Lectures overview

- Characteristics
- Kinetics
- Regulation
- Mechanisms
Definitions

- **Enzyme** – One or more polypeptide chains forming a catalytic active site

- **Substrate** - Molecule which binds active site and undergoes a chemical reaction

- **Product** – The result of enzyme action
Types of product

Light: Firefly

Enzyme: **Luciferase**

Heat: Bombadier beetle

Enzyme: **Catalase**
What do enzymes do?

- Digestion of food (pepsin)
- Clotting of blood (thrombin)
- Blood pressure (ACE)
- Defence (lysozyme)
- Breakdown of toxins (cytochrome P450)
- Routine cell processes
Lysosomes

- All are acid-sensitive, requiring low pH for activity
- Acid phosphatase is a marker enzyme for lysosomes

Contain 40-50 different digestive enzymes
- Proteases
- Lipases
- Phospholipases
- Nucleases
- Glycosidases
- Phosphatases
- Sulphatases
Enzyme classification

- Most enzyme names end in -ase
- Some have common names e.g. trypsin (a protease)
- Typically named for the reaction they catalyse or their substrate/product
  - E.g. Glycogen synthase → Synthesis of glycogen

- A few types of enzyme:
  - Dehydrogenases → Remove/add hydrogen with NAD+/NADH
  - Kinases → Transfer PO₄³⁻ from ATP to OH groups
  - Phosphatases → Remove PO₄³⁻ groups to leave OH
Enzyme classification

- **Enzyme Commission number**
- **Class.Subclass.Sub-subclass.Serial number**
- **Classes:**
  1. **Oxidoreductases** – Transfer electrons (as H⁺ or H)
  2. **Transferases** – Transfer chemical groups *e.g.* methyl
  3. **Hydrolases** – Break bonds with water
  4. **Lyases** – Reactions involving double bonds
  5. **Isomerases** – Transfer of groups within a molecule
  6. **Ligases** – Formation of bonds using energy from ATP

*(E.g. E.C. 3.1.3.1 - Alkaline phosphatase)*
Why are enzymes necessary?

1. Pace of life

\[ 2H_2O_2 \rightarrow 2H_2O + O_2 \]

Uncatalysed: 41 years
Platinum catalyst: 9.25 hours
Catalase: 1 second

2. Conditions of life

- Body temperature
- Neutral pH

\textit{i.e.} no high temp or harsh treatment to speed up reactions
Properties

- Reusable
- Specific
- Efficient
- Controllable
The active site

- Active site is a small part of the whole enzyme
  - 3D arrangement of amino acids
  - Contains binding and catalytic residues
  - Source of substrate and reaction specificity

- Often only a small part of the substrate e.g. a chemical group enters the active site \( \rightarrow \) range of substrates which all have that group
Substrate specificity

- Lock and Key (Fischer)
- Induced fit (Koshland)
Substrate specificity

Induced fit (Koshland)
Substrate specificity

- Lock and Key (Fischer)
- Induced fit (Koshland)
Hexokinase
Ogston 3-point binding
Reaction specificity

Determined by:

- 3D arrangement of residues
- Chemical properties of residues

- Often only 3 (carefully positioned) amino acids perform the actual catalysis - *catalytic triad*

Active site may also contain:

- Metal cofactors *e.g.* Mg$^{2+}$, Zn$^{2+}$ (*A.* Phosphatase)
- Coenzymes *e.g.* NAD, NADP
- Prosthetic groups *e.g.* Flavins, Haem (*Catalase*)
Metal Cofactors
Co-enzymes

- Organic molecules which provide/remove groups
  - Sometime called co-substrates. E.g. NADH $\rightarrow$ NAD$^+$
Coenzymes can act as hydrogen shuttles in redox reactions.
Types of reaction

- $A + B \rightarrow C$  Anabolic/synthetic
- $A \rightarrow B + C$  Catabolic/degradative
- $A + B \rightarrow C + D$  Interconversions

- Many biological reactions are reversible – substrate and product exist in an equilibrium
Progress of reaction

Equilibrium reached
Reaction appears to stop
Rate = zero
Reaction rate

- Reaction rate depends on:
  - Speed of 1 reaction → rate constant, $k \ (\text{reactions/s})$
  - Number of reactions happening → [reactants]
Overall rate of reaction

- Depends on rate constants and concentrations

\[ k_{S \rightarrow P} \times [S] = k_{P \rightarrow S} \times [P] \]

At equilibrium: \( k_{S \rightarrow P} \times [S] = k_{P \rightarrow S} \times [P] \)
Reaction rate

- Reaction rate depends on:
  - Speed of 1 reaction → rate constant, $k$ (reactions/s)
  - Number of reactions happening → [reactants]

Enzymes change $k$ by decreasing the Activation Energy
How does energy relate to speed?

- Each change in activation energy of ~5 kJ/mol = 10 times faster