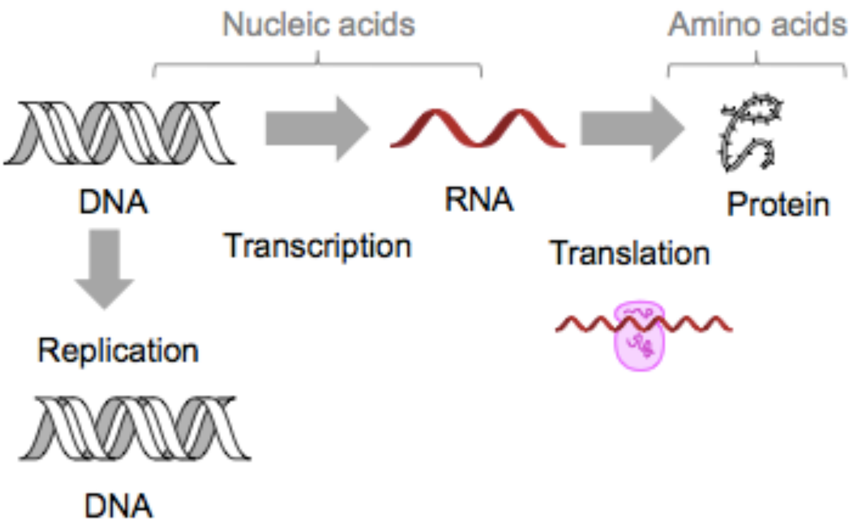
Lecture 1: Introduction to Molecular Biology

1. Present the central dogma of genetic information flow
2. Explain why life is carbon based
3. Identify the main biopolymers
4. Describe the general properties of biopolymers

1. Present the central dogma of genetic information flow

Information Technology and information must be able to be:
- Stored (stable/corruption-free, protected)
- Accessed easily
- Transferred accurately
- Read (de-coded easily& selectively)
- Used

Central Dogma → Carbon based IT (*The FLOW of GENETIC INFORMATION*)
- Genome (DNA)
- Transcriptome (RNA)
- Proteome (Protein)



- DNA in almost every cell in your body contains the SAME information with usually only one copy of each gene.
- Each cell will need a few proteins in large no. & many at low copy no.
- Many sequences are NOT represented at all

2. Explain why life is carbon based

Although it is not the most abundant element on the Earth's crust, life DEPENDS on carbon → *all MAJOR biopolymer have a substantially carbon BACKBONE*

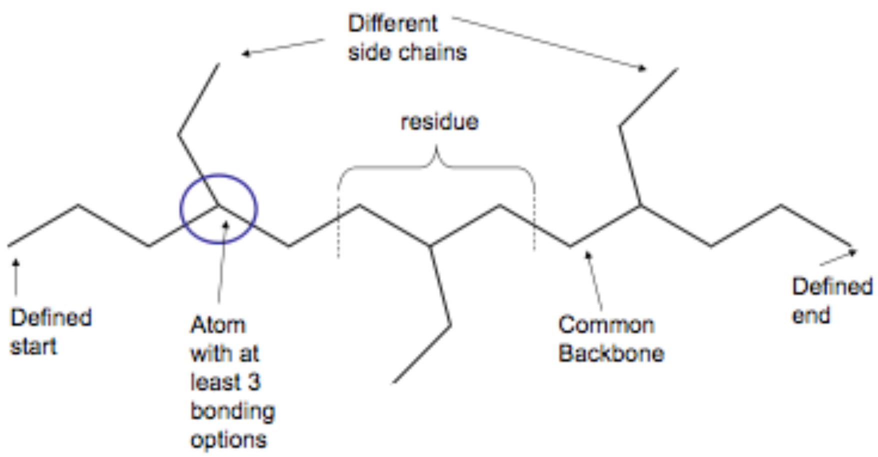
Unique properties of carbon:
- Can directly bond to itself & form long chains ==> **catenation**
- Side chain "hang off" the polymer backbone
- 4 valence e^- ==> able to form 4 bonds

- Form stronger bonds with itself than with oxygen (reason why life isn't silicon based → silicon readily form strong bonds with oxygen, exist naturally as O-Si-O & silicon has a larger atomic radius)
- Carbon compound are relatively inert or kinetically stable to hydrolysis and oxidation
- General organic reactions tend to be under **kinetic control** (rate of reaction) rather than **thermodynamic control** (internal energy available to do work, outcome of equilibrium) → **attractive for enzyme control**

3 & 4. Identify & describe the general properties of the main biopolymers

- Fat
- Carbohydrate
- Nucleic Acid
- Protein

- All linear biopolymer have a defined beginning and end
- Biopolymer synthesis ==> *anabolic process* (require energy input)
- All biopolymer are synthesised in *ONE DIRECTION* only
- Some monomer lost in polymerisation, leaving behind a "residue" incorporated in the growing chain



Lecture 2: Molecules of Life - Biopolymers

1. Explain the differences between covalent, ionic and polar covalent bonding
2. Recall the peptide bond formation reaction
3. Appreciate the thermodynamics of peptide bond formation and its implications to protein synthesis inside the cell.
4. Appreciate the groupings of the 20 amino acids: aliphatic hydrophobic, aromatic hydrophobic, polar non-ionic, acidic and basic.
5. Predict the grouping/properties of an amino acid side- chain given its structure

1. Explain the differences between covalent, ionic and polar covalent bonding

- **Covalent (X:Y):** *equal electron distribution* between the 2 atoms (e.g. H-H, C-C, C-H)
  - Fat (Hydrophobic) ==> general formula $(-CH_2-)_n$
    - Long carbon chain very non-polar (consisting of C-H and C-C bonds)
    - Aliphatic chian, longer it is, more hydrophobic
- **Polar covalent (δ+X:δ-Y):** *partial charges* – asymmetrical electron distribution (e.g. H2O, C=O, C-N, C-S, amide [CO-NH2], alcohol [C-OH])
  - Polysaccharides (Hydrophilic) ==> Hydrated carbon, $(H-C-OH)_n$
    - Components of nucleic acid
    - Very water soluble (OH group responsible)
- **Ionic (X+Y-):** full charge on each atom (e.g. NaCl -> Na+ Cl-, -COOH, $-^{+}NH_3$, $-HPO_4^{2-}$)

2 & 3. Recall the peptide bond formation reaction, the thermodynamics of peptide bond formation and its implications to protein synthesis inside the cell.

Information biopolymers:

- Nucleic acid (NA): DNA & RNA
- Protein

- Consisting of variety of monomers
- **Order is important**
- ***Template** required*
- Processes of copying the template faithfully

NA: (DNA & RNA)

- 4 monomers
  - Sugar moiety
  - Ribose/deoxyribose
  - Phosphate
- Consists of repeating sugar phosphate backbone

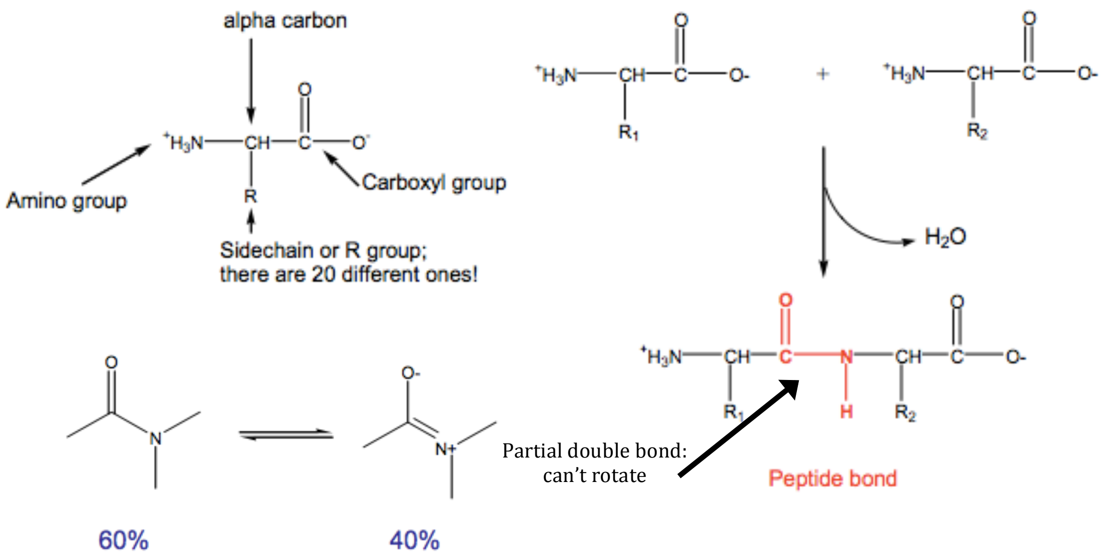
Proteins:

- Made up of 20 AA, differing in their side chain
- Each AA side chain have very different chemical properties
  - Hydrophobic (aliphatic and aromatic)
  - Polar non-ionic
  - Acidic
  - Basic

- **AA sequence determine structure** (give cell its shape) ==> **determine function** (receptors, transporters, ***ENZYMES***, hormones, growth factors, toxins, transporters and antibodies)
- Make up >50% of cell by dry weight

Peptide bond formation ==> **condensation polymerisation** to form a dipeptide

- Strong *COVALENT BOND*
- Extremely thermodynamically unfavourable reaction in aqueous environment → abundance of water around, relative conc. of products and reactants is going to favour reverse reaction (hydrolysis)
- Inside the cell, water is *EXCLUDED* from the *ACTIVE SITE* of the peptide bond formation
- Happens in translation, occurring in ribosomes
- Catalysed by RNA (23S rRNA in prokaryotes)
- AA must be activated by ATP first
- 2 resonance structures
    - Has a polarity (O is δ-ve and N is δ +ve) → can form H-bonds
    - Has a partial double bond (resonating between C=O and C=N) → **restrict rotation** ==> *impacts the 3-D conformations* the protein can exist as



In eukaryotic cells transcription and replication are carried out in the nucleus and translation is carried out in the cytoplasm.
In prokaryotes, which have no organelles to compartmentalize the processes, **transcription is tightly coupled to translation**. One follows the other almost simultaneously. Replication is carried out by DNA polymerases; transcription by RNA polymerases and translation is performed on ribosomes.

4 & 5. Appreciate the groupings of the 20 amino acids: aliphatic hydrophobic, aromatic hydrophobic, polar non-ionic, acidic and basic. Predict the grouping/properties of an amino acid side- chain given its structure

Hydrophobic

- Aliphatic
  - E.g. Glycine, Leucine
  - Branched aliphatic chain with no dipole
  - Doesn't participate in H-bonding/Ionic interactions BUT interact with other hydrophobic side chains
  - Found buried in the interior of water-soluble protein or exposed on the outside of membrane embedded portions of proteins.
- Aromatic
  - E.g. Phenylalanine, Tyrosine (also polar non-ionic), Tryptophan
  - Hydrophobic aromatic side chain that absorb UV light @ 280nm
    - The fact it absorbs UV strongly is used as a quick and inexpensive method to detect proteins experimentally w/o destroying the sample

Polar non-ionic

- E.g. Serine
- Contain –OH, giving the side chain polar properties
- Act as H-bond donor
- Serine is a common mechanism for enzyme regulation

Acidic

- E.g. Glutamate, Aspartate
- Contain carboxylic side chain which dissociates with a pKa of ~4
- At neutral pH, carry –ve charge, enabling ionic interaction with +ve side chains.
- Hydrophilic → found outside of water soluble proteins
- $HA \leftrightarrow H^+ + A^-$

Basic

- E.g. Lysine, Arginine, Histidine
- Characterised with a protonated N
- At physiological pH, carry +ve charge
- Found on DNA binding proteins, interacting with the –ve sugar phosphate backbone
- $BH^+ \leftrightarrow B + H^+$