Good morning!
Your tests are graded. They will be returned at the end of the period.
Anyone who wants to RETAKE this exam is welcome to; however,
The retake will be next THURSDAY at 2:45 pm.

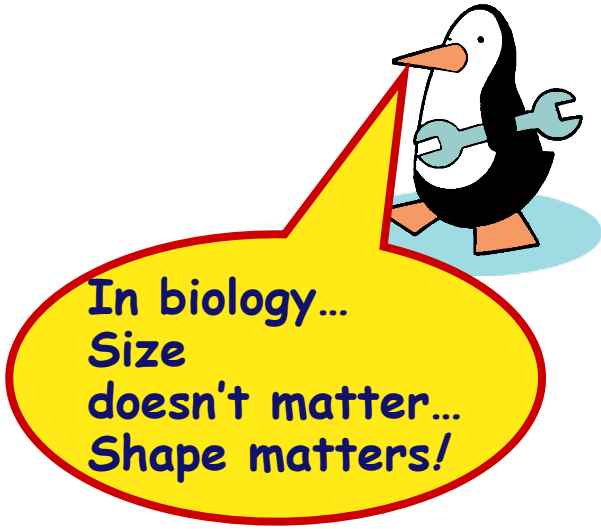
Enzymes and Metabolism

Chapter 8, Part II

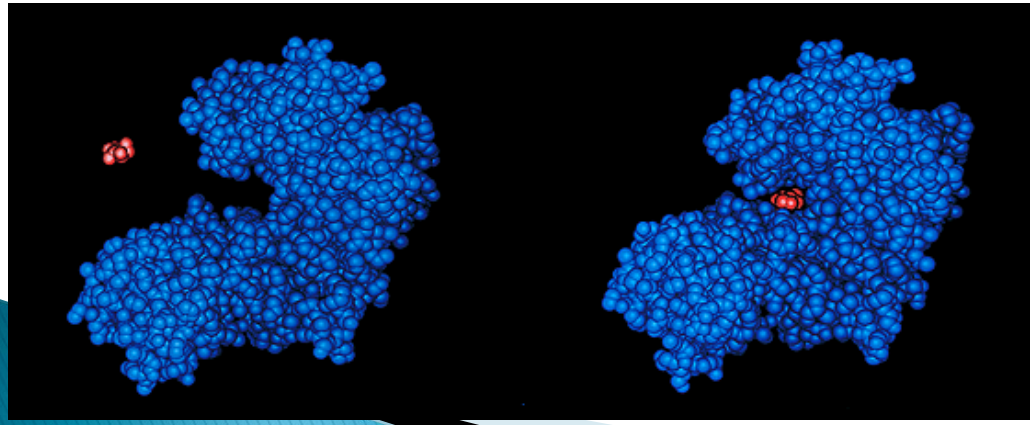
Today I will…

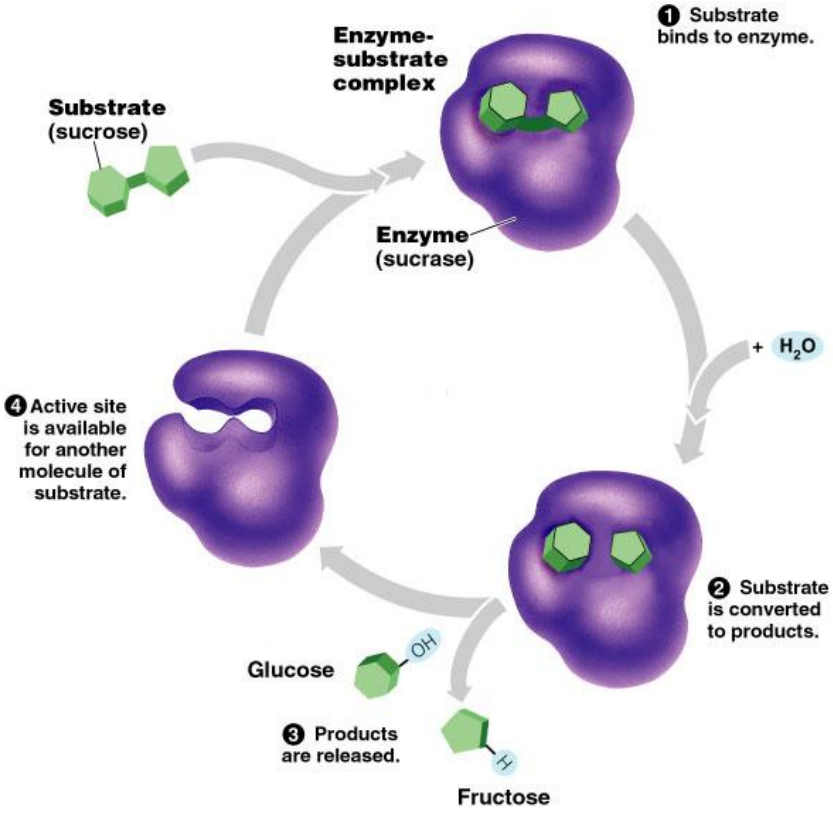
1. Review factors that affect enzyme activity.
2. Describe a laboratory procedure that will be used to study enzyme activity.

Lock and Key model



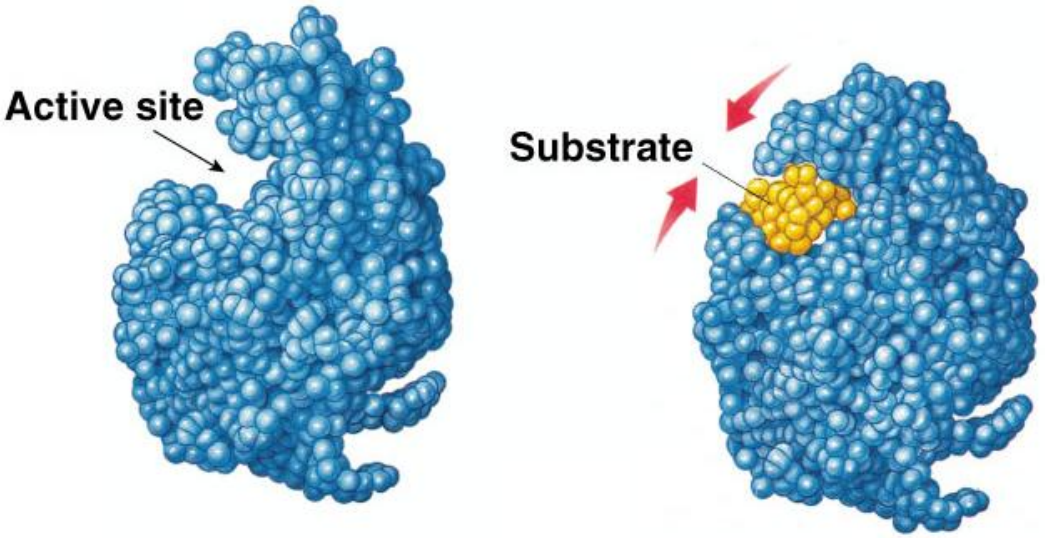
- Simplistic model of enzyme action
  - substrate fits into 3-D structure of enzyme' active site
    - H bonds between substrate & enzyme
  - like "key fits into lock"





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



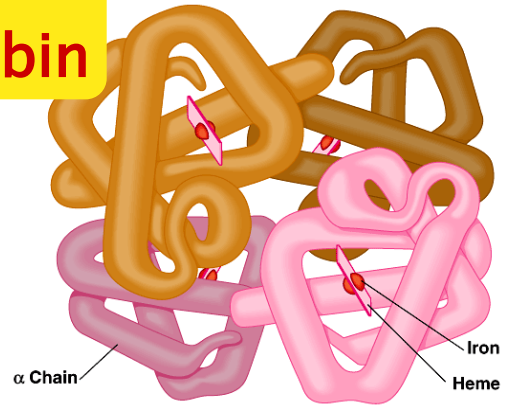
How does it work?

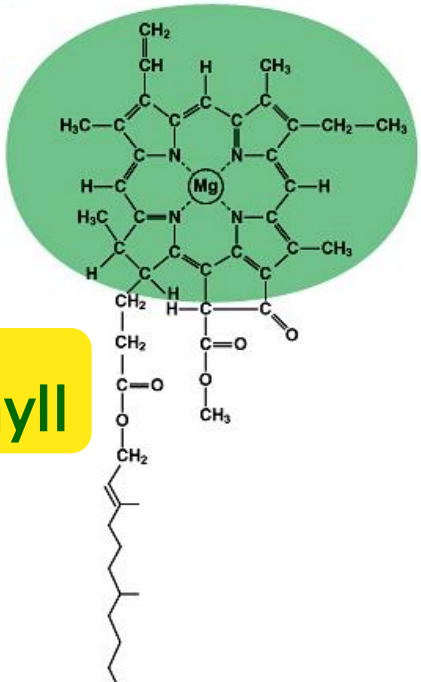
- Variety of mechanisms to lower activation energy & speed up reaction
  - synthesis
    - active site orients substrates in correct position for reaction
      - enzyme brings substrate closer together
  - digestion
    - active site binds substrate & puts stress on bonds that must be broken, making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

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

Fe in hemoglobin

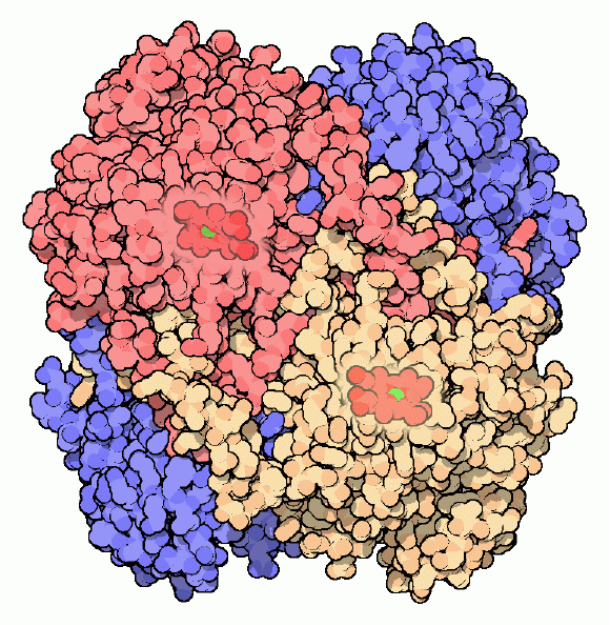




Mg in chlorophyll

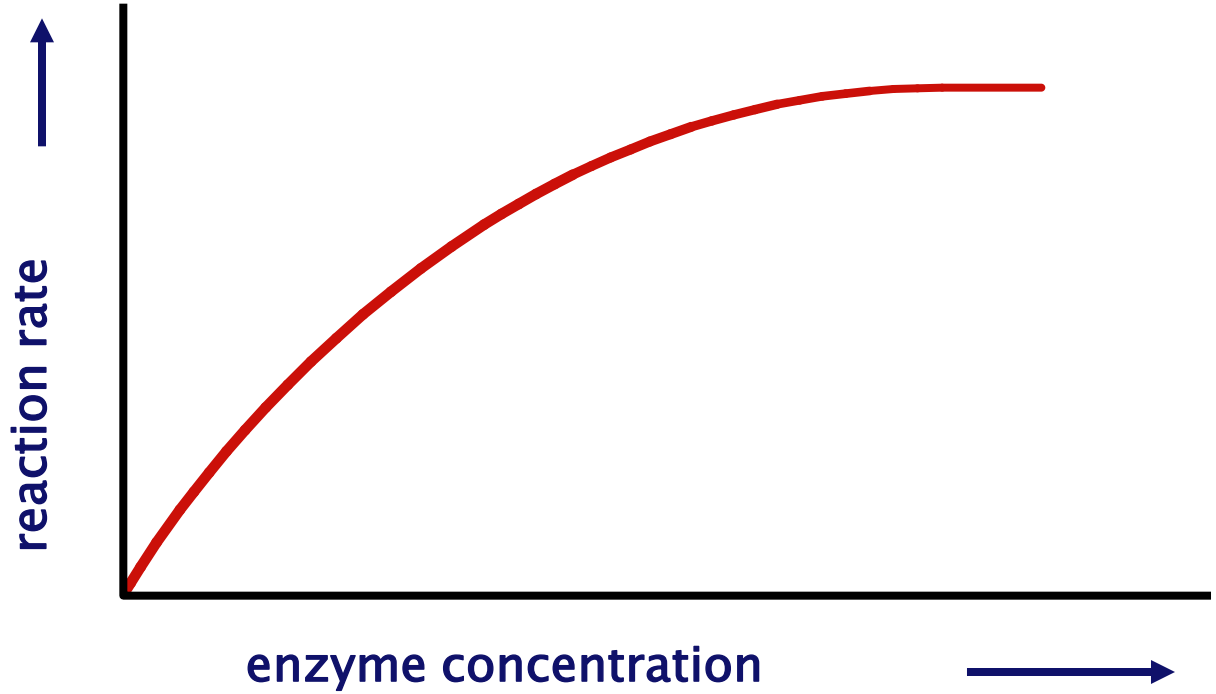
Factors Affecting Enzyme Function

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



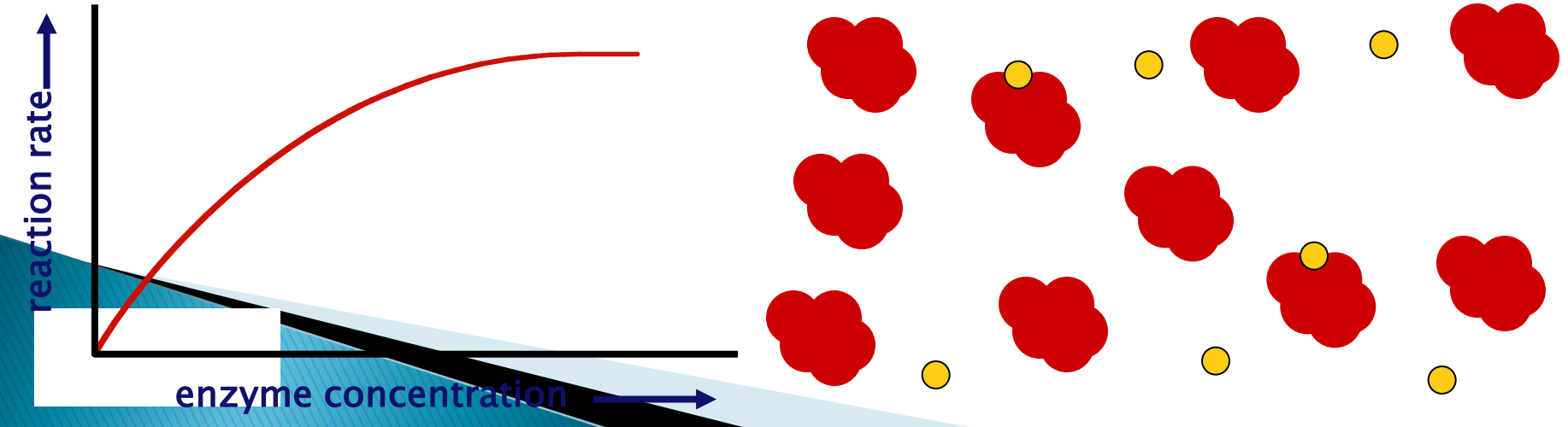
catalase

Enzyme concentration

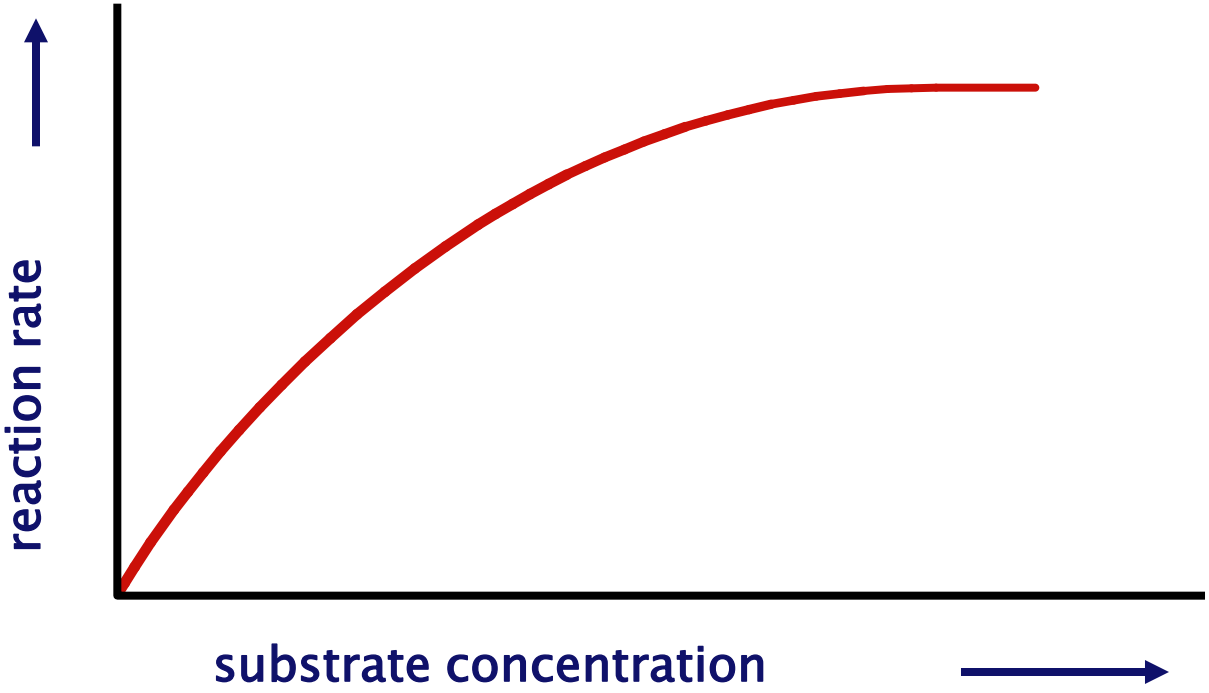


Factors affecting enzyme function

- 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

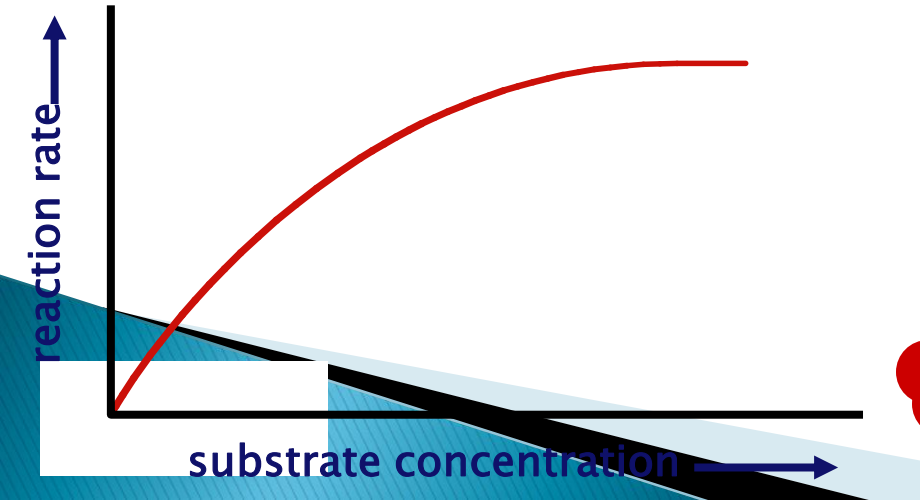


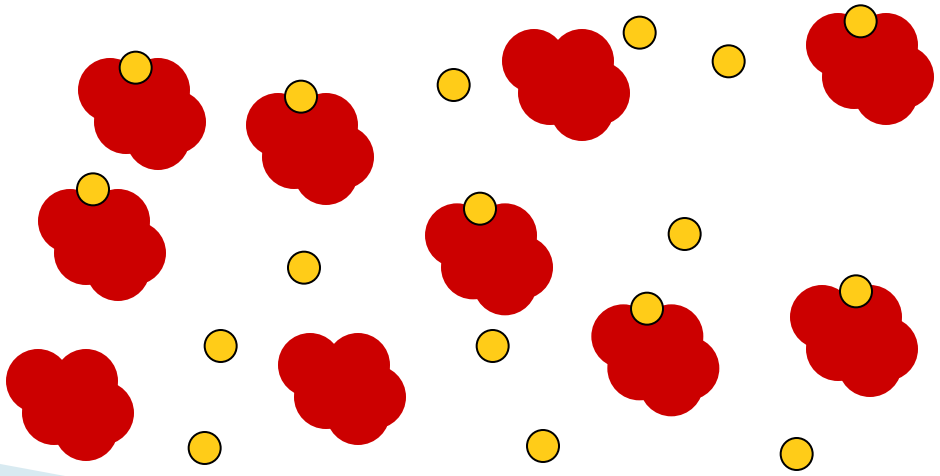
Substrate concentration



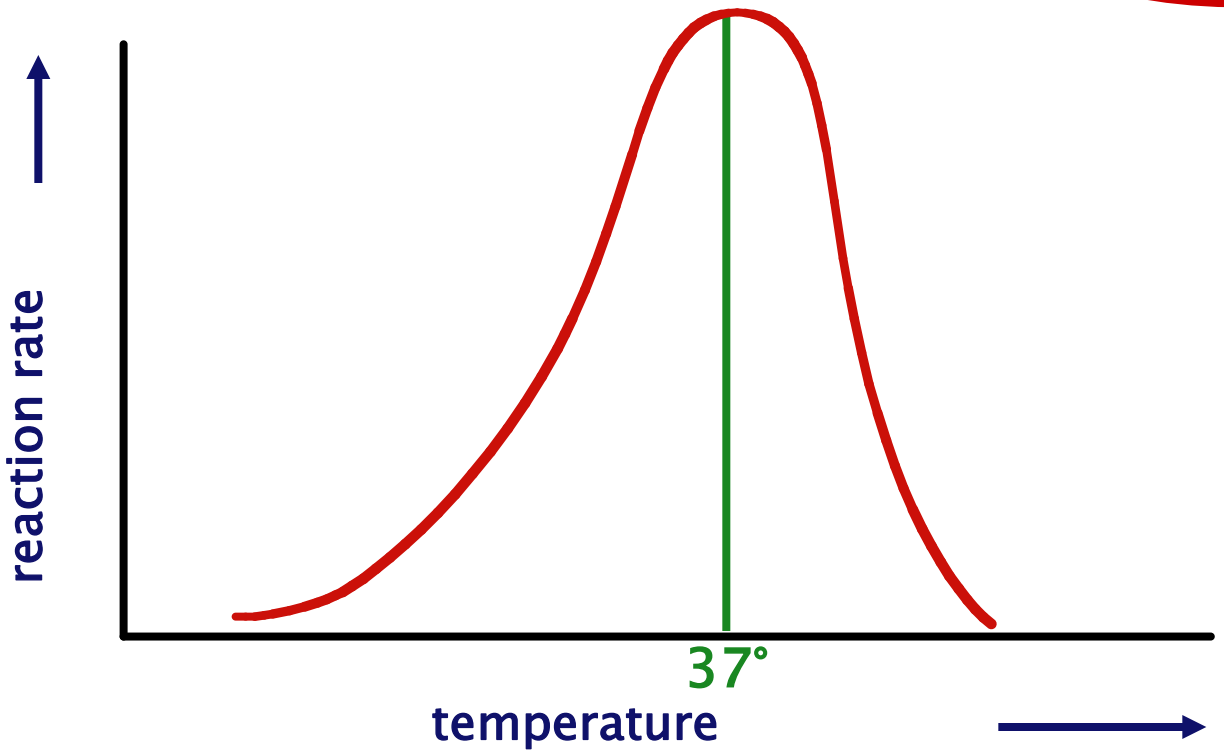
Factors affecting enzyme function

- 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

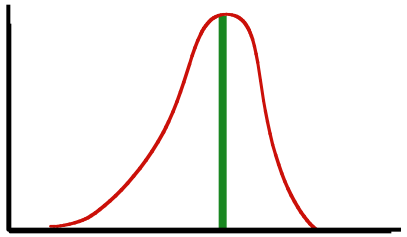




Temperature



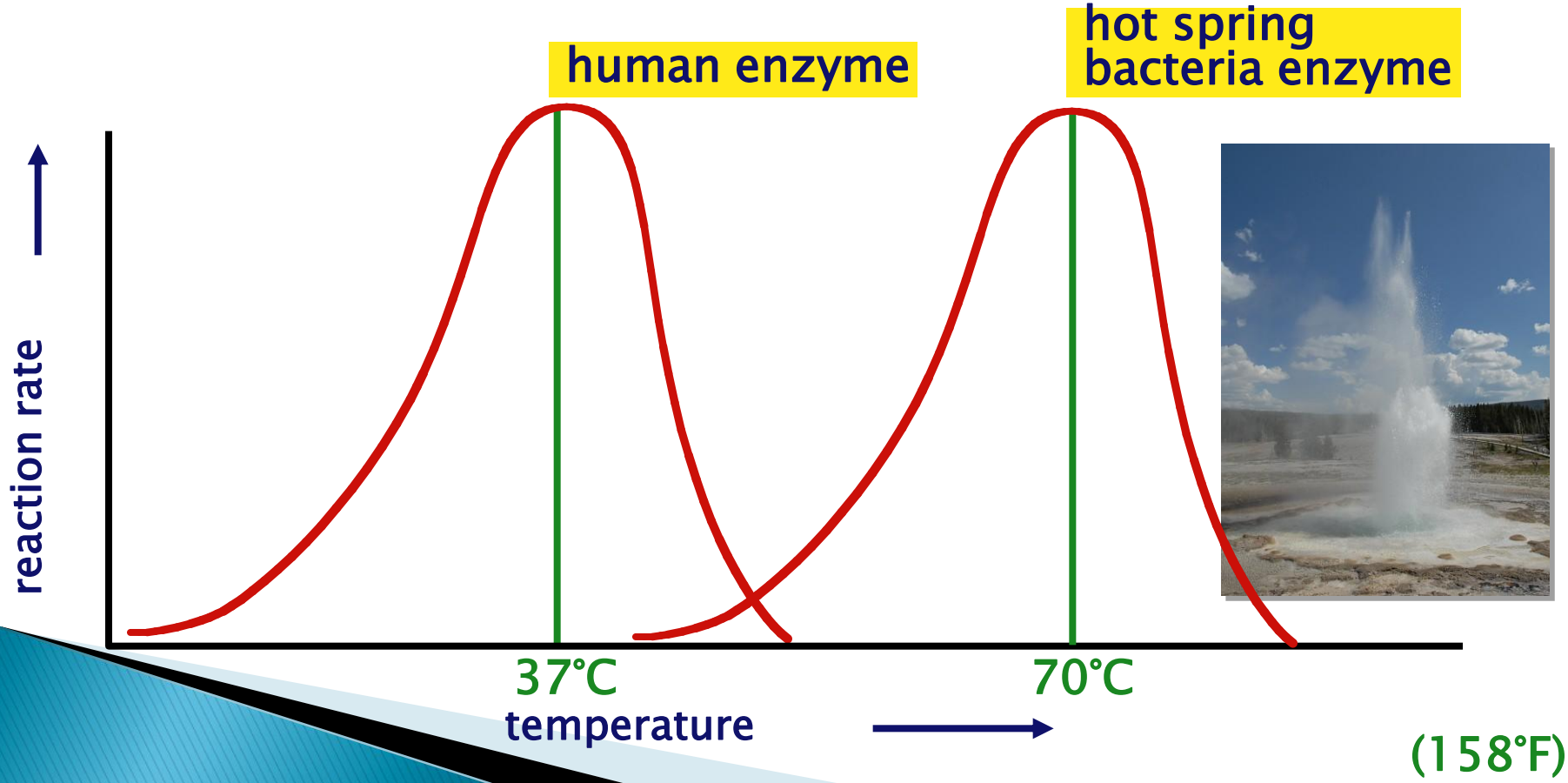
Factors affecting enzyme function



- 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

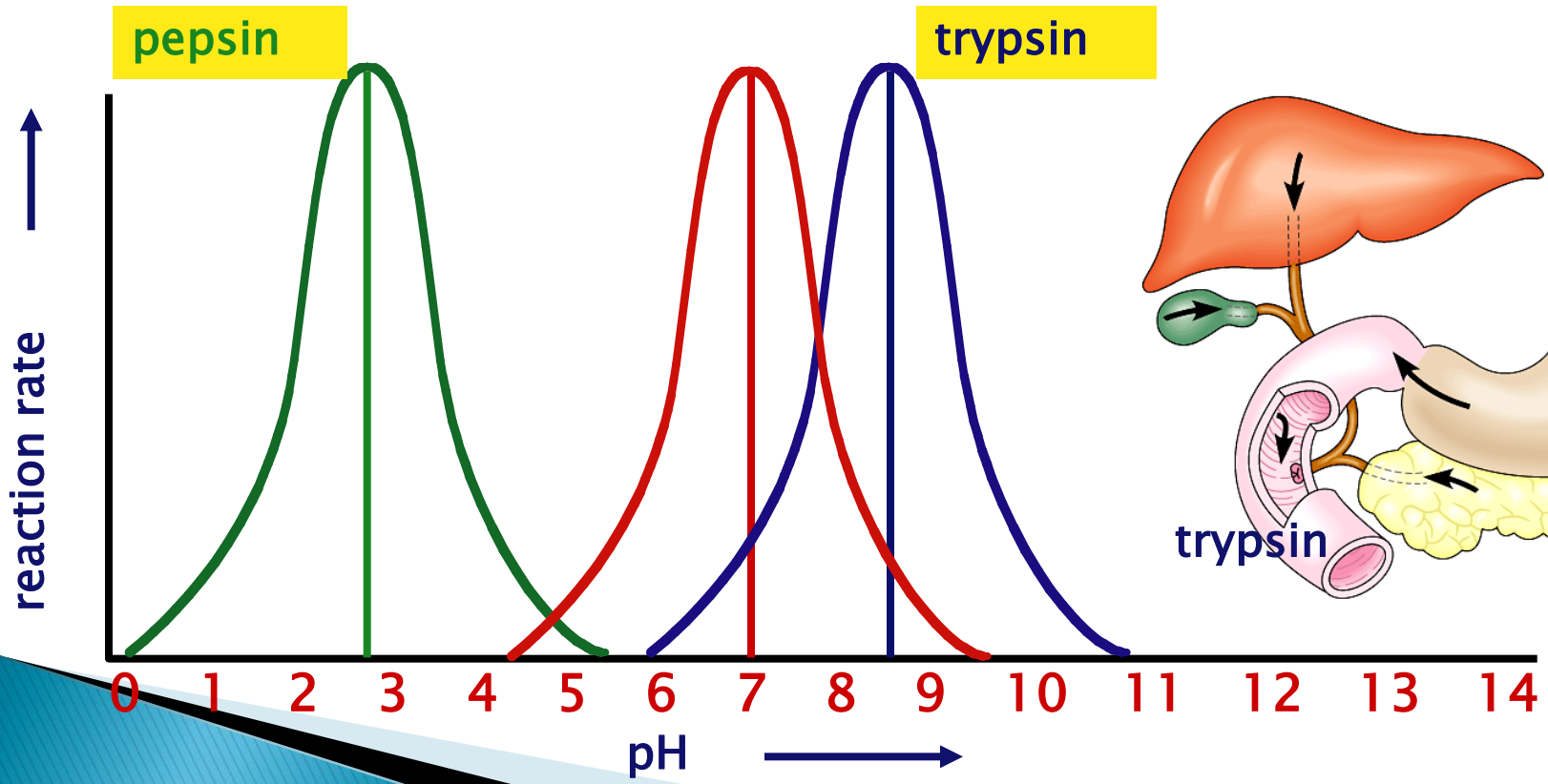
Enzymes and temperature

- Different enzymes function in different organisms in different environments



pH

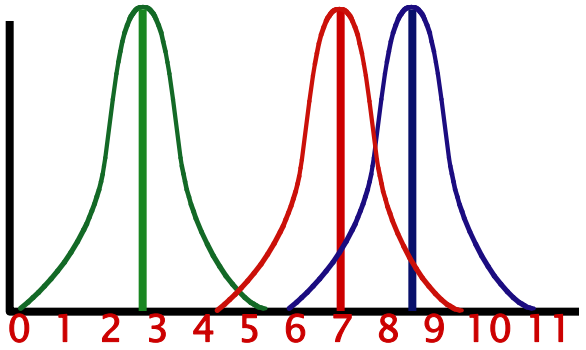

What's happening here?!


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

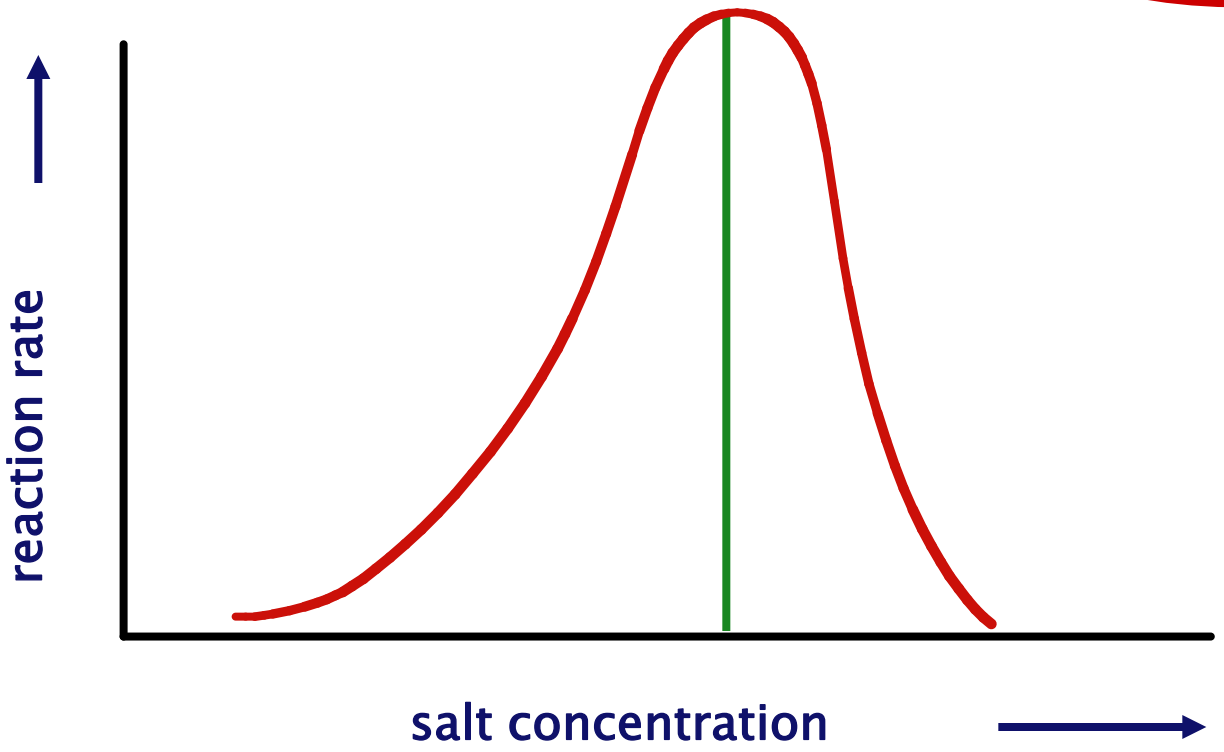
pepsin
trypsin

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

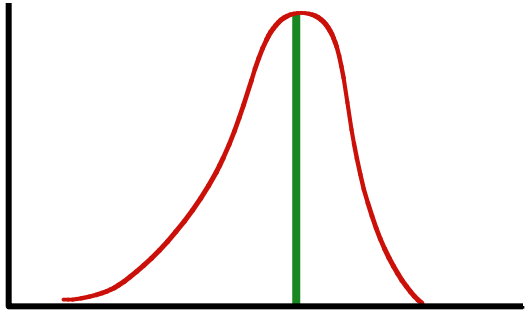


Salinity



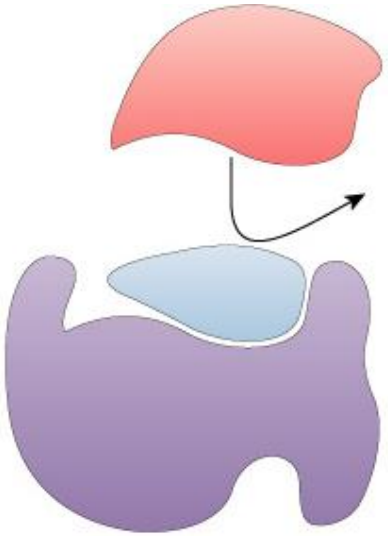
Factors affecting enzyme function

- 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!



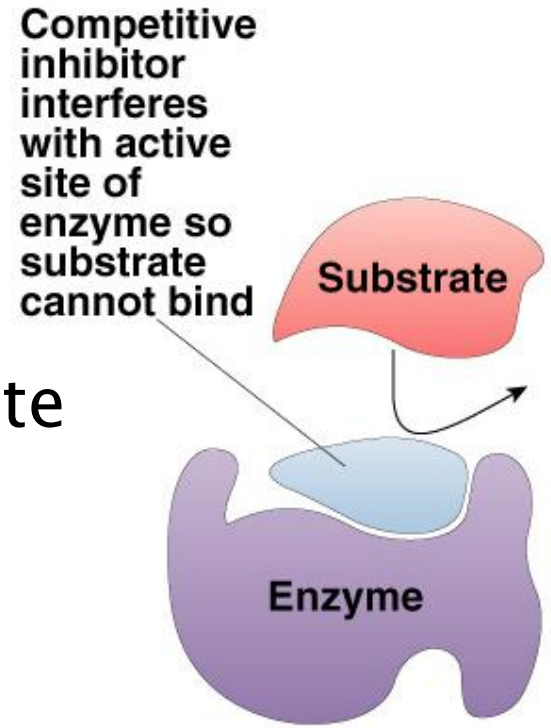
Compounds which regulate enzymes

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



Competitive Inhibitor

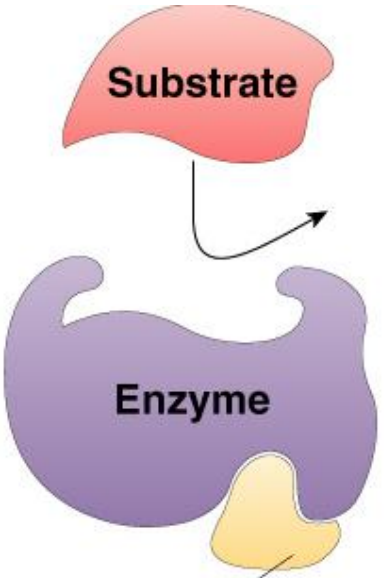
- Inhibitor & substrate "compete" for active site
  - penicillin
    blocks enzyme bacteria use to build cell walls
  - disulfiram (Antabuse)
    treats chronic alcoholism
    - blocks enzyme that breaks down alcohol
    - severe hangover & vomiting 5-10 minutes after drinking
- Overcome by increasing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



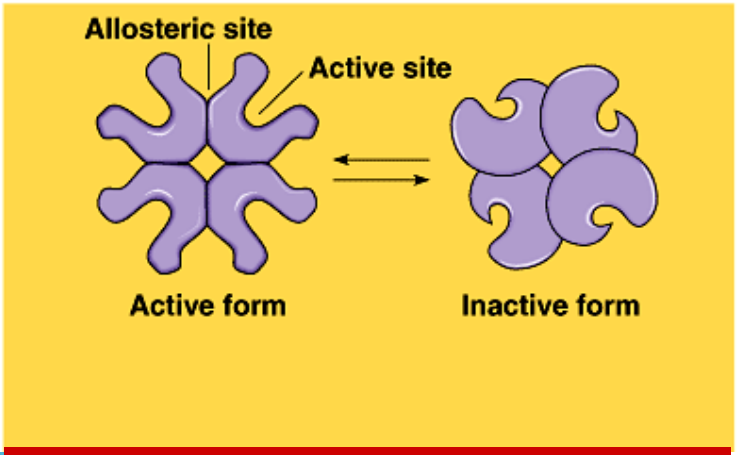
(b) Noncompetitive inhibition

Irreversible inhibition

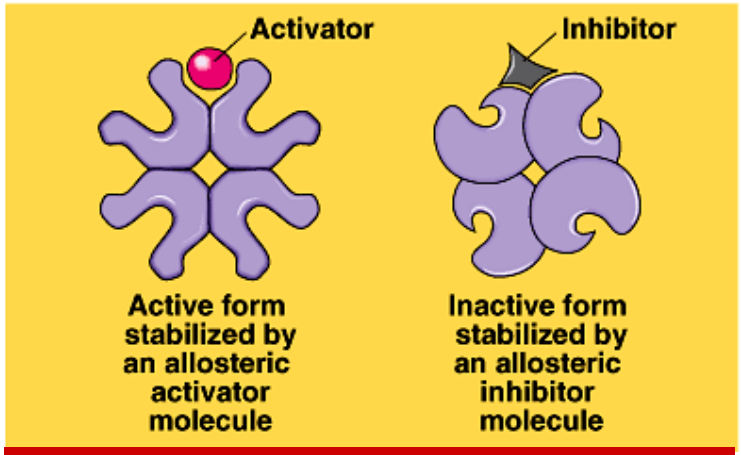
- Inhibitor permanently binds to enzyme
  - competitor
    - permanently binds to active site
  - allosteric
    - permanently binds to allosteric site
    - permanently changes shape of enzyme
    - nerve gas, sarin, many insecticides (malathion, parathion…)
      - cholinesterase inhibitors
        - 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

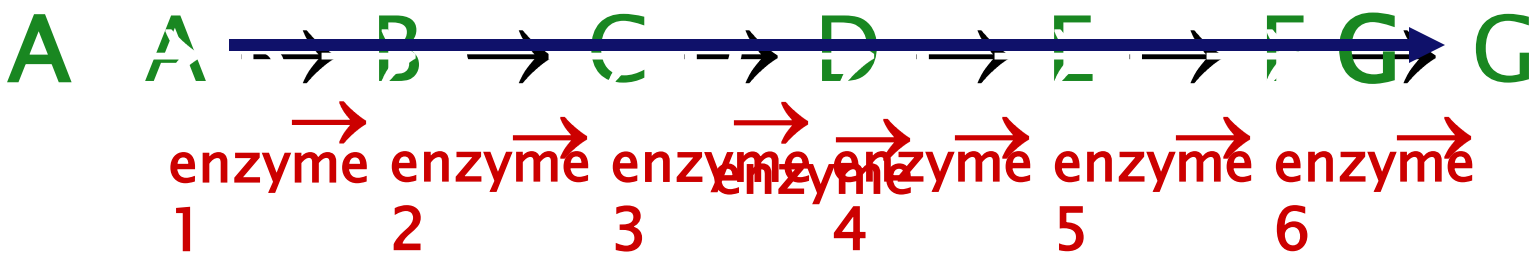


Conformational changes

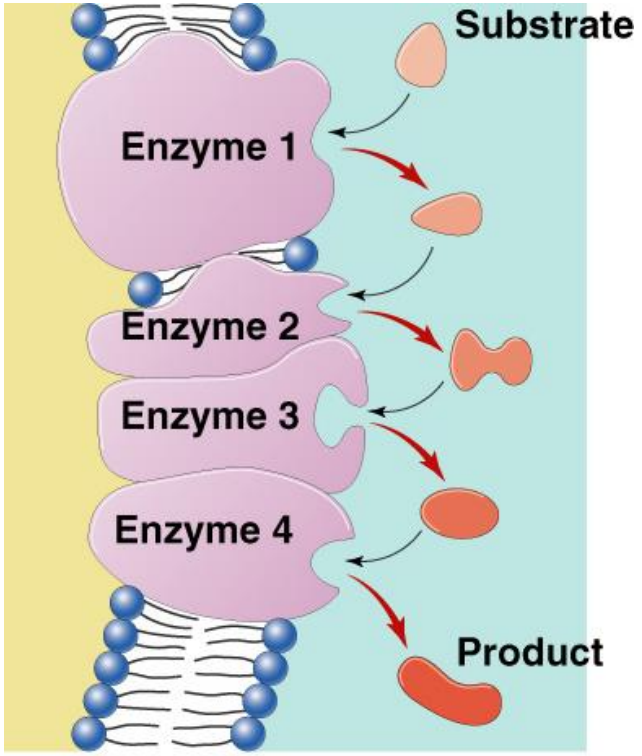


Allosteric regulation

Metabolic pathways

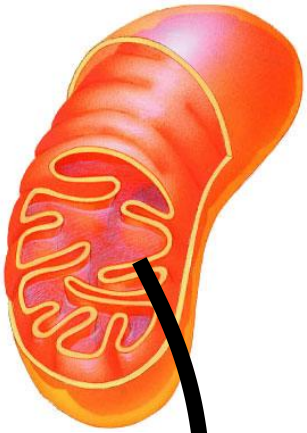


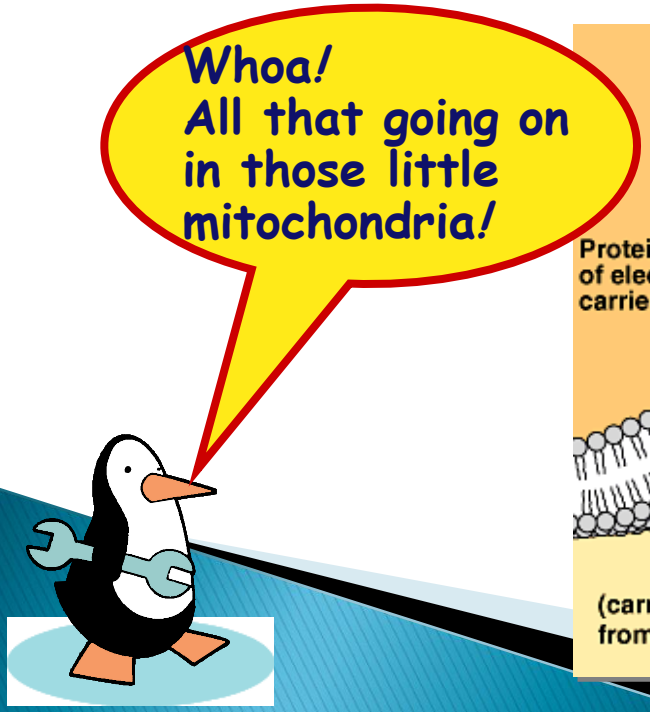
- Chemical reactions of life are organized in pathways
  - divide chemical reaction into many small steps
    - artifact of evolution
    - ↑ efficiency
      - intermediate branching points
    - ↑ control = regulation

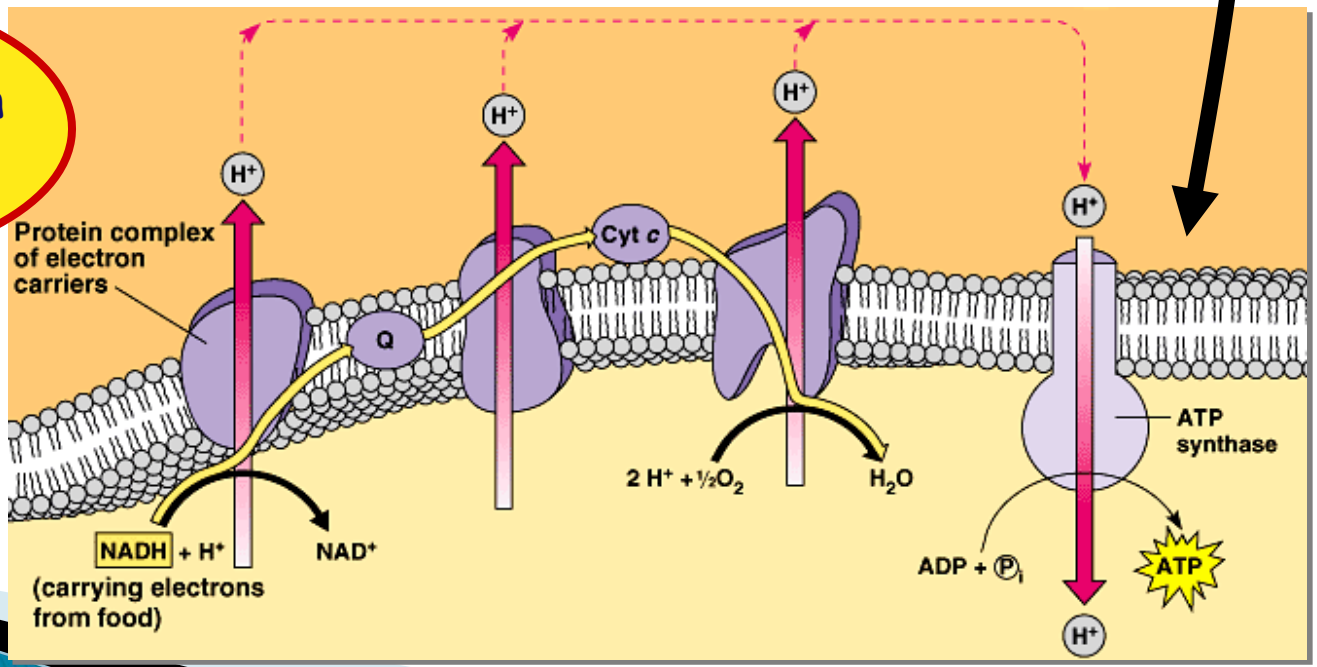


Efficiency

- Organized groups of enzymes
  - enzymes are embedded in membrane and arranged sequentially
- Link endergonic & exergonic reactions

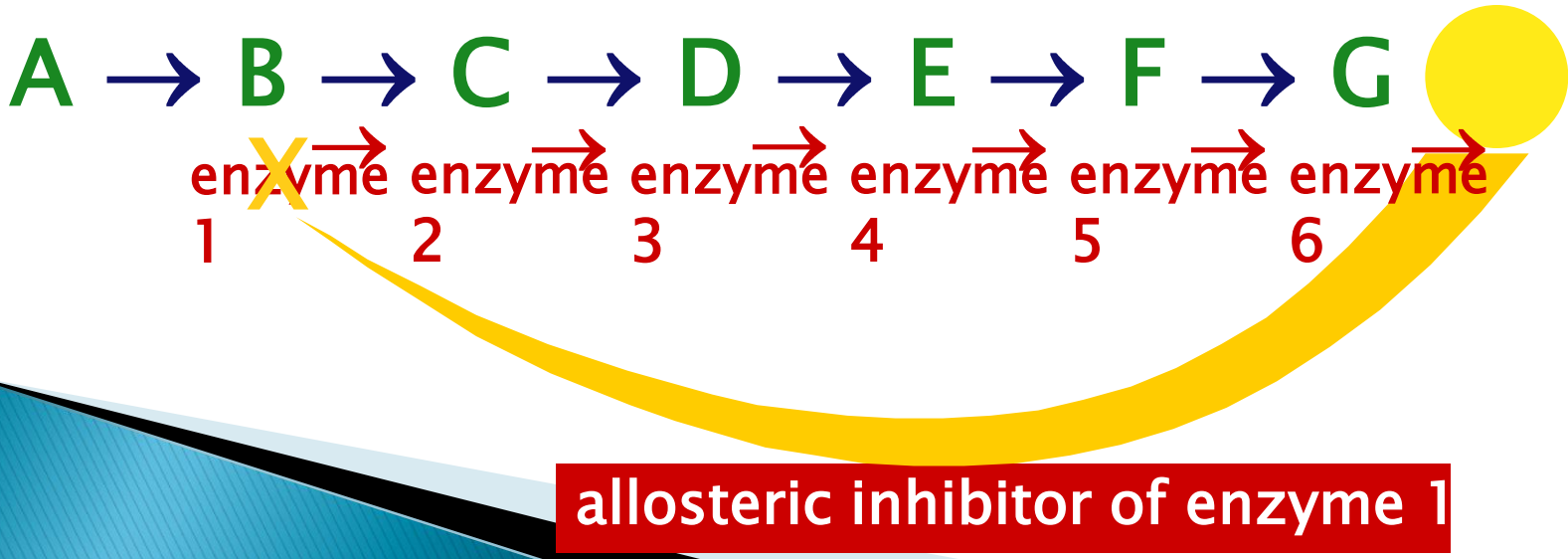






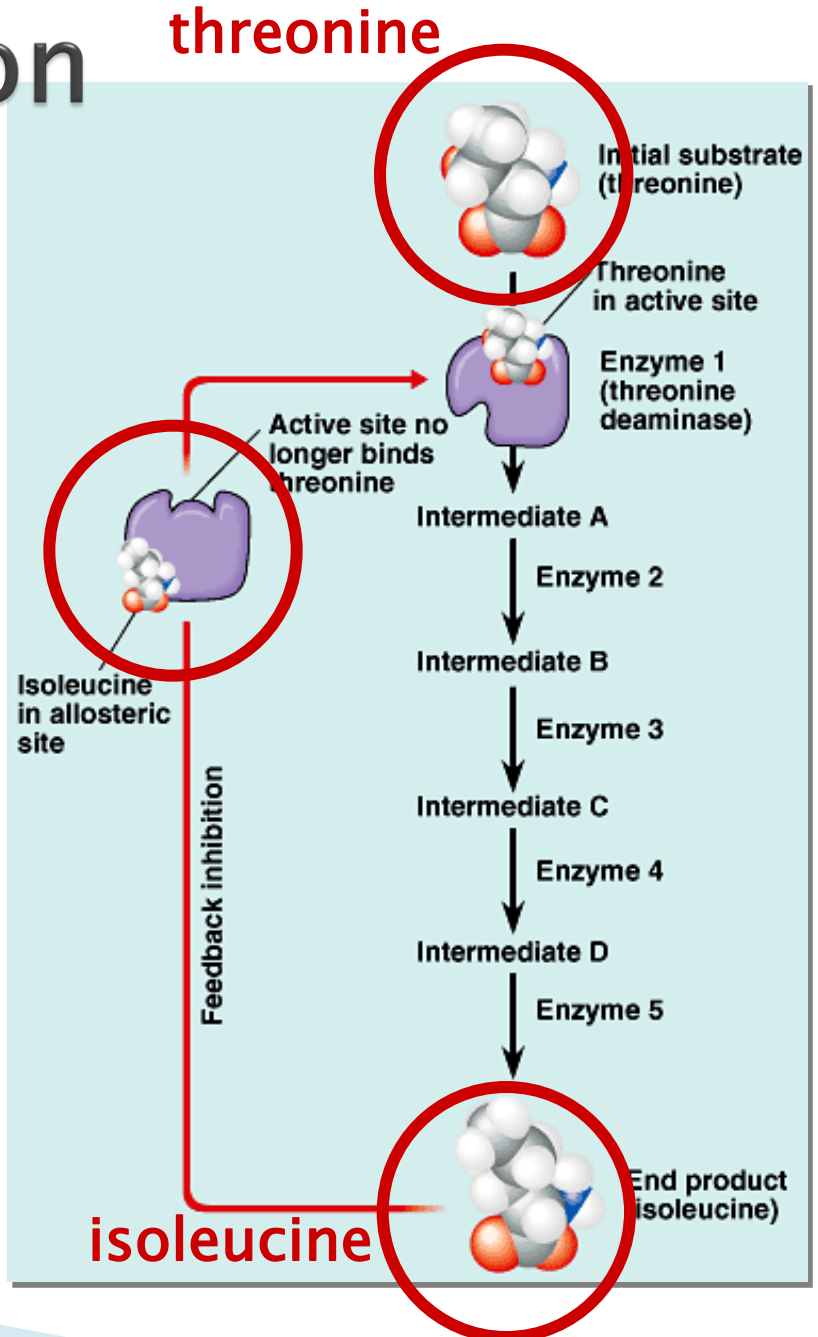
Feedback Inhibition

- 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

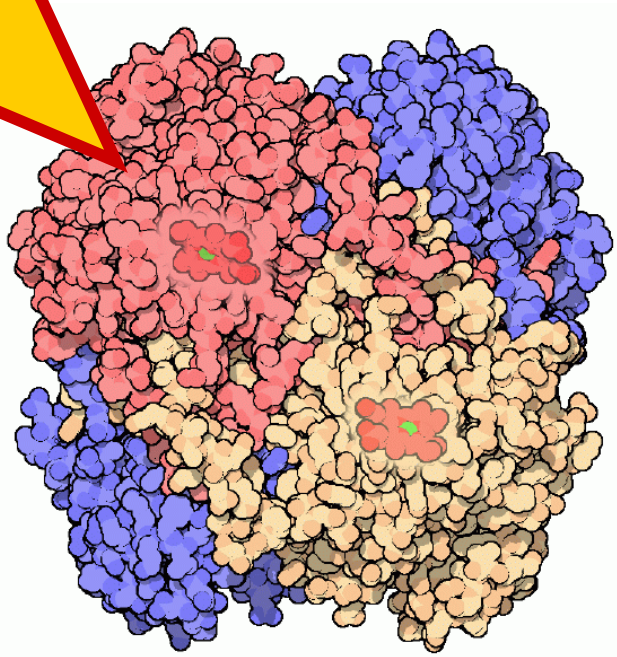


Feedback inhibition

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



Don't be inhibited!
Ask Questions!



Energy Principles

Two Pathways

CATABOLIC pathways:

break down complex molecules into smaller ones

- hydrolysis/digestion reactions
  - **RELEASES** energy
  - Example: respiration

ANABOLIC pathways:

consume or **ABSORB** energy

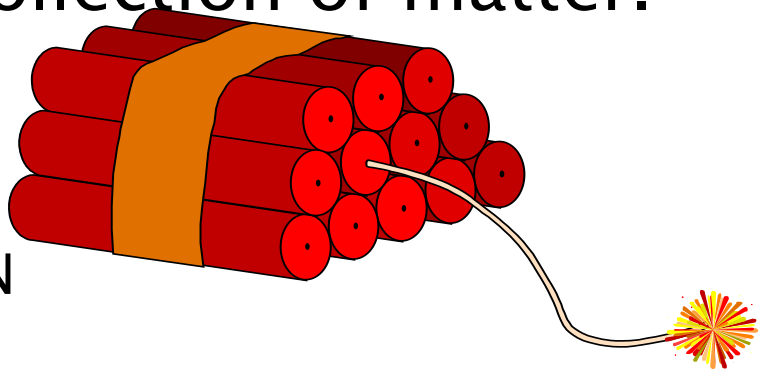
-building complex molecules from smaller ones.

-condensation/dehydration synthesis

- Example: Photosynthesis

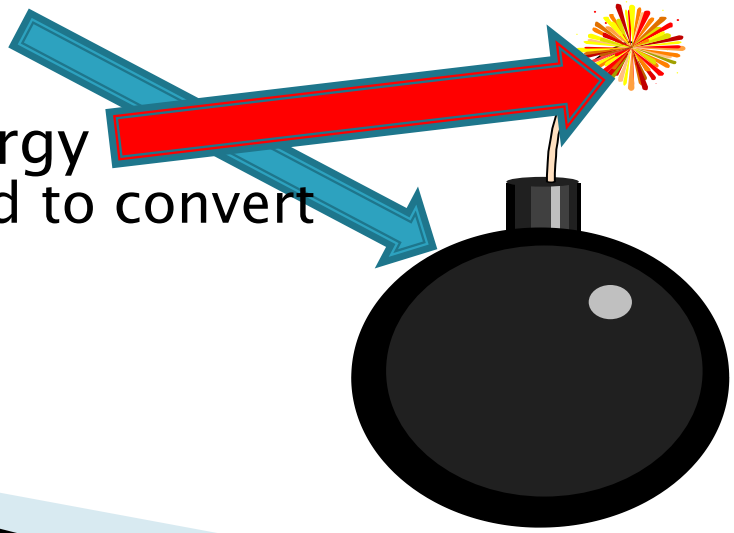
Energy–What is it?

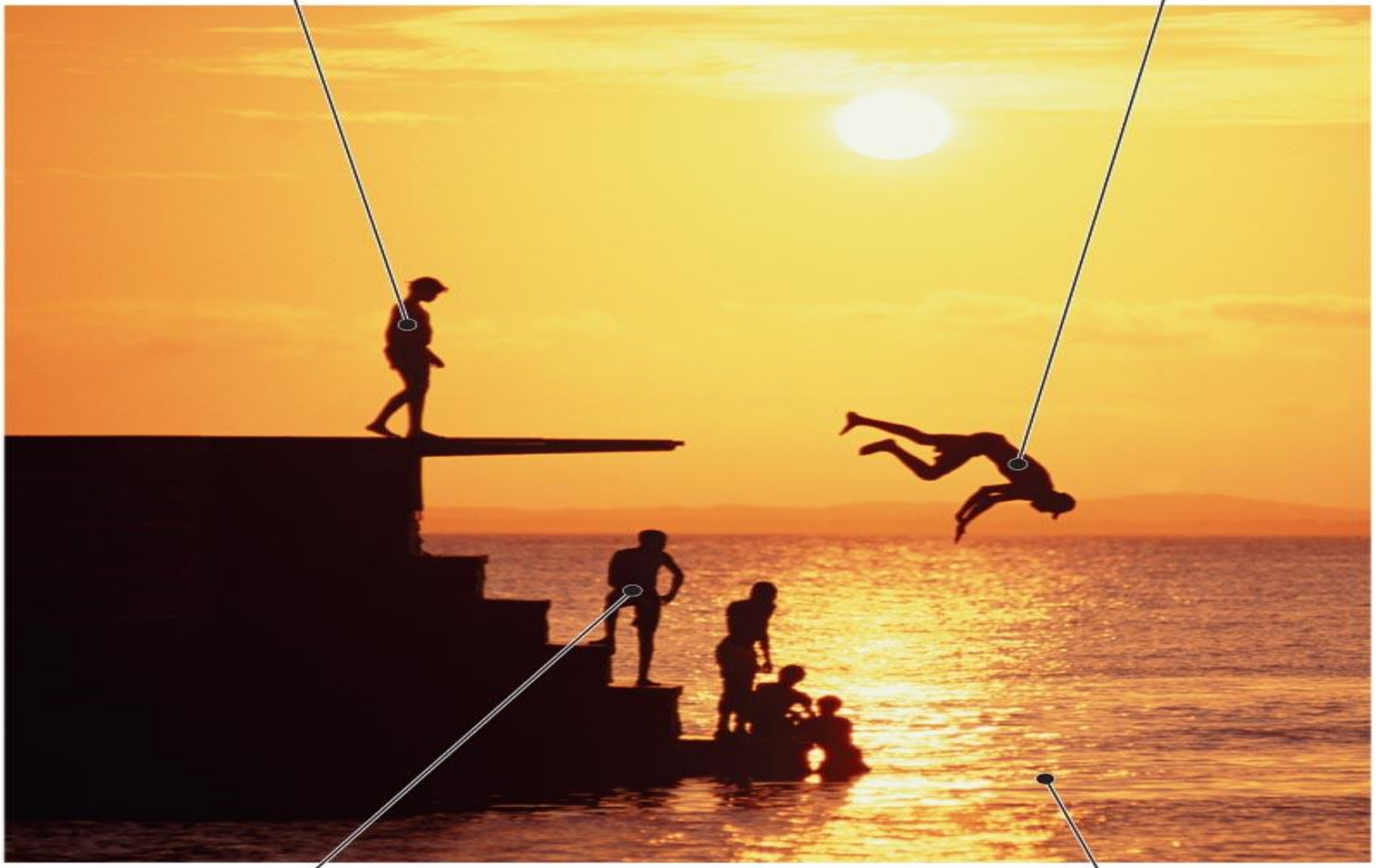
- ENERGY is the ability to do work.
- The ability to rearrange a collection of matter.



Forms of energy:

- Kinetic (KE)
  - Energy of ACTION or of MOTION
- Potential (PE)
  - Stored energy
- Activation Energy
  - Energy needed to convert PE to KE.





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SECOND LAW OF THERMODYNAMICS

Each energy transfer or transformation increases the entropy of the universe.

So what is ENTROPY?

- A measure of disorder or chaos
- The *quantity* of energy in the universe is constant, but its *quality* is not.

So HOW DOES LIFE WORK to minimize ENTROPY?

- By using energy from the environment or external sources (e.g. food, light).

Free energy

- The portion of a system's energy that can perform work.

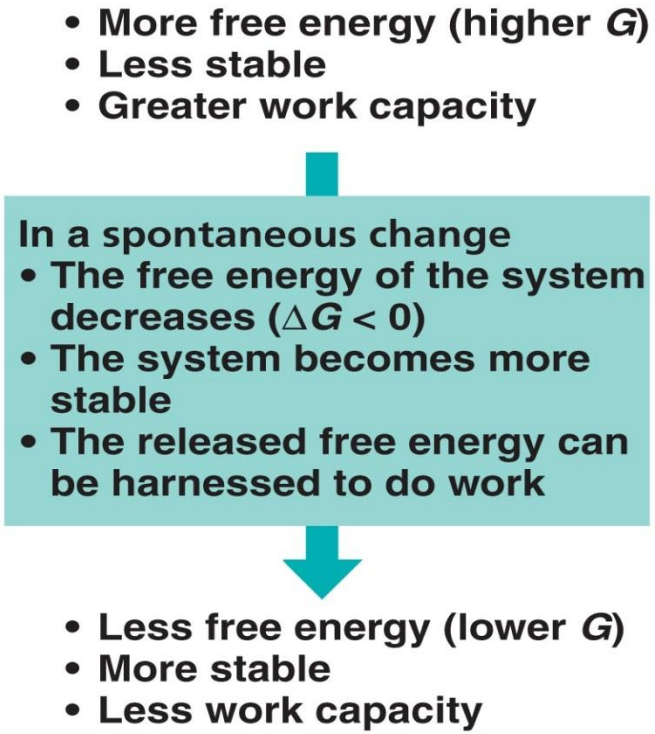
$$\Delta G = H - (T)S$$

G = free energy of a system
H = total energy of a system
T = temperature in ^{o}K
S = entropy of a system

- If the system has:
  - more free energy
  - it is less stable
- It has greater work capacity

Spontaneous vs. Stabile

- If the system is **unstable**, it has a greater tendency to change spontaneously to a more stable state.
  - This change provides free energy for work.



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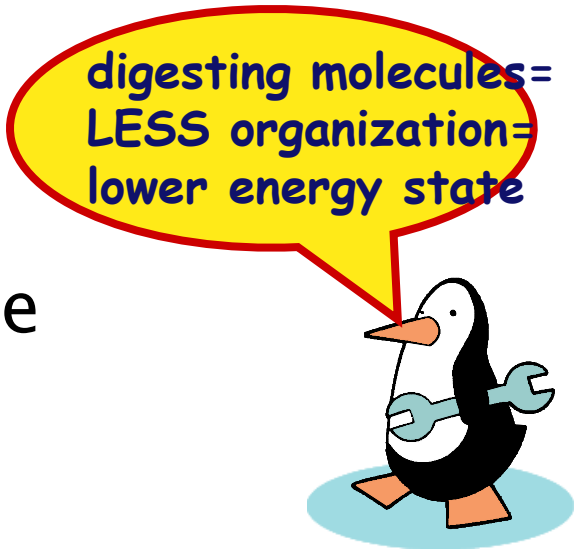
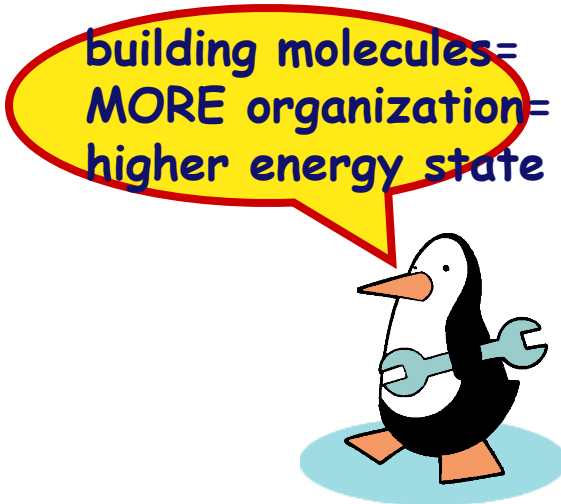
Chemical reactions & energy

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

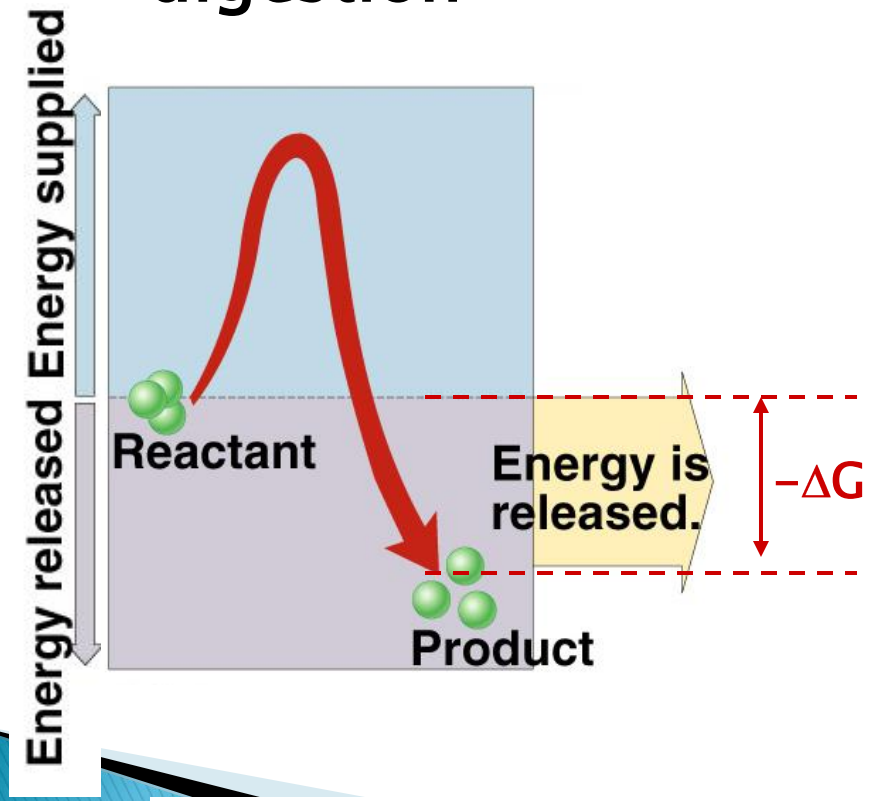




Endergonic vs. exergonic reactions

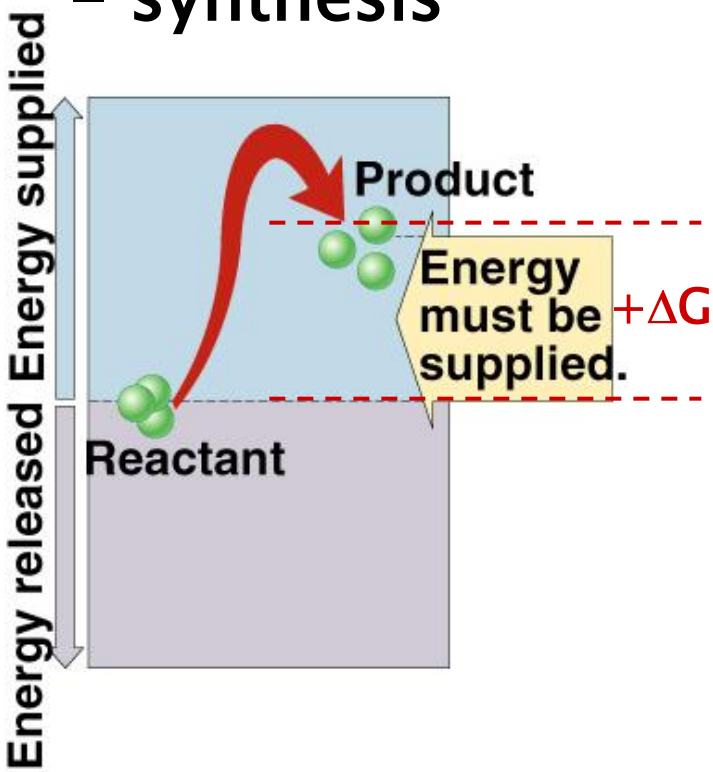
exergonic

- energy released
- digestion



endergonic

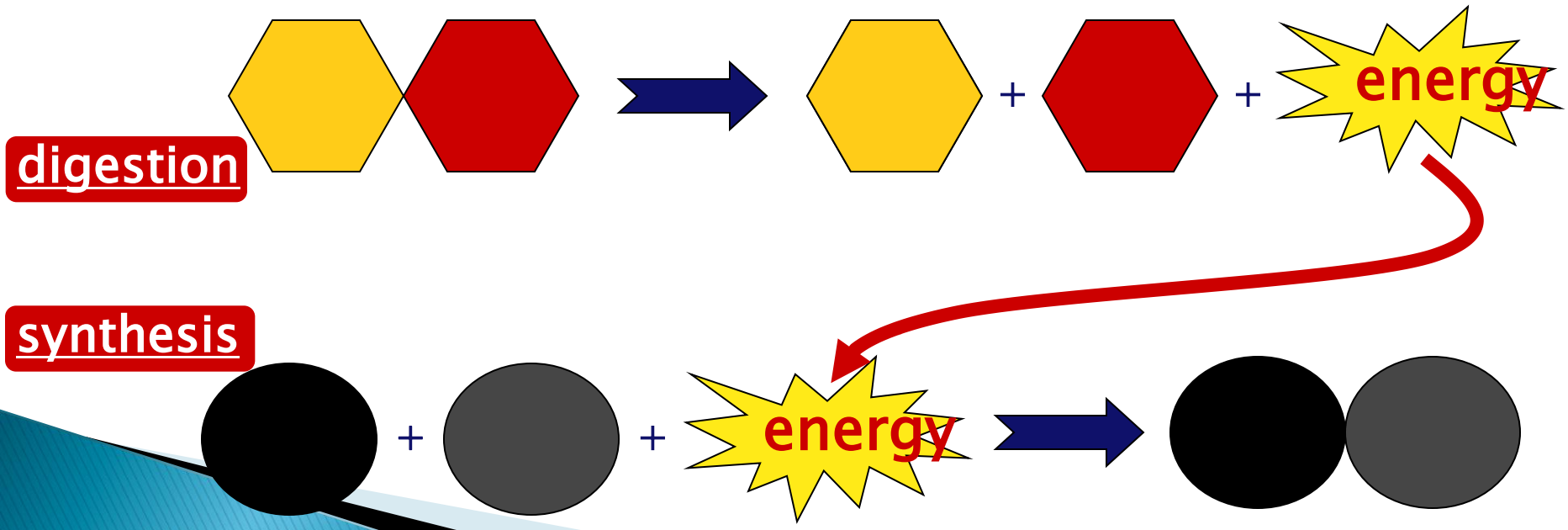
- energy invested
- synthesis



ΔG = change in free energy = ability to do work

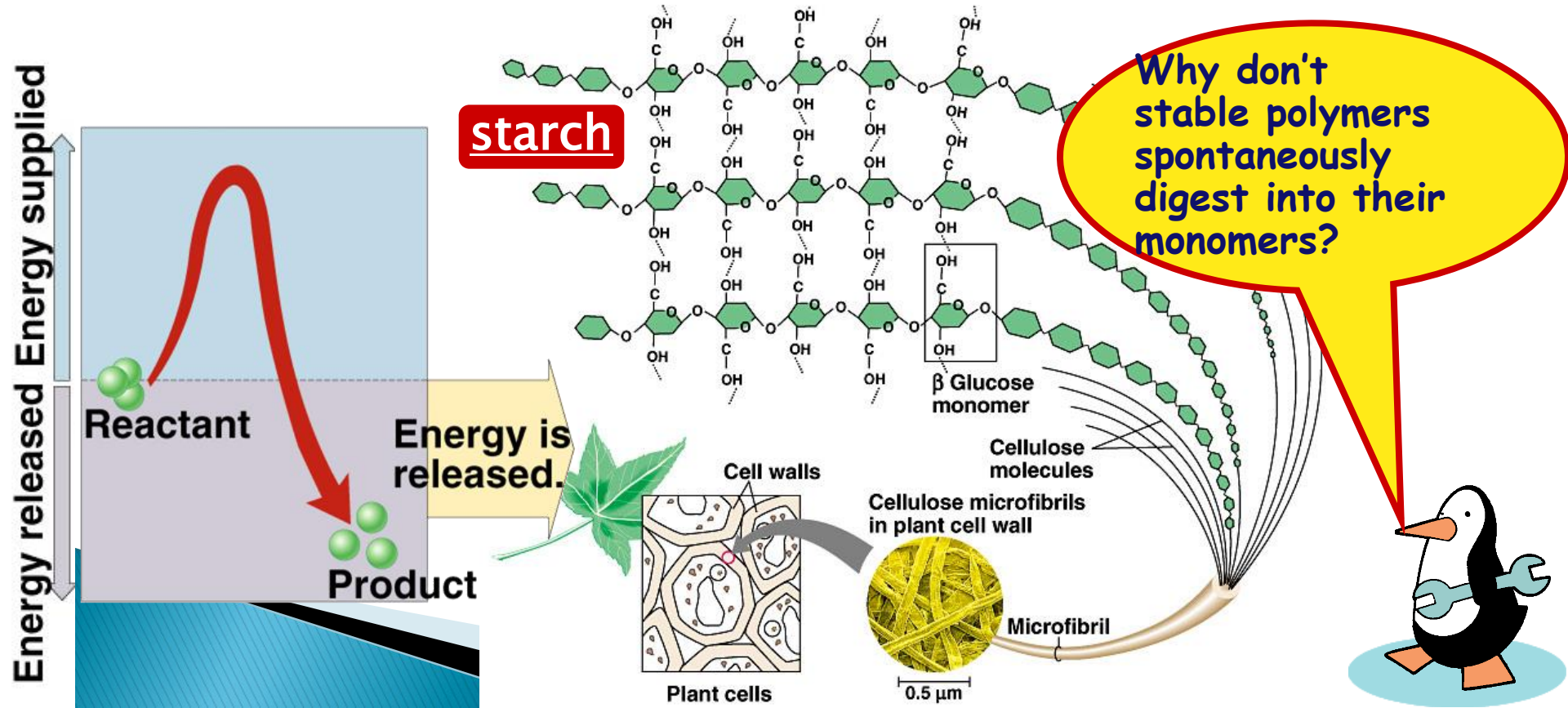
Energy & life

- 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



Cells must "do" work

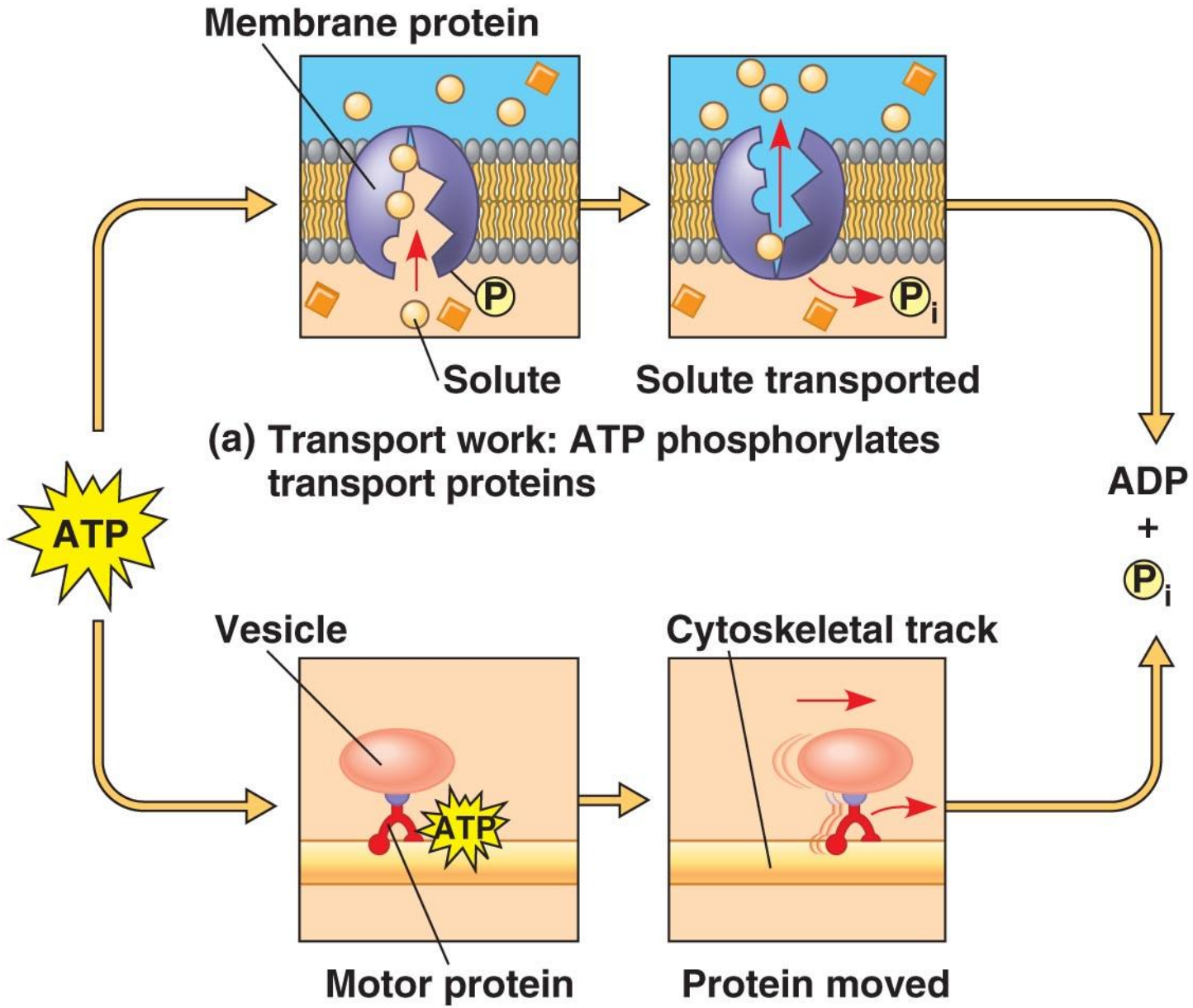
Examples of cellular work:

- Mechanical – muscle contractions
- Transport – pumping across membranes
- Chemical – making polymers

Cells must use ENERGY to do work…

–Couples an *exergonic* process to drive an *endergonic* one.

- ATP is used to couple the reactions together.



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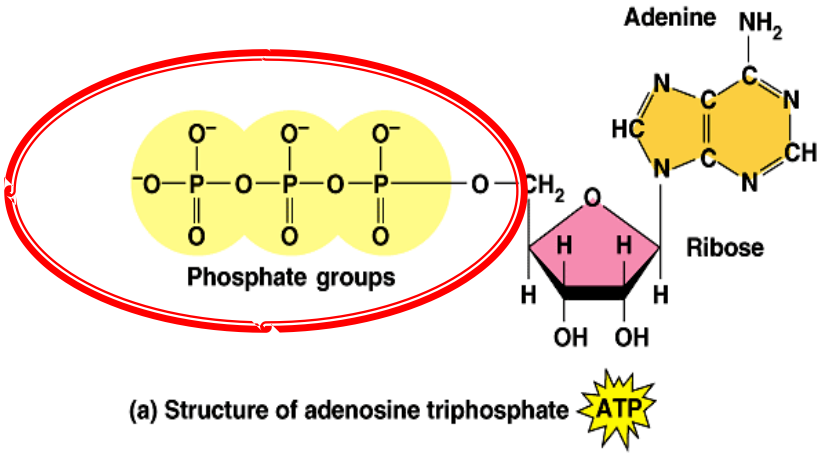
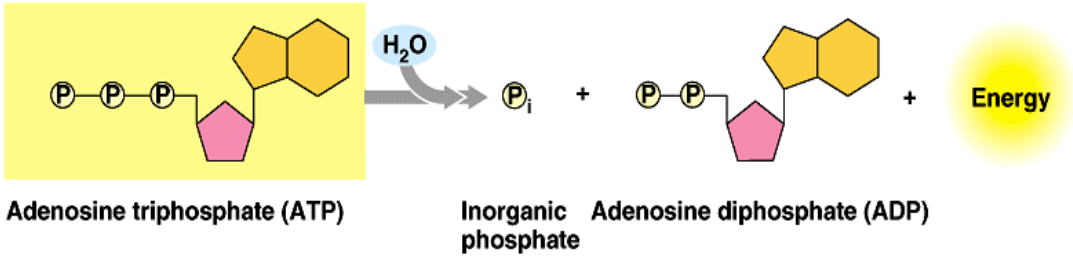
ATP (Adenosine TriPhosphate)

- Made of:
  - Adenine (nitrogenous base)
  - Ribose (pentose sugar)
  - 3 phosphate groups



Key to ATP:
3 PO_4



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ATP performs work

- Works by energizing other molecules
  - by transferring **phosphate groups**.

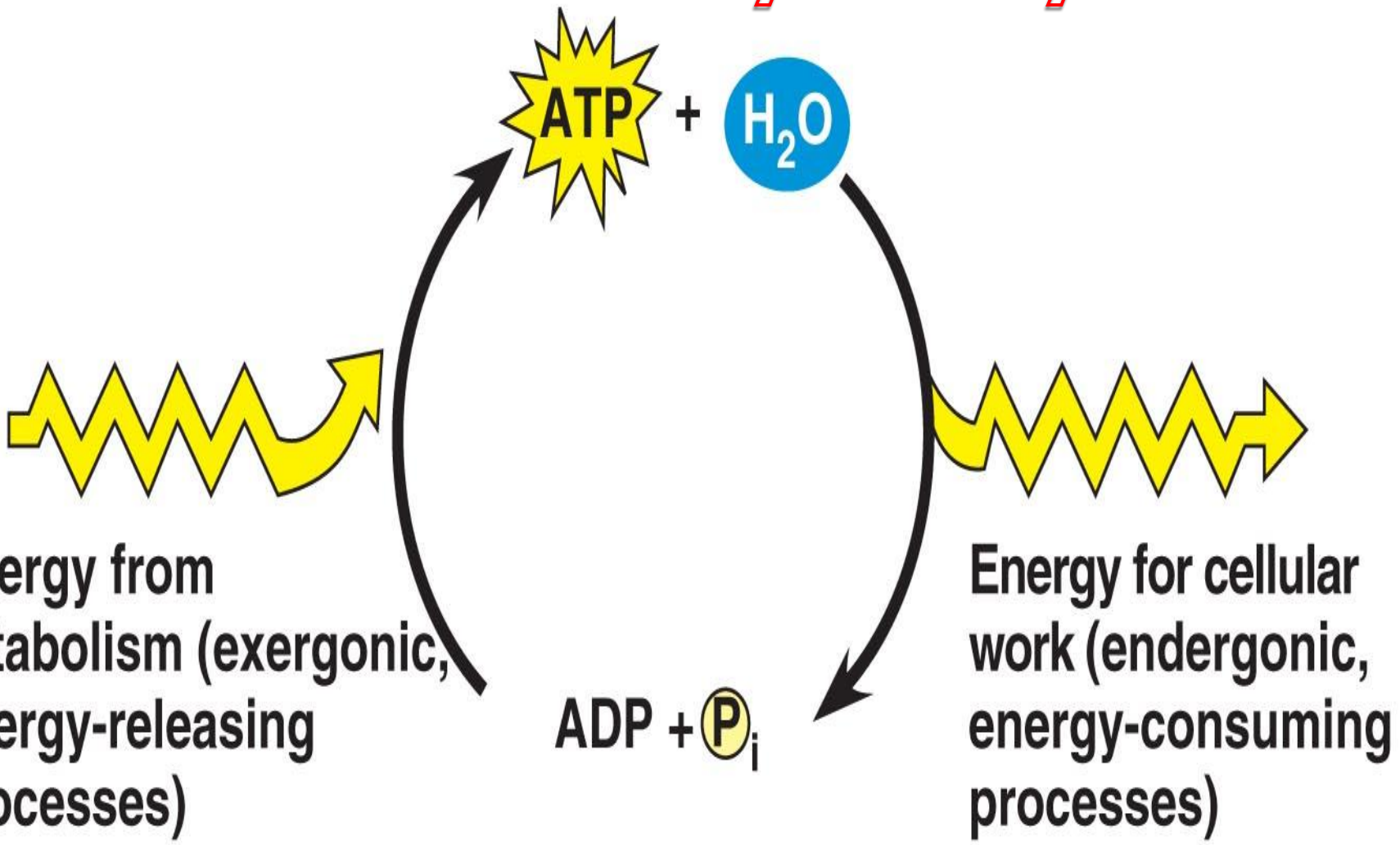
- ATP:
  - Renewable energy resource.
  - Unstable bonds
- Food:
  - Long term energy storage
  - Stable bonds

ATP Cycles

- Energy released from ATP drives anabolic reactions.
- Energy from catabolic reactions “recharges” ATP.

ATP Cycle

hydrolysis



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