TRANSLATION

Content Statements:

B1.2.6	Chemical diversity in the R-groups of amino acids as a basis for the diversity in proteins
B1.2.7	Impact of primary structure on the conformation of proteins
B1.2.8	Pleating and coiling of secondary structure of proteins
B1.2.9	Dependence of tertiary structure on hydrogen bonds, ionic bonds, disulphide covalent bonds and hydrophobic interactions
B1.2.10	Effect of polar and non-polar amino acids on tertiary structure of proteins
B1.2.11	Quaternary structure of non-conjugated and conjugated proteins
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D1.2.17	Initiation of translation
D1.2.18	Modification of polypeptides into their functional state
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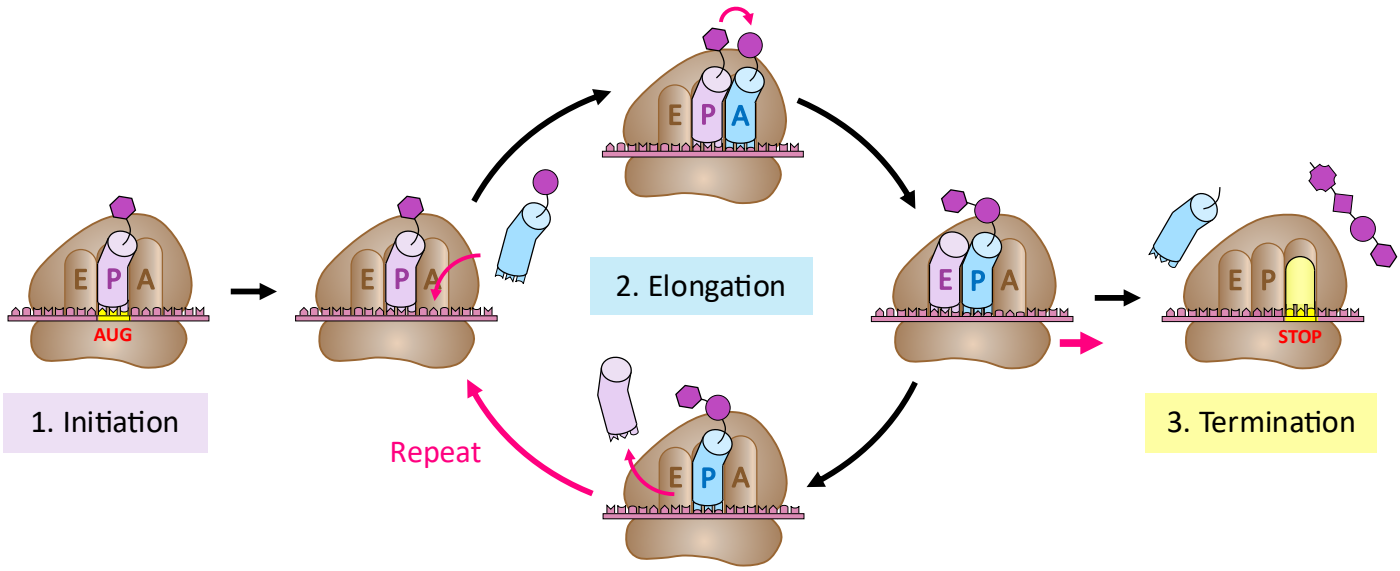
B2.2.7	Structure and function of free ribosomes and of the rough endoplasmic reticulum
B2.2.8	Structure and function of the Golgi apparatus

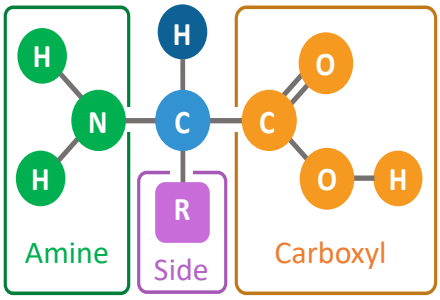
TRANSLATION

Protein synthesis (translation) occurs at the ribosome, which is composed of a large and small subunit. The small subunit binds to mRNA and moves along in a 5' → 3' direction until it reaches a start codon (AUG) to which an **initiator tRNA** has attached. A large ribosomal subunit binds to the initiator tRNA (via the **P site**), completing the ribosomal complex. Another tRNA molecule binds to the ribosomal **A site** and the tRNA in the P site transfers its amino acid to this new molecule. The ribosome moves along one codon position (in a 5' → 3' direction). The deacylated tRNA is now in the **E site** and is released. A new tRNA molecule enters the unoccupied A site and the process of amino acid transfer is repeated. This cycle continues the length of the codon sequence until a stop codon is reached. At this point, a **release factor** binds and causes both the ribosome and the polypeptide chain to dissociate from the mRNA – completing the process of translation.



PROTEIN DIVERSITY

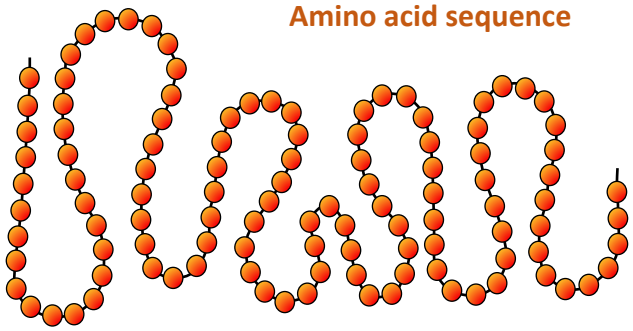
Proteins are comprised of long chains of recurring monomers called **amino acids**. Amino acids all share a common basic structure, with a central carbon atom bound to an amine group, a carboxyl group and a variable side chain. There are 20 different amino acids, each with a distinct side chain (i.e. *R group*). The different chemical properties of these side chains cause a protein to **fold differently** according to the sequence of amino acids (different order = altered protein structure).



PROTEIN STRUCTURE

Amino acids are joined via condensation reactions to form polypeptide chains that are linked together by peptide bonds. These polypeptide chains may be organised into four hierarchical levels of protein structure:

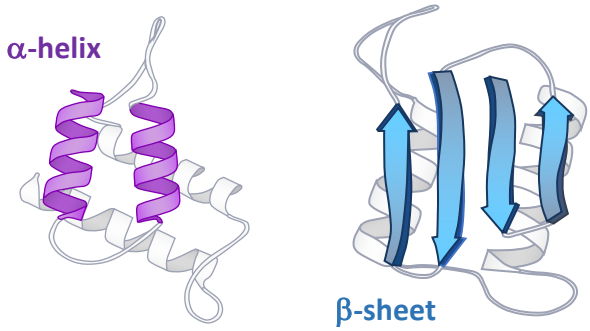
PRIMARY STRUCTURE:



The order of amino acids in a polypeptide chain (determines all subsequent levels of structure)

Formed by covalent bonding between the amine and carboxyl groups of adjacent amino acids

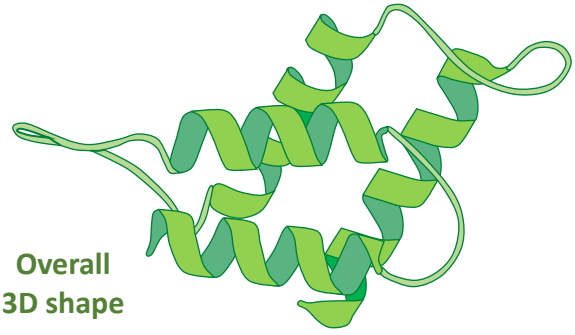
SECONDARY STRUCTURE:



The folding of a polypeptide chain in a repeating arrangement to form α-helix or β-pleated sheet

Formed by hydrogen bonding between the amine and carboxyl groups of non-adjacent amino acids

TERTIARY STRUCTURE:

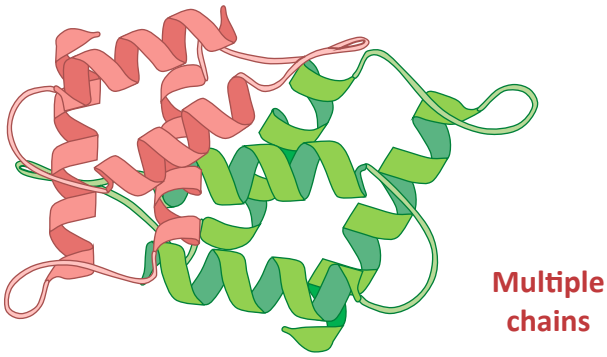


Folding of a polypeptide into a complex 3D shape

Formed by interactions between variable groups (e.g. H bonds, ionic bonds, disulphide bonds, etc.)

Can be described as globular (functional proteins) or described as fibrous (structural proteins)

QUATERNARY STRUCTURE:



Interaction of multiple polypeptides or prosthetic groups to form a single biologically active protein

Quaternary structures may be held together by a variety of bonds (similar to tertiary structure)

Not all proteins will have a quaternary structure

TYPES OF PROTEINS

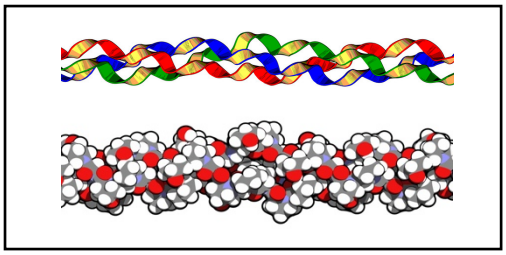
Proteins may be broadly categorised according to their tertiary structure organisation or core functionality. Examples of these protein categories include fibrous proteins, globular proteins and membrane proteins.

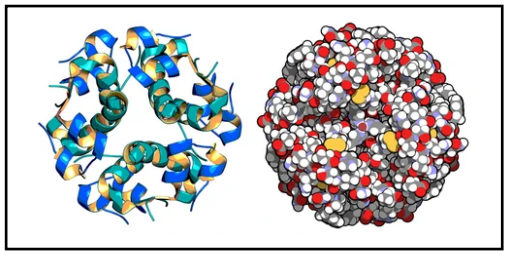
Fibrous Proteins

Fibrous proteins are typically long and narrow in shape due to a repetitive amino acid sequence. They have **structural roles** within organisms and are typically insoluble in water (external amino acids are non-polar). An example of a fibrous protein is collagen (prominent in the extracellular matrix and connective tissues).

Globular Proteins

Globular proteins are typically round and spherical with an irregular amino acid sequence. They will possess **functional roles** within an organism and are generally soluble in water (the external amino acids are polar). An example of a globular protein is insulin (hormone transported in the blood to regulate glucose levels).



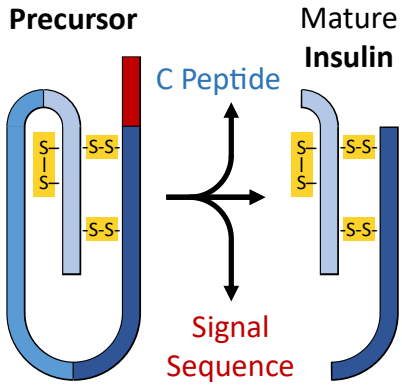


Fibrous (left image)
Have structural roles

Globular (right image)
Perform functions

PROTEIN MODIFICATIONS

Many proteins need to be modified before they can function. Insulin is a protein that requires post-translational modification. It is produced as an inactive precursor called **pre-proinsulin** and will undergo a two-step modification process. Pre-proinsulin is converted to **proinsulin** when a *signal sequence* is removed in the rough ER (this sequence was needed to direct the ribosome to the ER). As proinsulin folds in the Golgi body, the opposite ends of the protein (A and B chains) will become linked by disulphide bridges and the intervening segment (called the C peptide) is removed. Functional **insulin** molecule is stored in the Golgi until needed.



PROTEIN TRANSPORT

All proteins produced by eukaryotic cells are initially synthesised by **ribosomes** found freely floating in the cytosol. If the protein is targeted for intracellular use within the cytosol, the ribosome remains unattached. However, if the protein is destined for secretion (extracellular use), the will ribosome become bound to the endoplasmic reticulum. The **rough ER** packages these proteins into vesicles and transfers them to the Golgi complex. These proteins can either be released by the **Golgi body** immediately (constitutive secretion) or can be indefinitely stored in secretory vesicles for delayed – but sustained – release (regulatory secretion).

PROTEASOMES

Maintaining a functional proteome requires the continual breakdown of superfluous proteins to enable the synthesis of new ones. Proteasomes are protein complexes that degrade polypeptides that are misfolded or no longer needed by the cell. They are used by the cell to help regulate expression levels and recycle amino acids. Proteins are targeted to the proteasome after being tagged with a short polypeptide called **ubiquitin**.