Lecture 5
Discipline: Bioorganic Chemistry
Lecturer: Associate Professor, Dr. Gulnaz Seitimova

Title: Enzymes. Classification, structure, physiological role.
Objective: The aim of this lecture is to provide a comprehensive understanding of enzymes, their chemical nature, mechanisms of action, structural organization, physiological significance, and classification principles used in modern biochemistry.
Main Questions: Definition and general characteristics of enzymes. Structural organization of enzymes: apoenzyme, cofactor, coenzyme, holoenzyme. Active site: structure, specificity, catalytic mechanisms. Enzyme classification according to the International Union of Biochemistry and Molecular Biology (IUBMB). Factors affecting enzyme activity. Enzyme kinetics and Michaelis–Menten principles. Physiological role of enzymes in metabolism and regulation. Examples of enzyme disorders and their medical relevance.

Key Notes and Theses
Definition and General Characteristics
- Enzymes are biological macromolecules, primarily proteins, that catalyze biochemical reactions by lowering the activation energy.
- Almost all metabolic reactions require enzymes to proceed at biologically relevant rates.
- Enzymes exhibit remarkable specificity, efficiency, and regulation.

Chemical Structure of Enzymes
- Most enzymes are globular proteins with a well-defined tertiary or quaternary structure.
- Structure includes:
  - Apoenzyme – the protein part.
  - Cofactor – non-protein component (metal ions: Mg^{2+}, Zn^{2+}, Fe^{2+}).
  - Coenzyme – organic molecules, often derived from vitamins (NAD^{+}, FAD, coenzyme A).
  - Holoenzyme – the active enzyme complex (apoenzyme + cofactor/coenzyme).

Active Site and Specificity
- The active site is a small, three-dimensional region where substrate binding and catalysis occur.
- Enzyme specificity types:
  - Absolute specificity – one substrate only.
  - Group specificity – molecules with similar functional groups.
  - Stereospecificity – distinguishes between stereoisomers.
- Catalytic mechanisms include:
  - Acid–base catalysis
  - Covalent catalysis
  - Metal ion catalysis
  - Proximity and orientation effects

Classification of Enzymes (IUBMB System)

All enzymes are divided into six major classes:

1. Oxidoreductases – catalyze oxidation–reduction reactions

Examples: dehydrogenases, oxidases

2. Transferases – transfer functional groups

Examples: kinases, aminotransferases

3. Hydrolases – catalyze hydrolysis reactions

Examples: proteases, lipases, nucleases

4. Lyases – add or remove groups without hydrolysis or oxidation

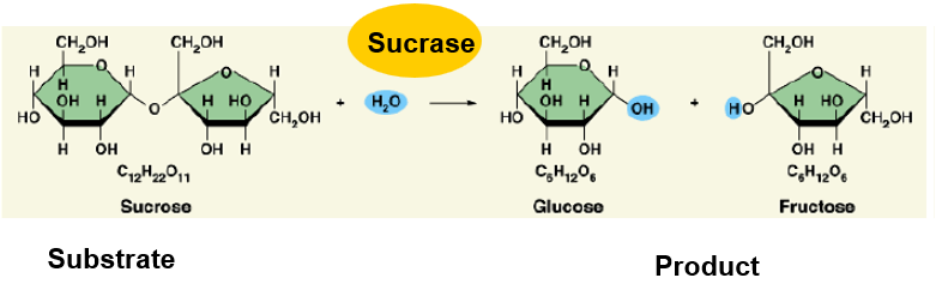
Examples: decarboxylases, aldolases

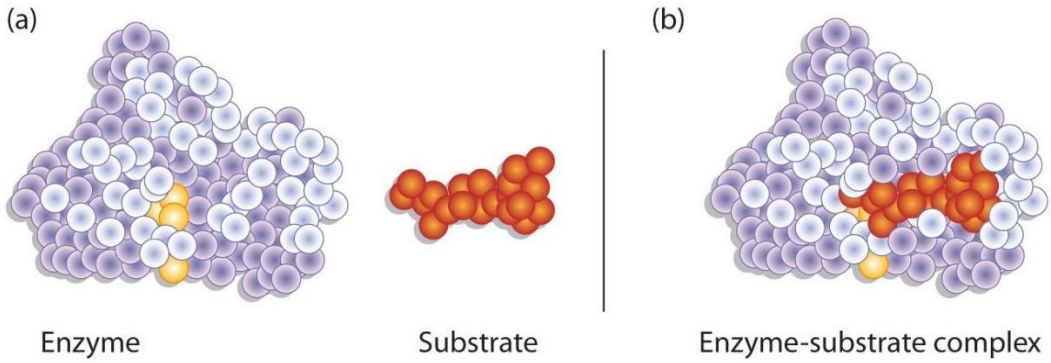
5. Isomerases – catalyze intramolecular rearrangements

Examples: epimerases, mutases

6. Ligases (synthetases) – catalyze synthesis using ATP

Examples: DNA ligase, carboxylases





Substrate Binding to the Active Site of an Enzyme. The enzyme dihydrofolate reductase is shown with one of its substrates: $NADP^+$ (a) unbound and (b) bound. The $NADP^+$ (shown in red) binds to a pocket that is complementary to it in shape and ionic properties.

Factors Affecting Enzyme Activity

- Temperature: activity increases until denaturation occurs.
- pH: each enzyme has an optimum pH (e.g., pepsin pH 1.5–2.0).
- Substrate concentration: follows Michaelis–Menten kinetics.
- Enzyme inhibitors:
  - Competitive

- Noncompetitive
- Uncompetitive

Enzyme Kinetics

- Described by the Michaelis–Menten model: v = (Vmax [S]) / (Km + [S])
- Km reflects the affinity of enzyme for substrate.
- Turnover number (kcat): number of substrate molecules converted per second by one enzyme molecule.

Physiological Role of Enzymes

Enzymes participate in all major biochemical processes:

- Digestion (amylase, trypsin, lipase)
- Energy production (ATP synthase, glycolytic enzymes)
- DNA replication and repair (polymerases, helicases)
- Detoxification (cytochrome P450 enzymes)
- Cellular signaling (kinases, phosphatases)
- Immune response (lysozyme, complement enzymes)

Medical Relevance of Enzymes

- Enzyme deficiencies cause diseases:
  - Phenylketonuria (phenylalanine hydroxylase deficiency)
  - Lactose intolerance (lactase deficiency)
  - Gout (xanthine oxidase overactivity)
- Enzymes as therapeutic agents:
  - Asparaginase (leukemia therapy)
  - Streptokinase (thrombolytic therapy)
  - Digestive enzyme supplements
- Enzymes as clinical biomarkers:
  - ALT, AST (liver damage)
  - CPK (myocardial infarction)
  - Amylase, lipase (pancreatitis)

Enzymes are proteins

In general, a protein is a chain of amino acids (aa) covalently linked (when the chain is short ~5-10 aa, the protein is often called oligopeptide/polypeptide or simply peptide)

Thousands of different proteins are built with the same ubiquitous set of 20 amino acids (the protein “alphabet”)

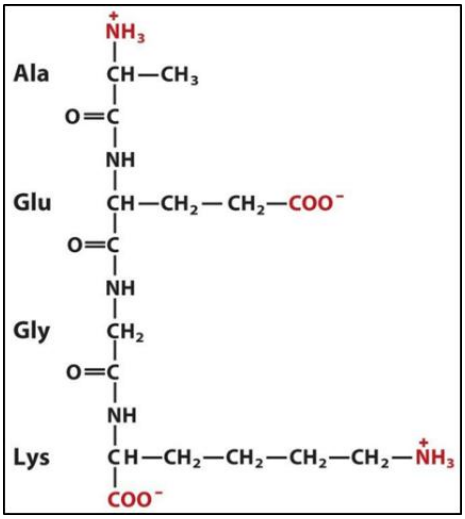
Some proteins have structural roles (e.g. actin in the muscles), other have catalytic (chemical-reaction-making) activity and are called enzymes

A polypeptide with 4 amino acids (Ala-Glu-Gly- Lys)

The electrically charged groups are shown in red

In a longer protein the electrically charged lateral groups can line a pocket of the enzyme 3D structure to generate an active reaction site (see following slides)

Enzymes are proteins and their activities depends on the 3D structure of the amino acids that compose them



Questions for Knowledge Assessment

1. What structural components make up an active holoenzyme?
2. Describe the difference between a cofactor and a coenzyme.
3. What determines enzyme specificity?
4. Name the six major enzyme classes and give examples.
5. What is the active site and how does it function?
6. What is Km and what does it indicate about enzyme–substrate interactions?
7. Explain the main types of enzyme inhibition.
8. Why are enzymes essential for metabolism?
9. Provide examples of clinically important enzyme biomarkers.
10. How do temperature and pH affect enzyme catalysis?

Recommended Literature

1. Nelson, D. L., Cox, M. M. (2017). *Lehninger Principles of Biochemistry* (7th ed.). New York: W.H. Freeman and Company.
2. Voet, D., Voet, J. G. (2011). *Biochemistry* (4th ed.). Hoboken, NJ: John Wiley & Sons.
3. Garrett, R. H., Grisham, C. M. (2016). *Biochemistry* (6th ed.). Boston, MA: Cengage Learning.
4. Stryer, L., Berg, J. M., Tymoczko, J. L., Gatto, G. J. (2015). *Biochemistry* (8th ed.). New York: W.H. Freeman and Company.
5. McMurry, J. (2010). *Organic Chemistry with Biological Applications* (2nd ed.). Belmont, CA: Brooks/Cole, Cengage Learning.
6. McMurry, J., Castellion, M. E. (2002). *Fundamentals of General, Organic, and Biological Chemistry* (4th ed.). Upper Saddle River, NJ: Prentice Hall.
7. Fromm, H. J., Hargrove, M. (2012). *Essentials of Biochemistry*. Berlin, Heidelberg: Springer-Verlag.
8. Hunter, G. K. (2000). *Vital Forces: The Discovery of the Molecular Basis of Life*. San Diego, CA: Academic Press.

9. Tyukavkina, N. A., Baukov, Y. I. (2014). *Bioorganic Chemistry* (in Russian). Moscow.

10. Ovchinnikov, Y. A. (1987). *Bioorganic Chemistry* (in Russian). Moscow.

11. Rouessac, F., Rouessac, A. (2007). *Chemical Analysis: Modern Instrumentation Methods and Techniques*. Hoboken, NJ: John Wiley & Sons.

12. Jeffery, G. H., Bassett, J., Mendham, J., Denney, R. C. (1989). *Vogel's Textbook of Quantitative Chemical Analysis* (5th ed.). London: Longman; John Wiley & Sons.