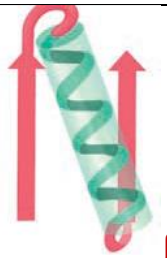
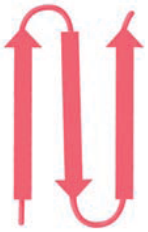
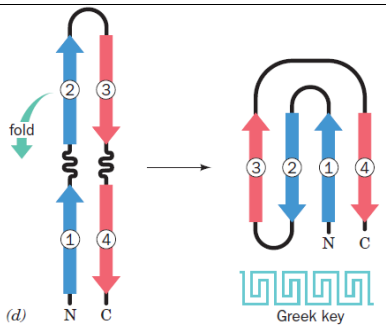
Protein Motifs and Folds

A motif or fold is a recognizable folding pattern involving two or more elements of secondary structure and the connection(s) between them.

A domain, as defined by Jane Richardson in 1981, is a part of a polypeptide chain that is independently stable or could undergo movements as a single entity with respect to the entire protein.

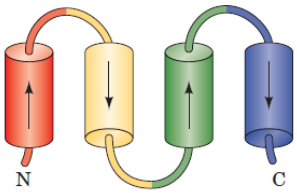
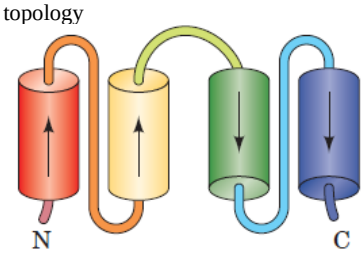
Motifs

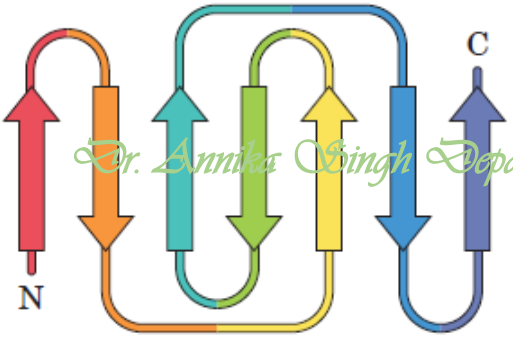
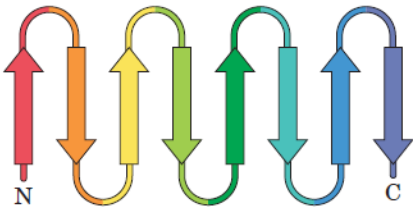
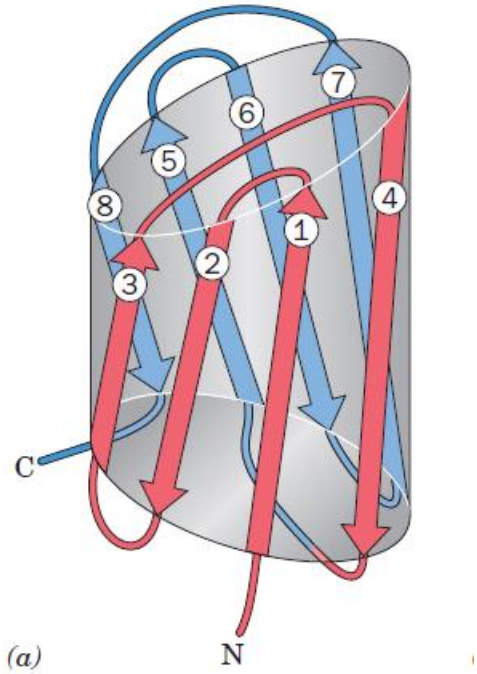
Certain groupings of secondary structural elements, named **supersecondary structures** or **motifs**

1. The most common form of supersecondary structure is the βαβ **motif** , in which the usually righthanded crossover connection between two consecutive parallel strands of a β sheet consists of an _α helix.	 βαβ **motif**
2. Another common supersecondary structure, the β **hairpin motif**, consists of an antiparallel β sheet formed by sequential segments of polypeptide chain that are connected by relatively tight reverse turns.	 β **hairpin motif**
3. In an α α, two successive antiparallel helices pack against each other with their axes inclined so as to permit their contacting side chains to interdigitate efficiently. Such energetically favorable associations stabilize the coiled coil conformation of α keratin	 α α motif
4. In the **Greek key motif** , a β _ hairpin is folded over to form a four-stranded antiparallel β sheet. Of the 10 possible ways of connecting the strands of a four-stranded antiparallel β sheet, the two that form Greek key motifs are, by far, the most common in proteins of known structure.	

PROTEIN FOLD

Groups of motifs combine in overlapping and nonoverlapping ways to form the tertiary structure of a domain, which is called a **fold.**
There are less than 8000 naturally occurring folds.
Domain structures might be classify as
α Domains (containing secondary structural elements that are exclusively α helices)
β Domains (containing only β sheets)
α/β Domains (containing both α helices and β sheets).
The α/βdomain category may be further divided into two main groups:
α /β barrels and open β sheets.

α domains a. Cytochrome b_{562} (106 residues) has up-down-up down topology  b. human growth hormone (191 residues) has up-up-down-down topology  	**X-ray structures of 4-helix bundle proteins.** (*a*) *E. coli* cytochrome *b*562 and (*b*) human growth hormone. Cytochrome *b*562 (106 residues) has up-down-updown topology, whereas human growth hormone (191 residues) has up-up-down-down topology. Note that the N- and C-terminal αhelices of human growth hormone are longer than its other two helices, so that, at one end,these longer helices associate as an α α motif.
β domains **β sandwich**	The X-ray structure of the N-terminal domain of the human immunoglobulin fragment **Fab New** shows its immunoglobulin fold, consists of a 4-stranded antiparallel sheet in face-to-face contact with a 3-stranded antiparallel sheet. The inset is the topological diagram of the immunoglobulin fold showing

	the connectivity of its stacked 4-stranded and 3-stranded antiparallel β sheets
β barrel 	**Retinol binding protein** X-ray structure shows its up-and down β barrel (residues 1_142of this 182-residue protein). which consists of 8 successive antiparallel strands that are arranged like the staves of a barrel.
	**X-ray structure of the C-terminal domain of bovine γ-B crystallin.** (*a*) A topological diagram showing how its two Greek key motifs are arranged in a β barrel. One Greek key motif (*red*) is formed by strands 1 to 4 and the other (*blue*) is formed by strands 5 to 8. The N-terminal domain of this two-domain protein is nearly superimposable on its C-terminal domain.

X-ray structure of chicken triose phosphate isomerase (TIM)

In α /β domains, a central parallel or mixed β sheet is flanked by α helices. The α /β barrel, is a remarkably regular structure that consists of 8 tandem _ units (essentially 8 overlapping β α β motifs) wound in a right-handed helical sense to form an inner 8-stranded parallel β barrel concentric with an outer barrel of 8 α helices. Each β strand is approximately antiparallel to the succeeding α helix and all are inclined at around the same angle to the barrel axis.

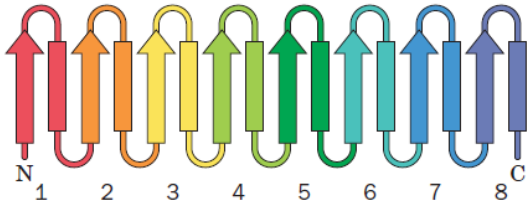


Fig: chicken **triose phosphate isomerase**

X-ray structures of open β sheet–containing enzymes.

Such folds consist of a central parallel or mixed β sheet flanked on both sides by α helices that form the right-handed crossover connections between successive parallel β strands

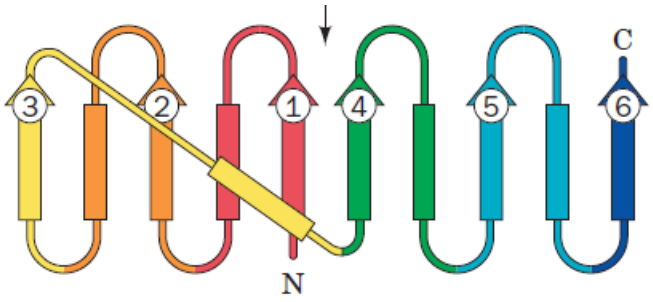


Fig: lactate dehydrogenase

PROTEIN STABILITY

Protein stability is determined by the characteristics of the protein itself as well as the surrounding solvent.

Native proteins are only marginally stable entities under physiological conditions. The free energy required to denature them is 0.4 kj/mol of amino acid residues, so that 100-residue proteins are typically stable by Only around 40 kj / mol. In contrast, the energy required to break a typical hydrogen bond is 20 kj /mol.

The various noncovalent influences to which proteins are subject— electrostatic interactions (both attractive and repulsive), hydrogen bonding (both intramolecular and to water), and hydrophobic forces—each have energetic magnitudes that may total thousands of kilojoules per mole over an entire protein molecule.

The interactions that hold proteins in their shape, like hydrogen bonds, can be affected by many factors. These include solvent, pH, salinity, temperature, and the presence of other molecules.