metal ions or disulfide bridges. Domains often form functional units, such as the calcium-binding EF hand (helix-loop-helix) domain of calmodulin.

Because they are independently stable, domains can be swapped by genetic engineering between one protein and another to make chimeric proteins. It is independent because domains may often be cloned, expressed, and purified independently of the rest of the protein, and they may even show activity if there is any known activity associated with them. Some proteins contain only a single domain, while others may contain several domains. A protein domain is assigned a certain type of fold. Domains with the same fold may or may not be related to each other functionally because nature has used and reused the same fold many times in different contexts. The currently available protein 3D structures in the Protein Data Bank (PDB; http://www.wwpdb.org/) are a repository for the 3D structural data of large biological molecules, such as proteins and nucleic acids.

The domains can be divided into four main classes based on the secondary structural content of the domain:

- All-α domains have a domain core exclusively built from α-helices. This class is dominated by small folds, many of which form a simple bundle of helices running up and down.
- All-β domains have a core composed of antiparallel β-sheets, usually two sheets packed against each other. Various patterns can be identified in the arrangement of the strands, often giving rise to the identification of recurring motifs, for example, the Greek key motif.
- The α+β domains are a mixture of all-α and all-β motifs. The classification of proteins into this class is difficult because of overlaps between the other three classes and, therefore, is not used in the CATH (class, architecture, topology, homologous superfamily) domain database.
- The α/β domains are made from a combination of β–α–β motifs that are predominantly from a parallel β-sheet surrounded by amphipathic α-helices.

Domains have limits on the size and vary from 36 residues in E-selectin to 692 residues in lipoxygenase-1, but the majority, 90%, have less than 200 residues with an average of approximately 100 residues. Very short domains, less than 40 residues, are often stabilized by metal ions or disulfide bonds. Larger domains, greater than 300 residues, likely consist of multiple hydrophobic cores.

1.4 Association and aggregation

The HOS is stabilized through a large number of weak and strong bonds including weak noncovalent bonds formed ionic, dipoles (hydrogen bonds), nonpolar (hydrophobic), and van der Waals interactions. These