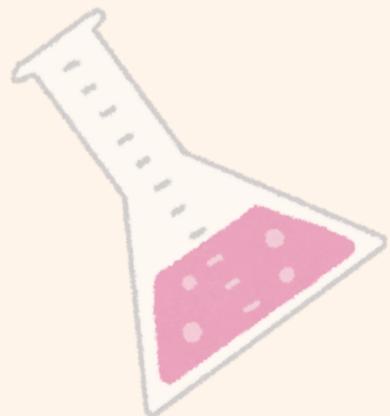
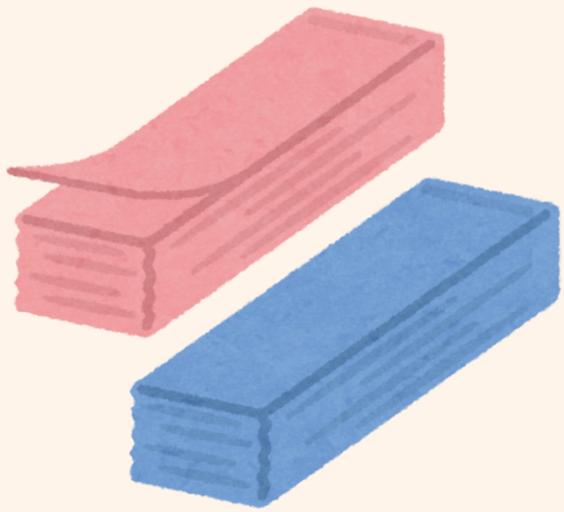


ENZYMES

SECOND STAGE

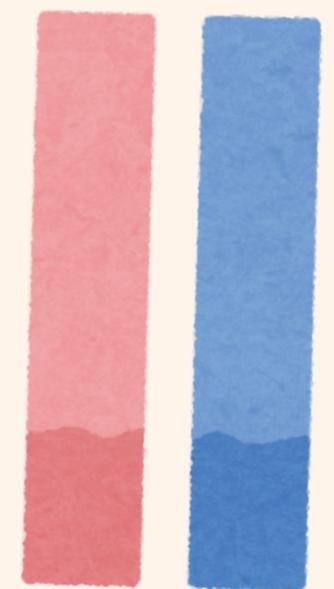
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Medical Biochemistry

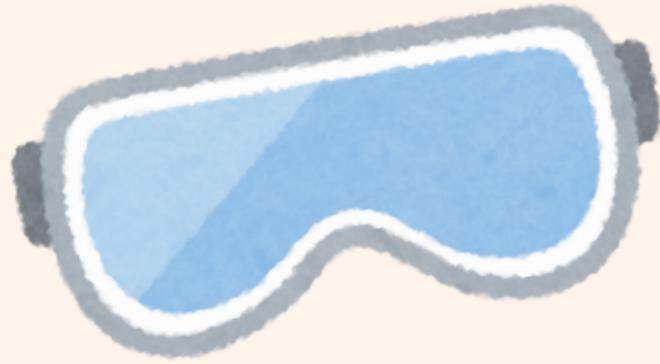




ENZYMES PART ONE

Enzymes are protein catalysts, usually within cells, that increase the rate of reactions without being changed in the overall process.





NOMENCLATURE

A. Recommended name

Recommended names have the suffix “-ase” attached to the substrate of the reaction, such as glucosidase and urease. Names of other enzymes include a description of the action performed, for example, lactate dehydrogenase (LDH) and adenylyl cyclase. There are also original trivial names, which give no hint of the associated enzymatic reaction, for example, trypsin and pepsin.



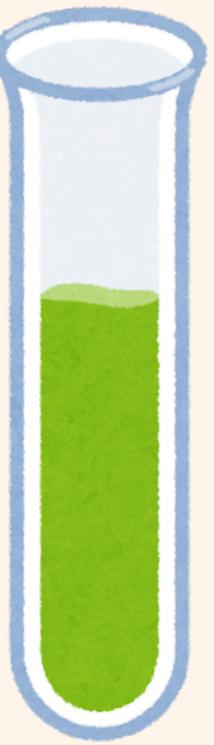
B. Systematic name: Six major classes

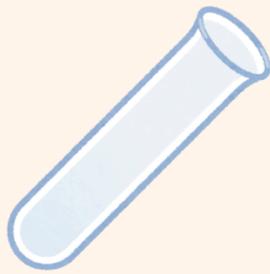
Enzymes are classified into six major classes:

Oxidoreductases: Catalyze oxidation-reduction reactions (e.g., Lactate to Pyruvate using NAD⁺).

Transferases: Catalyze transfer of C-, N-, or P-containing groups (e.g., Serine to Glycine).

Hydrolases: Catalyze cleavage of bonds by addition of water (e.g., Urea to CO₂ + NH₃).



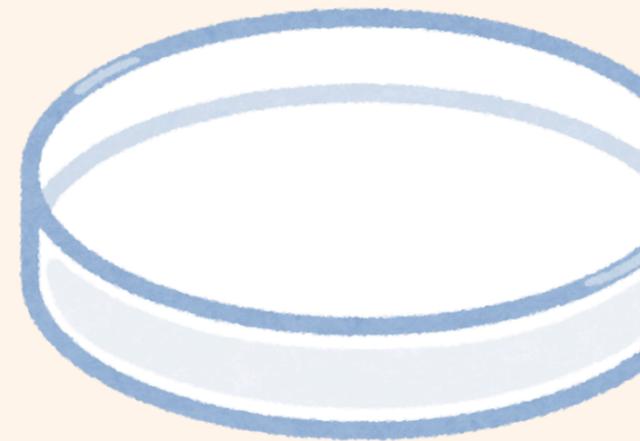
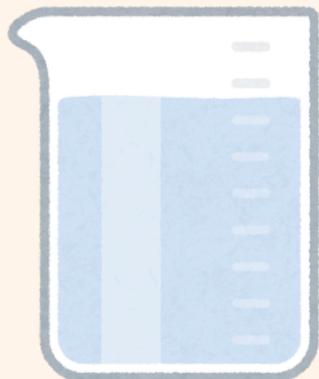


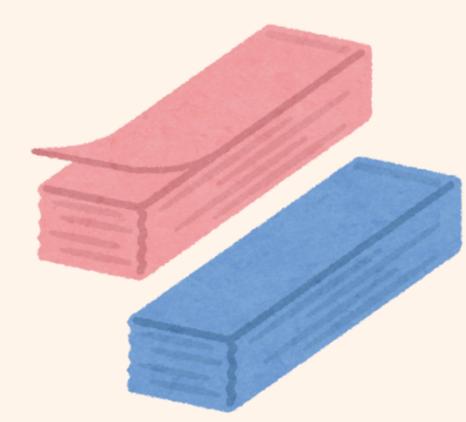
Lyases: Catalyze cleavage of C-C, C-S, and certain C-N bonds (e.g., Pyruvate to Acetaldehyde).



Isomerases: Catalyze rearrangement of optical or geometric isomers (e.g., Methylmalonyl CoA to Succinyl CoA).

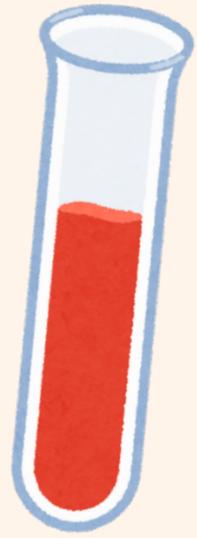
Ligases: Catalyze formation of bonds between carbon and O, S, and N coupled to hydrolysis of high-energy phosphates (e.g., Pyruvate to Oxaloacetate)..





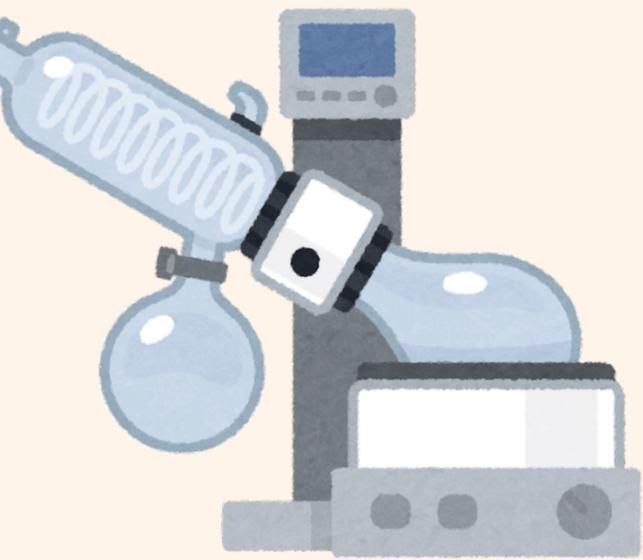
It is important to note that enzymes may have similar names but different functions or mechanisms. For example, synthetases require ATP, while synthases do not require ATP. Phosphatases use water to remove a phosphate group, while phosphorylases use inorganic phosphate to break a bond and generate a phosphorylated product. Dehydrogenases (using NAD⁺ or flavin adenine dinucleotide, FAD) accept electrons in a redox reaction. Oxidases use oxygen as the acceptor, with no oxygen atoms incorporated into the substrate, while oxygenases do incorporate oxygen atoms into their substrates.

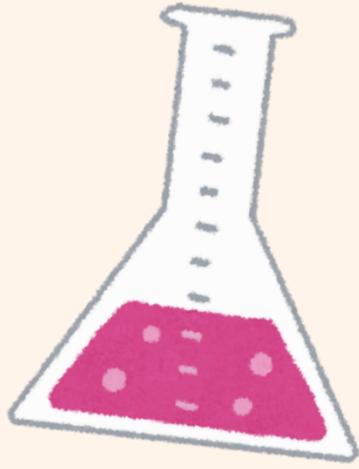




PROPERTIES

Some ribonucleic acids [RNAs] can catalyze reactions that affect phosphodiesterase and peptide bonds. RNAs with catalytic activity are called ribozymes and are much less common than protein catalysts.

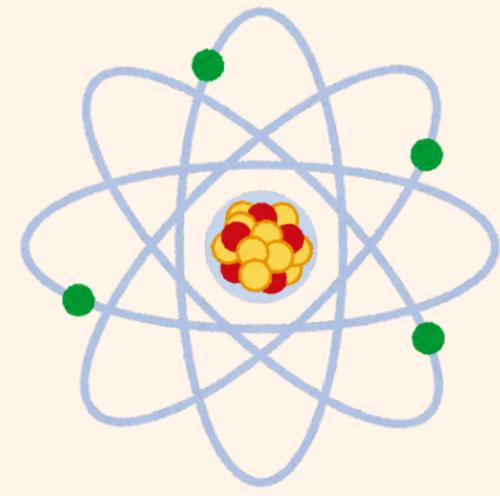
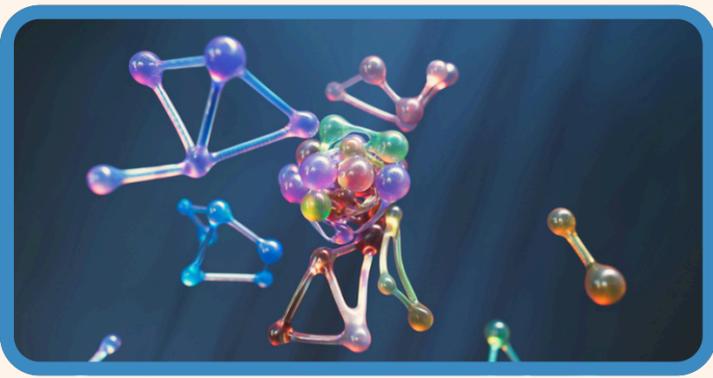




A . Active site

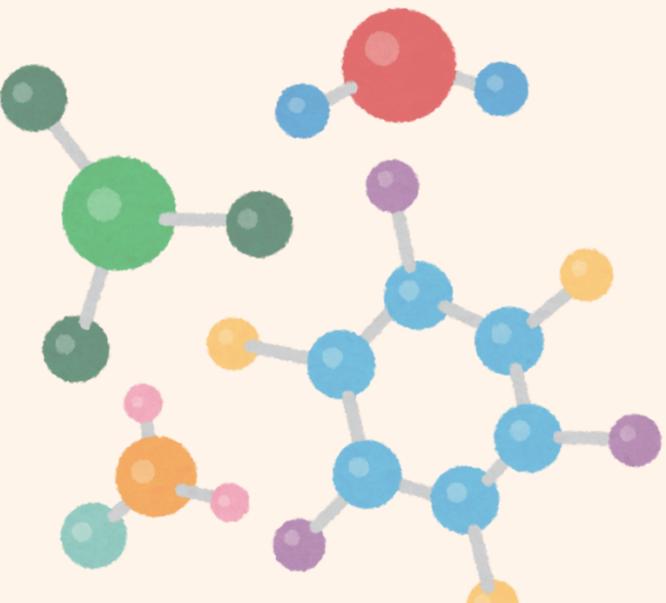
Enzyme molecules contain a special pocket or cleft called the active site which is formed by folding of the protein.

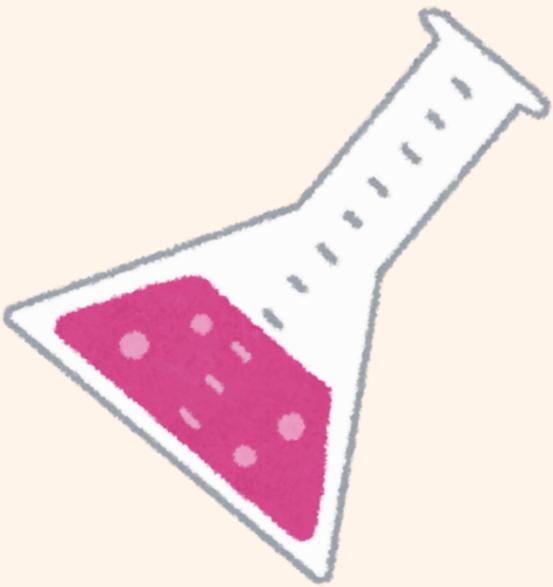
Binding is thought to cause a conformational change in the enzyme (induced fit model) that allows a rapid conversion of the ES to enzyme-product (EP) complex that subsequently dissociates to free enzyme and product.



B. Efficiency

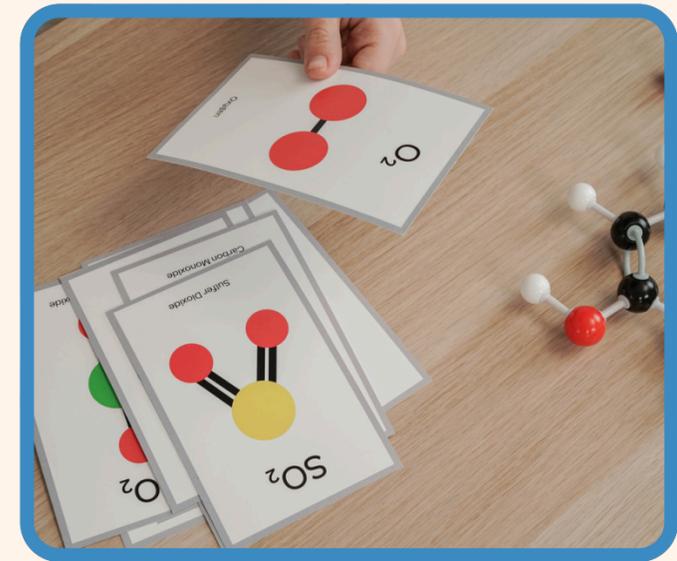
Enzymes are highly efficient, proceeding from 10^3 to 10^8 times faster than uncatalyzed reactions. The number of substrate molecules converted to product per enzyme molecule per second is called the turnover number, or k_{cat} , and typically is 10^2 to 10^4 second^{-1} . (Note: k_{cat} is the rate constant for the conversion of ES to E + P).

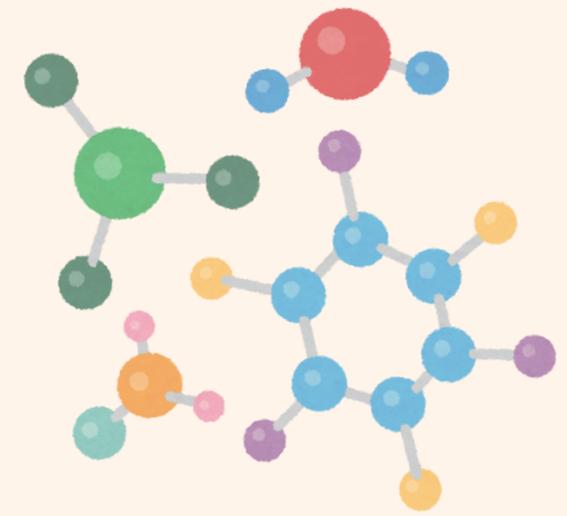
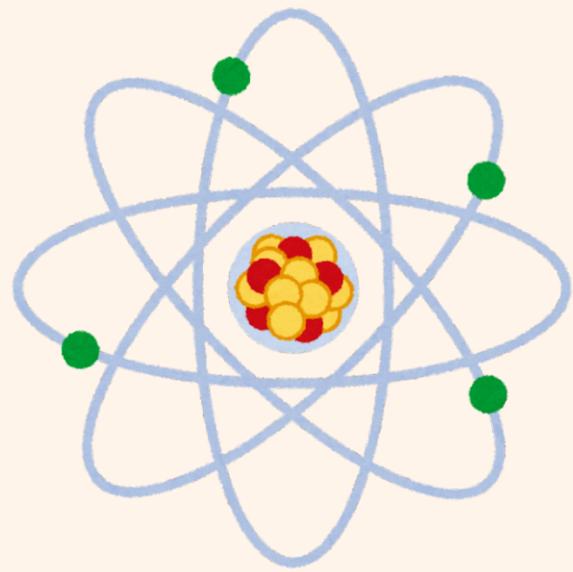




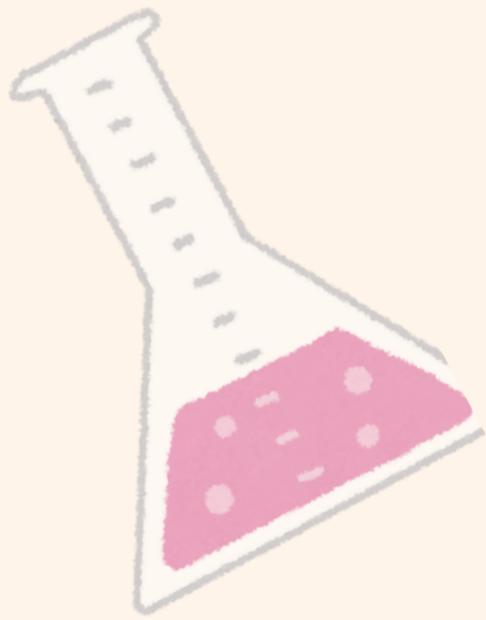
C. Specificity

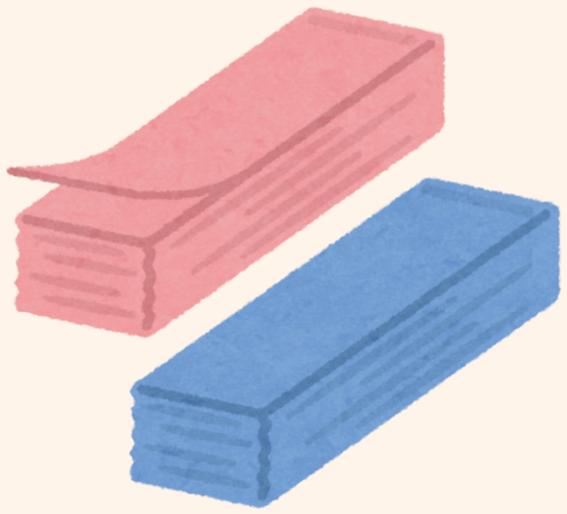
Enzymes are highly specific and are capable of interacting with one or a very few substrates and can catalyze only one type of chemical reaction.



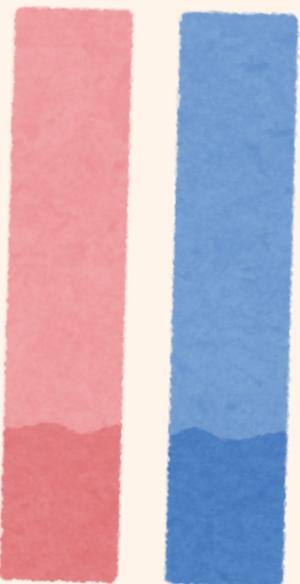


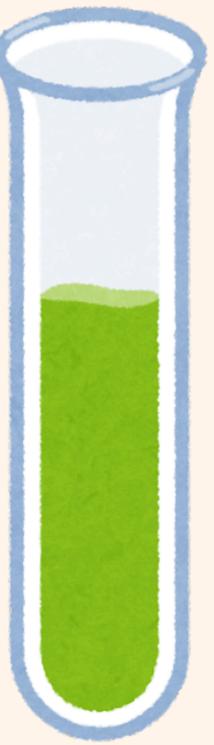
D. Holoenzymes, apoenzymes, cofactors, and coenzymes
Holoenzyme refers to the protein component of the enzyme. The enzyme without its nonprotein moiety is termed an apoenzyme and is inactive. If the nonprotein moiety is a metal ion, such as zinc (Zn^{2+}) or iron (Fe^{2+}), it is called a cofactor. Coenzymes or cosubstrates only transiently associate with the enzyme and dissociate from the enzyme in an altered state (for example, NAD^+). If the coenzyme is permanently associated with the enzyme and returned to its original form, it is called a prosthetic group (for example, FAD). Coenzymes commonly are derived from vitamins; for example, NAD^+ contains niacin, and FAD contains riboflavin.





E. Regulation Enzyme
The rate of product formation responds to the present cellular needs.

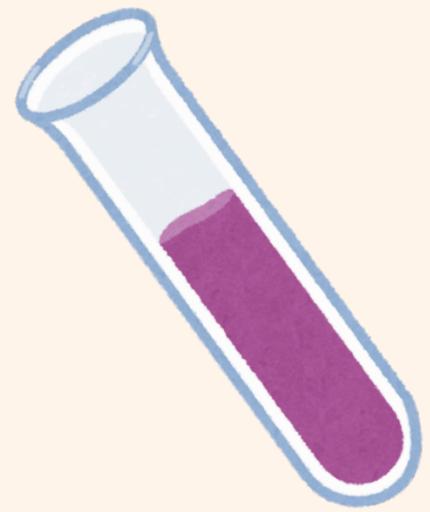
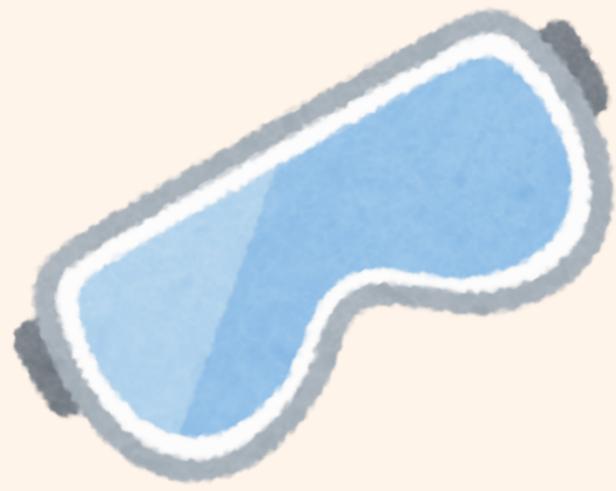




F. Location within the cell

Most enzymes function inside cells, within the confines of plasma membranes. Many enzymes are localized in specific organelles within the cell, such as the mitochondria (TCA cycle, fatty acid oxidation), cytosol (Glycolysis, PP pathway), nucleus (DNA and RNA synthesis), and lysosome (degradation of complex macromolecules). Such compartmentalization serves to isolate the reaction substrate or product from other competing reactions. This provides a favorable environment for the reaction and organizes the thousands of enzymes present in the cell into purposeful pathways.

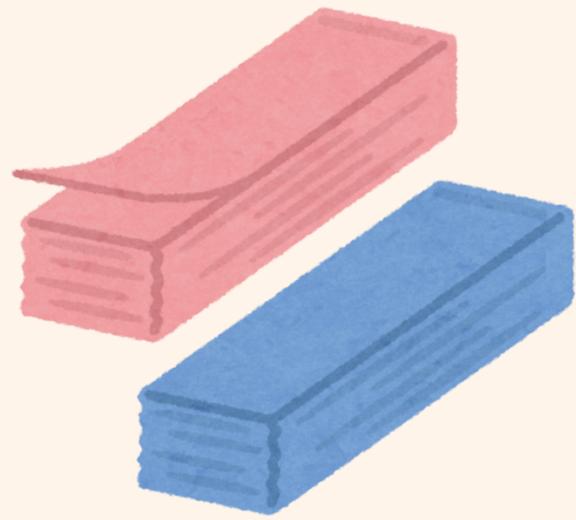




IV. MECHANISM OF ENZYME ACTION

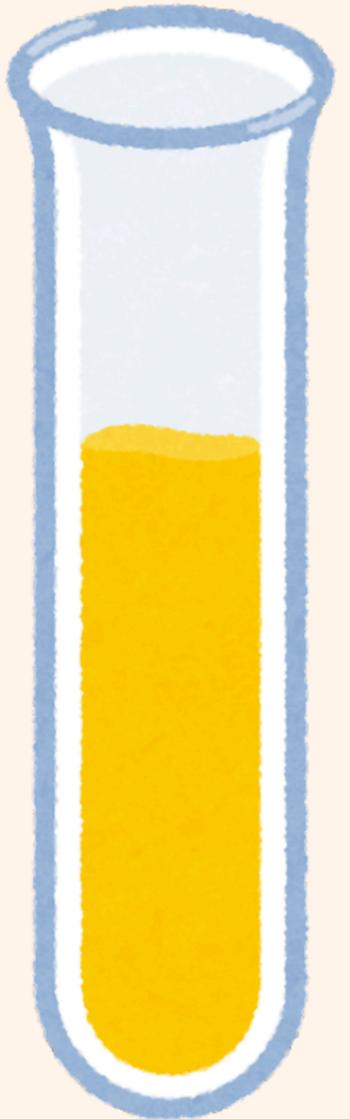
The mechanism of enzyme action is treated from two perspectives: first, in terms of energy changes, and second, describing how the active site chemically facilitates catalysis.



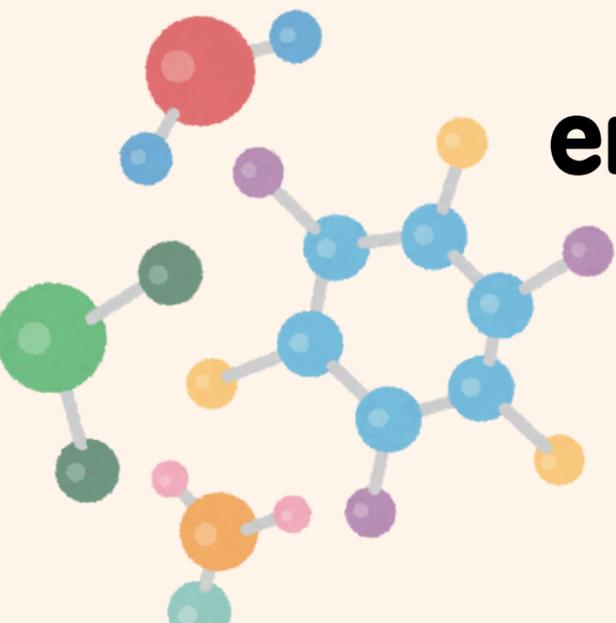
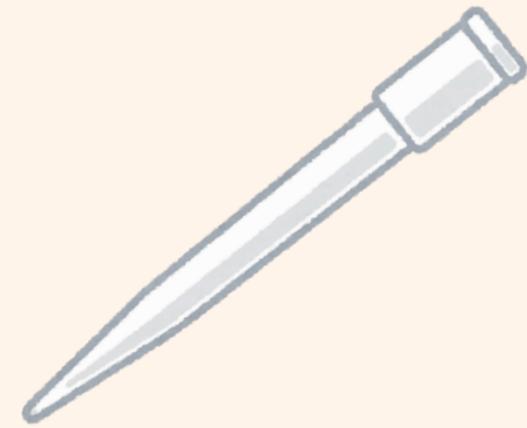


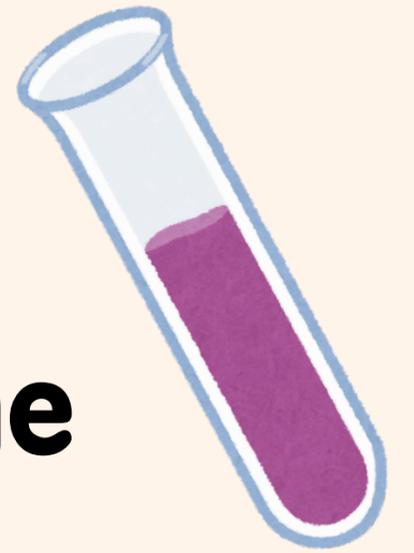
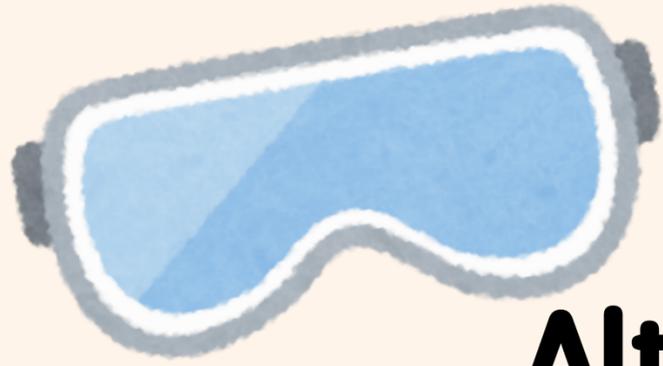
A. Energy changes

Virtually all chemical reactions have an energy barrier separating the reactants and the products. This barrier, called the activation energy (E_a), is the energy difference between that of the reactants and a high-energy intermediate, the transition state (T^*), which is formed during the conversion of reactant to product.



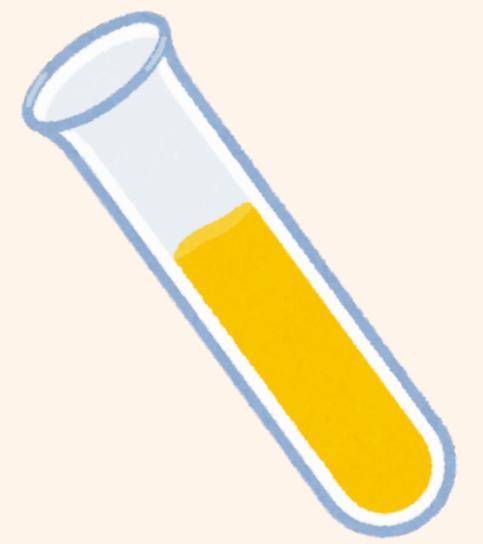
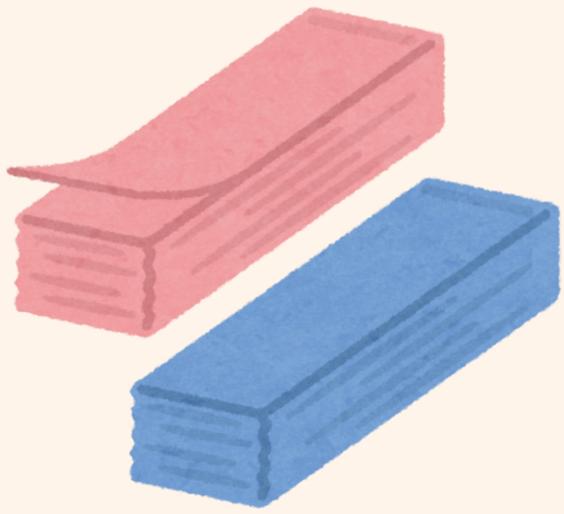
Activation energy: The peak of energy is the difference in free energy between the reactant and T^* . Rate of reaction: For molecules to react, they must contain sufficient energy to overcome the energy barrier of the transition state. In the absence of an enzyme, only a small proportion of a population of molecules may possess enough energy to achieve the transition state. The rate of reaction is determined by the number of such energized molecules





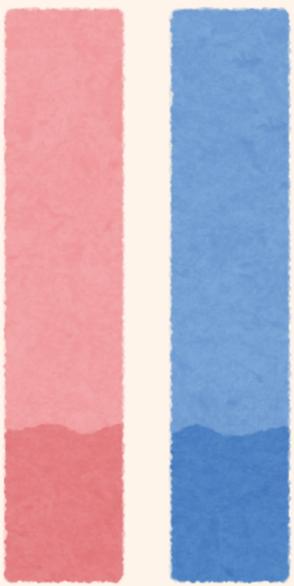
Alternate reaction pathway: The enzyme does not change the free energies of the reactants (substrates) or products and, therefore, does not change the equilibrium of the reaction. It does, however, accelerate the rate by which equilibrium is reached.

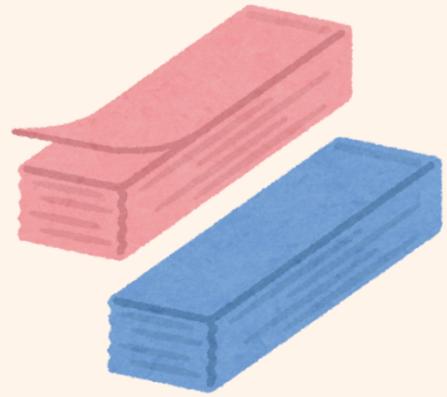




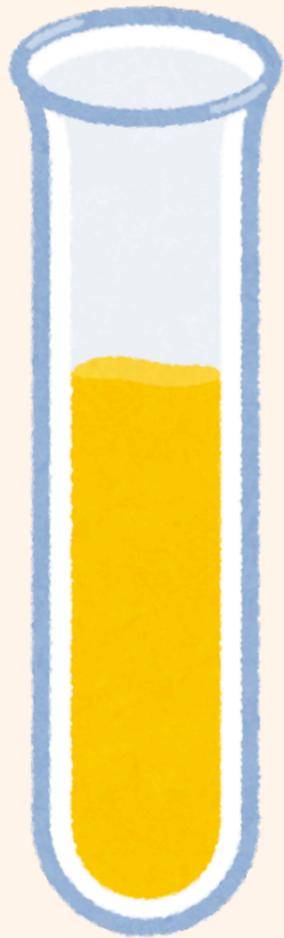
B. Active site chemistry

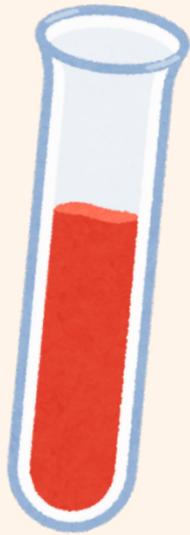
The active site is not a passive receptacle for binding the substrate but, rather, is a complex molecular machine that can employ diverse chemical mechanisms to facilitate the conversion of substrate to product. A number of factors are responsible for the catalytic efficiency of enzymes



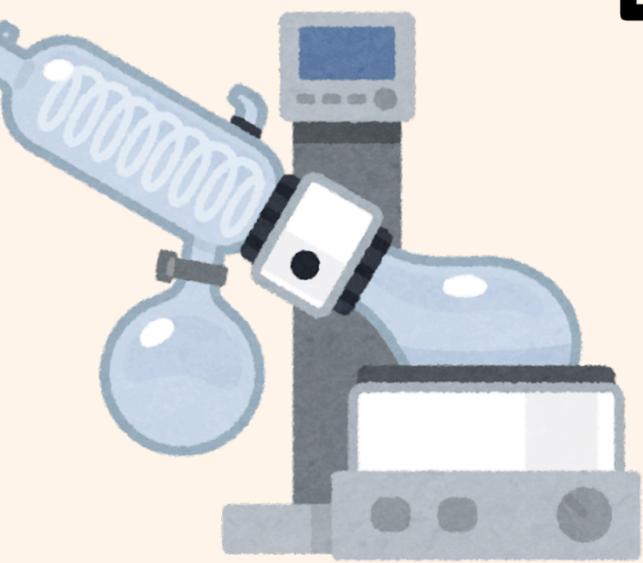


Transition-state stabilization: The active site often acts as a flexible molecular template that binds the substrate and initiates its conversion to the transition state. By stabilizing the transition state, the enzyme greatly increases the concentration of the reactive intermediate that can be converted to product and, thus, accelerates the reaction.



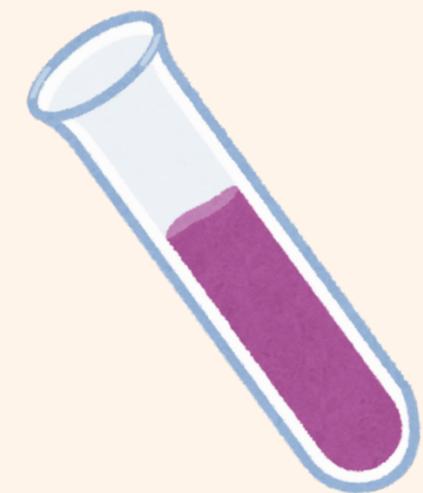
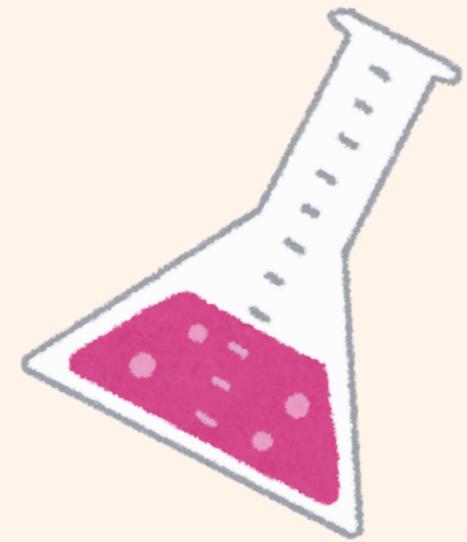


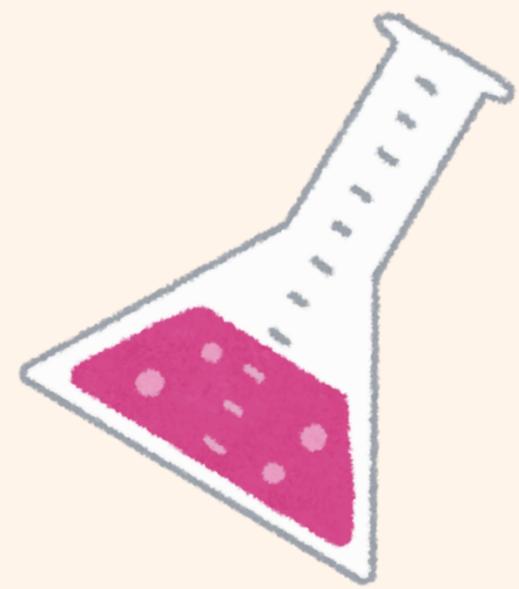
Catalysis: The active site can provide catalytic groups that enhance the probability that the transition state is formed. In some enzymes, acid-base catalysis occurs where amino acid residues provide or accept protons. In other enzymes, the transient formation of a covalent ES complex occurs. For example, chymotrypsin includes general base, general acid, and covalent catalysis



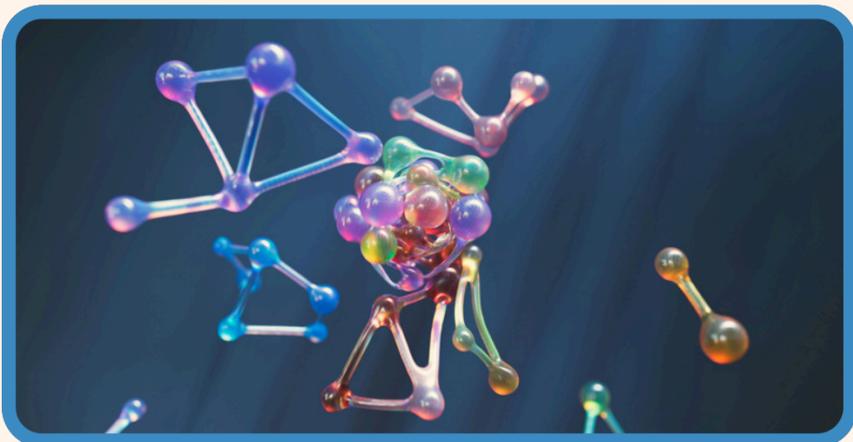
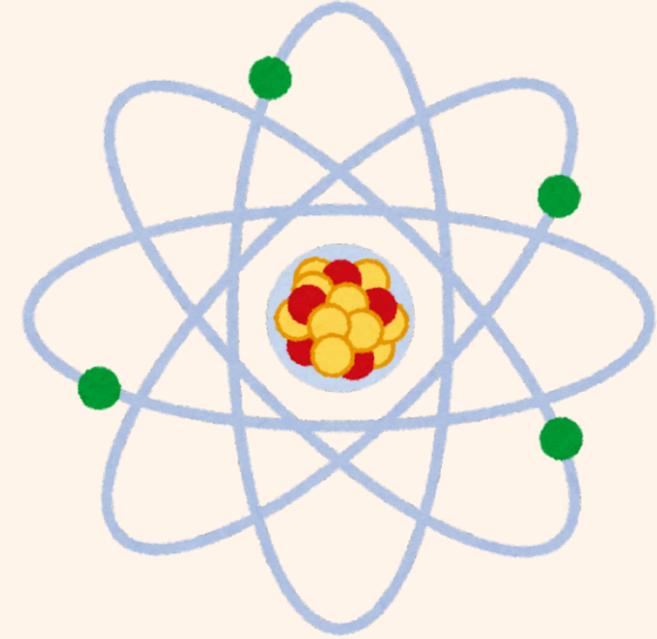


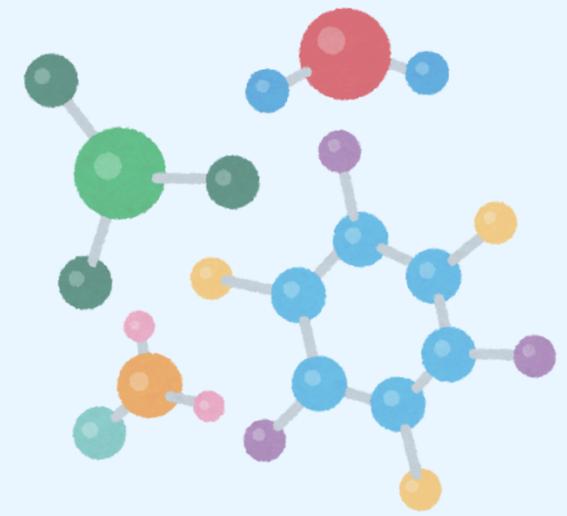
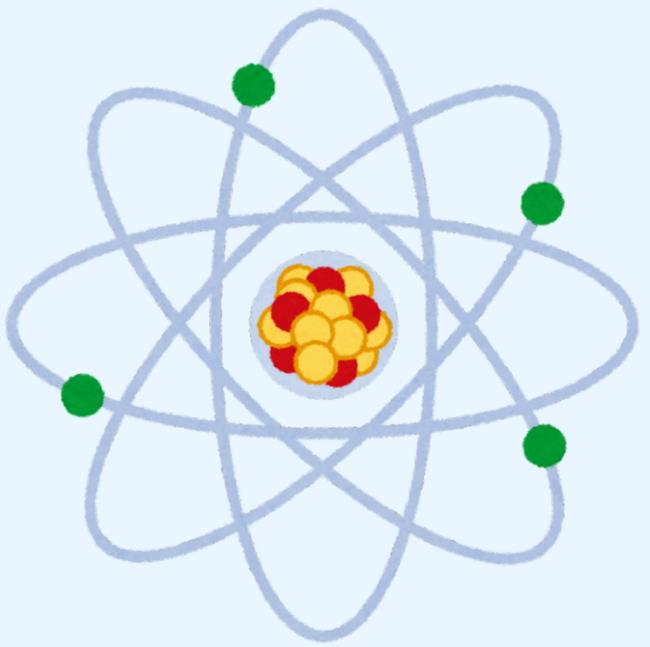
**A histidine at the active site
of the enzyme gains
(general base) and loses
(general acid) protons,
being close to physiologic
pH. Serine at the active site
forms a transient covalent
bond with the substrate.**





**Transition-state
visualization: The substrate
bound to the enzyme [ES] is
at a slightly lower energy
than unbound substrate [S]
and explains the small dip in
the curve at ES.**





Thank

You

