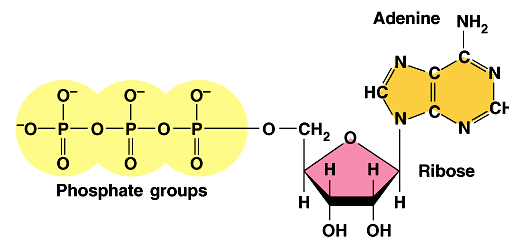


BI107 CHAP 6A

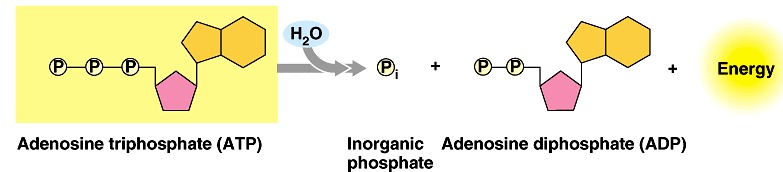
ATP, Enzymes and Metabolic
Control

ATP

- ATP powers cellular work by coupling exergonic reactions to endergonic reactions
- 3 main types of work done by a cell
 - 1) mechanical – muscle contraction, cilia beating
 - 2) transport – pumping ions against concentration gradients
 - 3) chemical – pushing endergonic reactions – must push to go



(a) Structure of adenosine triphosphate **ATP**

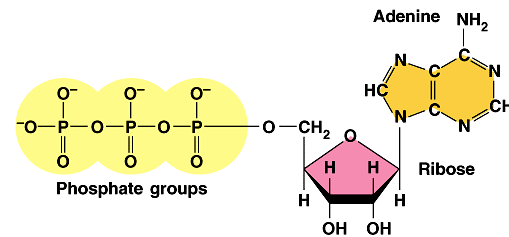


(b) Hydrolysis of ATP

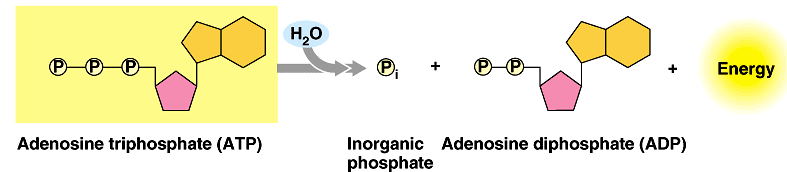
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ATP cont.

- ATP is immediate source of energy for all those types of reactions
- Structure – nitrogenous base adenine bonded to ribose – 5 carbon sugar & 3 phosphate groups attached to ribose



(a) Structure of adenosine triphosphate **ATP**

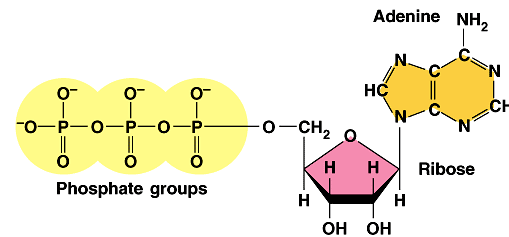


(b) Hydrolysis of ATP

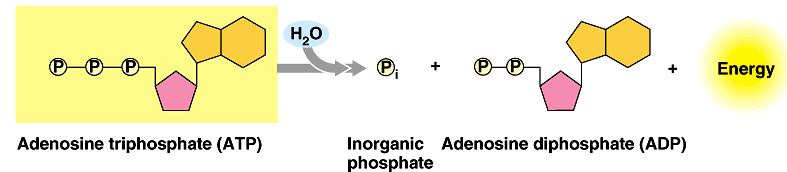
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ATP cont.

- Bonds between phosphates broken by hydrolysis forming ADP & inorganic phosphate (P_i) & reaction is exergonic – in standard lab conditions - -7.3 kcal/mol or 31 kJ/mol but in cell -13 kcal/mol 78% greater



(a) Structure of adenosine triphosphate **ATP**

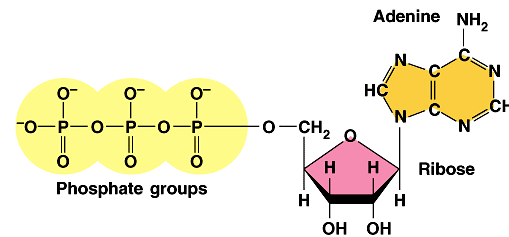


(b) Hydrolysis of ATP

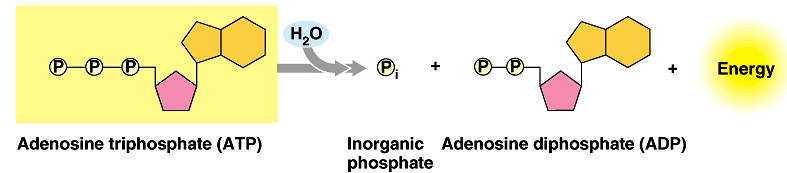
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ATP cont.

- Energy released because ADP plus P_i are more stable than ATP (when system changes in direction of greater stability change is exergonic)
- Phosphate bond is fragile due to negative charges of 3 phosphates crowded together



(a) Structure of adenosine triphosphate **ATP**

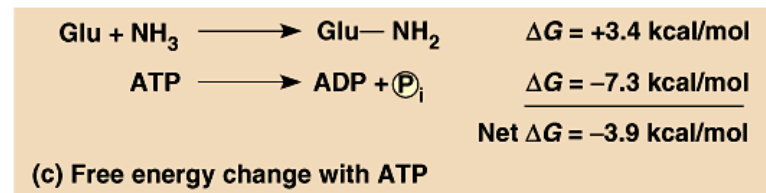
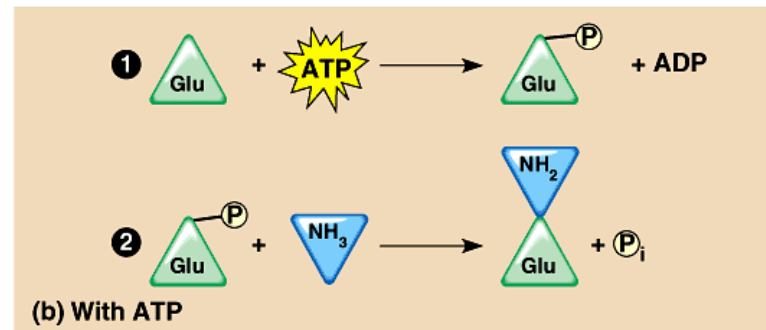
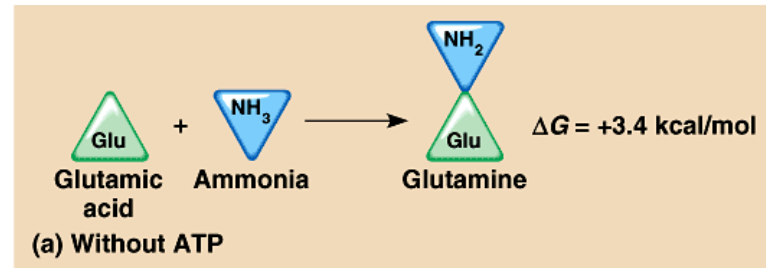


(b) Hydrolysis of ATP

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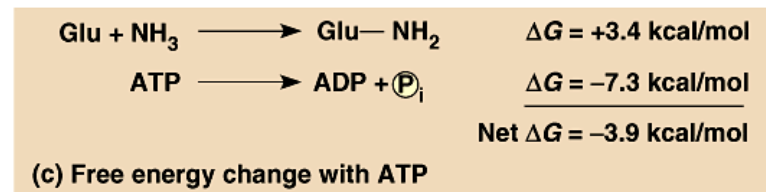
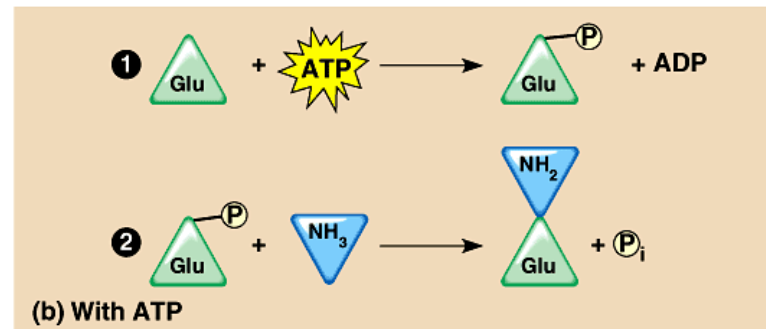
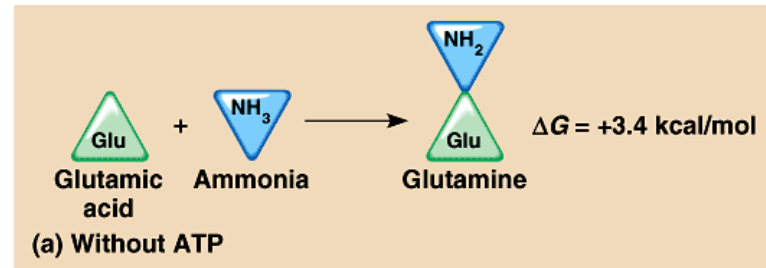
ATP cont.

- How ATP works – specific enzymes in cell couple energy of ATP hydrolysis directly to endergonic processes by transferring phosphate group from ATP to some other molecule which is ‘phosphorylated’ & phosphorylated intermediates are more reactive than unphosphorylated ones



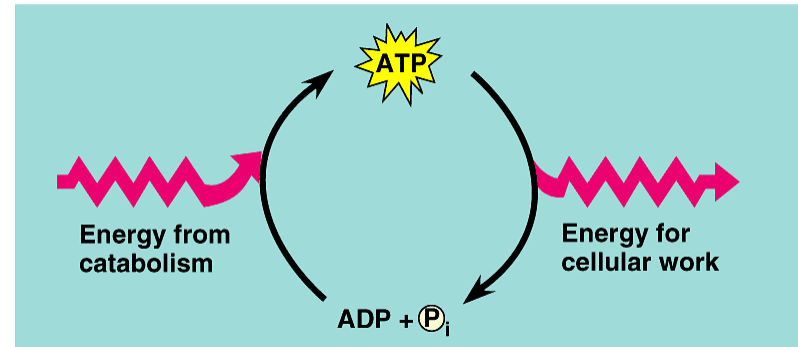
ATP cont.

- Almost all cellular work depends on ATP's ability to energize other molecules by transferring phosphate groups



ATP cont.

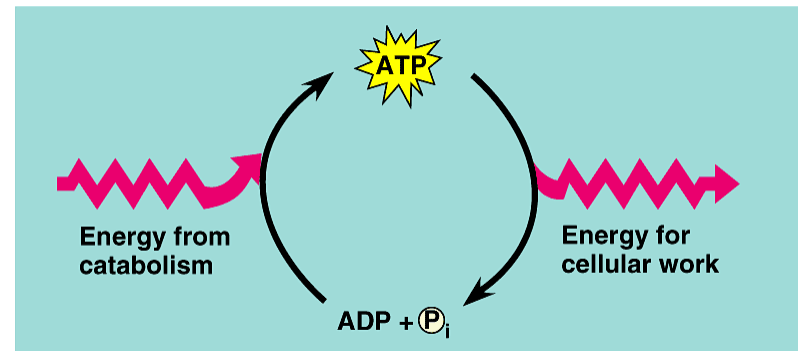
- Regeneration of ATP – ATP continuously used so must be regenerated continuously
- Free energy required to phosphorylate ADP to ATP comes from catabolism – breakdown reactions in the cell



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ATP cont.

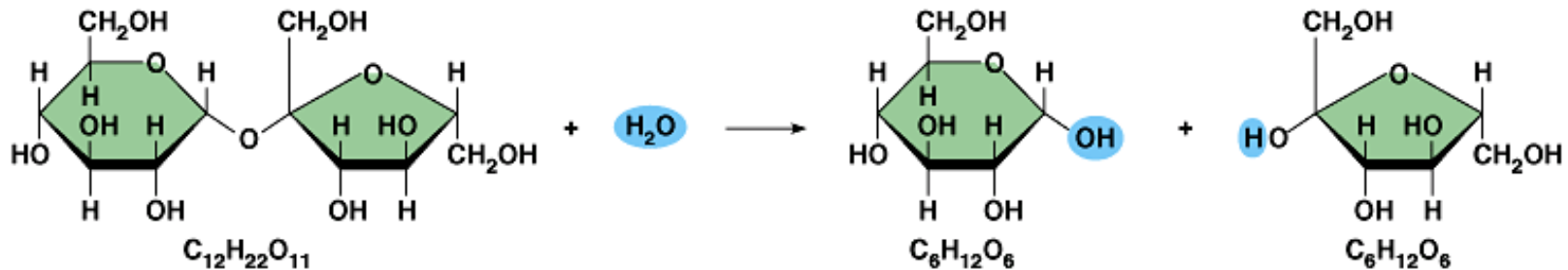
- ATP cycle couples energy yielding to energy producing reactions
working muscle - each cell uses 10 million ATP/sec/cell with regeneration being endergonic - +7.3 kcal/mol std. Reaction & catabolic or exergonic reactions esp. cellular respiration providing energy for endergonic production of ATP



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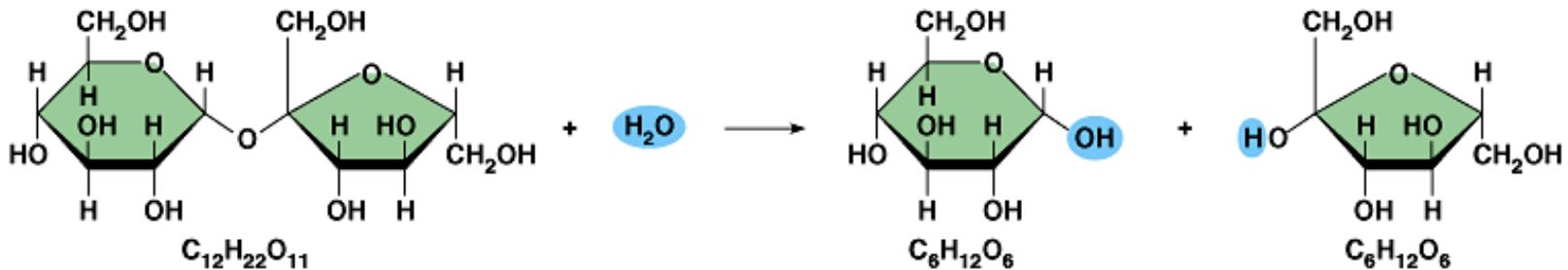
ENZYMES

- Catalyst is chemical agent that changes rate of a reaction without being consumed by the reaction
- Enzyme is a catalytic protein
- Chemical reactions involve bond breaking & bond forming & reactants must absorb energy for bonds to break & energy is released when bonds form



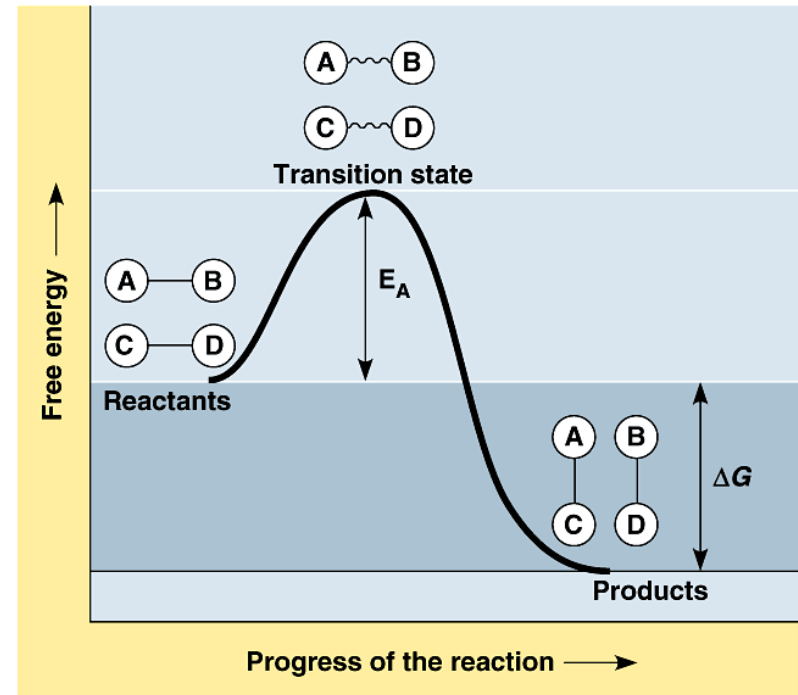
Enzymes cont.

- Initial energy required to break bonds of reactant molecules called free energy of activation or activation energy (E_A in the text) which occurs in the form of heat which increases thermal energy of reactants – causes more frequent & more forceful collisions – so thermal agitation increases chance of bonds breaking



Enzymes cont.

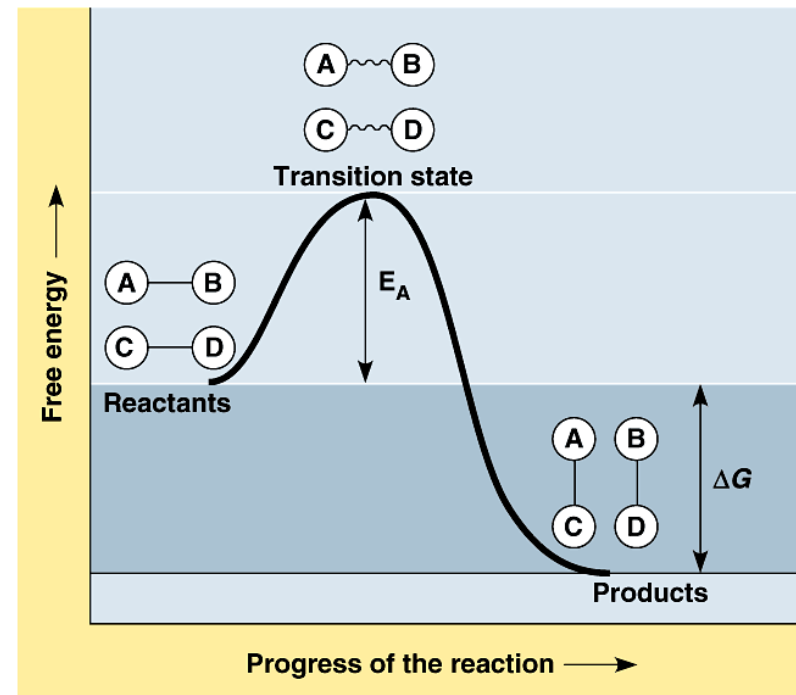
- Activation energy is amount of energy needed to push reactants over a hill so downhill part of reaction can occur
AB + CD \rightarrow AC + BD
energizing or activation of reactants is the uphill part of graph where free energy content of molecules increases & at top of graph reactants are activated & unstable



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Enzymes cont.

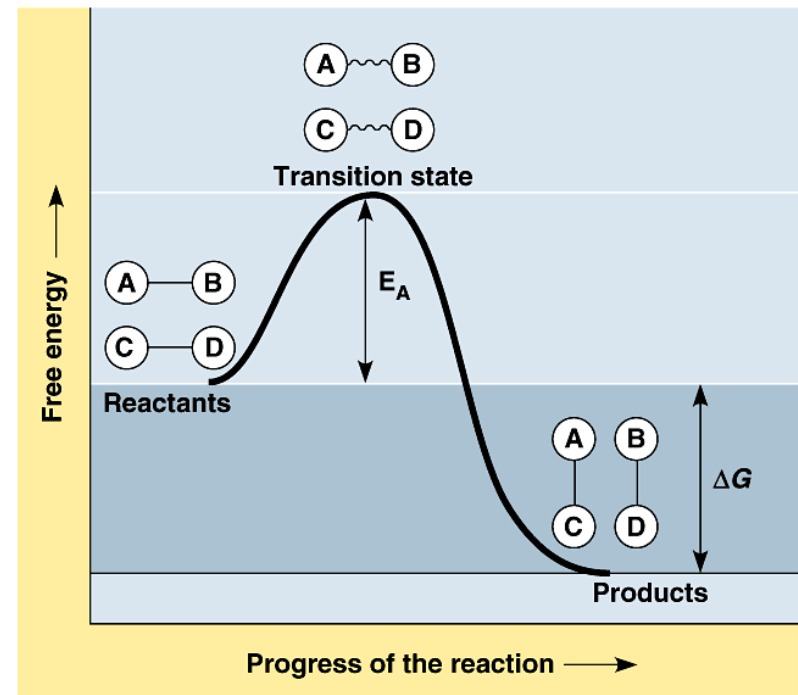
- At top of graph making & breaking of bonds can occur
- Bond forming phase of reaction is downhill portion where molecules lose free energy which is released to surroundings & difference between free energy of reactants & free energy of products is called delta G & is negative for exergonic reactions



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Enzymes cont.

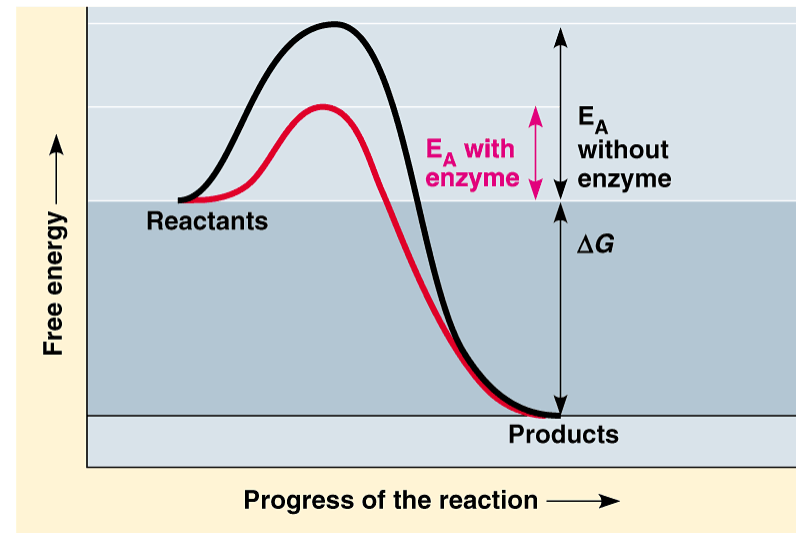
- Even exergonic reactions require reactants to overcome activation energy barrier as most reactions will not occur at any rate at room temp. Require the addition of heat example – spark plugs for car
- Adding heat energy is not compatible with life – proteins denature & cells die



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Enzymes cont.

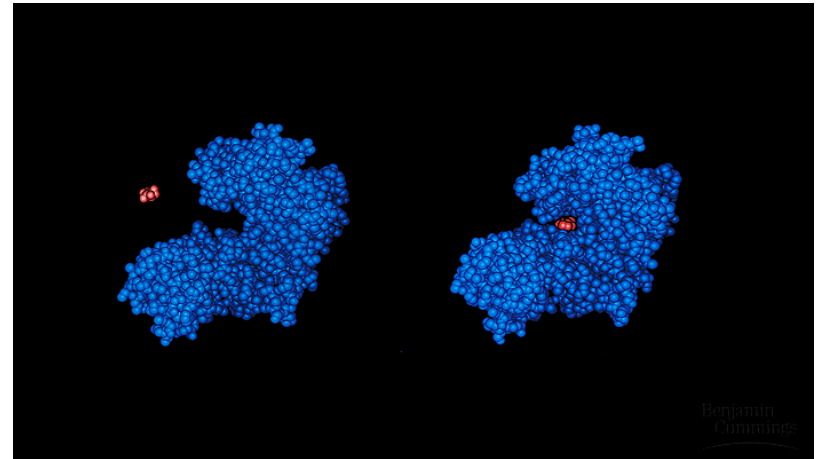
- Organisms use a catalyst (enzyme) which lowers EA barrier so reaction can occur at moderate temp
- Enzyme cannot change ΔG for the reaction & cannot make endergonic reactions exergonic – only speeds reactions which would occur anyway
- Enzymes are very selective in reactions they catalyze so determine which reactions occur



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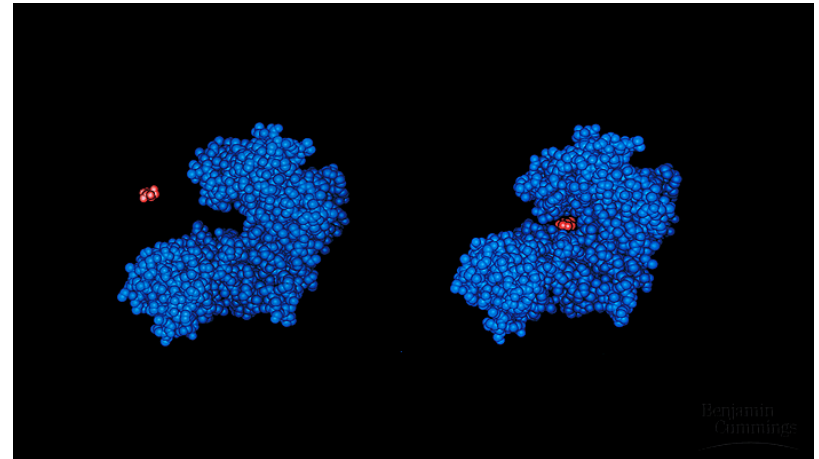
Enzymes cont.

- Enzymes act on substrate(s) converting them to products while enzyme & substrates are joined
- Enzyme acts only on specific substrates because enzymes are proteins with 3D structure so specificity comes from 3D shape



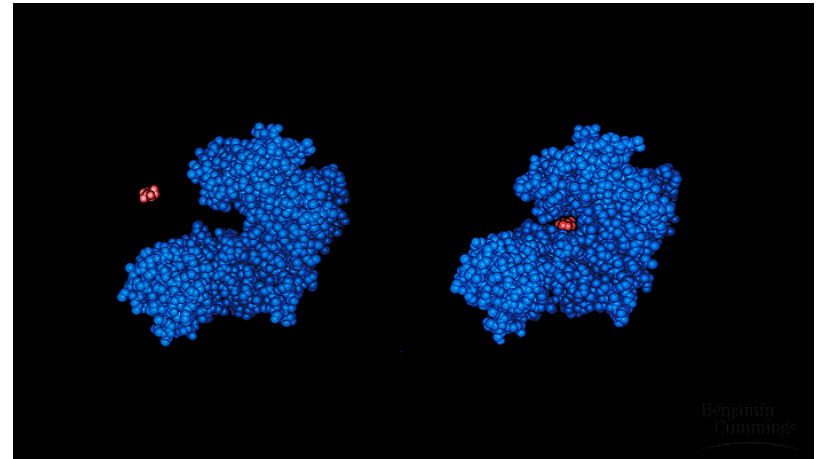
Enzymes cont.

- Active site (pocket or groove in surface of enzyme) of enzyme is small region which binds the substrate(s)
- Formed by small number of aa with rest of protein used for framework – side chains (R group) of a few aa making up active site catalyze conversion of substrates to products



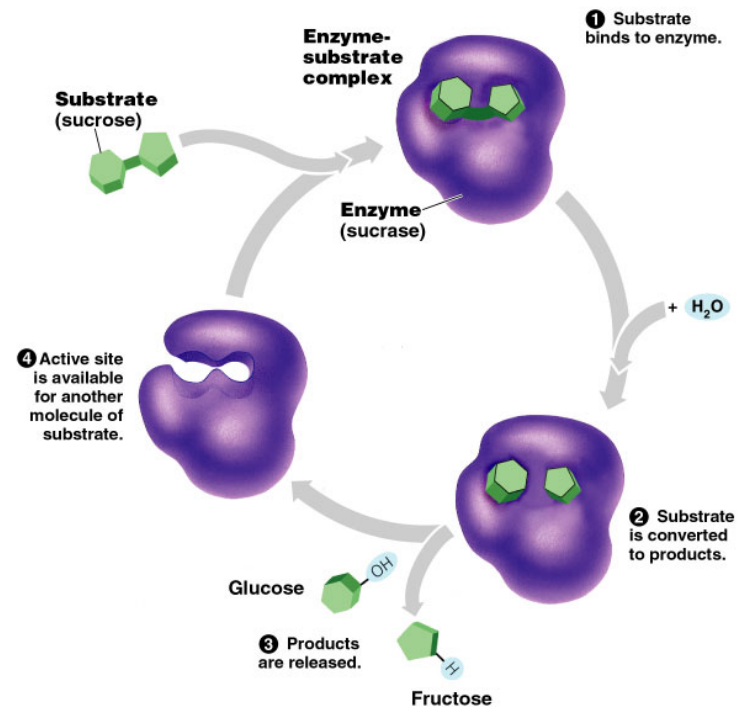
Enzymes cont.

- Shape of active site & shape of substrate must be compatible – substrate & enzyme held together by weak interactions – hydrogen or ionic bonds
- When substrate binds enzyme changes shape slightly to better bind to substrate – called induced fit which enhances ability of chemical groups in active site to catalyze reaction



Enzymes cont.

- Enzyme is not destroyed in chemical reaction but is used repeatedly so small amount of enzyme can have very large effect
- Enzymes use several mechanisms to lower E_A & speed a reaction



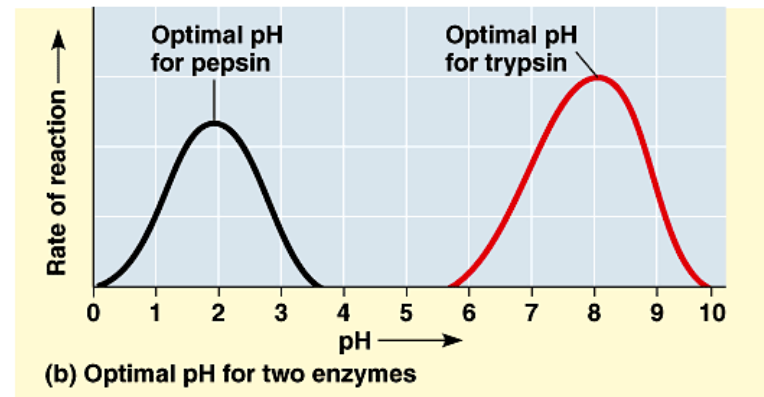
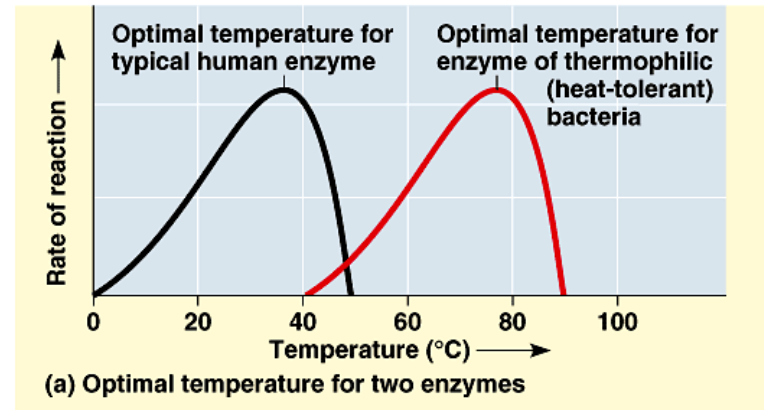
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Enzymes cont.

- 1) may stress substrate molecules stretching & bending critical chemical bonds that must be broken
- 2) may provide microenvironment conducive to particular type of reaction (acidic groups in active site may make pocket of low pH where H^+ ions can be transferred
- 3) direct participation of enzyme in chemical reaction by having substrate briefly bind to enzyme
- Rate of reaction depends on substrate concentration up to a point – saturation point when all enzyme molecules have active sites engaged then reaction rate depends on catalytic rate of the enzyme

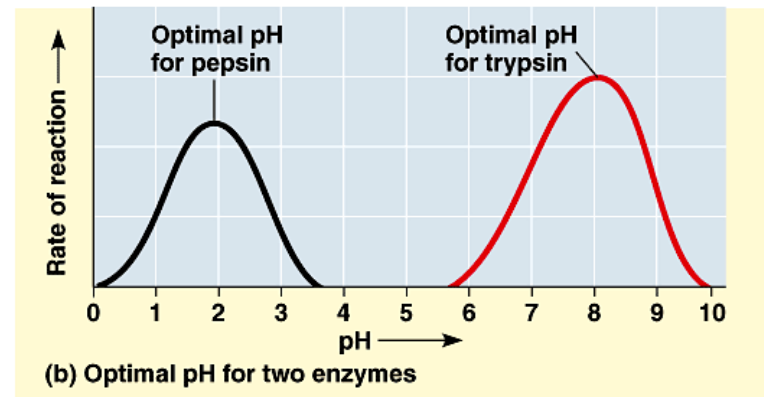
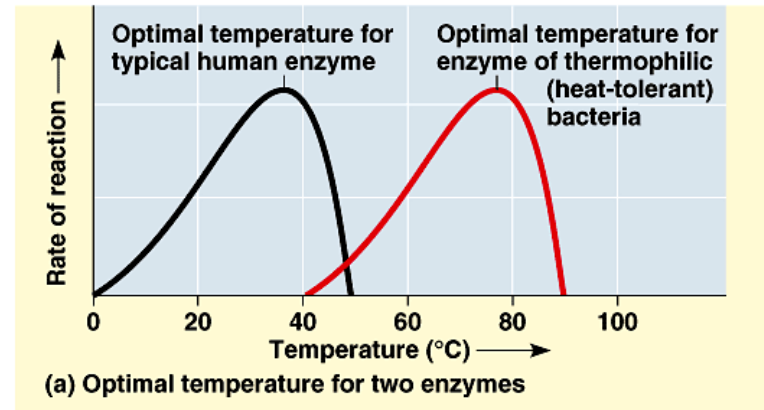
Enzymes cont.

- Activity affected by cell environment – temperature, pH, chemical composition, ions, etc.
- 3D structure of proteins affected by environment & 3D shape needed for enzyme activity



Enzymes cont.

- Up to optimal temp. enzyme activity increases as temp increases (substrates collide with active site more frequently) but after optimal temp increased heat called thermal agitation disrupts weak bonds holding protein structure together get similar effects for pH

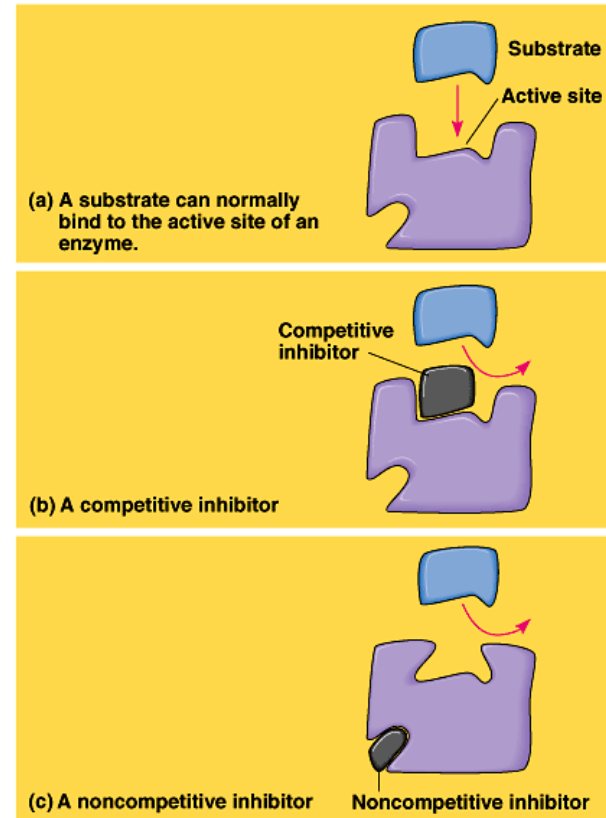


Enzymes cont.

- Cofactors – nonprotein helpers for catalytic activity – ions such as zinc, iron, copper
- Coenzymes – cofactor is an organic molecule – vitamins or molecules derived from vitamins
- Enzyme inhibitors – reversible if inhibitor binds to enzyme by weak bonds but irreversible if binds by covalent bonds
- Competitive inhibitors resemble normal substrate & compete for binding to active site & overcome by adding more substrate

Enzymes cont.

- Noncompetitive inhibitors do not compete with substrate for active site but bind to another part of enzyme & impede enzyme activity
- Selective inhibition & activation by natural molecules is essential for metabolic control

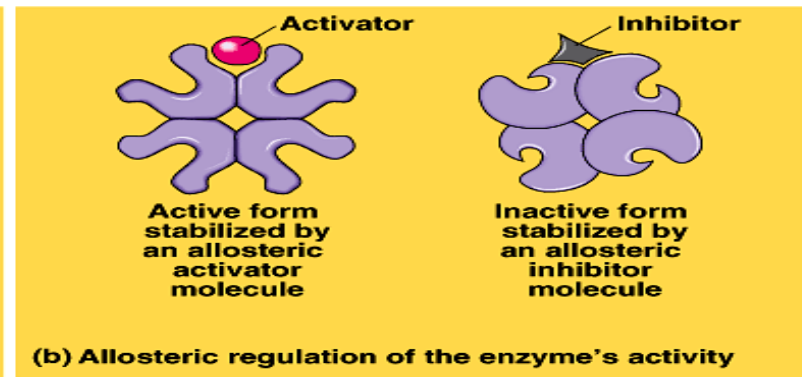
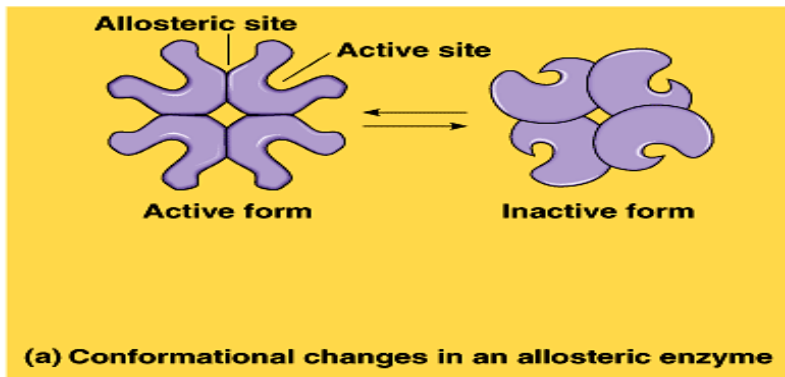


Metabolic Control

- Cell controls metabolic pathways by controlling when & where various enzymes are active – regulates amount of enzyme or activity of enzyme already present
- Naturally occurring regulators of enzyme activity act as noncompetitive inhibitors – changing an enzyme's shape & thus function by binding weakly to a site remote from active site – effect could be stimulation or inhibition

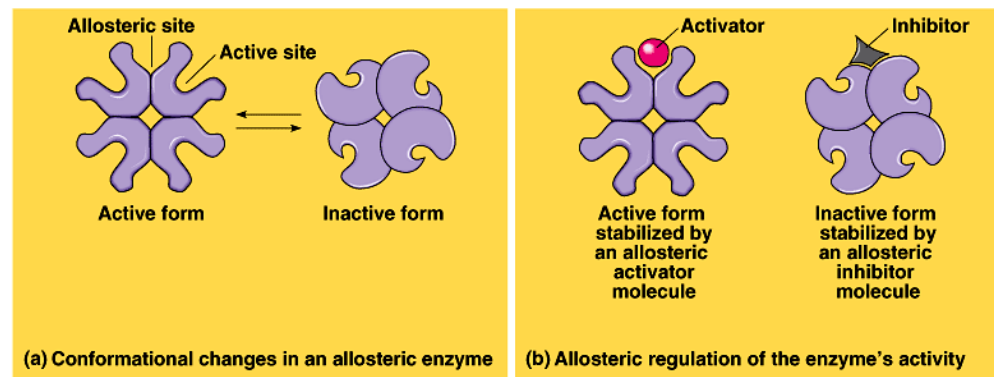
Metabolic Control cont.

- Allosteric regulation most often involves enzymes with more than 1 polypeptide chain where each has an active site and allosteric sites are located at juncture of polypeptides – complex moves between 2 conformational states – active & inactive



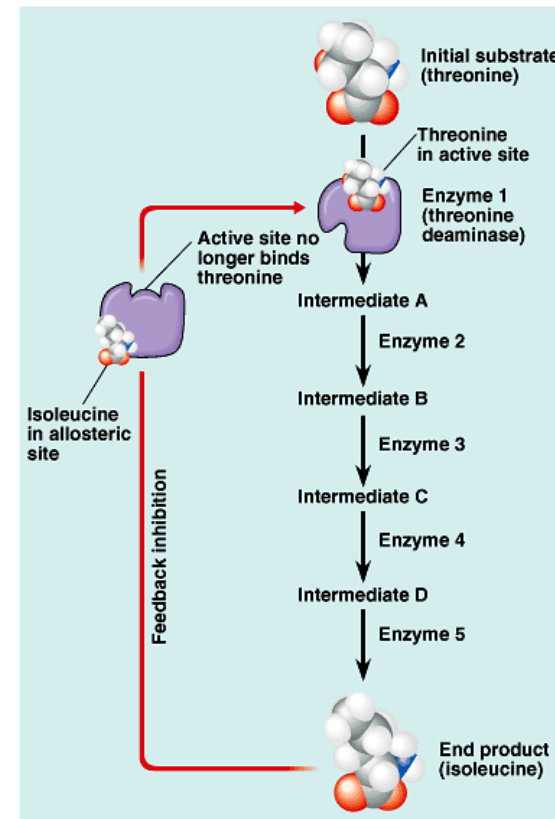
Metabolic Controls cont.

- Binding of activator to allosteric site stabilizes conformation with functional active site & binding of allosteric inhibitor stabilizes inactive form of enzyme
binding to 1 allosteric site affects all active sites in all subunits



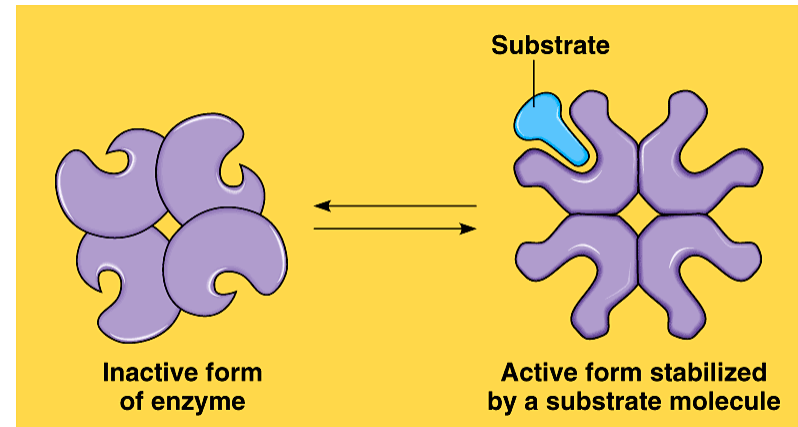
Metabolic Controls cont.

- Feedback inhibition – one of most common methods of metabolic control where metabolic pathway switched off by the end product
- Example – amino acid threonine deaminated to isoleucine which inhibits threonine deaminase by binding to allosteric site



Metabolic Controls cont.

- Cooperativity – mechanism amplifies response of enzymes to substrates – 1 substrate molecule primes the enzyme to accept additional substrate molecules readily



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Metabolic Controls cont.

- Cellular location helps order metabolism
- Cell brings order to metabolism by assembling enzymes for specific pathways together – can be in an organelle or can be a multienzyme complex

