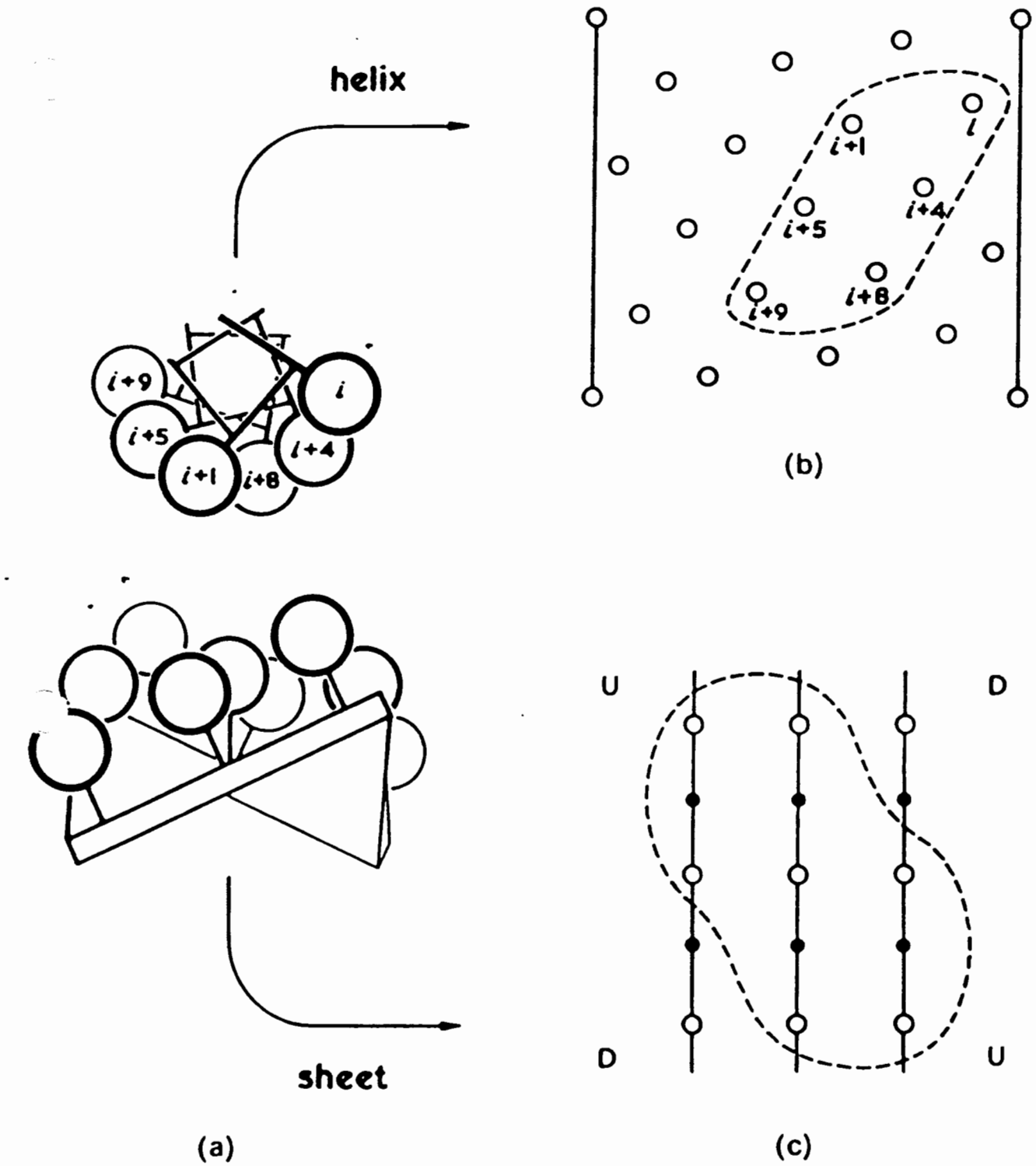
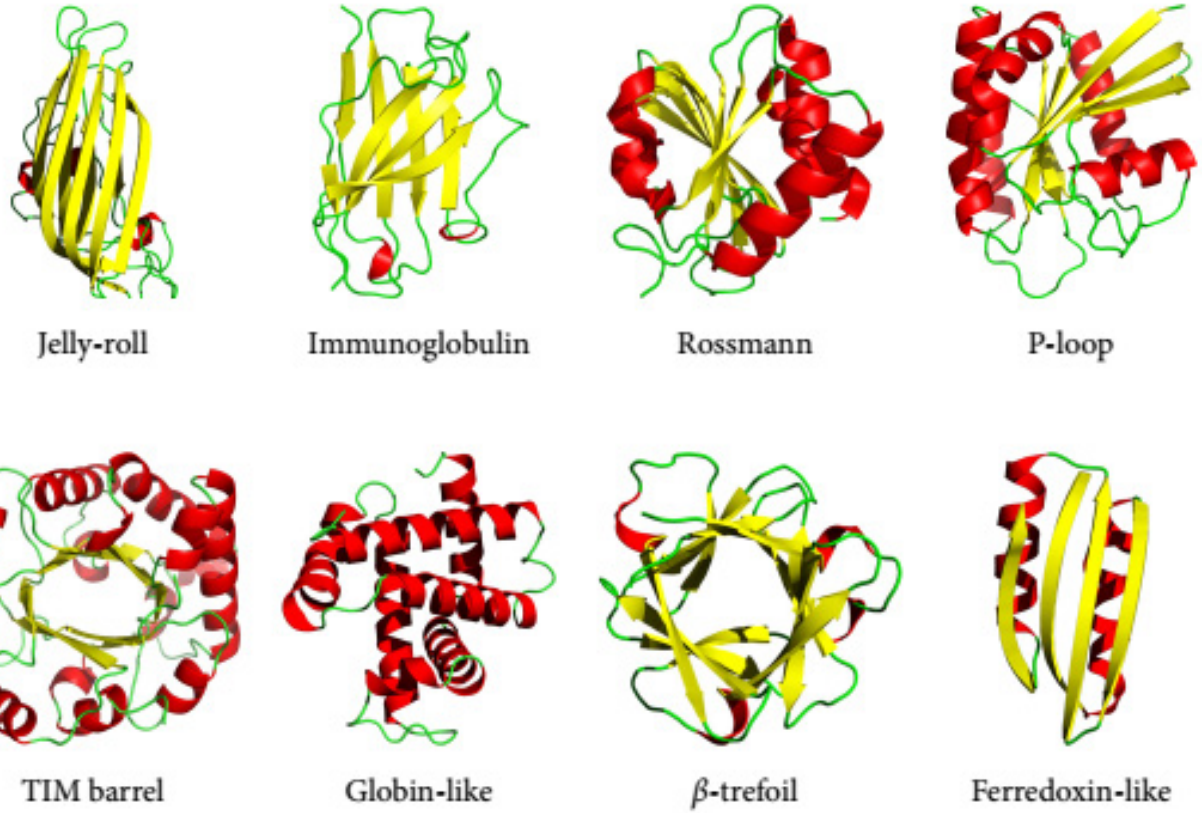


Figure 9 The complementary twist model for α-helix to β-sheet packing. Side chains on one side of an α helix and a twisted β sheet are shown as open circles (*a*). When the helix axis is parallel to the strand direction, the helix residues $i, i+1, i+4, i+5, i+8, i+9, \ldots$ form a twisted surface that is complementary to that of the twisted β sheet. The patterns formed by the residues in contact at the interface are shown on flattened projections of the α helix (*b*) and β s... (*c*). U and D mark the corners of the β sheet that move up and down from the plane when the β sheet is twisted. Note that the β-sheet contact residues cluster about a line joining U to U, the concave diagonal of the β sheet. [Reprinted with permission from (44).]

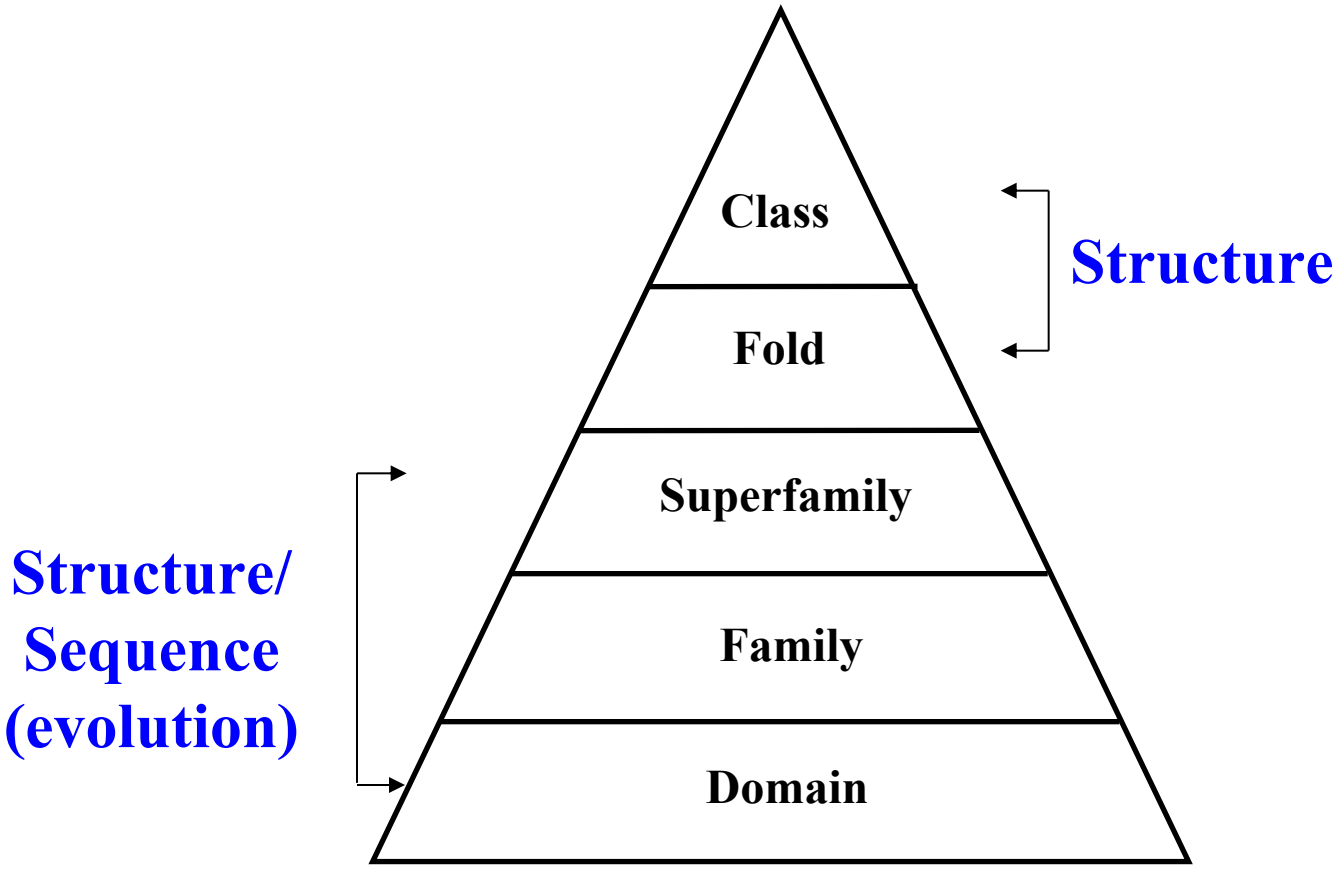
Common Superfolds

- **Structural stability** - amino acid packing, 2nd structures
- **Functional efficiency** - create binding/active sites



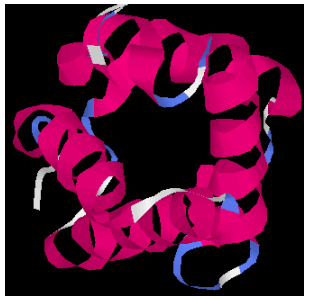
Protein Classification

- **SCOP (Structural Classification Of Proteins)**



- URL: http://scop.mrc-lmb.cam.ac.uk/scop/

Protein Classification



Classes:

1. All alpha proteins [46456] (226)
2. All beta proteins [48724] (149)
3. Alpha and beta proteins (a/b) [51349] (134)
   Mainly parallel beta sheets (beta-alpha-beta units)
4. Alpha and beta proteins (a+b) [53931] (286)
   Mainly antiparallel beta sheets (segregated alpha and beta regions)
5. Multi-domain proteins (alpha and beta) [56572] (48)
   Folds consisting of two or more domains belonging to different classes
6. Membrane and cell surface proteins and peptides [56835] (49)
   Does not include proteins in the immune system
7. Small proteins [56992] (79)
   Usually dominated by metal ligand, heme, and/or disulfide bridges
8. Coiled coil proteins [57942] (7)
   Not a true class
9. Low resolution protein structures [58117] (24)
   Not a true class
10. Peptides [58231] (116)
    Peptides and fragments. Not a true class
11. Designed proteins [58788] (42)
    Experimental structures of proteins with essentially non-natural sequen

Table 4.1. Classification of protein topologies

Property	Class		Characteristic	Examples
Secondary structure content	1.	α-helical	secondary structure almost exclusively α-helical	myoglobin, cytochrome c, citrate synthase
	2.	β-sheet	secondary structure almost exclusively β-sheet	chymotrypsin, immunoglobulin domain
	3.	$\alpha+\beta$ and α/β	secondary structure contains both α-helix and β-sheet	papain, alcohol dehydrogenase, triose phosphate isomerase
Tertiary structure	2.1	parallel β-sheet	double β-sheet sandwich, strands roughly parallel	immunoglobin domain
	2.2	orthogonal β-sheet	double β-sheet sandwich, strands of different sheets roughly perpendicular	chymotrypsin domains
	2.3	β-sheet (other)	other types of spatial relationships between sheets	neuraminidase, interleukin-1β
	3.1	$\alpha+\beta$	α-helices and strands of β-sheet separated in different parts of molecule. Absence of β–α–β supersecondary structure	papain, staphylococcal nuclease
	3.2	α/β	helices and sheet assembled from β–α–β units—strands of sheet parallel	alcohol dehydrogenase, triose phosphate isomerase
	3.2.1	α/β-linear	line through centres of strands of sheet roughly linear	alcohol dehydrogenase
	3.2.2	α/β-closed	line through centres of strands of sheet roughly circular	triose phosphate isomerase

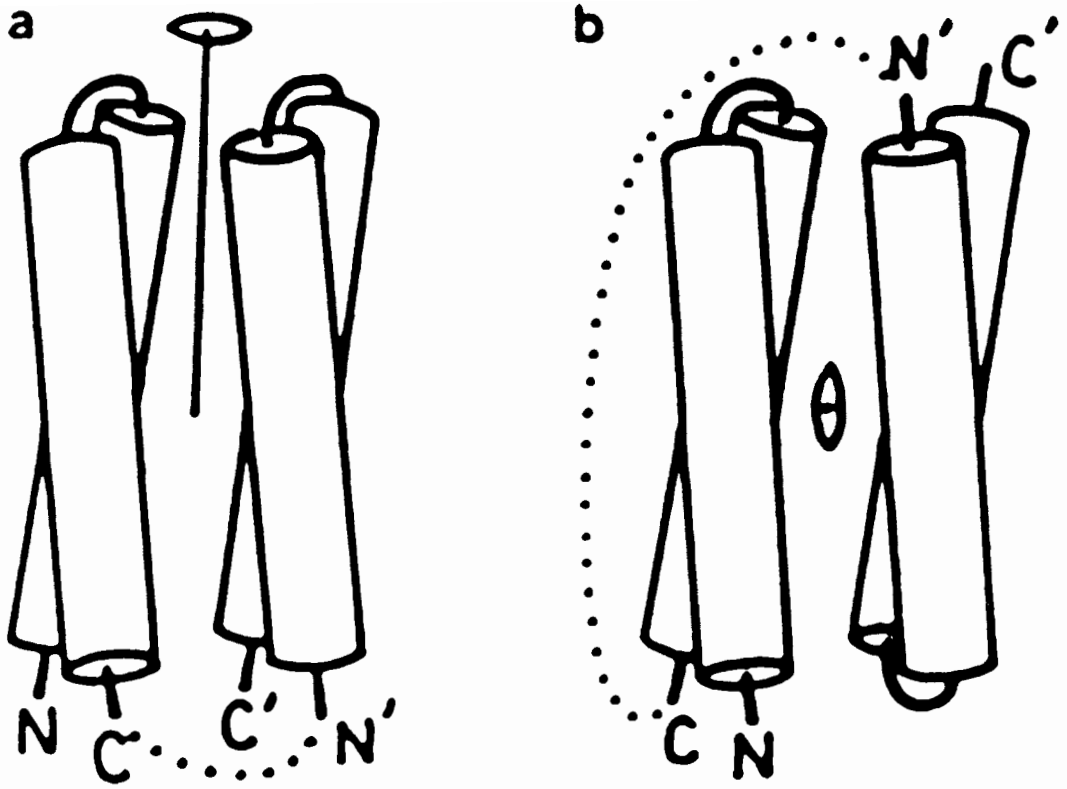


Figure 37. Diagram of two alternative arrangements for helix-pair dimers, with dotted lines to show the type of connection needed to join them into a single covalent chain. (a) The dimers are related by a lengthwise twofold axis, and they can be joined by a short connection into an up-and-down helix bundle (like those in Fig. 36). (b) The dimers are related by a crosswise twofold axis (as is the case for the ROP dimer), and they can only be joined by a long crossover connection of the type seen in ferretin and growth hormone.

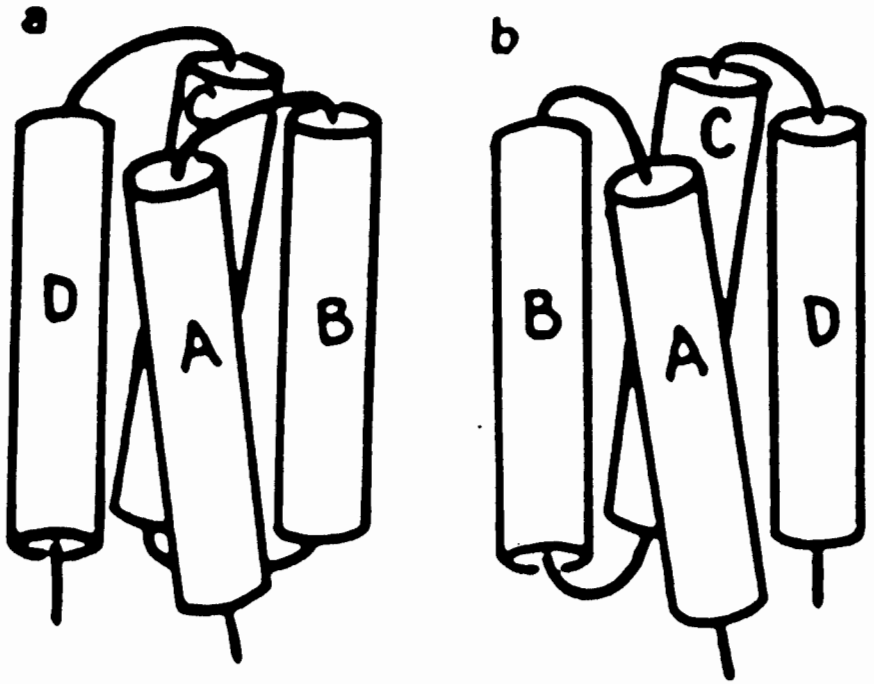


Figure 39. Diagrams of the two directions in which an up-and-down helix bundle can pack: (a) the more common version turns right at the top of the first helix, as in the proteins of Fig. 36; (b) the alternative version turns left at the top of the first helix, as seen in cytochrome b_5 and ROP protein.

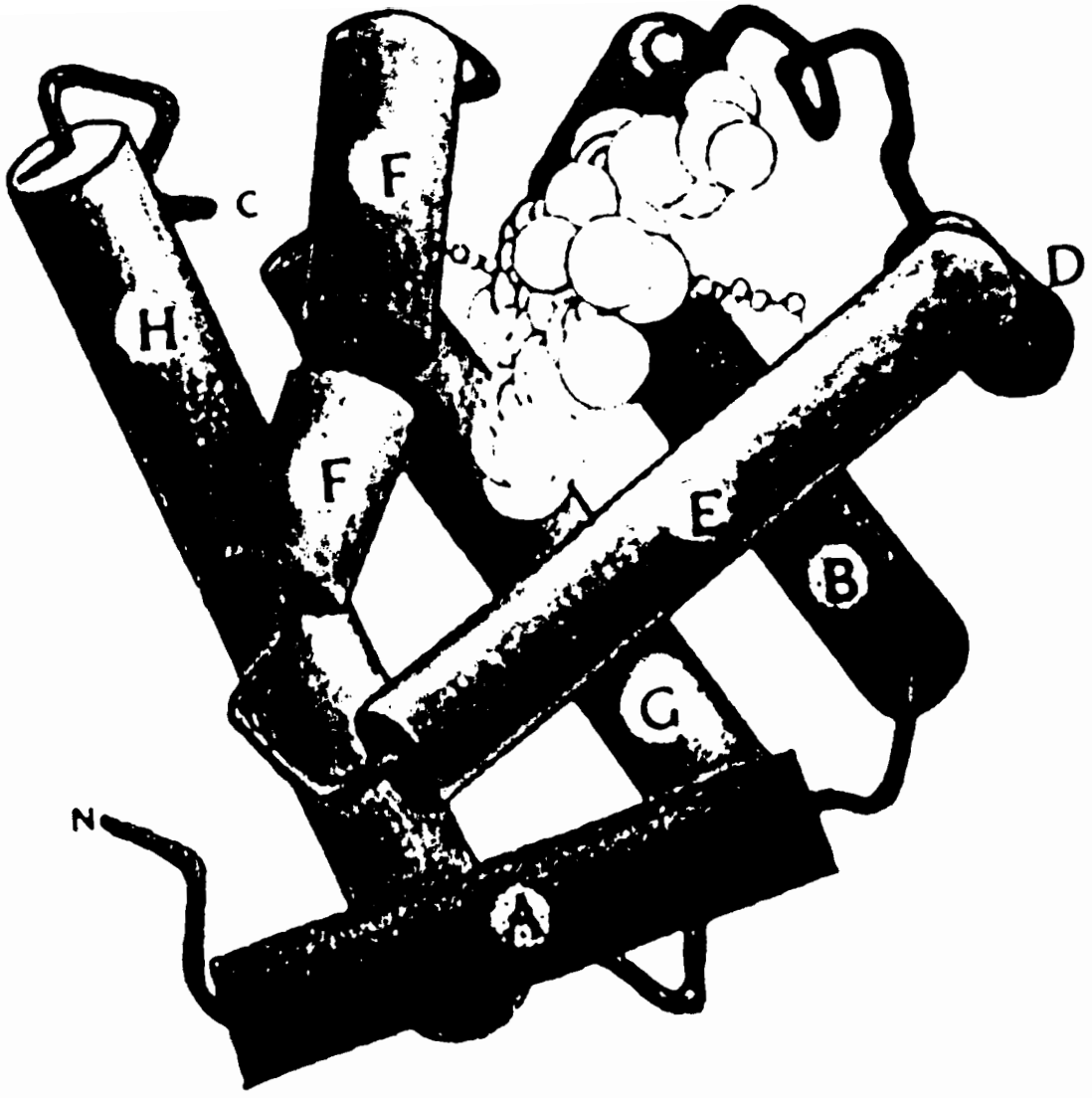
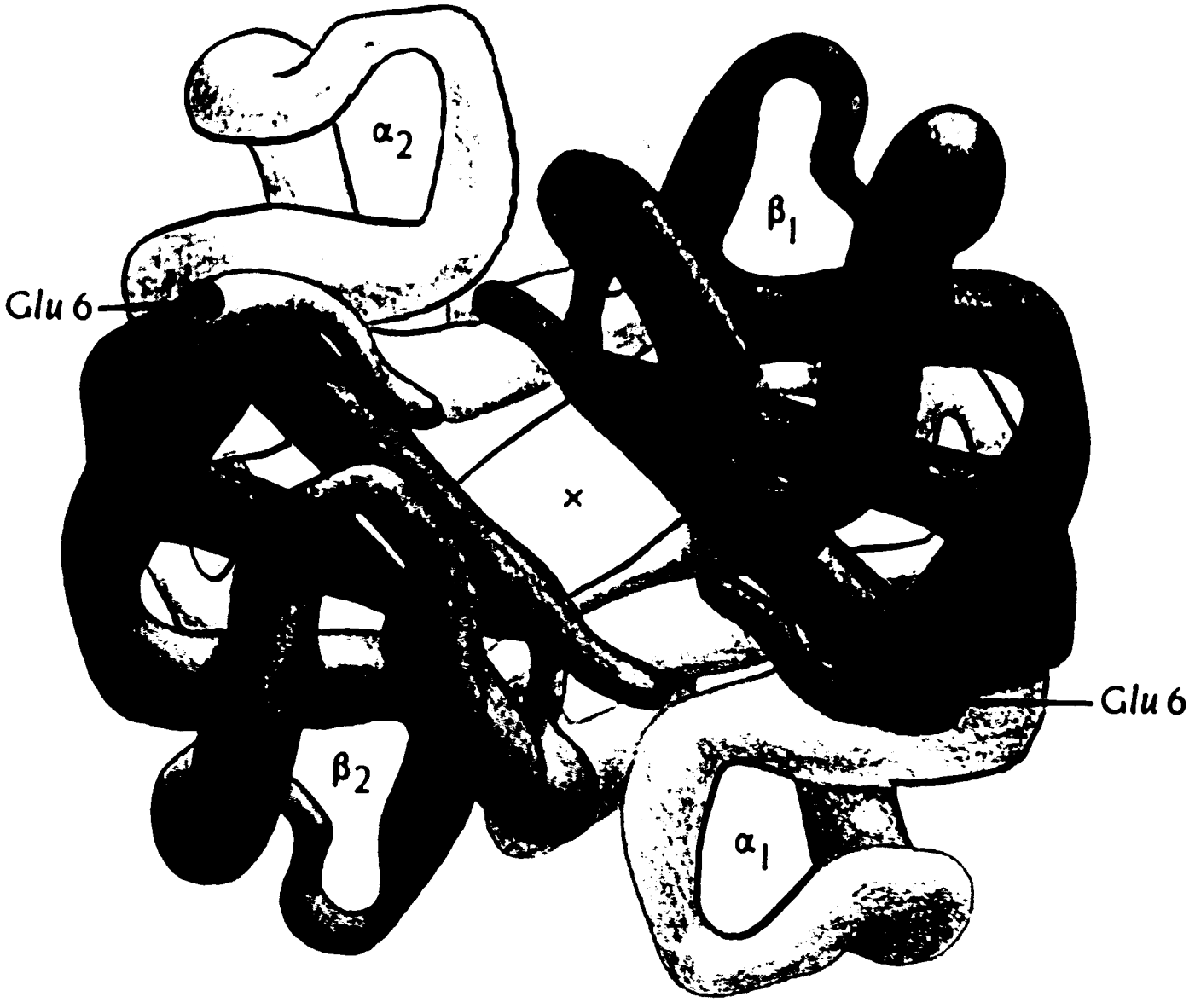
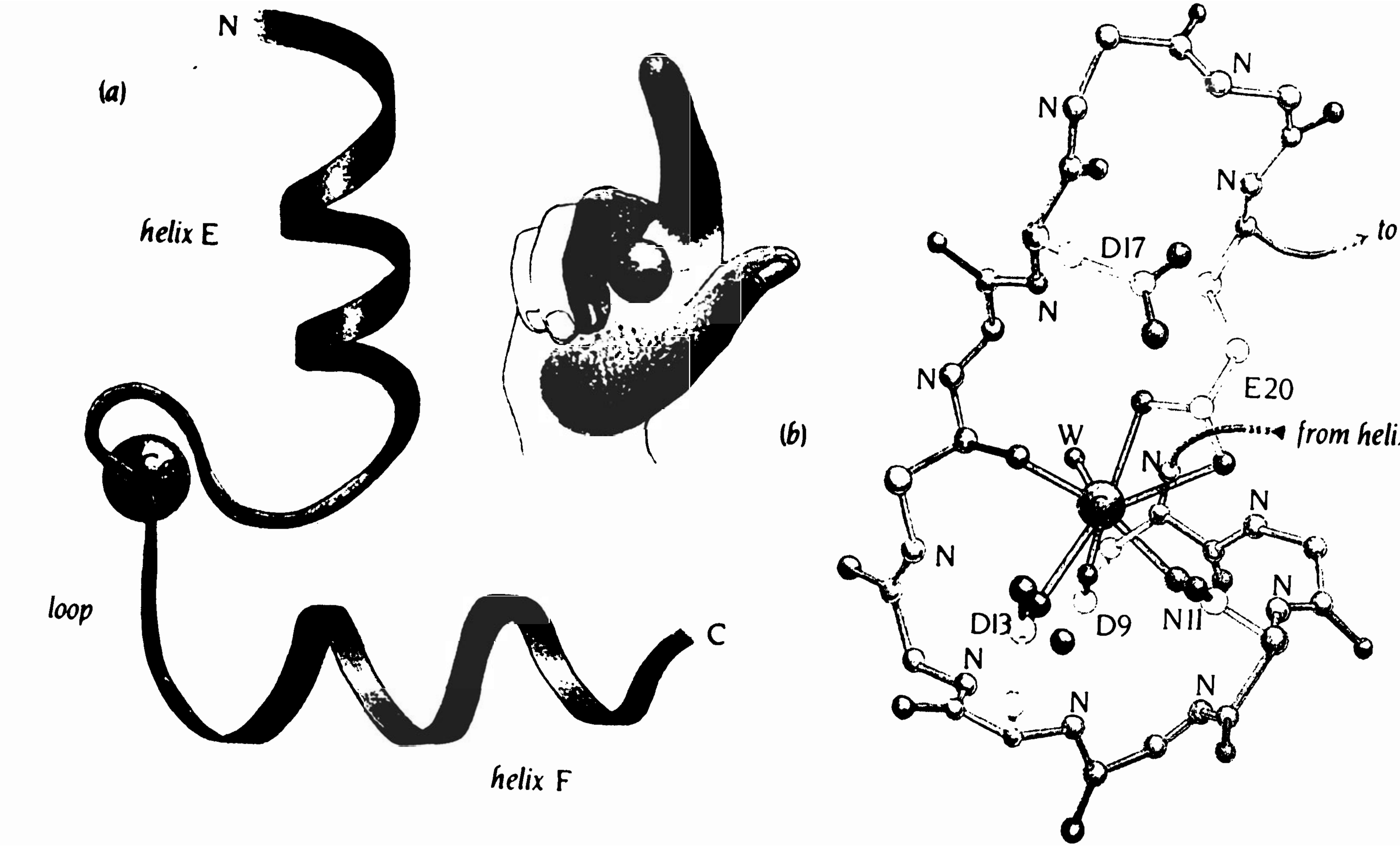
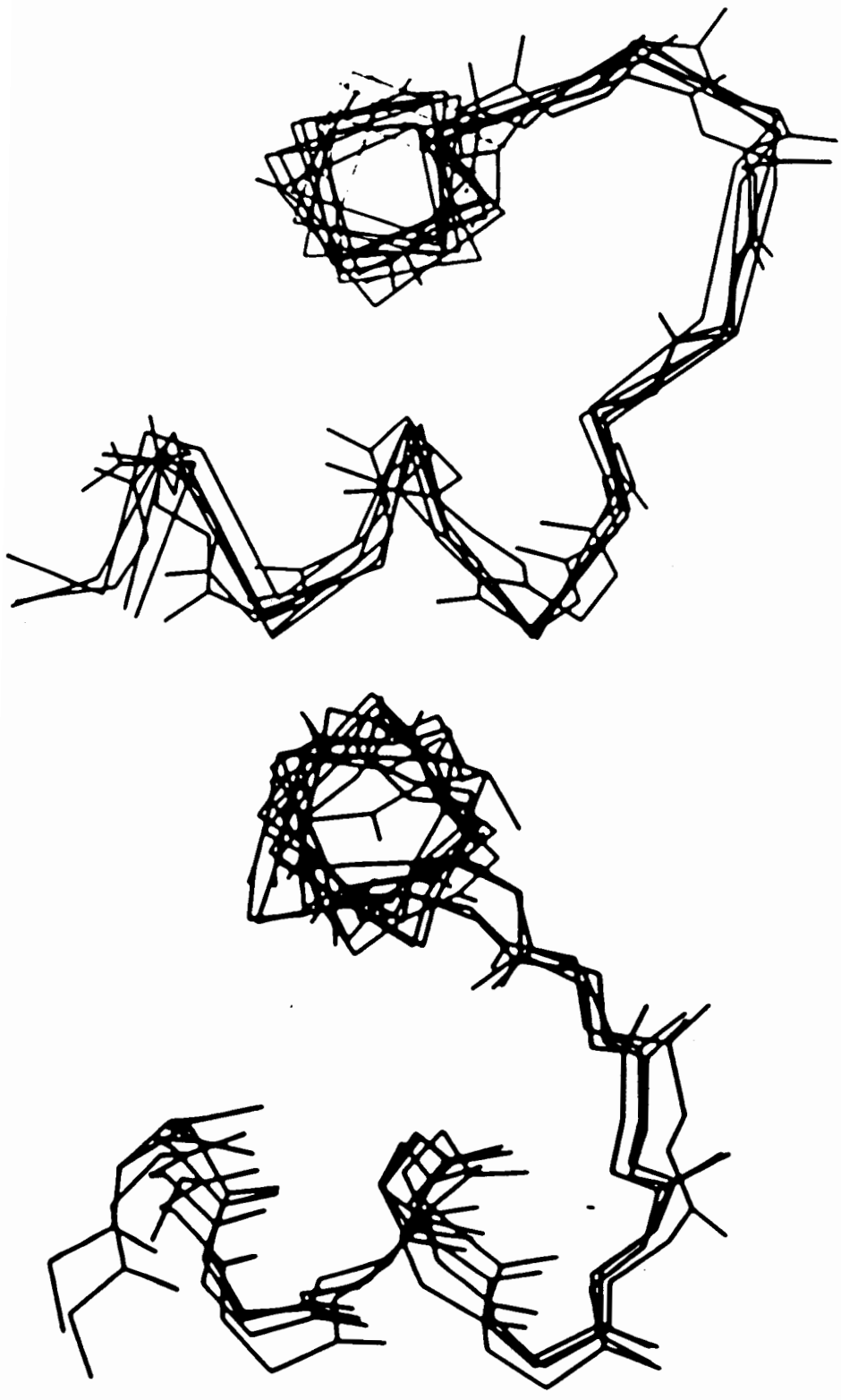


Figure 3.4 Schematic drawing of the globin domain. The eight α helices are labeled A to H. A–D are red, E and F green, and G and H blue. (Adapted from originals provided by A. Lesk.)


α2
β1
Glu 6
x
Glu 6
β2
α1



(a)
N
helix E
loop
helix F
C
(b)
N
D17
E20
W
D13
D9
N11
to



(a) six superimposed examples of Ca-binding

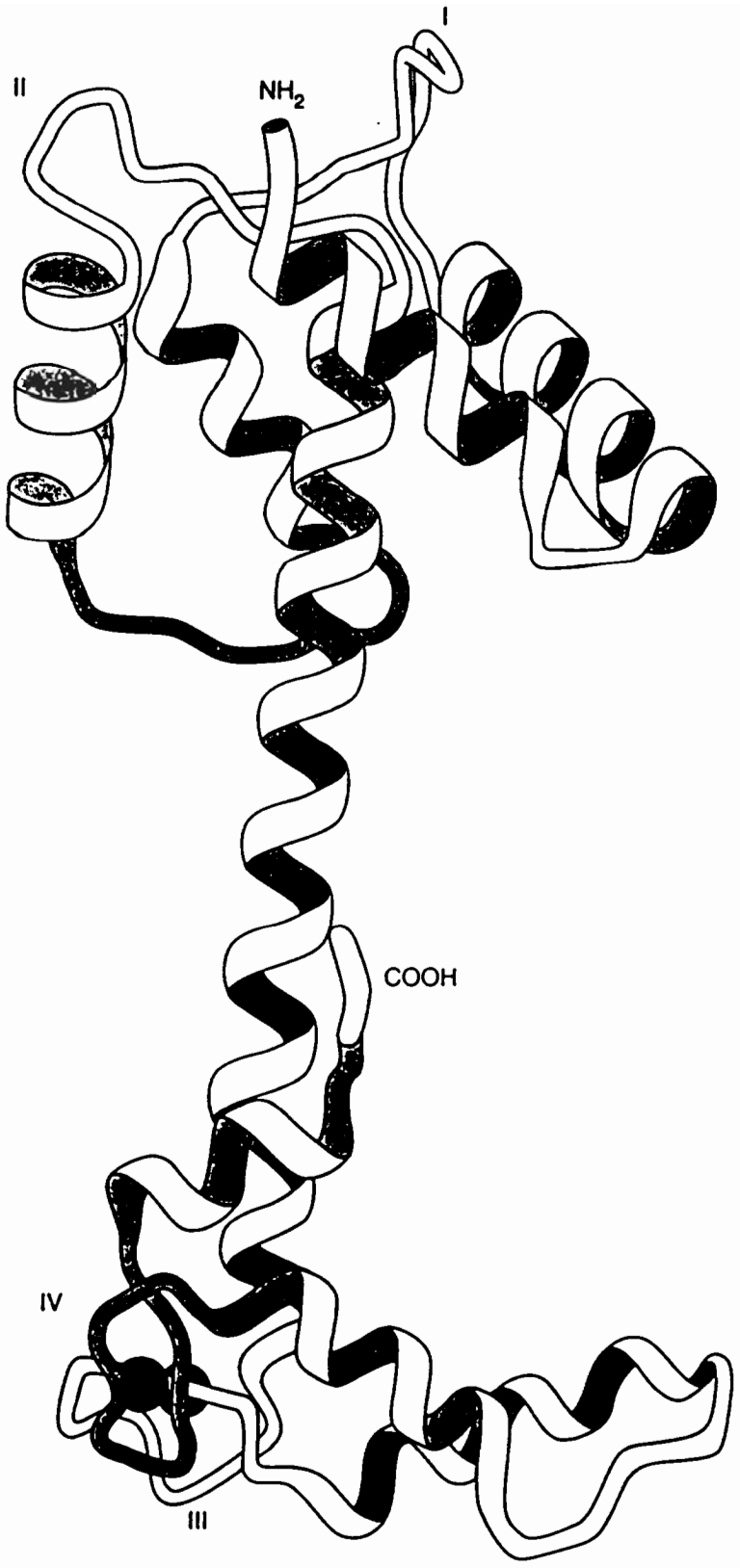
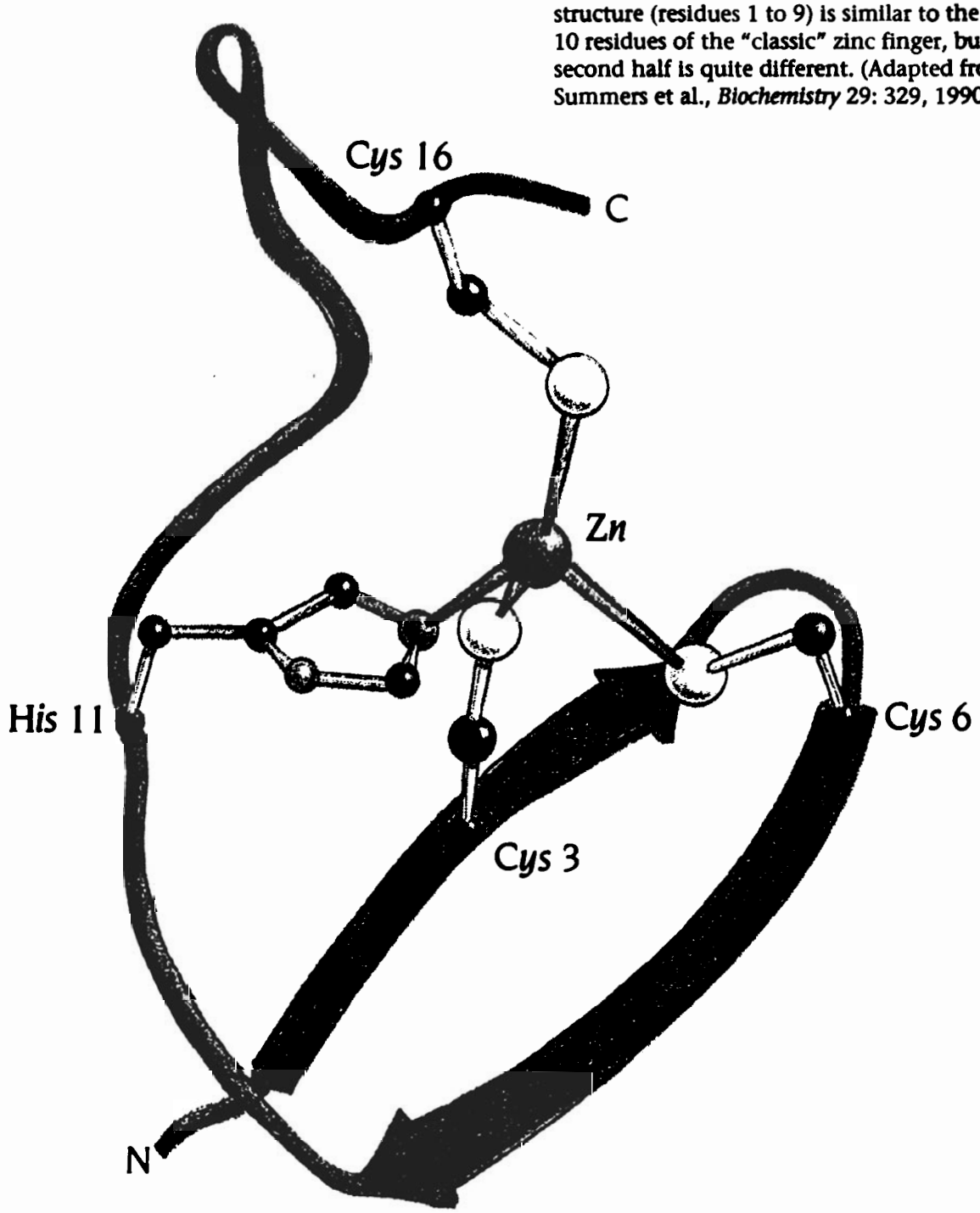


Figure 4.1. The structure of troponin C with Ca^{2+} bound at two of its four EF hands. Sites II and IV have been highlighted in orange. Note the differences in their conformation due to the presence of Ca^{2+} at sites III and IV and its absence at sites I and II. Reproduced with permission from Herzberg, O. and James, M.N.G. (1988) *J. Mol. Biol.*, **203**, 761.

Figure 8.10 Schematic diagram of the three-dimensional structure of a complex between zinc and a synthetic peptide with an amino acid sequence corresponding to one of the zinc fingers in the gag protein of retrovirus HIV. The zinc atom is coordinated to three cysteine residues and one histidine. The first half of the structure (residues 1 to 9) is similar to the first 10 residues of the "classic" zinc finger, but the second half is quite different. (Adapted from M. Summers et al., *Biochemistry* 29: 329, 1990.)



H_2N–V–K–C–F–N–C–G–K–E–G–[■]–I–A–R–N–C–R–A–COOH

1 3 6 11 16 18

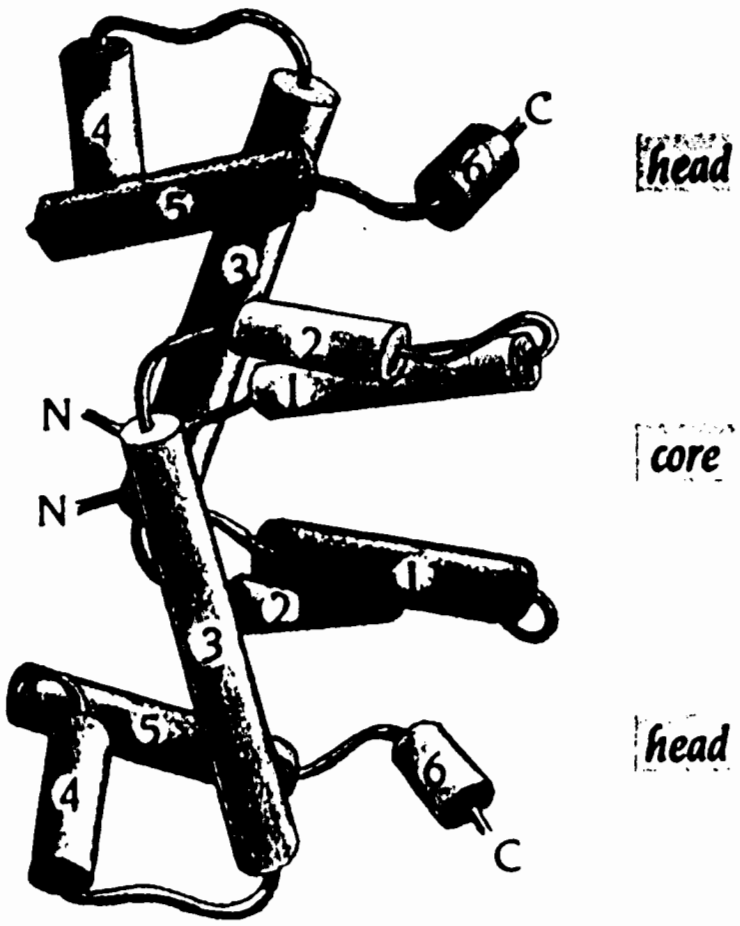


Figure 7.23 The α helices of the N-terminal region of the *trp* repressor are involved in subunit interactions and form a stable core in the middle of the dimer. α helices 4–6, which include the helix-turn-helix motif, form two "head" regions at the two ends of the molecule. α helix 3 connects the core to the head in both subunits. (Adapted from Schevitz et al., *Nature* 317: 782, 1985.)

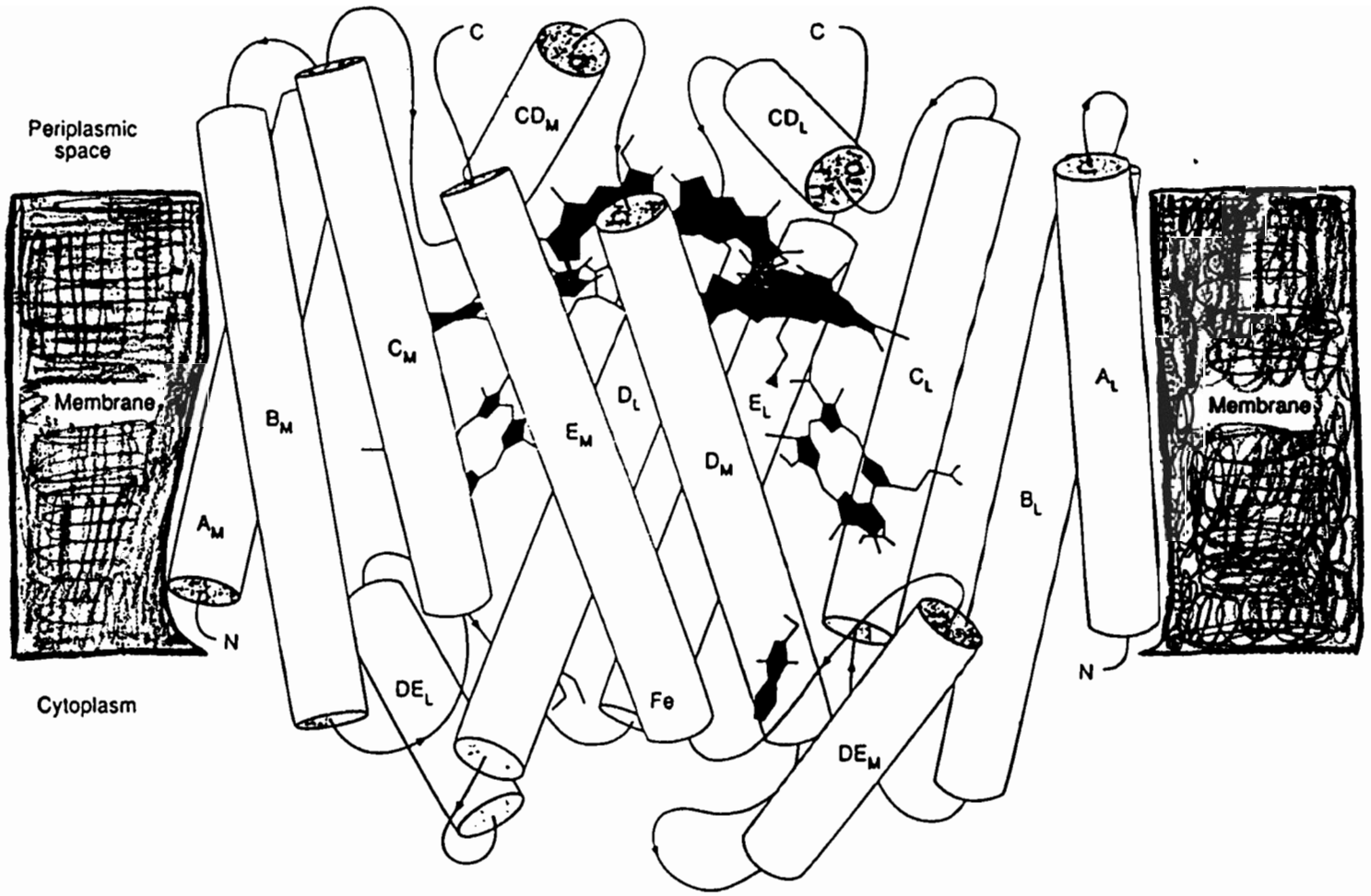
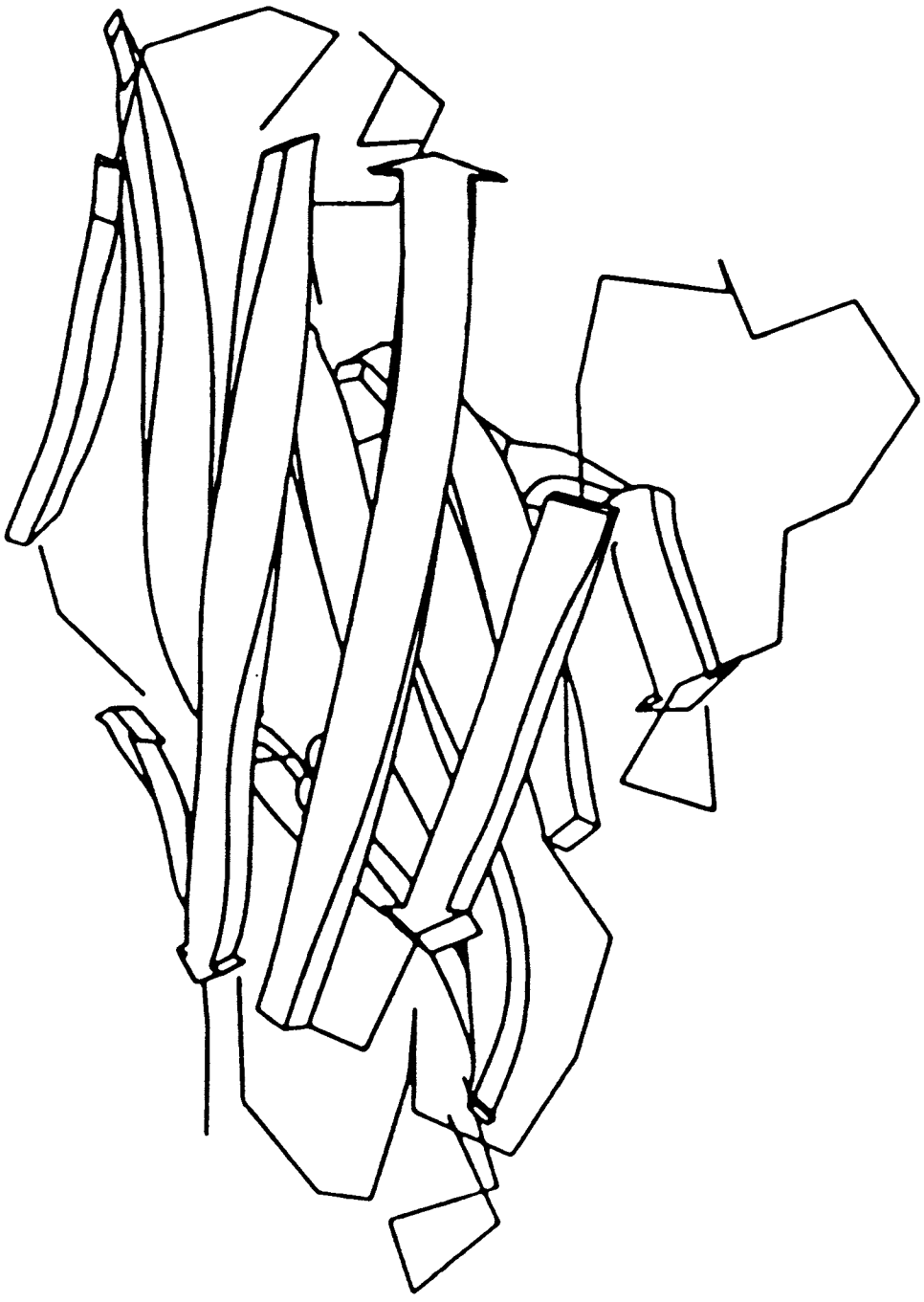


Figure 3.1 Schematic diagram of the L (grey) and M (pale orange) subunits of the photosynthetic reaction centre; the major α-helices are labelled A to E for each subunit; minor helices are labelled by the major helices they connect. Note the 2-fold pseudo-symmetry axis; the L and M subunits probably arose from a common ancestral protein that functioned as a dimer. The H subunit of the protein (not shown) is mainly located on the cytoplasmic face of the membrane, but also has one transmembrane helix. A cytochrome subunit binds to the periplasmic side of the membrane by protein–protein interactions. Co-factors and prosthetic groups are shown in orange. Reproduced with permission from Michel, H. and Diesenhofer, J. (1988) *Biochemistry*, **27**, 1.

Jelly Roll

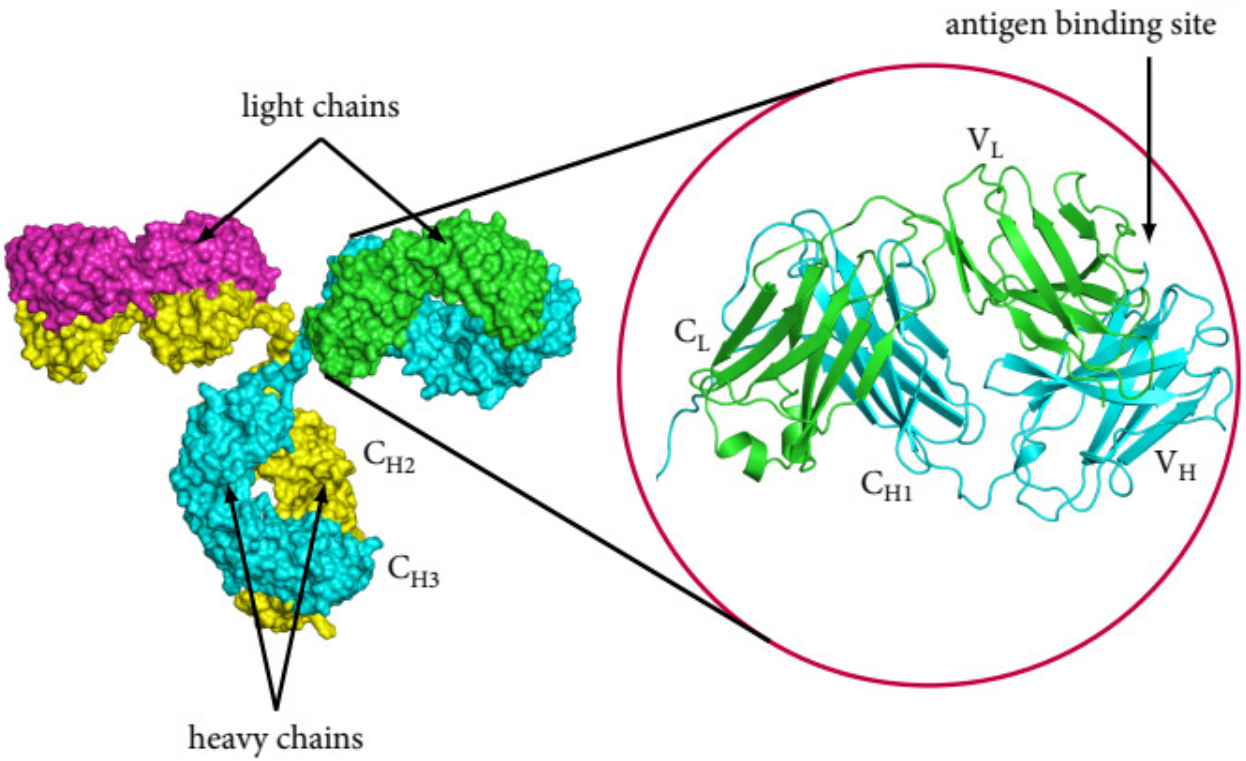
Immunoglobulin (Ig)



immunoglobulin domain (V_H KOL)

- Found in **immune system molecules (Ab, TCR, MHC)** and other recognition molecules
- Based on the **β-sandwich** motif
- Antibodies: 2 heavy chains + 2 light chains
- Antigen binds to **loops**

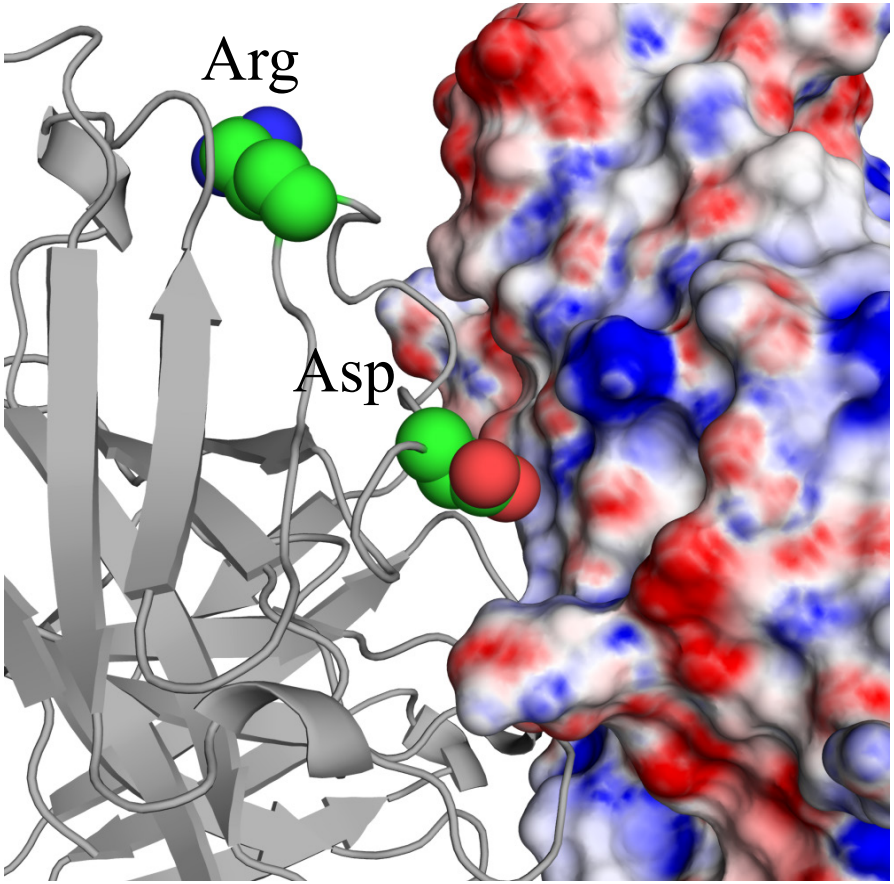
- **Ig Fold**



- **The immunoglobulin (Ig) fold**

➢ Binding **specificity** result from **shape complementarity** and **electrostatic interactions**

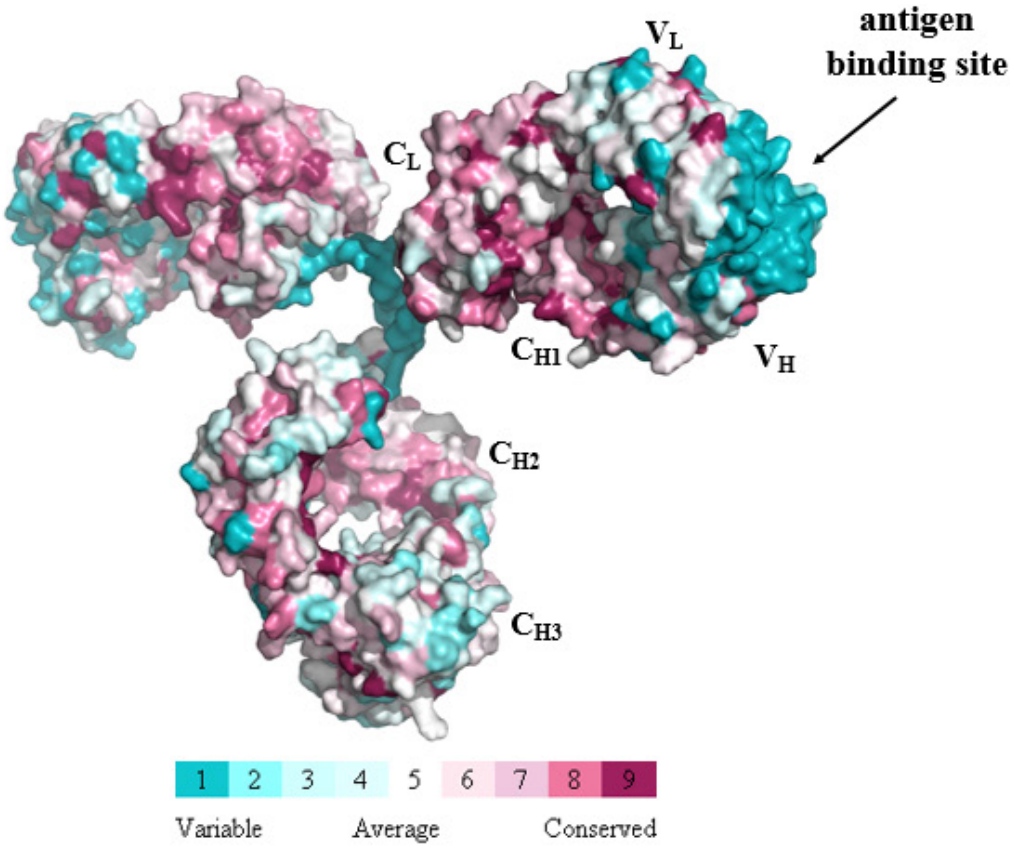
Antibody

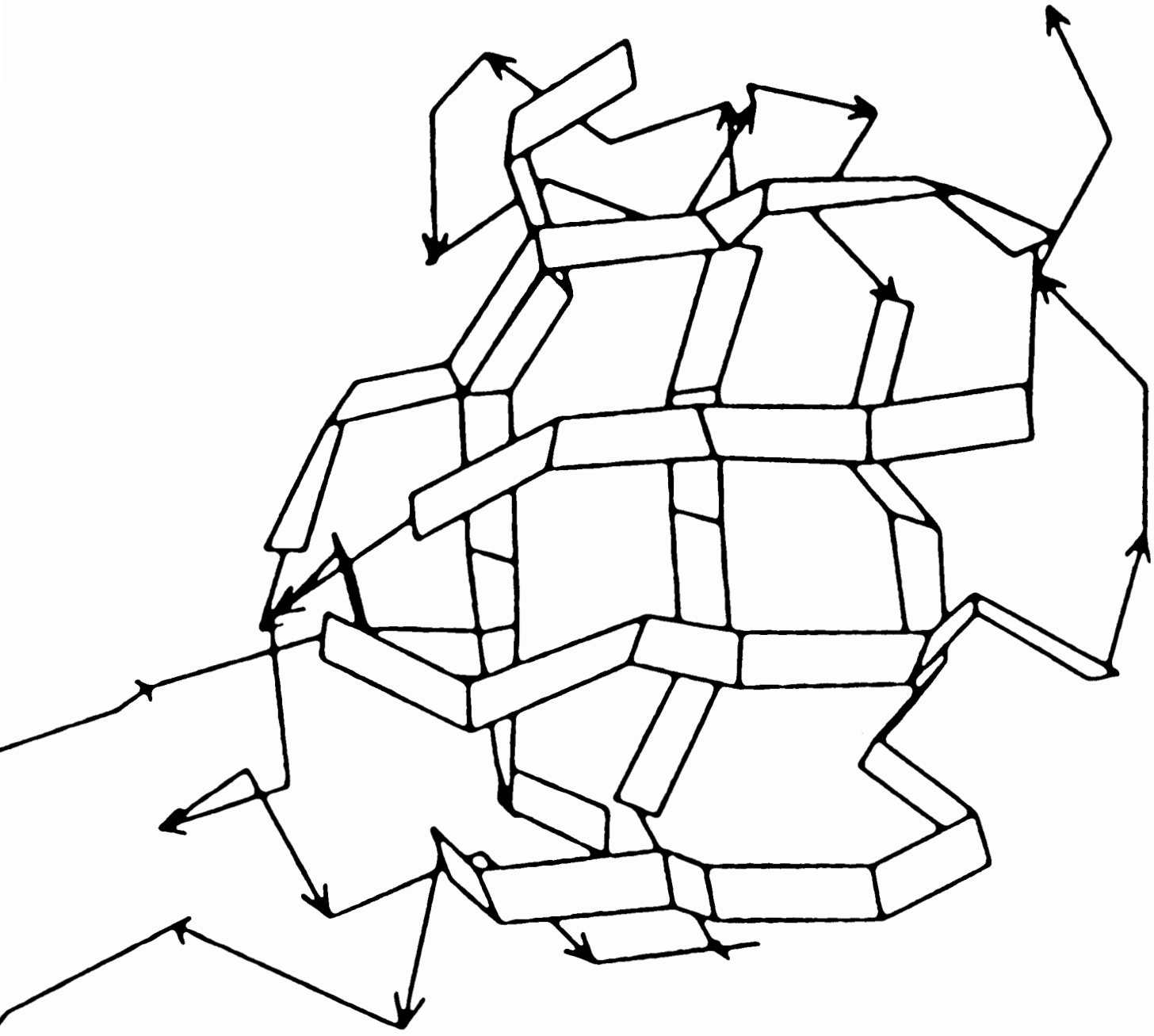


Antigen

- **The immunoglobulin (Ig) fold**

➢ The antigen-binding site has **very low evolutionary conservation** → allows **variability** despite common structure





N-terminal domain of γ-chymotrypsin

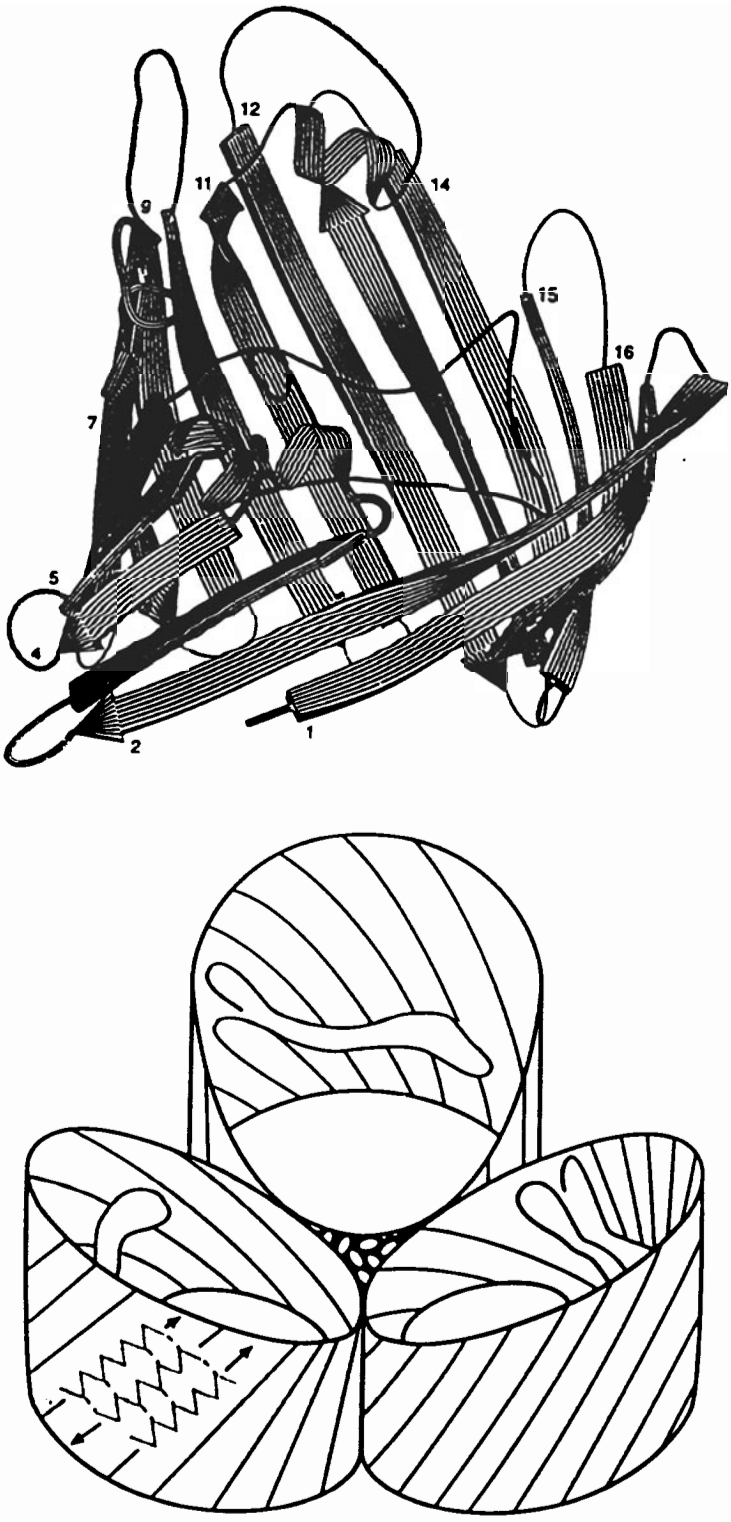
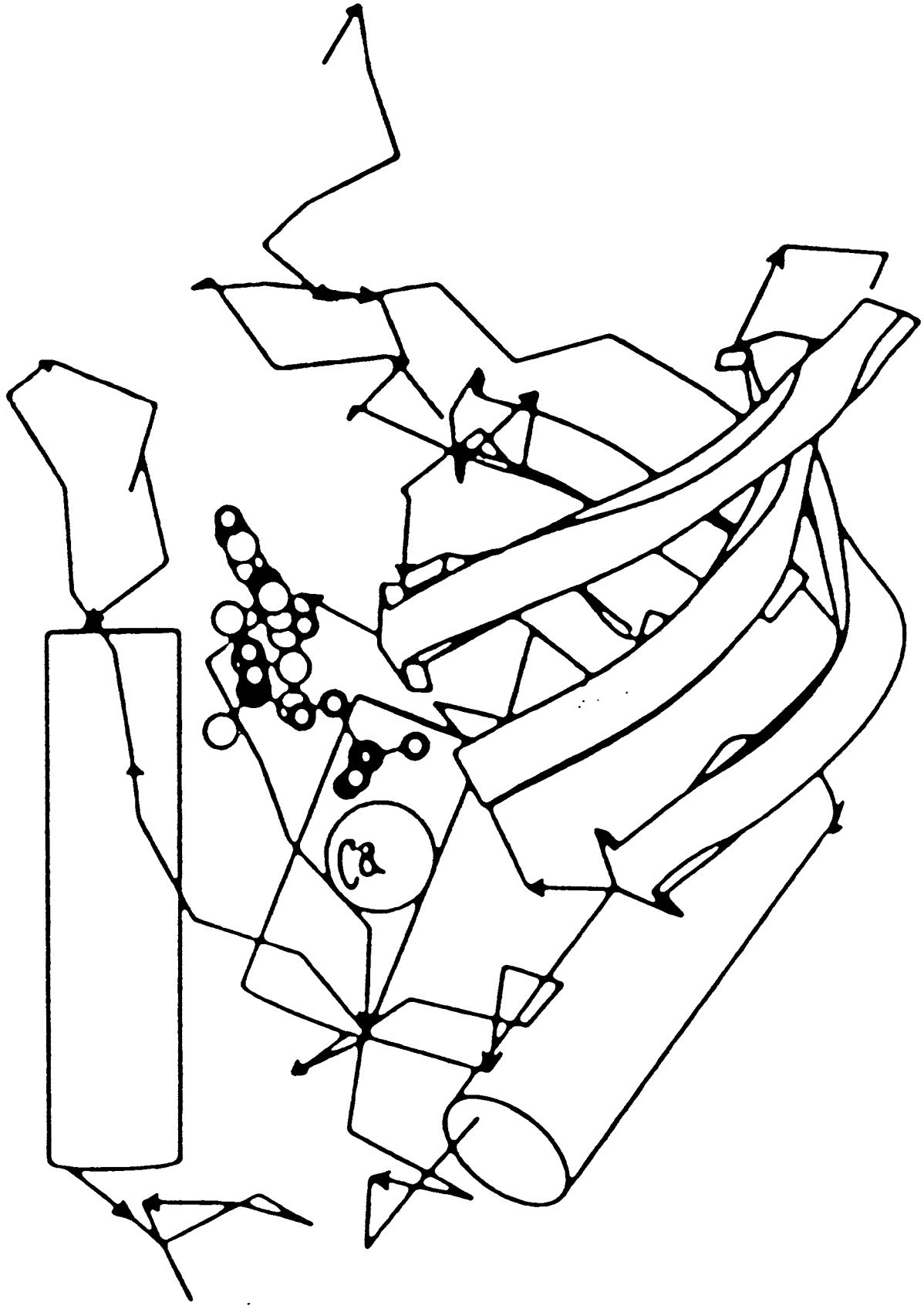
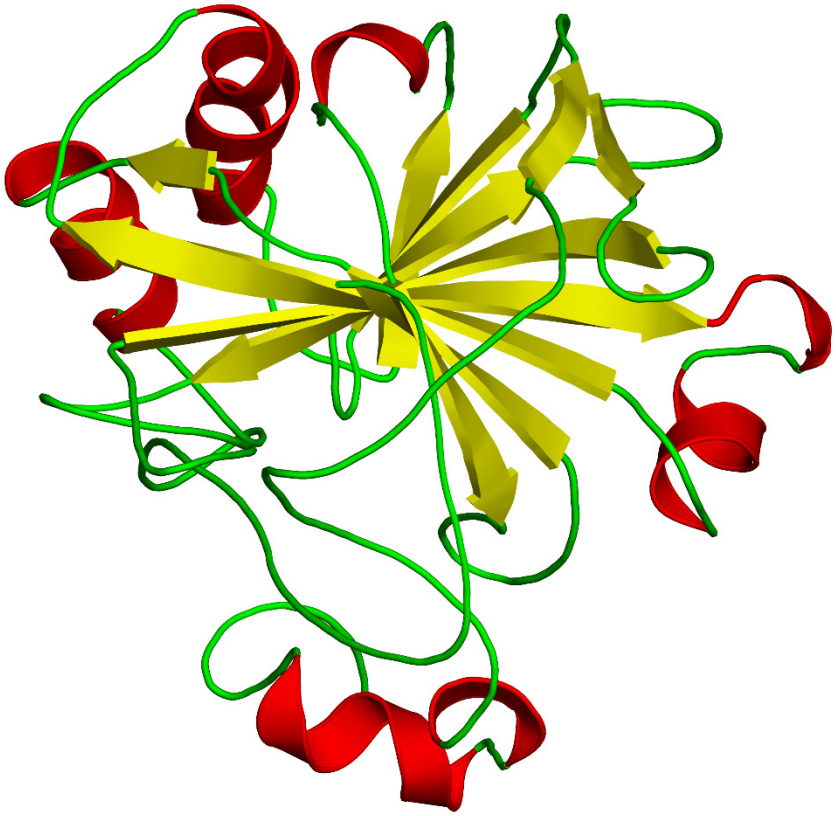
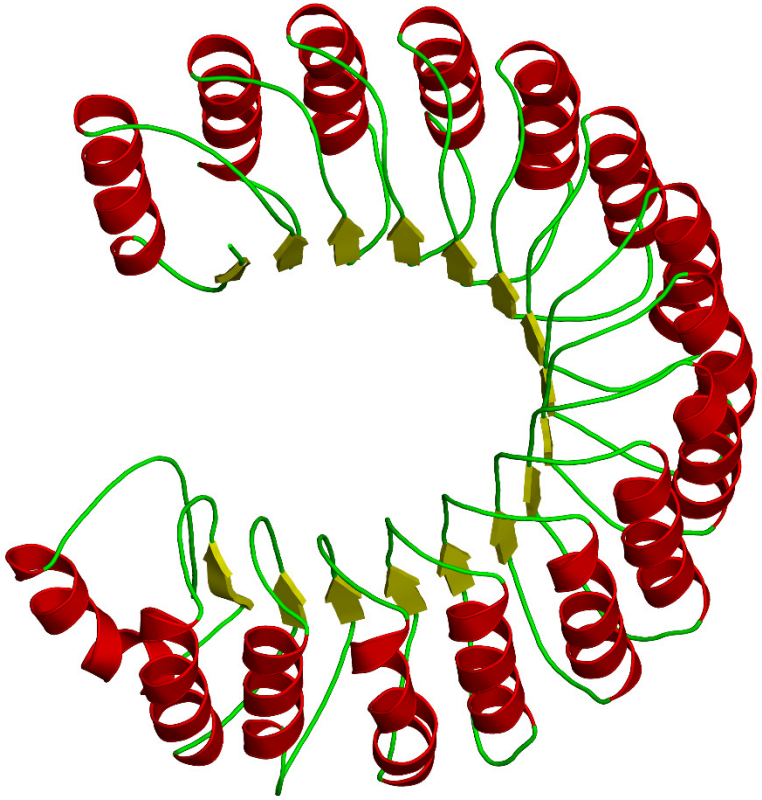


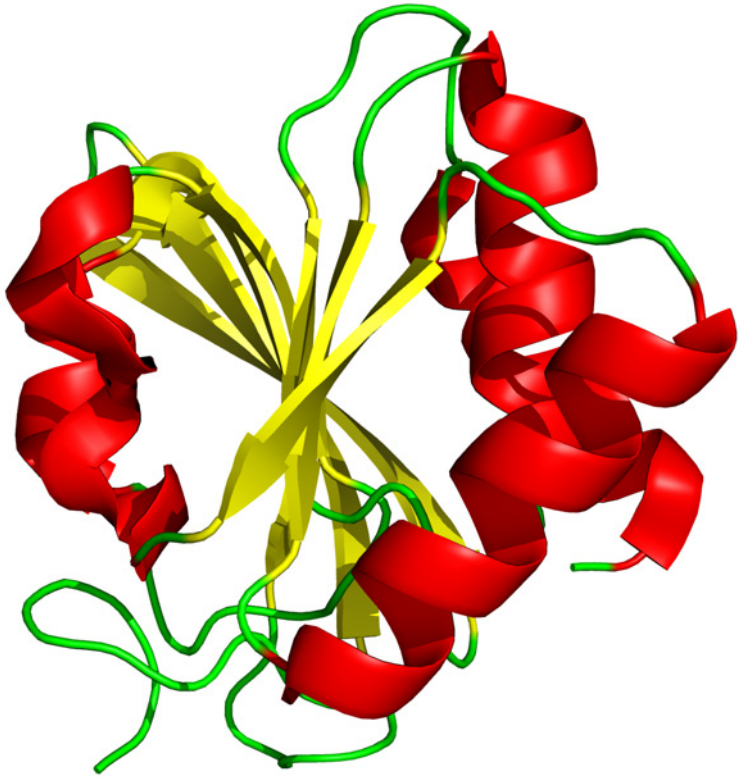
Figure 3.2. (a) Schematic view of one subunit of porin, which consists of 16 antiparallel β-strands, each 6–17 residues long, linked together by short lengths of α-helix or by loops to form a barrel. One loop of 44 residues (shown in orange) linking an α-helix after strand 5 to strand 6 protrudes into the barrel and restricts the channel. The bottom rim of the barrel faces the periplasm and is relatively flat, while the top rim with its longer and more irregular connections is slanted and also less regular. Reproduced, with permission from ref. 14. (b) Schematic representation of a porin trimer, with the channel-restricting loop shown in orange. Reproduced with permission from Schirmer, T. and Rosenbusch, J.P. (1991) *Curr. Opinion Struct. Biol.*, **1**, 539.



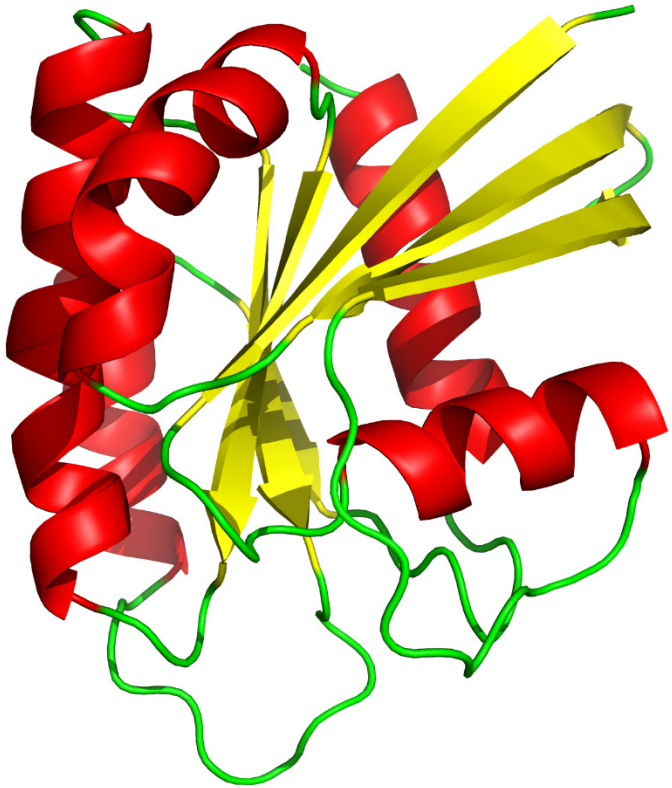
Staphylococcal nuclease





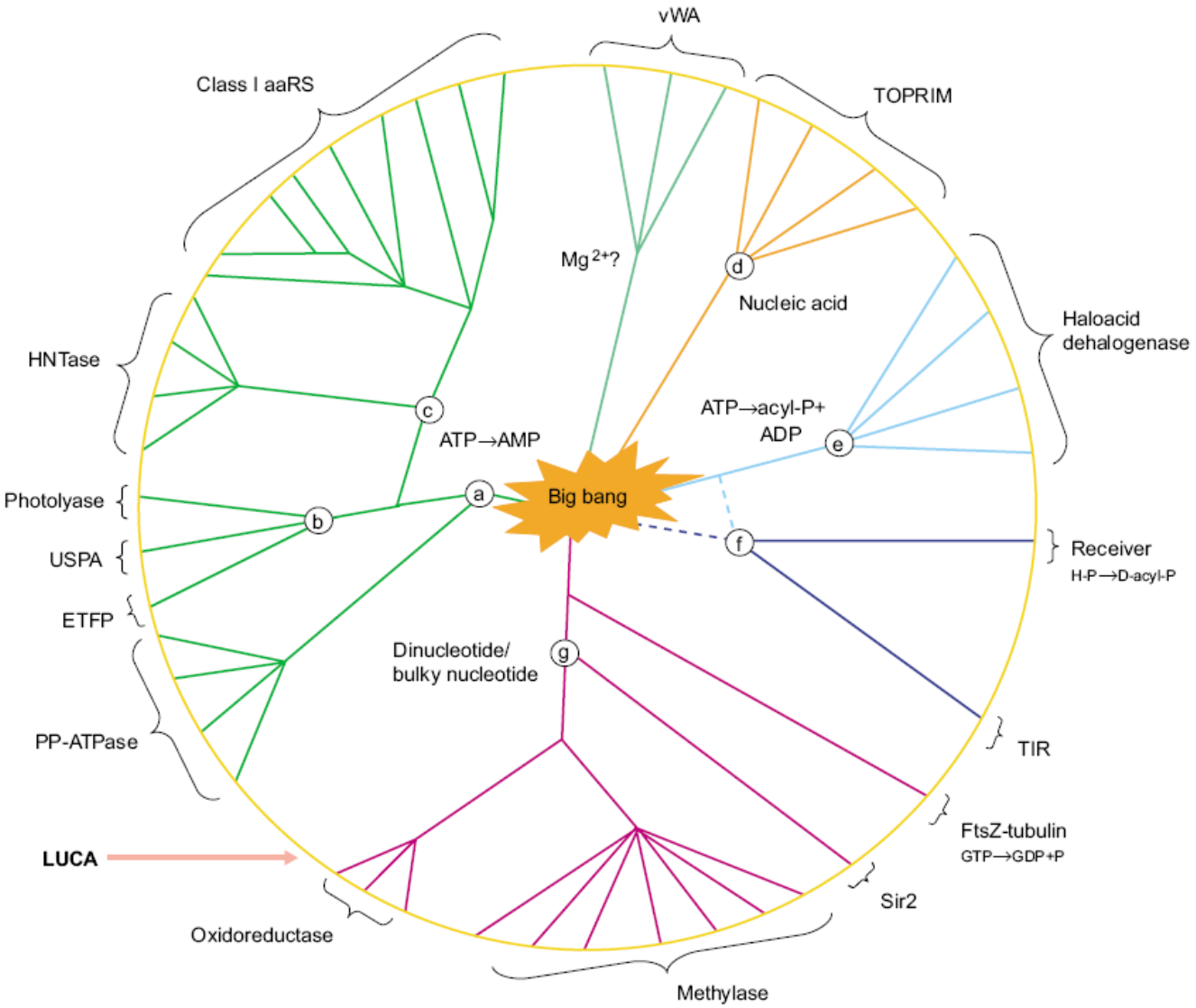


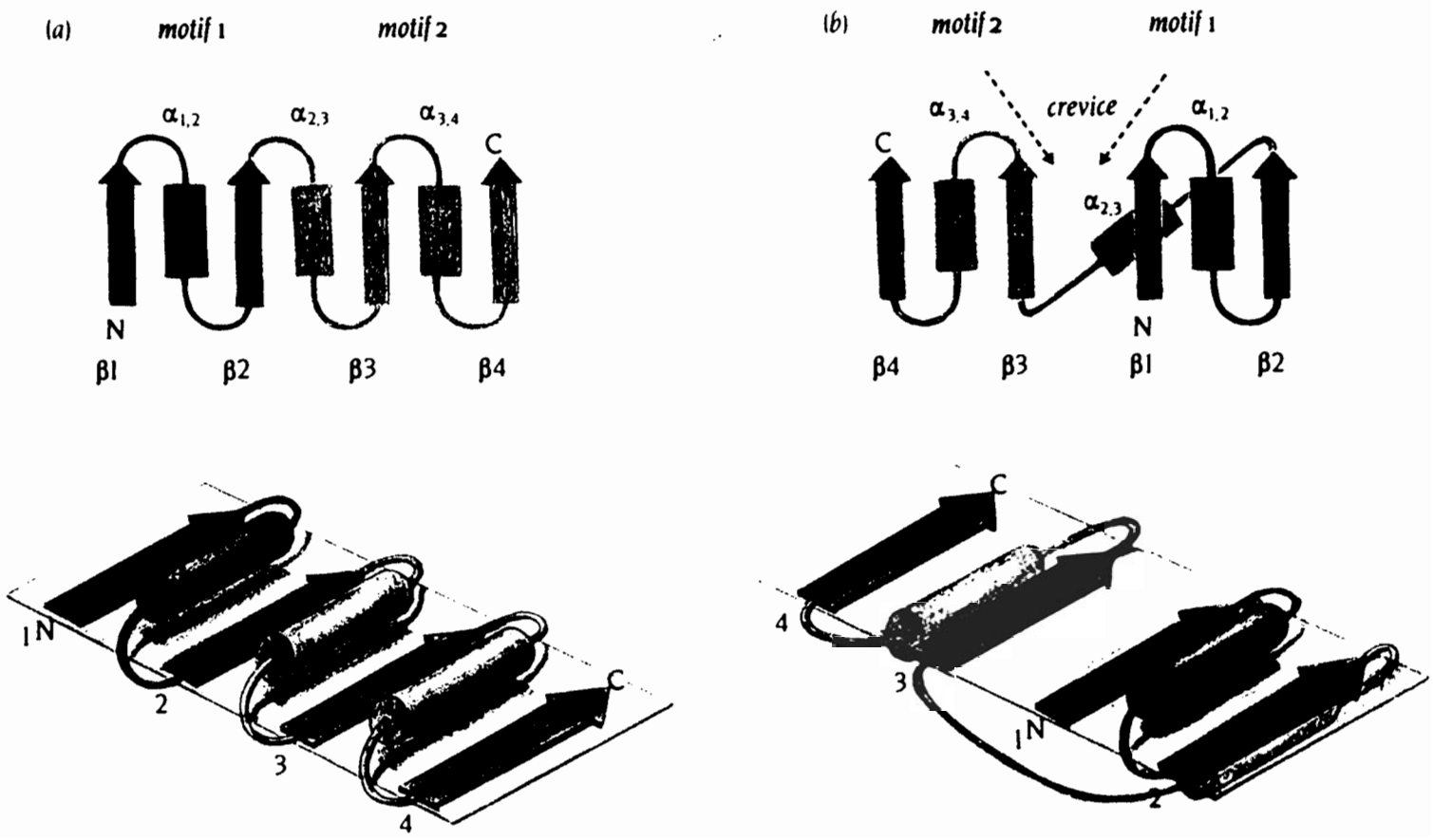
Rossmann

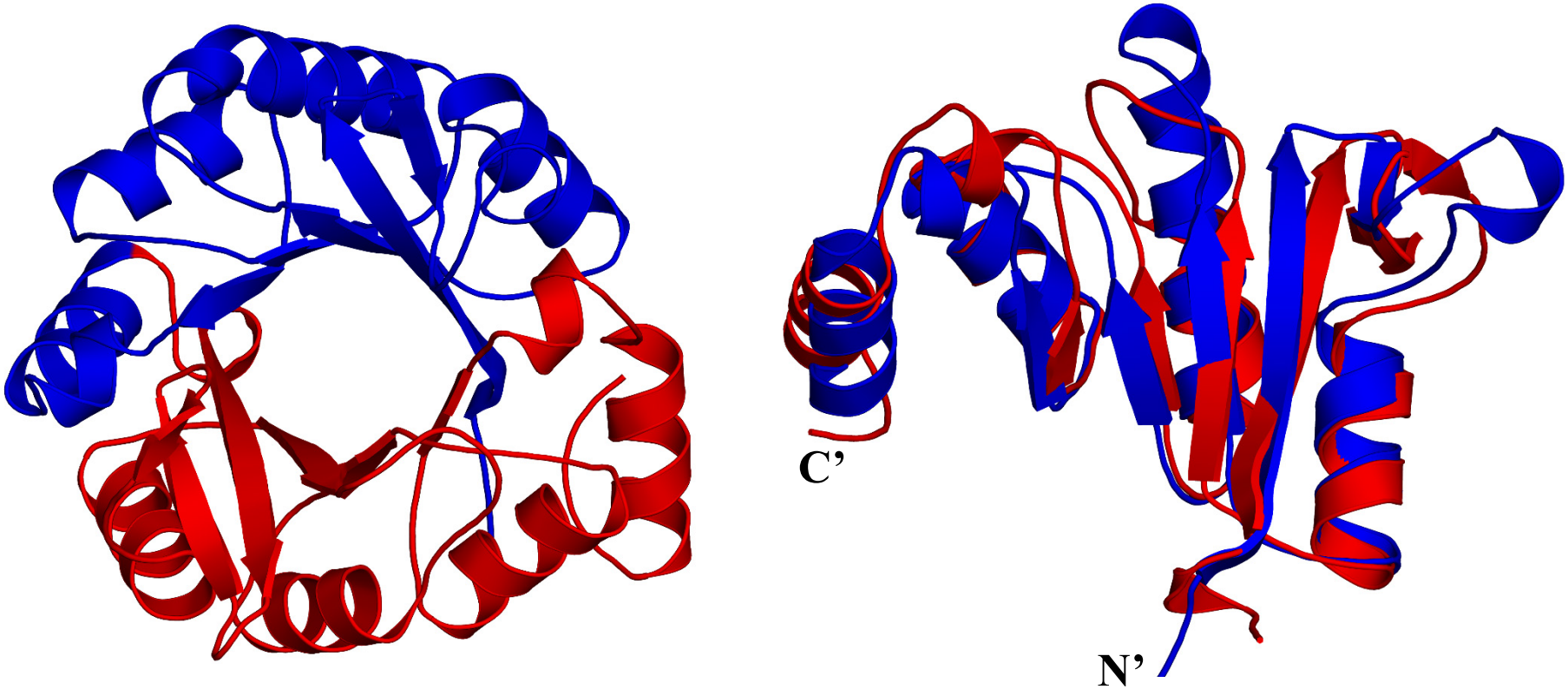


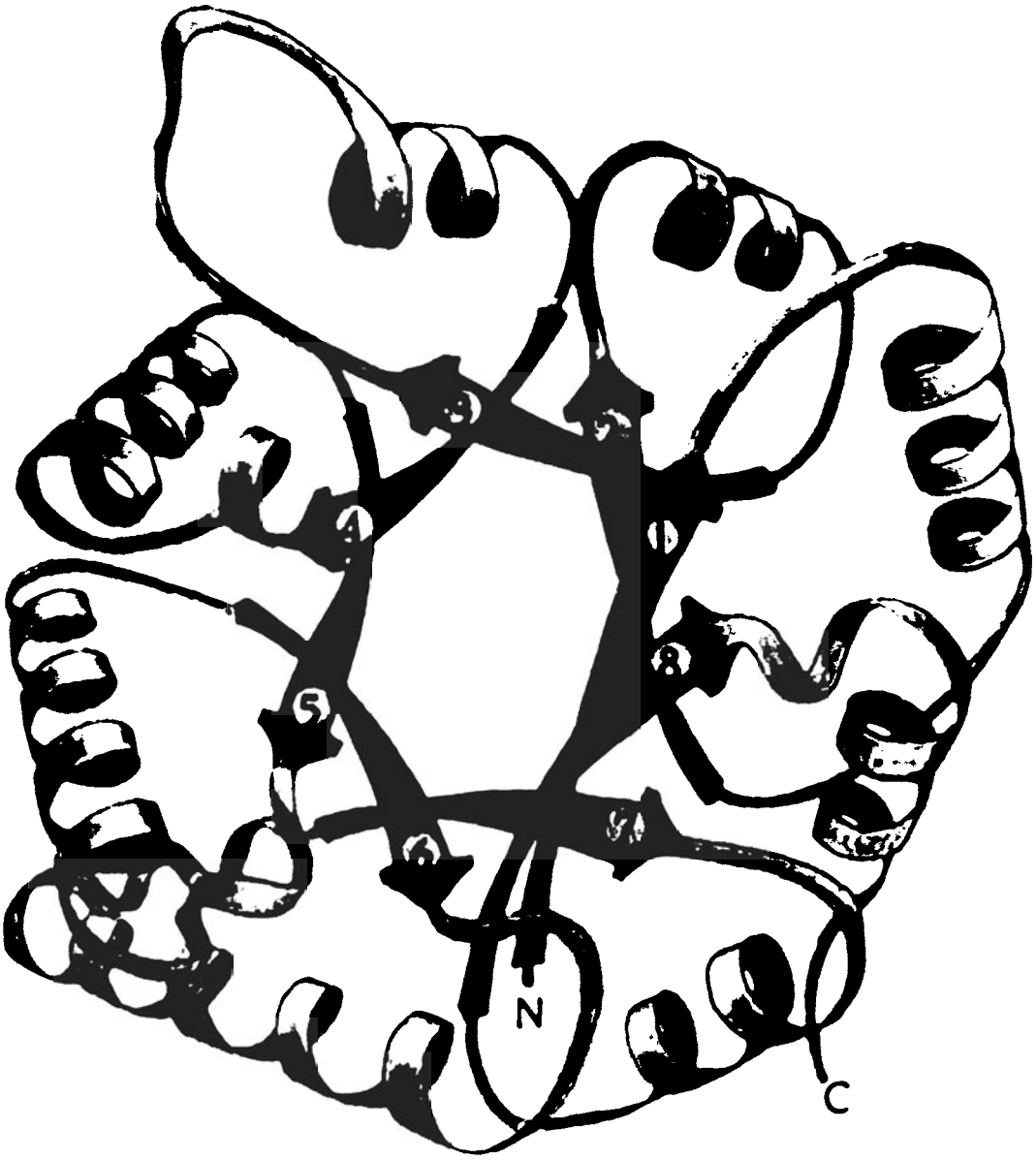
P-loop

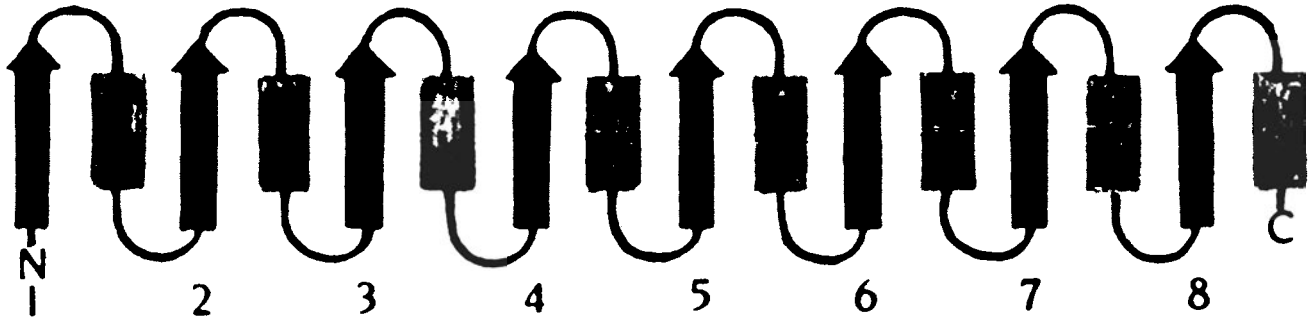
Rossmann Folds Have a Variety of Functions

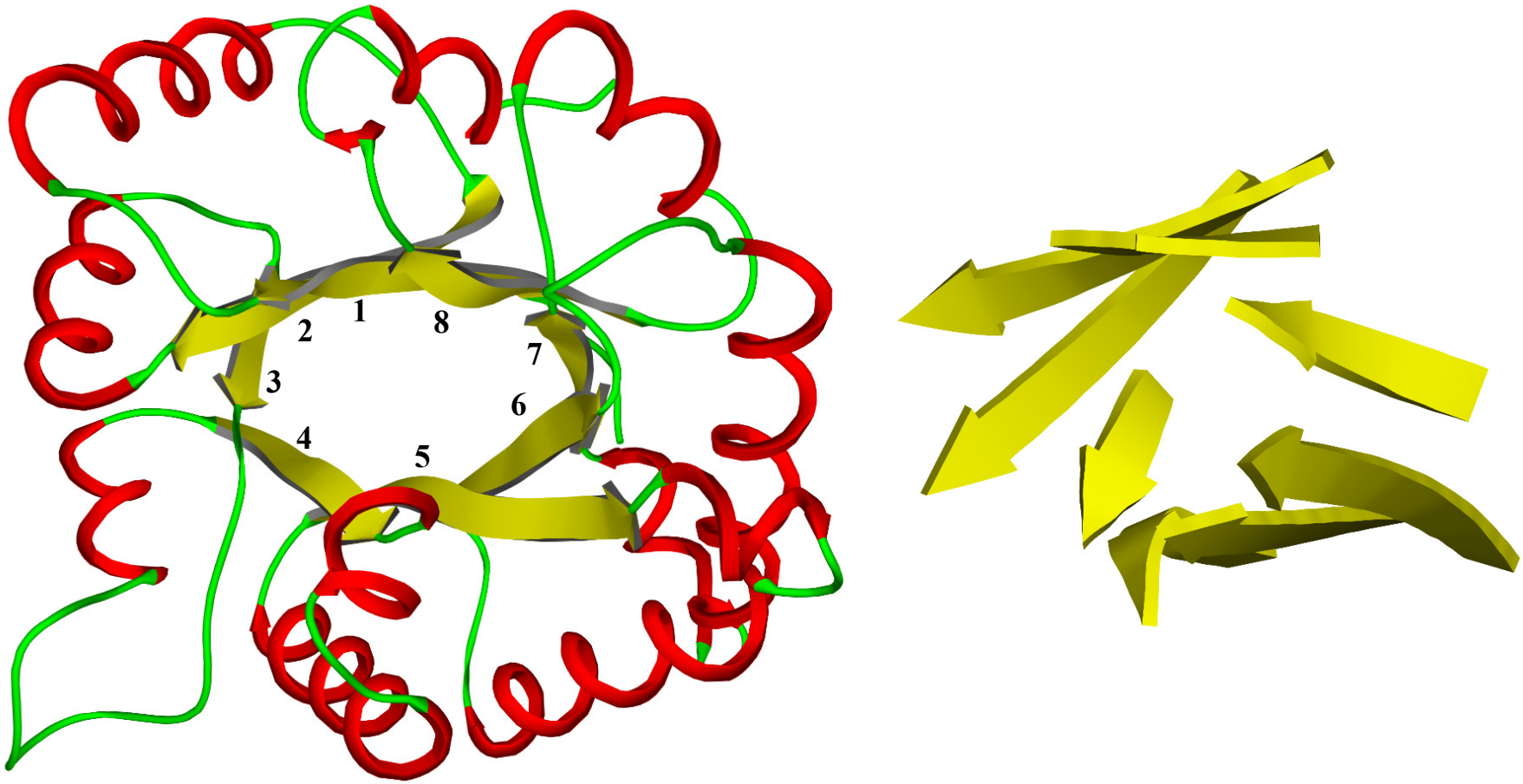


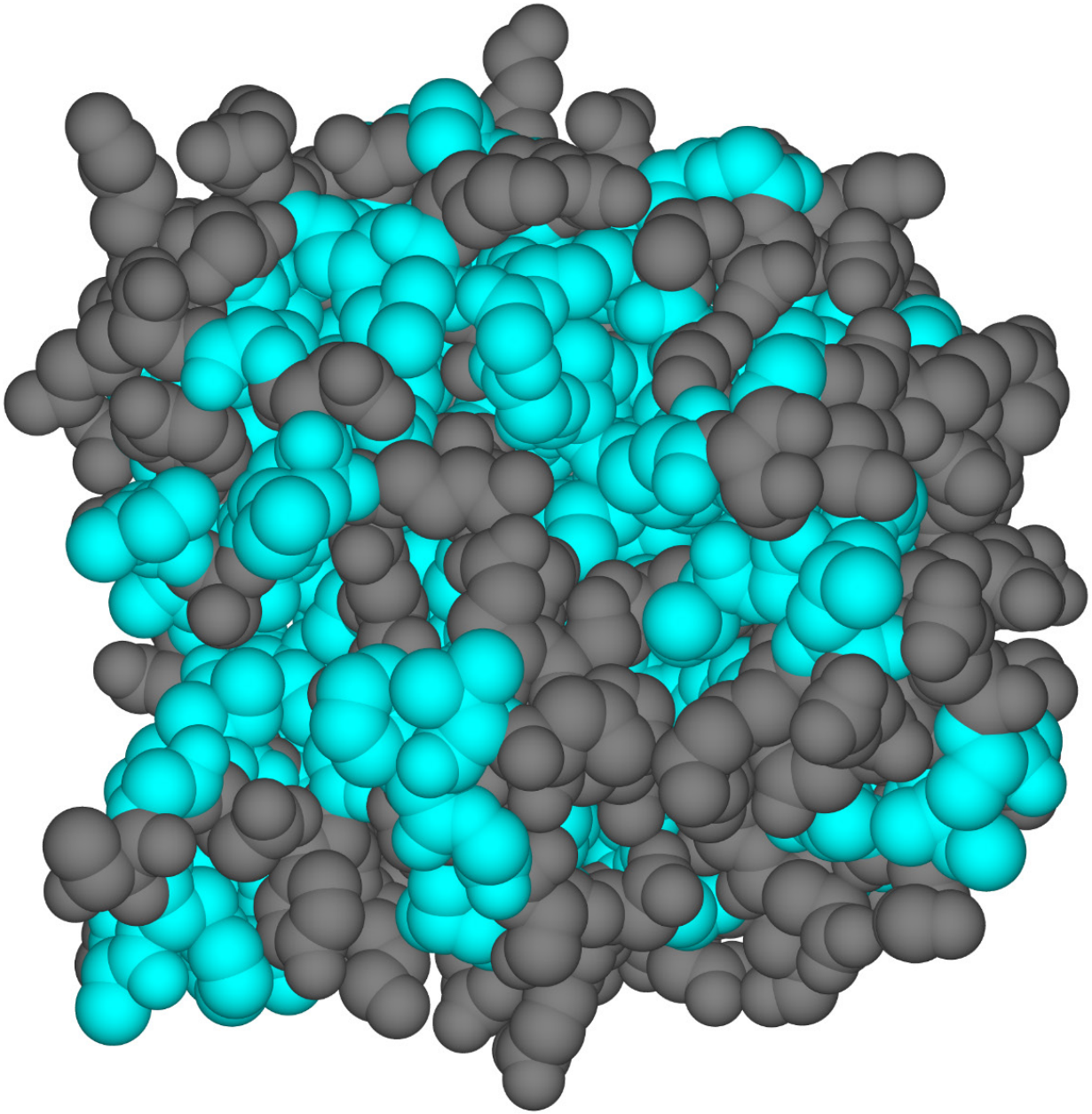

(a)
motif 1
motif 2
α1,2
α2,3
α3,4
C
N
β1
β2
β3
β4
1
N
2
3
C
4
(b)
motif 2
motif 1
crevice
α3,4
α1,2
α2,3
C
N
β4
β3
β1
β2
C
4
3
1
N
2

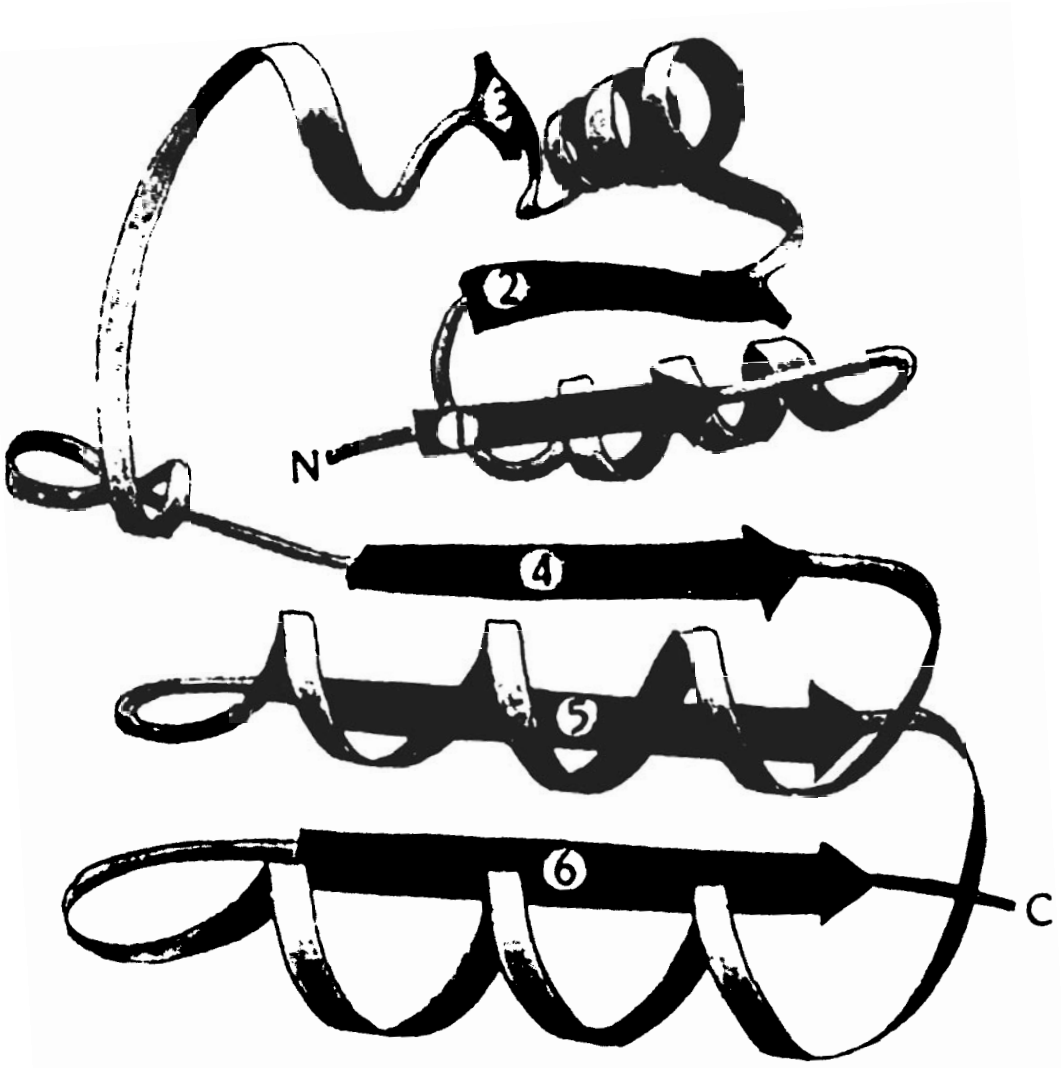

C’
N’

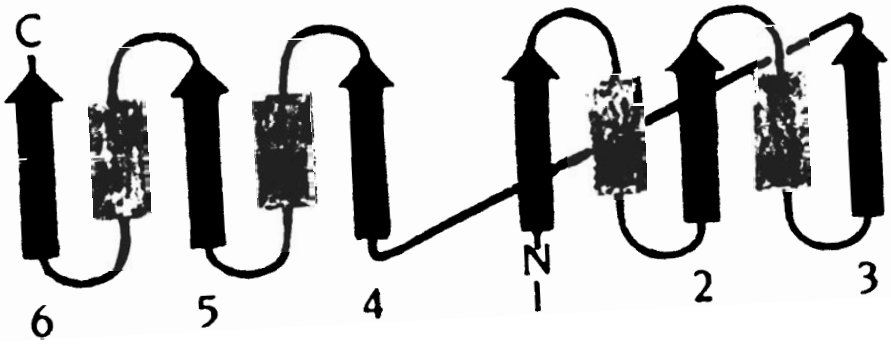

N
C

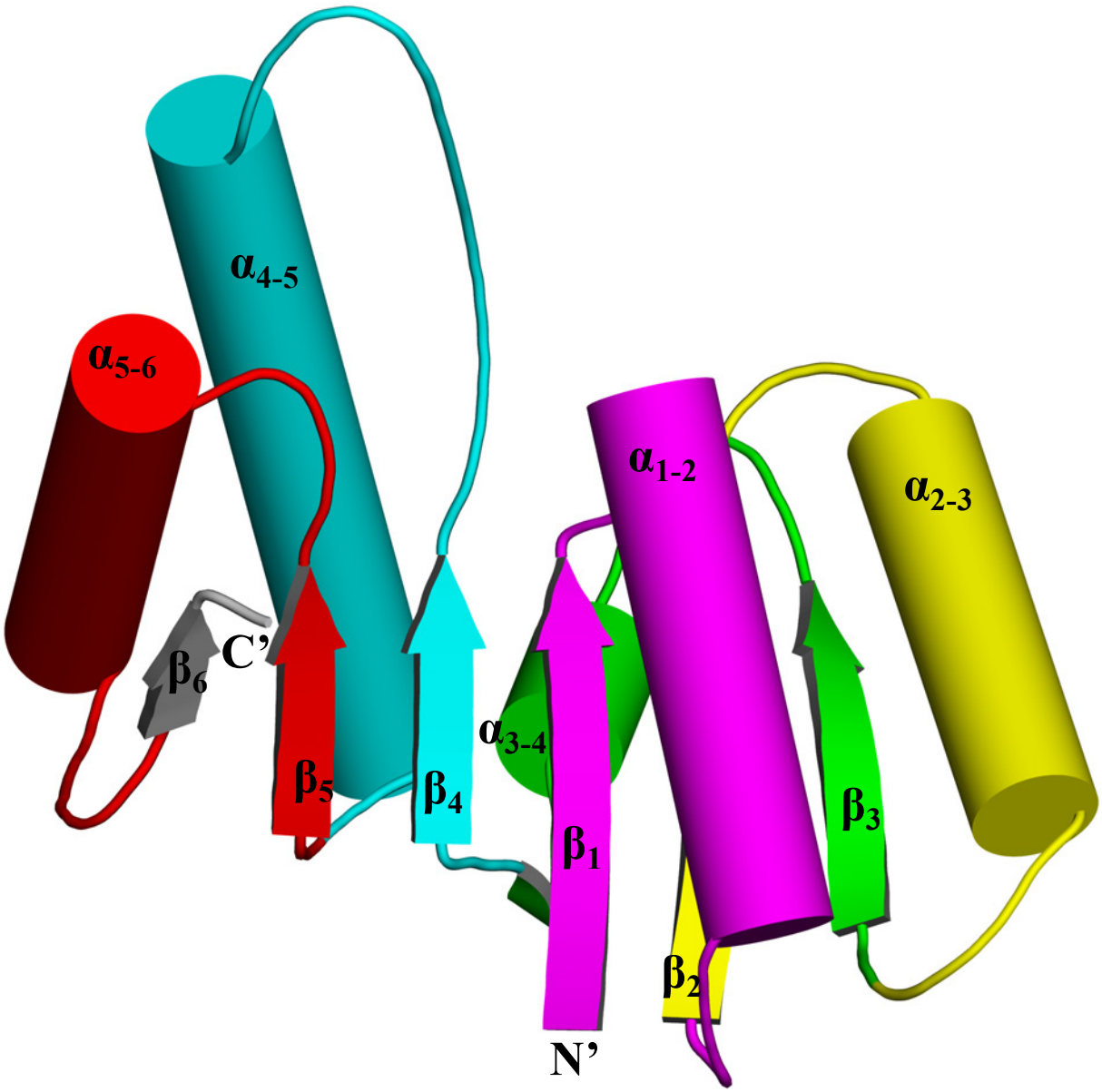

N
C
1
2
3
4
5
6
7
8


1
2
3
4
5
6
7
8

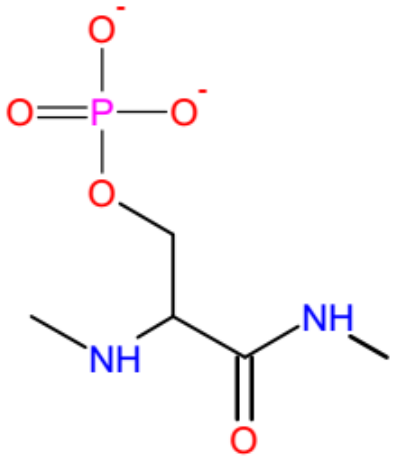



3
2
N
4
5
6
C

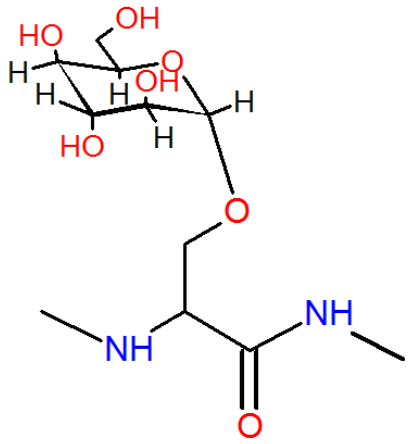

C
N
6
5
4
1
2
3


α4-5
α5-6
α1-2
α2-3
β6
C'
β5
β4
α3-4
β1
β3
β2
N'

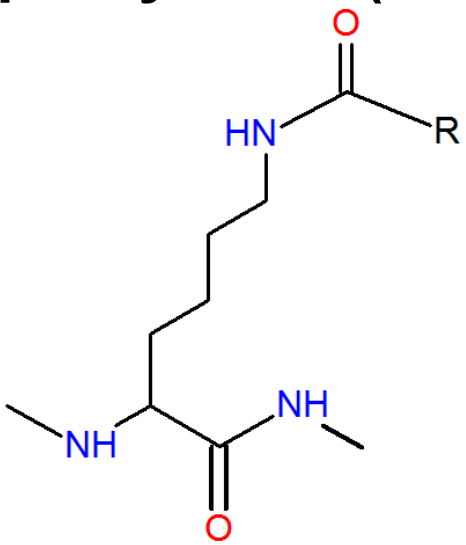
Proteins Contain Various Modifications



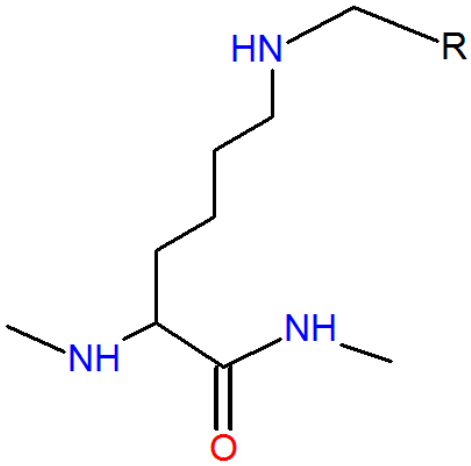
Phosphorylation (Ser/Thr/Tyr)



***O*-glycosylation (Ser/Thr)**



***N*-acylation (Lys)**



***N*-alkylation (Lys)**