BCH2011: Structure and Function of Cellular Biomolecules

Lecture 1: Introduction

- Aim: provide students with an understanding of biochemistry
- Blood cells are the same size as capillaries- squeeze through them
- Glucose molecule = quite small
- Prac session manual- hard copy distributed at session 1
- Must complete pre-prac questions/exercise

Lectures 2-5: Chemical Foundations of Biology

OBJECTIVES:

- To review fundamental chemical concepts needed to understand introductory biochemistry
- To understand the structure of water, particularly the role of hydrogen bonds
- To understand the importance of hydrogen bonds to the structures and behaviour of biomolecules, particularly DNA and RNA
- To understand that water ionises and this gives rise to the concepts of pH and ionisation of biomolecules in water
- To understand the importance of bonding systems (particularly hydrogen bonds) to the behaviour of biomolecules
- To understand the influence of water on the association of nonpolar molecules in an aqueous environment

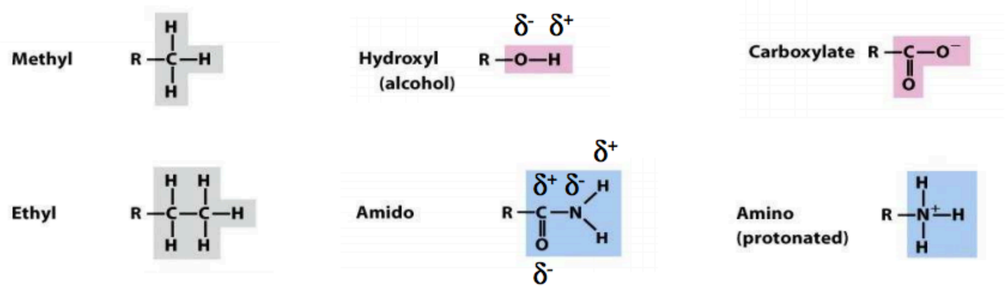
KEY CONCEPTS:

- Molecular structure and (covalent) bonding
- Organic molecules and functional groups
- Ionisation
- Non-covalent interactions
- Equilibrium, free energy, enthalpy and entropy
- Kinetics (rates of reactions)

1. Chemical Structure and Bonding:

- Bonding controls structure
  - Structure controls interaction of molecules with one another
  - Molecular Shape
  - Bond rotation
  - Groups want to maximise distance to minimise repulsion
  - Chirality → property of a molecule that means it's mirror image isn't identical to it
- Molecular Structure and Bonding
  - Functional Groups
    - OH- hydroxyl
    - COO-, carboxylate
  - Electronegativity: H,C<N,O

- Polarity:



Non-polar Polar Charged

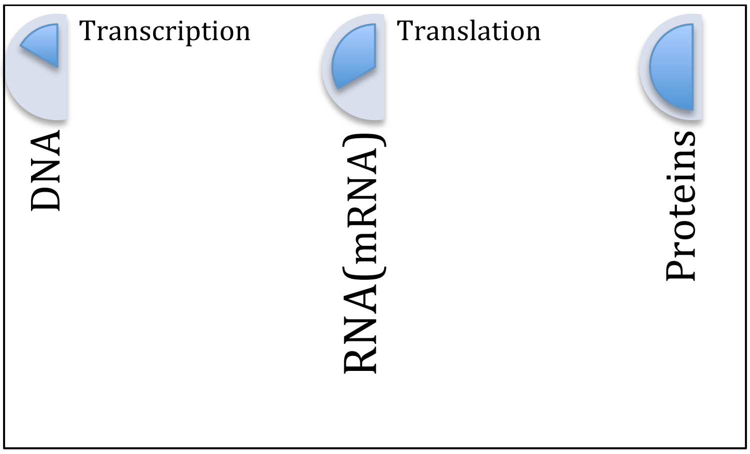
- Structure of Water
  - H2O
  - Bonds are polar
  - Condensation reactions (removing water)
  - Hydrolysis reactions (adding water)
  - Addition (adding water with only one product)
  - Elimination (removing water with only one reactant)

2. The Structure of Water and Hydrogen Bonds:

- Water forms hydrogen bonds
  - Non-covalent interactions
  - Far weaker than covalent bonds
  - Longer than covalent bonds
  - Easily broken and reformed
  - In ice, each water molecule forms four hydrogen bonds
  - Vapour form- no hydrogen bonds
- Structure of Liquid Water: Flickering Cluster Model
  - ~85% of molecules live in small hydrogen bonded clusters
  - Clusters of variable size
  - Other 15% of water molecules are “free” → not hydrogen bonded to any other molecules
  - All molecules are in a rapid flux; clusters are constantly growing, shrinking, breaking apart & reforming
  - Number of H bonds is not max and they are constantly being broken and reformed
  - Clusters progressively breakdown as the temp is raised
- Hydrogen bonds are common non-covalent interactions
- Occur in biological molecules containing N and O atoms
  - Strongest when the three atoms involved lie in a straight line
  - Linear = strong, Bent=weaker

3. Hydrogen Bonds in the Structures of DNA and RNA:

- DNA and RNA carry information to encode the structures/functions of proteins



- Structure of DNA
  - Polymer
  - Repeating string of many similar units
  - Double stranded (2 polymer)
  - Starts at 5’ and finishes at 3’ end
    - Opposite stand starts from bottom at 5’ → 3’ (antiparallel)
  - T→A (2 bonds), G→C (3 bonds), isomorphus
- Structure of RNA
  - When made is a single strand
  - Sugar is ribose (not deoxyribose like DNA)
  - Thymine is replaced with Uracil (U)
  - RNA hairpin look
  - tRNA- involved in translation (how cell translates from mRNA to protein sequence)
- Transcription (DNA → RNA)
  - Double-stranded DNA
  - Single-stranded DNA
  - Double stranded DNA-RNA hybrid (Thymine replaced with Uracil on RNA strand)
  - Single stranded RNA

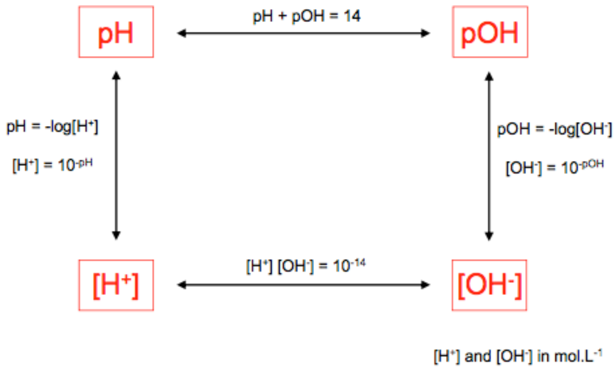
4. Chemical Equilibrium and Free Energy:

- Many Biochemical Processes are Reversible
  - Dynamic Equilibrium → rate of forward reaction equals rate of reverse reaction
  - Equilibrium is the constant rate of the complex
- Equilibrium Constant (Keq) and Free Energy Change (delta G)
  - A + B ←→ AB
  - At Equilibrium: [AB] = Keq[A][B]
  - Keq is relative stability of AB compared to A+B
  - More stability= lower Gibbs Free Energy (G)
  - Delta G = -RT ln(Keq)
  - Delta G < 0 ←→Keq>1
- Association and Dissociation Equilibrium Constant
  - Association: Ka = [AB]/([A][B])
  - Dissociation: Kd = ([A][B])/[AB] = 1/Ka

5. The Acid-Base Chemistry of Water:

- H_2O ←→ H^+ + OH^-, H2O can ionise to release a proton

- $H_2O + H^+ \leftrightarrow H_3O^+$, Can also accept a proton to form a hydronium ion
- In pure water, H^+ (or H_3O^+) and OH^- are present in equal concentrations (10^{-7}M at 25°C)
    - $[H^+][OH^-] = 10^{-14}\ M^2$
- High pH, high concentration, OH^- ions, basic
- Most enzymes and other biomolecules have optimum pH values for:
    - their activities, and
    - maintenance of their structures



- Enzymes are the result of evolution, producing them the right way with the appropriate properties
- pH and molecular charge: weak acids and bases
    - **pK_a = pH at which the group is 50% deprotonated**
    - High pH → deprotonated form only
    - Low pH → protonated form only
- Weak acids deprotonate faster
- pK_a is a different value for different acidic groups
- Many biological molecules contain more than one dissociable proton
- The charge on such molecules is dependent on pH in a complex manner
- Buffering region → either side of pK_a value
- RULE OF THUMB:
    - When $pH=pK_a$ the ratio [A]:[HA] = 1:1
    - For each pH unit above the pK_a, the ratio [A]:[HA] increases 10-fold
    - For each pH unit below the pK_a, the ratio [A]:[HA] decreases 10-fold

6. Energy and Entropy; Water as a Solvent and the Hydrophobic Effect

- Formation of bonds/interactions decreases the energy (enthalpy, H) of a system
- Entropy (s) opposes formation of interactions
- Some times energy(H) wins & sometimes Entropy (S) wins
- Free energy, Enthalpy and Entropy
    - $A + B \leftrightarrow AB$
    - A decrease in enthalpy (Delta H<0) favours a process
    - A increase in entropy (Delta H> 0) favours a process
    - Most processes involve both Delta H and Delta S