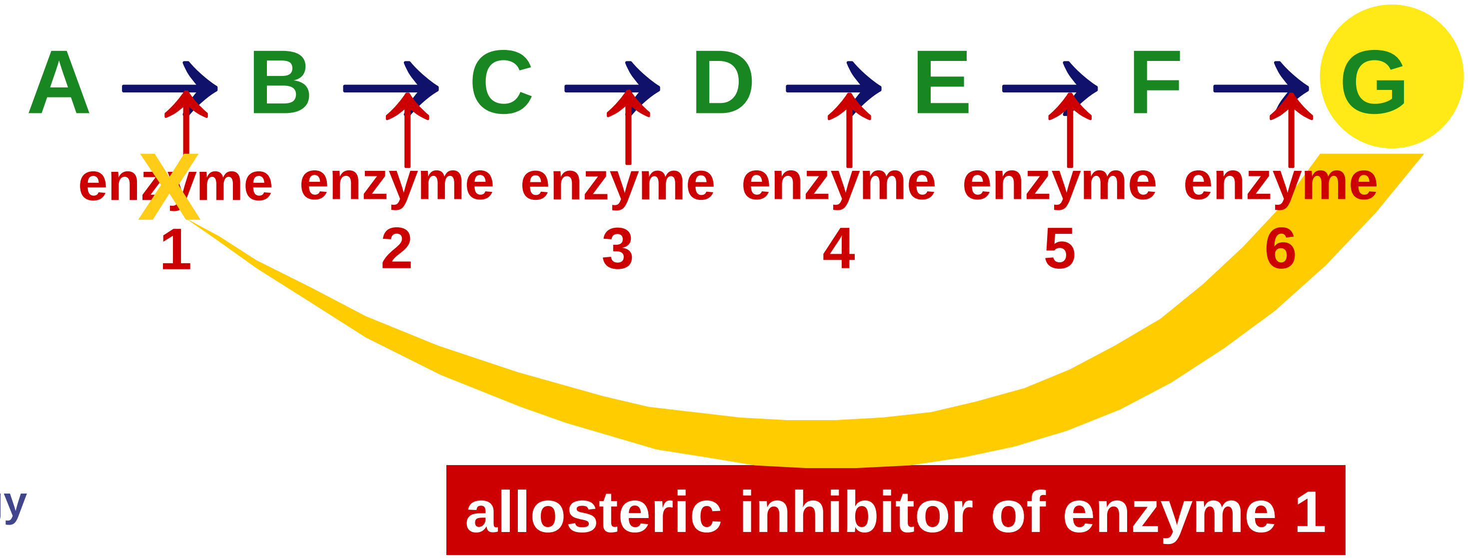






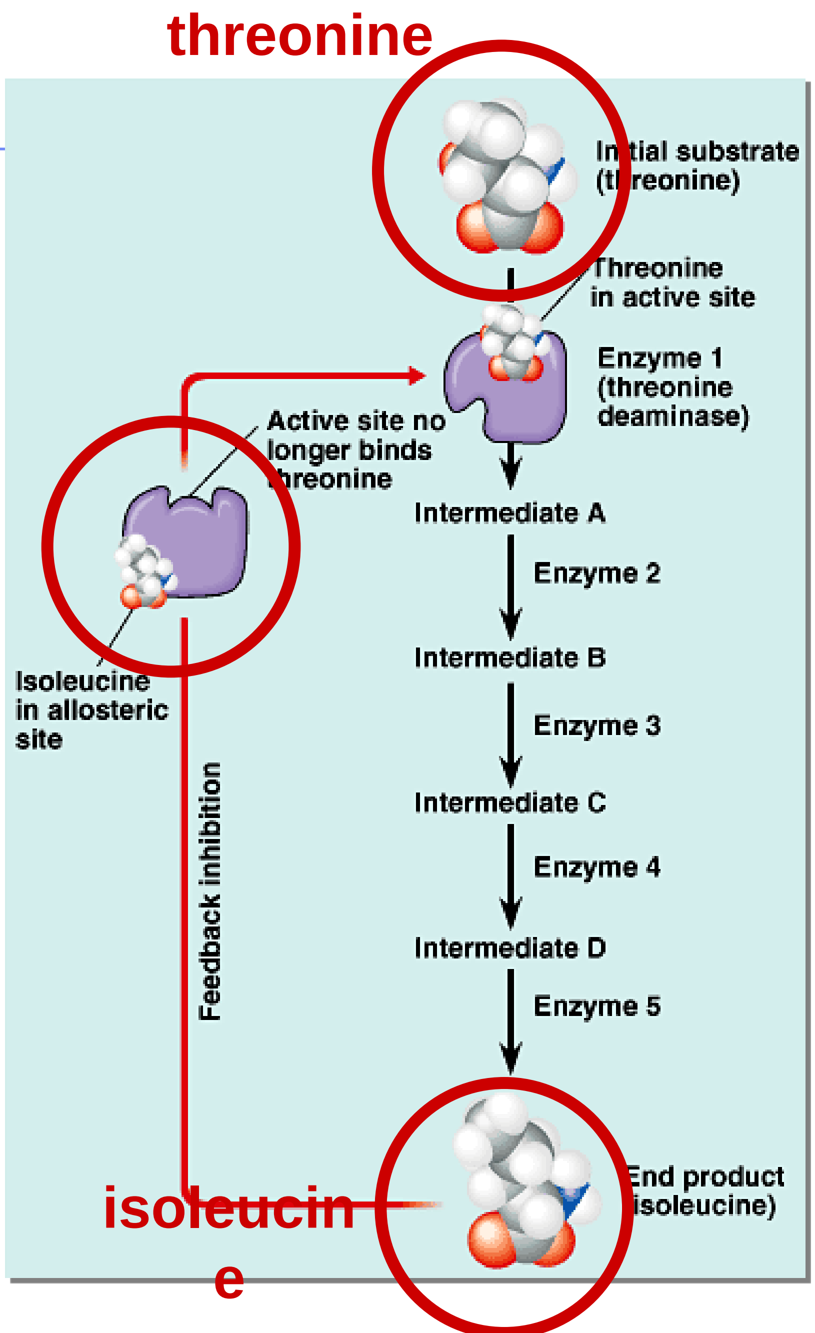
Feedback Inhibition

- **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



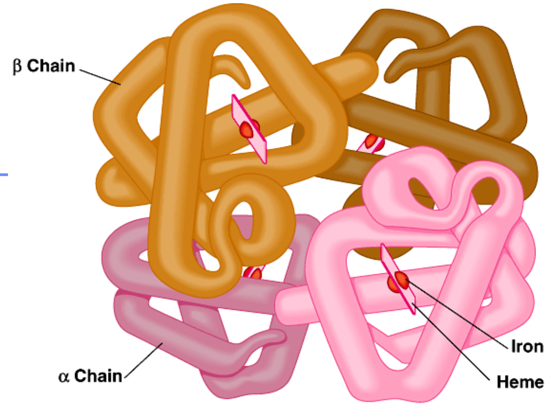
Feedback inhibition

- Example
  - synthesis of amino acid, **isoleucine** from amino acid, **threonine**
  - isoleucine becomes the **allosteric inhibitor** of the first step in the pathway
    - as product accumulates it collides with enzyme more often than substrate does

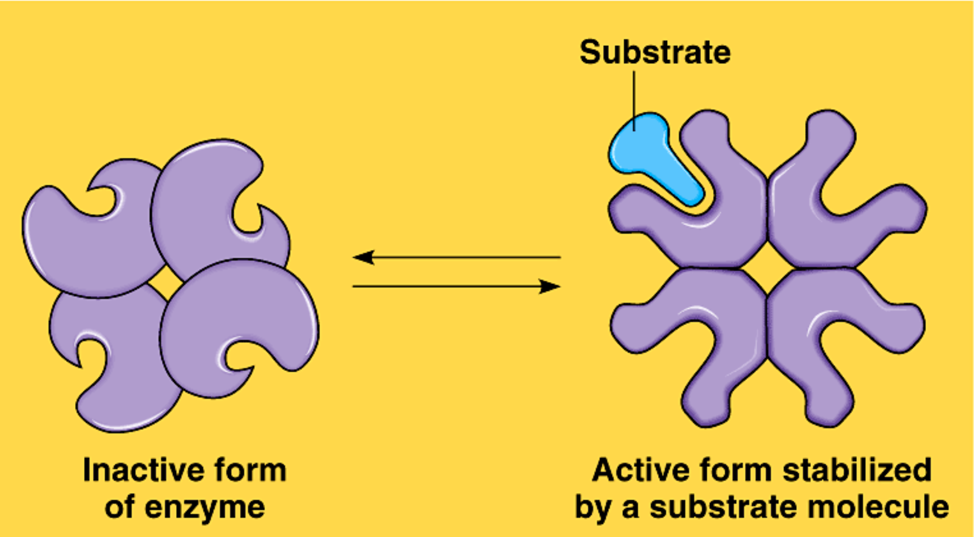


Cooperativity

- 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
    - hemoglobin



Hemoglobin
- 4 polypeptide chains
- can bind 4 O_2;
- 1st O_2 binds
- now easier for other 3 O_2 to bind



Don’t be inhibited!
Ask Questions!