Enzymes: Introduction

Enzymes are proteins.

– (ribozymes: catalytic RNA molecules)

• biological catalysts

– not chemically altered in reaction

– do not change equilibrium constant (Keq) for reaction

– increase rate of reaction by providing a pathway of lower

activation energy to get from reactants to products

– operate under physiological conditions (moderate temps., around

neutral pH, low conc. in aqueous environment)

– work by forming complexes with their substrates (binding), thus

providing unique microenvironment for reaction to proceed, the

active site

– VERY HIGH SPECIFICITY for both reaction catalyzed and substrate

used

– VERY HIGH CATALYTIC EFFICIENCY

– ACTIVITIES of some enzymes REGULATED

• Enzymes very specific

– for substrate acted upon

– for reaction catalyzed

• Example: Proteases are a whole class of enzymes that all catalyze

hydrolysis of peptide bonds:

Substrate specificity (e.g., of proteases) due to precise interaction of

enzyme with substrate

– result of 3-D structure of enzyme active site where substrate has

to bind and be properly oriented for catalysis to occur

Berg et al., Fig. 8-1

(A) Trypsin catalyzes hydrolysis

of peptide bonds on carboxyl

side of Lys and Arg residues

(digestive function in small

intestine, cleaves just about

any protein it encounters after

(eventually) every Lys and Arg)

(B) Thrombin (involved in blood

clotting cascade) catalyzes

hydrolysis of peptide bonds

between Arg and Gly residues

in specific sequences in

specific protein substrates

(activated only where blood

needs to clot, works only on

very specific target protein)

• substrate specificity of proteases --

another example, chymotrypsin:

– cleaves on carboxyl side of aromatic and hydrophobic amino acid

residues

– evolutionarily related to trypsin

– Genes for trypsin and chymotrypsin are homologous.

• Ancestral gene duplicated and sequences diverged through

evolution.

• Substrate specificities for site of cleavage diverged, but catalytic

mechanism and overall tertiary structure was conserved.

Specificity of reaction catalyzed:

Many proteases also catalyze hydrolysis of carboxylic ester bonds:

Some enzymes need cofactors for their activity.

• COFACTORS: small organic or metalloorganic molecules (coenzymes)

or metal ions

• Cofactors can bind tightly or weakly to enzymes. (Equilibrium below

can lie far to left, weak binding, or far to right, tight binding.)

• Prosthetic groups (e.g. heme in hemoglobin): tightly bound cofactors

(either coenzymes or metals)

– remain associated with their enzymes even between reaction cycles.

• Weakly bound coenzymes (which are NOT prosthetic groups) can

associate and dissociate from enzymes between reaction cycles, behaving

like substrates

– sometimes referred to as "cosubstrates"

TRANSITION STATE THEORY

• transition state: an activated complex at the highest free

energy point on the reaction coordinate a PEAK on the free

energy diagram

• not isolatable as structures (lifetimes ~10–13 sec) -- they’re "in

transition", sort of with bonds half-made, half-broken.

• Chemical example: an SN2 reaction, attack of a thiolate anion on

iodoacetate: transition state (in brackets)(‡): a trigonal

bipyramid, with 3 covalent bonds + 2 more "half" bonds:

Dependence of rate constant on ΔG‡, the activation energy

• Rate constant (k) depends on ΔG‡, the Arrhenius activation energy

(i.e., the free energy of activation for the reaction)

• ΔG‡ = G‡ – GS = difference in free energy between transition state

and starting state (S in this case), the "barrier" over which the reaction

must go in order to proceed.

• ΔG‡ has POSITIVE values (ΔG‡ > 0) -- it's a free energy BARRIER.

• k is rate constant for the reaction.

• κ is Boltzmann’s constant and

h is Planck’s constant.

• NOTE: Rate constant k is inversely

and exponentially dependent

on the activation energy, ΔG‡.

Velocity of the reaction:

(rate constant k is what’s inside large brackets.)

How could you increase the

reaction rate of S

Dependence of rate constant on ΔG‡, the activation energy

• Rate constant (k) depends on ΔG‡, the Arrhenius activation energy

(i.e., the free energy of activation for the reaction)

• ΔG‡ = G‡ – GS = difference in free energy between transition state

and starting state (S in this case), the "barrier" over which the reaction

must go in order to proceed.

• ΔG‡ has POSITIVE values (ΔG‡ > 0) -- it's a free energy BARRIER.

• k is rate constant for the reaction.

• κ is Boltzmann’s constant and

h is Planck’s constant.

• NOTE: Rate constant k is inversely

and exponentially dependent

on the activation energy, ΔG‡.

Velocity of the reaction:

(rate constant k is what’s inside large brackets.)

How could you increase the

reaction rate of S