Protein Structure

Proteins are said to have 4 levels of structure

- Primary
- Secondary
- Tertiary
- Quaternary

Primary Sequence

The order of amino acids is the primary sequence. This is determined by the information contained within DNA.

The linear sequence must contain all of the information required to specify all other orders of structure.

Primary Sequence

Many times changes in primary sequence will change protein function.

Generally substitutions of similar amino acids (leucine for isoleucine) are fairly well tolerated.

Changes at the surface often have less effect than changes in the interior.

Code

Can code for 20 amino acids.

No code for hydroxyproline, methyl lysine, hydroxylysine, etc.

These occur in some proteins.

Also no code for some modifications such as phosphorylation of selected serine molecules.

Modifications

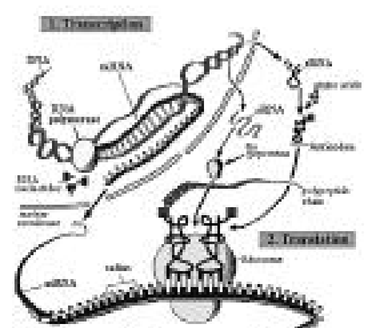
These modifications are very specific and do not occur in all proteins.

Information for where to make modifications must exist within the genetic code, but can use no new codons.

Sequence of amino acids can determine modifications.

Changes occur in Golgi

Protein Synthesis



Protein synthesis

Primary

The number of possible proteins is extremely large.

A protein with 70 amino acids (very small) could have 20^{70} possible sequences.

This is 1.18×10^{91}

Few of these could ever have existed.

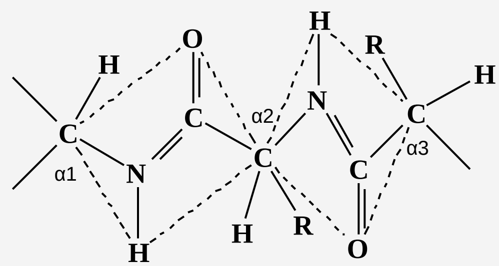
Energy

When two amino acids are joined together, they form a planer structure.

The bonds between planes are able to rotate.

The amino acids attempt to assume a structure that minimizes their free energy.

Peptide Bond



Angles

Not all angles between adjacent planes are energetically allowed.

Angles that force bulky side chains into close contact or groups with like charges are not allowed.

Low energy areas lead to regular, repeating structures.

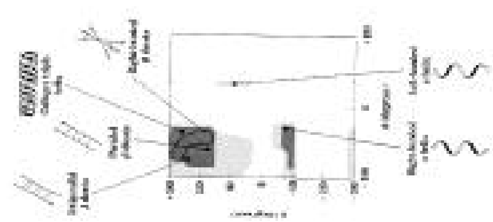
Bond Angles

Ramachandron used space filling models and computer programs to calculate the energies of various combinations of planar angles.

The resulting Ramachandron plots show areas of high and low bond energy.

Low energy areas are where typical protein secondary structures are observed.

Plot



Secondary Structure

Secondary structure can be defined as regular repeating three dimensional regions resulting from the primary structure of protein molecules. Types include:

- α−helix
- β-sheet
- Triple helix
- β-turns

α-helix

Pauling and Corey (1951) Given:

1. Bond lengths and angles in proteins will be the same as in small compounds
2. N-H and C=O hydrogen bonding should be maximized and should have a length of 2.79 Å

This can be accomplished by a helical structure. In this case, called the α-helix

Properties

Each peptide bond can be considered a plane that is tangent to a cylinder around the axis of the helix.

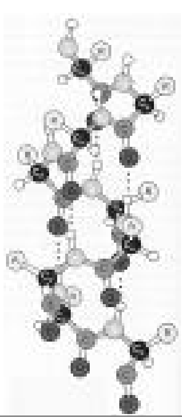
From one amino acid to the next, there is a rotation of 100° and a translation of 1.5Å.

Each peptide group is hydrogen bonded to the third peptide group along the chain in either direction.

Properties

There are 3.6 amino acids per turn of the helix, that is, 18 amino acid residues per 5 turns of the helix.

The helix is a very tight structure with no room for water in the center.



Alpha Helix

Some proteins contain very large amounts of α-helix (90%).

Others contain very little (5%).

The helices can not be bent so that folds in proteins must occur in areas between helices.

β-pleated Sheets

Built from extended peptide chains with hydrogen bonding between neighboring chains.

Best hydrogen bonds are formed when the chain is not fully extended, hence the term pleated.

Structures give strength, but not extensibility.

Proteins contain from very little to greater than 60% (silk) β-sheets.

Beta Structure

The antiparallel sheet has neighboring hydrogen bonded polypeptide chains running in opposite directions.

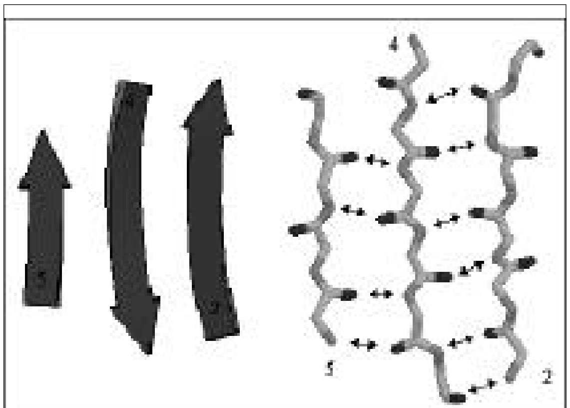
Parallel sheets have the hydrogen bonded chains running in the same direction.

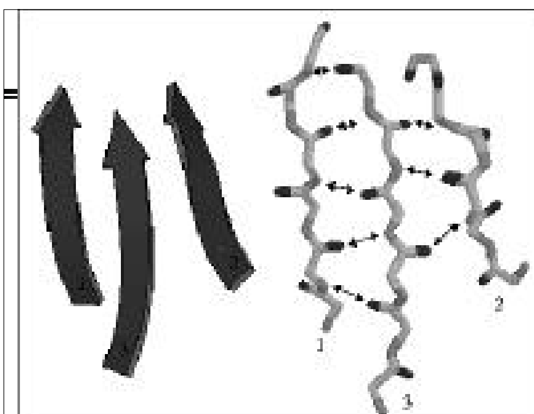
Parallel

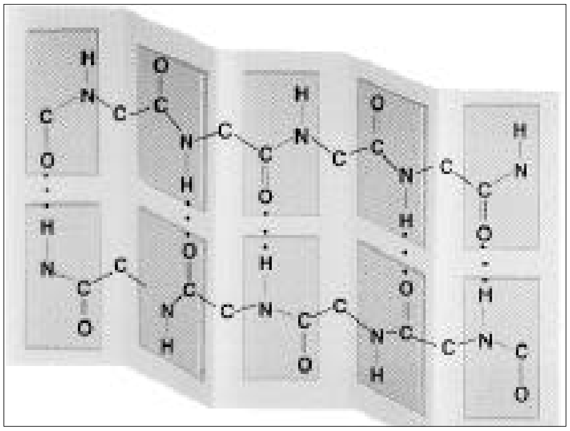
Hydrogen bonds in parallel sheets are distorted.

Less stable than antiparallel sheets

Rarely found with less than five polypeptide chains

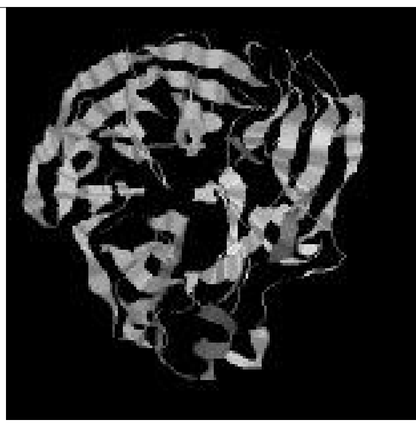






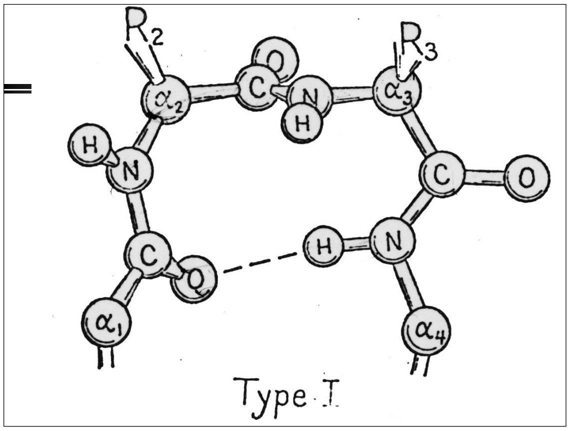
β-barrels

- Structures made up of several β-sheets
- Usually from 5 to 15 strands
- May form pockets
- Structure may be hydrophilic, hydrophobic or mixed



Turns

- Proteins need a mechanism for structures to change direction.
- Must be reproducible
- β-turns provide a way for proteins to fold back on themselves
- May be stabilized by hydrogen bonds or by bond energies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