

Membrane Proteins

11/8/07

Biomolecular Structure

Lynmarie Thompson

Fewer Structures Known

Listings of membrane protein structures

- http://blanco.biomol.uci.edu/Membrane_Proteins_xtal.html

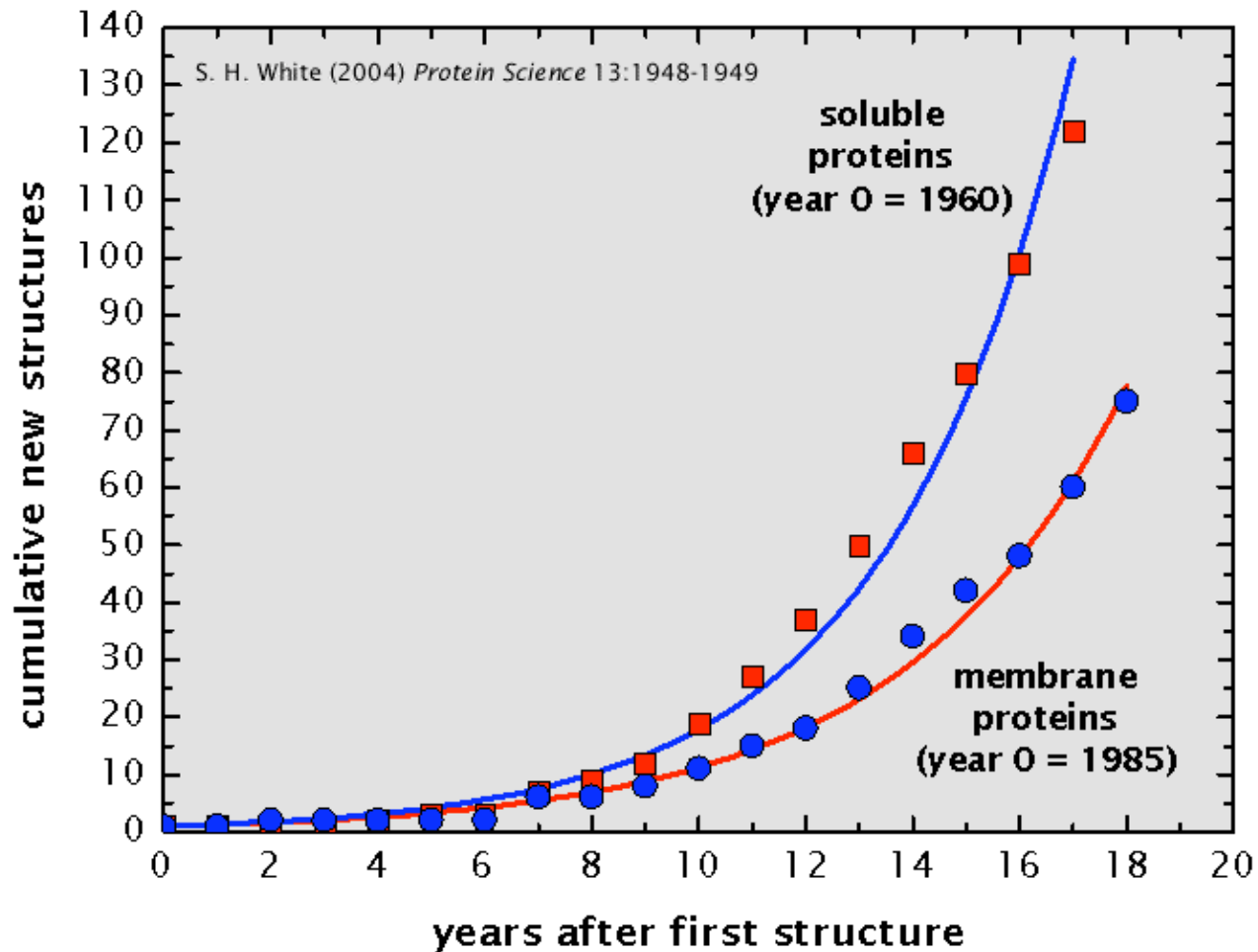
134 unique (281 total)

- <http://www.mpibp-frankfurt.mpg.de/michel/public/memprotstruct.html>
- <http://www.mpdb.ul.ie/>

177 unique (749 total)

Growing fast - 125 in 2006!

- <http://pdbtm.enzim.hu/>



- Exponential growth, with lag
- # structures doubles every ≈ 3 years

Classic picture

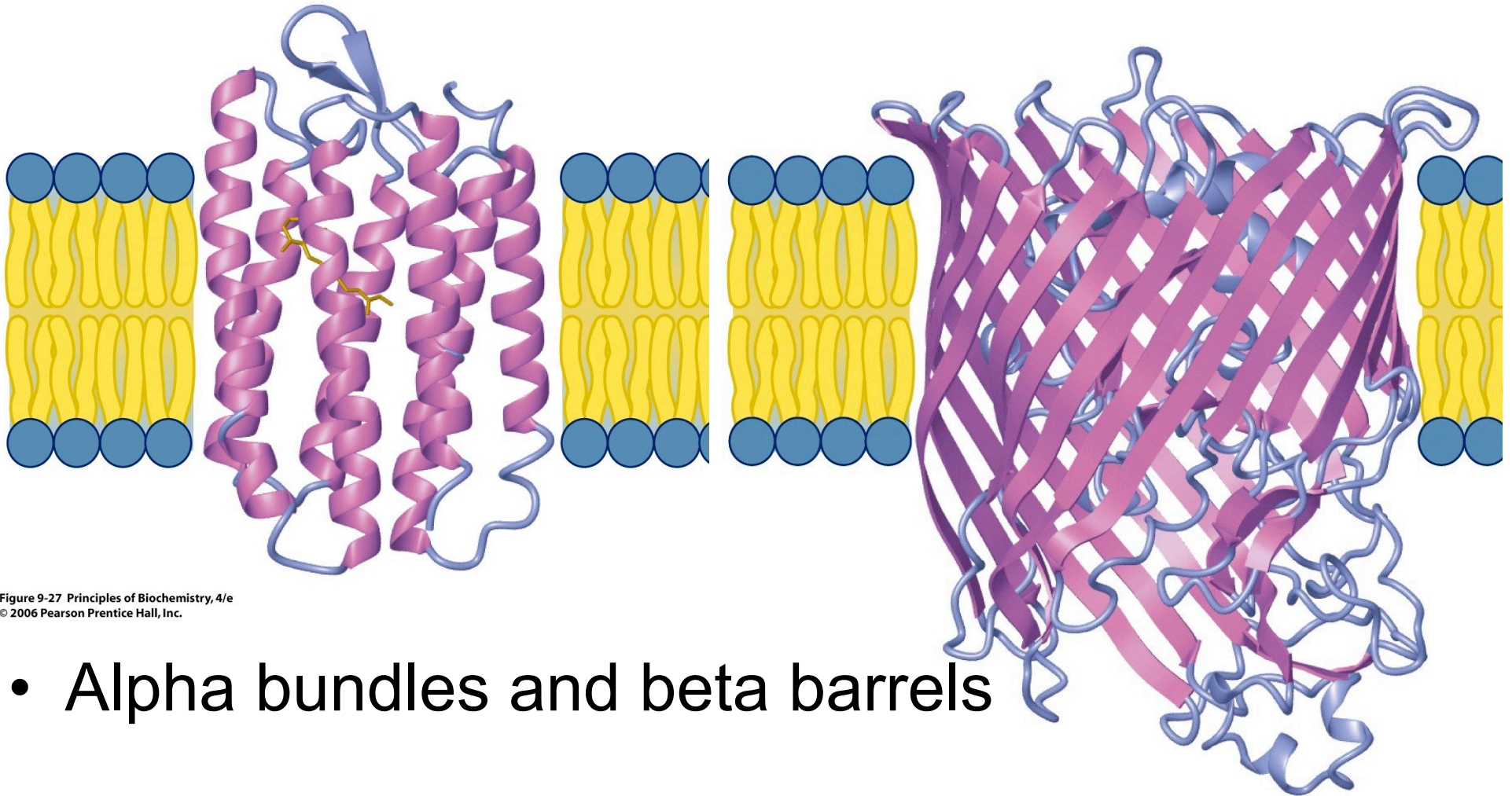


Figure 9-27 Principles of Biochemistry, 4/e
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- Alpha bundles and beta barrels
- New twists emerging

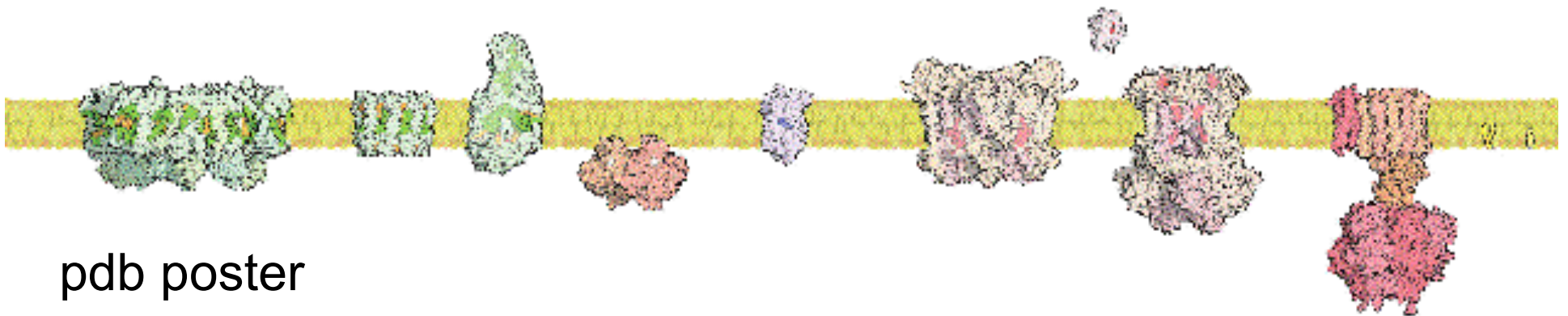
Figure 9-28 Principles of Biochemistry, 4/e
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Critical Functions

- Energy conversion
 - Light or metabolism-driven electron transport
 - Light or electron-xfer driven proton pumps
 - Proton-driven motor or ATP synthesis
- Signaling
 - Receptors
 - Channels
- Transport
 - Pumps
 - Channels

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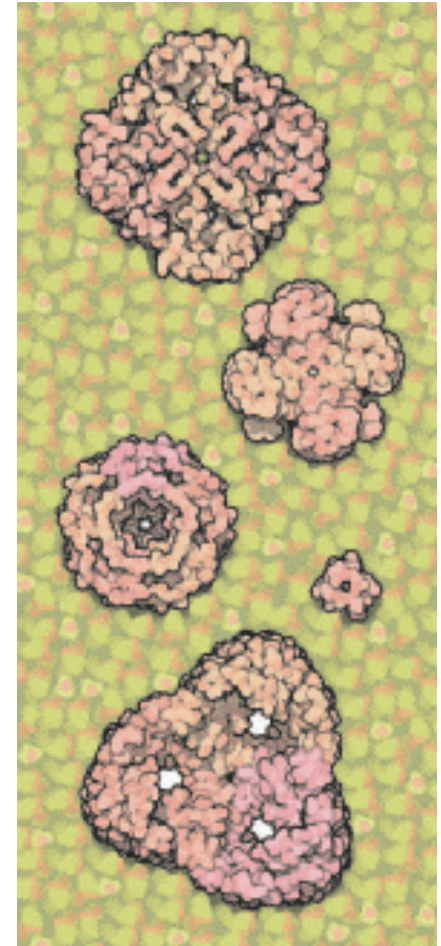
Earliest structures; not flexible.

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Pump: Ca-ATPase

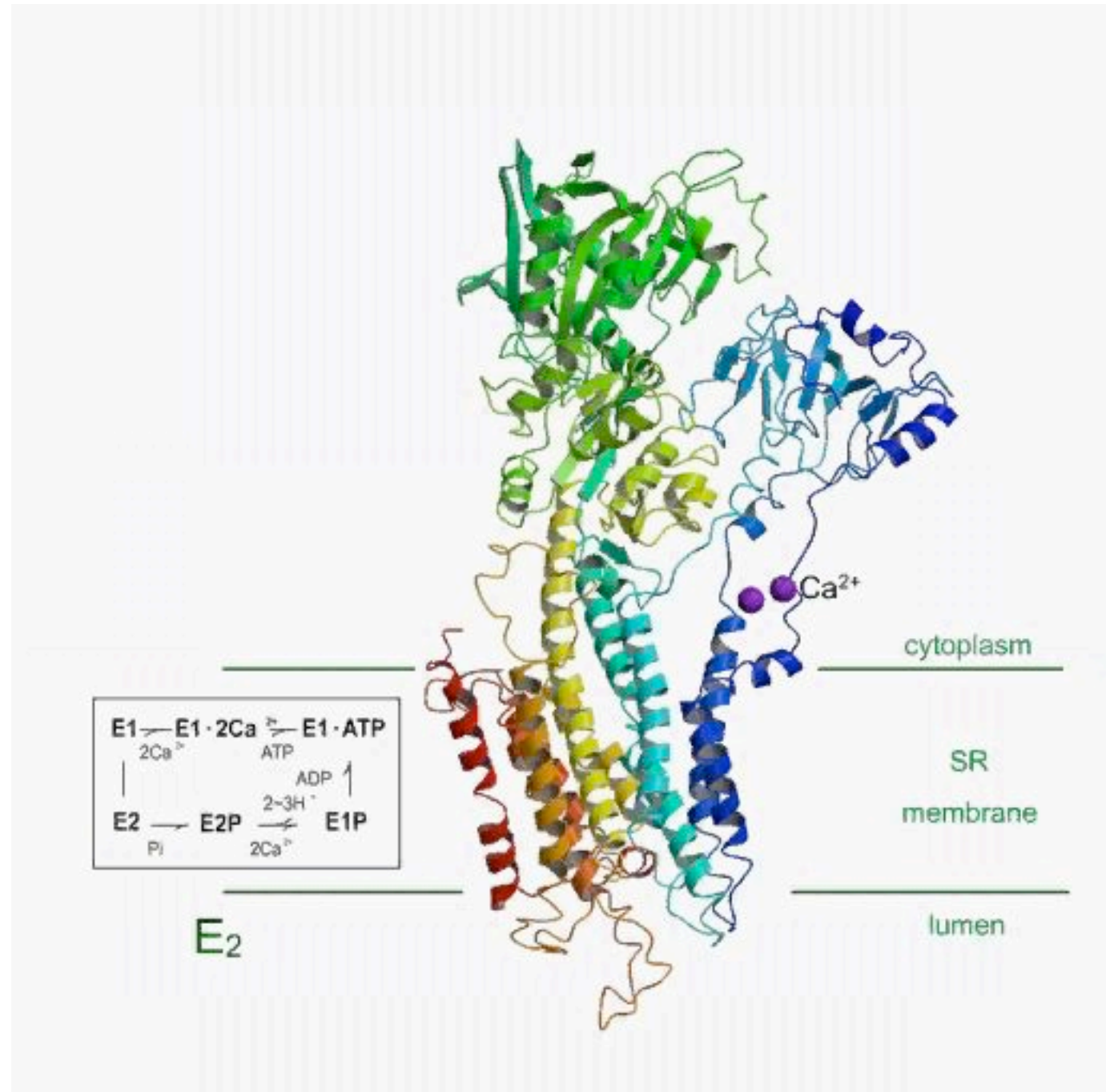
Channels



Recently solved structures include more flexible proteins...

Bovine Ca^{2+} -ATPase.

Toyoshima, C.,
Nomura, H. &
Tsuda, T.
Luminal gating
mechanism
revealed in
calcium pump
crystal
structures with
phosphate
analogues.
*Nature***432**, 361-
368 (2004).



pdb gives biased view of proteins

- Those with good properties for structural biology
 - Not dynamic
 - Not membrane bound
 - Folded
- What else are we missing...?

Beta barrels

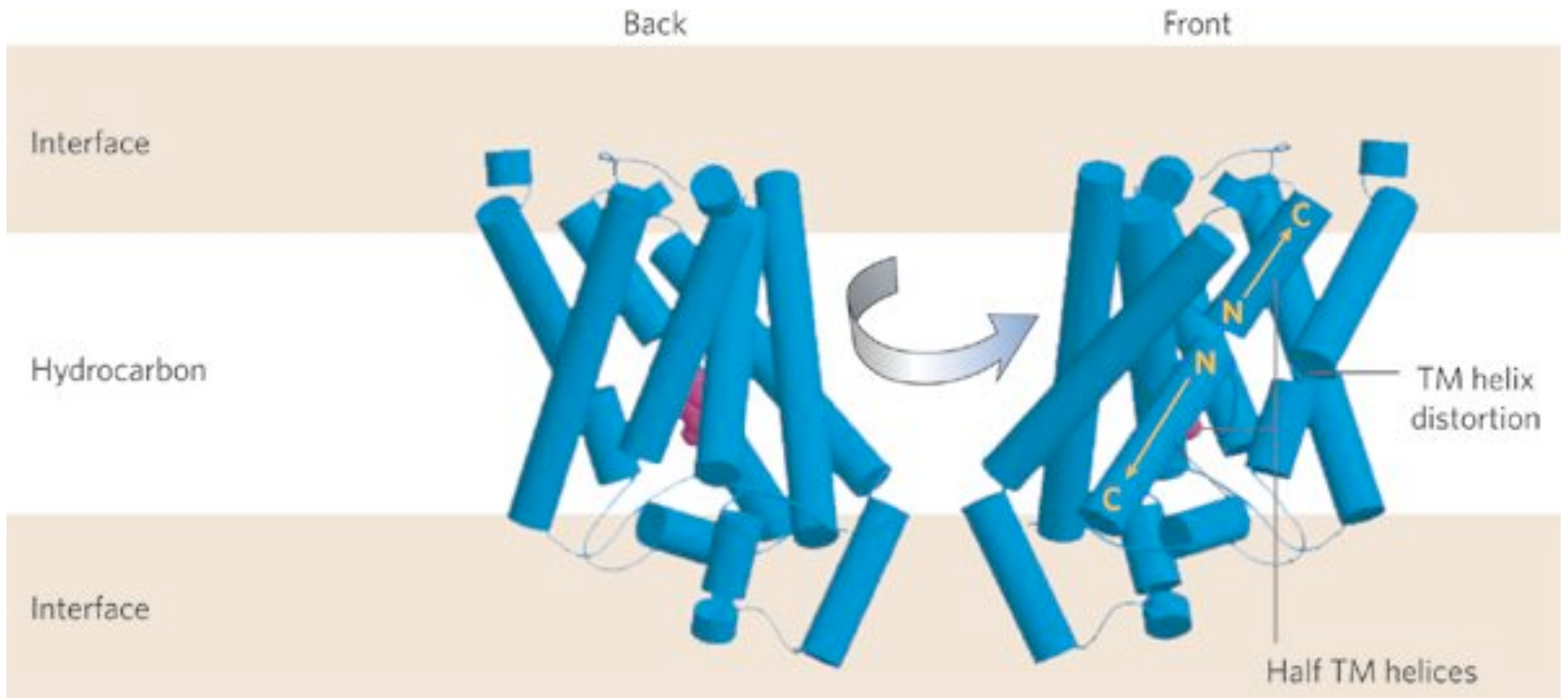
- Outer membrane of E coli & mitochondria
- Rest so far are alpha helical
- A cool beta barrel: α -hemolysin

<http://tm.chem.umass.edu/martin/Jmol/MembrProts/>

Alpha helical bundles

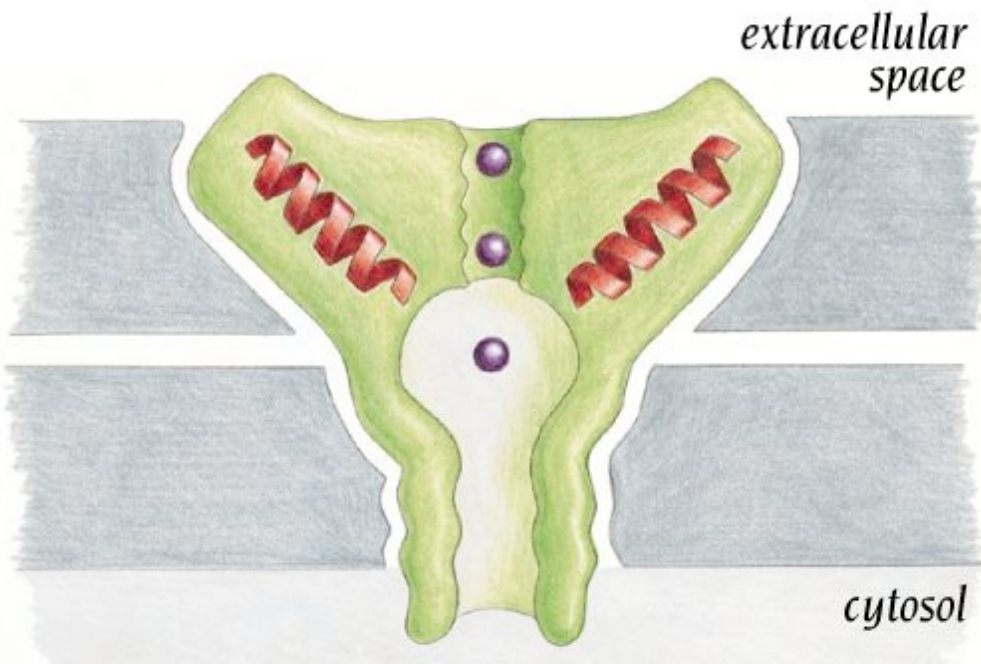
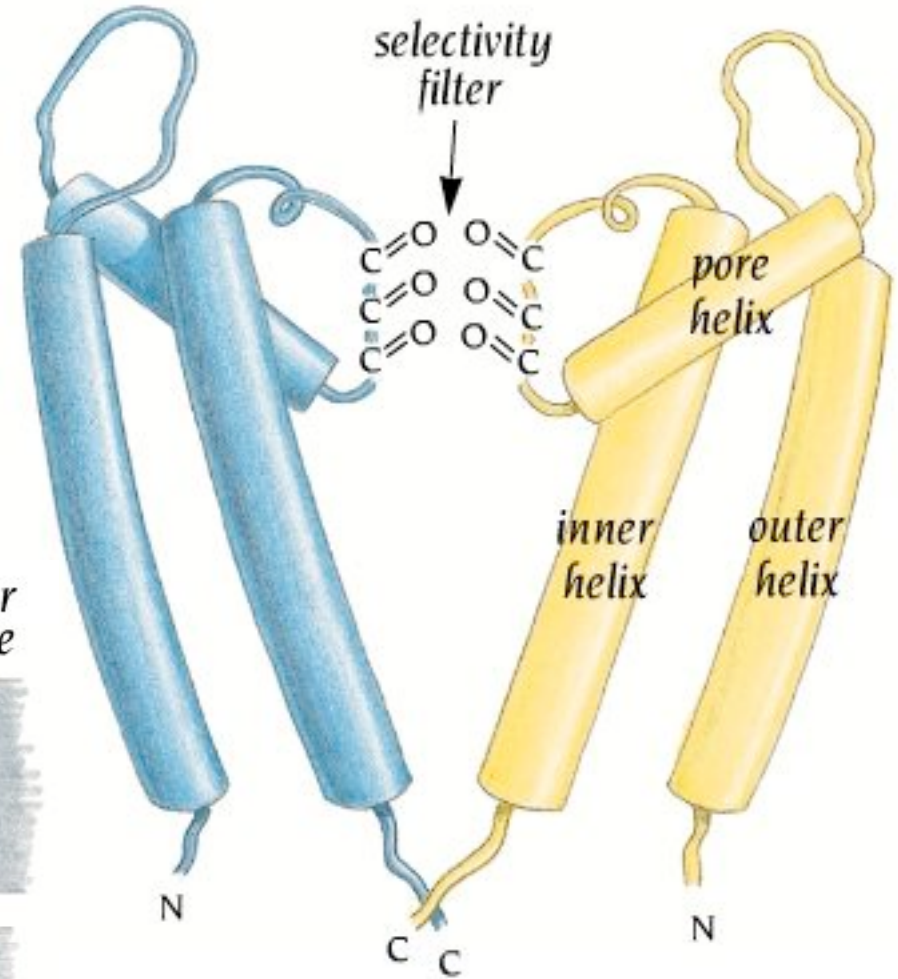
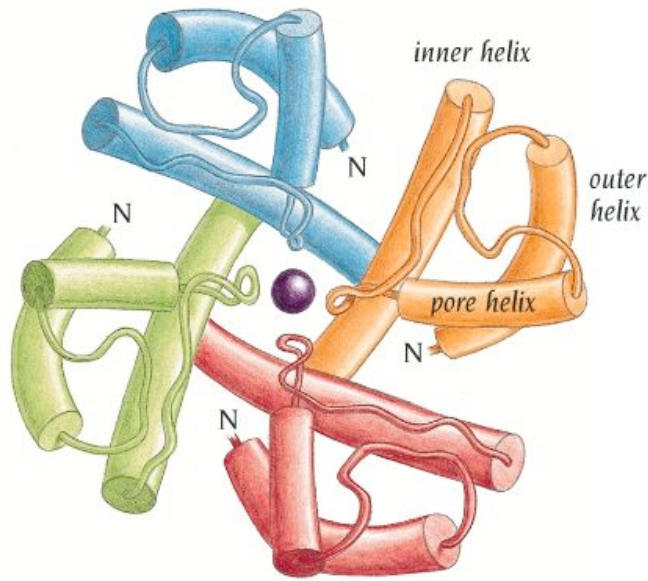
- All TM helices
 - Bacteriorhodopsin is the classic & first
- New structural twists
 - Half-helices: GlpF
 - Buried non-helices: K⁺ channel
- Functional significance

GlpF



JU Bowie (2005) Nature 438, 581-589.

Potassium Channel KcsA

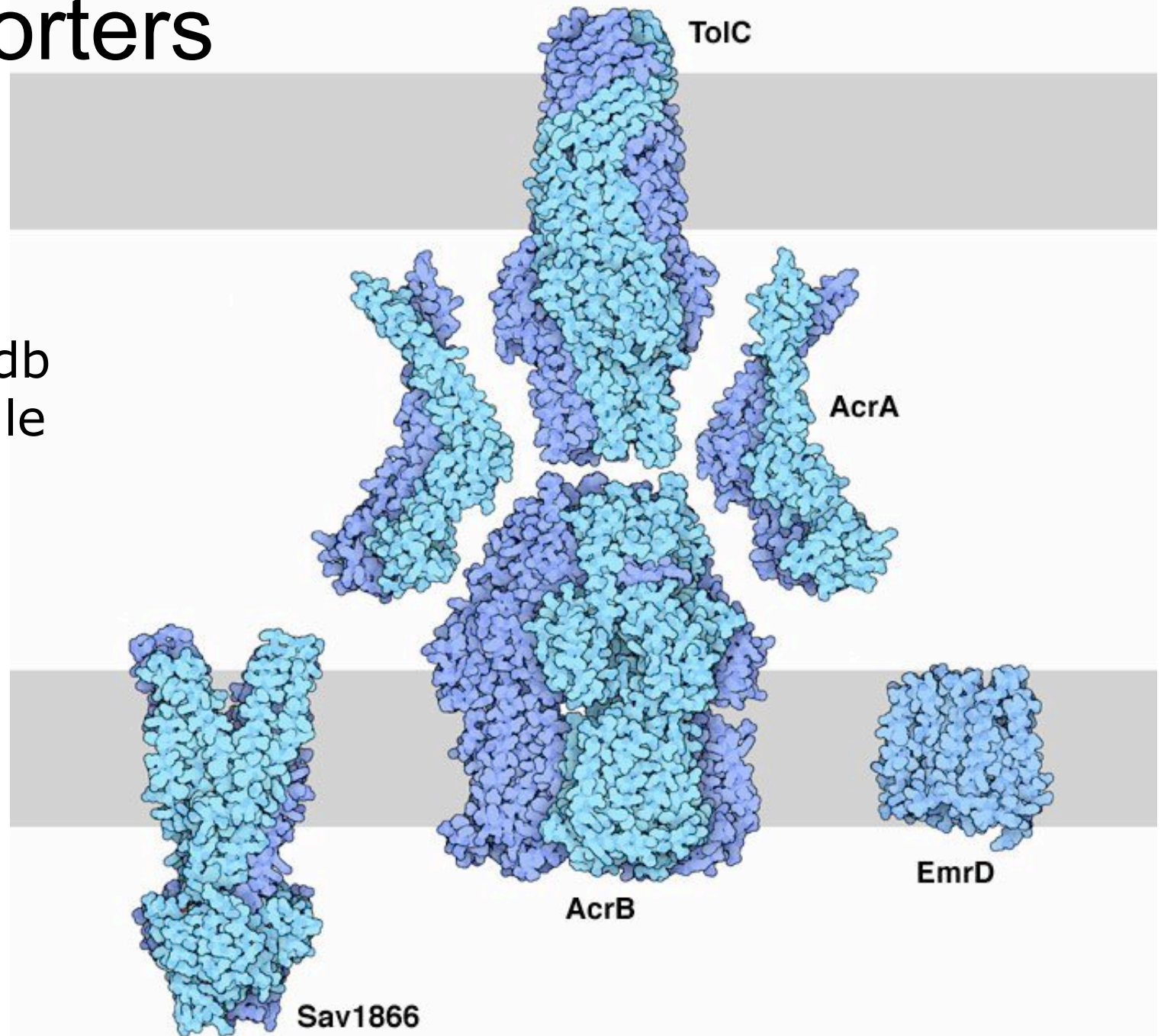


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Branden & Tooze
Intro to Protein Structure

Transporters

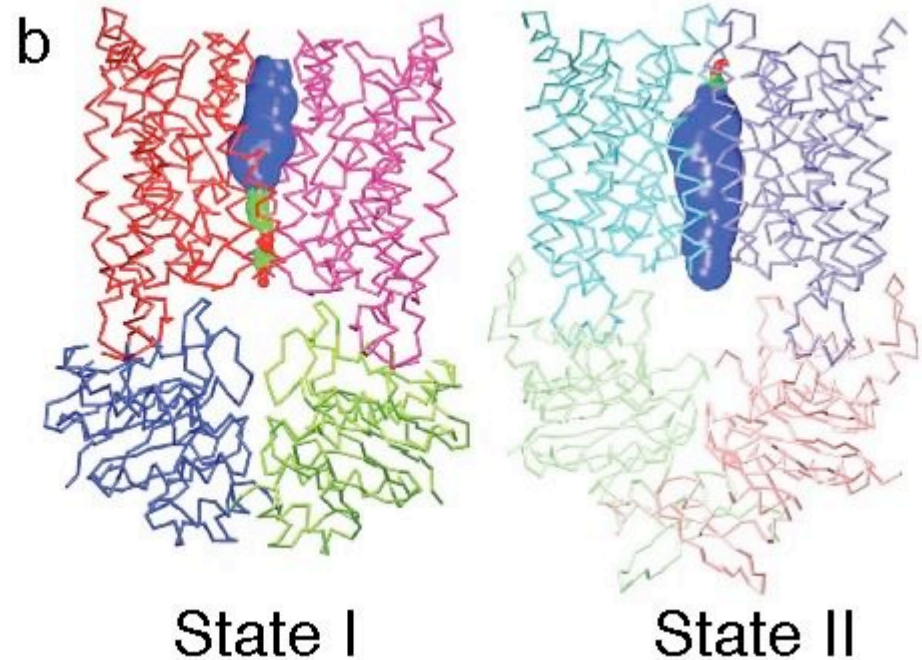
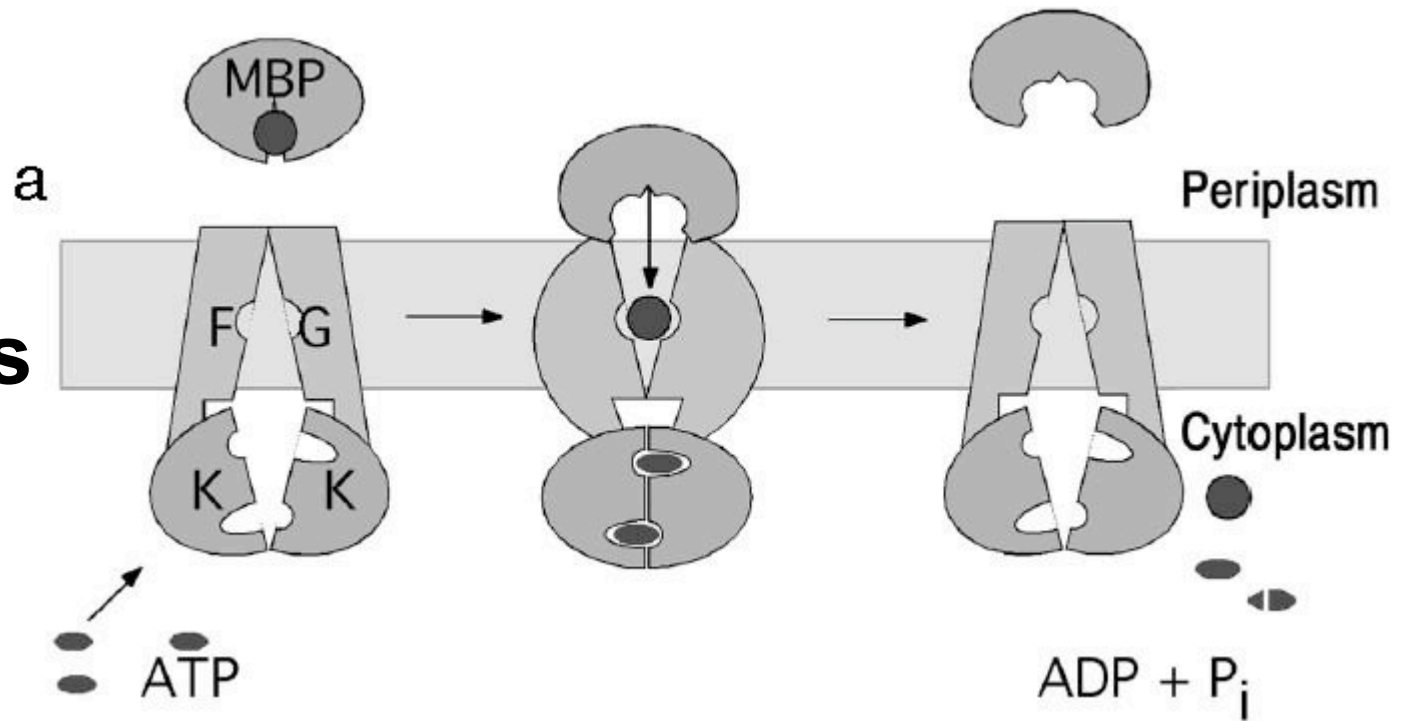
Current pdb
"Molecule
of the
Month"



ABC Transporters

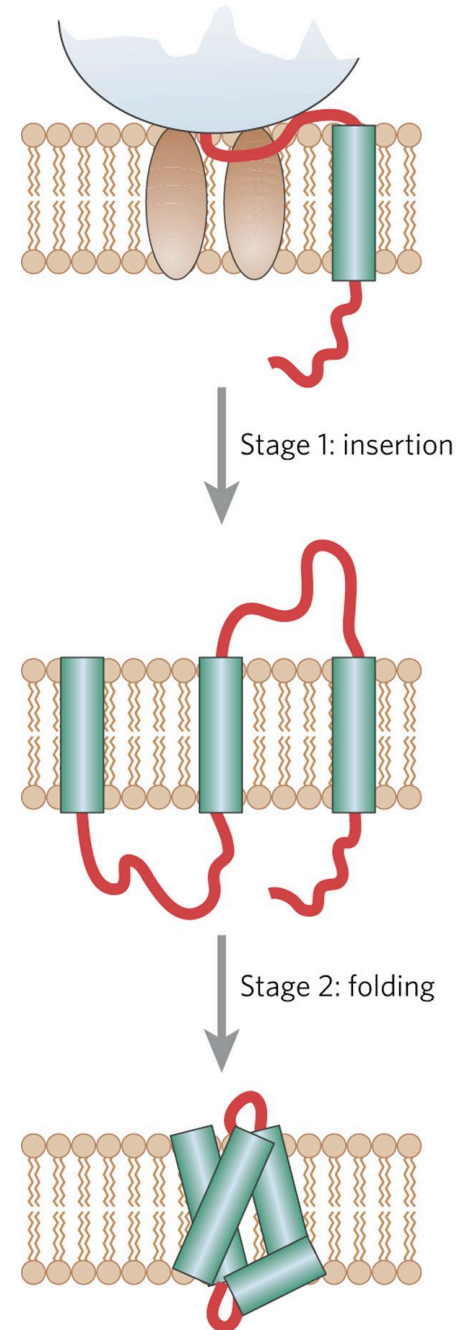
ATP hydrolysis-driven pumps for import or export

Proposed alternating access mechanism



Membrane Protein Folding

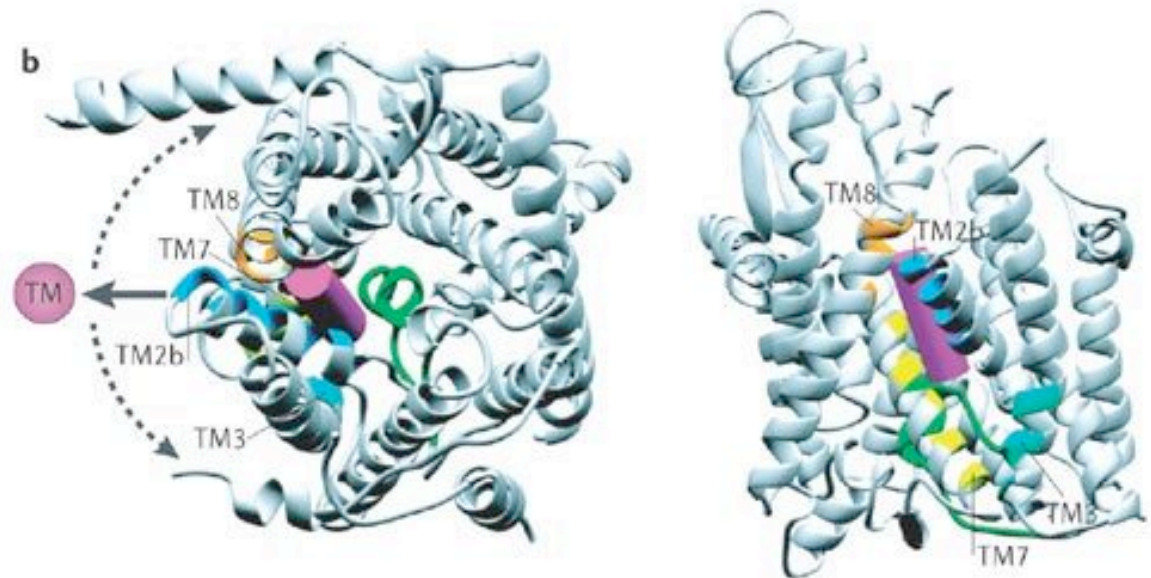
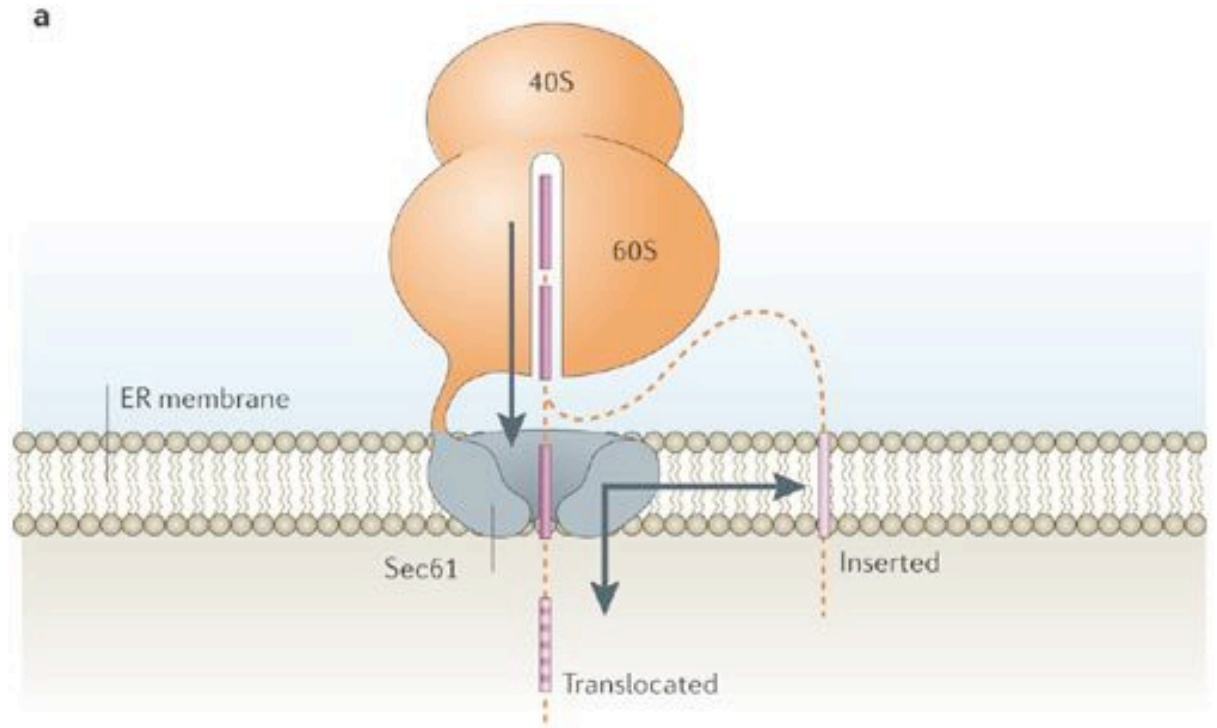
2-stage model



Membrane Protein Folding

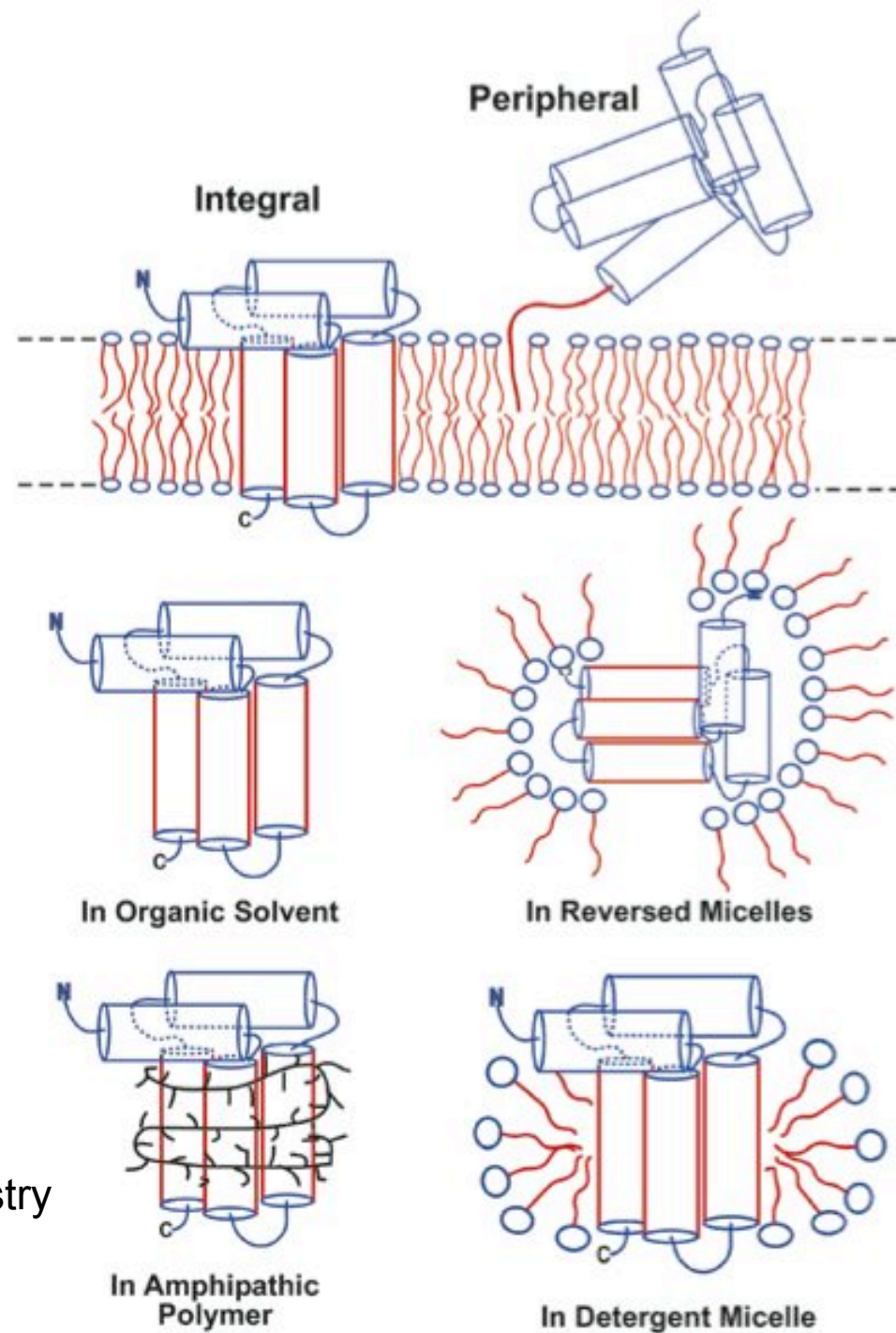
Translocon
measures
thermodynamics

G von Heijne (2006) Nature Reviews Molecular Cell Biology 7, 909-918 .



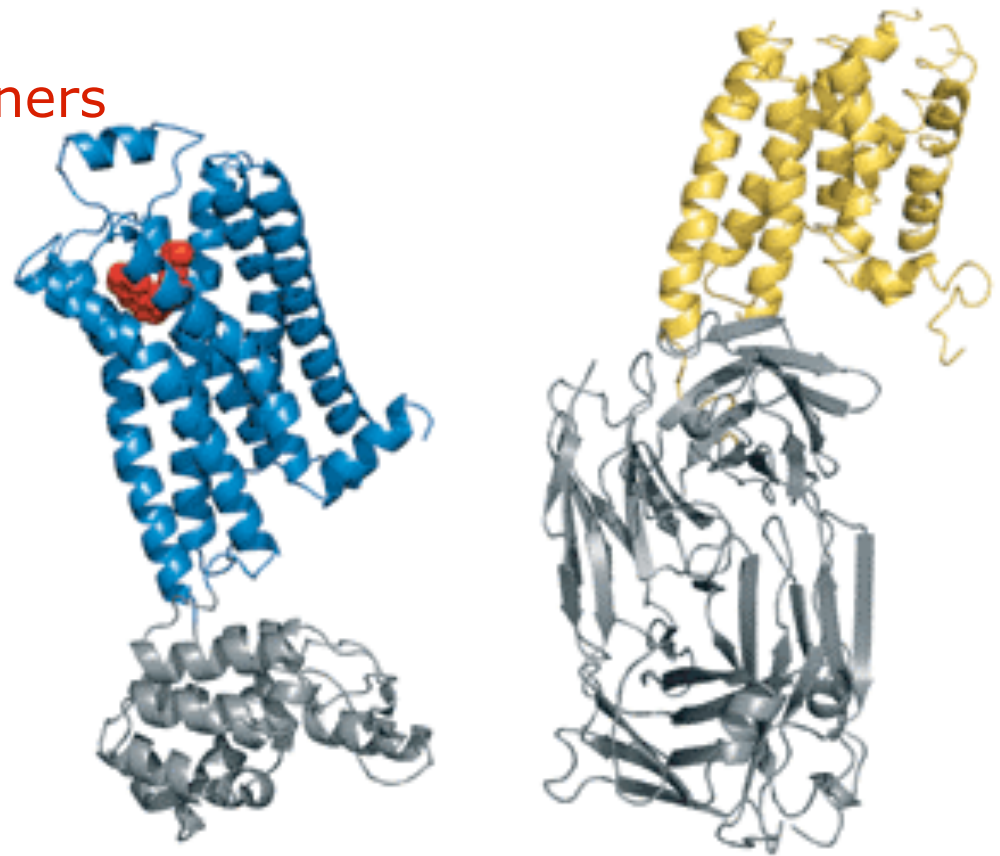
Why are structures difficult?

Sanders & Sonnichsen (2006)
Magnetic Resonance in Chemistry
44, S24 - S40.



Current structural efforts

- Crystallization
 - Funnel approach
 - Retain lipids
 - Fusion protein/binding partners
 - quaternary contacts?
- Solution NMR
 - Structures as of 2005
- Solid-state NMR
 - 1-2 TM's
- Electron diffraction
 - 1.9 Å with lipids!

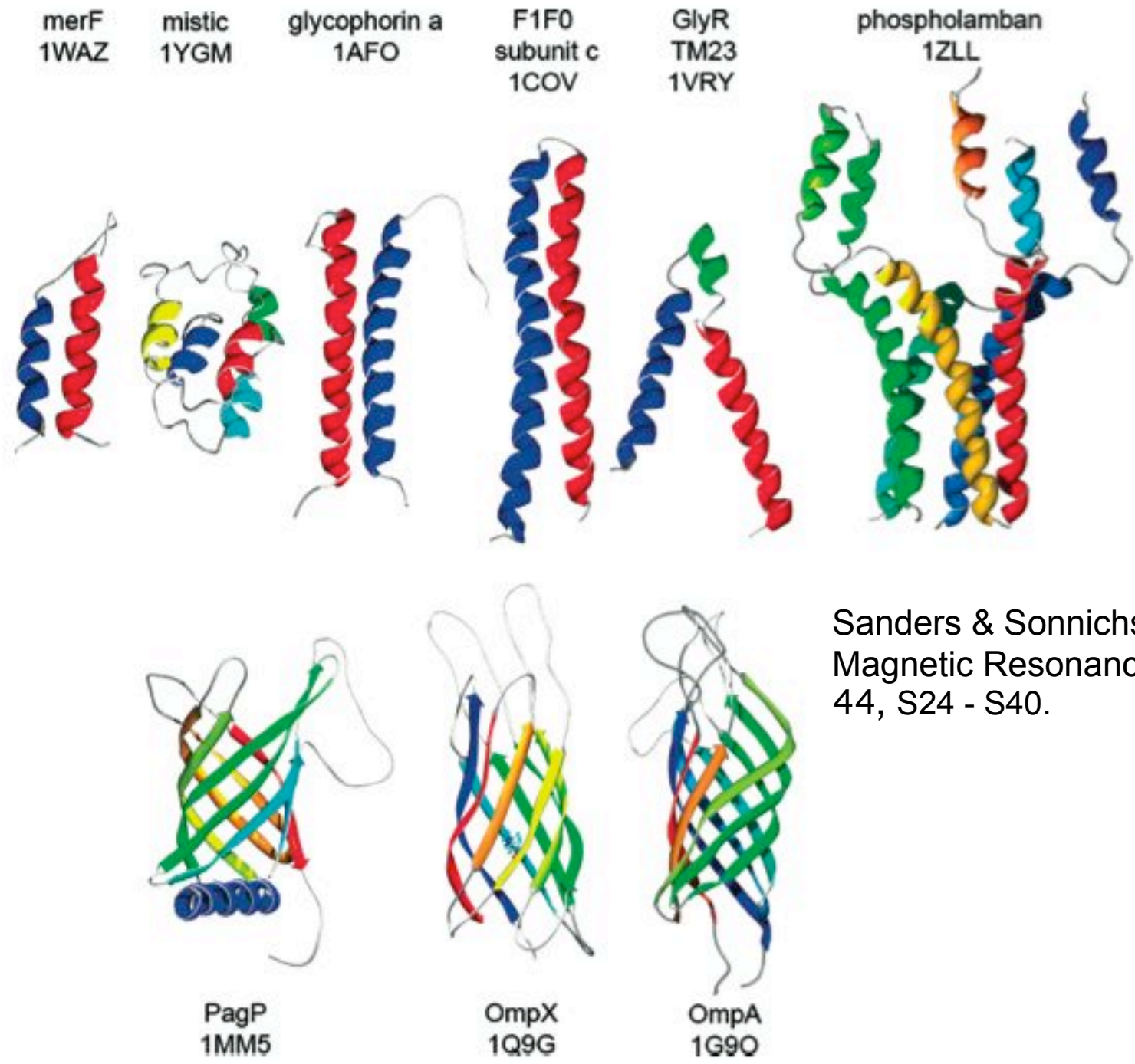


C&E News 10/29/07

Kobilka & coworkers Science 2007

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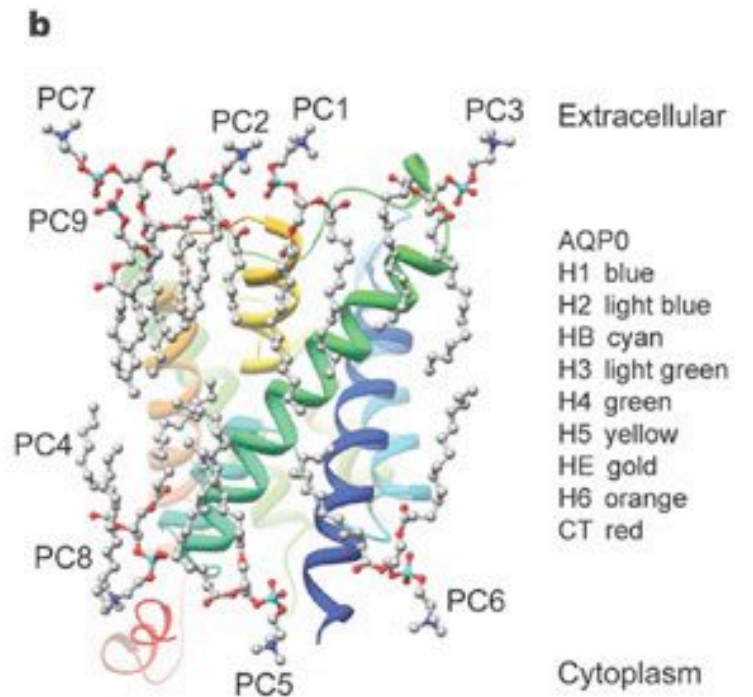
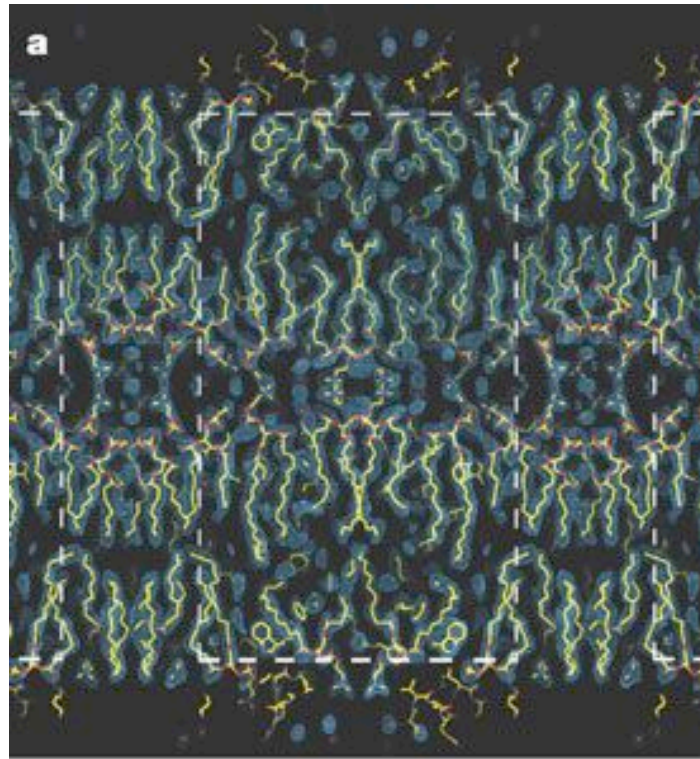


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Can be done in membrane - pellets or 2-D crystals.



Gonen et al
 (2005) Nature
 438, 633-638.

