TOPIC 8.1: METABOLISM

Metabolic Pathways

Metabolism describes the sum total of all chemical reactions that occur within an organism in order to maintain life

- Metabolic processes are controlled and coordinated by a series of enzyme-catalysed reactions
- Metabolic pathways are typically organised into chains (e.g. glycolysis) or cycles (e.g. Krebs cycle, Calvin cycle)

Enzyme Action

Every chemical reaction requires a certain level of energy in order to proceed – this is called the **activation energy (E_A)**

Enzymes speed up reaction rates by *lowering* the activation energy threshold (destabilise substrate bonds = ⬆ product conversion)

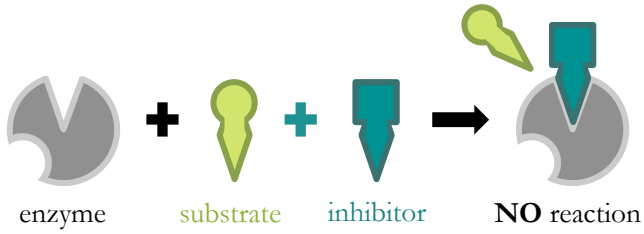
- If reactants contain *more* energy than the products, the reaction is **exergonic** as energy is released (e.g. catabolic reactions)
- If reactants contain *less* energy than the products, the reaction is **endergonic** as energy is absorbed (e.g. anabolic reactions)

Enzyme Inhibition

Competitive Inhibition

- Inhibitor is structurally similar to the substrate
- It directly blocks the active site of the enzyme
- Increasing substrate concentration will reduce inhibition

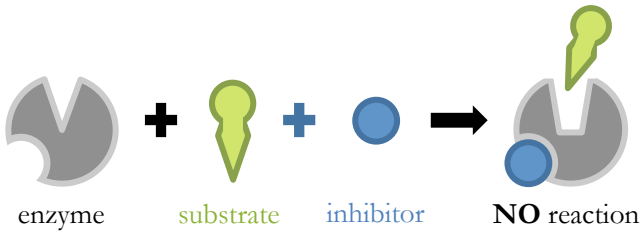
Example: Treating influenza with a neuraminidase inhibitor



Non-Competitive Inhibition

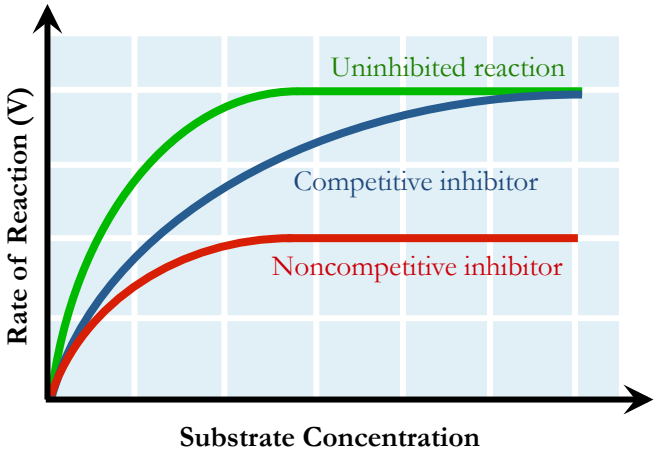
- Inhibitor is not structurally similar to the substrate
- It binds to an allosteric site (not the active site)
- It induces a conformational change in the active site

Example: Cyanide as an inhibitor of cytochrome oxidase



Enzyme Kinetics

Enzyme inhibitors lower reaction rates by reducing levels of uninhibited enzymes *(reaction rate = 1 / time taken)*



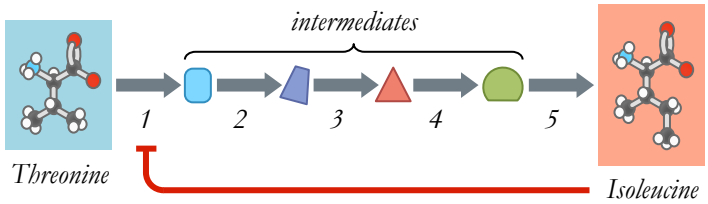
Feedback Inhibition

Metabolic pathways can be controlled by feedback inhibition *(end product inhibition)*, where a product inhibits an earlier step

- This ensures product levels are always tightly regulated

Example: Isoleucine Synthesis

- Threonine deaminase convert threonine into isoleucine
- Isoleucine inhibits the enzyme's activity *(non-competitive)*
- Thus, isoleucine synthesis inhibits further formation



Rational Drug Design

Inhibitors can be used to treat infectious diseases by targeting the enzymes involved in pathogenesis (e.g. anti-malaria drugs)

- Inhibitors can be identified by database mining (bioinformatics) or constructed via combinatorial chemistry techniques