Metabolism

- *Metabolism* is the sum of all chemical reactions occurring within a living organism
- *Anabolism* is the type of reaction that uses energy to build complex organic molecules from simpler ones
- *Catabolism* is the type of reaction that breaks down complex organic molecules with the release of energy

Anabolic reactions	Catabolic reactions
Build complex molecules	Breaks down complex molecules
Are endergonic	Are exergonic
Are biosynthetic	Are degradative
Example: photosynthesis	Example: cellular respiration

- *Endergonic reactions* occur when the products of a chemical reaction have more energy than the reactants or the substrates of the reaction
  - Tend to occur in *biosynthetic reactions* in which more complex molecules are produced
  - Energy flows into a system
- *Exergonic reactions* occur when the products of a chemical reactions have less energy than the reaction's reactants or substrates
  - Tend to occur in *degradative reactions* in which complex molecules are broken down into simpler materials
  - Energy flows out of a system

Metabolic pathways

- Almost all metabolic reactions in organisms are catalysed by enzymes
- *Metabolic* or *biochemical pathways* are specific sequences in which many of the metabolic reactions occur
- Enzymes cause one substrate to be changed to another until the final product of the pathway is formed
- Some metabolic pathways consist of cycles of reactions and some of chains of reactions. Others include both

- Metabolic pathways are usually carried out in designated compartments of the cell where the necessary enzymes are clustered and isolated
- The enzymes required to catalyse every reaction in these pathways are determined by the cell's genetic makeup

Enzyme action

- *Enzymes* are complex protein molecules with high molecular weights
- The higher levels of protein structure allow enzymes to form unique areas, such as the active site
    - The *active site* is the region on the enzyme that binds to a particular substrate(s)
        - This binding results in the reaction occurring much faster
- Enzymes are globular proteins, that as a minimum, have the tertiary level of organisation
- E. Fisher, 1890's, proposed the lock-and-key model of enzyme action
    - Substrate molecules fit into a rigid section of the enzyme like a key fits into a lock
    - This model has been modified
- Enzymes undergo significant changes in their conformation when substrates combine with their active site
    - This new model is called *induced-fit model*
    - Think of a glove and a hand. The glove (enzyme) looks like a hand (substrate), but when the hand is placed in the glove, there's a interaction that results in a conformational change of the glove
    - These changes and induced fit are the results of changes in the R-groups of the amino acids at the active site of the enzyme, as the enzyme interacts with the substrate

Activation energy

- *Activation energy (AE)* is the energy necessary to destabilise the existing chemical bonds in the substrate on an enzyme-substrate catalysed reaction
- Enzymes work by lowering the AE required
    - The enzymes cause chemical reactions to occur faster, due to this reduction
    - Enzymes do not alter the proportion of reactants to products

Mechanism of enzyme action

1. Substrate contacts the active site
2. The enzyme changes shape to accommodate the substrate
3. A temporary complex called the *enzyme-substrate complex* forms
4. The AE is lowered and the substrate is altered by the rearrangement of the existing atoms
5. The transformed substrate (product) is released from the active site
6. The unchanged enzyme is then free to combine with other substrate molecules

$$E + S \leftrightarrow ES \leftrightarrow E + P$$

- E: enzyme
- S: substrate
- ES: enzyme-substrate complex
- P: product

Inhibition

- If a molecule affects an active site in some way, the activity of the enzyme may be altered
- The activity of enzymes is strictly controlled in the body
- Competitive inhibition
  - A molecule called *competitive inhibitor* competes directly with the usual substrate for the active site or an enzyme
  - The substrate will have fewer encounters with the active site and rate of the chemical reaction will be decreased
  - The competitive inhibitor must have a structure similar to the substrate
  - No further reactions can take place
  - Example: the use of sulfanilamide (a sulfa drug) to kill bacteria during an infection
    - Folic acid is essential to bacteria as a coenzyme
    - It is produced by enzyme action on PABA (para aminobenzoic acid)
    - The sulfanilamide competes with PABA and blocks the enzyme
    - This prevents the production of folic acid resulting in the death of the bacteria
    - Humans are unaffected by the drug
  - *Reversible* competitive inhibition may be overcome by increasing the substrate concentration

        - There is more substrate molecules to bind with the active sites as they become available and the chemical reaction may proceed more rapidly

- ➢ Non-competitive inhibition
    - It involves an inhibitor that does not compete for the enzyme's active site
        - The inhibitor interacts with another site on the enzyme
    - Non-competitive inhibition is also referred to as *allosteric inhibition* and the site the inhibitor binds to is called *allosteric site*
    - Binding at the allosteric site causes a change in the shape of the enzyme's active site making it non-functional
    - Example: metal ions binding to the sulfur groups of the components amino acids of many enzymes
        - This results is shape changes of the protein causing inhibition of the enzyme
    - This type of inhibition may either be reversible or irreversible
    - There are examples of allosteric interactions activating an enzyme rather than inhibiting it

End-product inhibition

- ➢ It prevents the cell from wasting chemical resources and energy making more of a substrate than it needs
- ➢ Non-competitive inhibition
- ➢ Many metabolic reactions occur in an assembly line type of process so that a specific end product can be achieved
- ➢ Each step of the assembly line is catalysed by a specific enzyme
- ➢ When the end product is present in a sufficient quantity, the assembly line is shut down
    - The end product binds with the allosteric site of the first enzyme bringing about inhibition
- ➢ Lower concentrations of the end product results in fewer bindings and therefore the enzyme is activated
    - The enzyme that is inhibited and reactivated is an allosteric enzyme
- ➢ Example: E. coli uses a metabolic pathway to produce the amino acid isoleucine from threonine
    - A 5-step process