BIOCHEMISTRY LECTURES (III)ENZYME STRUCTURE AND FUNCTION

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INTRODUCTION

- The enormous variety of biochemical reactions that comprise life are nearly all mediated by a series of remarkable biological catalyst known as "ENZYMES"
- They differ from ordinary chemical catalyst in several important respects

✓ Higher reaction rates

✓ Milder reaction conditions

✓ Greater reaction specificity

✓ Capacity for regulation

MOST ENZYMES ARE PROTEINS

- With the exception of a small group of catalyst RNA molecules, all enzymes are proteins.
- Their catalytic activity depends on the integrity of their native protein conformation
- If an enzyme is denatured or dissociated into its subunits, catalytic activity is usually lost
- Thus the primary, secondary, tertiary and quaternary structures of protein enzymes are essential to their catalytic activity

ENZYME CLASSIFICATION AND NUMENCLATURE

- Many enzymes have been named by adding the suffix “ase” to the name of their substrate or to a word or phrase describing their activity
- In general, enzymes have been named for the following reasons:
- (a) Substrate acted upon by the enzyme e.g. sucrase (upon sucrose)
- (b) Types or reaction catalyzed e.g. transaminases (transamination)
- (c) Substrate acted upon and the type of reaction catalyzed e.g. succinate dehydrogenase (dehydrogenation of succinate)
- (d) Substrate synthesized e.g. Rhodonase (forms Rhodonate from hydrocyanic acid and sodium thiosulphate)
- (e) Chemical composition of the enzymes e.g. iron porphyrin enzymes-cytochrome c
- (f) Substances hydrolyzed and the group involved e.g. glycosidases

Under these classifications, sometimes the same enzyme has two or more names,or two different enzymes have the same name

ENZYME CLASSIFICATION AND NUMENCLATURE CONT'D

- Because of such ambiguities and the ever increasing numbers of newly discovered enzymes, biochemists by international agreement, have adopted a system for naming and classifying enzymes
- This system divides enzymes into six classes ,each with subclass, based on the type of reaction catalyzed
- Each enzyme is assigned a four-part classification number and a systematic name which identifies the reaction it catalyzes. This is called the ENZYME COMMISSSION NUMBER

ENZYME COMMISSION(EC) NUMBER

- **EC numbers are four digits, for example a.b.c.d, where “a” is the class, “b” is the subclass, “c” is the sub-subclass, and “d” is the sub-sub-subclass. The “b” and “c” digits describe the reaction, while the “d” digit is used to distinguish between different enzymes of the same function based on the actual substrate in the reaction.**
- **For example,The EC number of ATP:glucose phosphotransferase (Hexokinase) is 2.7.1.1**

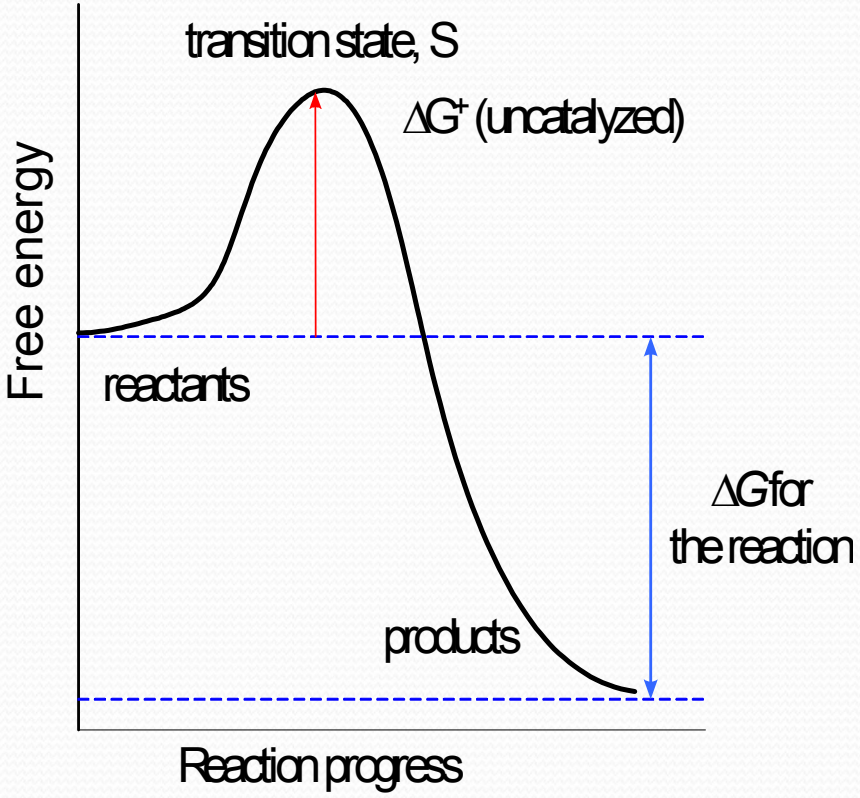
The first number (2) denotes the class name (transferase),the second number (7), the subclass (phosphotransferase),the third number (1), a phosphotransferase with a hydroxyl group as acceptor and the fourth number (1), D-glucose as the phosphoryl group acceptor

INTERNATIONAL CLASSIFICATION OF ENZYMES

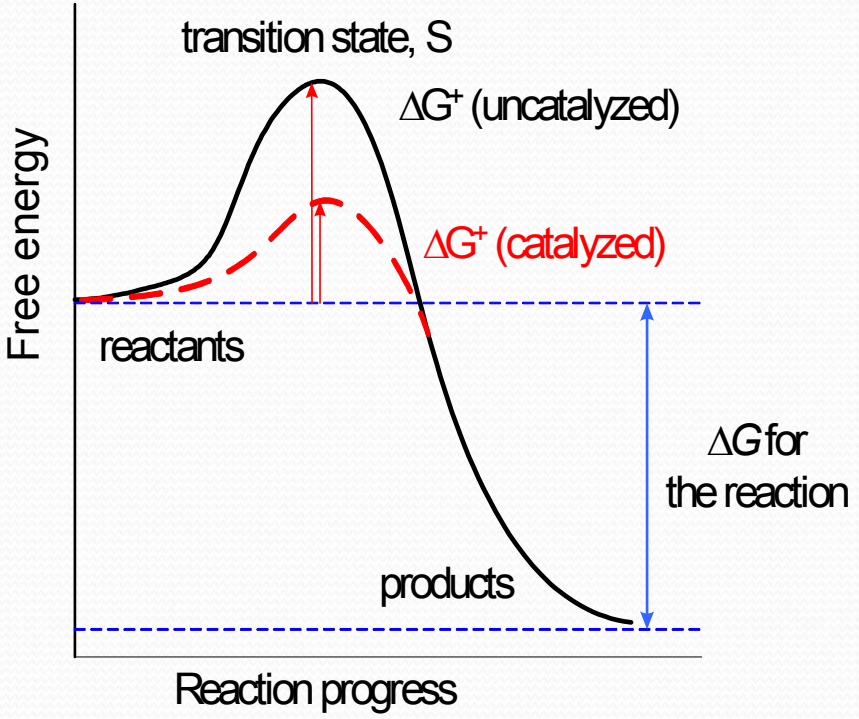
No.	Class	Type of reaction catalyzed
1	Oxidoreductases	Transfer of electrons (hydride ions or H atoms)
2	Transferases	Group transfer reactions
3	Hydrolases	Hydrolysis reactions (transfer of functional groups to water)
4	Lyases	Addition of groups to double bonds, or formation of double bonds by removal of groups
5	Isomerases	Transfer of groups within molecules to yield isomeric forms
6	Ligases	Formation of C—C, C—S, C—O, and C—N bonds by condensation reactions coupled to ATP cleavage

HOW ENZYMES WORK

Uncatalyzed reaction



Catalyzed reaction



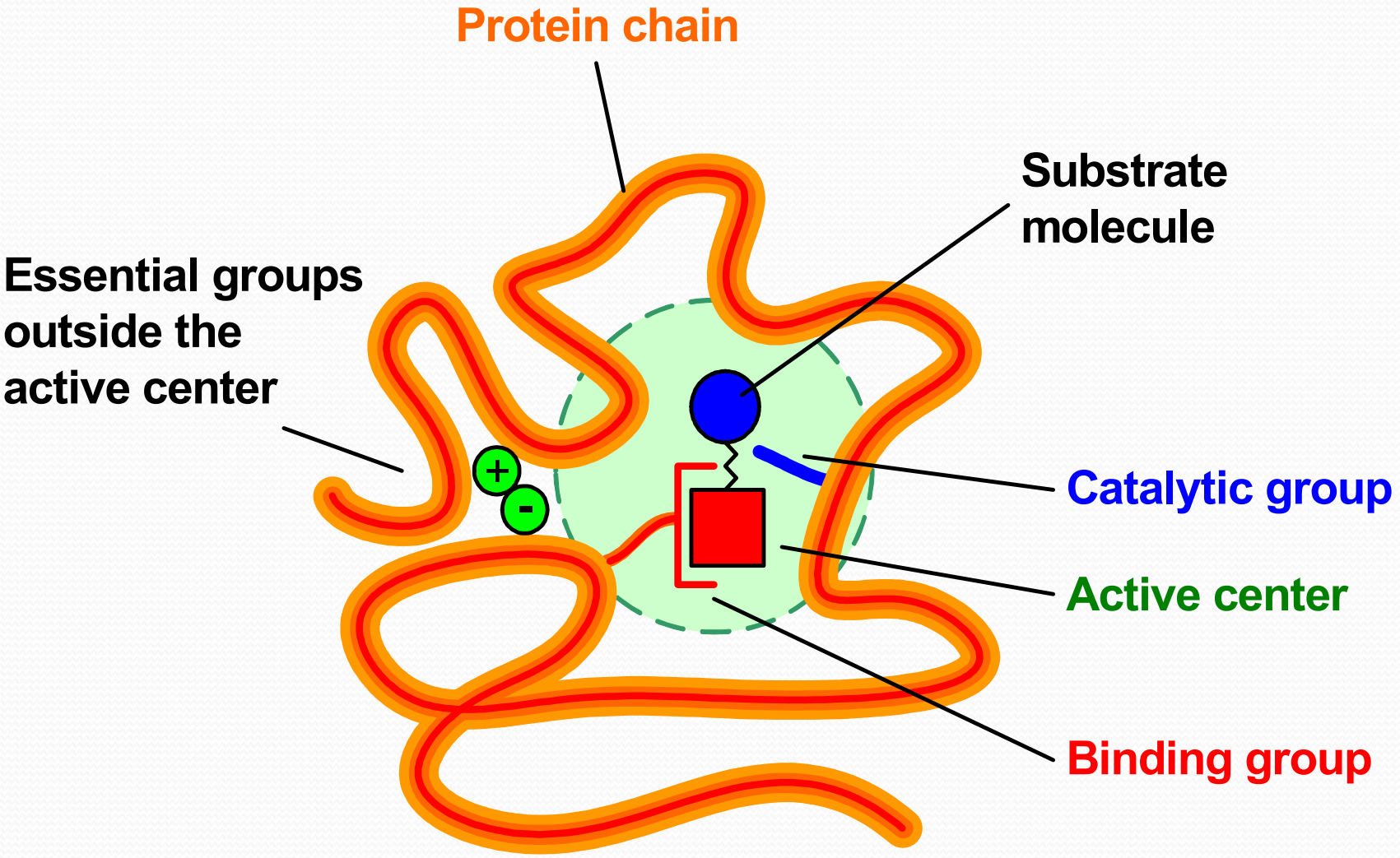
ACTIVE SITE

- A distinguishing feature of an enzyme-catalyzed reaction is that it takes place within the confines of a pocket on the enzyme called the "ACTIVE SITE"
- The active site is the part of an enzyme that directly binds to the substrate and carries out a reaction
- It contains both the BINDING group which helps in the proper binding of the entire enzyme to the substrate and the CATALYTIC groups which are amino acids that promote formation and degradation of bonds
- By forming and breaking these bonds, enzyme and substrate interaction promotes the formation of the TRANSITION STATE STRUCTURE – enzymes help a reaction by stabilizing the transition state intermediate
- The active site is formed by the groups that come from different part of the amino acid sequences
- The active site is only a small part of the total enzyme volume
- It enhances the enzyme to bind to substrate and catalysis by many different weak interaction because of its non polar microenvironment
- Active sites are hydrophobic

STRUCTURE OF THE ACTIVE SITE

- The active site is in the shape of a three dimensional cleft that is composed of amino acids from different residues of the primary amino acid sequence
- The amino acids that play a significant role in the binding specificity of the active site are usually not adjacent to each other in the primary structure, but forms the active site as a result of folding in creating the tertiary structure
- Enzyme specificity depends on the arrangement of atoms in the active site
- The unique amino acids contained in an active site promote specific interaction that are necessary for proper binding and resulting catalysis

ACTIVE SITE CONT'D



MODELS OF SUBSTRATE BINDING TO ENZYME ACTIVE SITE

- **There are two different models that represent enzyme- substrate binding**
- **(1)The LOCK and KEY model and (2)The INDUCED FIT model and**

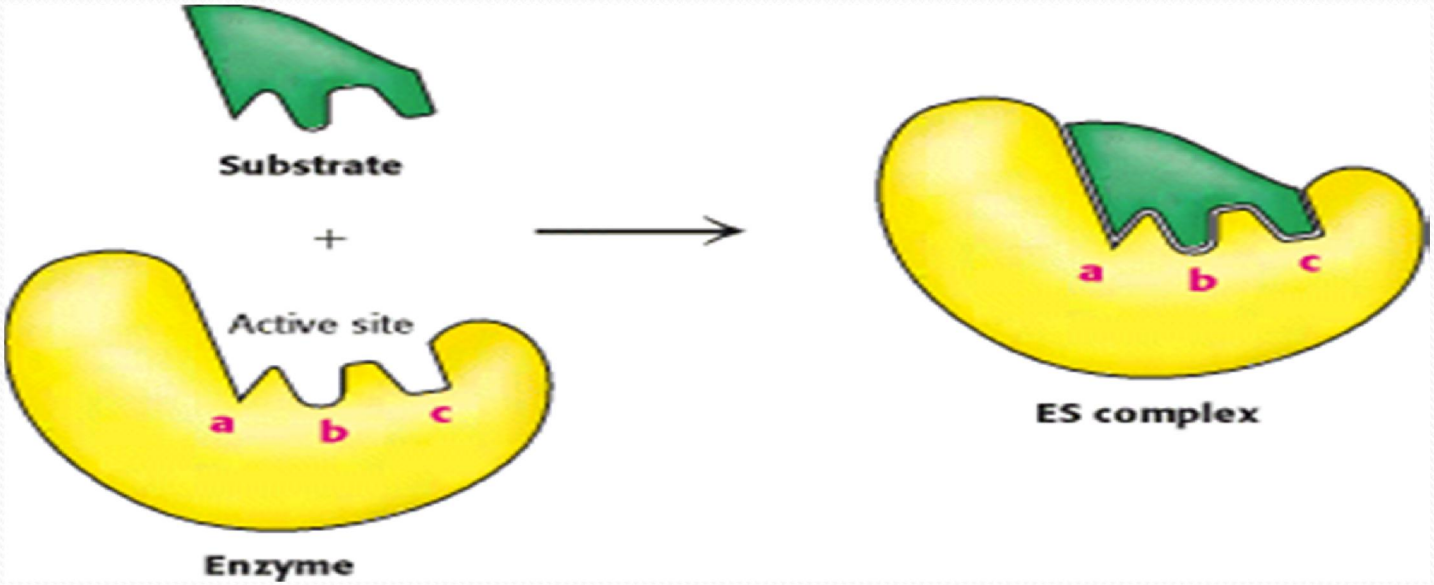
The lock and key model was proposed by emil fischer in 1980 .this model presumes that there is a perfect fit between the substrate and the active site – the two molecules are complementary in shape

Lock and key is the model such that the active site of enzyme is good fit for substrates that does not require change of enzyme after enzyme binds substrate

MODELS OF SUBSTRATE BINDING CONT'D

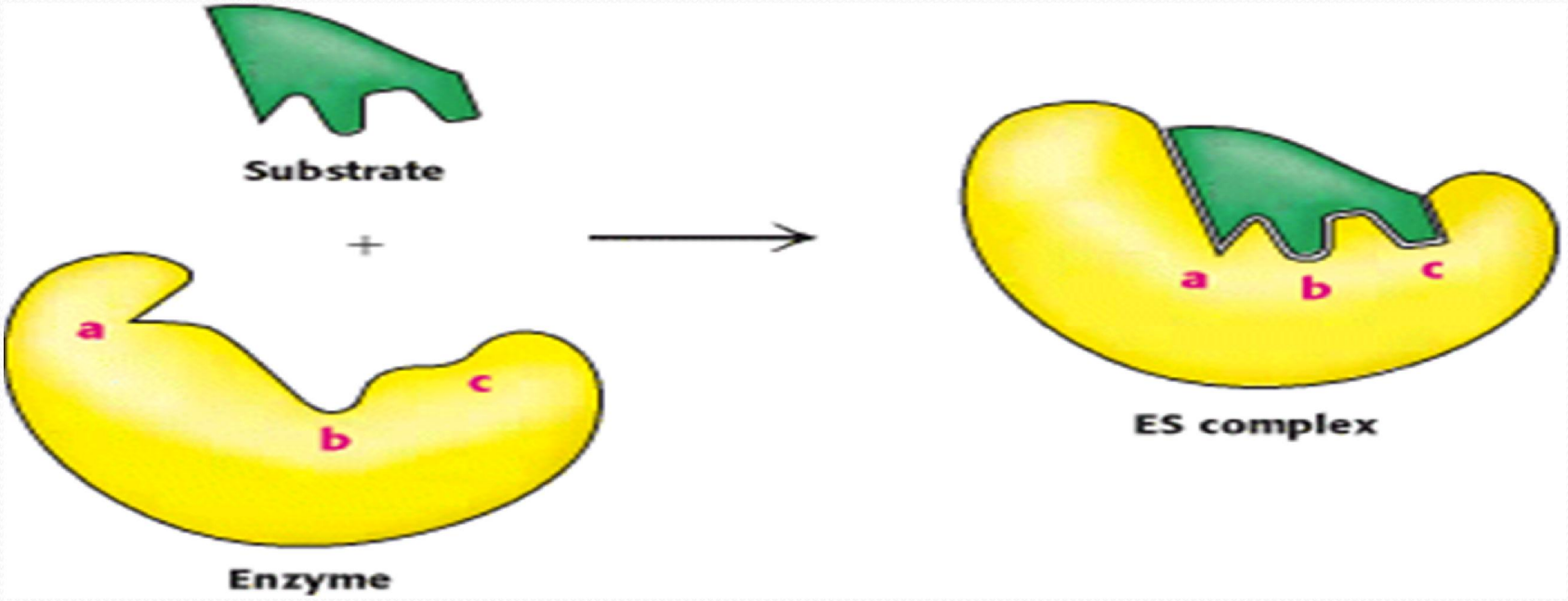
- The INDUCED FIT model was postulated by Daniel koshland in 1985
- It involves the changing of the conformation of the active site to fit the substrate after binding.
- Also in the induced fit model, it was stated that there are amino acids that aid the correct substrate to bind to the active site which leads to shaping of the active site to the complementary shape.
- Induced fit is the model such that the structure of the active site of enzyme can be easily changed after binding of enzyme and substrate
- The active site will then stabilize the transition state intermediate to decrease the activation energy
- The most common model of enzymatic binding site is the induced fit model

FISCHER'S LOCK AND KEY MODEL



Both E and S are rigid and fixed, so they must be complementary to each other perfectly in order to have a right match

KOSHLAND'S INDUCED FIT MODEL



The binding induces conformational changes of both E and S, forcing them to get a perfect match.

SPECIFICITY OF ENZYMES

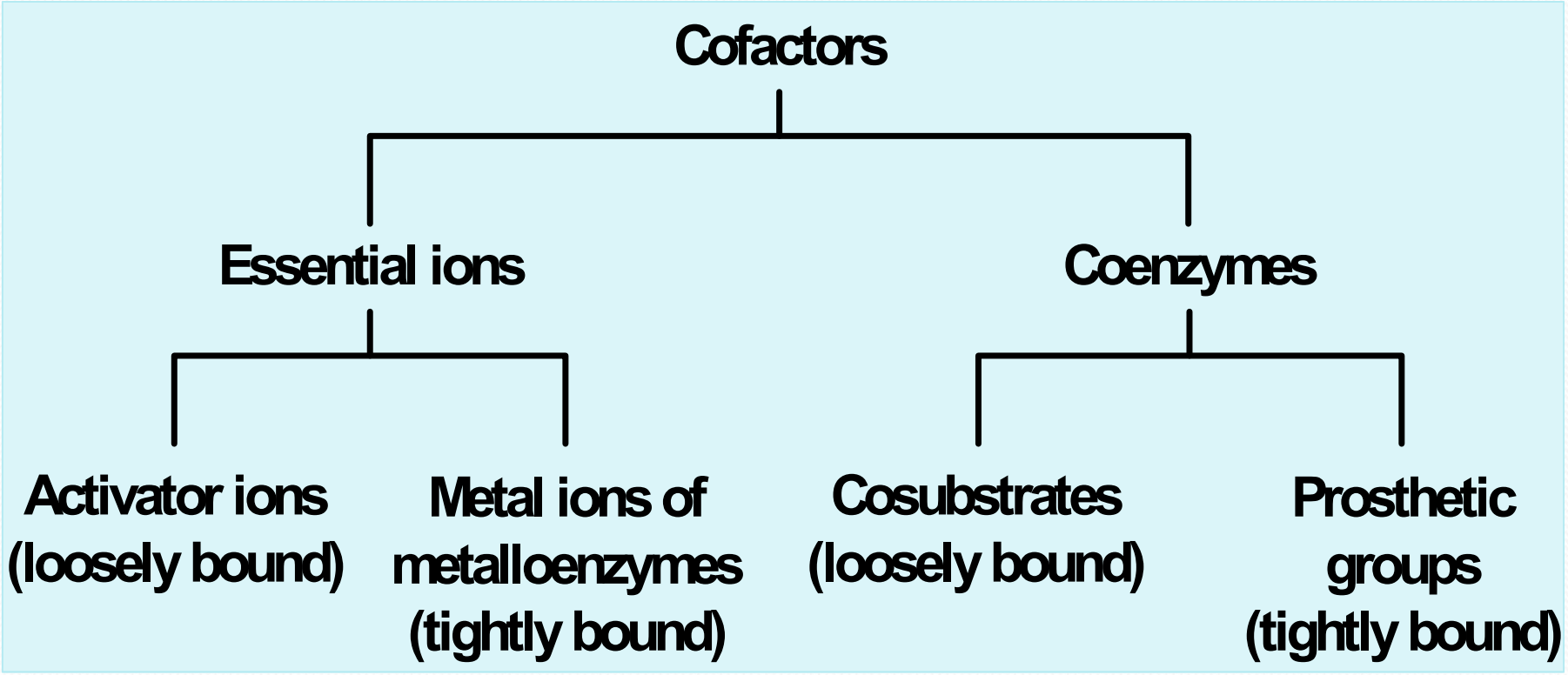
- The same binding energy that provides energy for catalysis also gives an enzyme its specificity, the ability to discriminate between a substrate and a competing molecule
- Specificity is derived from the formation of many weak interactions between the enzyme and its specific substrate molecule
- Specificity is the most distinct feature of enzyme catalyzed reaction
- Generally, there are four distinct types of specificty of enzymes
- (1) absolute specificity e.g. glucokinase
- (2) linkage specificity e.g. phosphatase
- (3) group specificity e.g. hexokinase
- (4) stereochemical specificity e.g. L-amino acid oxidase

ENZYME EFFICIENCY

- The best way to compare the catalytic efficiencies of different enzymes or the turnover of different substrate by the enzyme is to compare the ratio k_{cat}/K_m for the two reactions .
- k_{cat}/K_m is also called the *specificity constant* - used to rank an enzyme according to how good it is with different substrates
- K_{cat} is called the turn over number i.e. the number of substrate converted to products per unit time
- K_m is the substrate concentration at half maximal velocity

COENZYMES AND COFACTORS

- **Cofactors essentially act as enzymes' CHEMICAL TEETH**



MANY VITAMINS ARE COENZYME PRECURSORS

Coenzyme	*Examples of chemical groups transferred*	*Dietary precursor in mammals*
Biocytin	CO_2	Biotin
Coenzyme A	Acyl groups	Pantothenic acid and other compounds
5′-Deoxyadenosylcobalamin (coenzyme B_{12})	H atoms and alkyl groups	Vitamin B_{12}
Flavin adenine dinucleotide	Electrons	Riboflavin (vitamin B_2)
Lipoate	Electrons and acyl groups	Not required in diet
Nicotinamide adenine dinucleotide	Hydride ion ($:H^-$)	Nicotinic acid (niacin)
Pyridoxal phosphate	Amino groups	Pyridoxine (vitamin B_6)
Tetrahydrofolate	One-carbon groups	Folate
Thiamine pyrophosphate	Aldehydes	Thiamine (vitamin B_1)