Metabolism

The totality of an organism’s chemical reactions, consisting of catabolic and anabolic pathways, which manage the material and energy resources of a cell. There are two metabolic pathways:

* Catabolism releases energy by breaking down complex molecules into simpler compounds e.g. respiration
* Anabolism consumes energy to build complex molecules from simpler ones e.g. protein synthesis

Energy Requirements

* To survive, organisms must obtain both energy and a carbon source from the environment
* Energy can be gained in one of two ways
  1. Phototrophs are organisms that use light energy
  2. Chemotrophs obtain energy from chemicals
* Carbon can be obtained through
  1. Autotrophs, which only use CO2 as a carbon source
  2. Heterotrophs, which require one or more organic carbon sources e.g. glucose

Human Metabolism

* Humans require carbohydrates (>55%), proteins (~15%) and lipids (<30%)
* Food is broken down in respiration to CO2 and H2O
* Energy is used for biosynthesis, membrane transport and muscle contraction
* Amino acids and fats can only be broken down by catabolism
* Skeletal muscles (intense exercise) and red blood cells (always) can use anaerobic respiration

Oxygen and Catabolism

Higher animals have aerobic catabolism; many protists and prokaryotes have anaerobic catabolism

Respiration

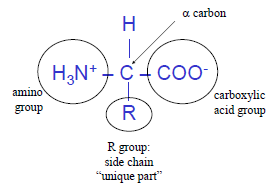
Fermentation

Tissue Specific Fuel Metabolism in Humans

* All human cells/tissues can use ATP as a metabolic fuel
* Brain tissues an red blood cells cannot use fat/amino acid breakdowns; glucose dependant
* Other tissues can work on breaking down fat and carbohydrates
* Skeletal muscles generates ATP faster when breaking down carbs than fats/amino acids 🡪 better supports intense exercise

Proteins

Proteins are strings of amino acids that function as catalysts, transport molecules, provide mechanical support (e.g. collagen), and generate movement

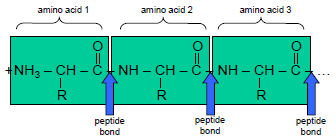
Amino Acids

Amino acids can exist in mirror (L and D) forms; L-amino acids are used on our planet by chance

Classifying Amino Acids

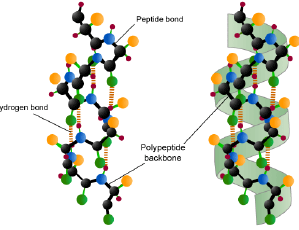
Classified through their R groups

1. Acidic – Side chain carries negative charge
2. Basic – Side chain carries positive charge
3. Polar – Uncharged but hydrophilic
4. Non-polar – Uncharged but hydrophobic

Note: Francis Crick proposed the central dogma of molecular biology in 1958 (DNA 🡪 RNA 🡪 protein)

Peptide Bonds

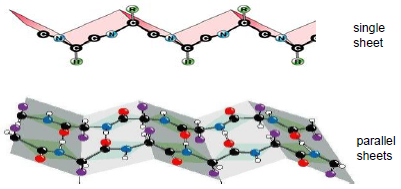
* Peptides and proteins have polarity or direction
* Amino acid terminus is the start and carboxyl terminus is the end

Protein Structure

Proteins have a primary, secondary and tertiary structure. Amino acids determine this; proteins are self-assembling

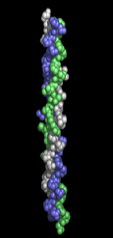
Secondary Structures

When polypeptide chains fold to form repeating structures; loops and turns exist between these

1. Alpha helix
   * Involves only one polypeptide chain
   * Stabilised by internal hydrogen bonds
   * R-groups project outwards from helix
2. Beta sheet (beta pleated sheet)
   * Involved one or more polypeptides
   * R-groups project outwards from the sheet
   * Hydrogen bonds stabilise adjacent sheets

Fun fact: Titin is the largest known protein; 26 000 amino acids, almost 1 micron in length



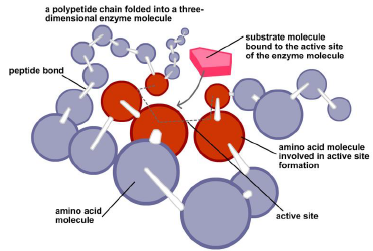
Tertiary Structure

Description of 3D position of all atoms; describes secondary structural elements

1. Fibrous
   * Long, extended and rod-lie
   * Insoluble, mostly alpha helices
   * E.g. Collagen, fibroin, titin, keratin
2. Globular 3D structures
   * Compact and fold back on themselves
   * Soluble; complex structures
   * E.g. hemoglobins, enzymes
   * Can contain both alpha helices and beta sheets
   * Have a hydrophobic core and hydrophilic surface e.g. thioredoxin

Diseases can occur when soluble proteins are modified to become insoluble e.g. Huntington’s, Alzheimer’s

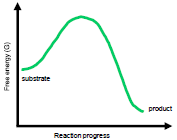
Enzymes and Catalysis

Enzymes are biological catalysts mostly made of proteins (some of RNA); highly specific

Substrates

* Reactants in enzyme-mediated reactions; converted into new products
* Products can be substrates for new reactions
* Protein 3D structures determine the substrate specificity by structure of active site

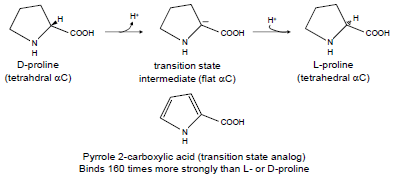
Note: Lock and key model is an oversimplification

Active Sites

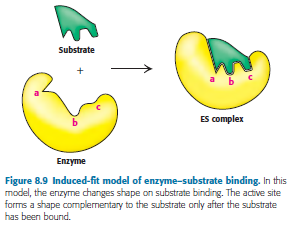
* Some active sites are not made of adjacent amino acids
* Protein can fold around
* Active sites are clefts or crevices
* Binding between enzymes and substrates are from weak forces like
  + Van der Waals
  + Hydrogen bonds
  + Ionic forces

Note: Catalysis is the acceleration of the reaction rate of a chemical reaction through a catalyst; same catalyst can be used many times

Free Energy

This is the amount of energy can be converted into work; enzyme substrates and products have free energy

* Differences in free energy account for the reaction equilibrium
* If a product has a lower free energy, the reaction can be spontaneous albeit slow
* Enzymes lower activation energy
  + Assist in formation of one or more reaction intermediates (also known as transition states)
  + Transition states known to exist due to inhibition by transition state analogs

Induced Fit Model of Catalysis

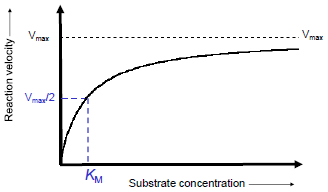
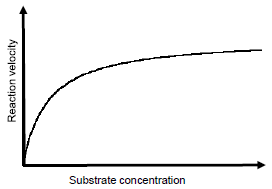
* Binding of substrate changes shape of active site
* Change in active site favours transition state
* Products are produced and released
* Enzyme resumes normal shape

Enzyme Kinetics

Enzyme reaction velocity is affected by substrate concentration; slows down as reached asymptote; fixed enzyme amount; based on unable to be found

Substrate preferences are reflected in different catalytic rates

Michaelis-Menten Constant



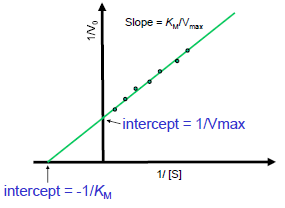
* indicates substrate concentration required for significant catalysis to occur
* Enzymes have varying values of
* An enzyme-substrate complex is formed as a step in a reaction mechanism

*Binding Strength*

* If rate k-1 >> k2, ES dissociates rapidly and product is not formed
* Km=k-1/k1 and so Km measures the affinity of the enzyme for the substrate
* When k-1 >> k2, low Km indicates strong binding and high Km means weak binding

Michaelis-Menten Equation

When [S] is very low and smaller than Km, V0 [S]; if [S] is high, V0=Vmax

Lineweaver-Burk Plots

Double reciprocal of Michaelis-Menten graph; able to derive values of KM and Vmax

Perfect Kinetics

A kinetically perfect enzyme is

* Limited only by the rate at which it encounters substrate
* In these cases, catalysis rates reflect those of diffusion
* Superoxide dismutase has kinetic perfection