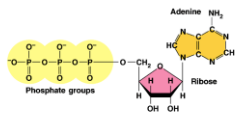
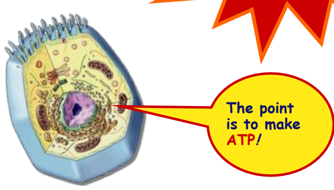
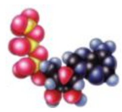
Making energy!





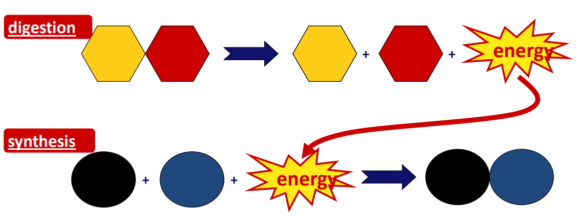


The energy needs of life

- Organisms are endergonic systems
  - What do we need energy for?
    - synthesis
      - building biomolecules
    - reproduction
    - movement
    - active transport
    - temperature regulation

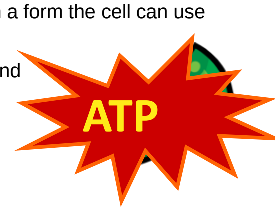
Where do we get the energy from?

- Work of life is done by energy coupling
  - use exergonic (catabolic) reactions to fuel endergonic (anabolic) reactions

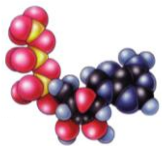


Living economy

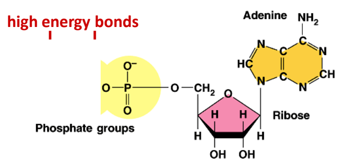
- Fueling the body's economy
  - eat high energy organic molecules
    - food = carbohydrates, lipids, proteins, nucleic acids
  - break them down
    - digest = catabolism
  - capture released energy in a form the cell can use
- Need an energy currency
  - a way to pass energy around
  - need a short term energy storage molecule



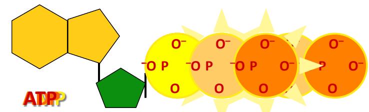
ATP



- Adenosine TriPhosphate
  - modified nucleotide
    - nucleotide = adenine + ribose + P_i → AMP
    - AMP + P_i → ADP
    - ADP + P_i → ATP
  - adding phosphates is endergonic



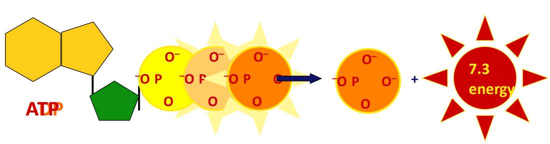
How does ATP store energy?



- Each negative PO_4 more difficult to add
  - a lot of stored energy in each bond
    - most energy stored in 3rd P_i
    - 3rd P_i is hardest group to keep bonded to molecule
- Bonding of negative P_i groups is unstable
  - *spring-loaded*
  - P_i groups "pop" off easily & release energy

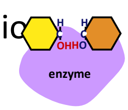
Instability of its P bonds makes ATP an excellent energy donor

How does ATP transfer energy?

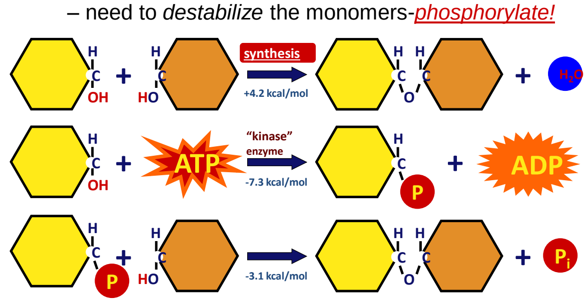


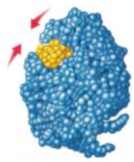
- ATP → ADP
  - releases energy
    - ΔG = -7.3 kcal/mole
- Fuel other reactions
- Phosphorylation
  - released P_i can transfer to other molecules
    - destabilizing the other molecules
  - enzyme that phosphorylates = "kinase"

An example of Phosphorylation

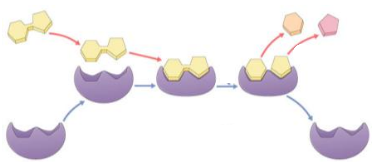


- Building polymers from monomers
  - need to *destabilize* the monomers-*phosphorylate!*



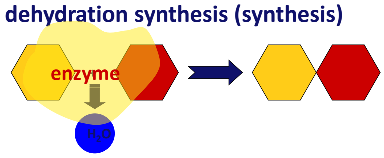


Metabolism & Enzymes

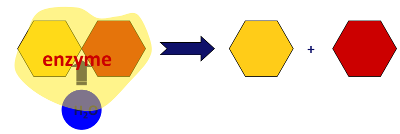


Examples

- **dehydration synthesis (synthesis)**



- **hydrolysis (digestion)**



Chemical reactions & energy

- Some chemical reactions release energy
  - exergonic
  - digesting polymers
  - hydrolysis = catabolism

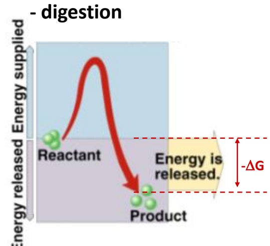
digesting molecules= LESS organization= lower energy state

- Some chemical reactions require input of energy
  - endergonic
  - building polymers
  - dehydration synthesis = anabolism

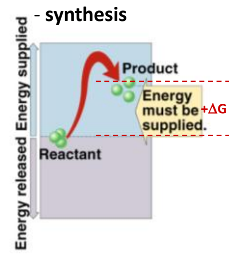
building molecules= MORE organization= higher energy state

Endergonic vs. exergonic reactions

exergonic
- energy released
- digestion



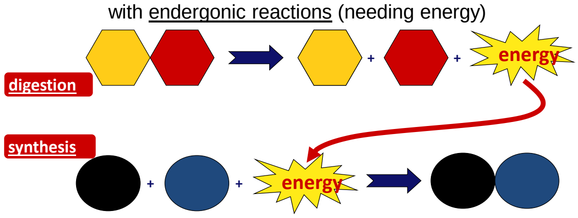
endergonic
- energy invested
- synthesis



ΔG = change in free energy = ability to do work

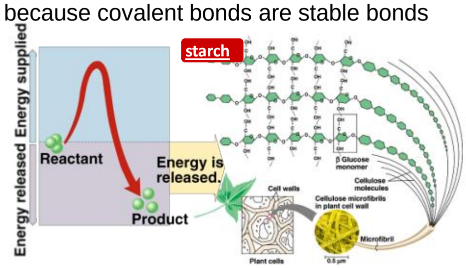
Energy & life

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



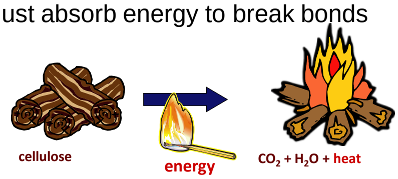
What drives reactions?

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



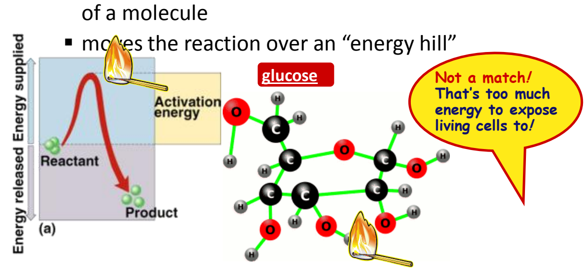
Activation energy

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



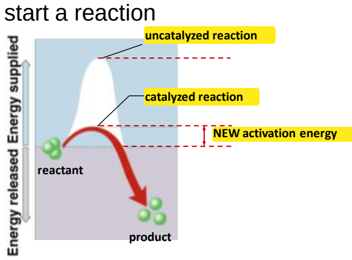
Too much activation energy for life

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



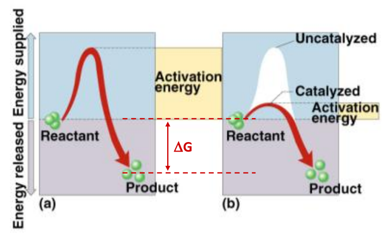
Reducing Activation energy

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

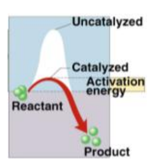


Catalysts

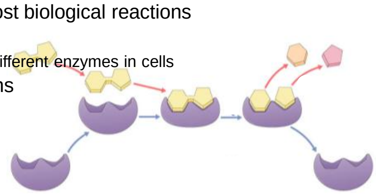
- So what's a cell got to do to reduce activation energy?
  - get help! … chemical help… **ENZYMES**



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

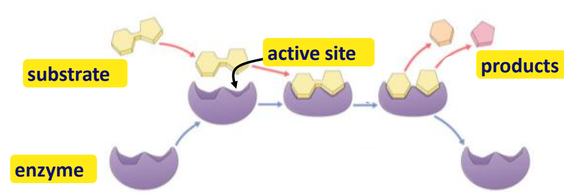


Enzymes vocabulary

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

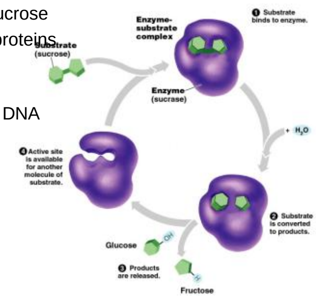


Properties of enzymes

- 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

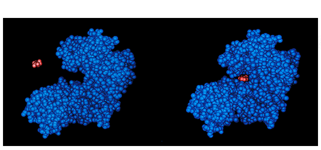
Naming conventions

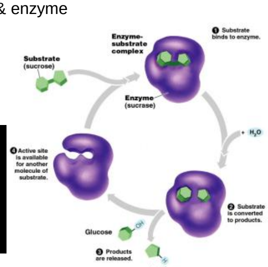
- Enzymes named for reaction they catalyze
  - sucrase breaks down sucrose
  - proteases break down proteins
  - lipases break down lipids
  - DNA polymerase builds DNA
    - adds nucleotides to DNA strand
  - pepsin breaks down proteins (polypeptides)



Lock and Key model

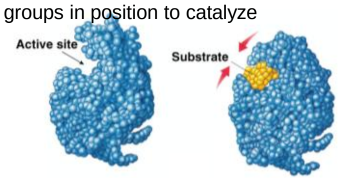
- Simplistic model of enzyme action
  - substrate fits into 3-D structure of enzyme' active site
    - H bonds between substrate & enzyme
  - like "key fits into lock"





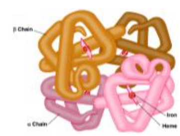
Induced fit model

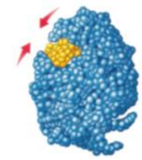
- More accurate model of enzyme action
  - 3-D structure of enzyme fits substrate
  - substrate binding cause enzyme to change shape leading to a tighter fit
    - "conformational change"
    - bring chemical groups in position to catalyze reaction



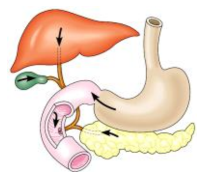
How does it work?

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



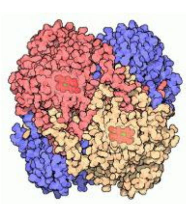


Factors that Affect Enzymes



Factors Affecting Enzyme Function

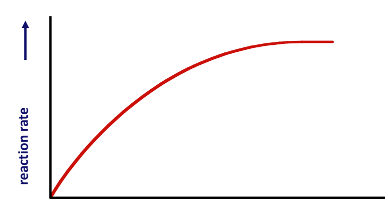
- Enzyme concentration
- Substrate concentration
- Temperature
- pH
- Salinity
- Activators
- Inhibitors



catalase

Enzyme concentration

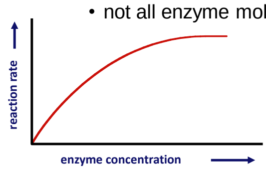
What's happening here?!

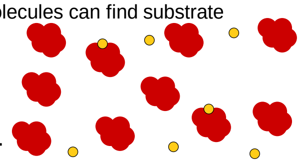


Reaction rate = disappearance of reactant or appearance of product per unit of time

Factors affecting enzyme function

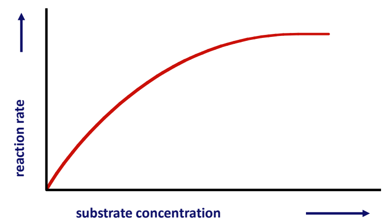
- Enzyme concentration
  - as ↑ enzyme = ↑ reaction rate
    - more enzymes = more frequently collide with substrate
  - reaction rate levels off
    - substrate becomes limiting factor
    - not all enzyme molecules can find substrate





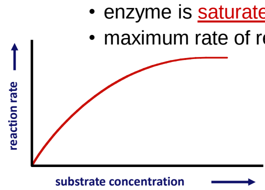
Substrate concentration

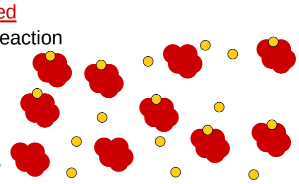
What's happening here?!



Factors affecting enzyme function

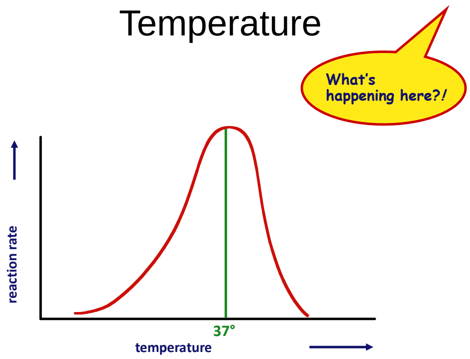
- Substrate concentration
  - as ↑ substrate = ↑ reaction rate
    - more substrate = more frequently collide with enzyme
  - reaction rate levels off
    - all enzymes have active site engaged
    - enzyme is saturated
    - maximum rate of reaction



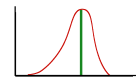


http://www.youtube.com/watch?v=0YGF5R9i53A

Temperature



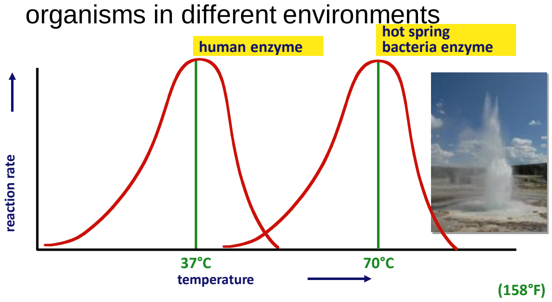
Factors affecting enzyme function



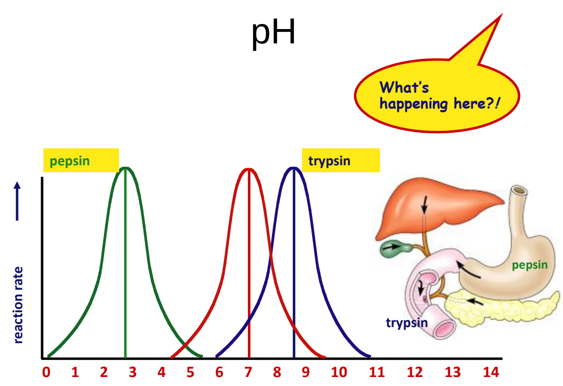
- Temperature
  - Optimum T°
    - greatest number of molecular collisions
    - human enzymes = 35°- 40°C
      - body temp = 37°C
  - Heat: increase beyond optimum T°
    - increased energy level of molecules disrupts bonds in enzyme & between enzyme & substrate
      - H, ionic = weak bonds
    - 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

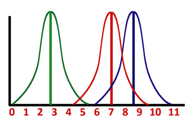


pH

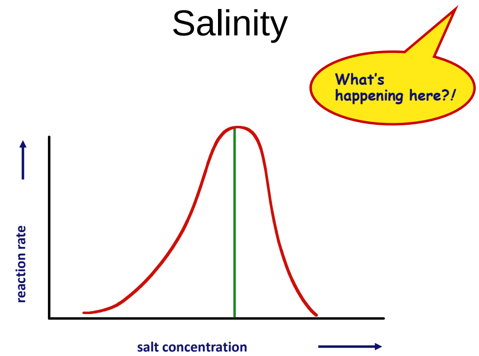


Factors affecting enzyme function

- 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

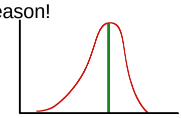


Salinity



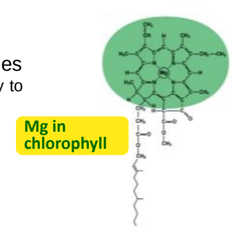
Factors affecting enzyme function

- 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!



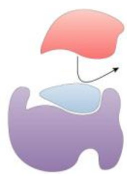
Compounds which help enzymes

- Activators
  - cofactors
    - non-protein, small inorganic compounds & ions
      - Mg, K, Ca, Zn, Fe, Cu
      - bound within 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



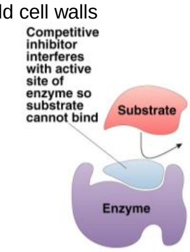
Compounds which regulate enzymes

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



Competitive Inhibitor

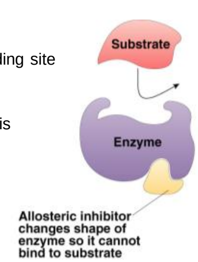
- Inhibitor & substrate "compete" for active site
  - penicillin
    blocks enzyme bacteria use to build cell walls
  - disulfiram (Antabuse)
    treats chronic alcoholism
    - blocks enzyme that breaks down alcohol
    - severe hangover & vomiting 5-10 minutes after drinking
- Overcome by increasing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



(a) Competitive inhibition

Non-Competitive Inhibitor

- 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



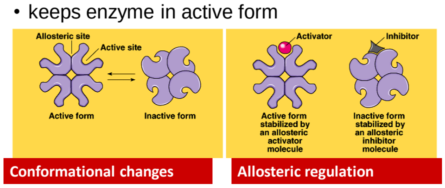
(b) Noncompetitive inhibition

Irreversible inhibition

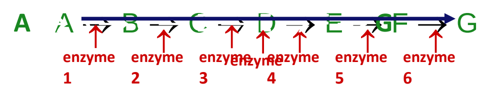
- Inhibitor permanently binds to enzyme
  - competitor
    - permanently binds to active site
  - allosteric
    - permanently binds to allosteric site
    - permanently changes shape of enzyme
    - nerve gas, sarin, many insecticides (malathion, parathion…)
      - cholinesterase inhibitors
      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

Allosteric regulation

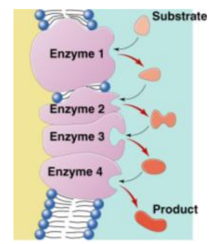
- Conformational changes by regulatory molecules
  - inhibitors
    - keeps enzyme in inactive form
  - activators
    - keeps enzyme in active form



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



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