Chou and Fasman formulated rules to predict the secondary structure of proteins from the sequence using the observed propensities of the a.a..

Let's consider what is referred to as the tertiary (3°) structure of proteins. The 3° structure of proteins refers to the three dimensional folding (twists and turns) of a polypeptide chain.

The handout figure shows the folding of the polypeptide chain in myoglobin. As noted earlier segments of the chain form α helices.

The twists and turns of the chain between α helical segments and the bonding between α helical segments are due to a large number of interactions of a.a. side chains.

One of these interactions is hydrophobic.

The globular shape of many proteins has often been compared to a micelle that is an aggregate of molecules that have a hydrocarbon chain terminated by a charged or polar group as represented below

Like micelles, globular proteins have a structure in which most polar a.a. are on the surface interacting with H_2O and most nonpolar a.a. are on the inside segregated from water.

Polypeptide chains tend to fold so that the interaction of nonpolar groups with H_2O are minimized as represented below

H-bonding between the side chains of a.a. residues also contributes to the folding of a polypeptide as represented below

Salt bonds also contribute to the 3° structure of proteins as represented below

Metal-ligand interactions are also important to the 3° structure of metalloproteins as represented below

An example of this type of interaction is Zn^{2+} binding in carboxypeptidase A.

The polypeptide chain has 307 a.a. folded in a roughly spherical shape. The Zn^{2+} is tetrahedrally coordinated to the side chains of his 69, glu 72, his 196 and a H_2O molecule suggesting that the metal ion contributes to the folding of the chain.

Fig 4-5 is a schematic representation which attempts to show how a variety of these noncovalent interactions of a.a. side chains contribute to the 3° structure of a protein.

Lastly, consider the quaternary (4°) structure of proteins.

The (4°) structure of proteins refers to the interaction between polypeptide chains in a protein for which each chain has its own 2° and 3° structure.

Hydrophobic, H-bonding, salt, metal-ligand and disulfide interactions may contribute to the bonding between chains.

Fig 6-1 shows a representation of the (4°) structure of hemoglobin, the protein in red blood cells responsible for O_2 transport.

In hemoglobin there are a few H-bonds and salt interactions between chains, but most of the interactions between chains are hydrophobic.