

Lecture 16: Membrane Proteins

Membrane proteins:

- 1) Overview: Types and Properties
- 2) Getting into the Membrane
- 3) What Membrane Proteins Do--
examples
- 3) Working with Membrane Proteins
- 4) Pymol/Chimera Tutorial

Membrane Overview

Membrane proteins are 25-35% of the genome.

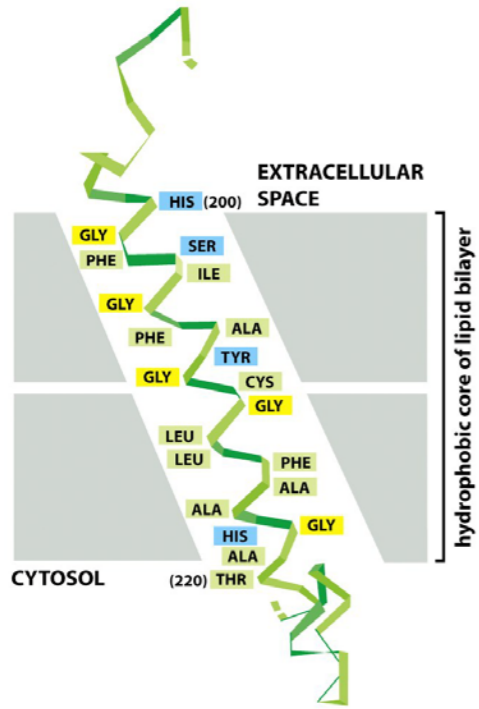


Figure 10-21 Molecular Biology of the Cell 5/e (© Garland Science 2008)

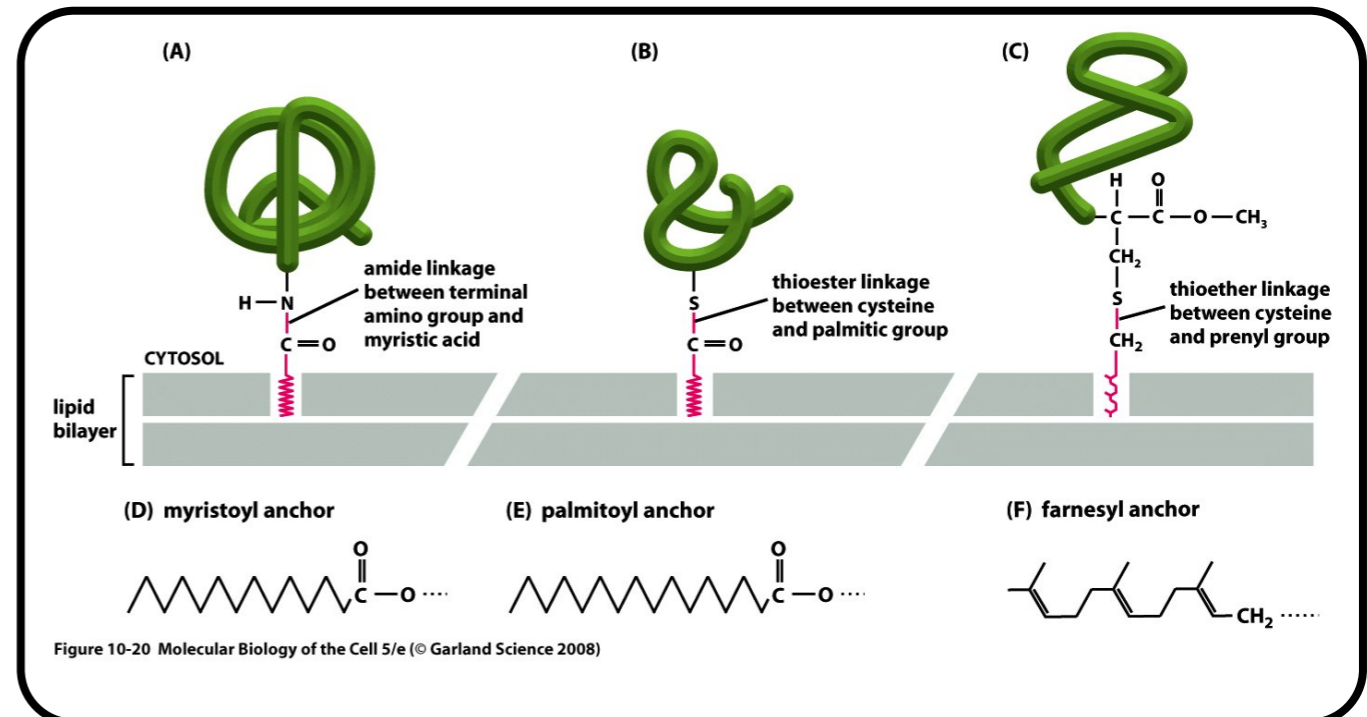


Figure 10-20 Molecular Biology of the Cell 5/e (© Garland Science 2008)

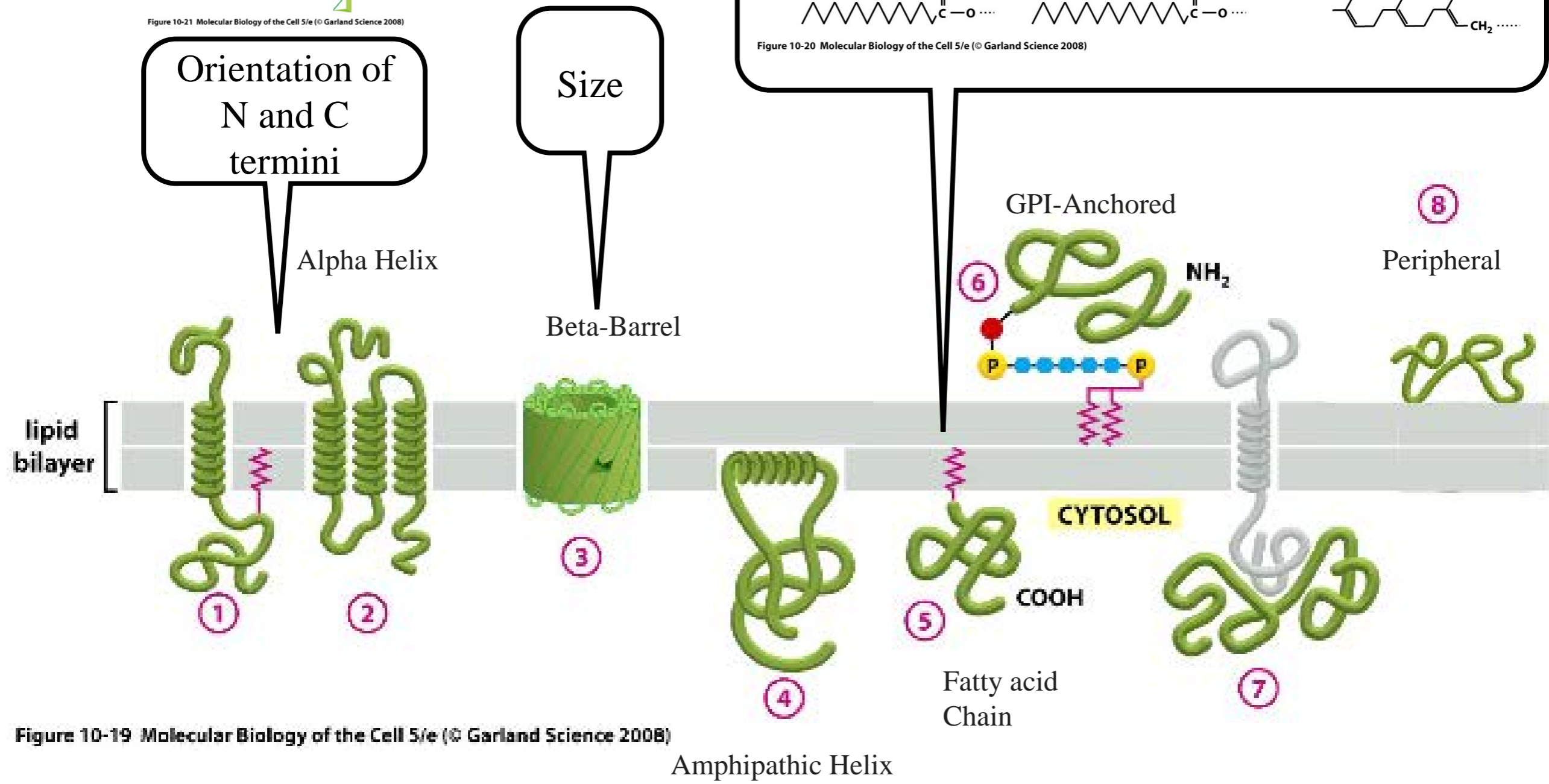


Figure 10-19 Molecular Biology of the Cell 5/e (© Garland Science 2008)

Amphipathic Helix

Beta-Barrel Proteins

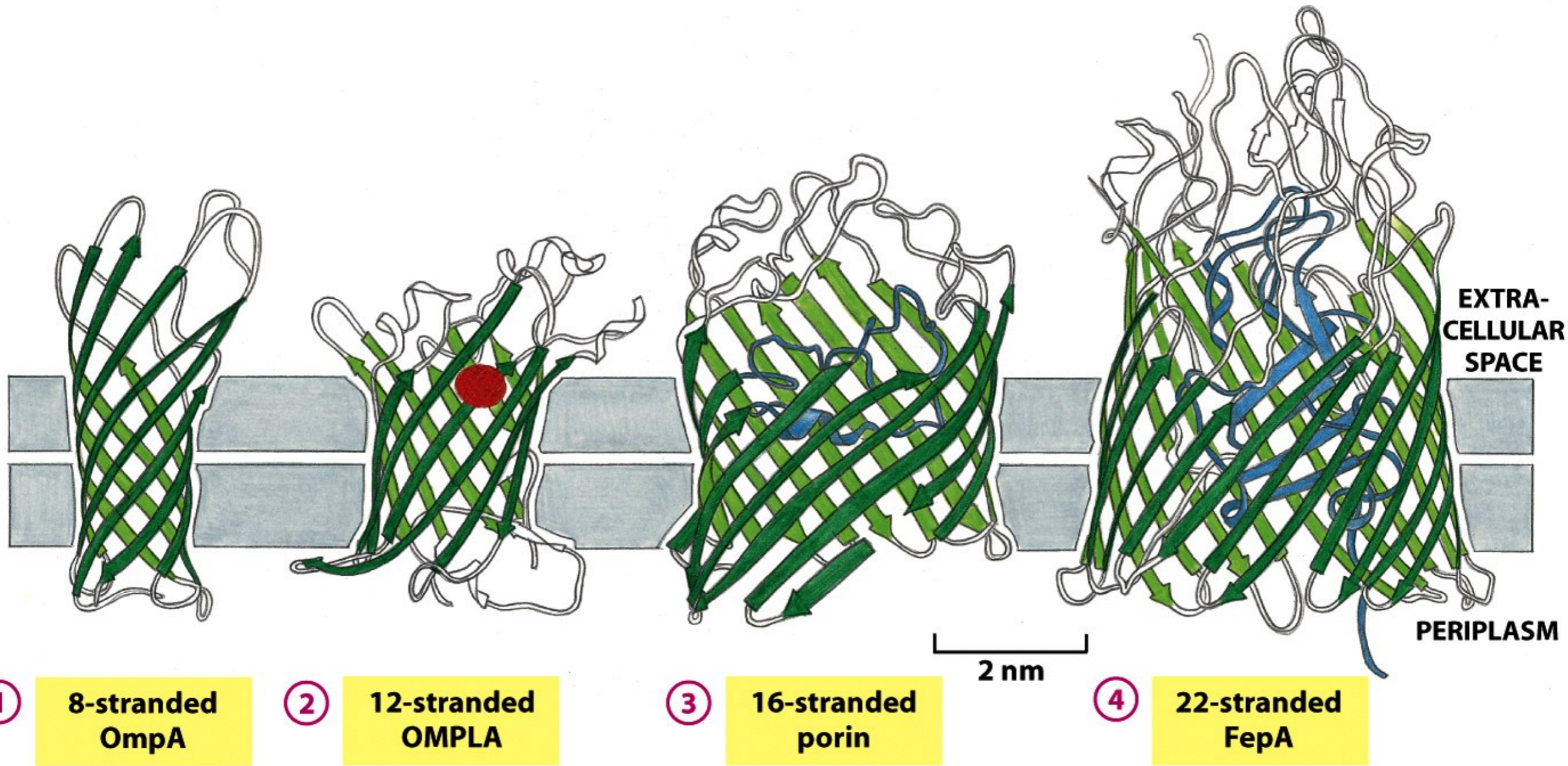
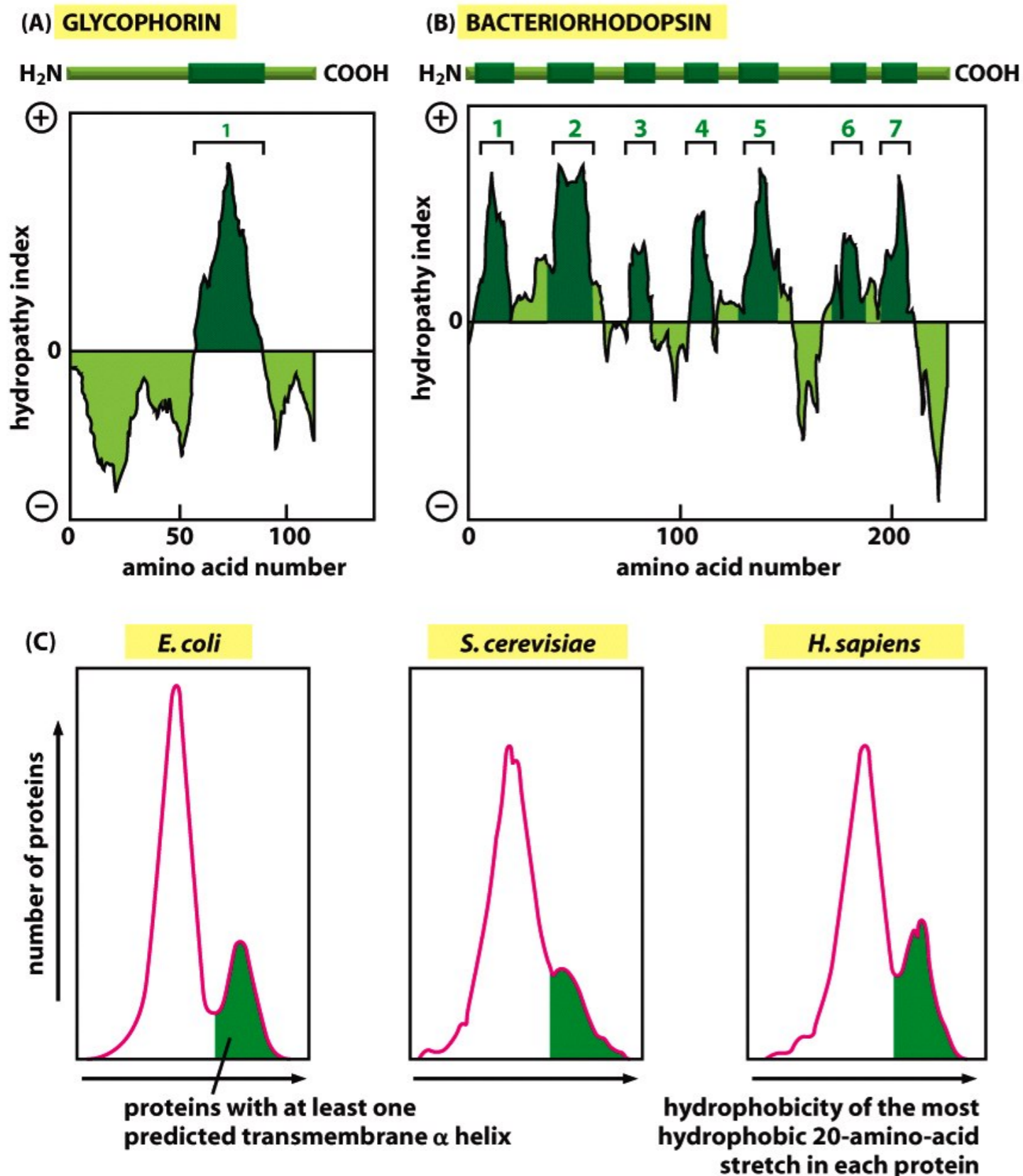


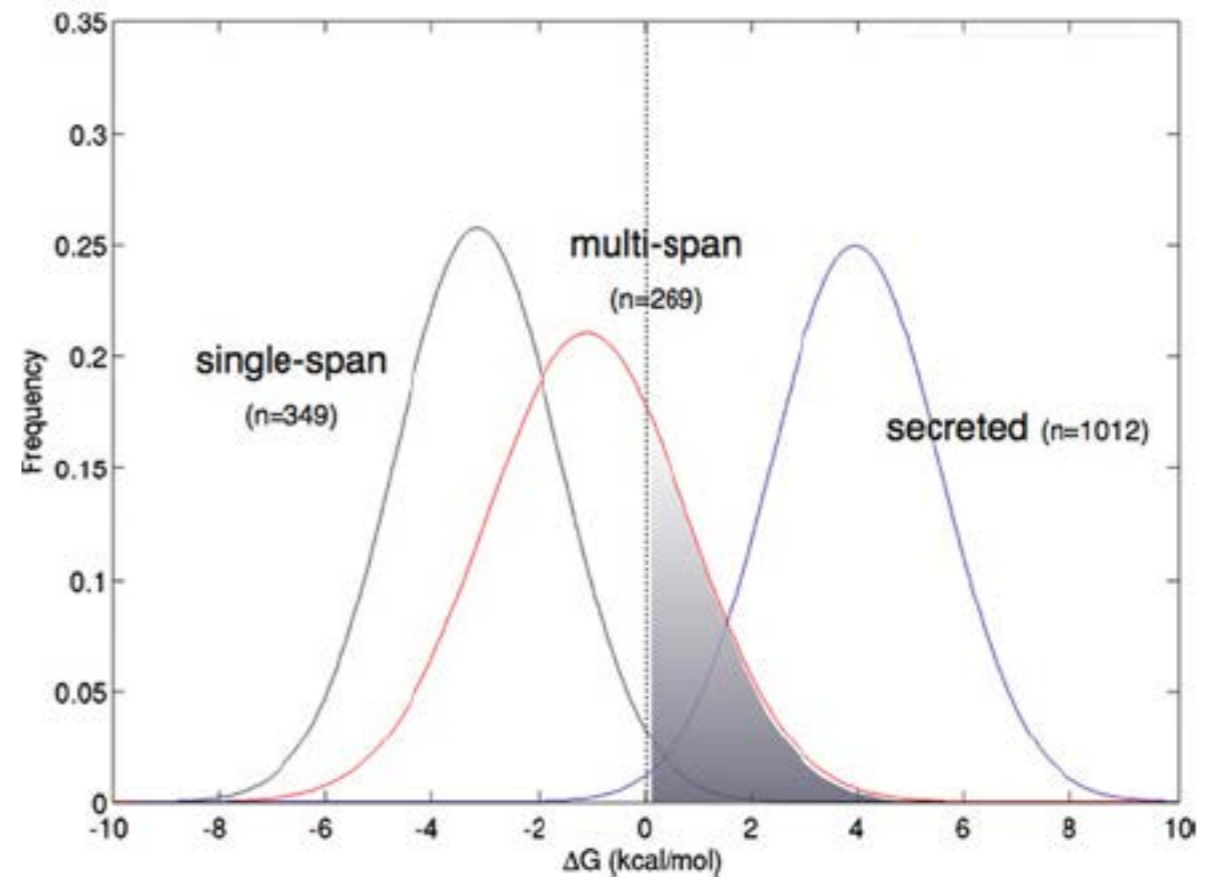
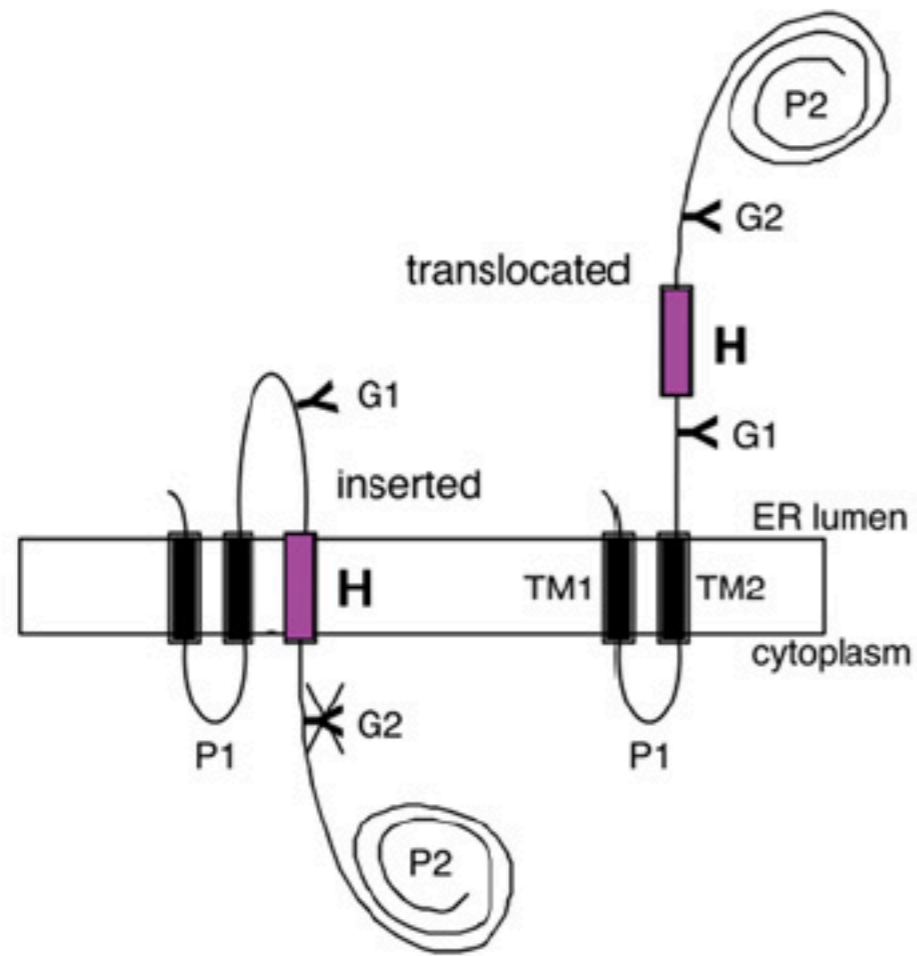
Figure 10-26 Molecular Biology of the Cell 5/e (© Garland Science 2008)

Hydropathy Plots for Alpha Helical Proteins: Classic Method



For alpha-helical membrane proteins, you can use hydropathy plots to predict the probability that a segment will be within the membrane. These are generated by measuring, for each amino acid, its partition coefficient between water and a non-interacting, isotropic phase such as Ethanol, and calculating from that partition coefficient a transfer free energy.

Hydropathy Plots: More Realistic Method



GGPG|AAAA**L**AAAA**L**AAAA**L**AAAA**L**AAAA|GPGG

The efficiency of membrane integration can be quantified from SDS/PAGE gels by measuring the amount of singly (f_1) and doubly (f_2) glycosylated protein. The apparent free energy of insertion is calculated as $\Delta G_{app} = -RT \ln \frac{f_1}{f_2}$. A typical H-segment is shown at the bottom.

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Getting into the Membrane: Destination Matters!

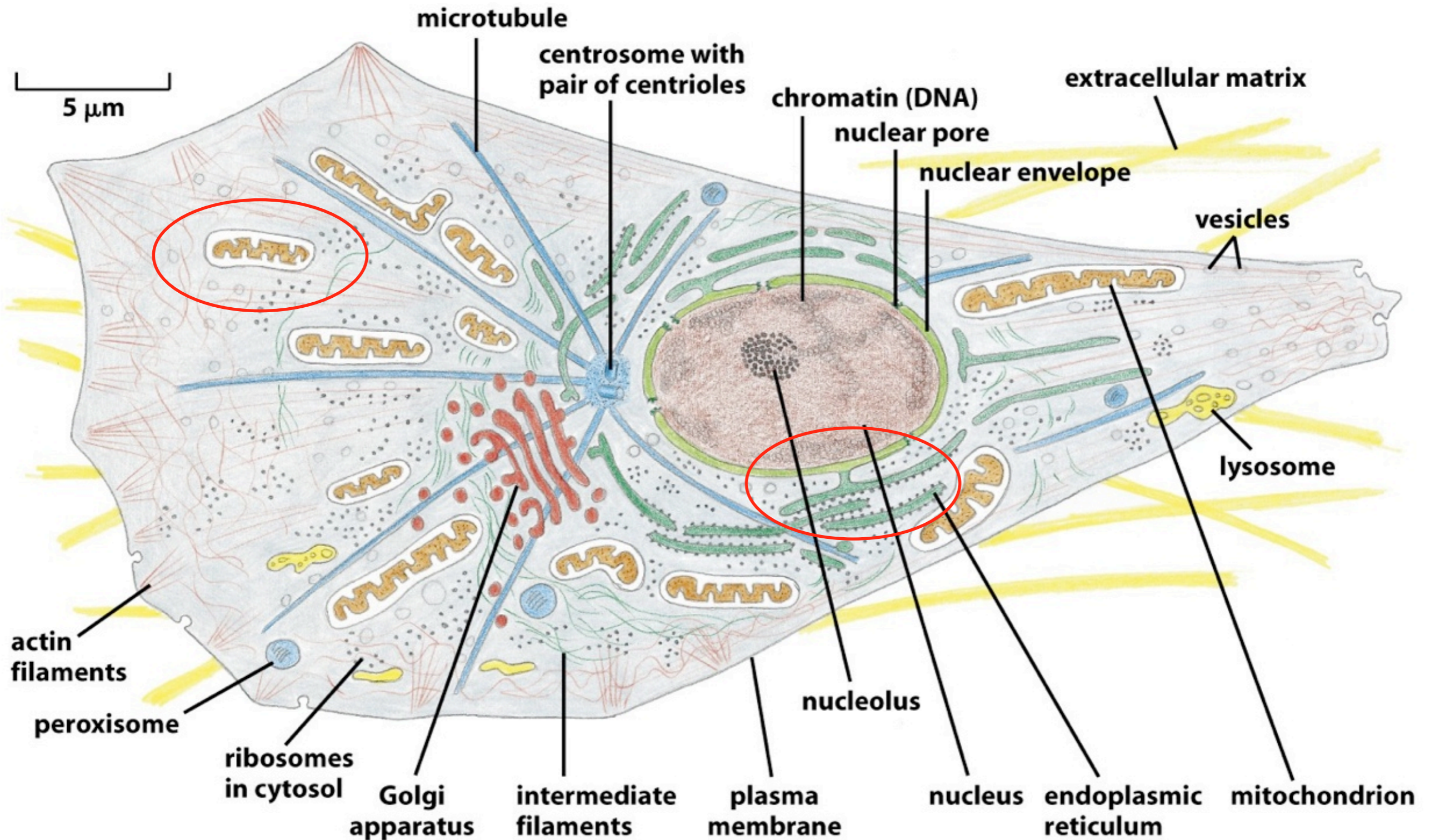


Figure 1-30 Molecular Biology of the Cell 5/e (© Garland Science 2008)

SRP Dependent Protein Targeting

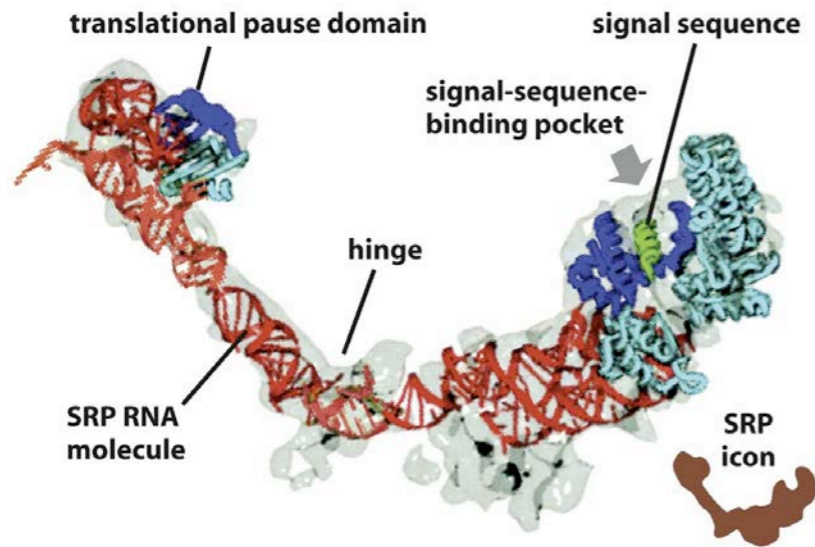


Figure 12-39a Molecular Biology of the Cell 5/e (© Garland Science 2008)

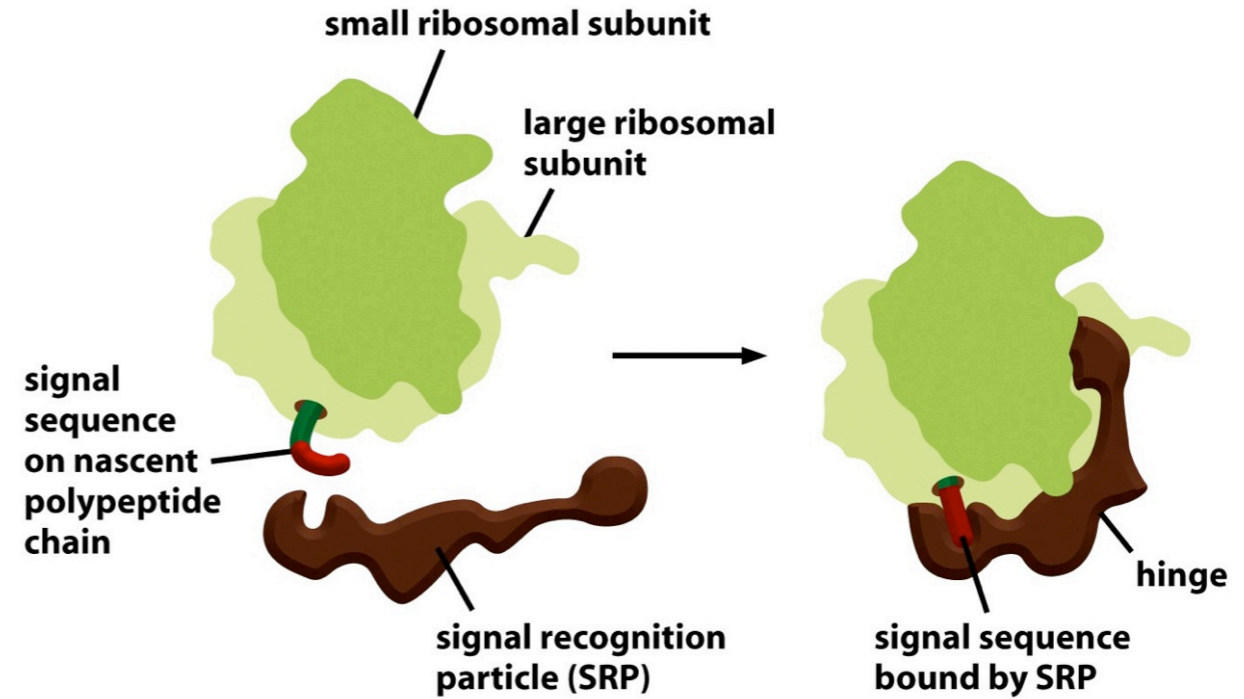


Figure 12-39b Molecular Biology of the Cell 5/e (© Garland Science 2008)

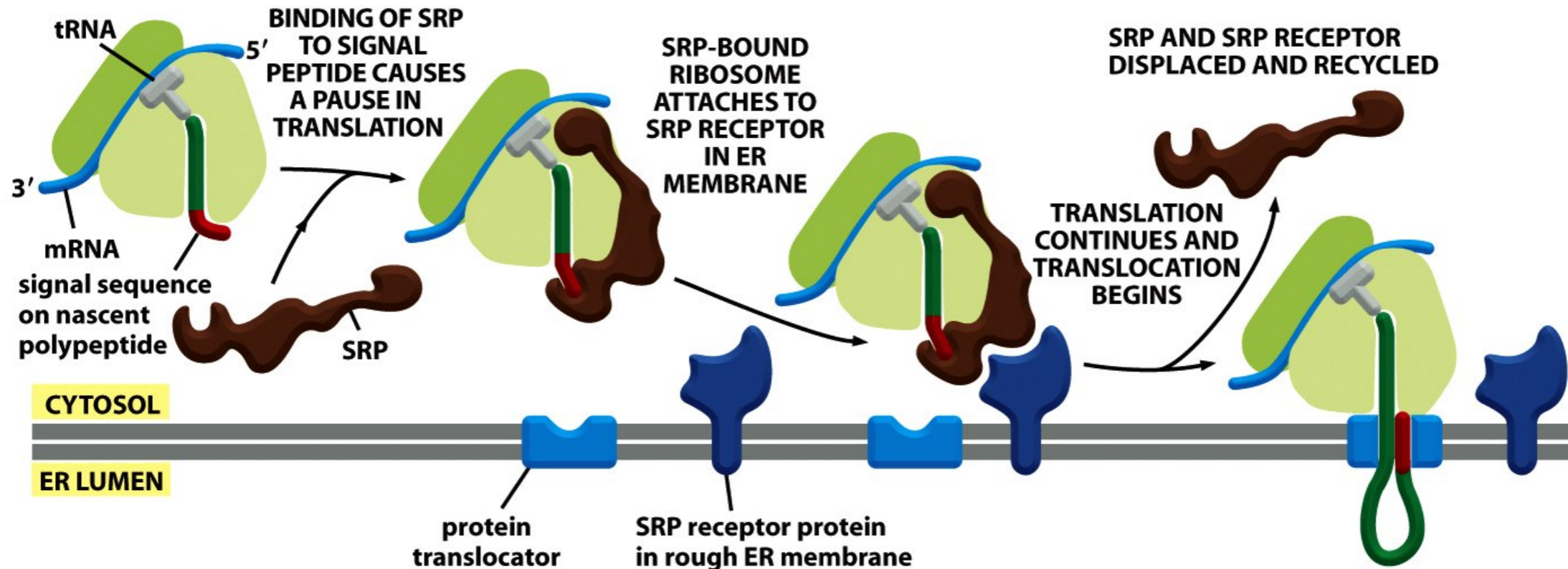
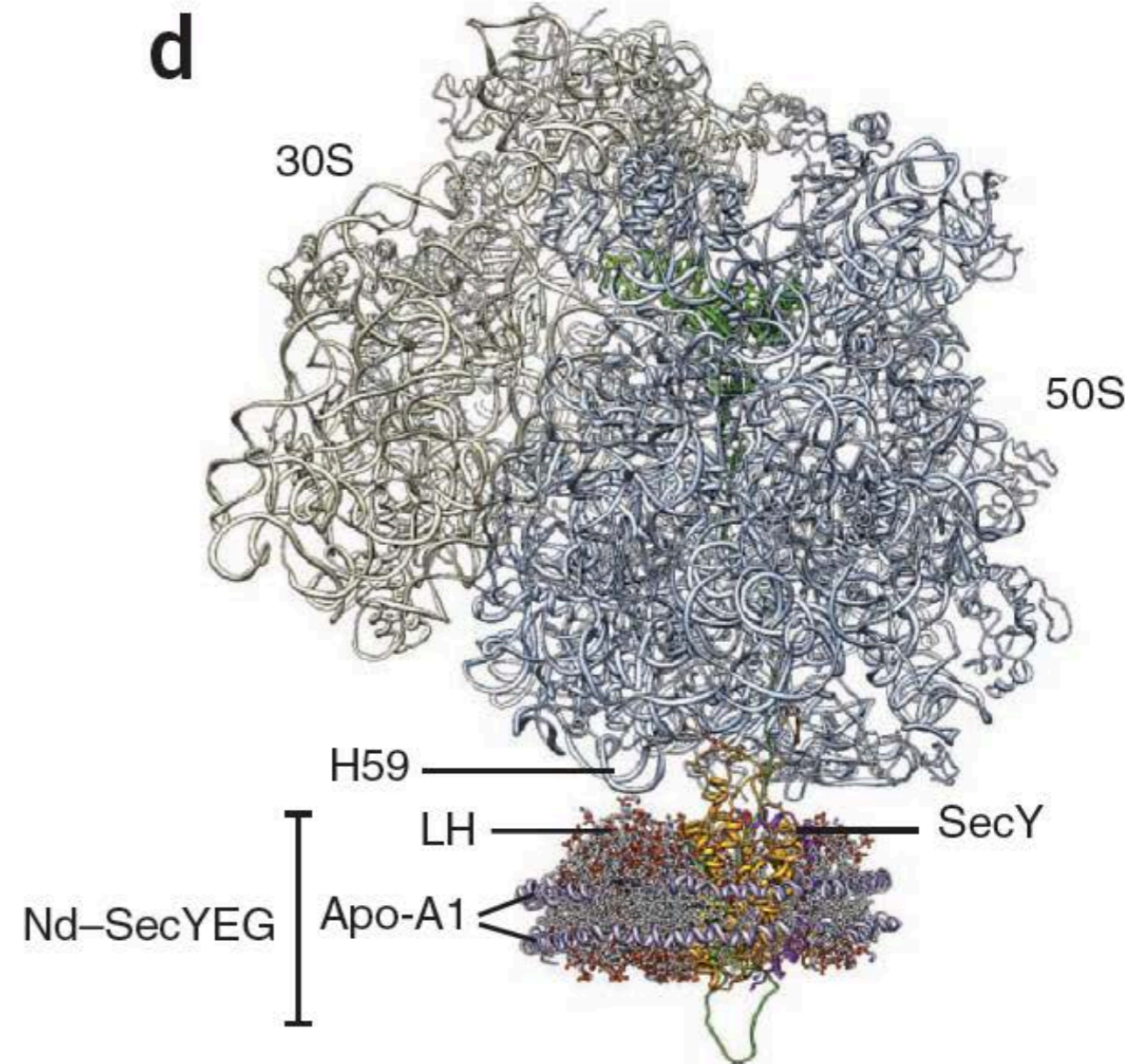
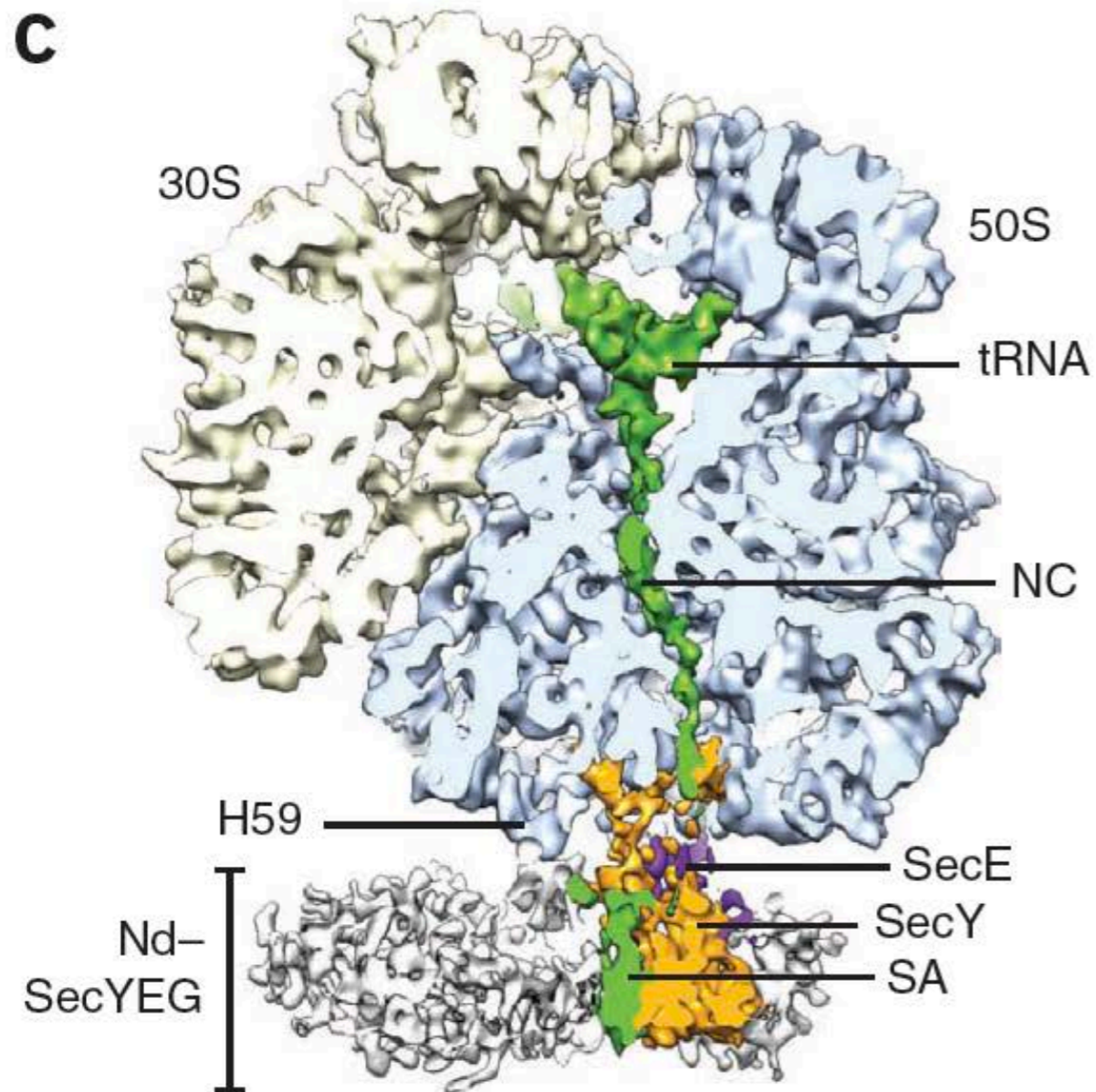
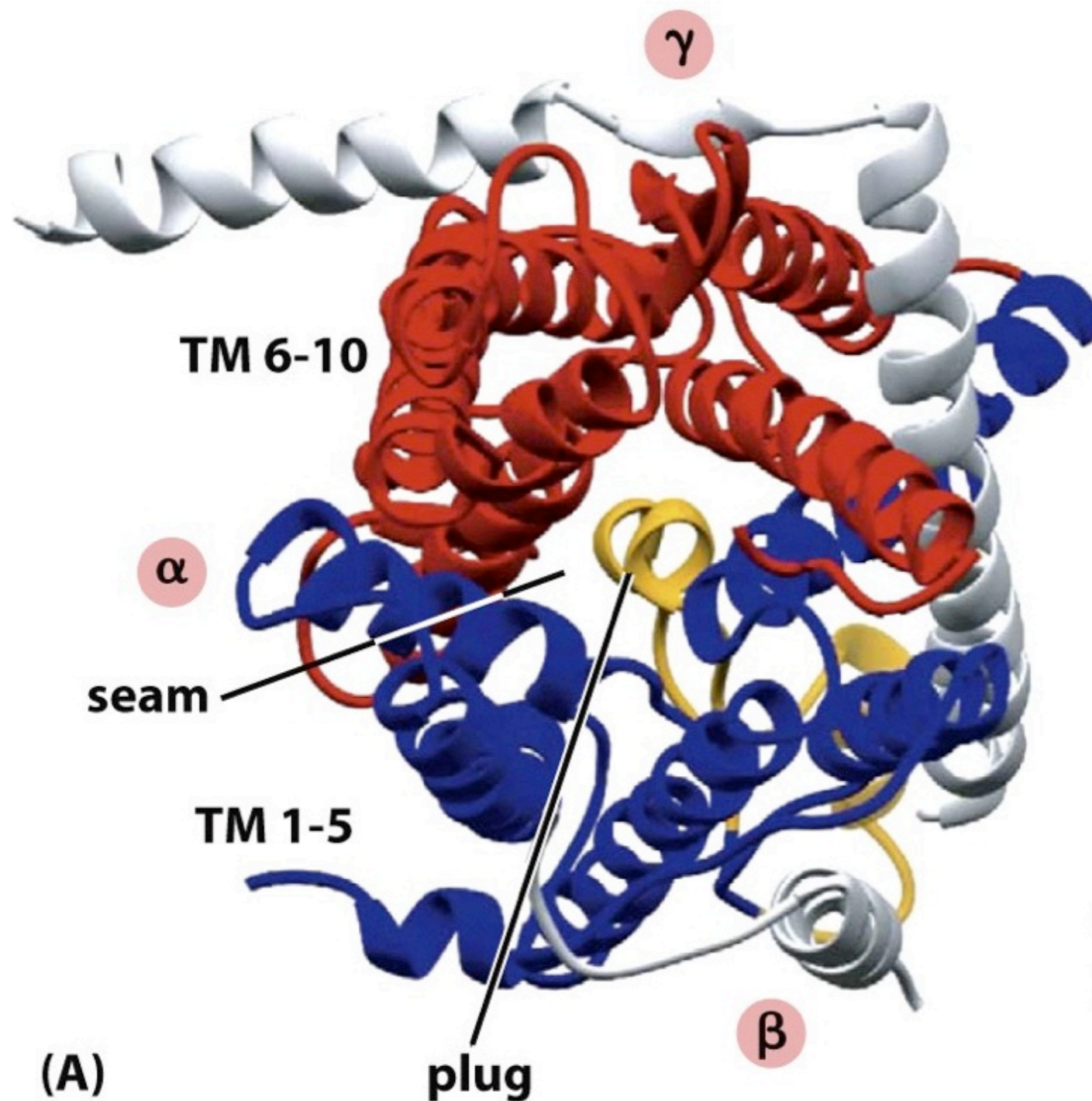


Figure 12-40 Molecular Biology of the Cell 5/e (© Garland Science 2008)

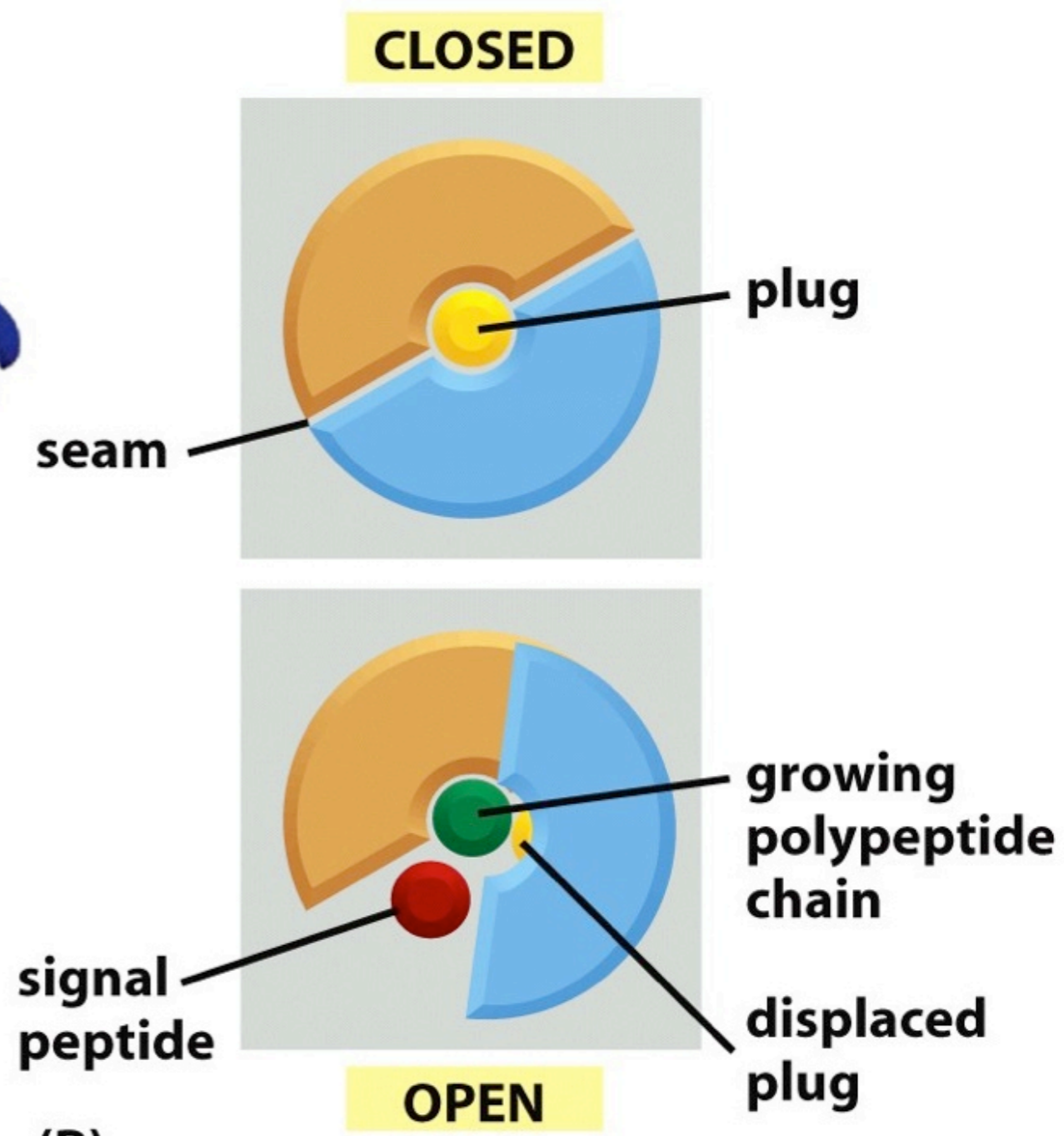
Ribosome Nascent Chain Translocon Complex!



Getting into the Membrane: The Lateral Gate

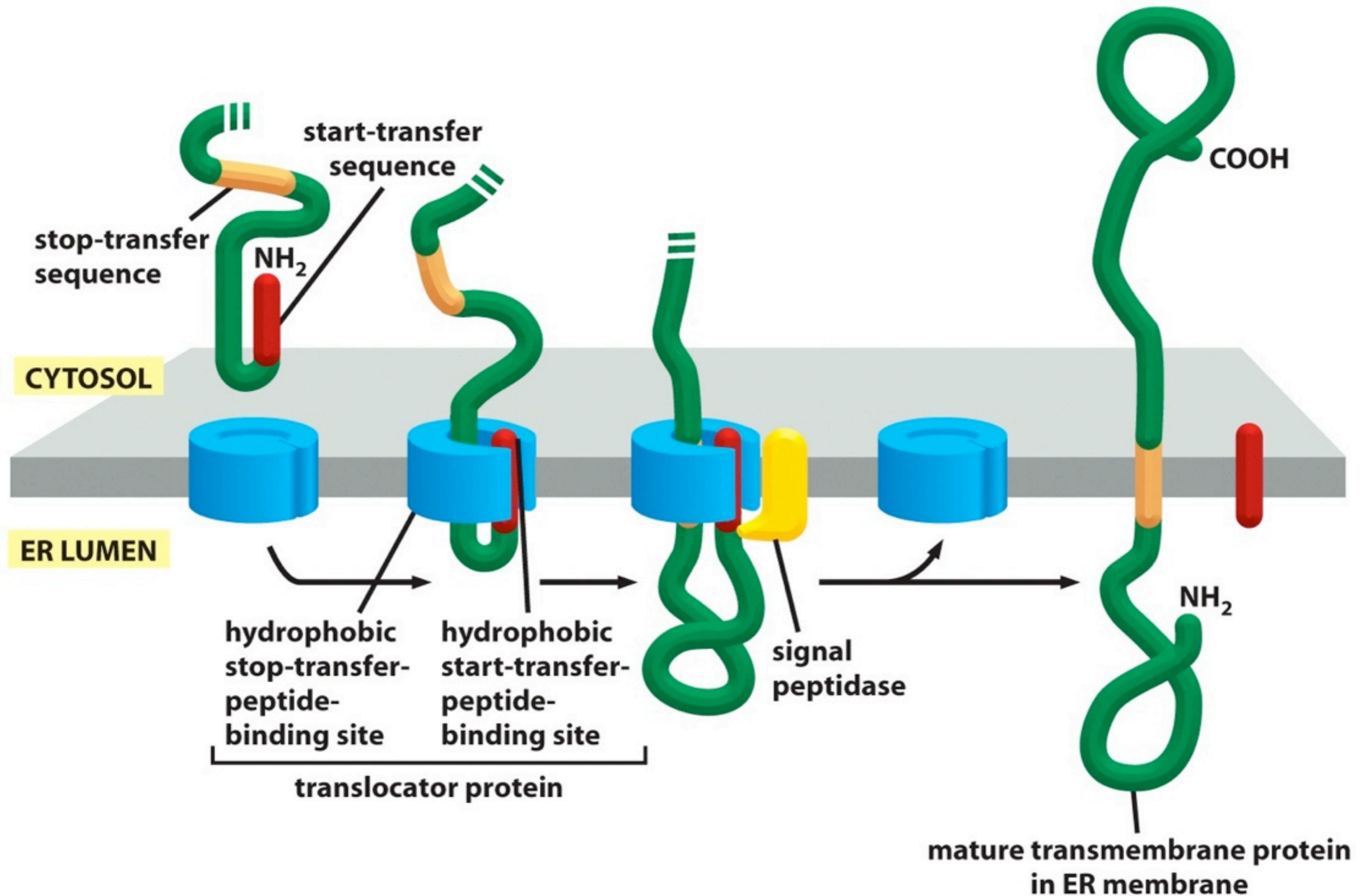


(A)



(B)

Getting into the ER: Single N-terminal TM Segment



Getting into the ER: Positive Inside Rule

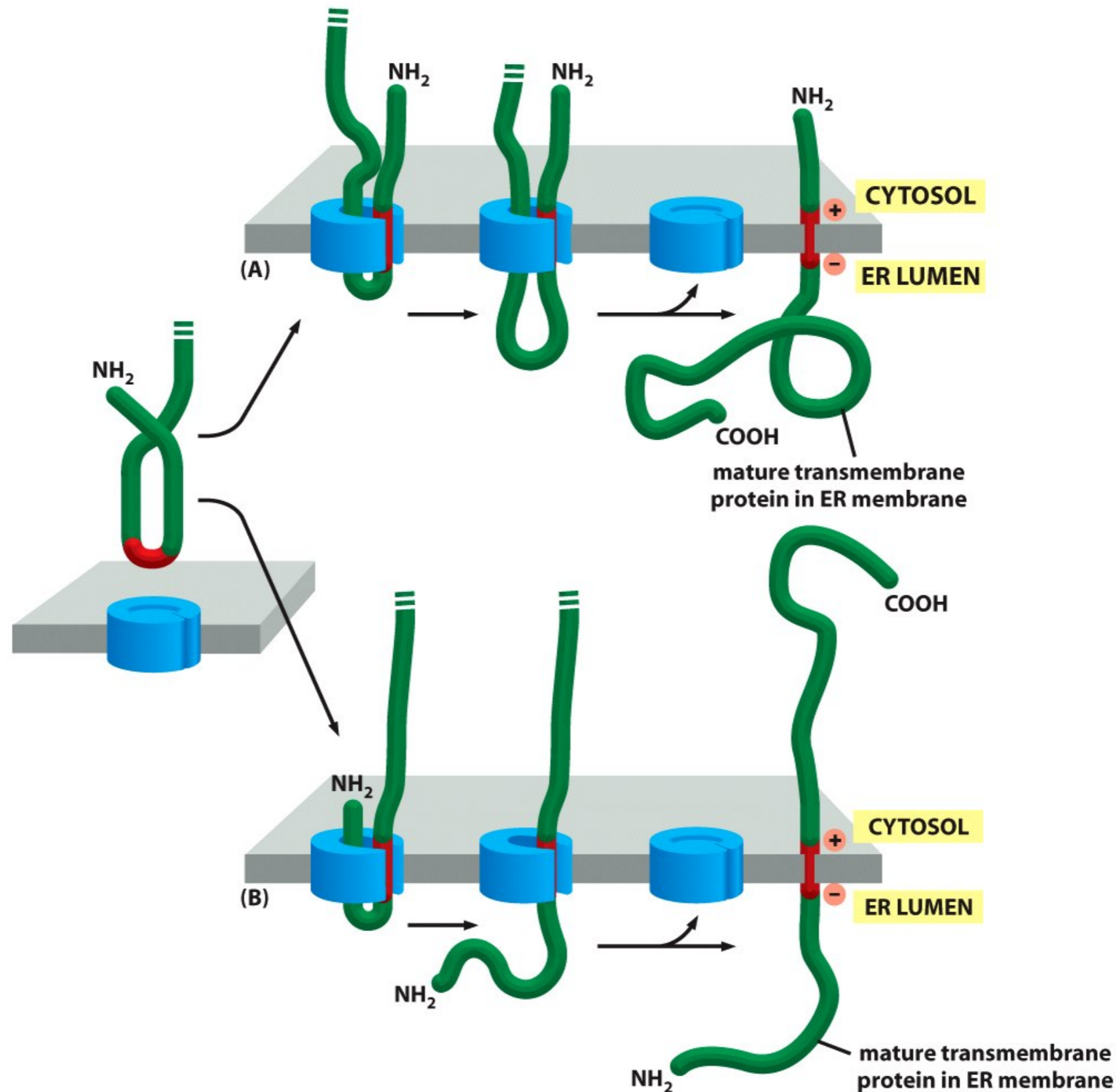
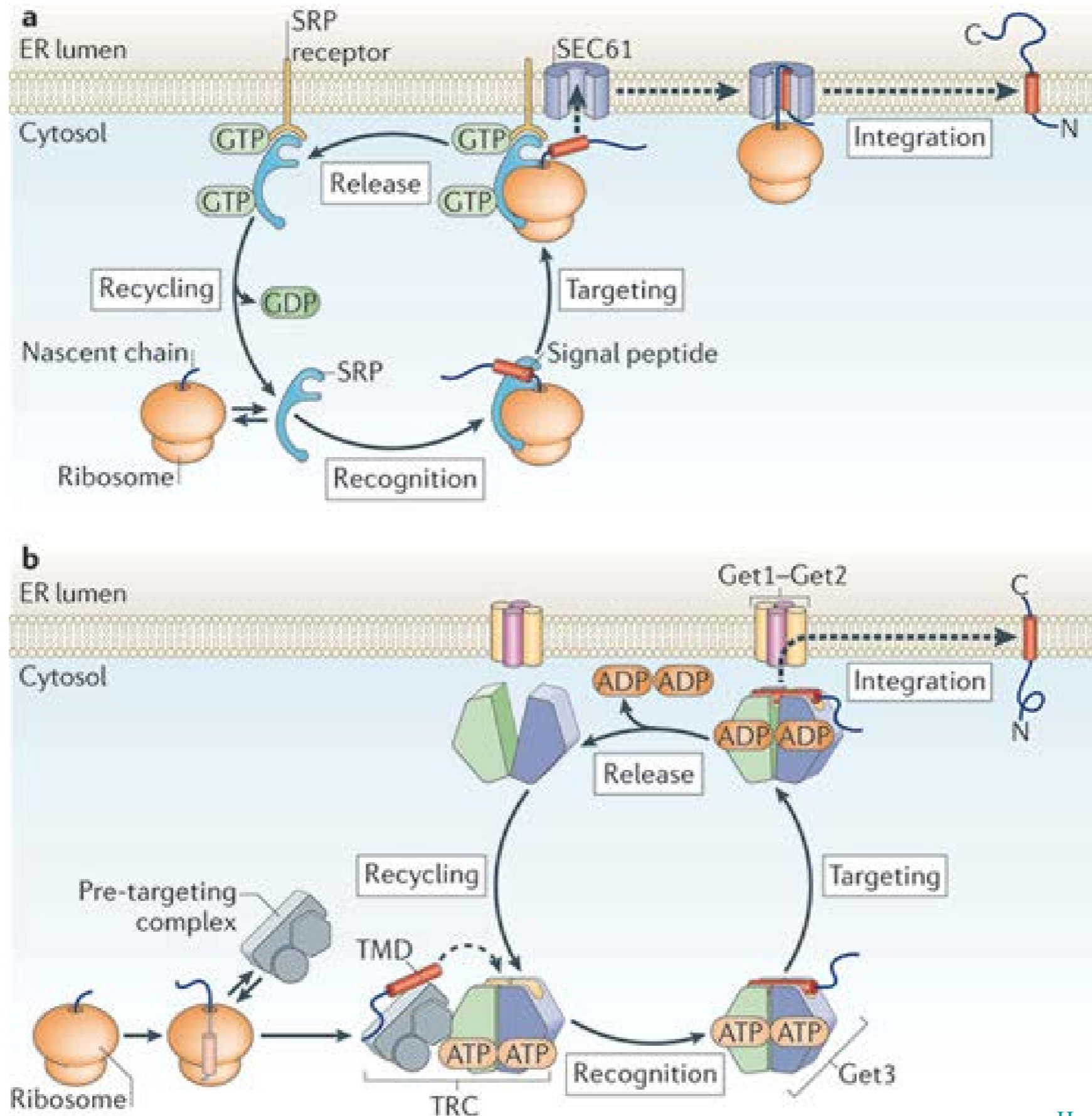
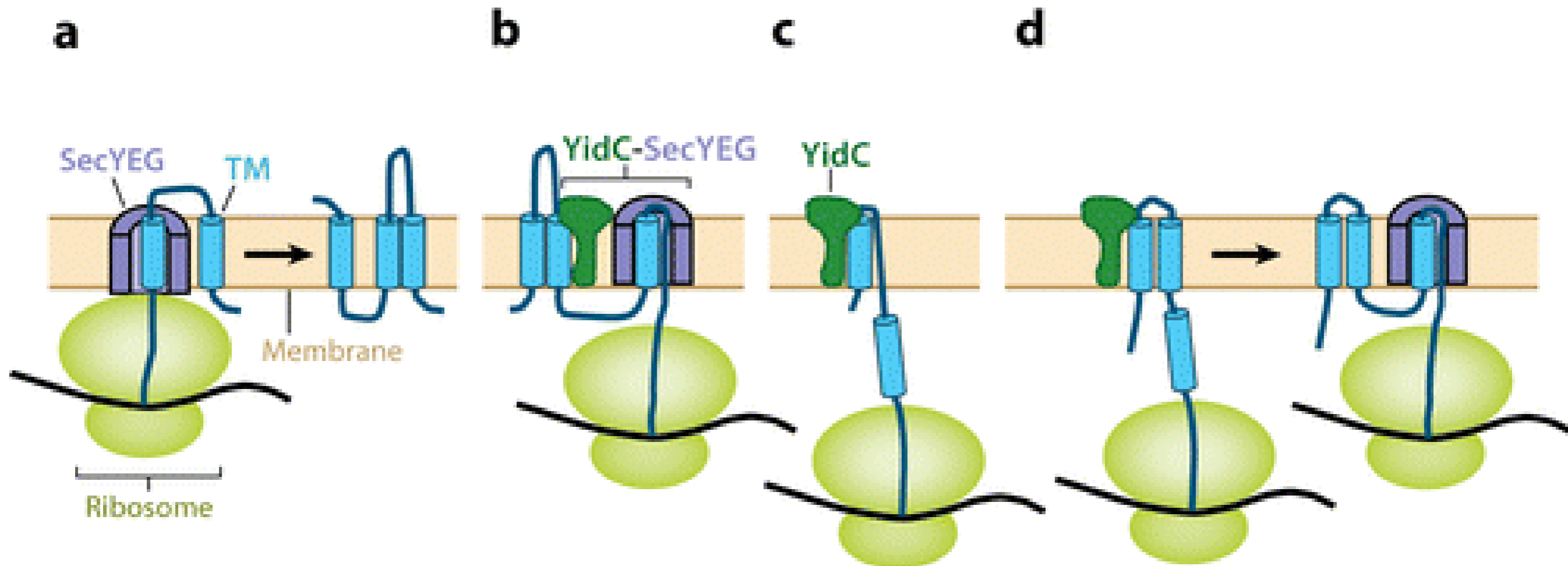


Figure 12-47 Molecular Biology of the Cell 5/e (© Garland Science 2008)

Getting into the ER: the Special Case of Tail-Anchored Proteins



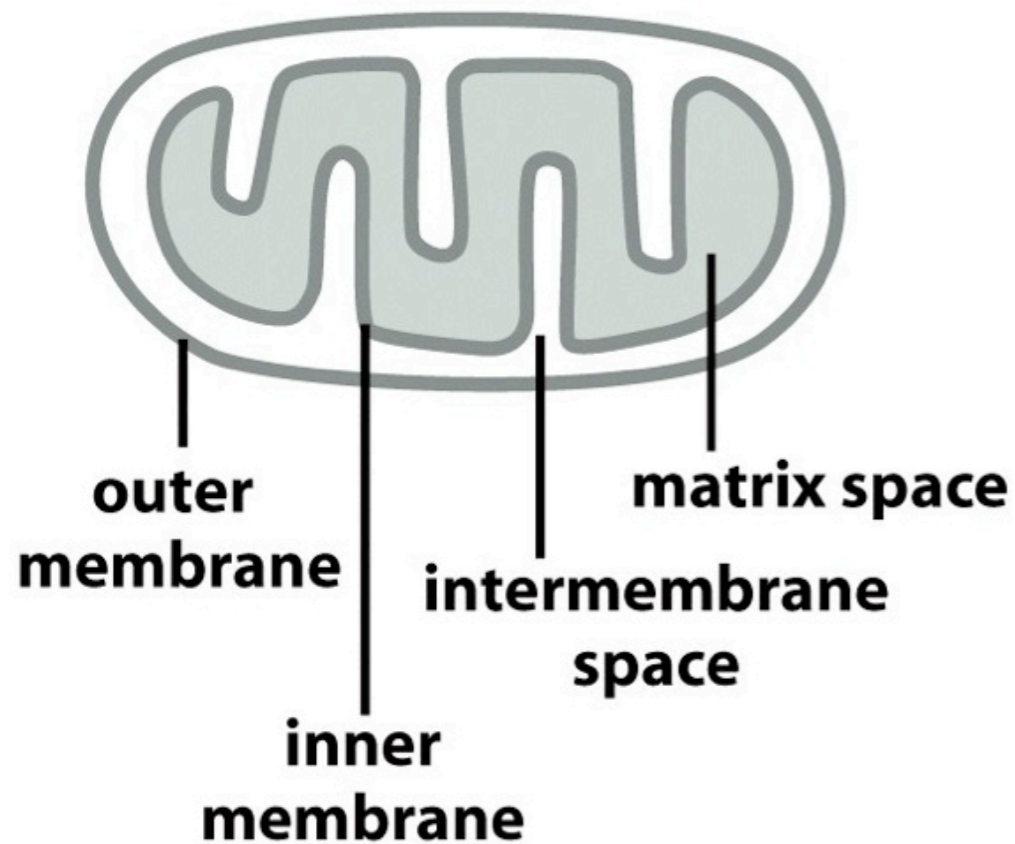
Extra Players in Prokaryotic Protein Targeting: YidC



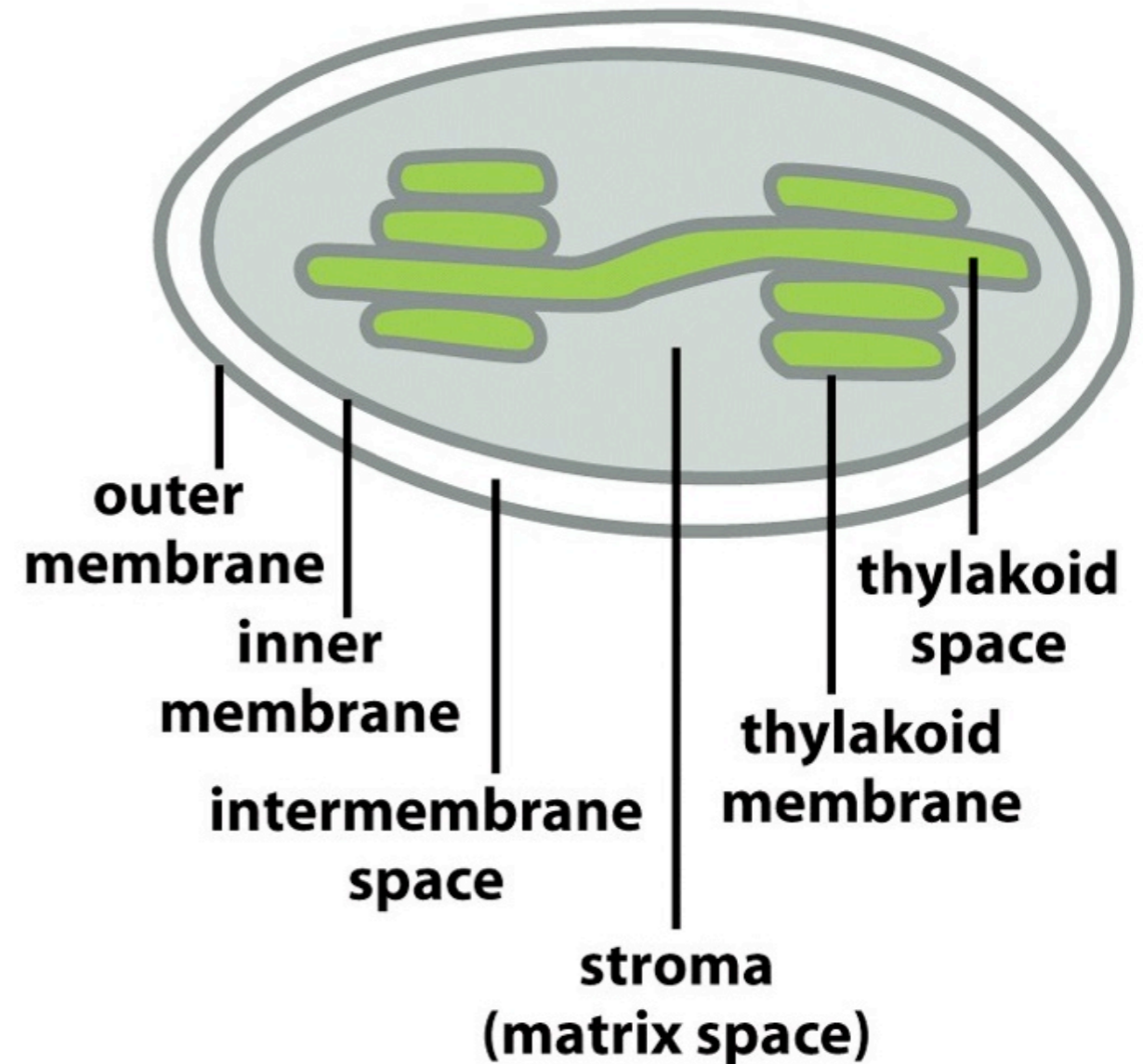
AR Dalbey RE, et al. 2011.
Annu. Rev. Biochem. 80:161–87

Chloroplasts and Mitochondria Have Their Own Genome but Most Proteins are Made in the Cytosol and Imported.

(A) MITOCHONDRION



(B) CHLOROPLAST



Trafficking to Mitochondrial Membranes

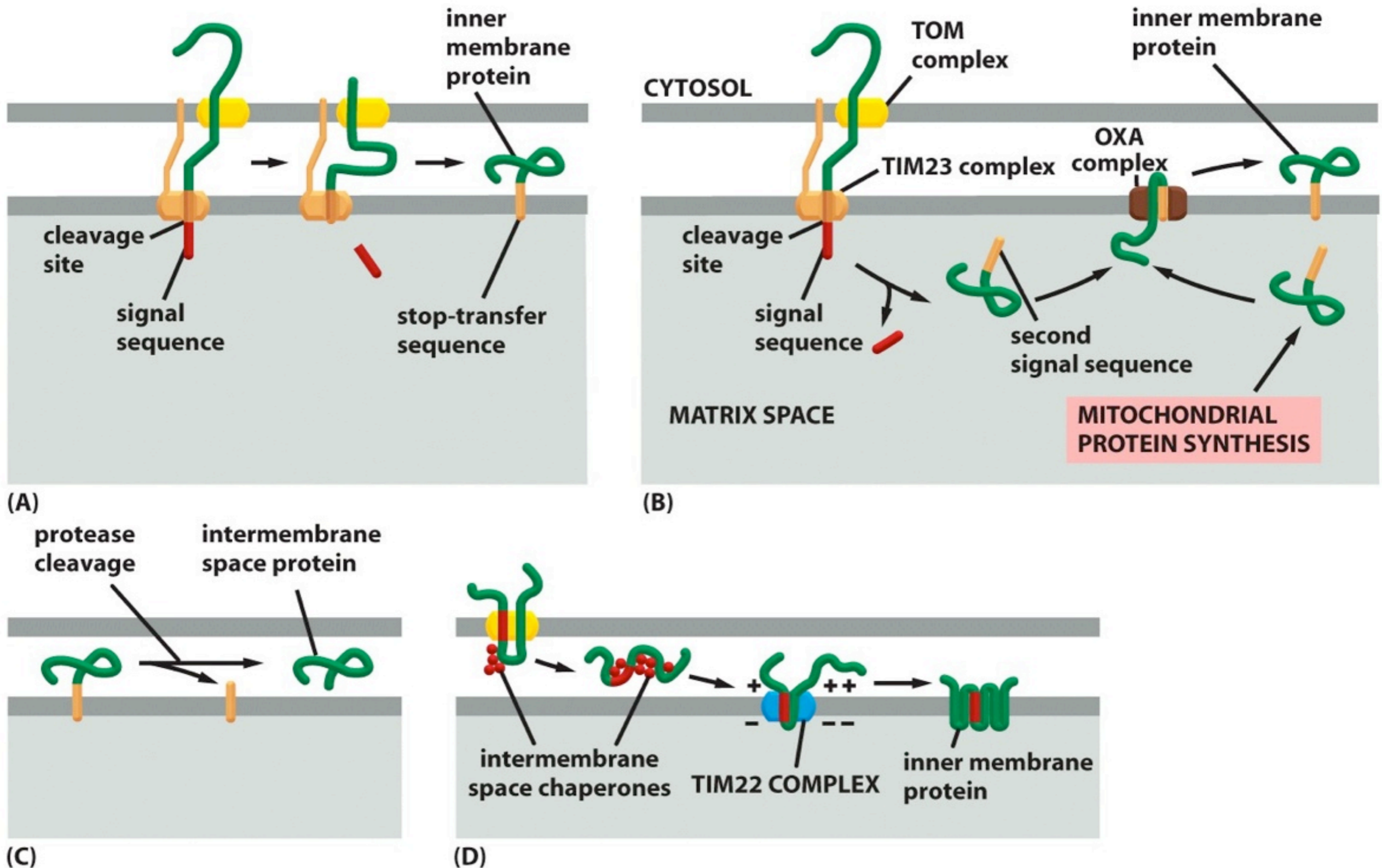


Figure 12-28 Molecular Biology of the Cell 5/e (© Garland Science 2008)

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Functions of Membrane Proteins:

Signaling

Transporters

Enzymes

Anchors

Signaling: IRE1 and the Unfolded Protein Response

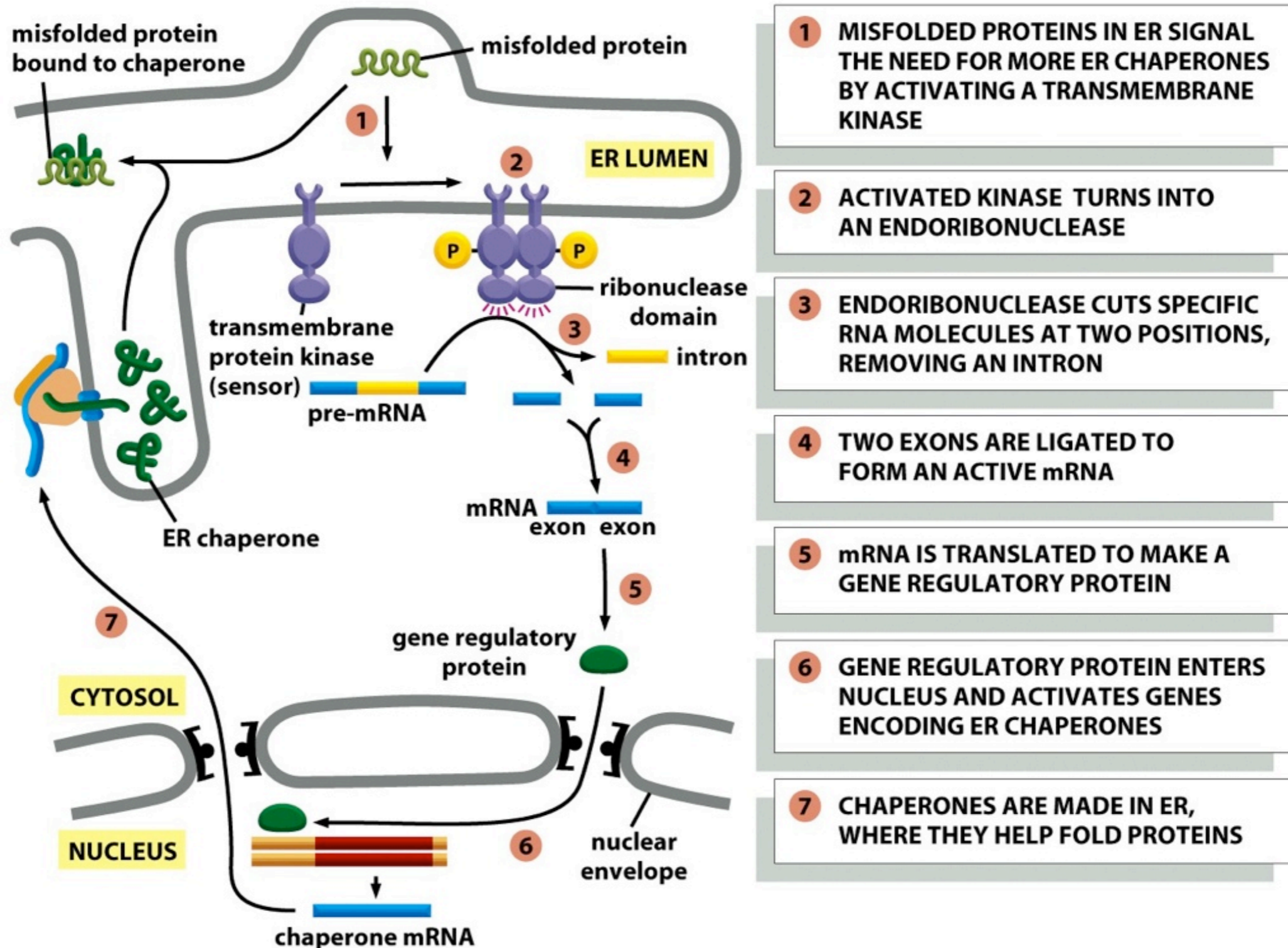
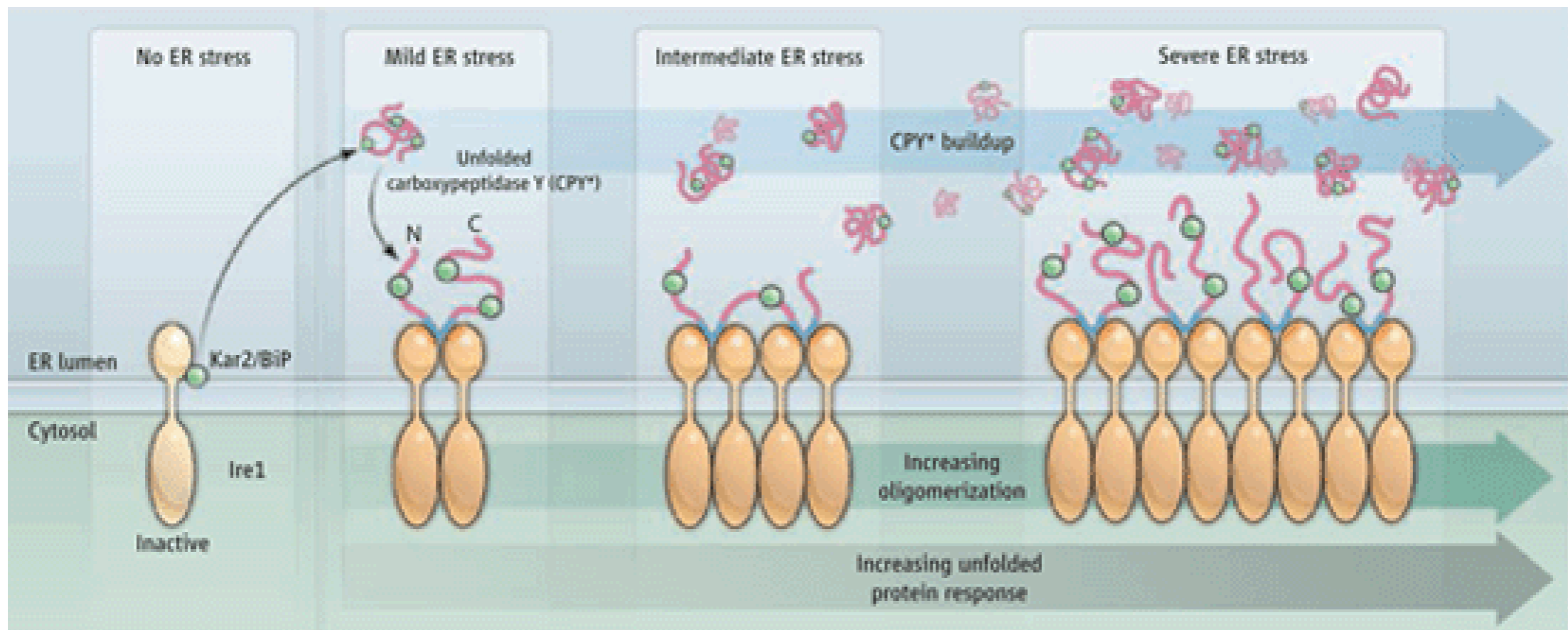


Figure 12-55b Molecular Biology of the Cell 5/e (© Garland Science 2008)

Signaling: IRE1 and the Unfolded Protein Response



Transporters: Aquaporins

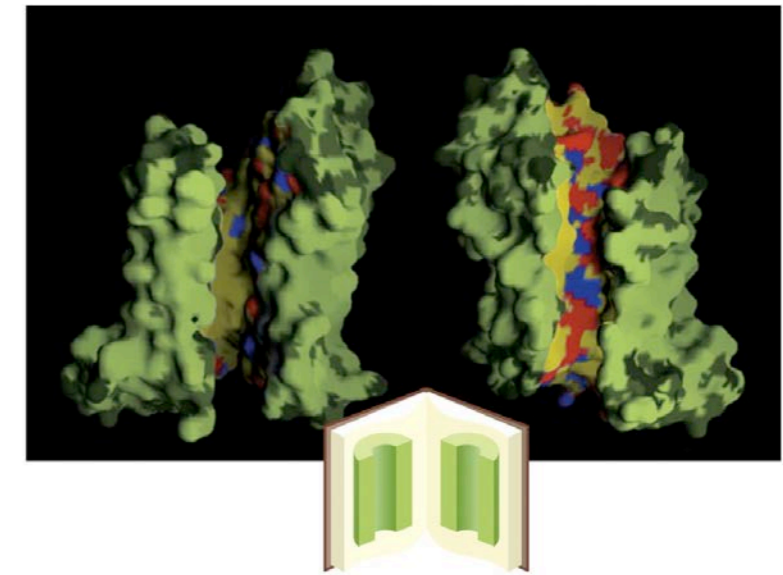
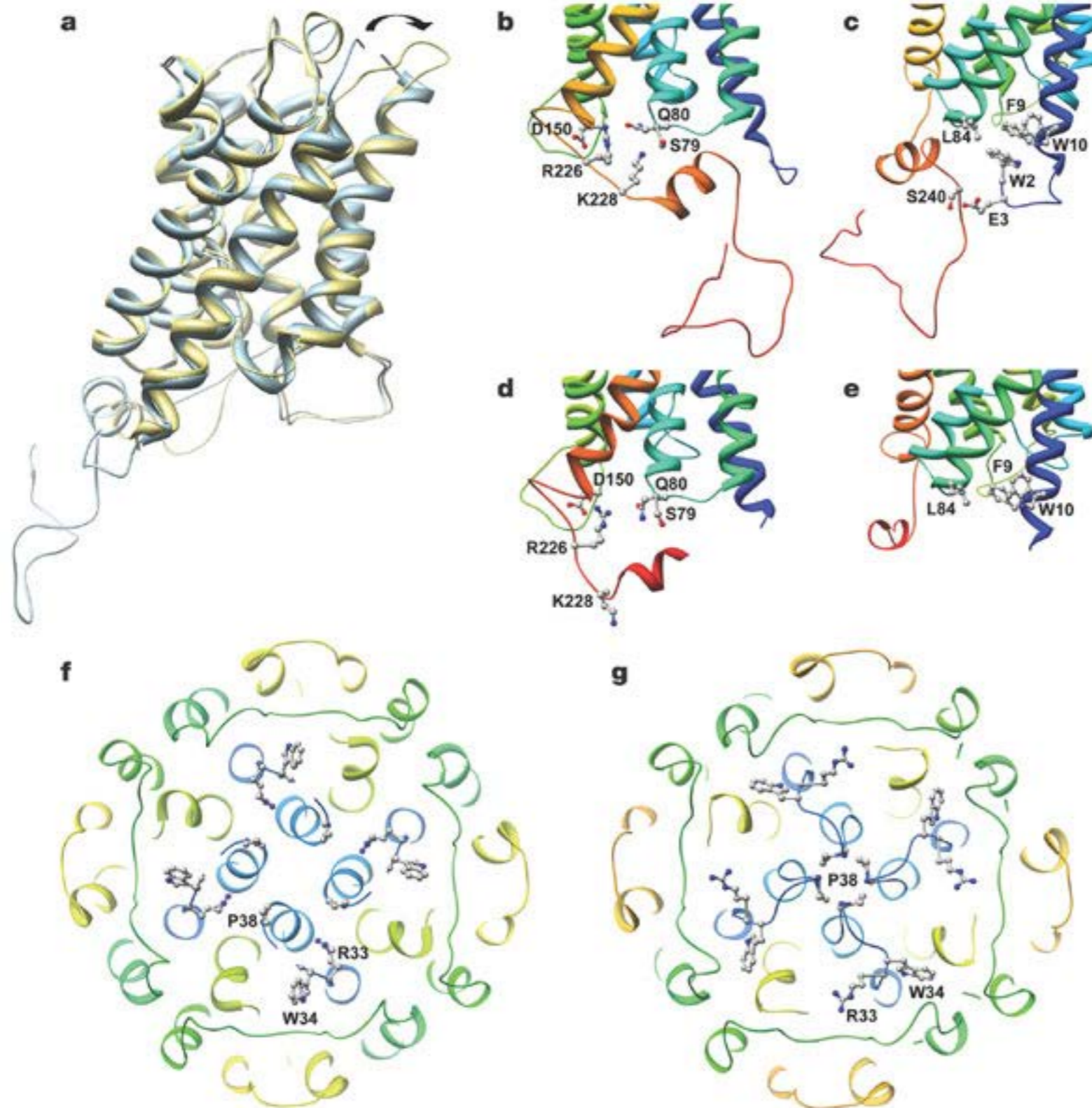
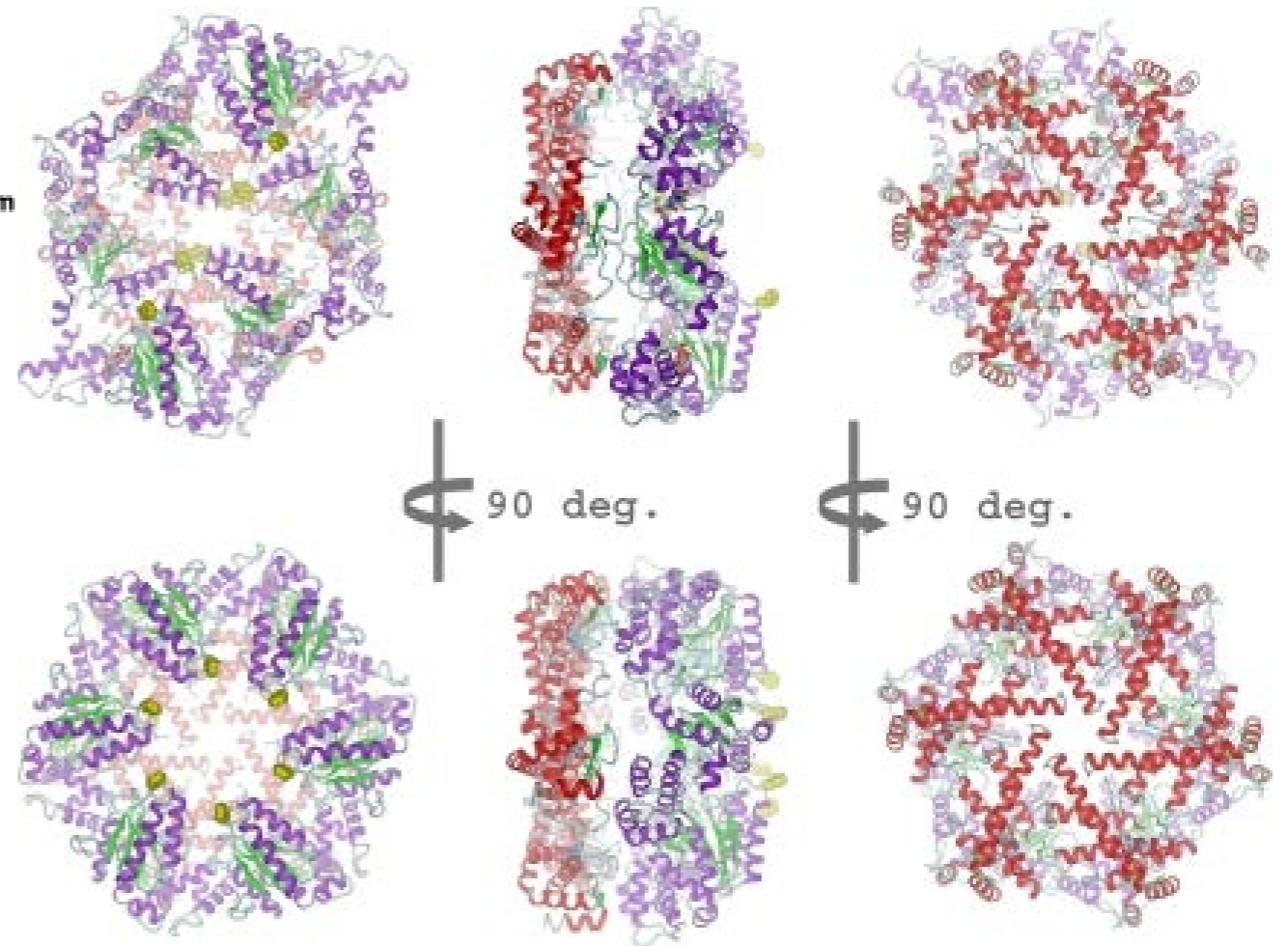
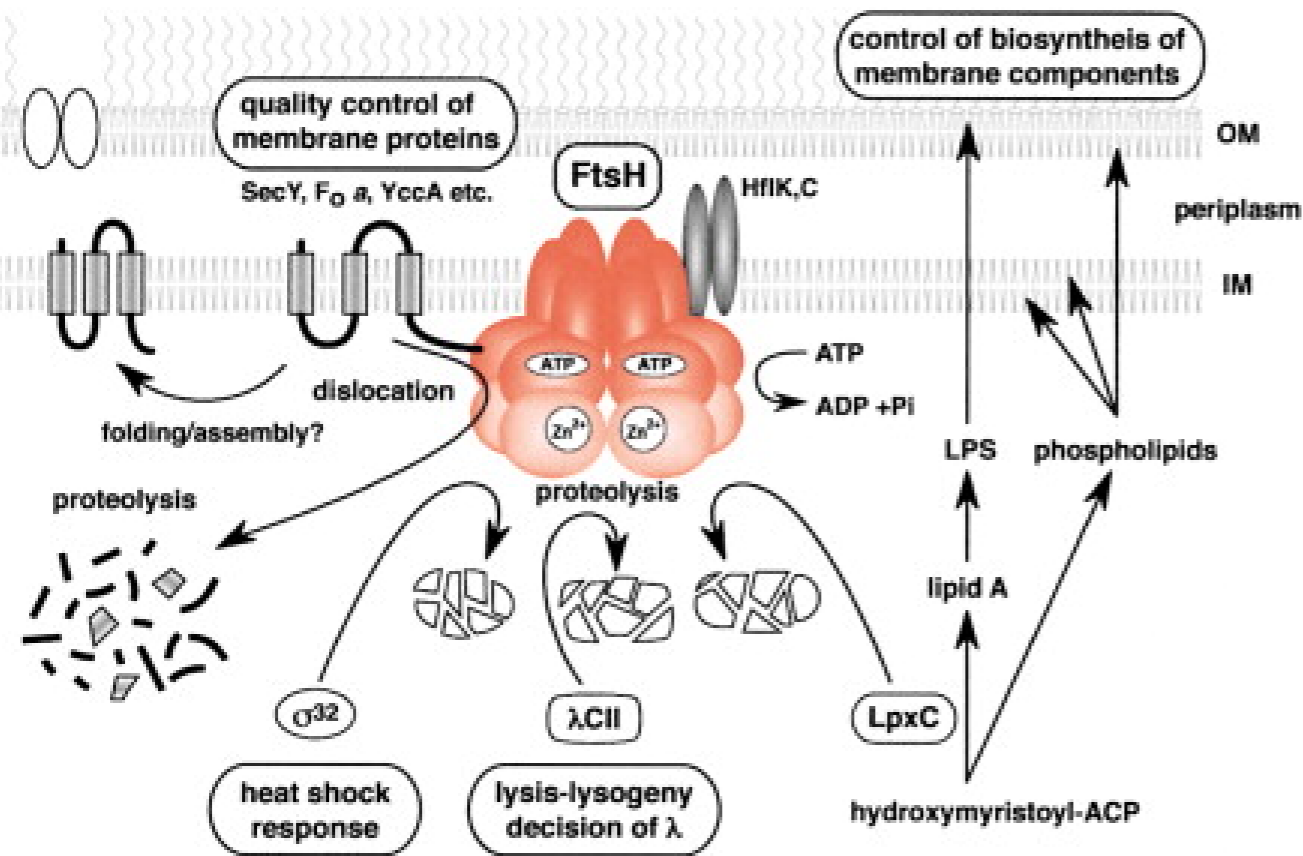


Figure 11-27b Molecular Biology of the Cell 5/e (© Garland Science 2008)

Enzymes: FtsH, a Membrane Bound Protease

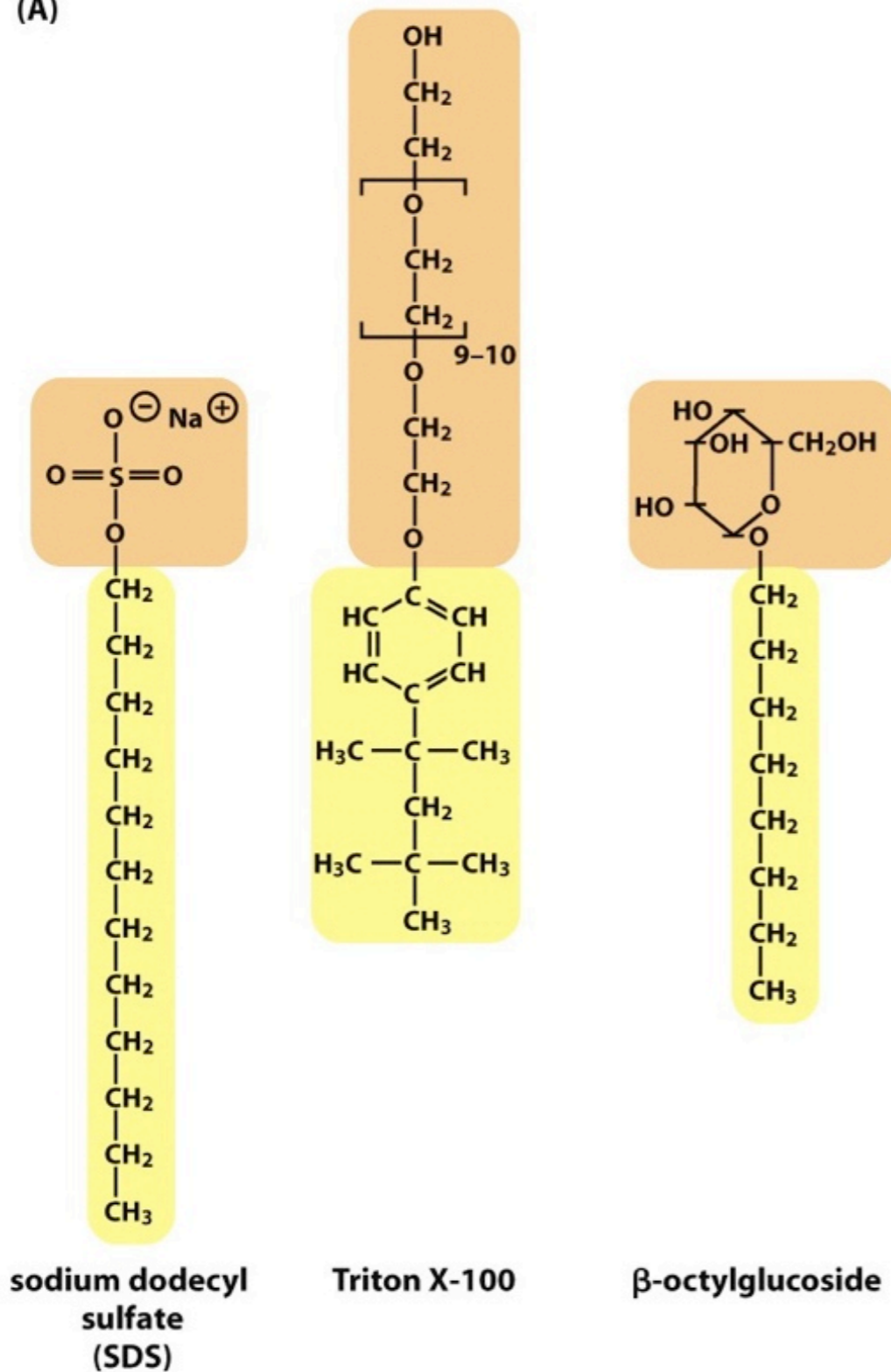


Membrane proteins:

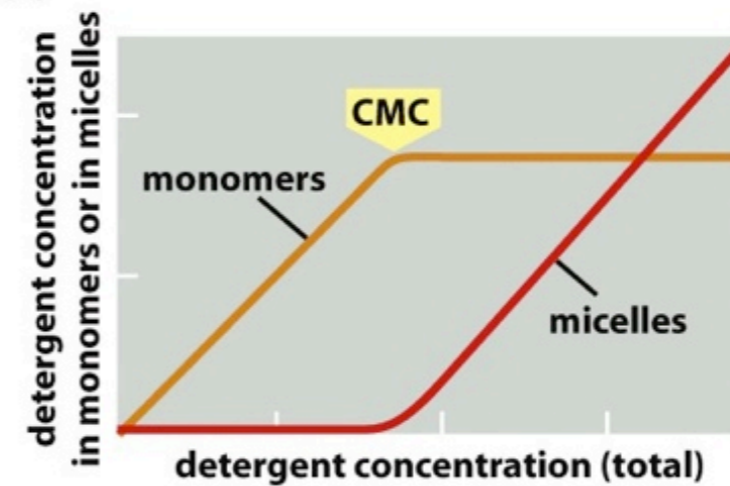
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Working with Membrane Proteins: Pick Detergents Wisely

(A)



(B)



(C)

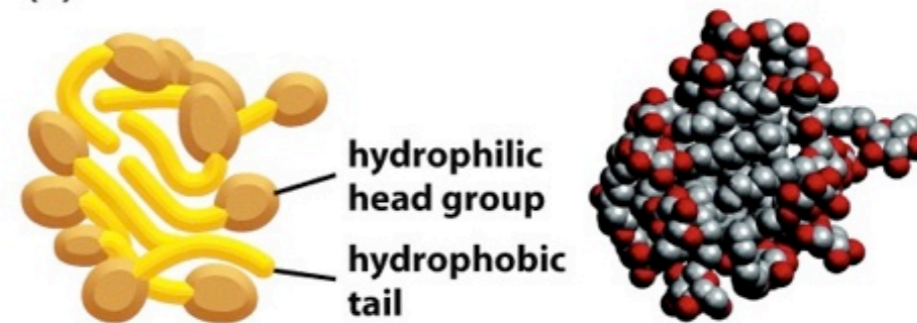


Figure 10-29 Molecular Biology of the Cell 5/e (© Garland Science 2008)

Proteoliposomes

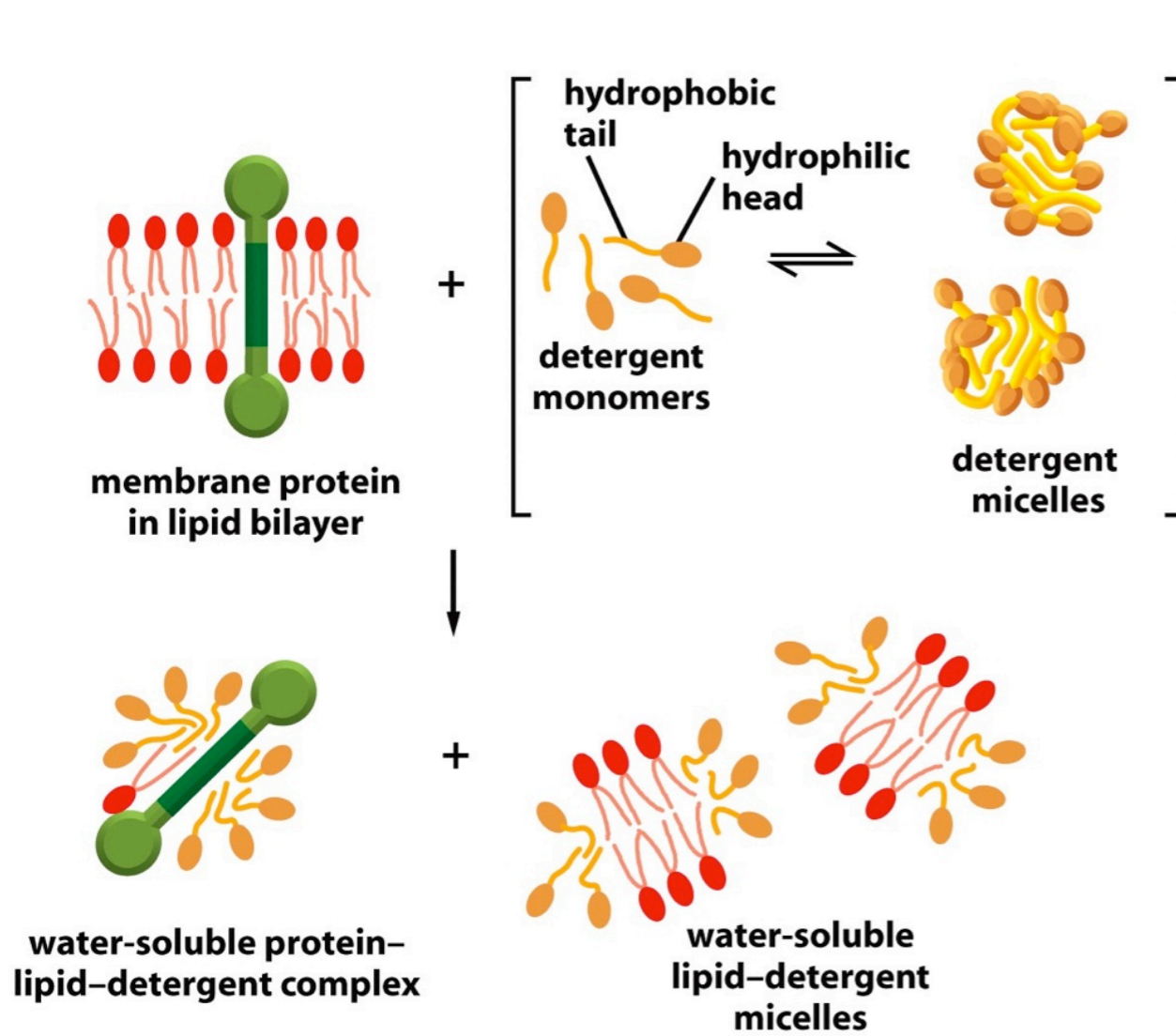


Figure 10-30 Molecular Biology of the Cell 5/e (© Garland Science 2008)

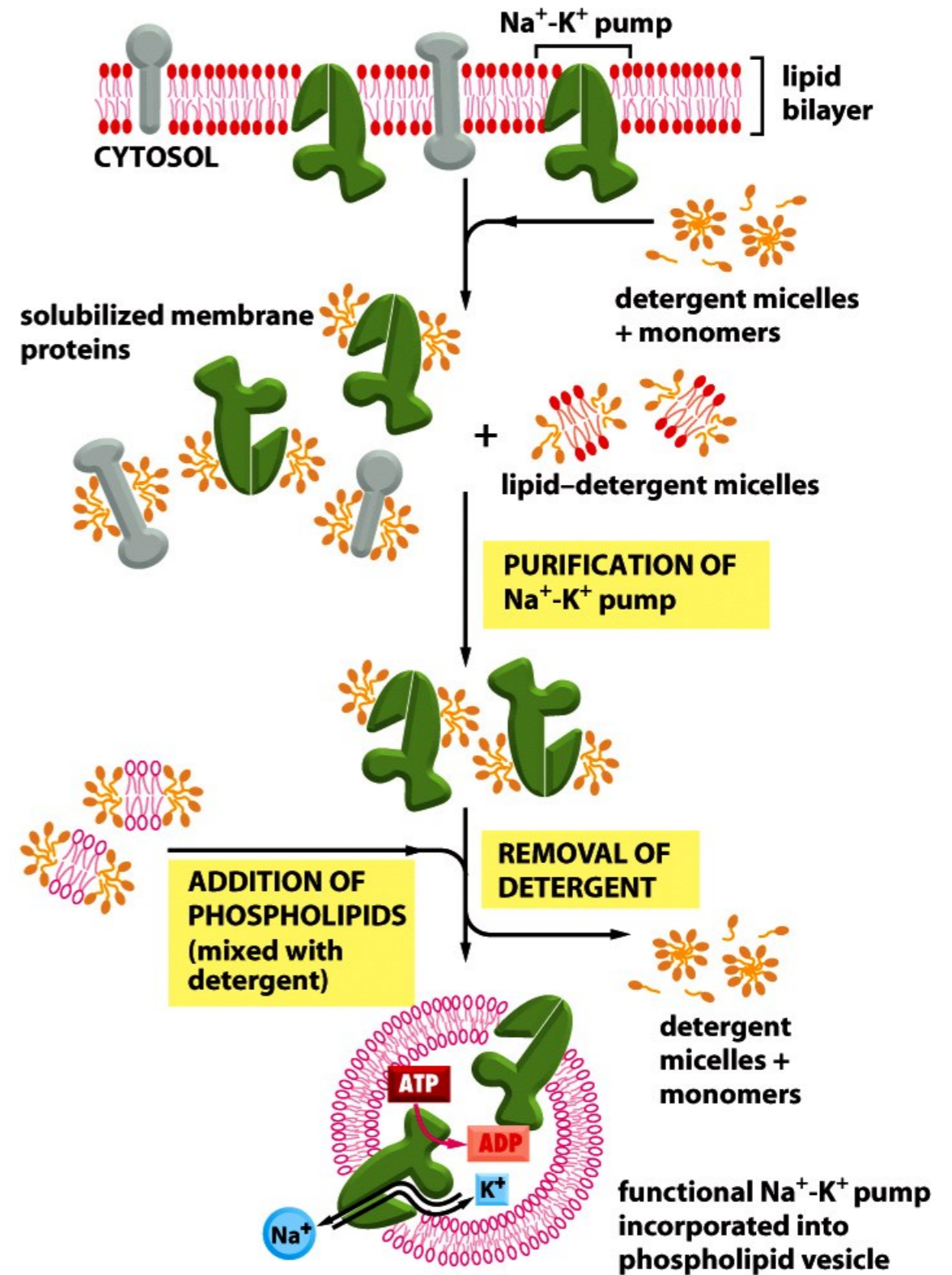
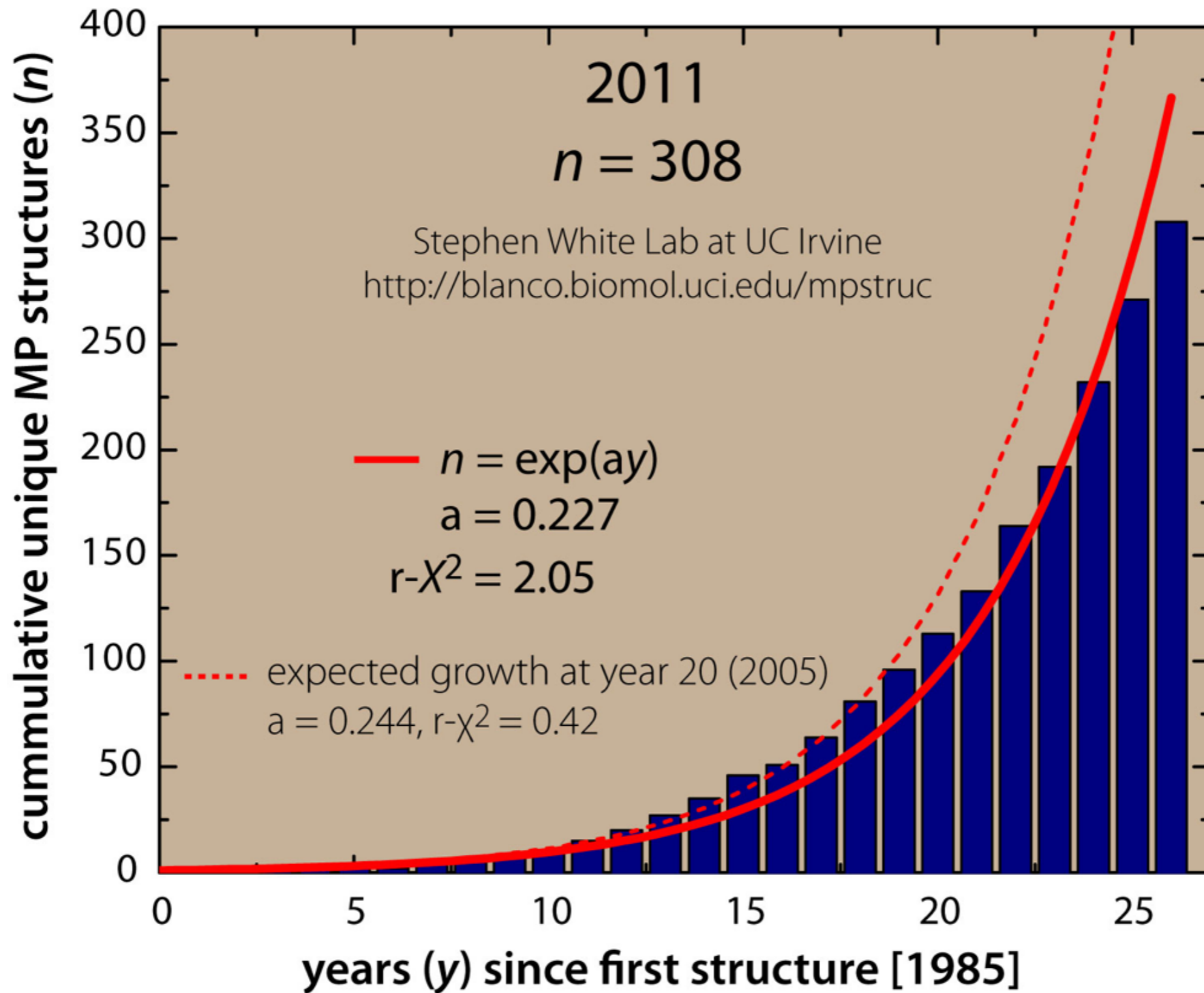
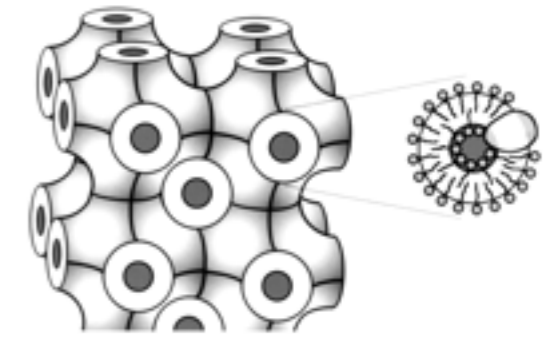


Figure 10-31 Molecular Biology of the Cell 5/e (© Garland Science 2008)

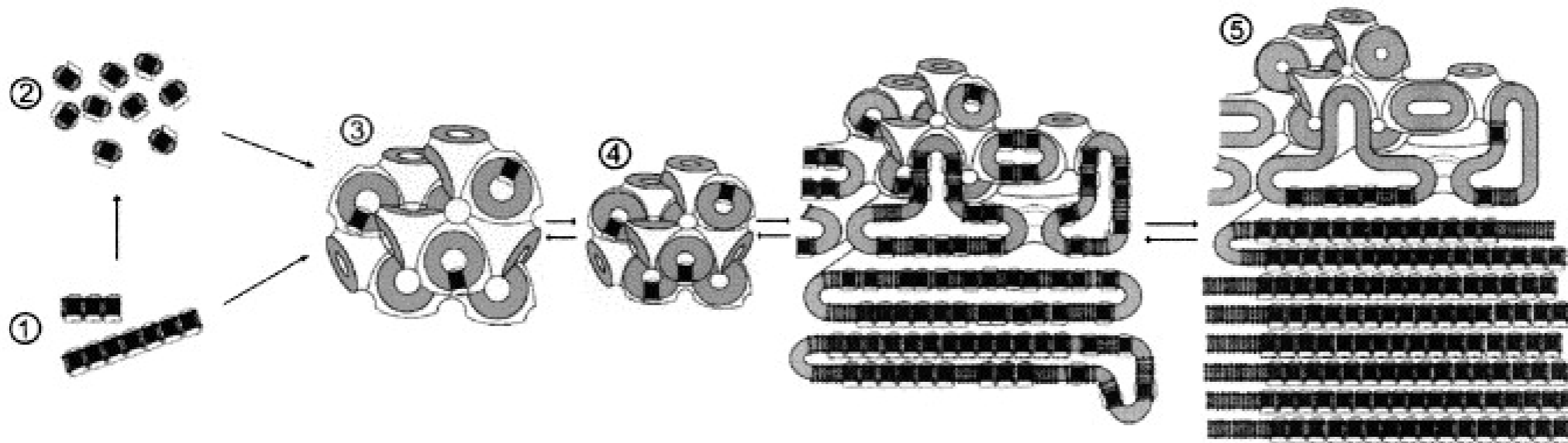
Not Many Membrane Protein Crystal Structures Solved



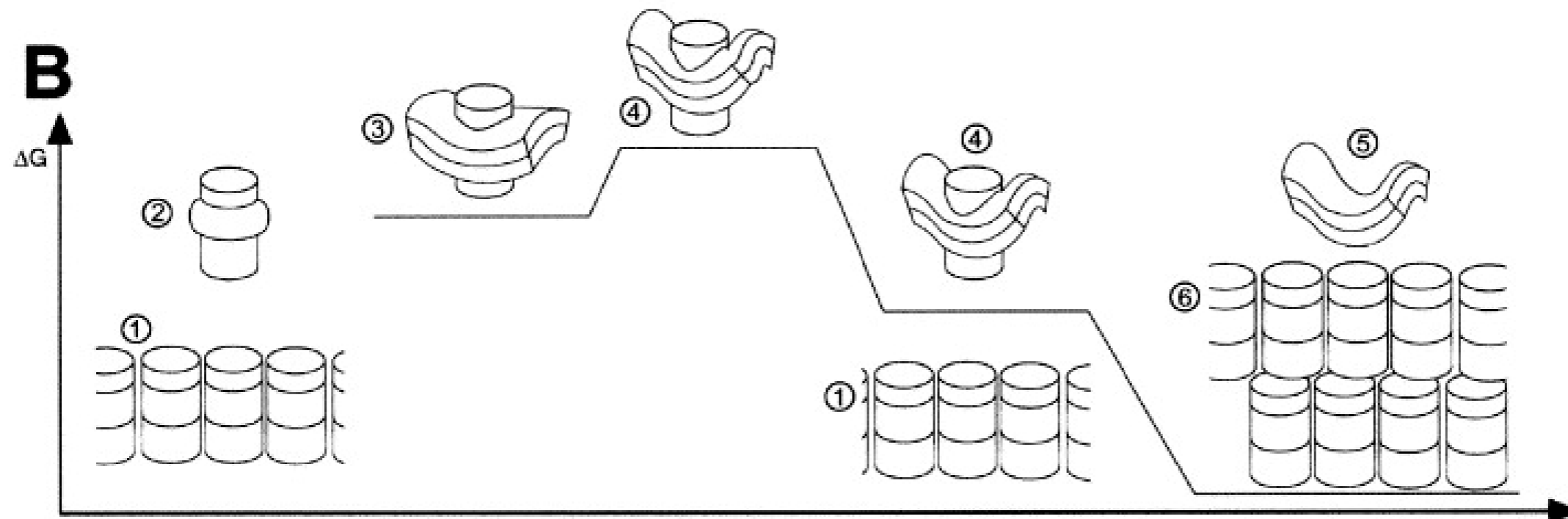
Lipidic Cubic Phase for Membrane Proteins



A

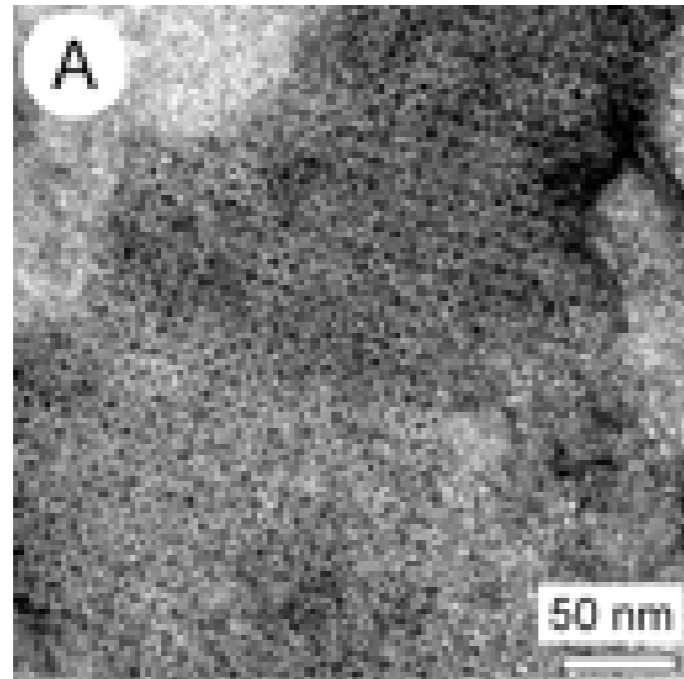


B

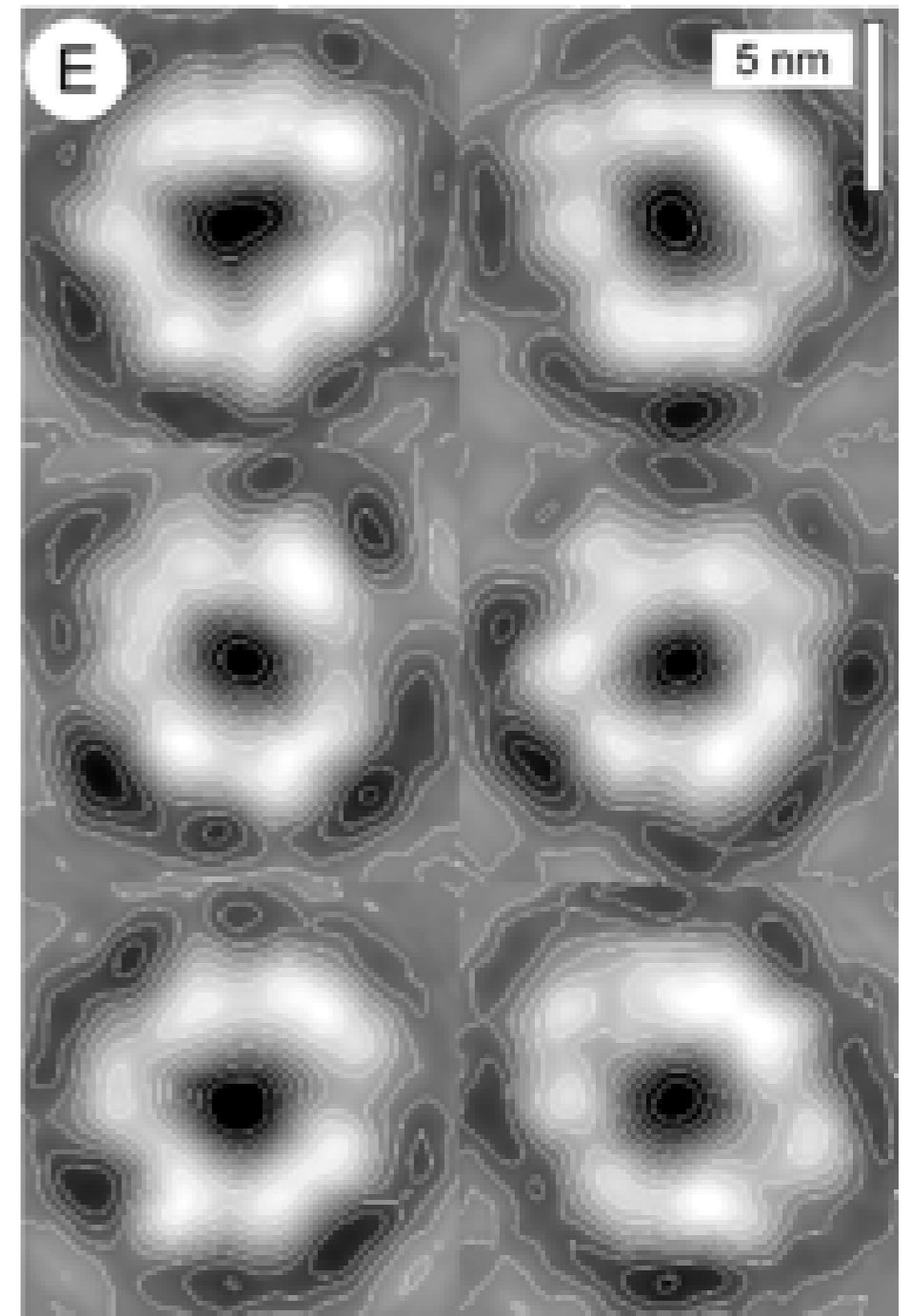
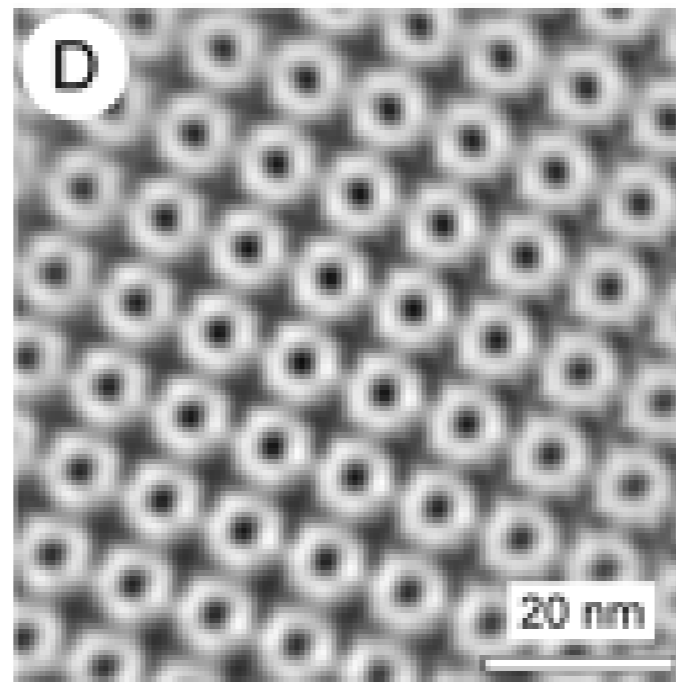
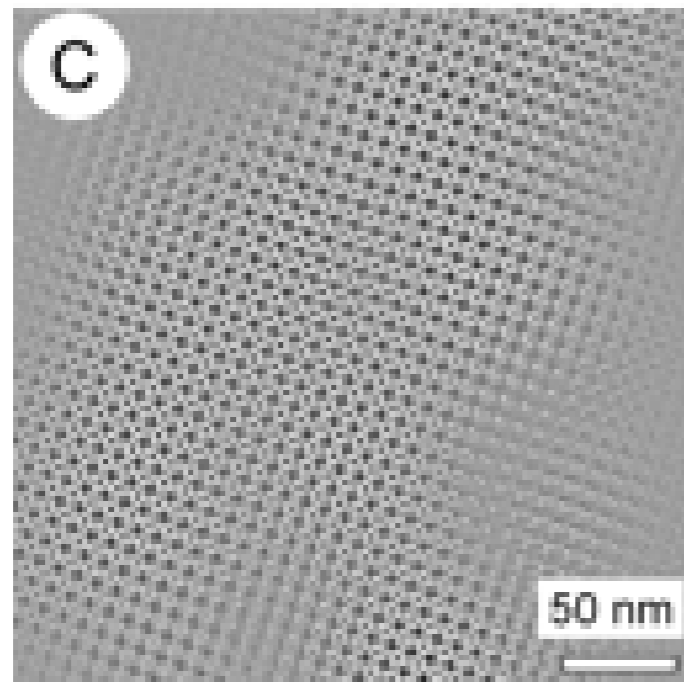
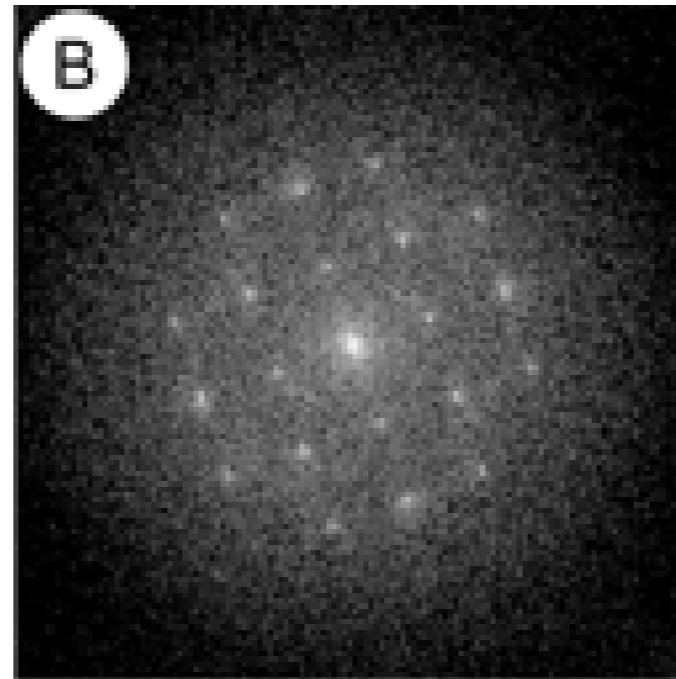


Electron Crystallography: An Example (Wza)

Neg. Stain



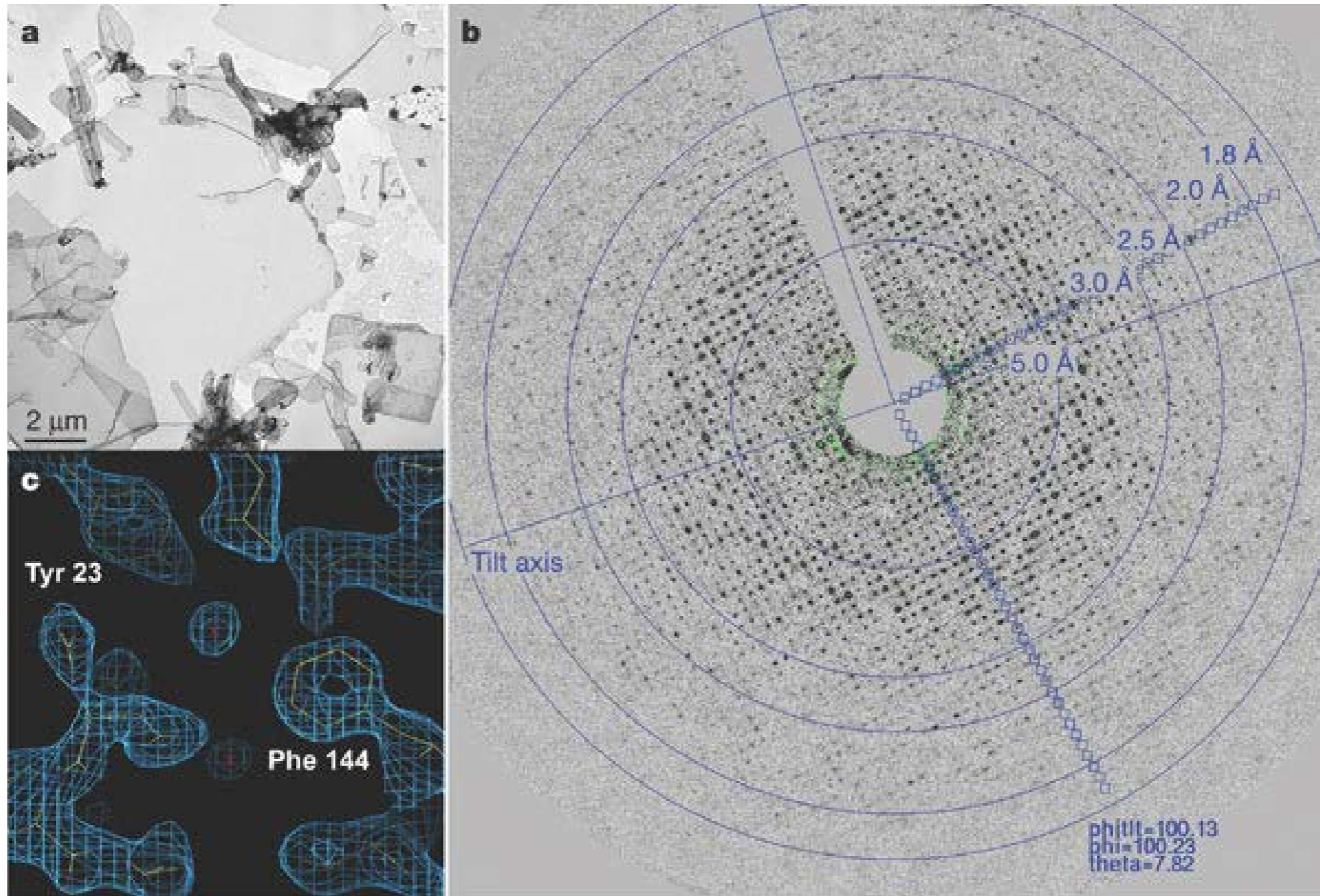
Diffraction Pattern



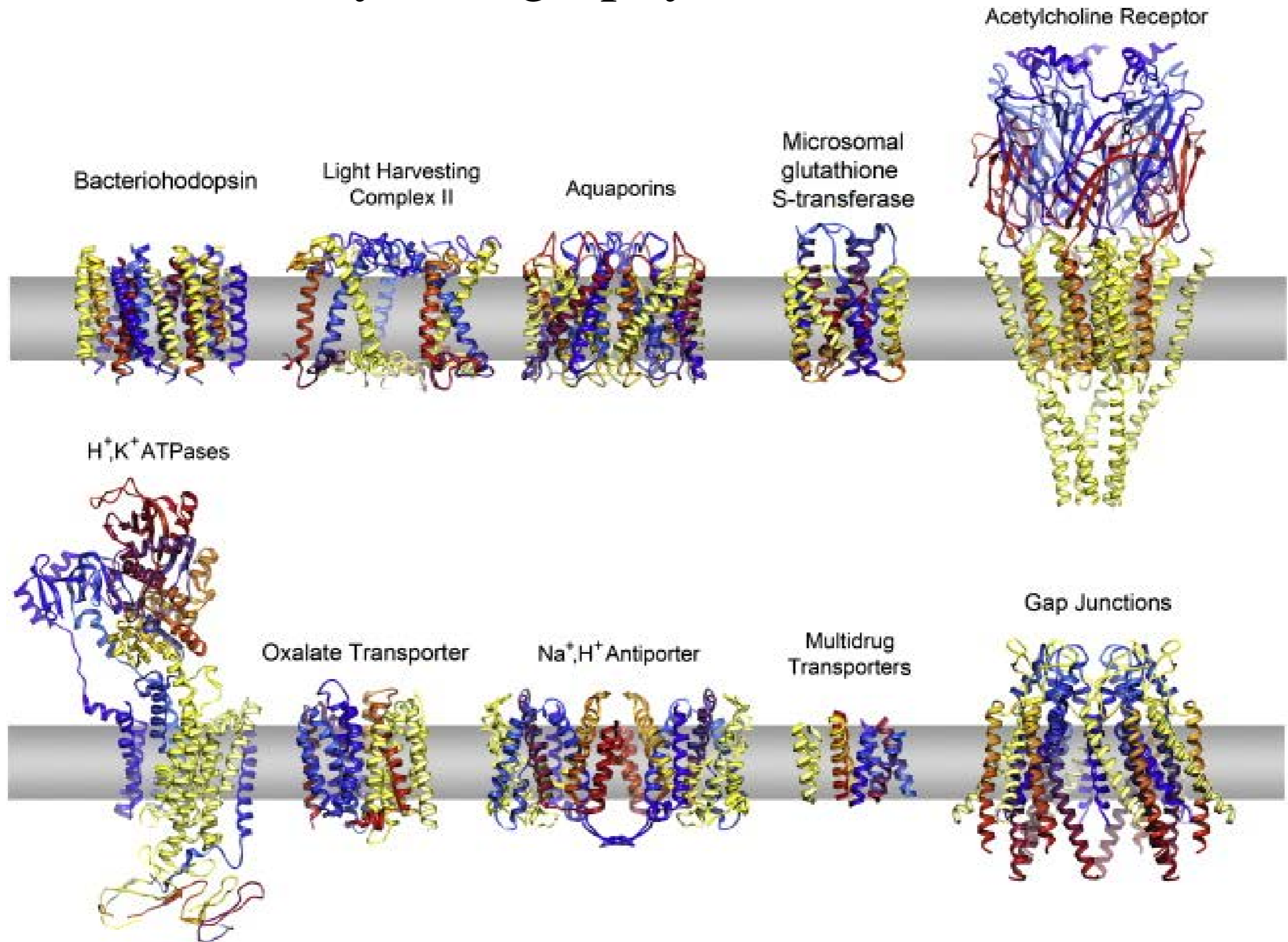
2-D crystals

Class averages of single particles

Electron Crystallography: Aquaporin



Electron Crystallography: Solved Structures



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