Bioorganic Chemistry. Academic Year 2019-2020.

Introduction.

- Catalyst definition. Kinetics and thermodynamics. Activation energy and Eyring equation.
- The Michaelis Menten equation. Meaning of k_{cat} and K_M. Catalytic efficiency of enzymes.

Structure and Properties of Amino Acids, Peptides, Proteins and Enzymes

- Structure and properties (review). Non-proteinogenic amino acids. Post-translational modifications in proteins. Reactivity of the side chains. Acids, bases and nucleophiles.
- The amide bond: peptides and proteins. Secondary and tertiary structure. Protein and enzyme structure.

Catalitic Efficiency

- Recognition and catalysis. The lock and key model. Induced fit. Affinity for the transition state.
- Enzyme-substrate interactions. Hydrogen bonds, non-covalent interactions.
- Bifunctional catalysis: glucose mutarotation; ketosteroid isomerase.
- Intramolecular catalysis. Effective molarity. Examples.
- Substrate distorsion.
- Specificity, selectivity and recognition.

Acid and Base Catalysis

- Specific and general acid-base catalysis. Mechanistic general acid-base catalysis. Examples: hydrolysis of esters, acetals and enoleters, α-halogenation of carbonyl compounds, aldol addition, condensation of carbonyl compounds with amines.
- Brønsted equation: halogenation of ketones. Extensions of the equation: β_{nu} and β_{lg}; transesterifications.
- Aspartyl proteases

Nucleophilic and Electrophilic Catlysis

- Nucleophilic catalysis: Williamson synthesis catalyzed by iodide, benzoin condensation, aldol addition, hydrolysis of esters catalyzed by tertiary amines.
- Serine and cystein proteases
- Electrophilic catalysis: Friedel-Crafts reactions; ring opening of epoxides; decarboxylation of β-keto acids; hydrolysis of aminoesters.
- Metalloproteases

Mechanisms of Enzyme Catalysis

- Hydrolysis and transfer reactions.
  - Lipases and esterases; ACE inhibitors; interfacial activation; biocatalysis.
  - Hydrolysis of phosphate esters. Phosphatases and phosphodiesterases.
  - ATP and energy storage: biosynthesis of esters and amides; ATPase, ATP synthase, SAM.
  - Glycosidases
  - Haloalkane and epoxide hydrolases (SN2)
- Enzyme-catalyzed transformations of amino acids and electrophilic catalysis
  - Pyridoxal
  - Aspartate aminotransferase
  - Alanine racemase
  - L-DOPA decarboxylase
  - Reactions at the β and γ positions
  - Histidine ammonia lyase
- Formation of C -C bonds
  - Via carbanions: class 1 and class 2 aldolases.
  - Via carbocations: squalene oxide cyclase.
  - Via radical reactions: methylmalonyl CoA mutase.
  - Via pericyclic reactions: chorismate mutase.
- Redox reactions .
  - NAD-dependent enzymes: alcohol dehydrogenase.
  - FAD-dependent enzymes: monooxygenase, glutathione reductase.
  - Metal-dependent enzymes: cytochromes P450.
- Catalytic RNA: ribosome and ribozymes.

- Enzyme inhibitors: reversible competitive inhibitors, reversible non competitive (allosteric) inhibitors; irreversible inhibitors.