

# Super secondary structure (Motif)

Secondary structures often group together to form a specific geometric arrangements known as motifs

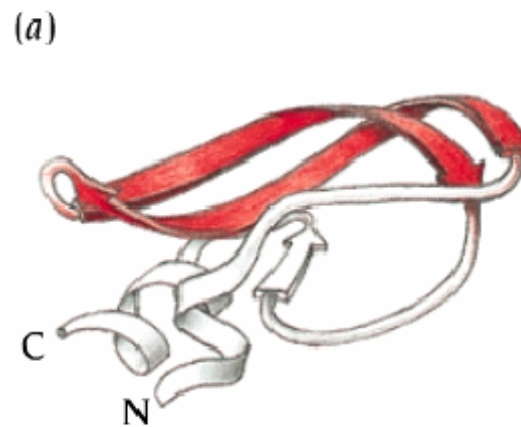
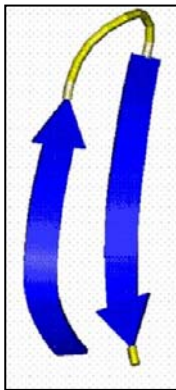
Since motifs contain more than one secondary structural element, these are referred to as super secondary structures

Simple motifs can combine to form more complex motifs

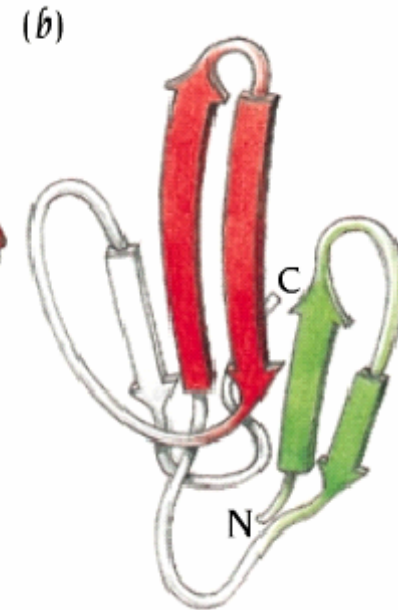
Recognizing motifs helps decompose complex protein structures into simpler units that can be readily understood

1. Beta-hairpin: two antiparallel beta strands connected by a “hairpin” bend, i.e. beta-turn

**2 x antiparallel beta-strands + beta-turn = beta hairpin**

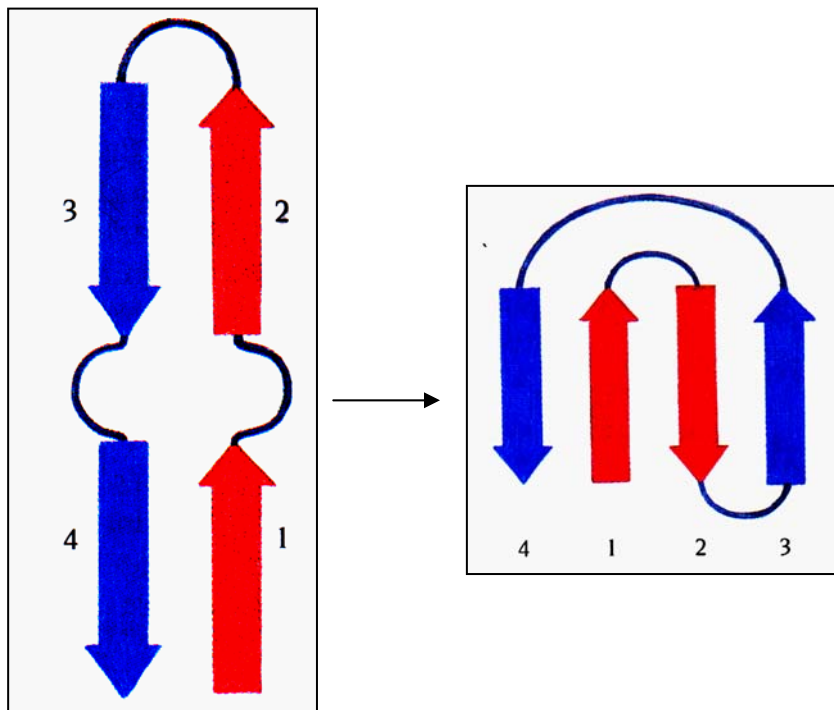


Bovine trypsin inhibitor

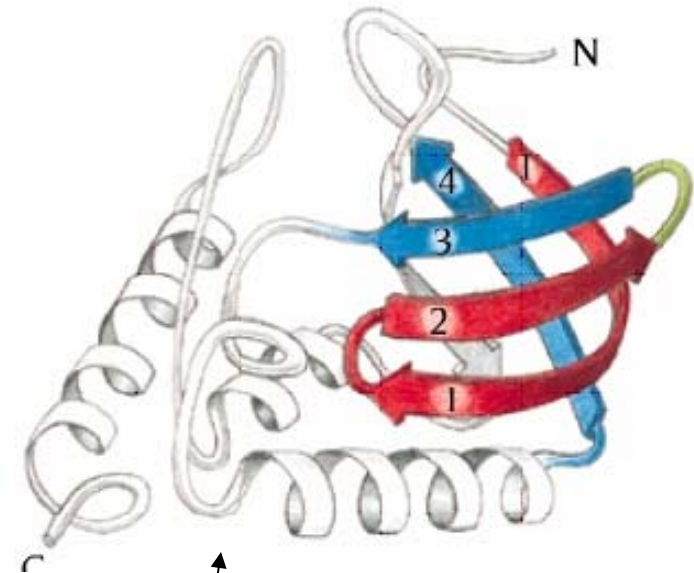


Snake venom erabutoxin

2. Greek keys : four adjacent antiparallel beta strands folded upon itself



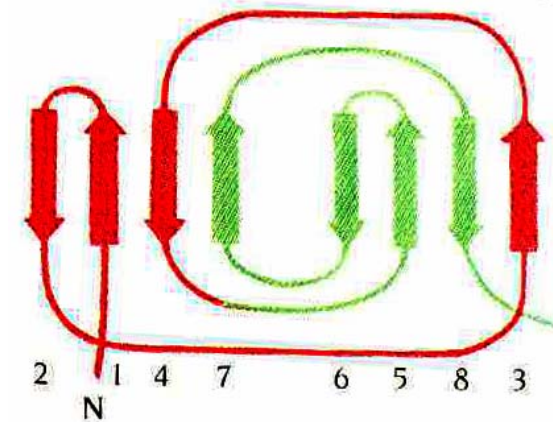
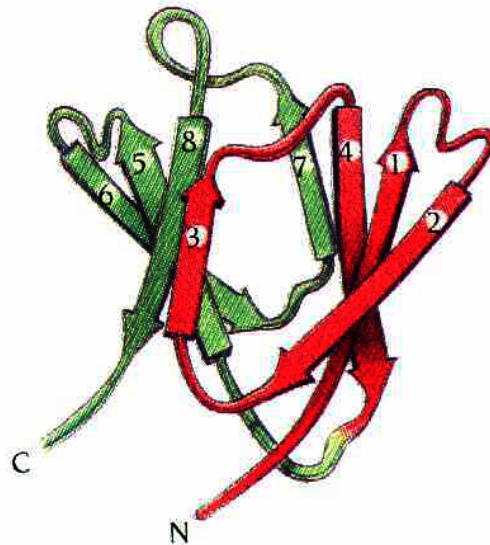
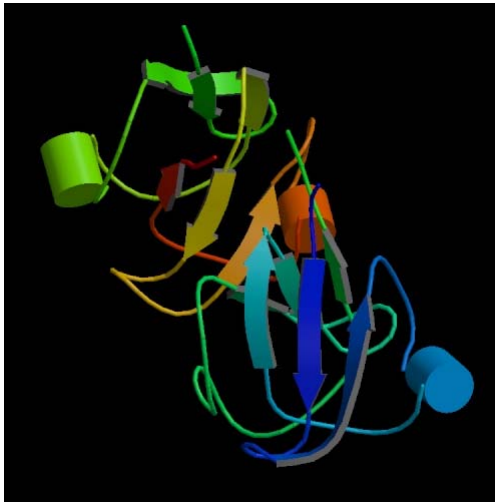
*Staphylococcus* nuclease



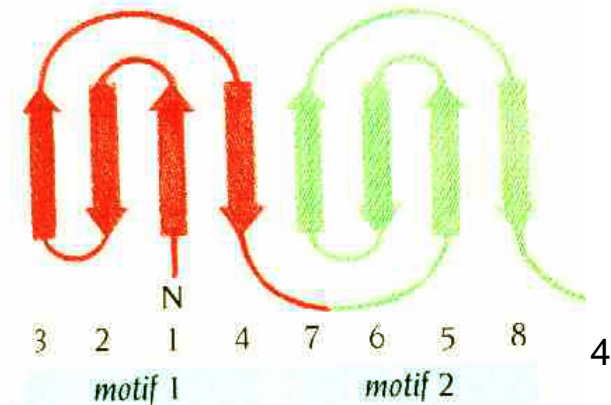
Long insertion between strands 3 and 4

# Gamma crystallin

- Monomeric protein of ~170 amino acids found in the eye lens
- Changing protein concentration gradient across the lens results in a smooth gradient of the refractive index for visible light that is crucial for vision

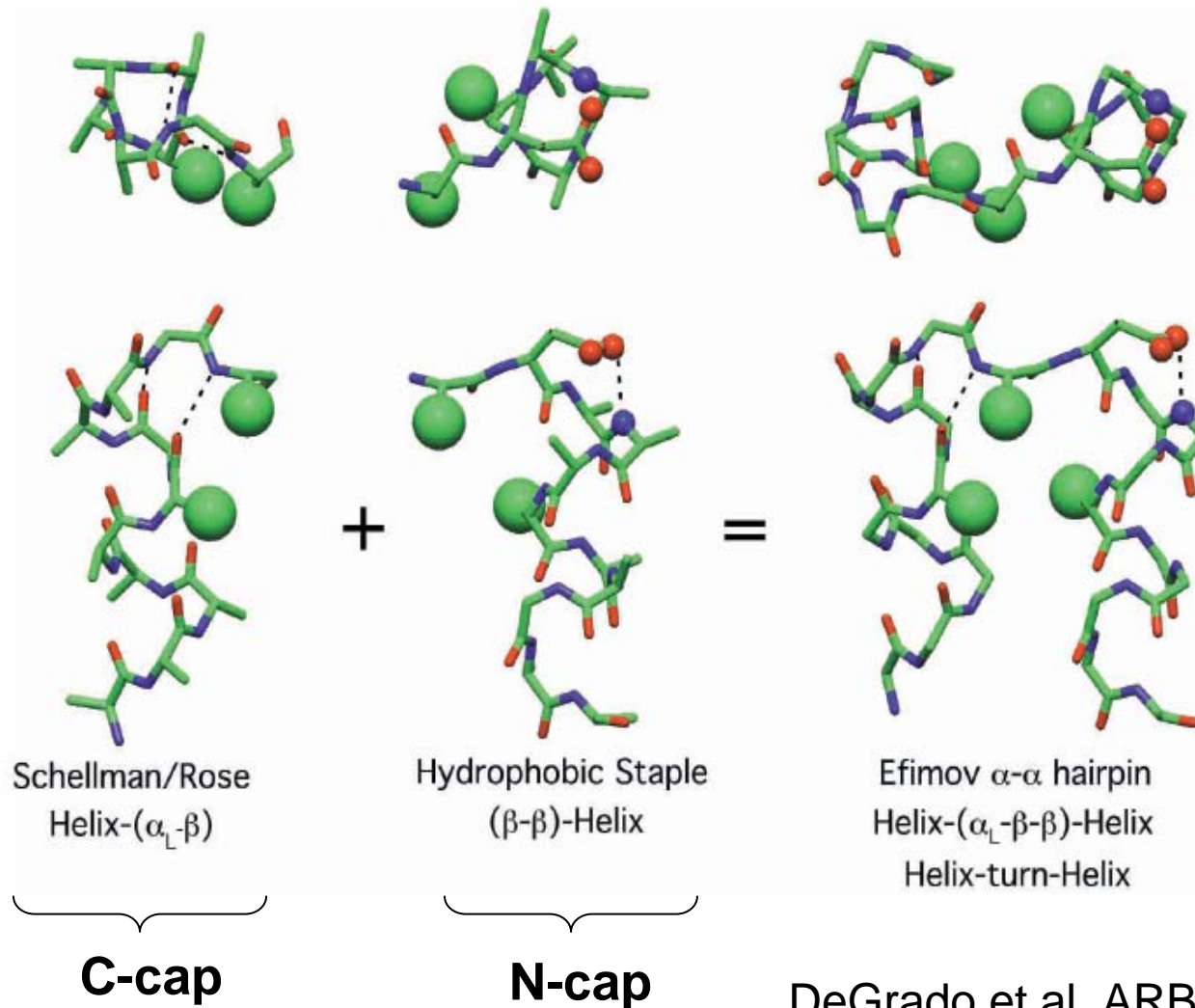


Domain 1



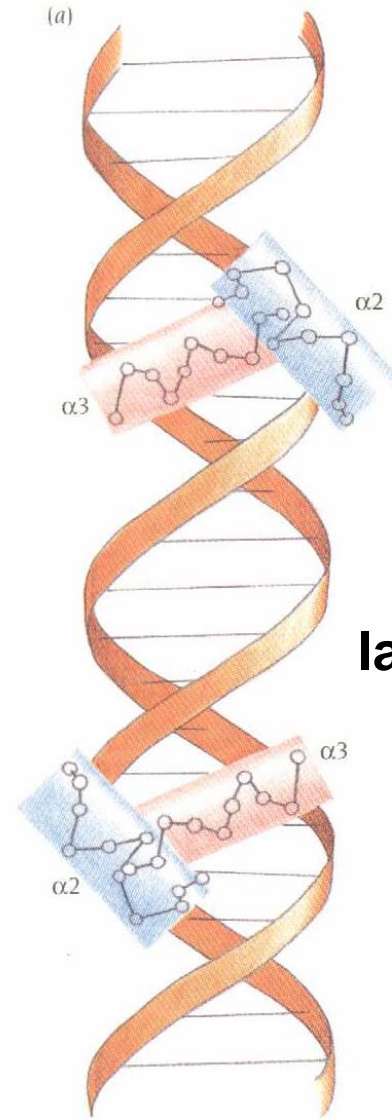
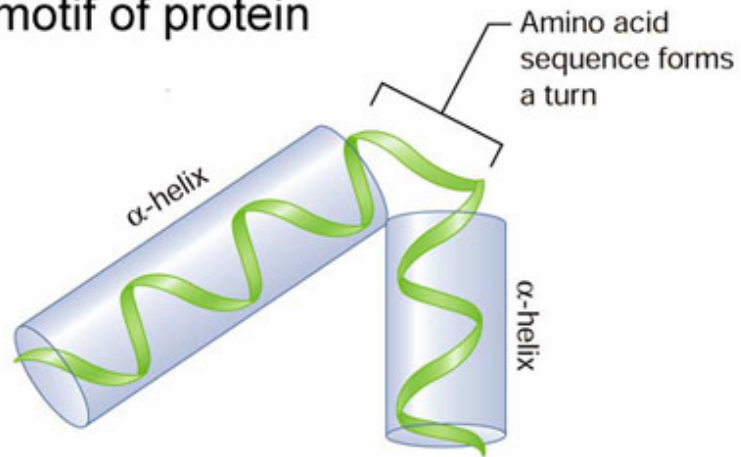
### 3. Alpha alpha hairpin: two helices connected by a short loop

- The interhelical loops are often composed of combinations of common helix N-cap and C-cap motifs



#### 4. Helix turn helix is a motif used in DNA recognition

Helix-turn-helix motif of protein

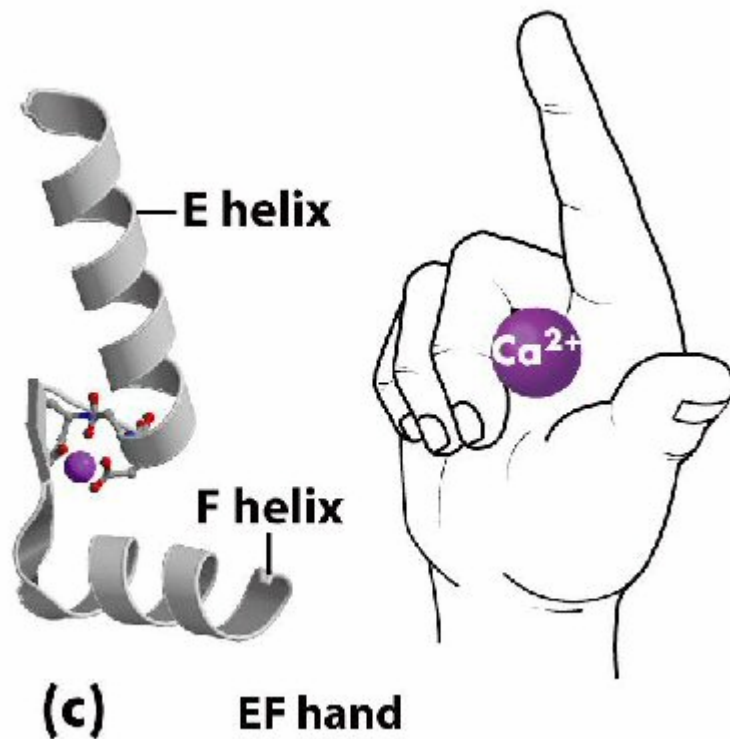


**lambda Cro**

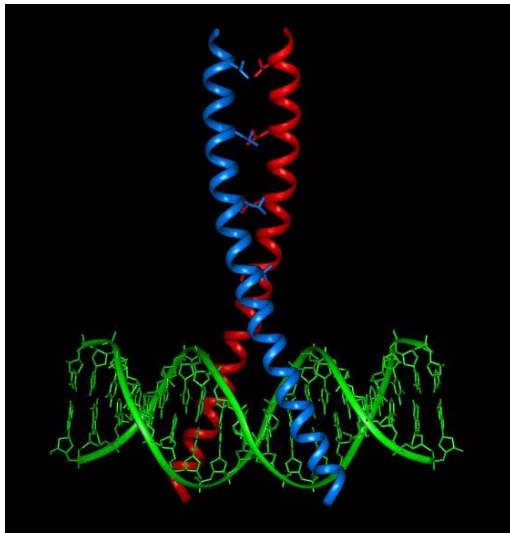
5. EF hand is two helices connected by a loop that contains residues to coordinate calcium ion ( $\text{Ca}^{2+}$ )

Name refers to the helices E and F in parvalbumin

Loop contains 12 amino acids, 5 bind  $\text{Ca}^{++}$

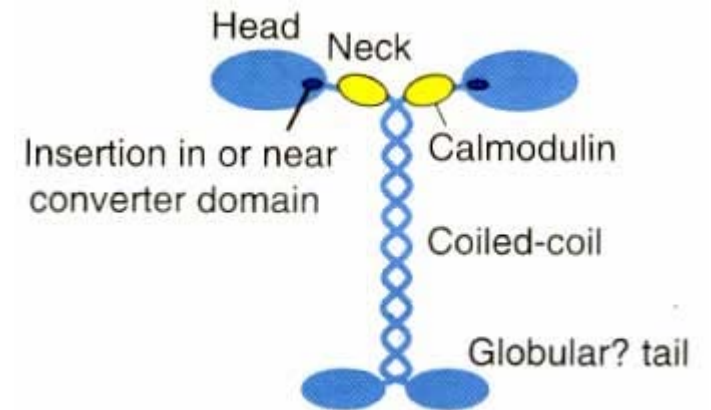
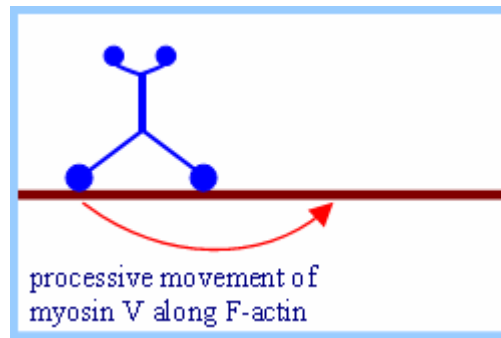


6. Coiled coils are two helices wound around either other in a super coil
- Found in fibrinogen (essential in blood coagulation), DNA binding protein (GCN4, AP1), structural proteins (spectrin), muscle protein myosin



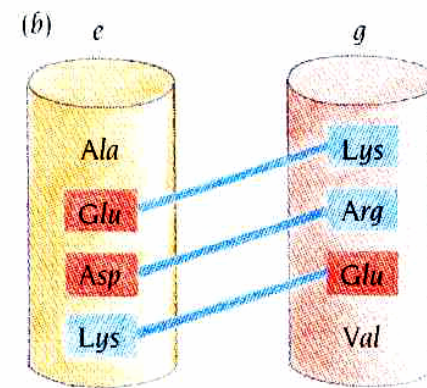
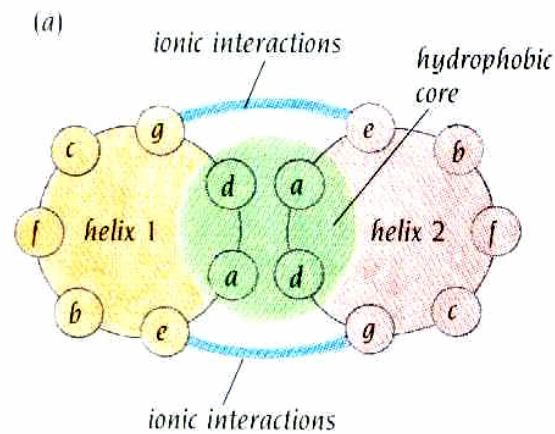
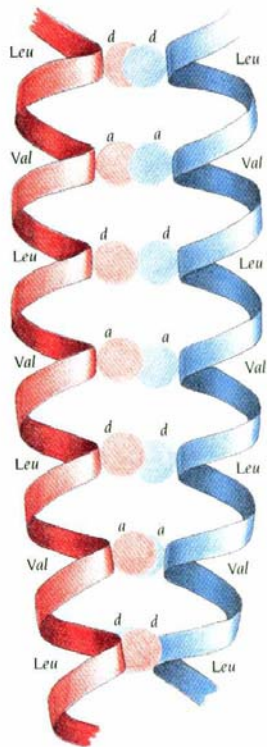
basic leucine zipper is a common motif among DNA binding proteins

### Myosin walks down an actin filament





- Stability is achieved by efficiently burying the hydrophobic residues
- Hydrophobic residues are arranged on one side of the helix



- Coiled coils have repetitive sequences with a period of seven residues (the **heptad** repeat)

**a**bc**d**efg

- The residues at positions “a” and “d” are hydrophobic

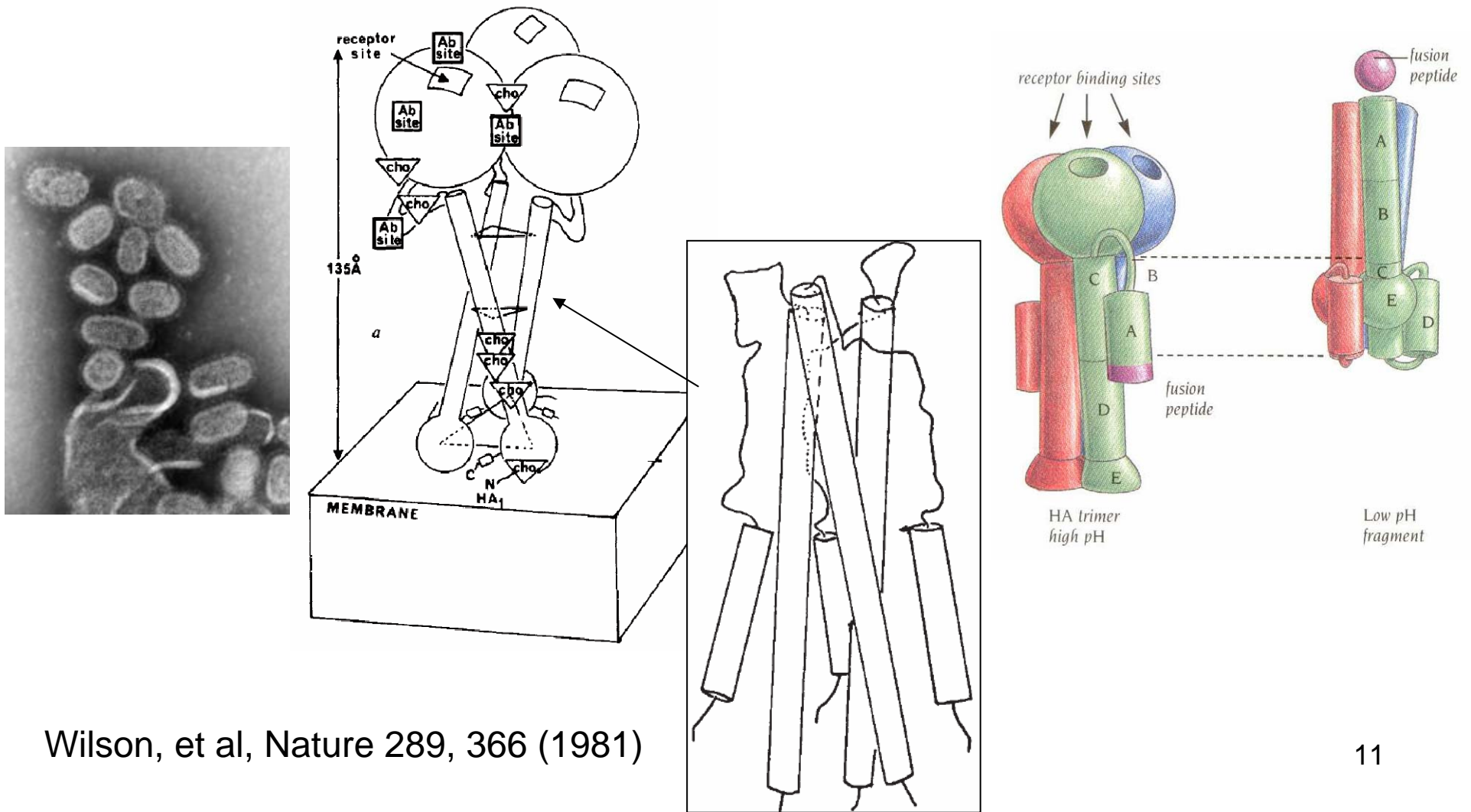
Coiled coil structures can be predicted from the amino acid sequences



Xklp3A/B, a newly cloned kinesin-II from *Xenopus laevis* – De Marco et al EMBO 20, 3370 (2001)

# Influenza attack

Influenza virus uses a protein with long 3 helix bundle to fuse into cells



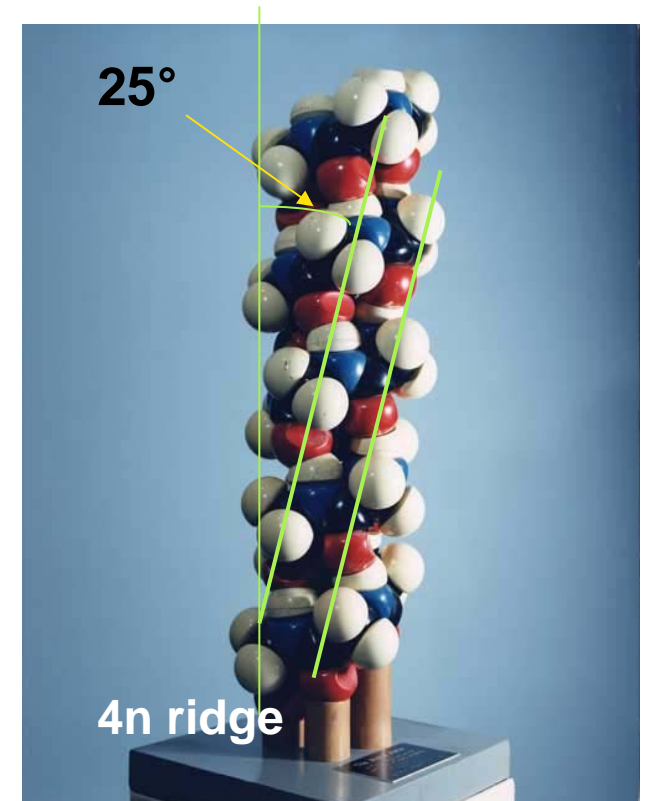
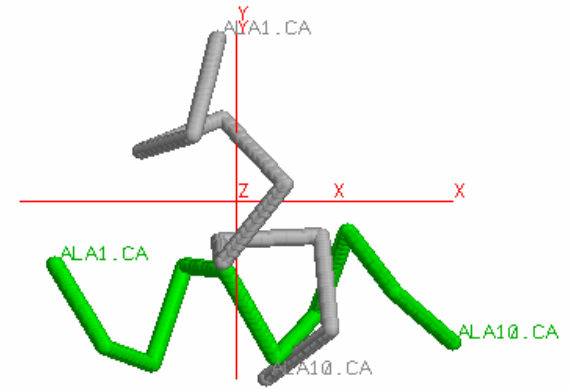
Wilson, et al, Nature 289, 366 (1981)

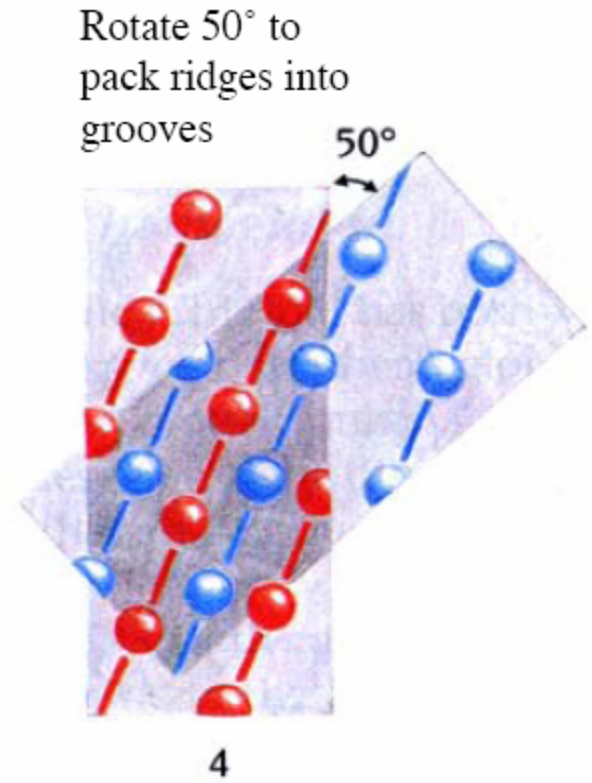
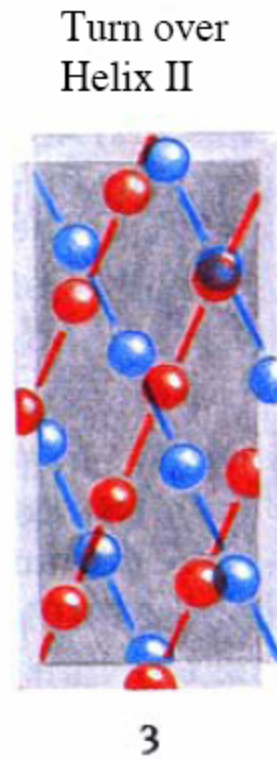
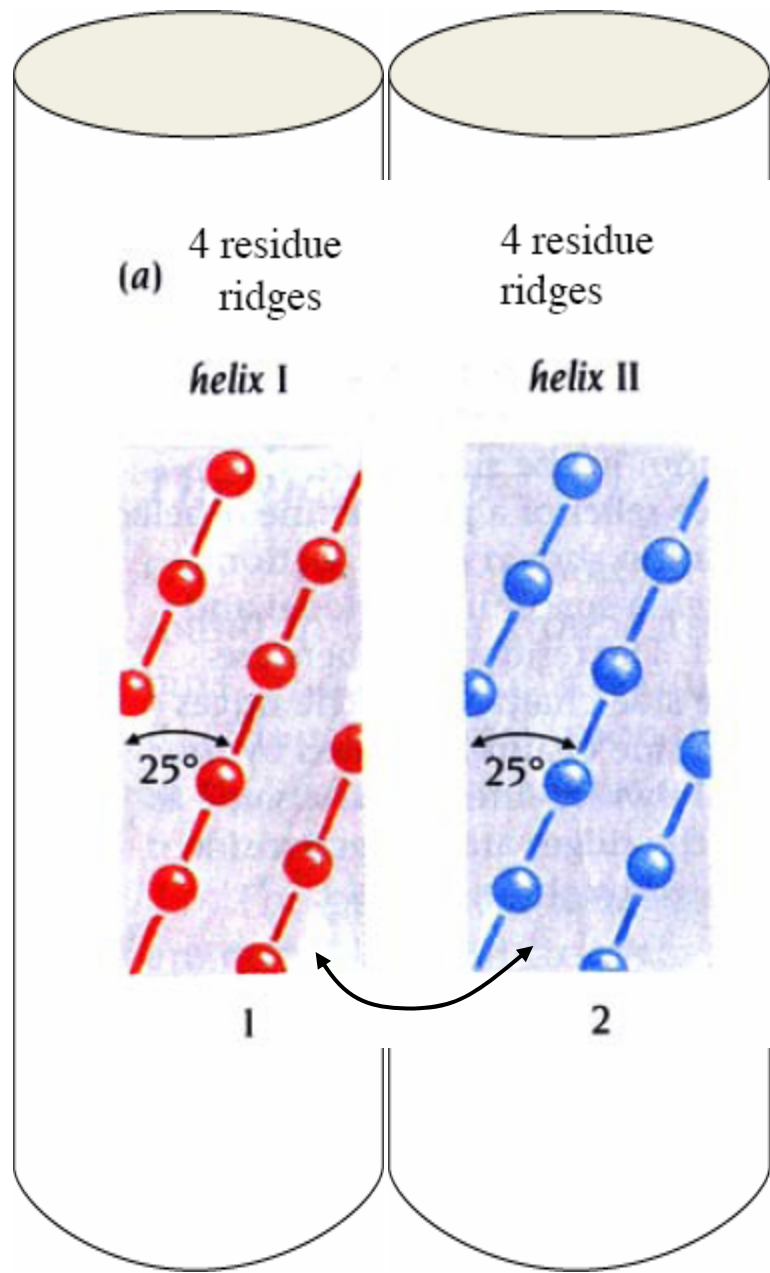
# Packing of helix

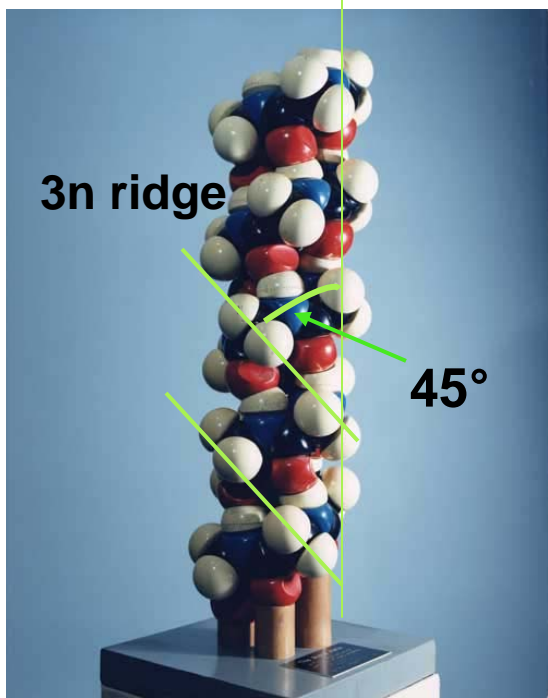
- Two a helices can pack against each other
- The interaxial distance between packed helices is 6.8 – 12.0 Å with an average = 9.4 Å. The two helices interdigitate by an average penetration depth of 2.3 Å
- Mostly the side chains make contact

## “Knobs into Holes”

- Side chains of every 4th residue form a ridge ( $\pm 4n$  ridge) that is  $\sim 25^\circ$  off the axis of the helix.
- Similarly, every 3<sup>rd</sup> residue forms a ridge ( $\pm 3n$  ridge) that is  $\sim 45^\circ$  off the axis of the helix
- Between two adjacent ridges lies a groove
- Helix packing occurs when the ridge of one helix fits within the groove of another helix

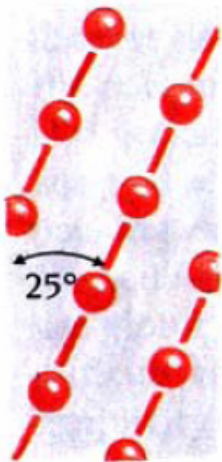






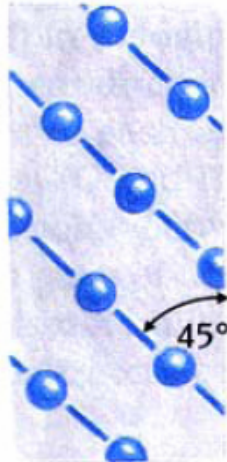
**Question**  
**How about 3n ridge on 3n ridge?**

(b) 4 residue ridges



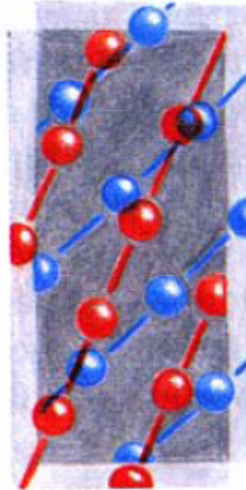
1

3 residue ridges



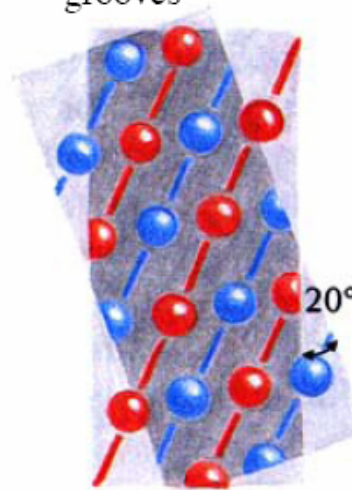
2

Turn over Helix II

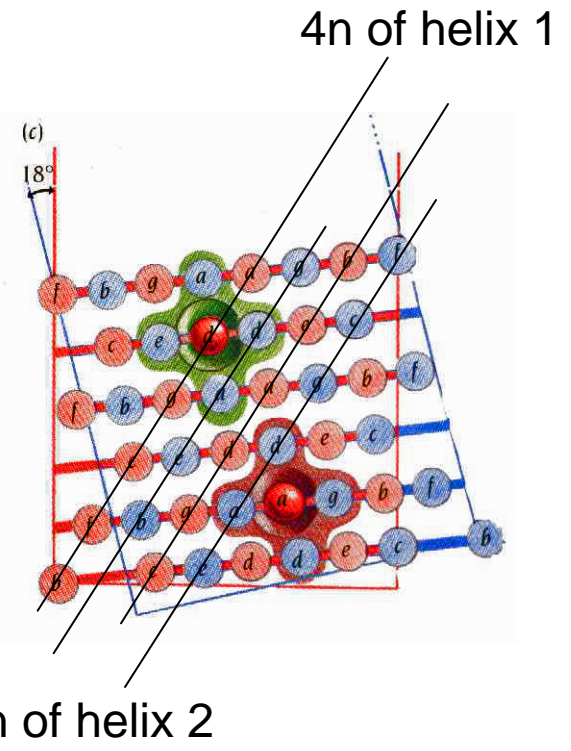
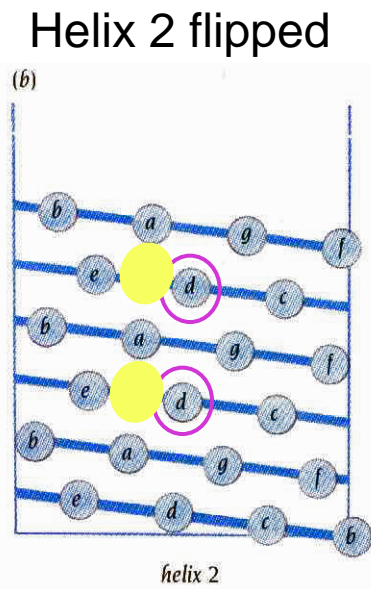
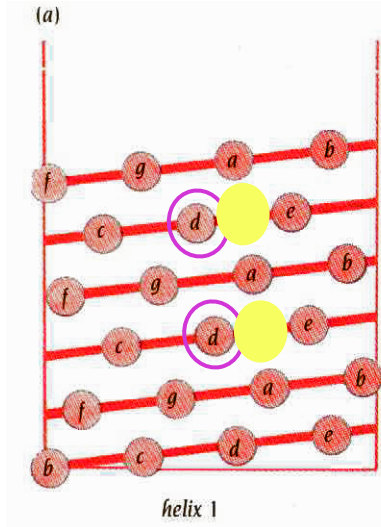
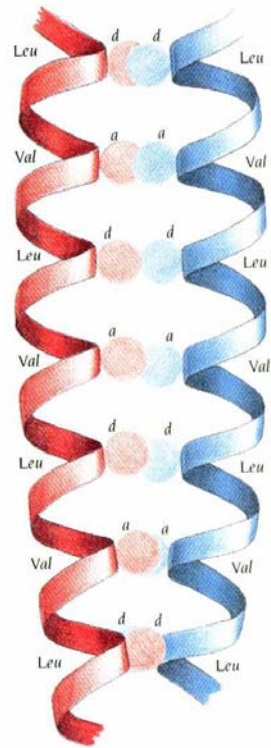


3

Rotate 20° to pack ridges into grooves



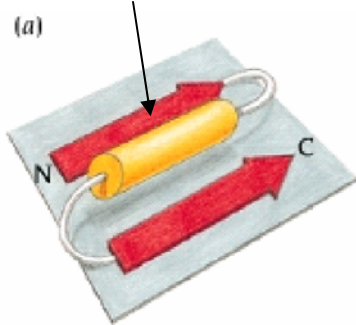
4



## 7. Beta-alpha-beta ( $\beta\alpha\beta$ ) motif allows two **parallel** beta strands

- There is a long crossover between the end of the first strand and the beginning of the second strand
- The crossover connections are frequently made by a helix

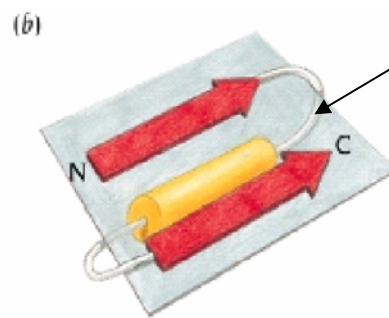
Helix above the plane



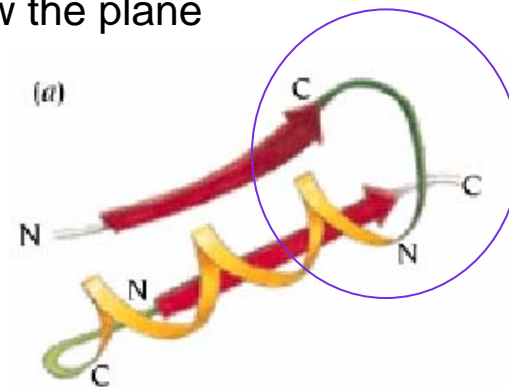
**Right-handed**  
**> 95%**

The rationale for this handedness is not clear

Helix below the plane



**Left-handed**

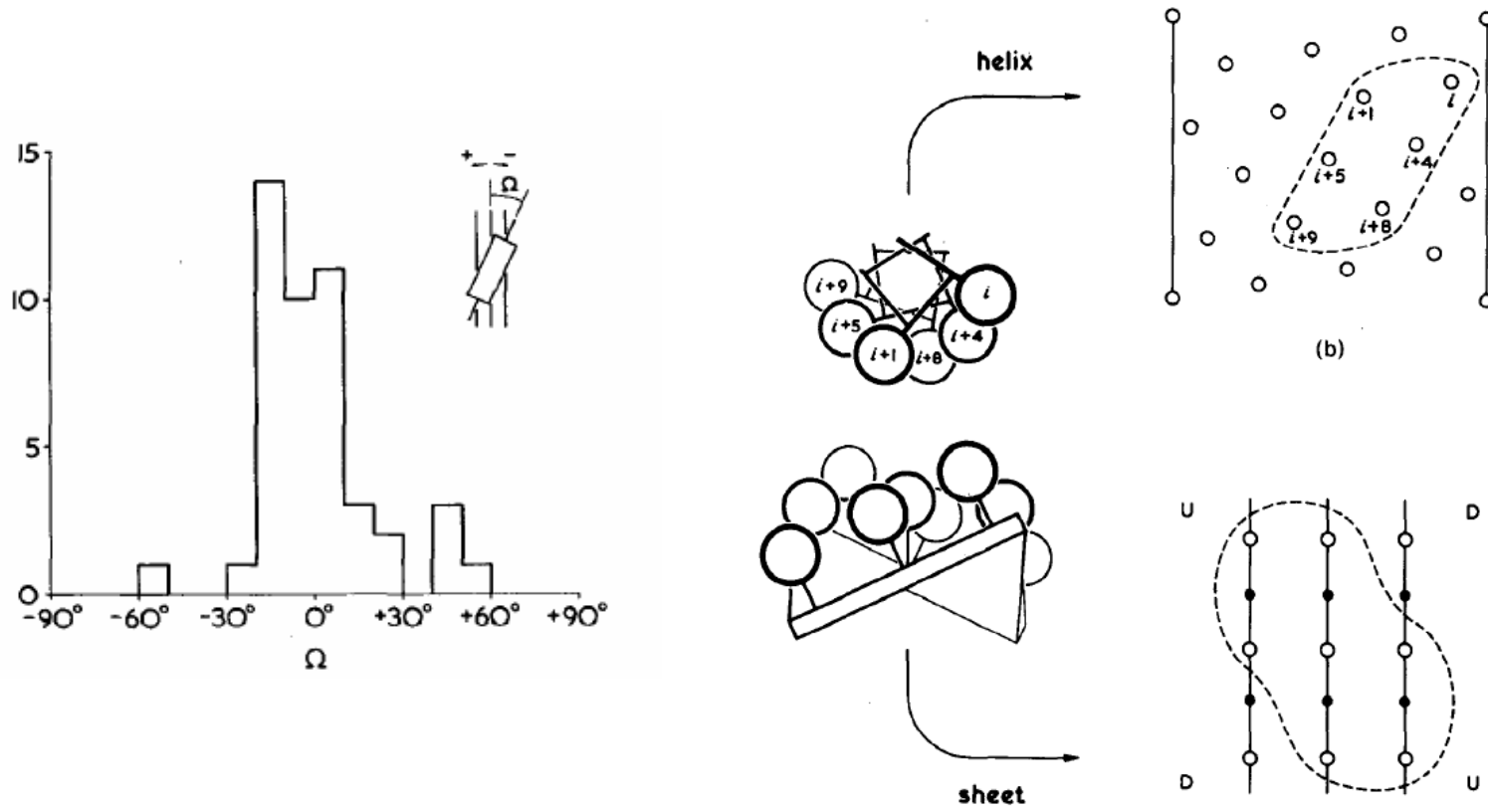


First loop is often evolutionarily conserved, whereas the second loop rarely has a known function



# Helix-sheet packing

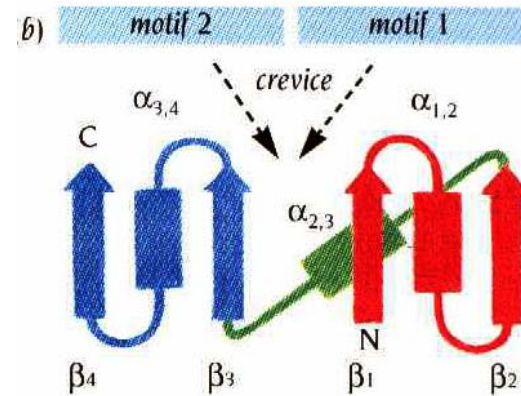
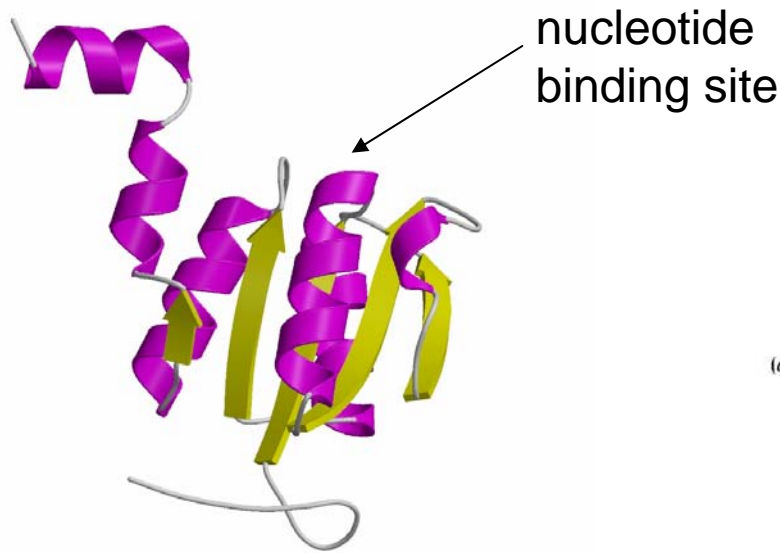
- Helices tend to pack against beta sheets with their axes parallel to the strands
- Intrinsic twist of the sheet complements the gradual rotation of the hydrophobic surface on a helix



Chothia, Annu Rev Biochem 53, 537 (1984)

# Simple motifs can combine to generate more complex structures

Rossmann fold (= 2 x  $\beta\alpha\beta$  motif with the middle  $\beta$  shared between the two units) binds nucleotides



Four helix bundle is two coiled coil packed against each other

