Lipids and Membrane Proteins

Biophysical Chemistry 1, Fall 2010

Fundamentals of lipid/membrane structure

Fundamentals of membrane protein structure

Channels and pores

Reading assignment: Chaps. 4 & 10

Back to the cell:

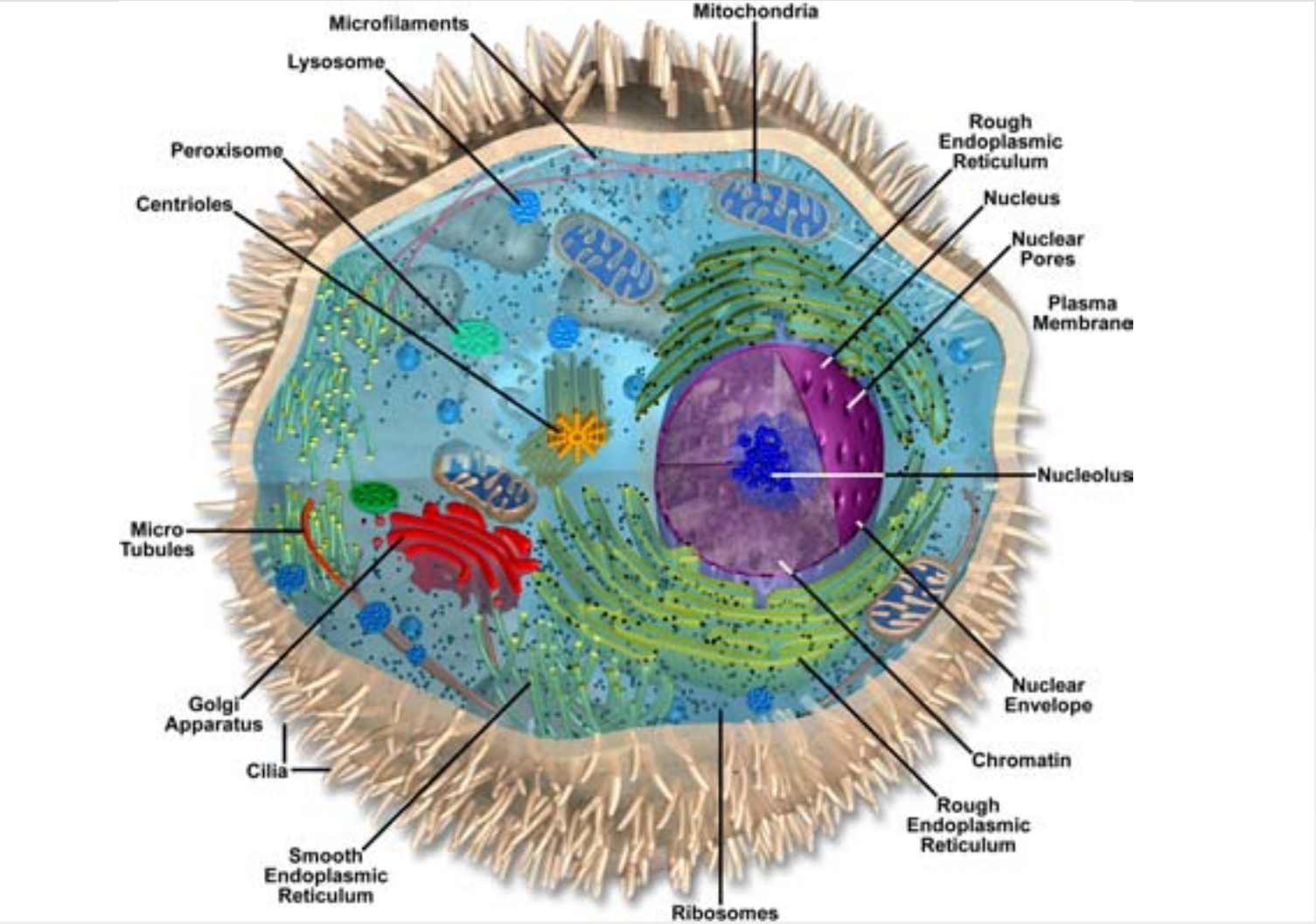


FIGURE 1.3 ■ A schematic picture of an animal cell showing sub-cellular structures, such as nucleus, membrane systems (ER), mitochondrion, etc. (Made by Michael W. Davidson, Florida State University.)

Basic chemistry of lipids

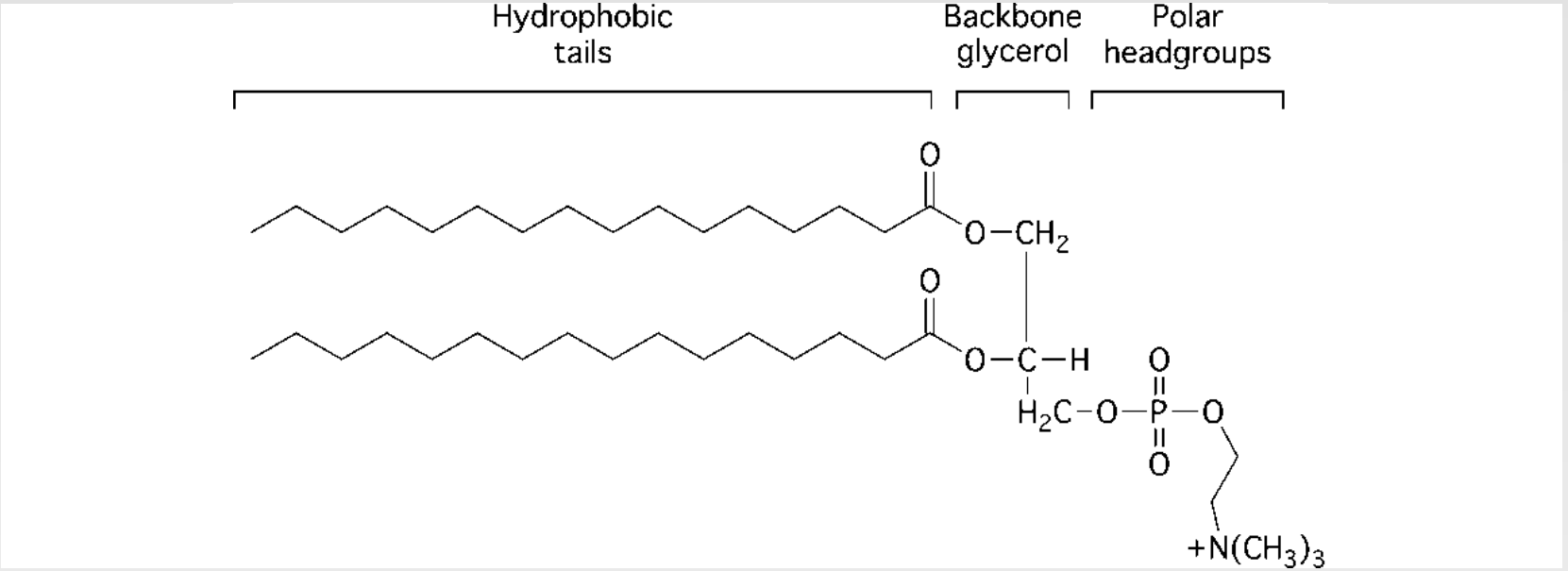
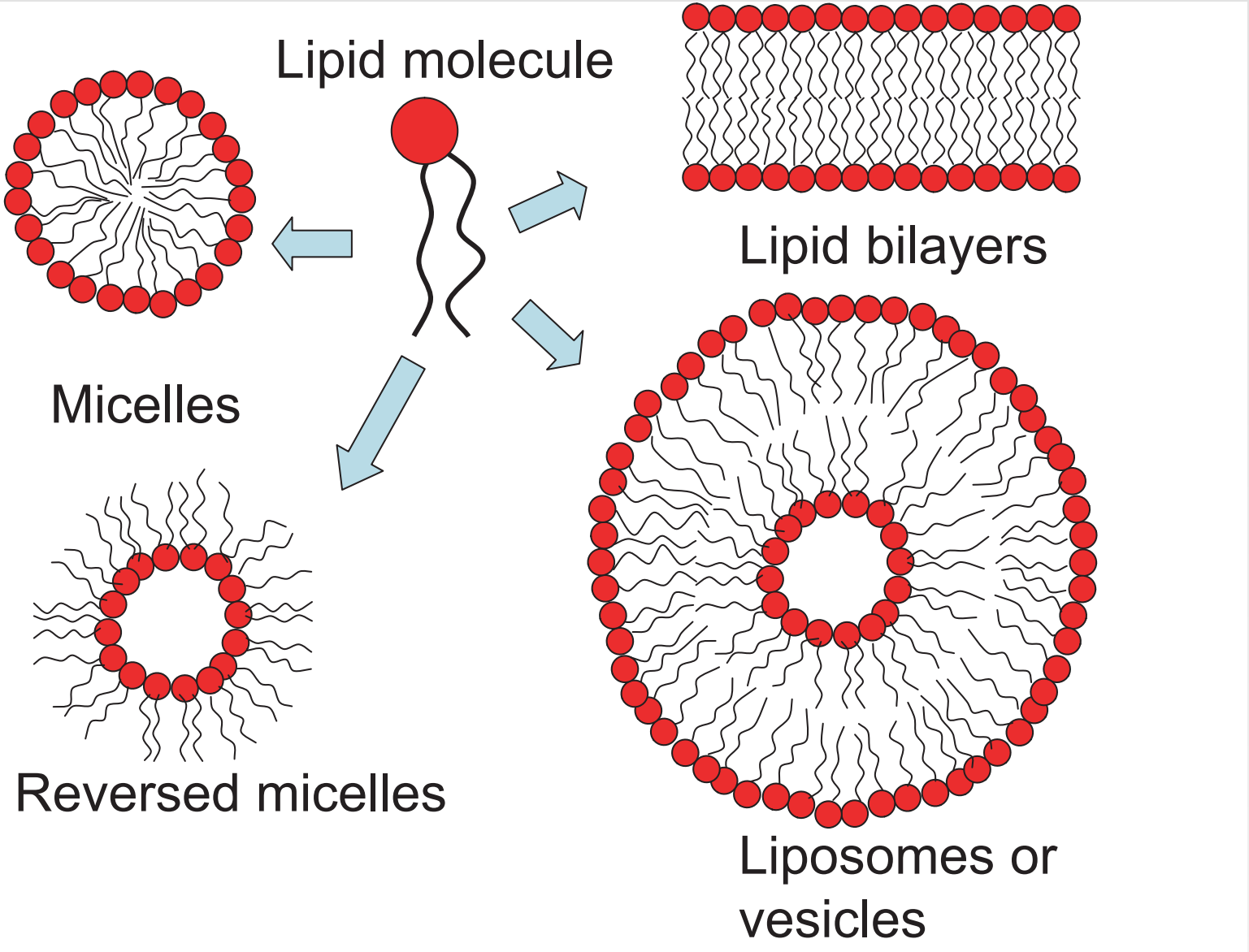
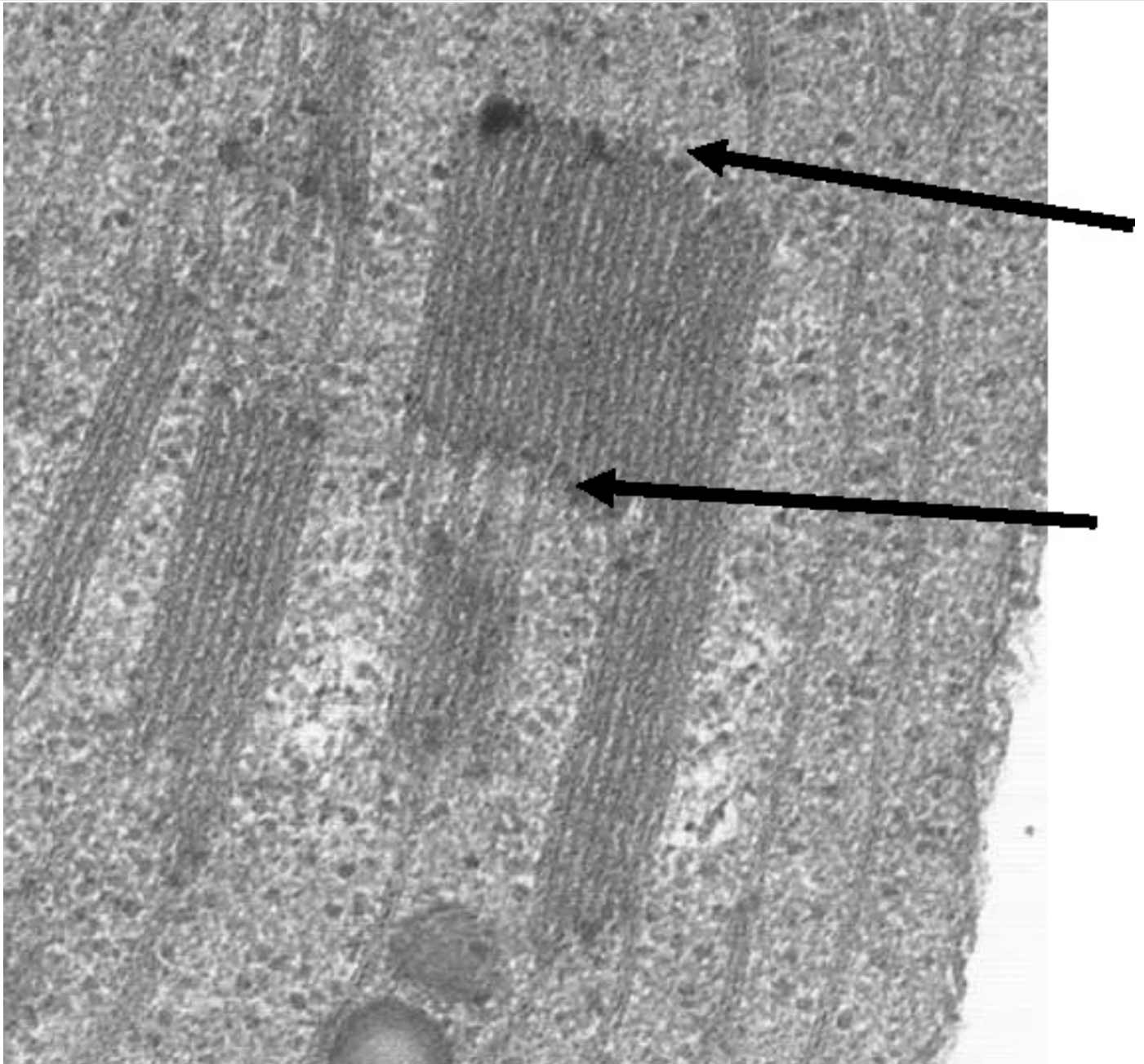


FIGURE 4.10 ■ As an example of a typical lipid, the figure shows a phospholipid (phosphatidylcholine, PC, often called lecithin). Its amphiphilic character is seen by the hydrophobic hydrocarbon acyl chains (tails) and the hydrophilic polar head group connected by the backbone, in this case glycerol.

Lipids self-assemble...



....and make complex membranes:



Controlling the amount of unsaturation

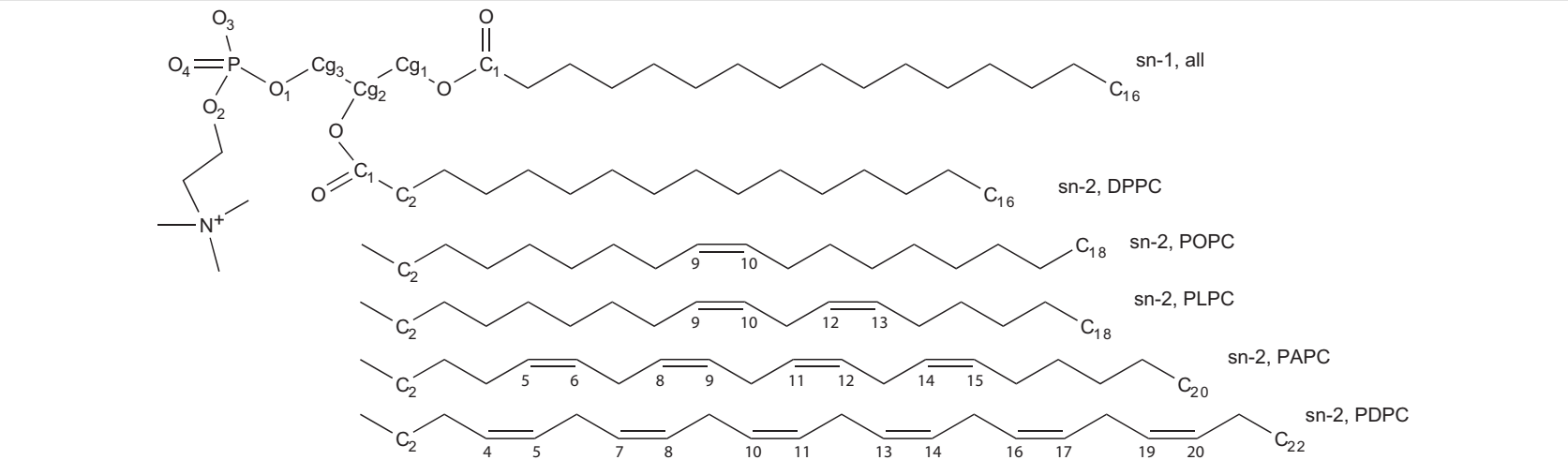


FIGURE 4.5 ■ Phosphatidylcholine with some of the most common fatty acyl chains. DPPC stands for dipalmitoyl-PC; POPC for palmitoyloleoyl-PC; PLPC for palmitoyllinoleoyl-PC; PAPC for palmitoylarachidonyl-PC; and PDPC for palmitoyldocosahexaenoyl-PC.

Lipid phase diagrams

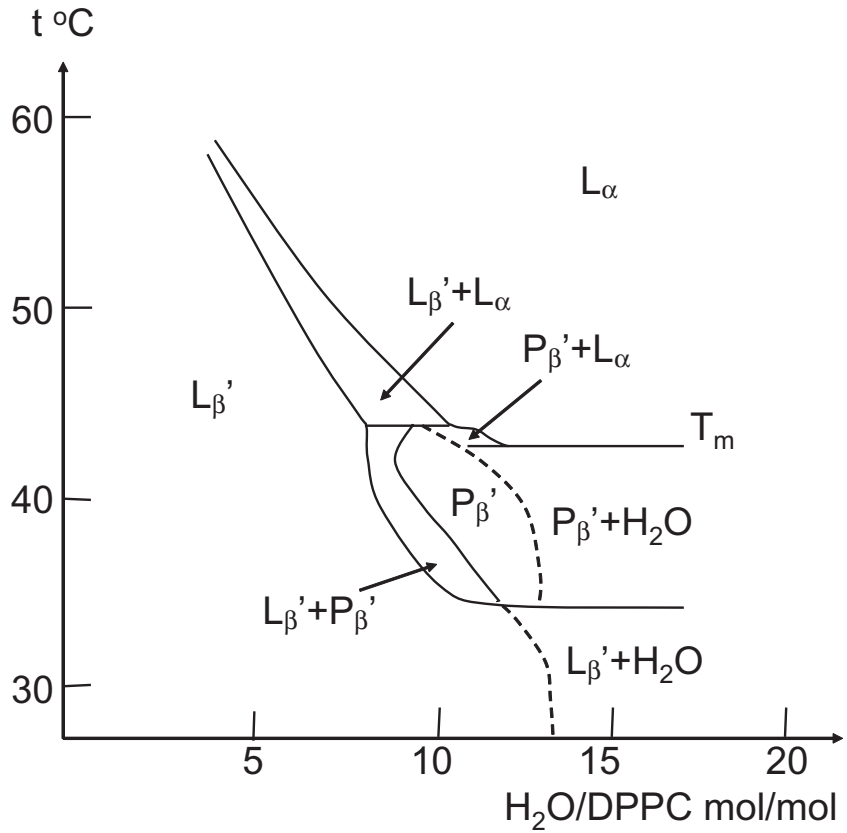
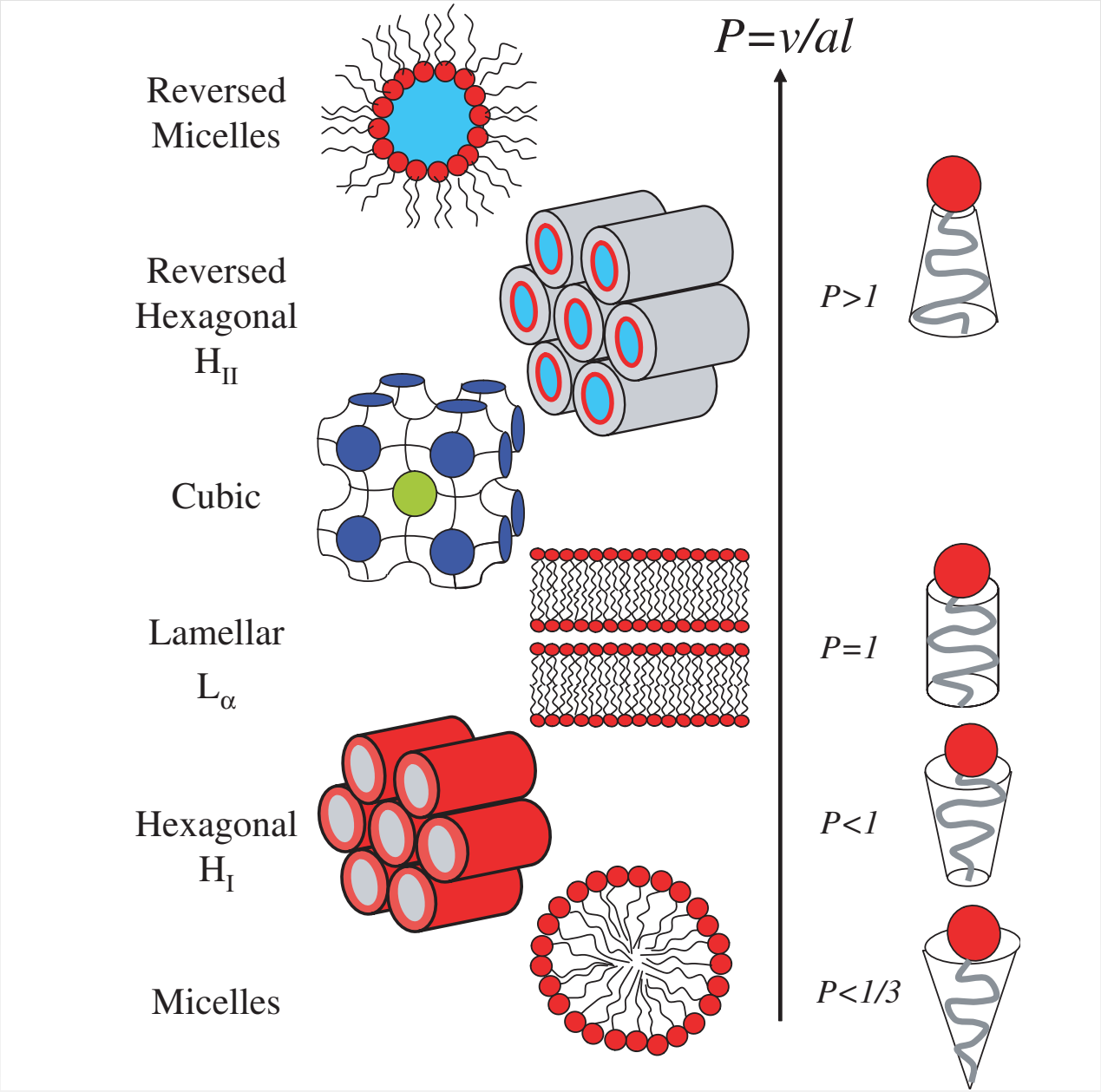
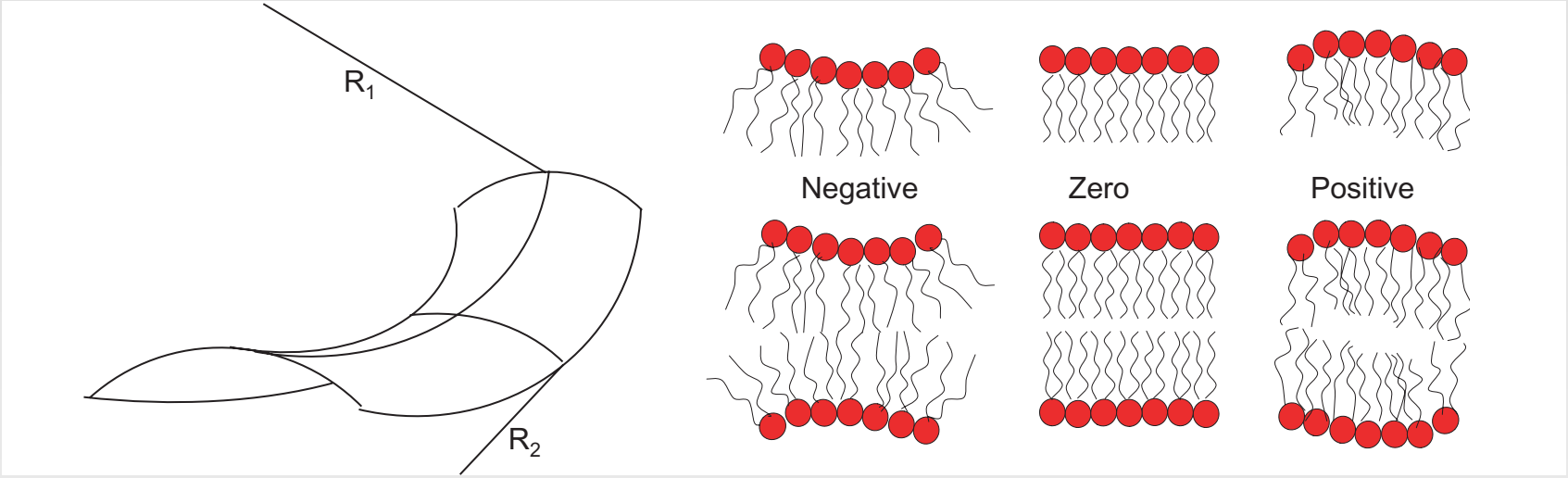


FIGURE 4.7 ■ A partial phase diagram of DPPC and water. At low temperature the gel, $L_{\beta'}$, phase is formed and at high temperature and relatively high water content, a lamellar liquid crystalline, $L_{\alpha'}$ phase is stable. In the middle of the phase diagram the ripple $P_{\beta'}$ phase is stable in a narrow region of temperature and water content. (Adapted with permission from Ulmius J, Wennerström H, Lindblom G, Arvidson G. (1977) Deuteron NMR studies of phase equilibria in a lecithin-water system. *Biochemistry* **16**: 5742–5745. Copyright (1997) American Chemical Society.)

Types of structures



Lamellar (membrane) phases have curvature



Lipid packing and lateral pressure

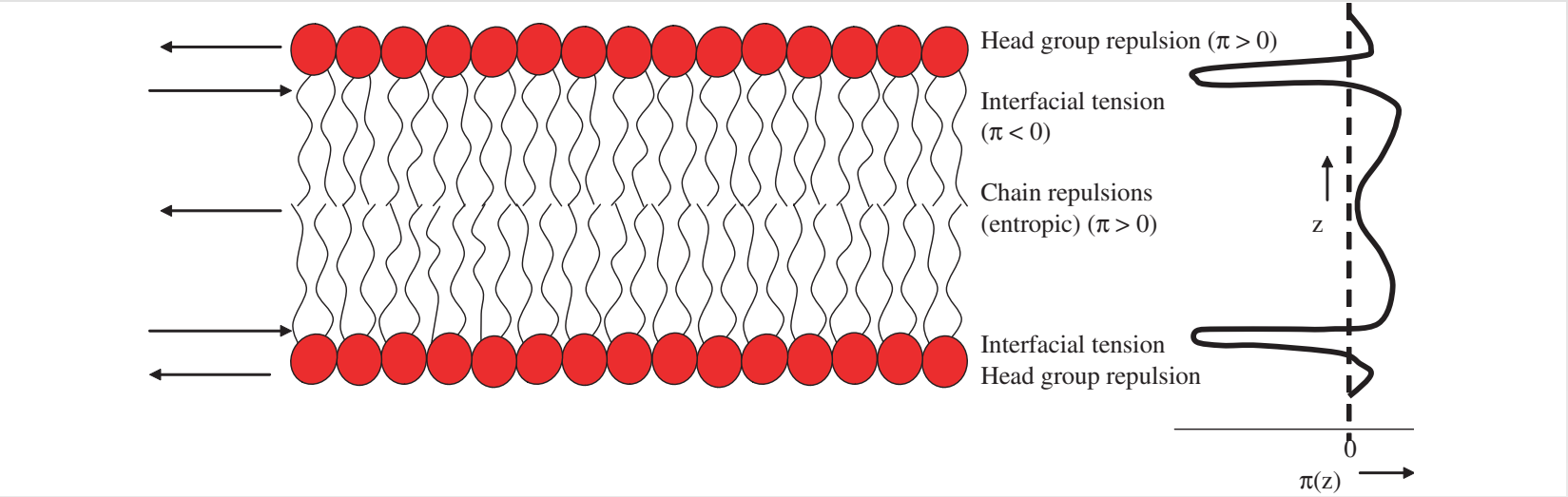
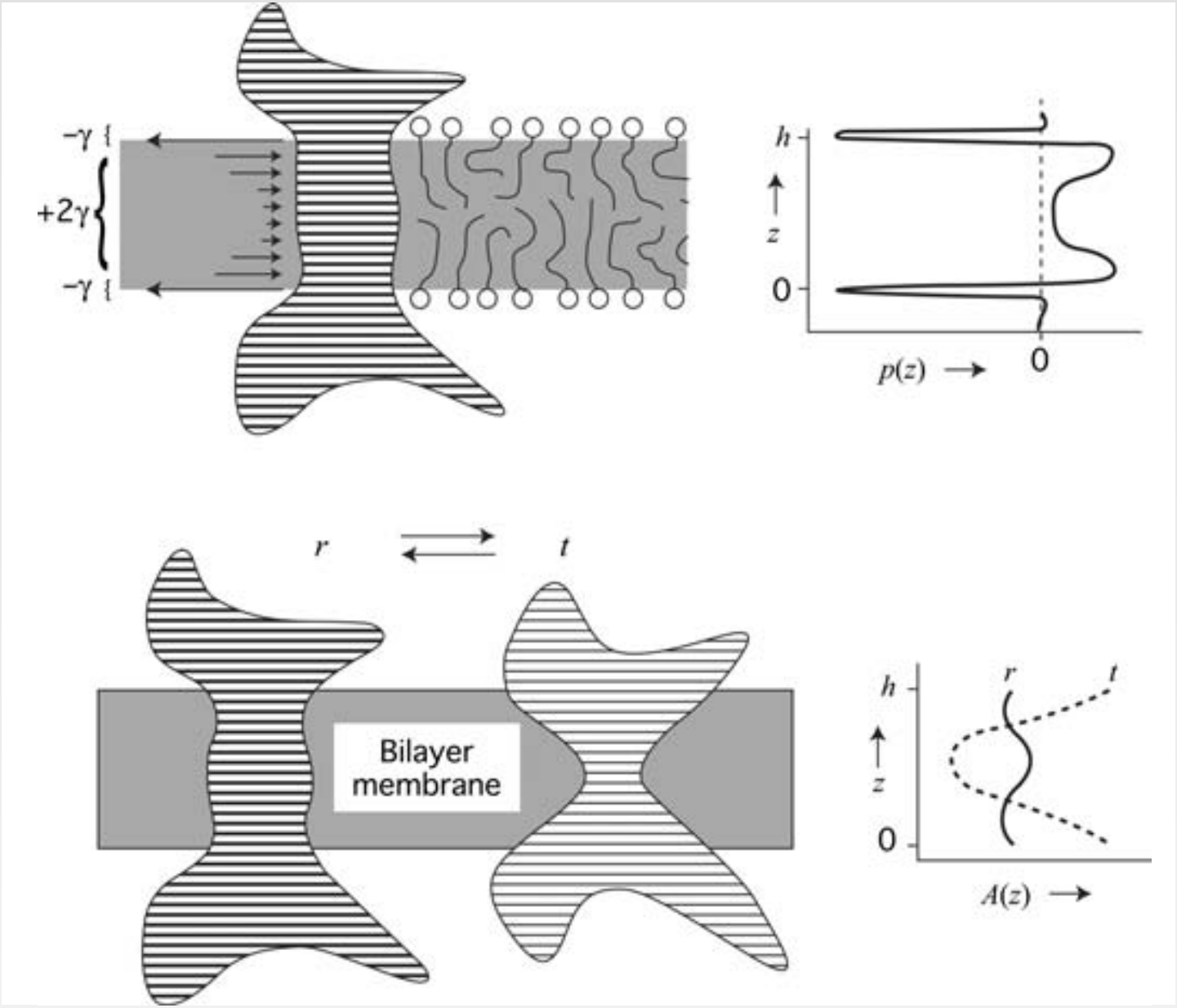
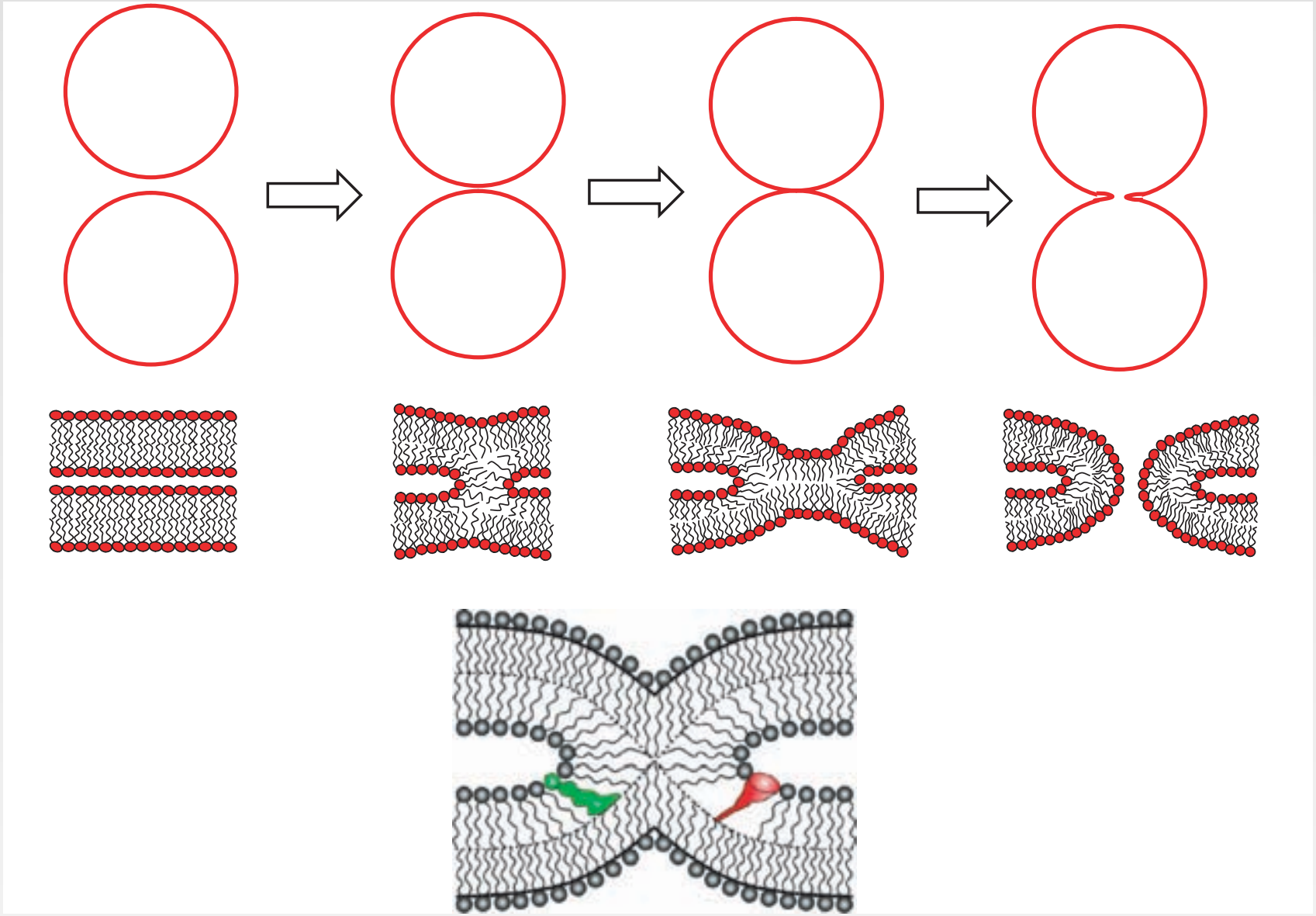


FIGURE 4.17 ■ Illustration of the lateral pressure, $p(z)$, profile in a lipid bilayer. A coordinate system, z, along the normal to lipid bilayer, showing the pressure distribution across the bilayer is schematically indicated to the right. The lateral pressure in the middle of the bilayer can be very high. However, the total pressure over the bilayer is zero. (Courtesy of Ole Mouritsen.)

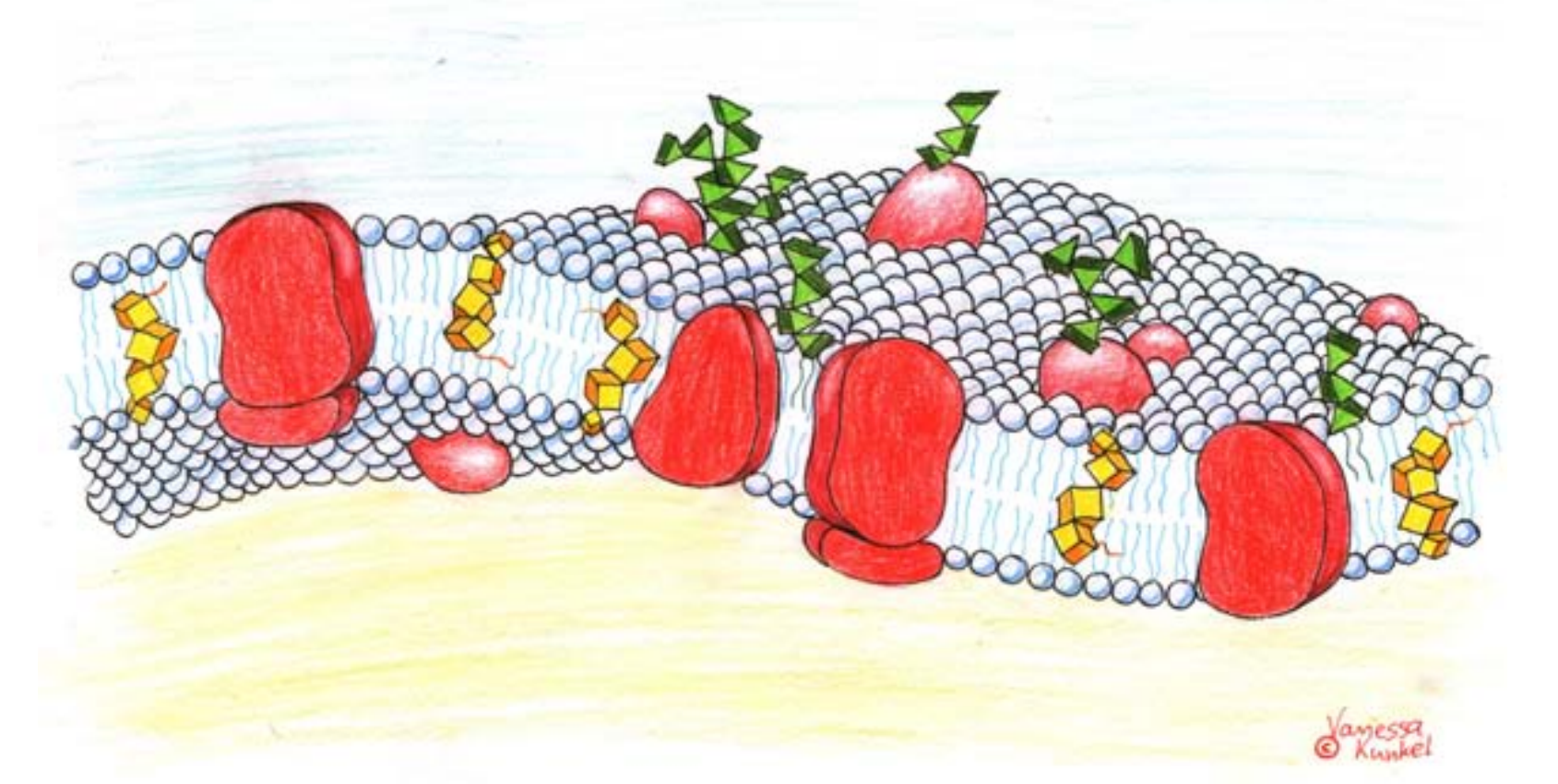
Pressure and conformation



Membrane fusion



Lipid domains and rafts



Basic classification scheme for membrane proteins

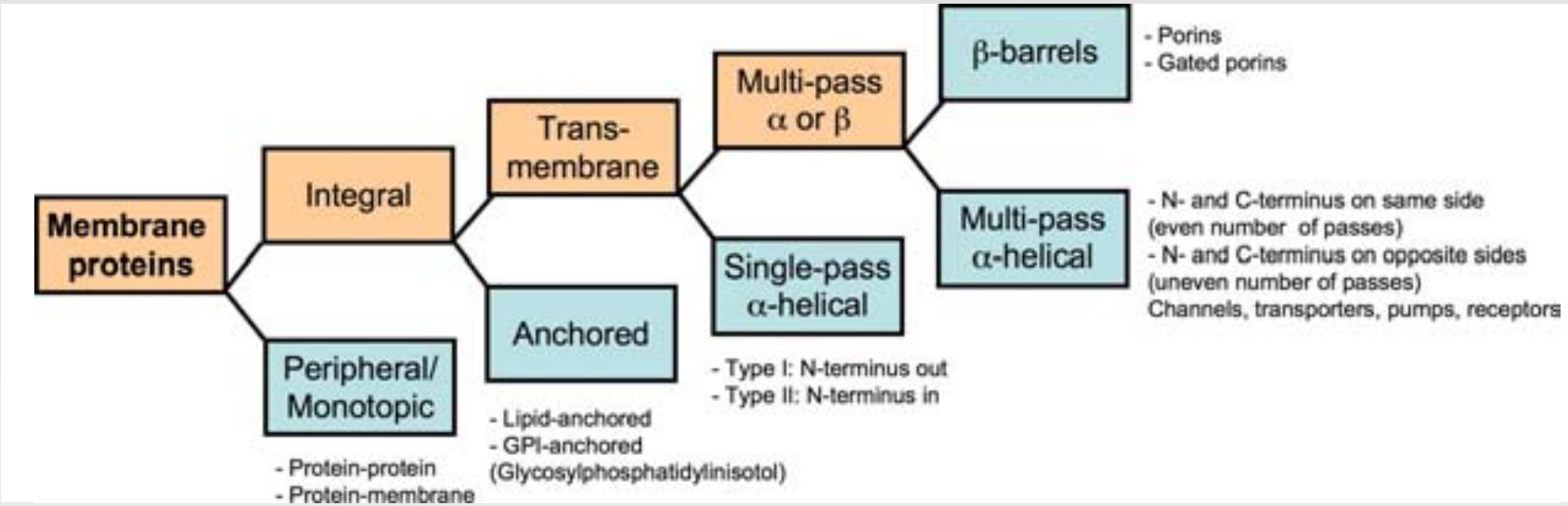


FIGURE 10.1 ■ Different categories of membrane proteins.

What we knew 5-10 years ago

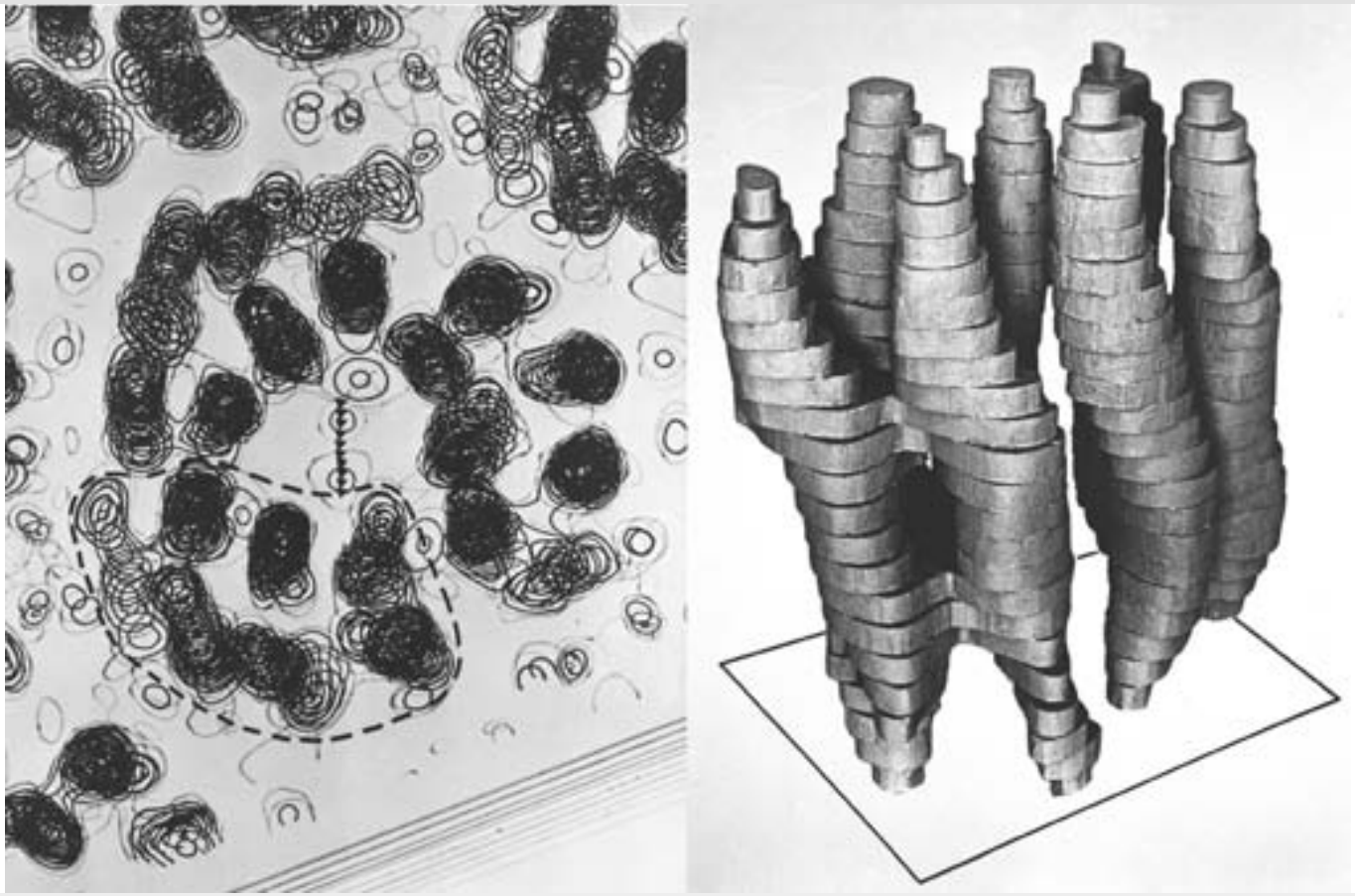


FIGURE 10.2 ■ Projection map (*left*) and 3D reconstruction from tilt series (*right*) of bacteriorhodopsin as derived by Henderson and Unwin in 1975 using electron microscopy on 2D crystals of "purple membranes." (Reprinted with permission from Henderson R, Unwin PNT. (1975) Three-dimensional model of purple membrane obtained by electron microscopy. *Nature* **257**: 28–32. Copyright (1975) Nature.)

Seven transmembrane helices

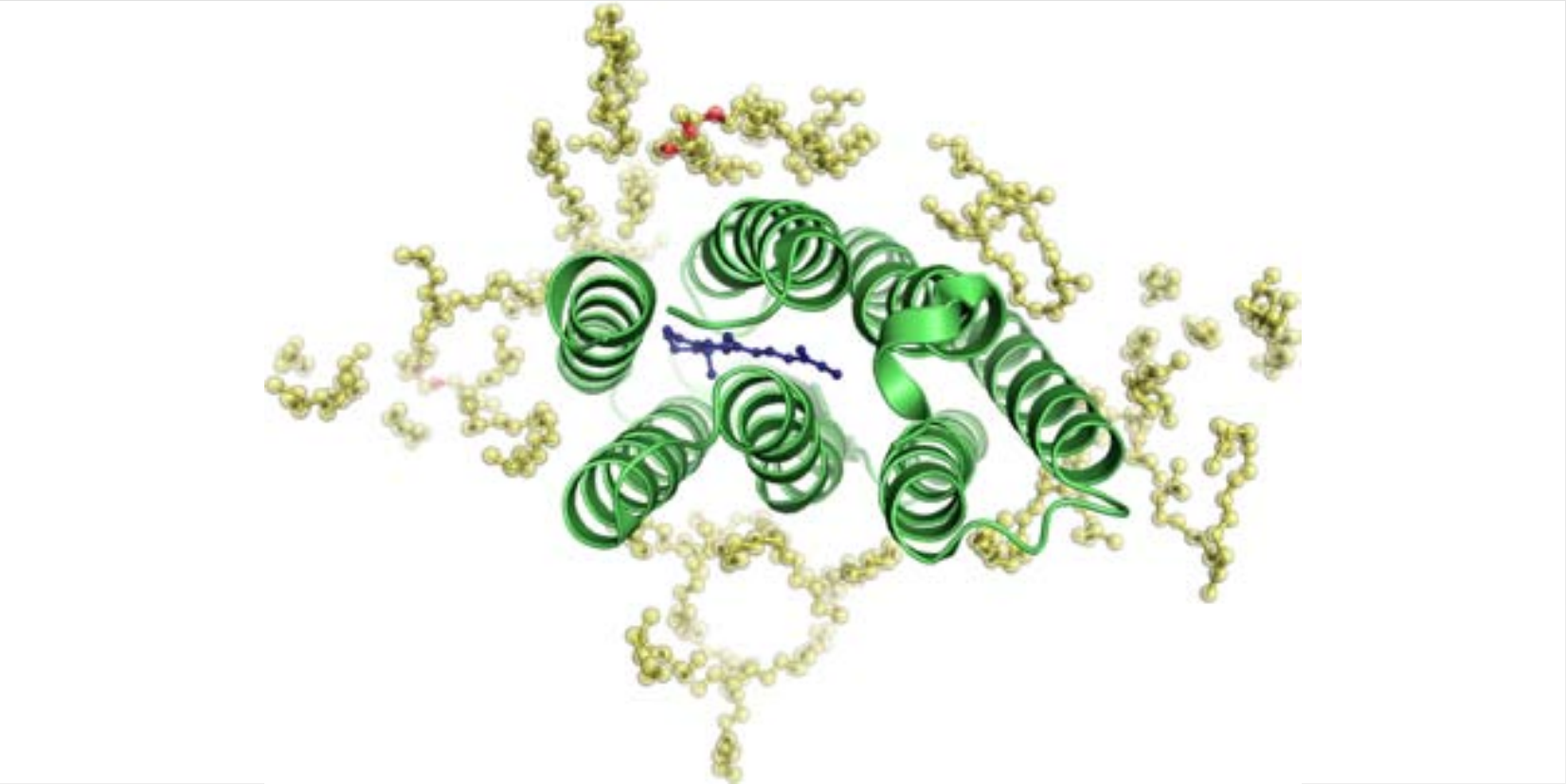
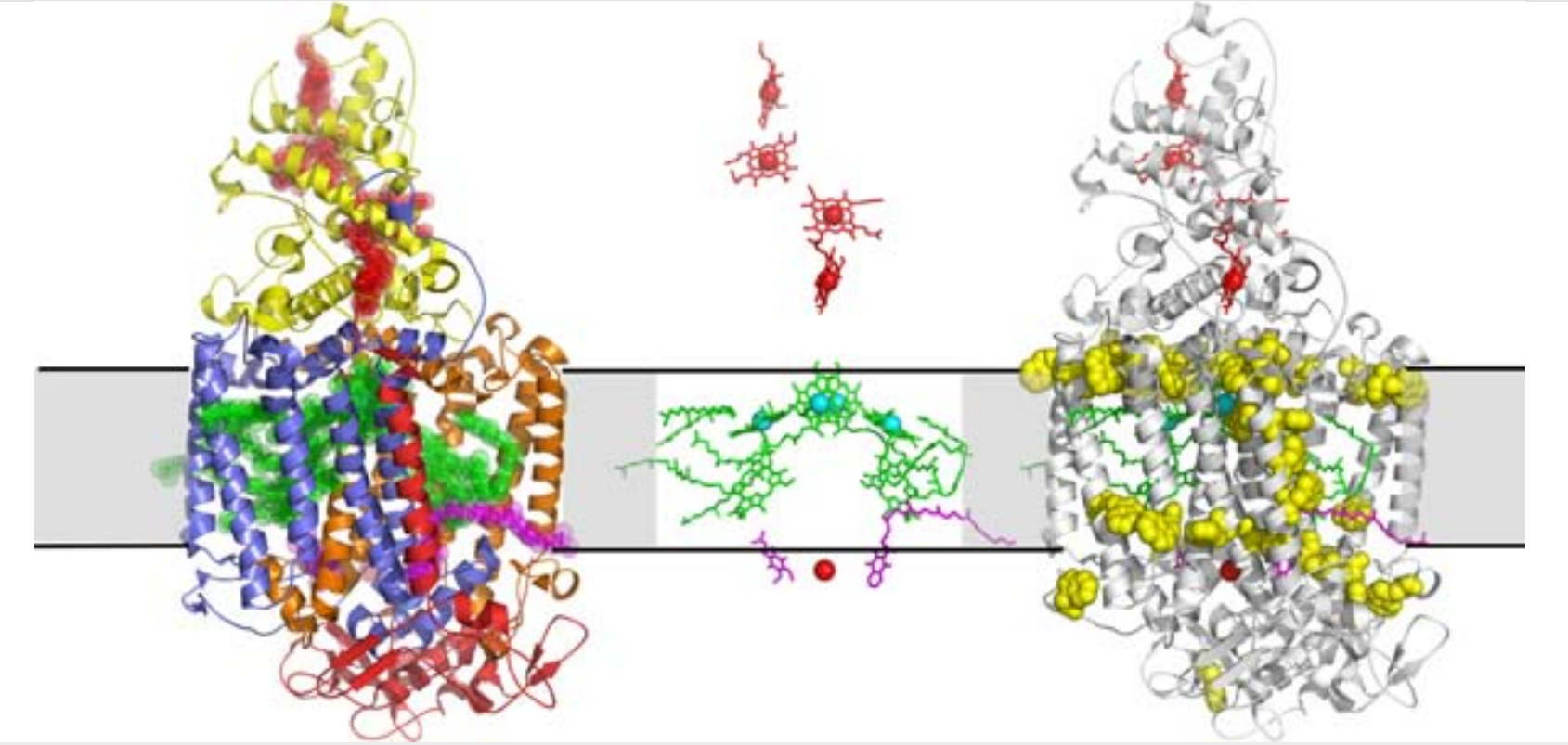
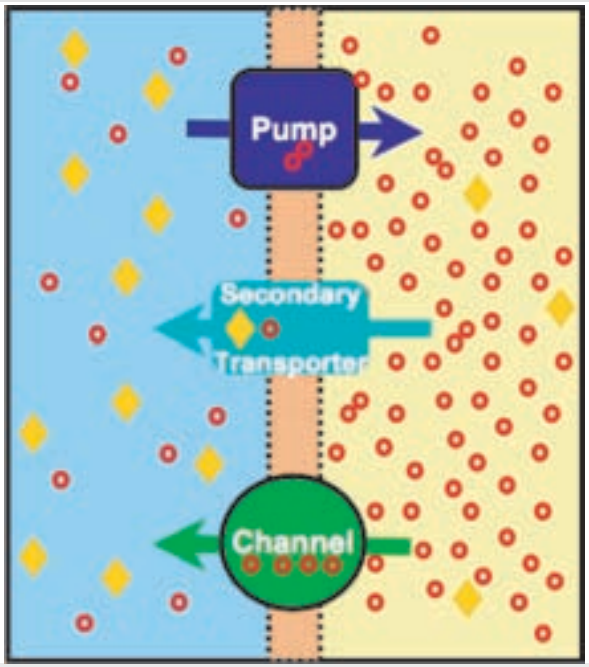


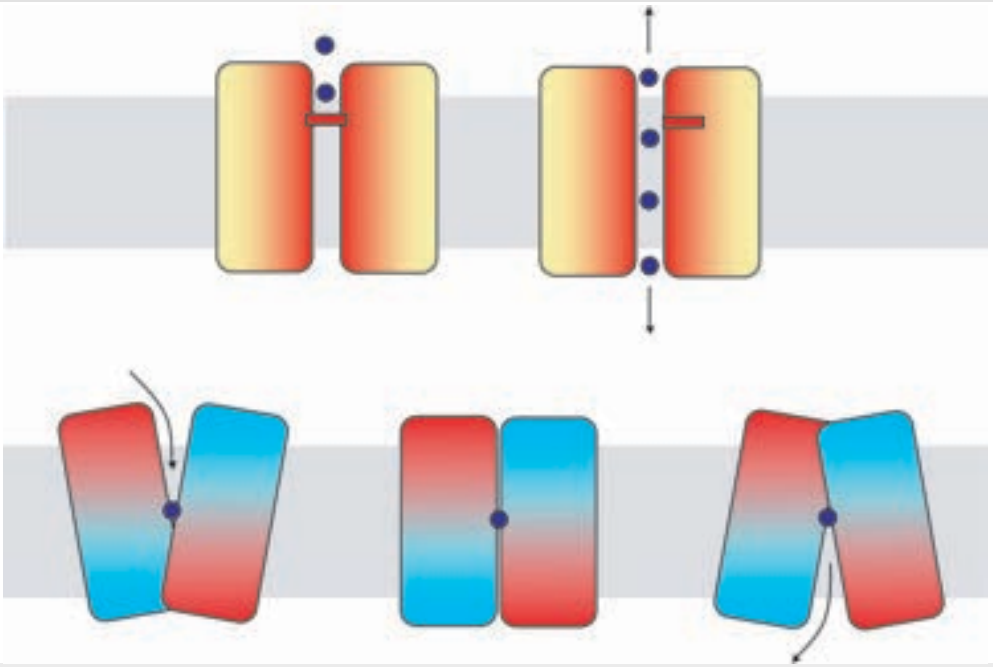
FIGURE 10.6 ■ Lipid molecules surrounding the structure of bacteriorhodopsin. The structure gives a nearly complete view of the lipidation of a membrane protein and is a basis for understanding the complex nature of protein-lipid-water interfaces. The retinal molecule is shown in blue and the lipids are in yellow (carbon atoms) and red (oxygen atoms) (PDB: 1C3W, 1QJH).

The photosynthetic reaction center



Pumps, transporters, and channels





Some nomenclature

- Channels
- Transporters
  - primary transporters (pumps) create gradients
  - secondary transporters use existing gradients
- Coupled transport
  - symporters take to species (often ions) in the same direction (sodium/glucose transport)
  - antiporters (exchangers) allow ions to exchange (e.g. sodium/calcium exchanger)
- Signal transduction (mostly G-protein coupled receptors)

β-barrel channels; porins

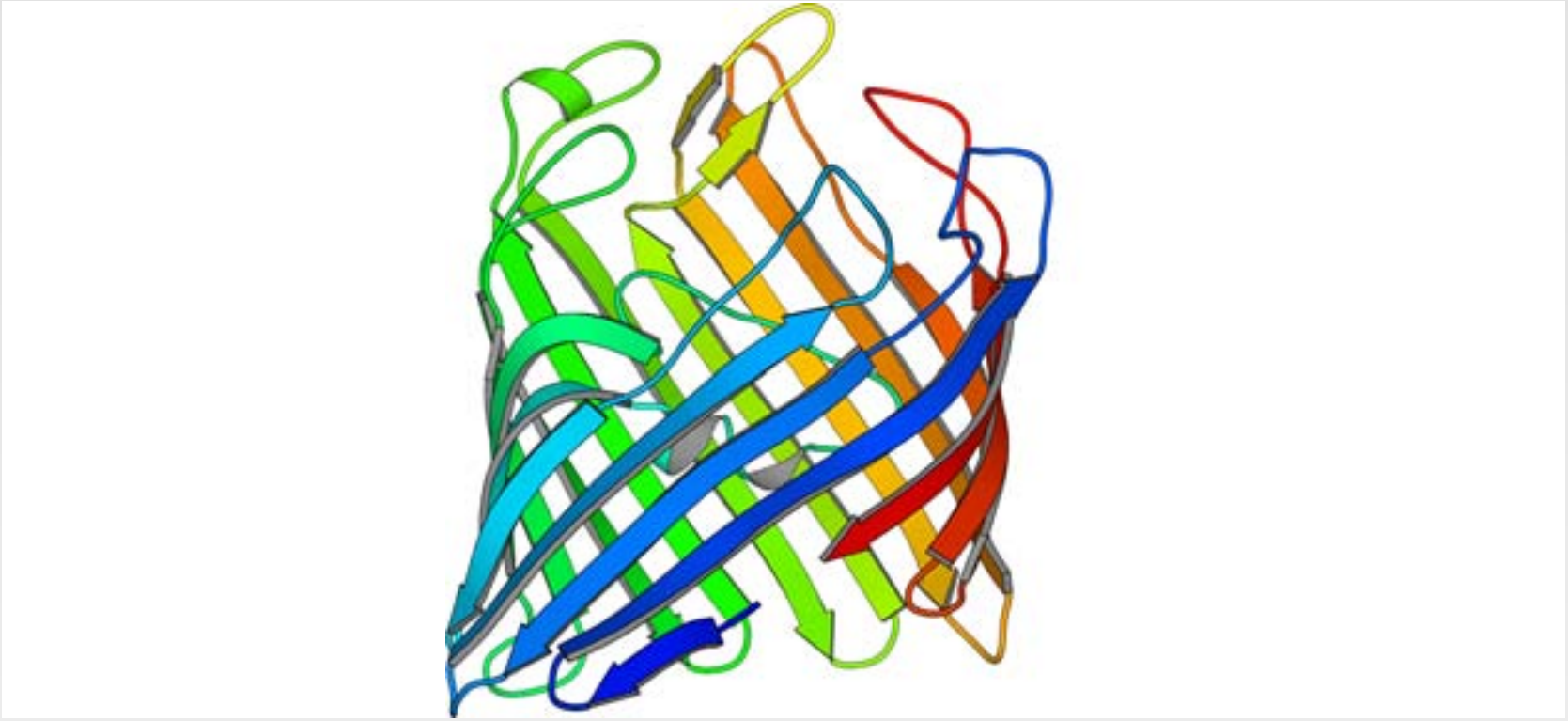


FIGURE 10.4 ■ The structure of the bacterial outer membrane protein porin, subsequently named OmpF, showing a transmembrane β-barrel structure (PDB: 2OMF).

The iron-citrate outer membrane transporter

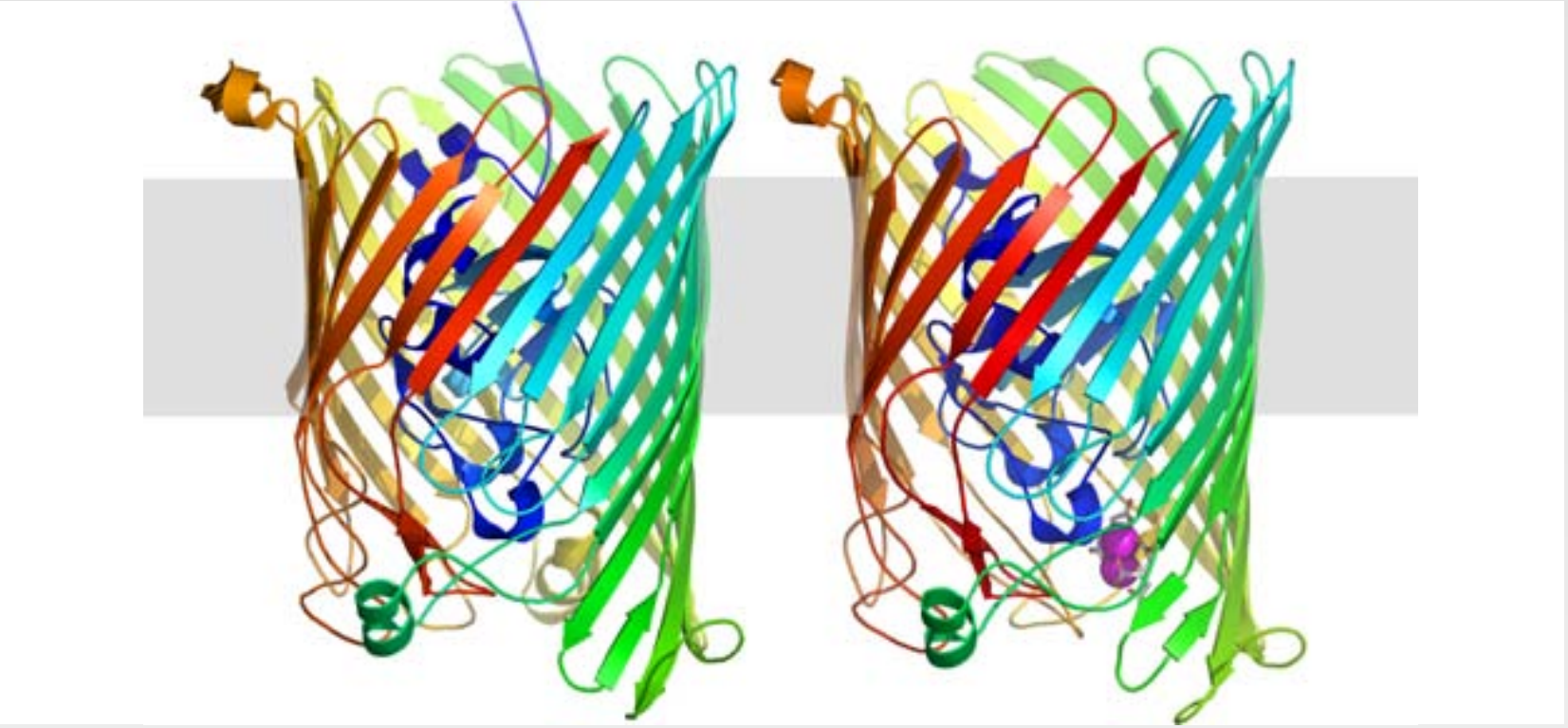


FIGURE 10.8 ■ The *E. coli* FecA iron-citrate outer membrane transporter (PDB: 1KMO, 1PO3) is based on a 22-stranded β-barrel structure (cyan to red spectrum) with an N-terminal domain (blue) plugged in the middle of the barrel that acts as a gating domain for two citrate-chelated Fe^{3+} ions (white sticks and magenta spheres in the substrate-bound complex to the *right*).

α vs. β secondary structure in channels

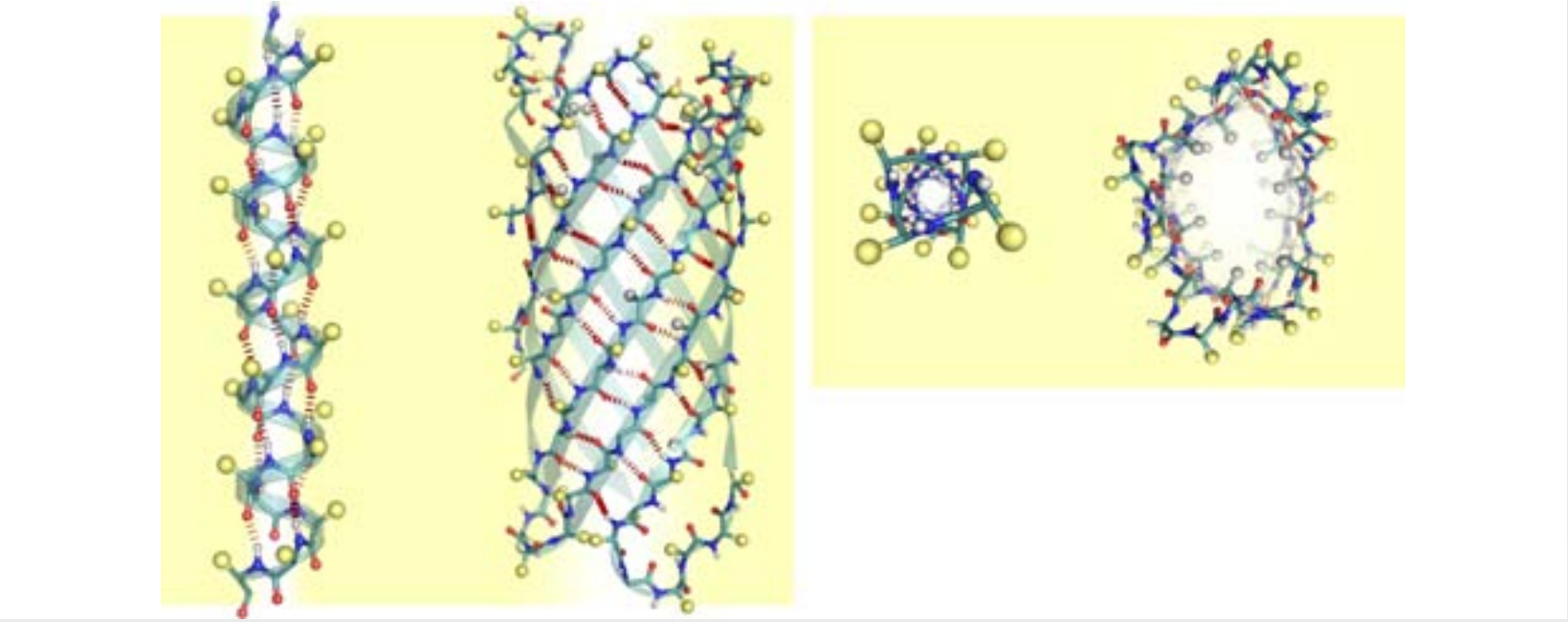
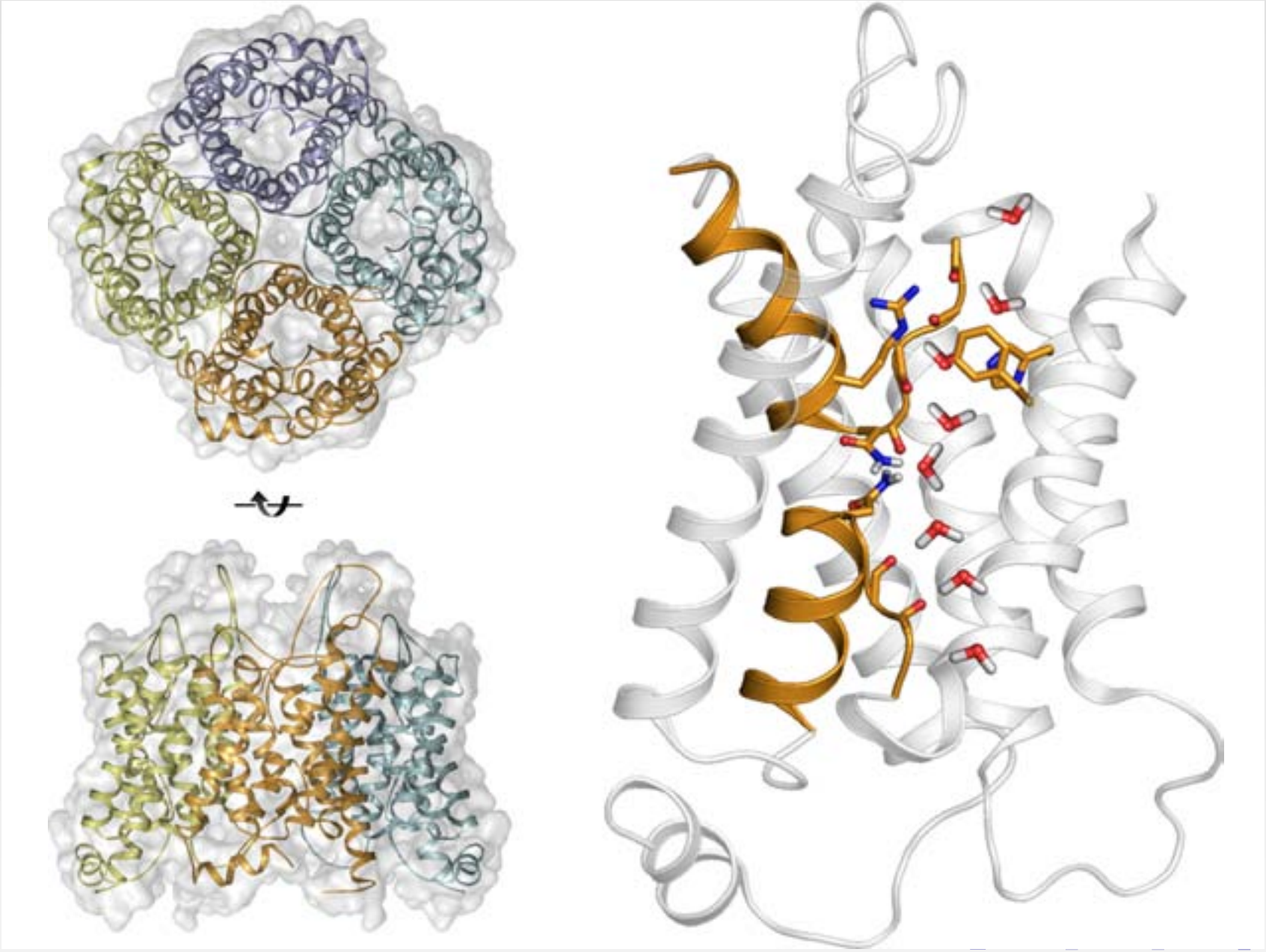


FIGURE 10.5 ■ *Left*: A comparison of the hydrogen-bonding schemes of α-helical and β-barrel structures. *Right*: An illustration of the very different patterns of exposure of side chains to the lipid phase. The α- and β-structures are not drawn to scale. The α-helical structure represents a 21-residue transmembrane helix. (Figure courtesy of Dr. Maike Bublitz.)

The aquaporin channel



The KcsA potassium channel

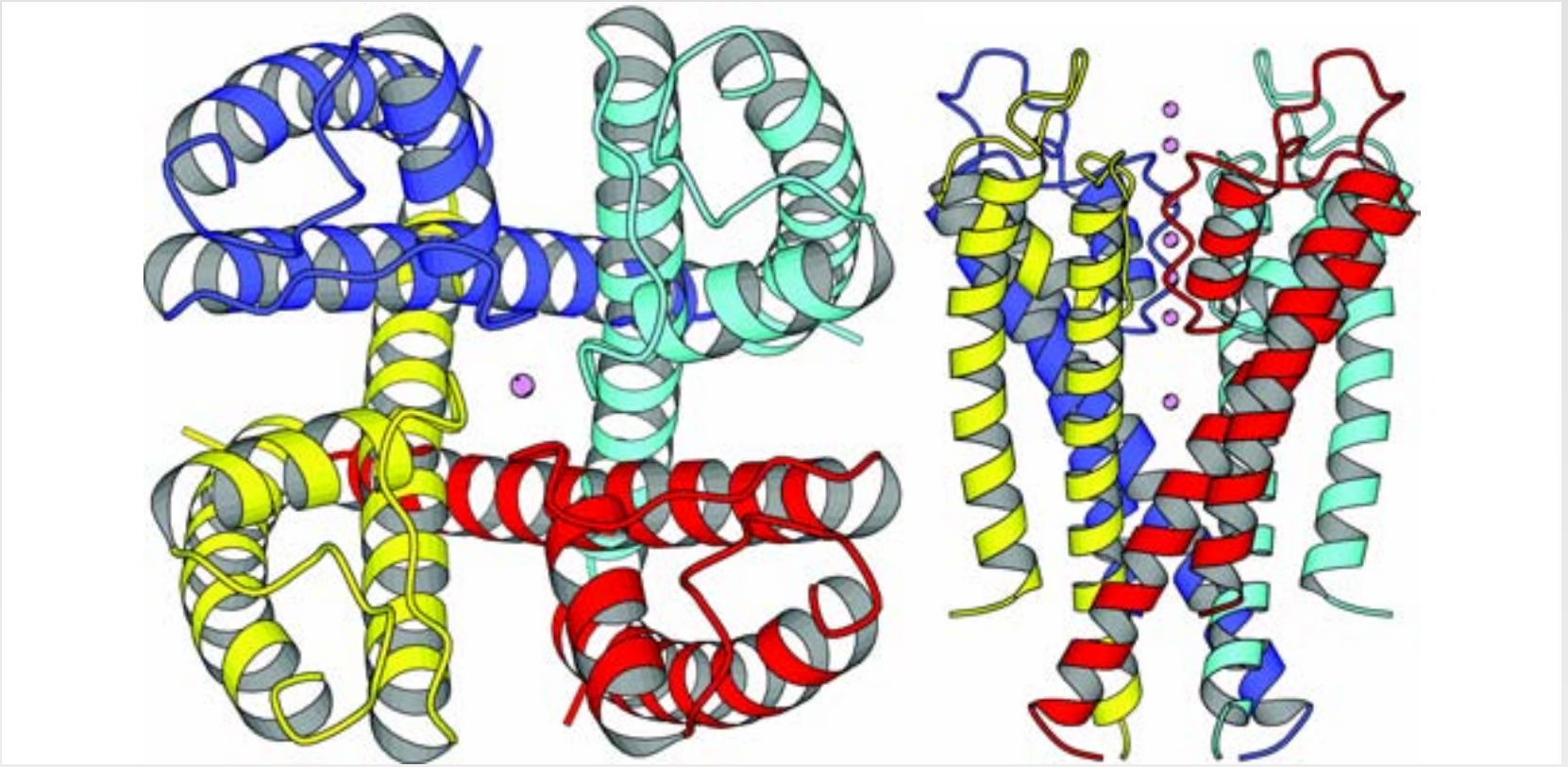


FIGURE 10.10 ■ The KcsA potassium channel. The tetramer as viewed from above (*left*) and from the side (*right*). The tetramer defines a selectivity filter and a central vestibule in the membrane stabilized by the dipoles of the helices forming the filter. Because of this, the effective transmembrane distance is significantly reduced. The conformation of the lower passage of the channel defines whether the gate is open or closed (PDB: 1K4C).

The KcsA potassium channel

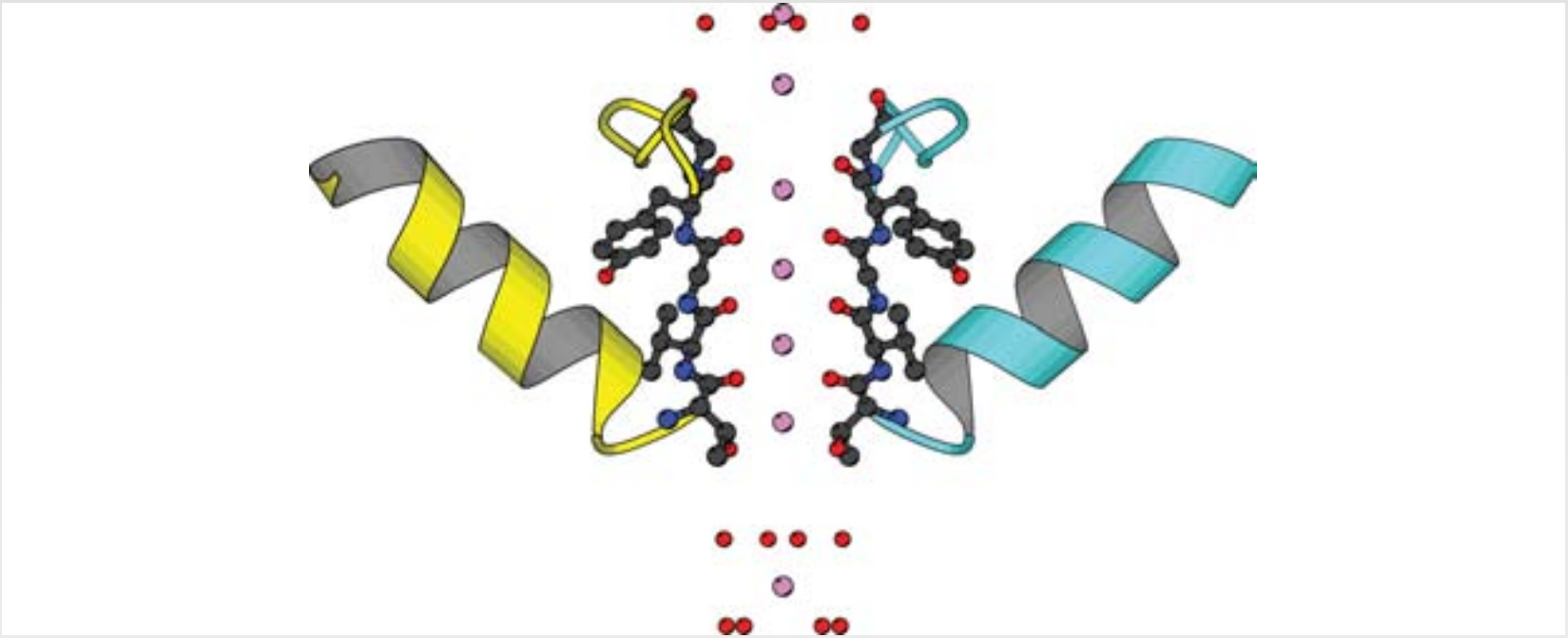


FIGURE 10.11 ■ The selectivity filter of KcsA at high potassium concentration. Only two subunits are drawn. A number of K^+ ions (lilac) are filling the filter, but only every second position in the filter can be occupied by one ion at a time. Carbonyl oxygens are facing the channel and restricting the passage to ions of suitable size to match the coordination distances provided by the tetrameric arrangement of carbonyl groups at the filter. Below the filter, one ion is found in the vestibule, coordinated again by eight water molecules and stabilized by the negatively charged end of four helix dipoles (two of which are shown).

The leucine transporter

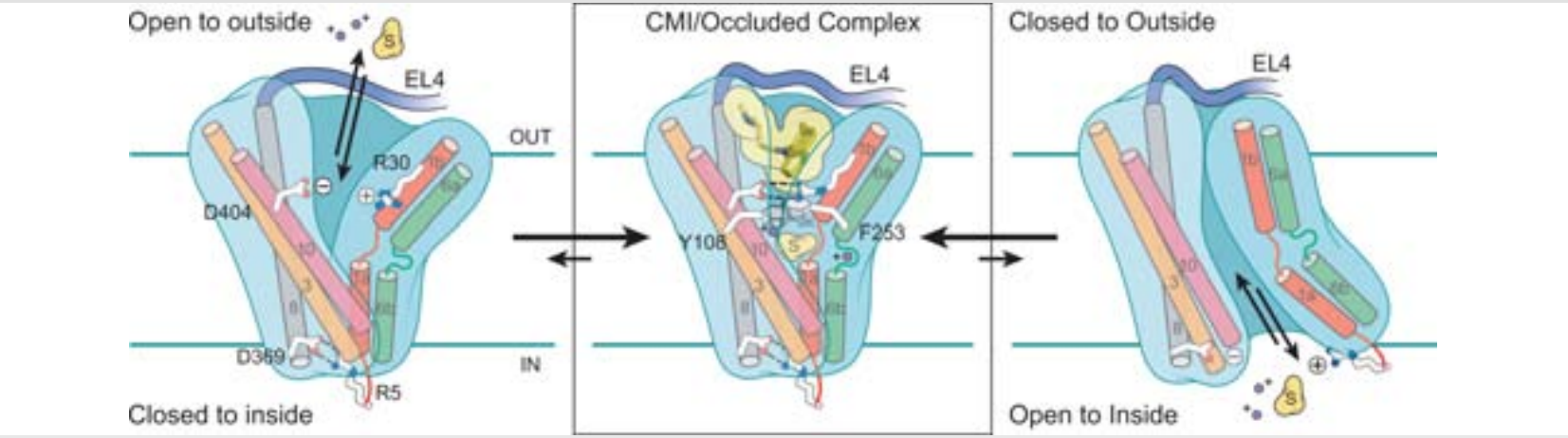


FIGURE 10.24 ■ A possible mechanism for transport of leucine and two sodium ions by the symporter LeuT. At least three states are needed: Open to outside when leucine and sodium can be exchanged with the solvent outside the cell; Occluded state when the transported ions are enclosed in LeuT; Open to inside when leucine and sodium can be exchanged with the solvent inside the cell. TCA inhibitors lock the transporter in the occluded state (Adapted with permission from Singh SK, Yamashita A, Gouaux E. (2007) Antidepressant binding site in a bacterial homologue of neurotransmitter transporters. *Nature* **448**: 952–956. Copyright (2007) Nature Publishing group).

Bacteriorhodopsin: light signaling

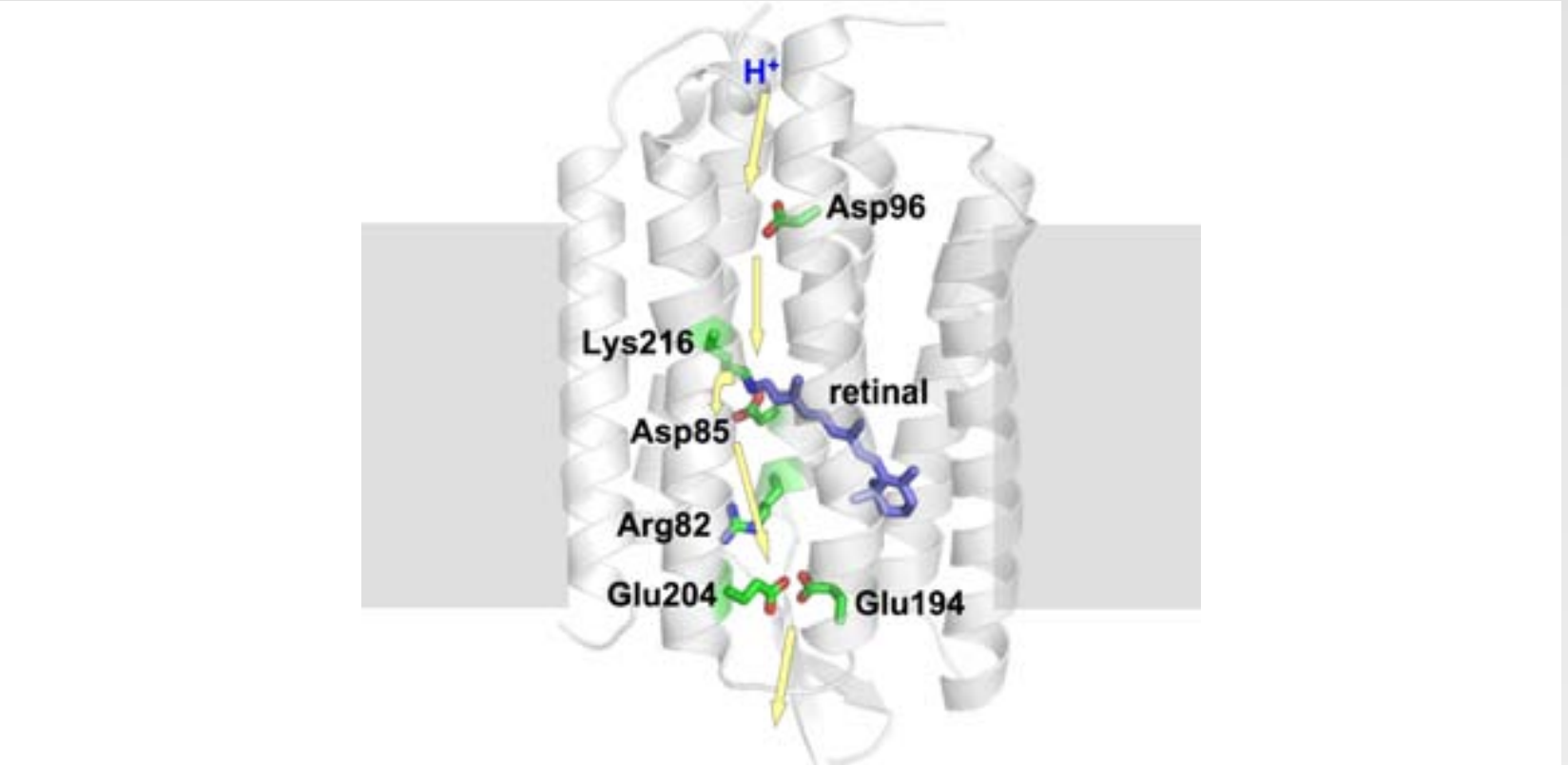
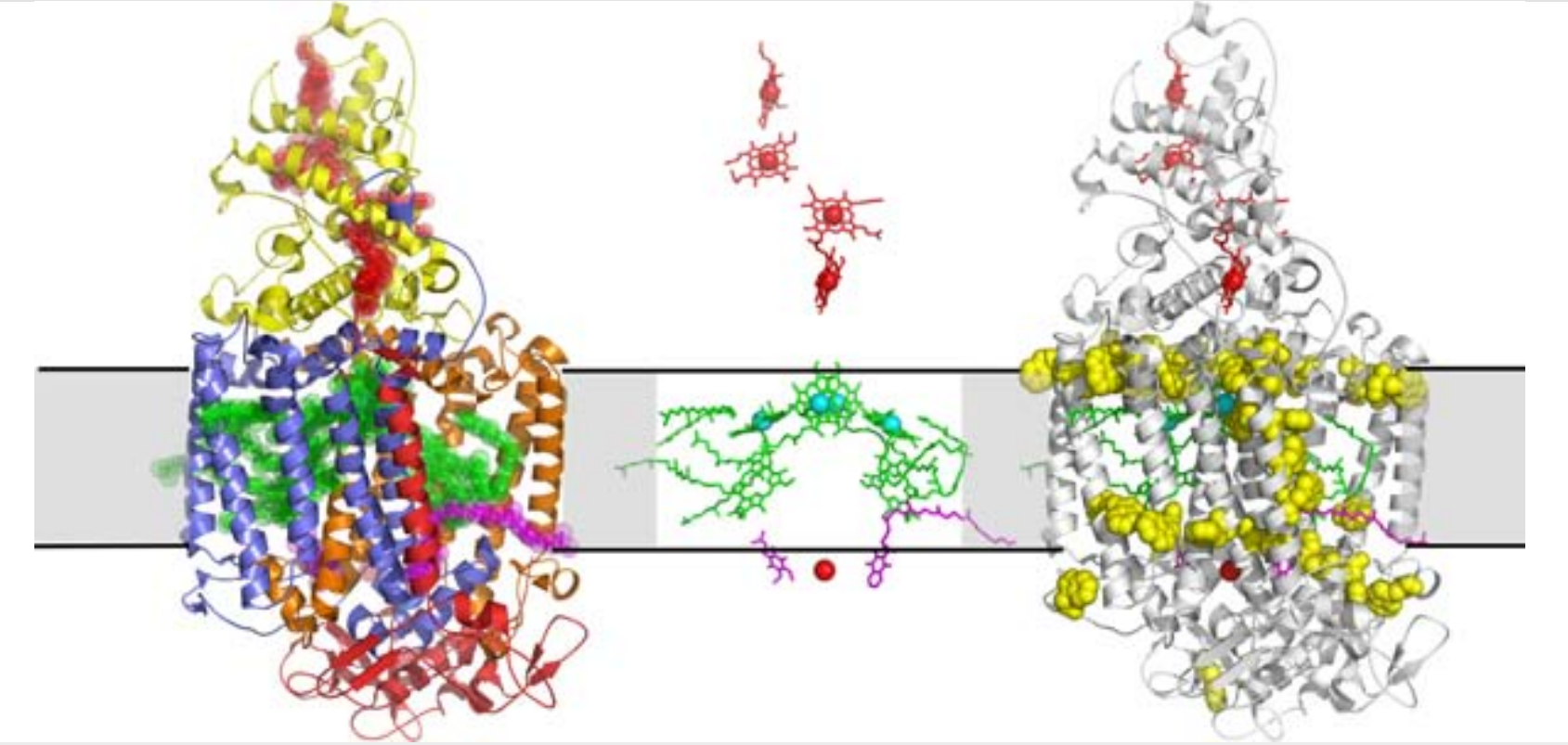


FIGURE 10.17 ■ The structure of bacteriorhodopsin with arrows and side chain indicating the proton translocation pathway, coupled to the light-driven *cis-trans* isomerization of retinal coupled by a Schiff's base link to the side chain amine of Lys216.

The photosynthetic reaction center



The photosynthetic reaction center

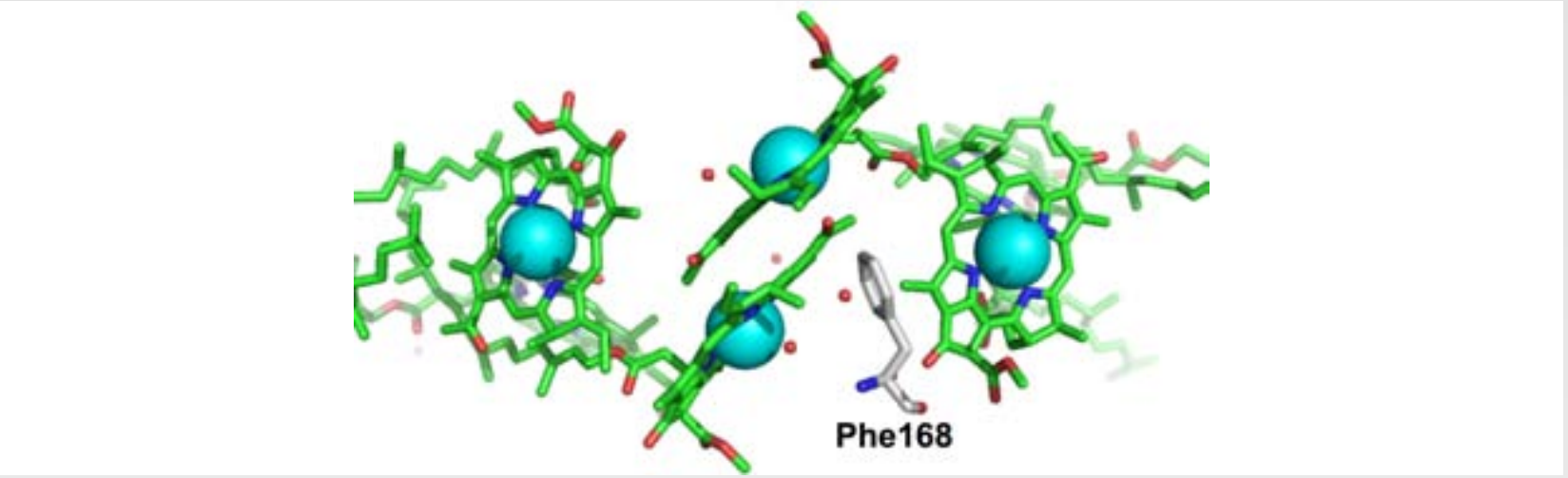
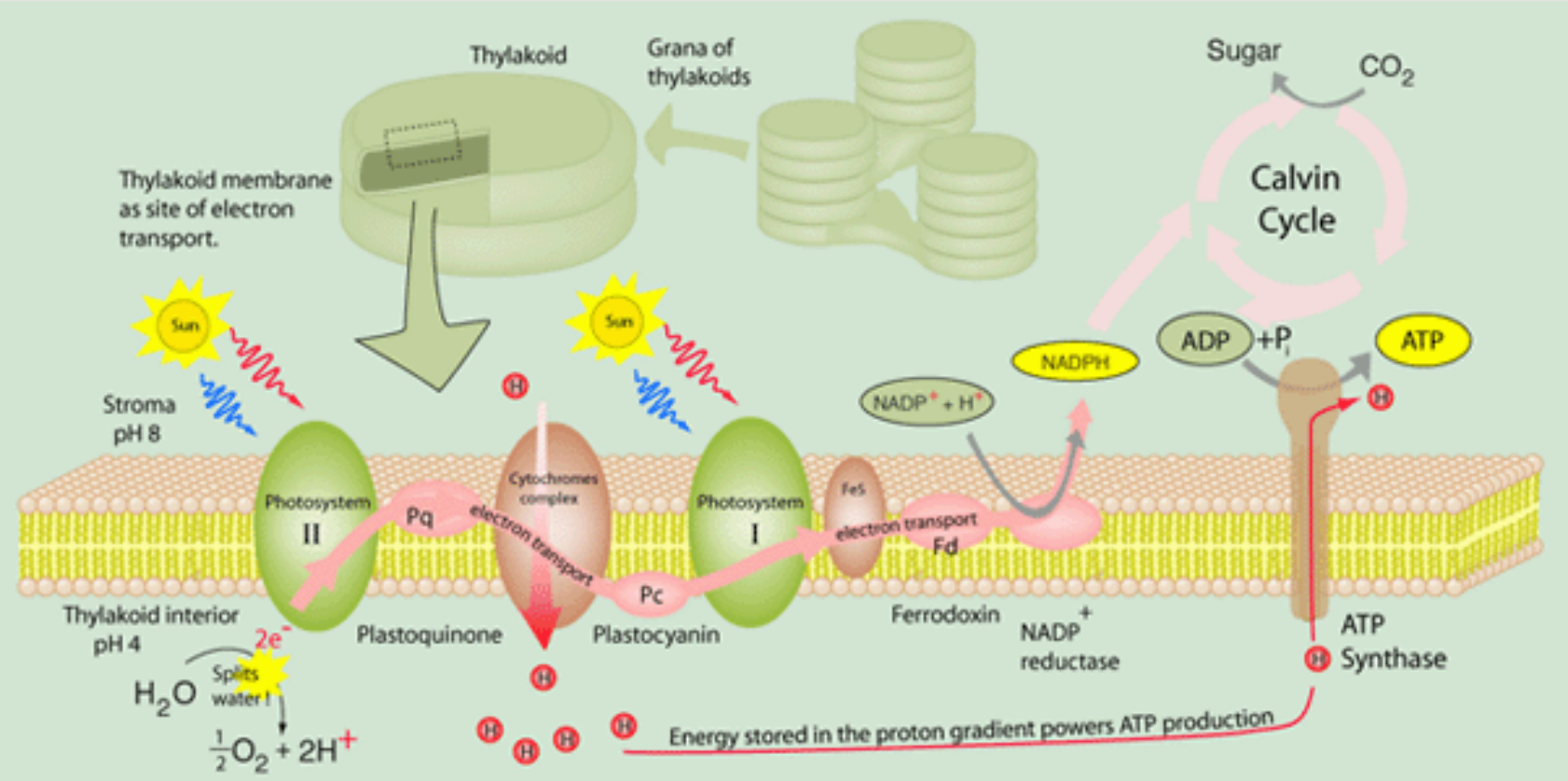
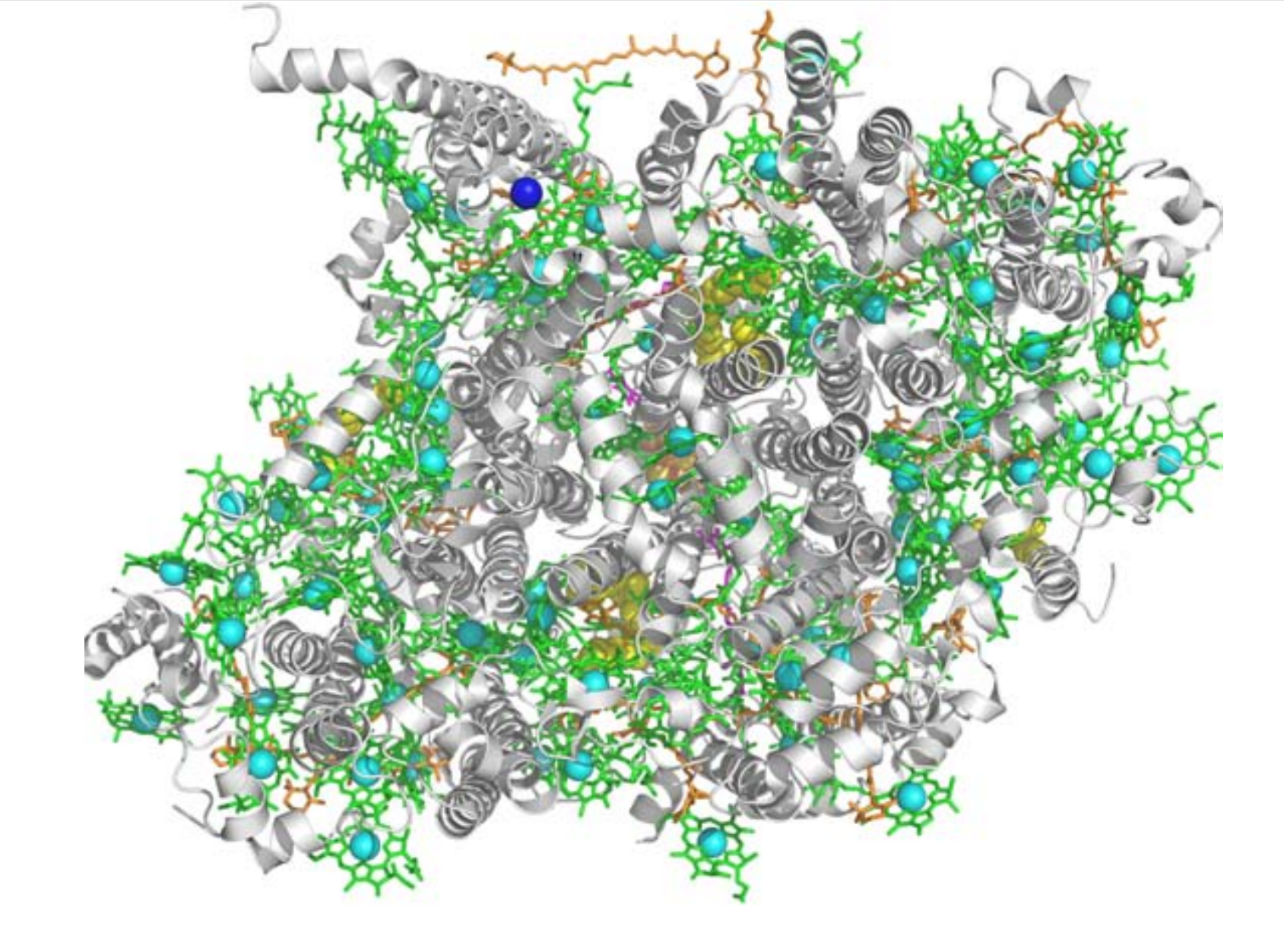


FIGURE 10.19 ■ The special pair of the L-chain His168Phe mutant of the photosynthetic reaction center from *R. viridis* displays a significant blue-shift and increased initial electron transfer rate. His168 (position indicated by Phe168 in white stick) interacts with the special pair (green sticks with Mg^{2+} ions as cyan spheres). The Phe side chain will provide poor stabilization of the polarized special pair (PDB: 1XDR).

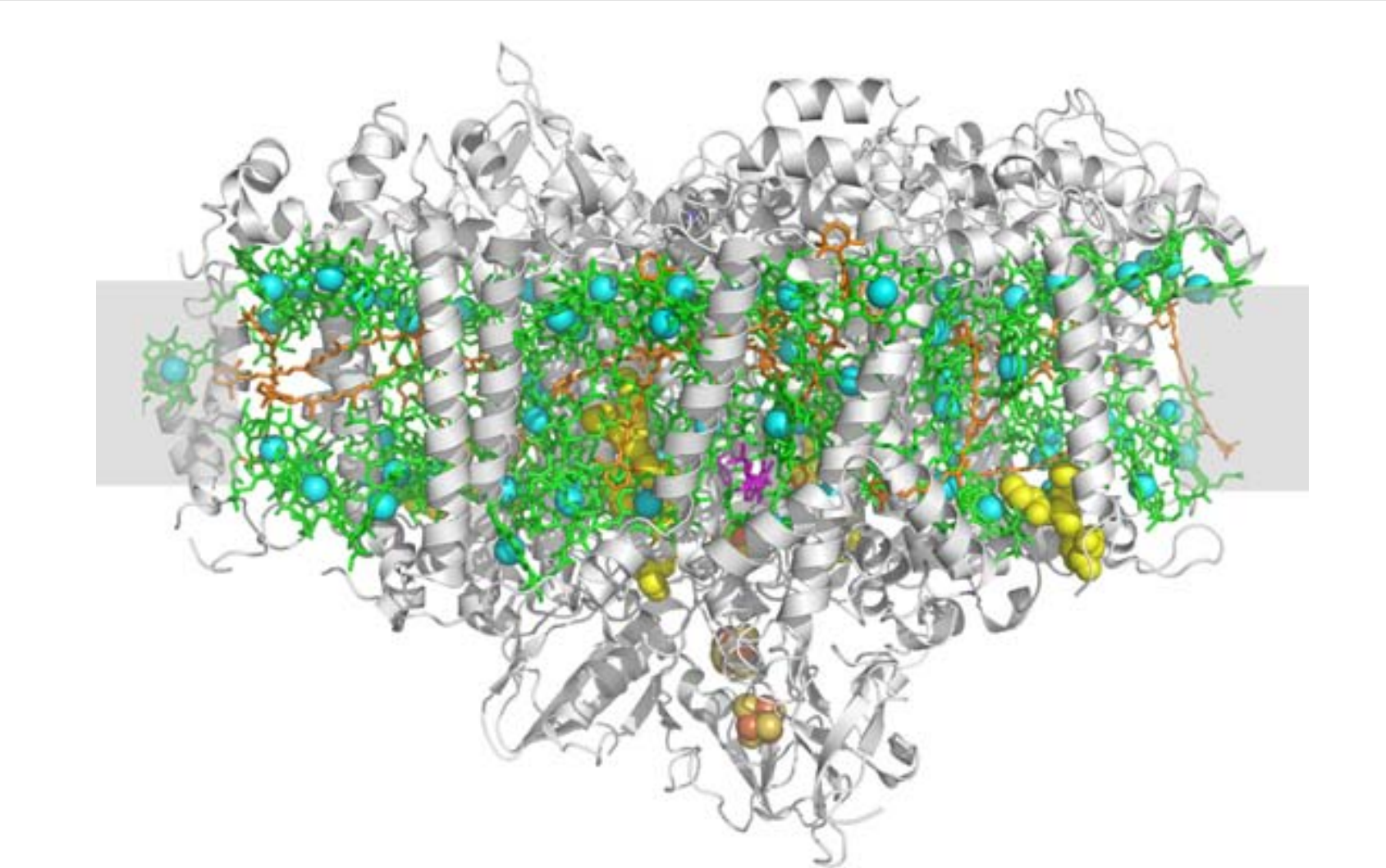
Phtosynthetic electron transfer in plants



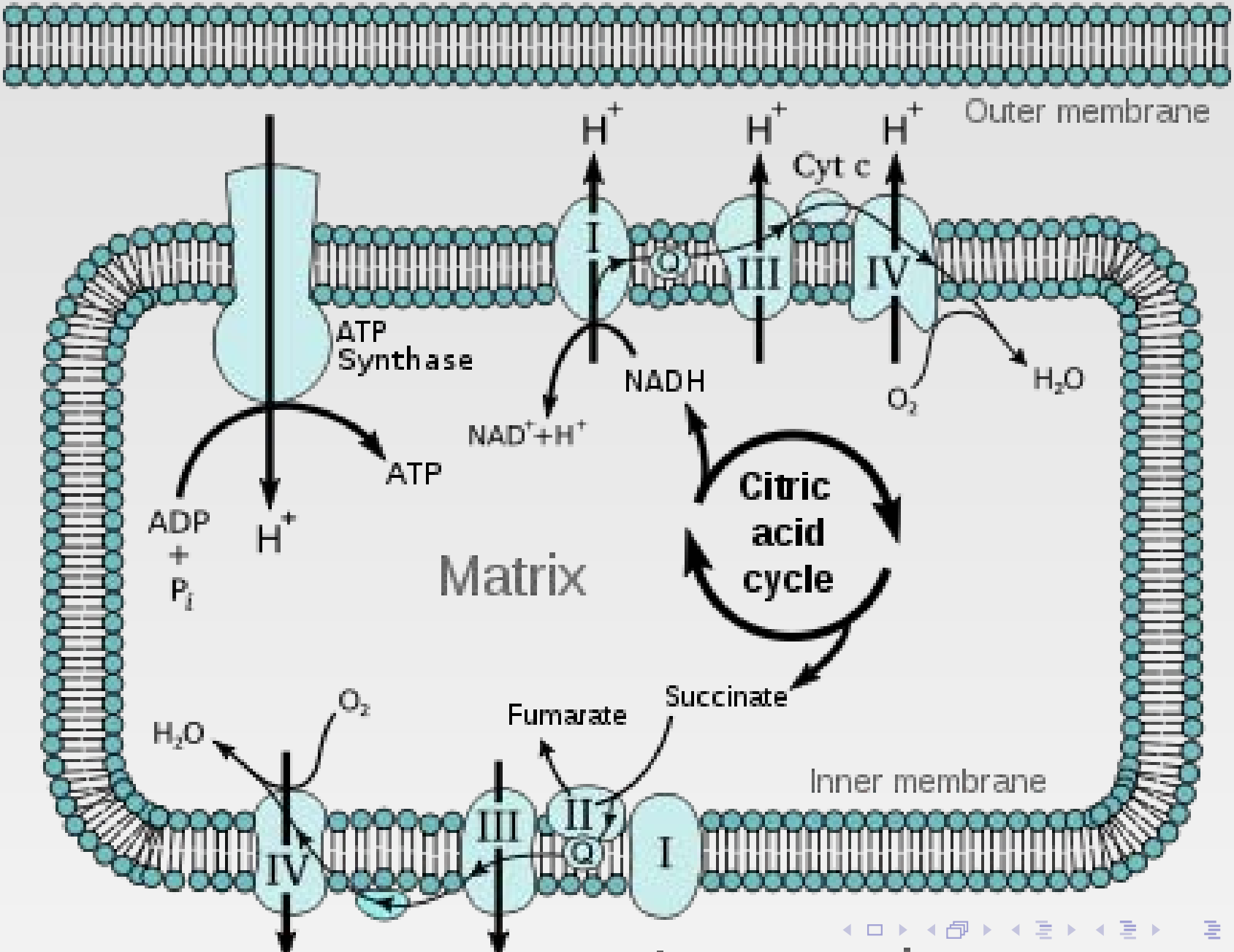
Getting more complex: photosystem I



Photosystem I



The mitochondrion



Complex electron transport chains