

Proteins can be

- soluble in the cytosol
- embedded in a membrane

**Membrane
bilayer**

Red blood cell
cytoplasm

Soluble protein :
hemoglobin

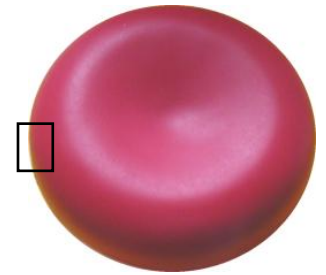
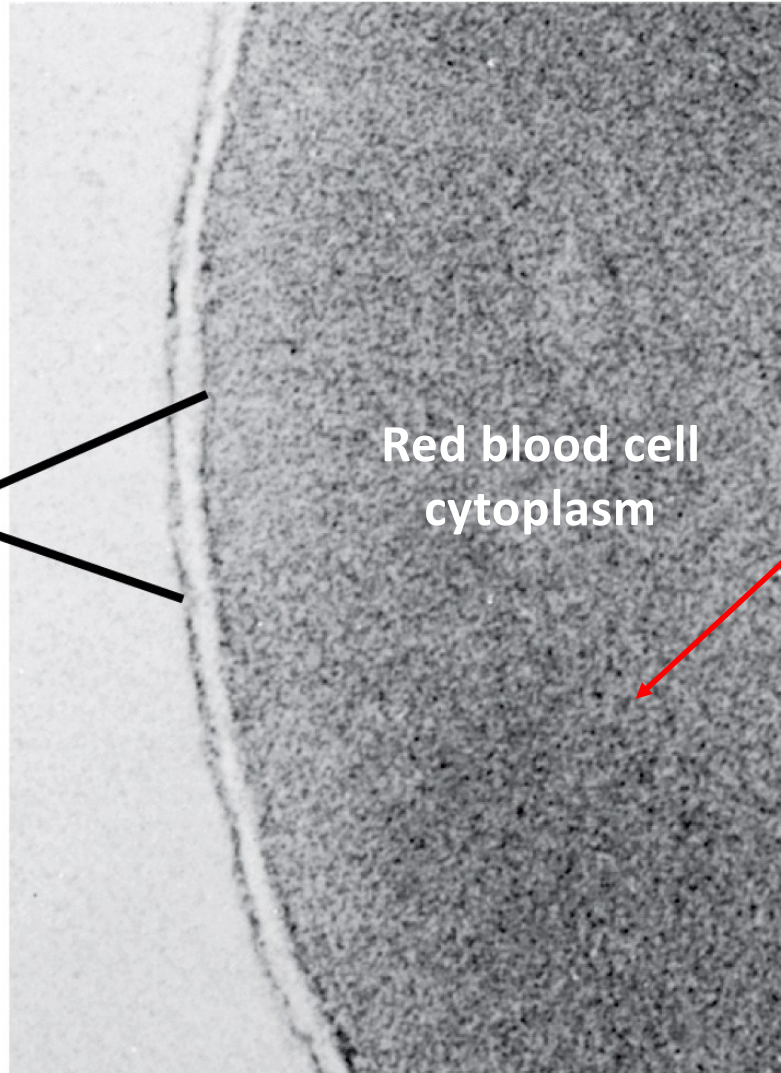


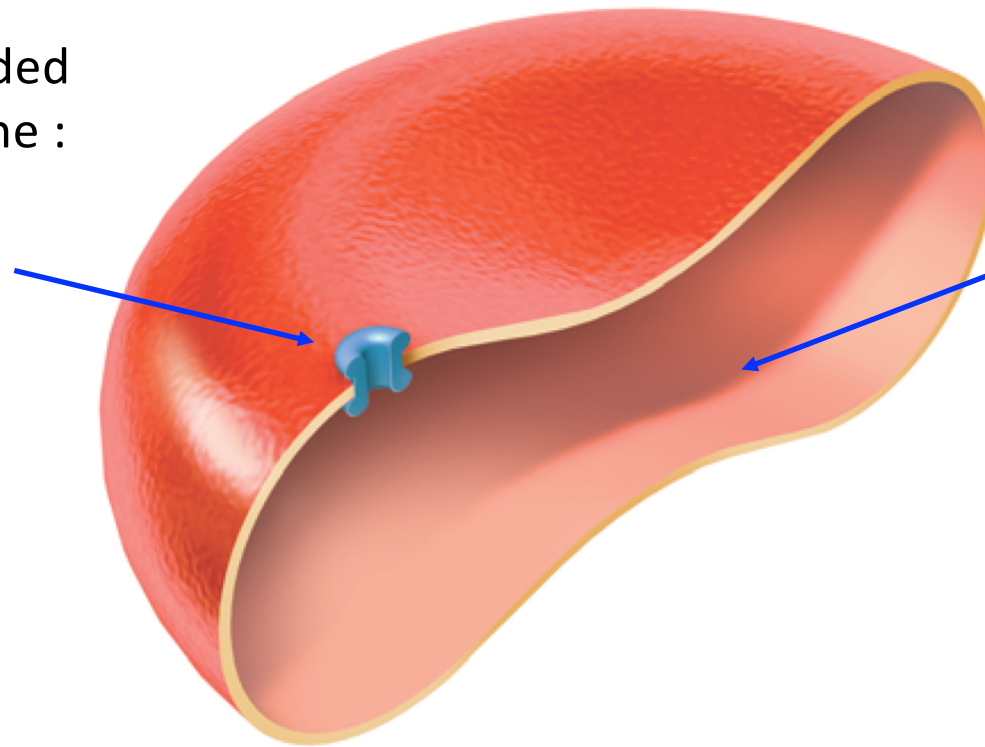
Figure 11-1

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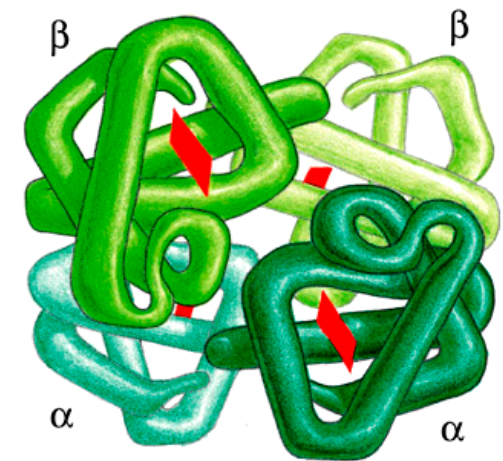
Protein embedded
in the membrane :

Aquaporin 1



Protein soluble
in the cytosol :

Hemoglobin



**Proteins often composed of several subunits:
-> either of identical subunits**

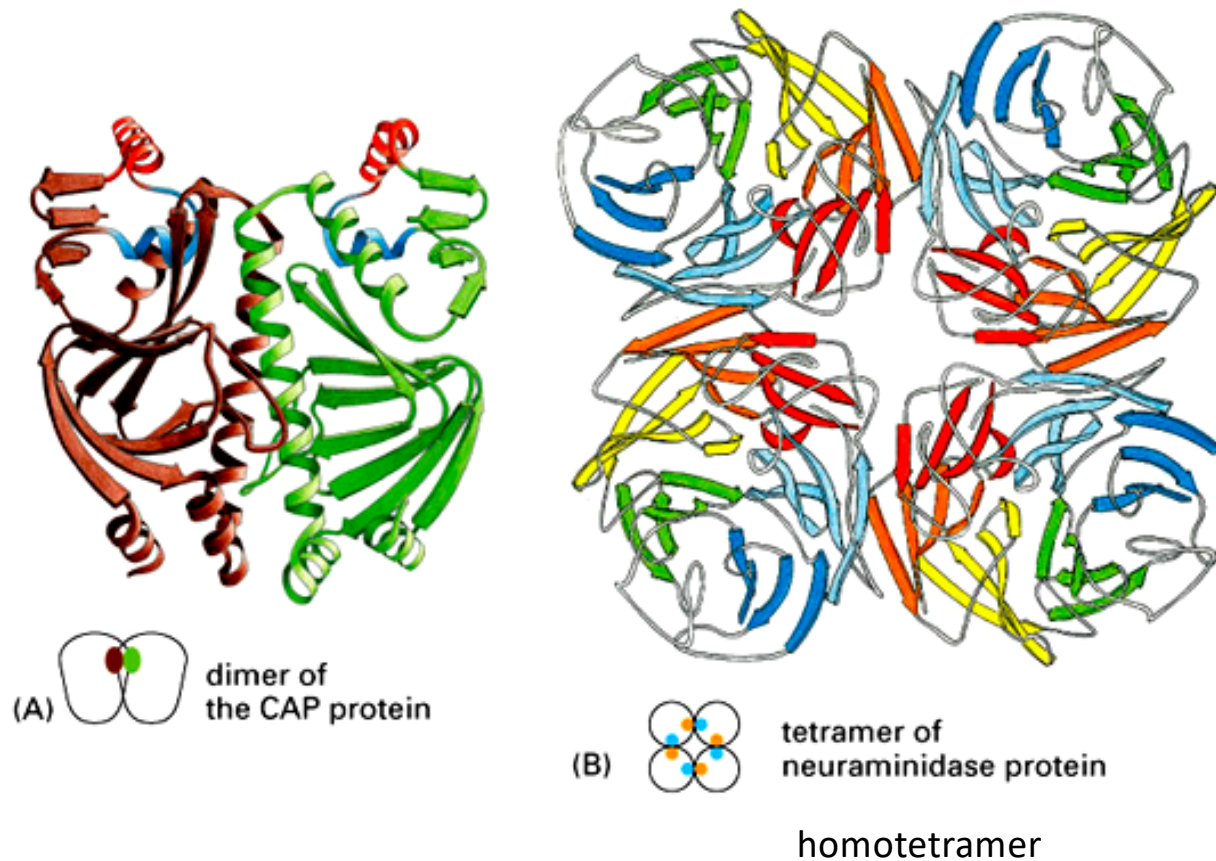
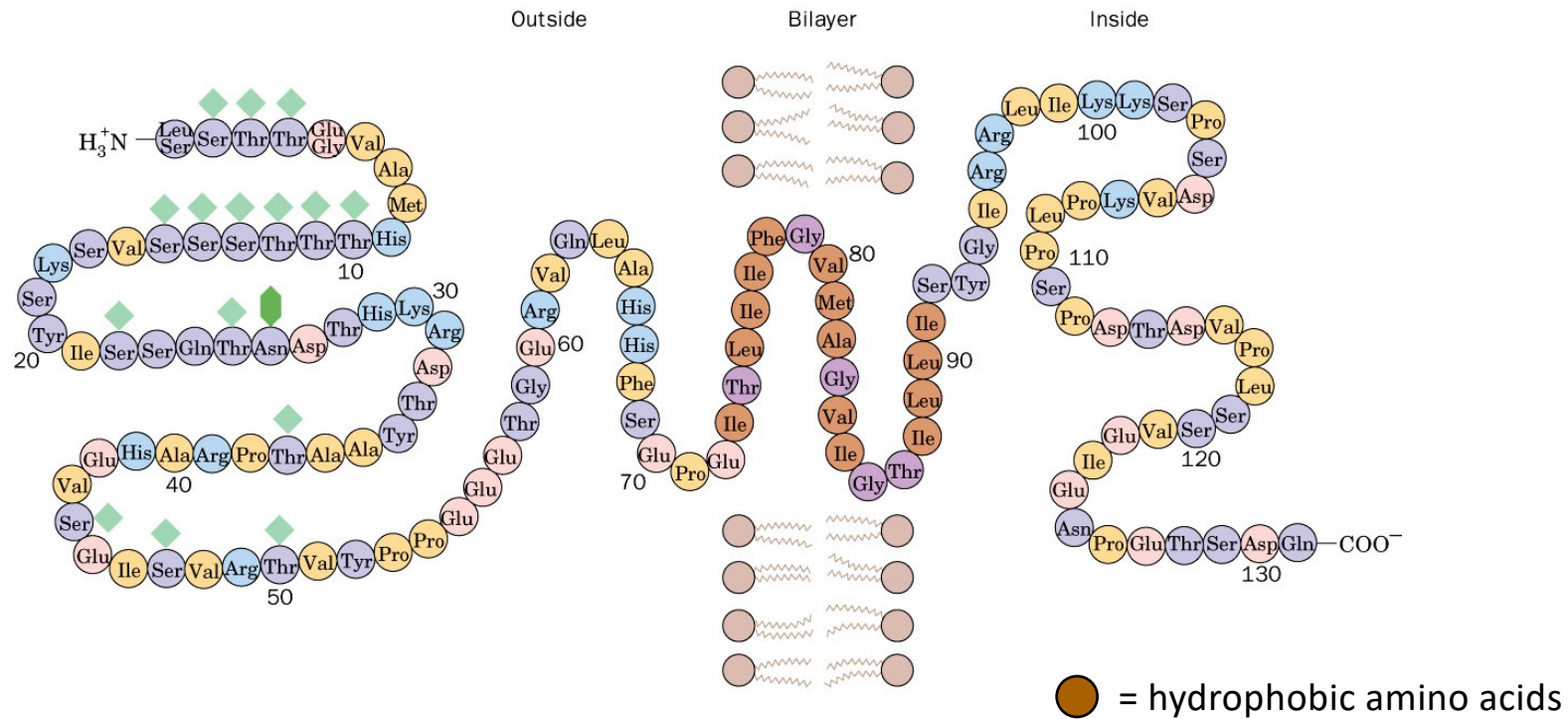


Figure 4-22 Essential Cell Biology, 2/e. (© 2004 Garland Science)

A protein is a chain of **amino acids**.



The transmembrane part is an **α -helix**

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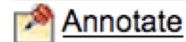
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Proteins



MP3 Tutor

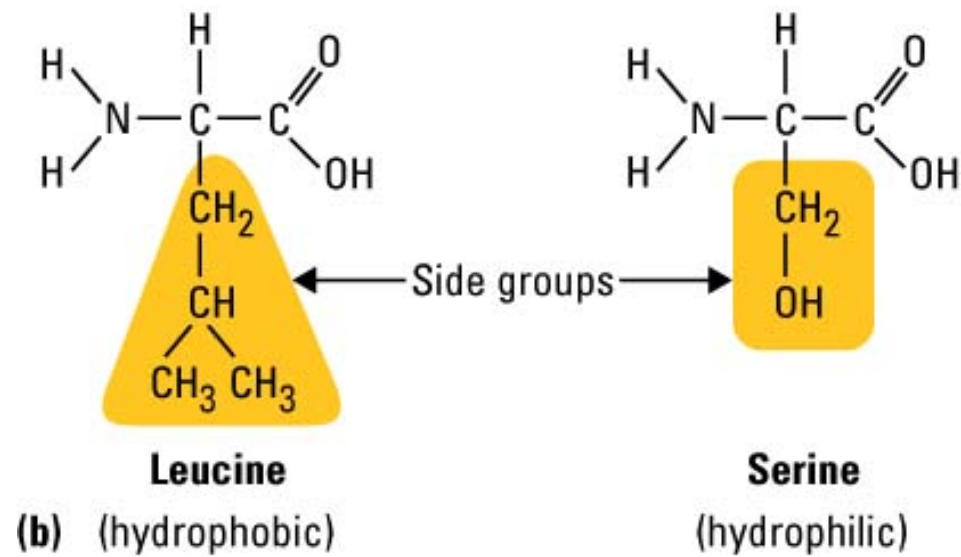
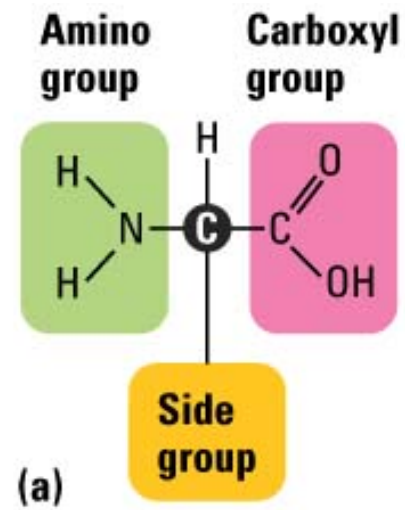
Protein Structure and Function

Proteins are the most elaborate of life's molecules. A **protein** is a polymer constructed from amino acid monomers. Your body has tens of thousands of different kinds of proteins, and each kind of protein has a unique three-dimensional shape that corresponds to a specific function. Proteins perform most of the tasks the body needs to function. **Figure 3.19** surveys the functions of four types of proteins: structural proteins, storage proteins, contractile proteins, and transport proteins. Other types of proteins include defensive proteins, such as antibodies of the immune system, and signal proteins, which convey messages from one cell to another. Enzymes (such as lactase), another important type of protein, change the rate of a chemical reaction without being changed in the process (as you will see in Chapter 5). Now let's take a look at the architecture of proteins.



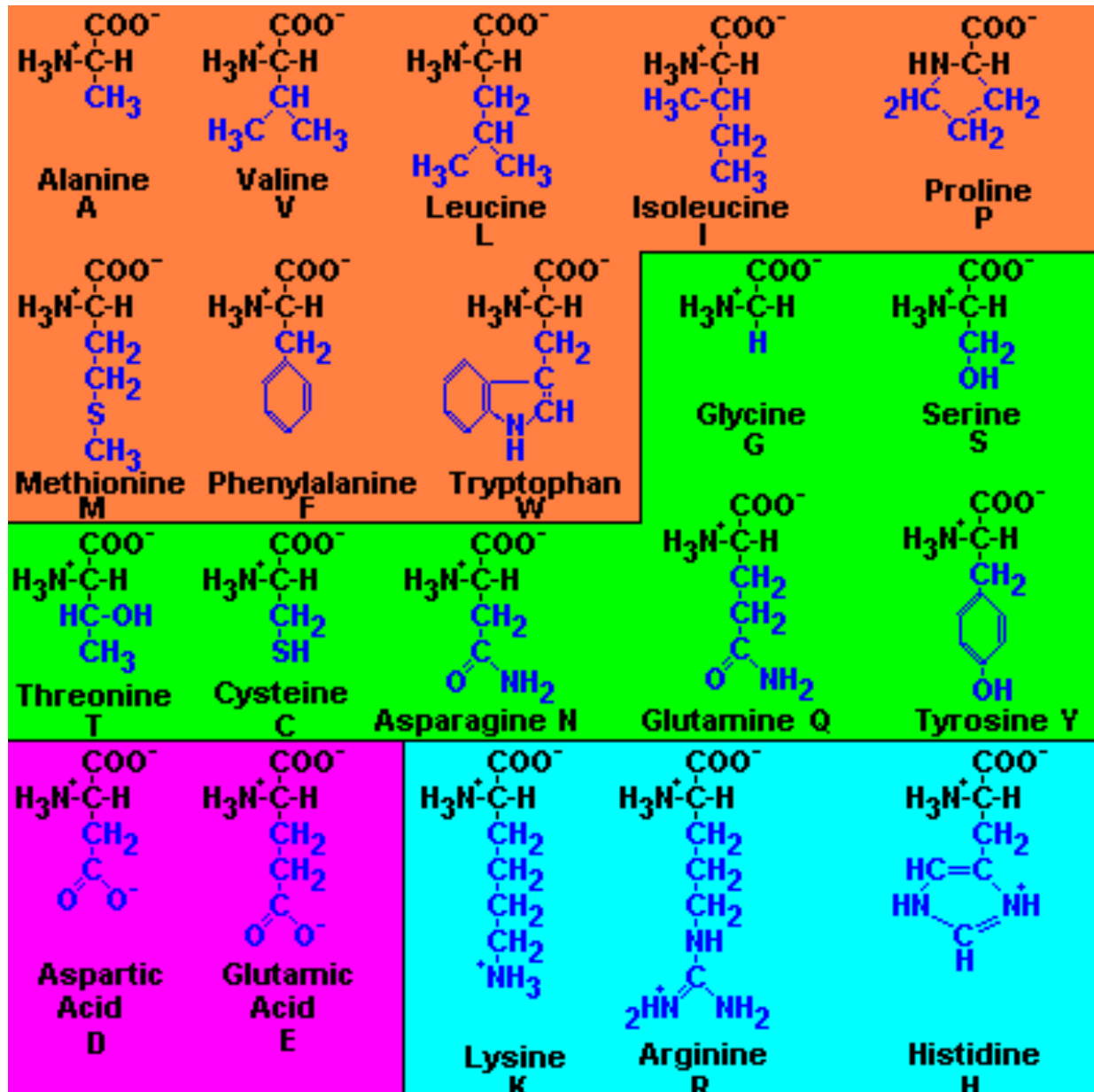
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Figure 3.19 Some functions of proteins.



Side chains can be hydrophilic or hydrophobic

non polar

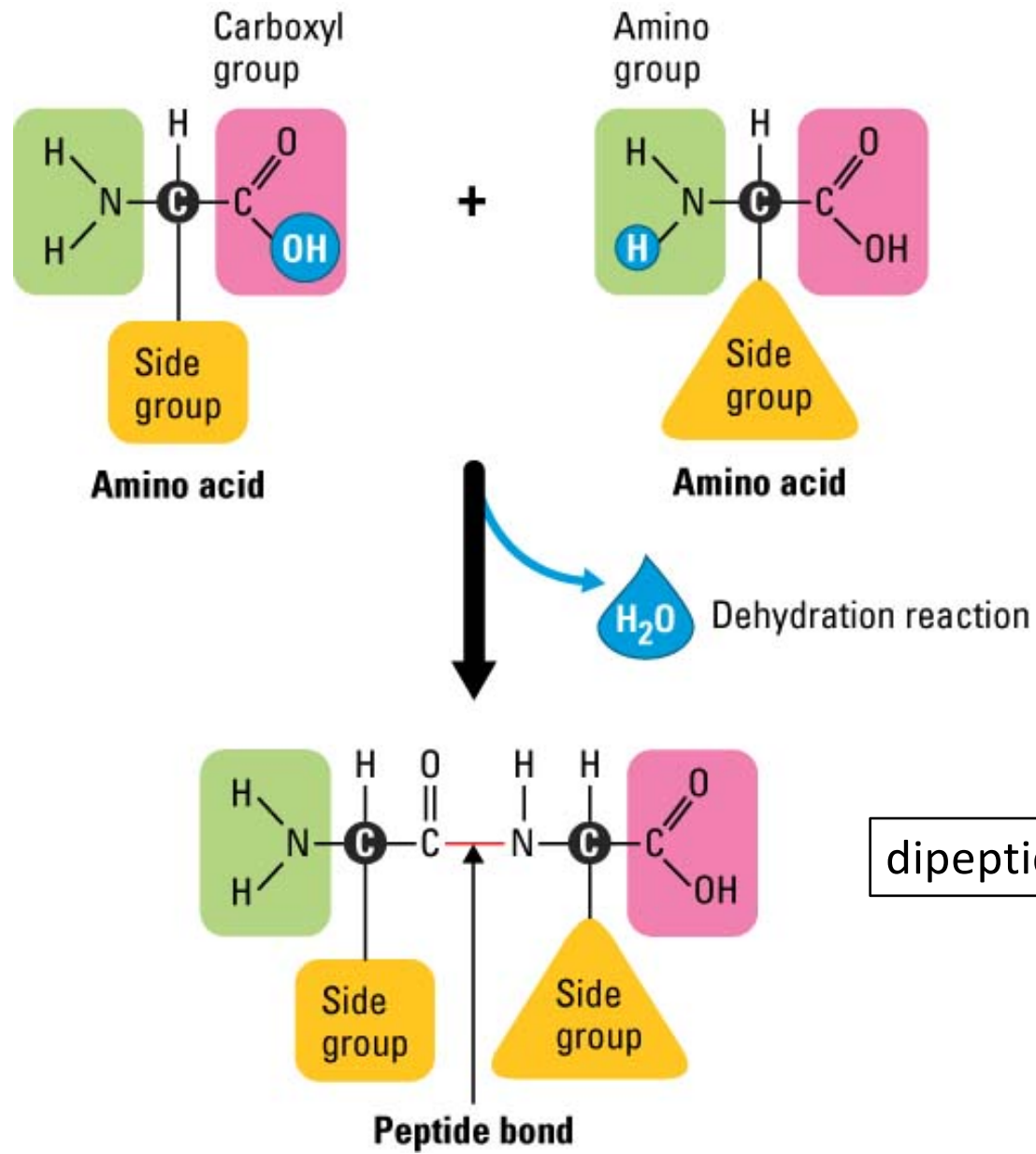


polar

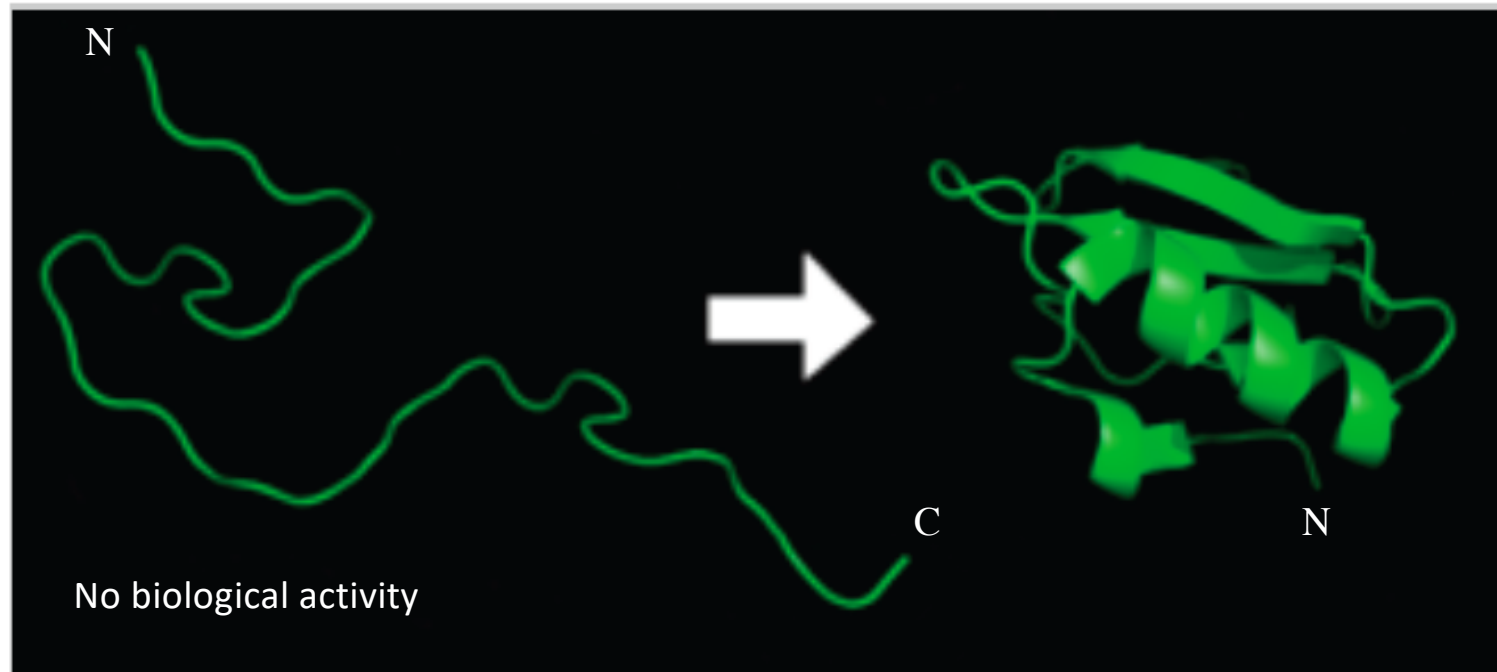
charged

The 20 amino acids used for protein synthesis

These amino acids have been separated according to the chemical properties of their side chains



Proteins are long polymers of amino acids.



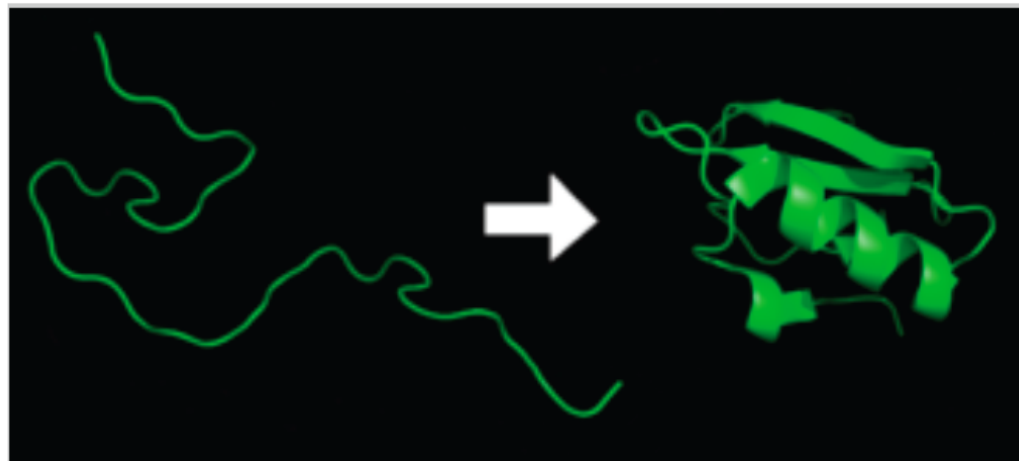
Protein before and after folding.

Only correctly folded proteins
Have a biological activity

Protein structure

- **Secondary structure** is the local spatial arrangement of a polypeptide's backbone atoms **without regard to the conformations of its side chains.**
- **Tertiary structure** refers to the three-dimensional structure of an entire polypeptide, **including that of its side chains.**
- Many proteins are composed of two or more polypeptide chains, loosely referred to as subunits. A protein's **quaternary structure** refers to the spatial arrangement of its subunits.

Side chains
are not shown



Protein before and after folding.

N terminus

Convention :
numbering starts at the
N-terminus

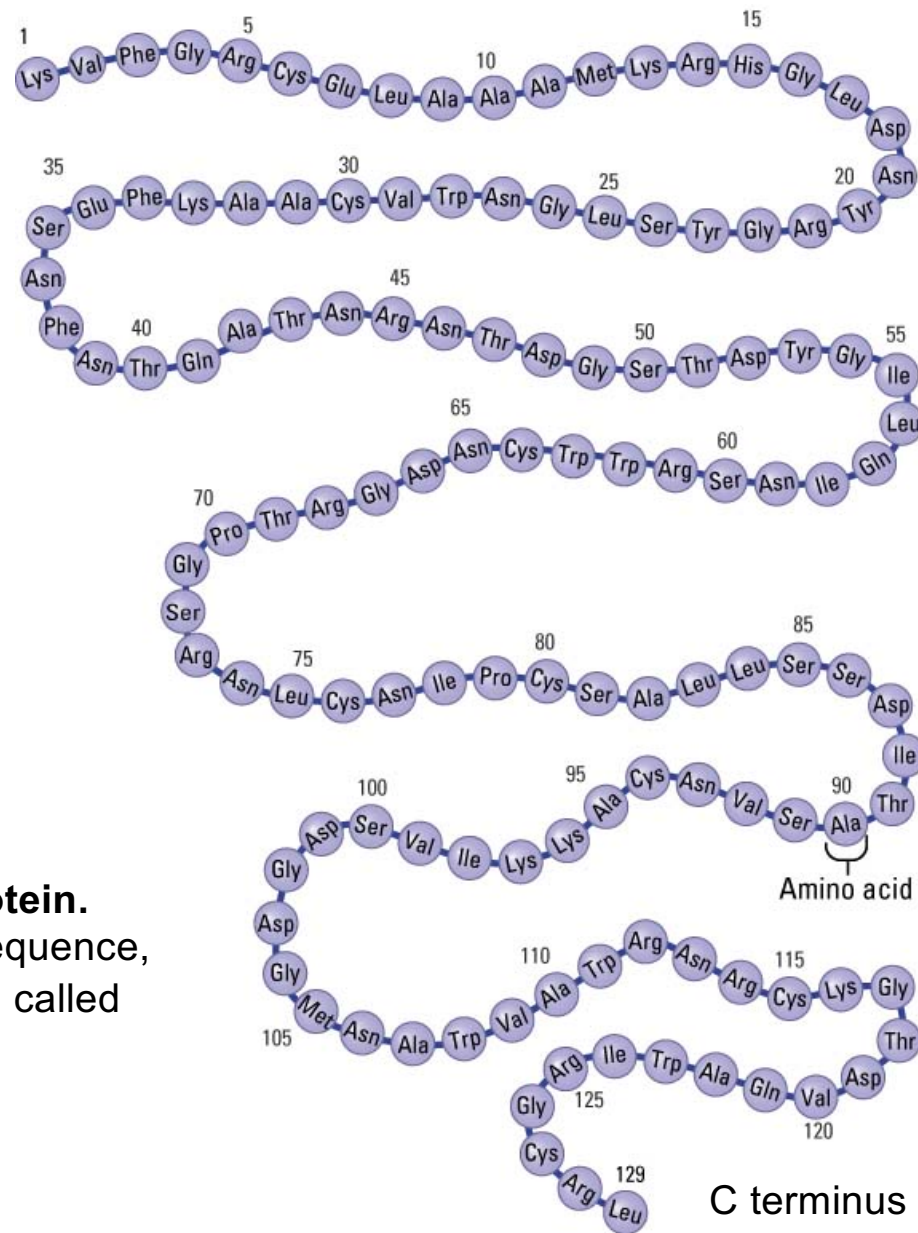


Figure 3.22

The primary structure of a protein.

This is the unique amino acid sequence, or primary structure, of a protein called lysozyme.

Folding of a polypeptidic chain

secondary structure:

structure produced by *regular repeated interactions* between atoms of the *backbone*.

→ α helix

→ β sheet



Hydrogen bond :

- donor
- acceptor

Which ones are the closest possible acceptor/donor ?

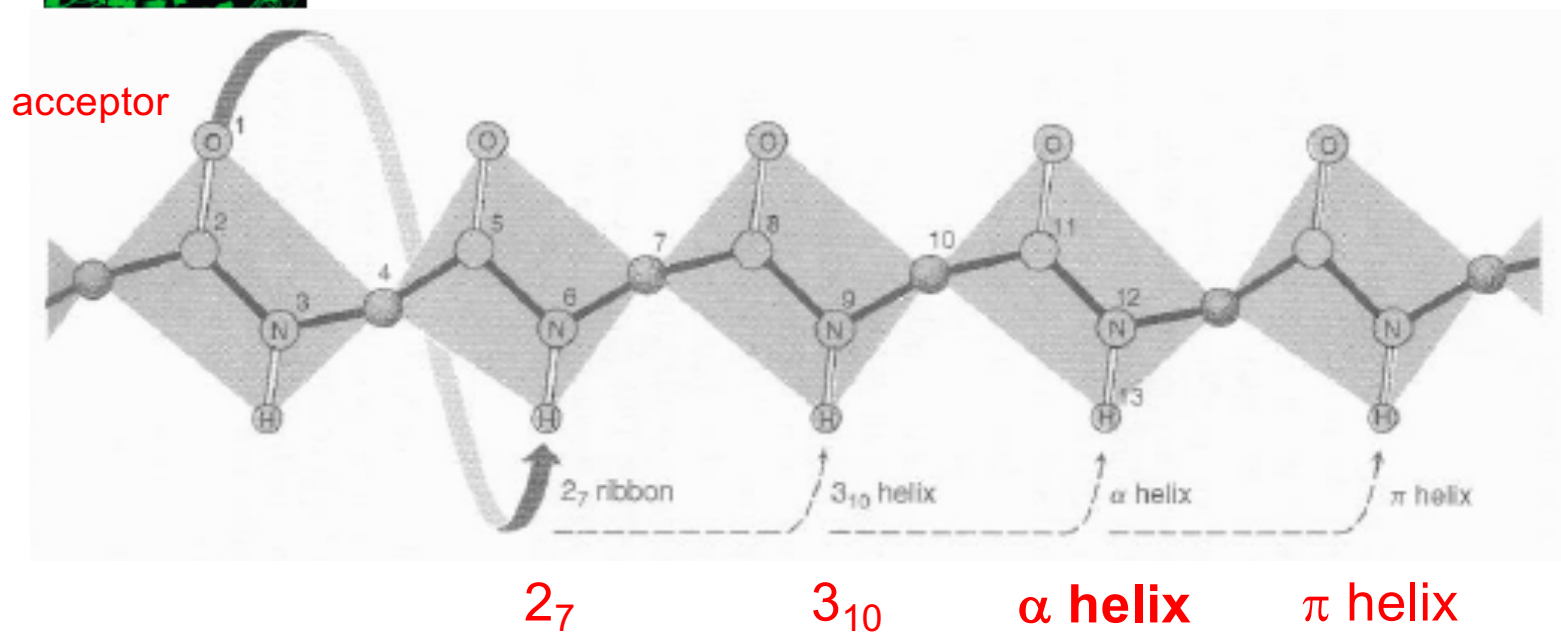
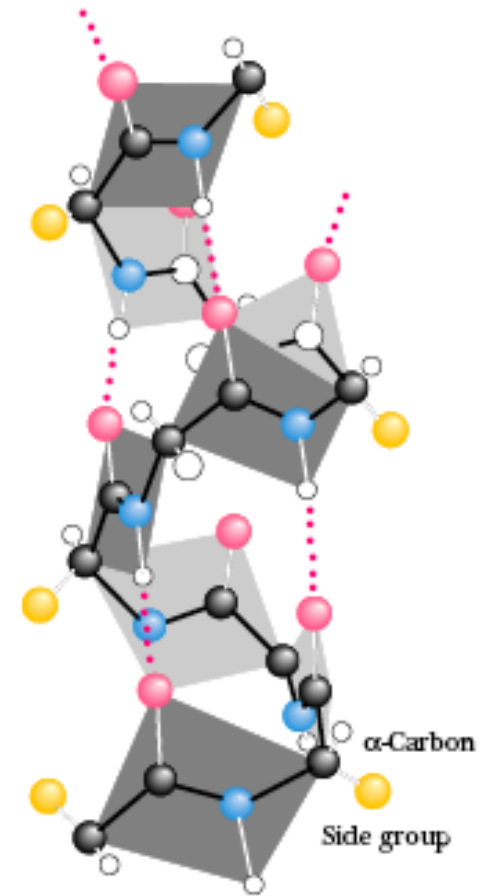
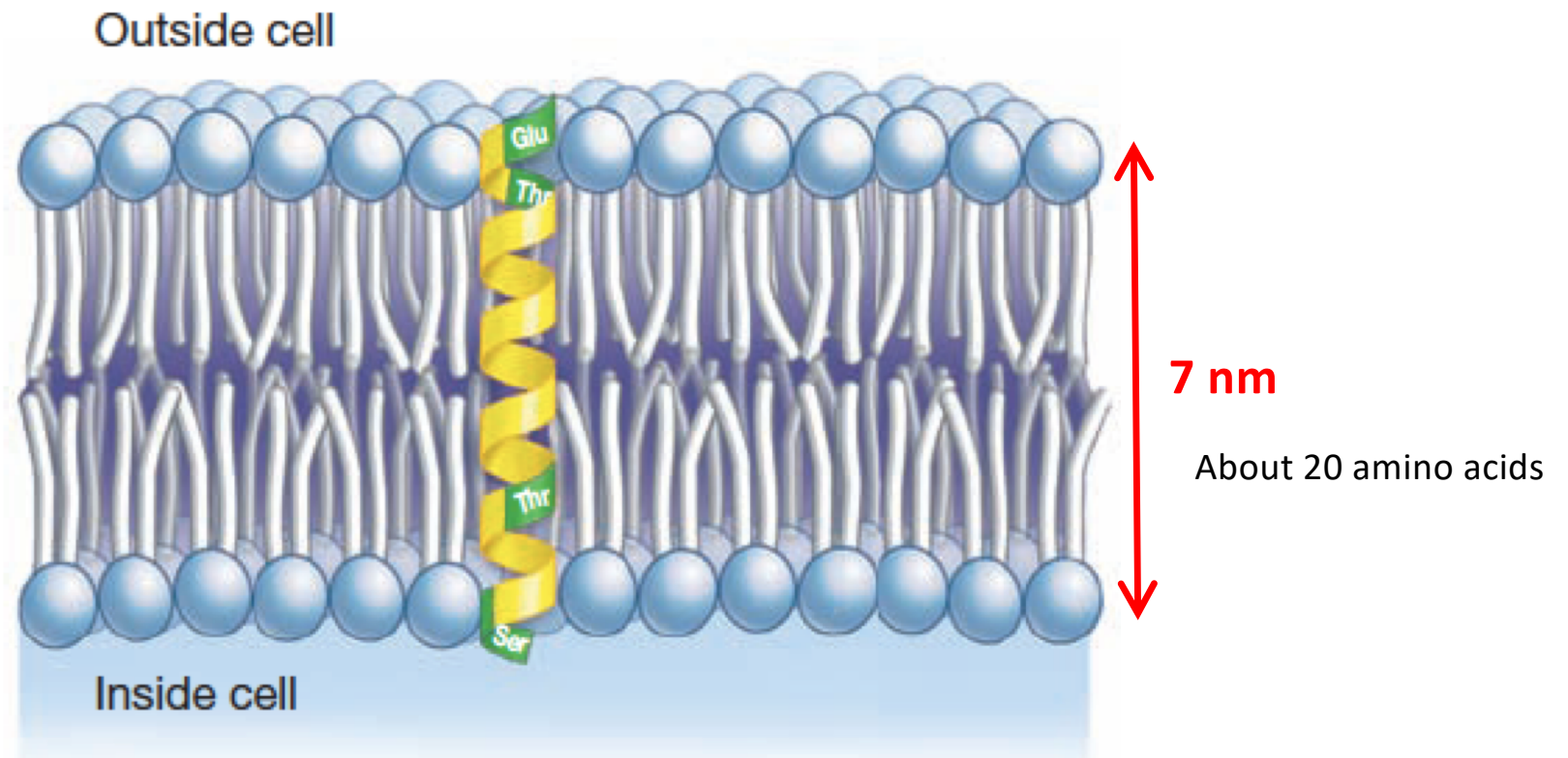


Fig 2-28



Linus Pauling and a model of the alpha helix.(1963)

Transmembrane domain :



Always an α helix .

Bacteriorhodopsin :

Outside

Protein with 7 TM

**Amino
terminus**

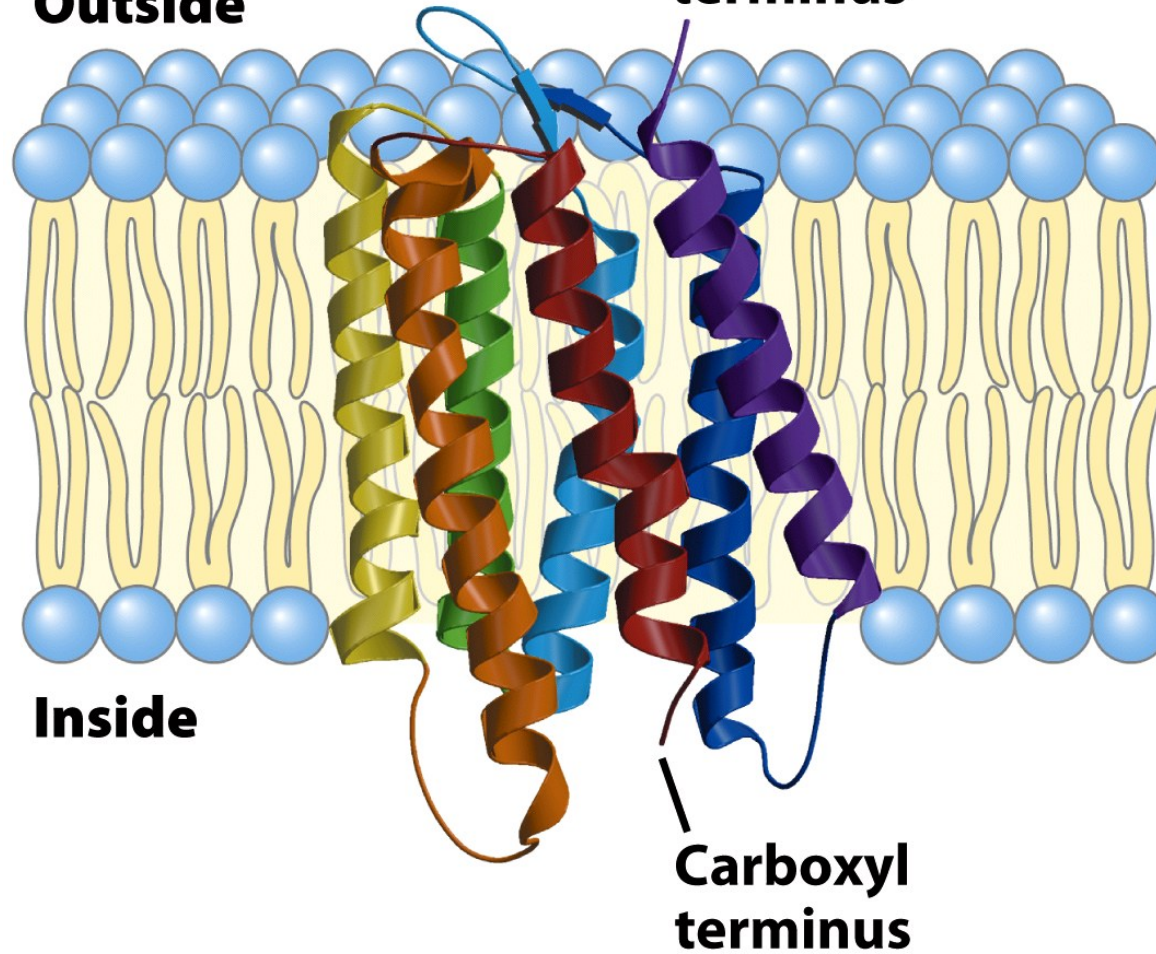
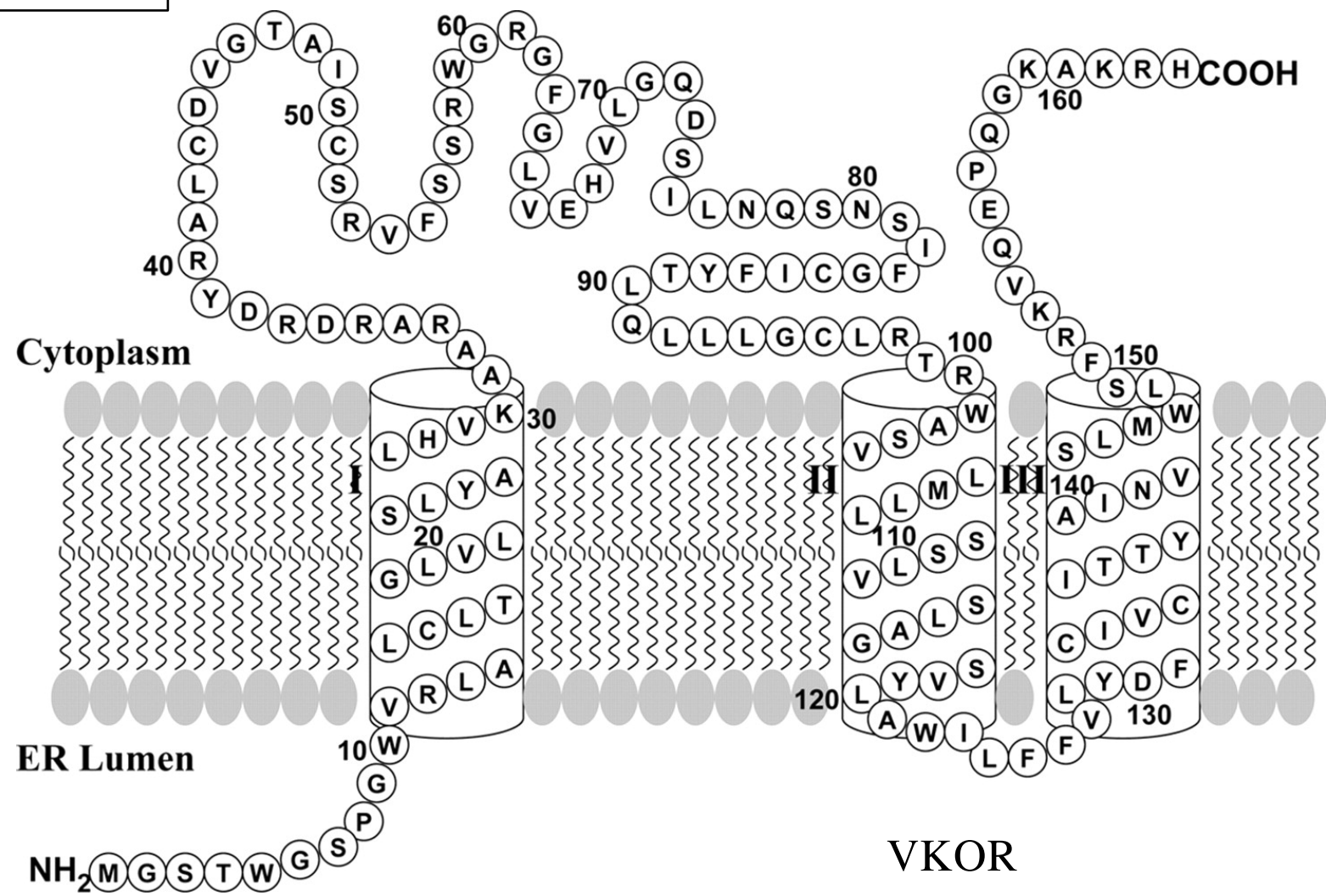


Figure 11-9
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Protein with 3 TM



Proposed structure of GLUT1 (12 TM)

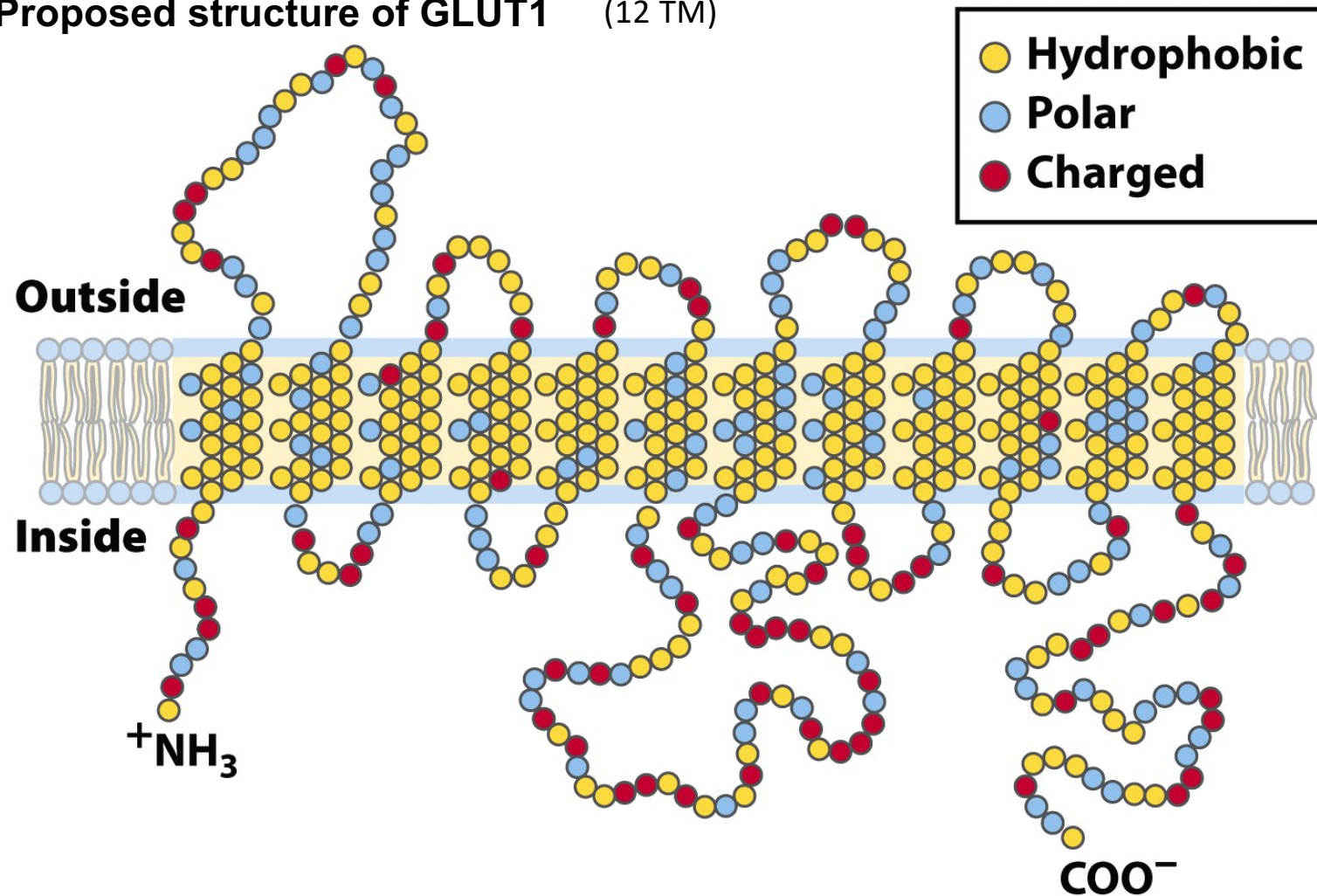
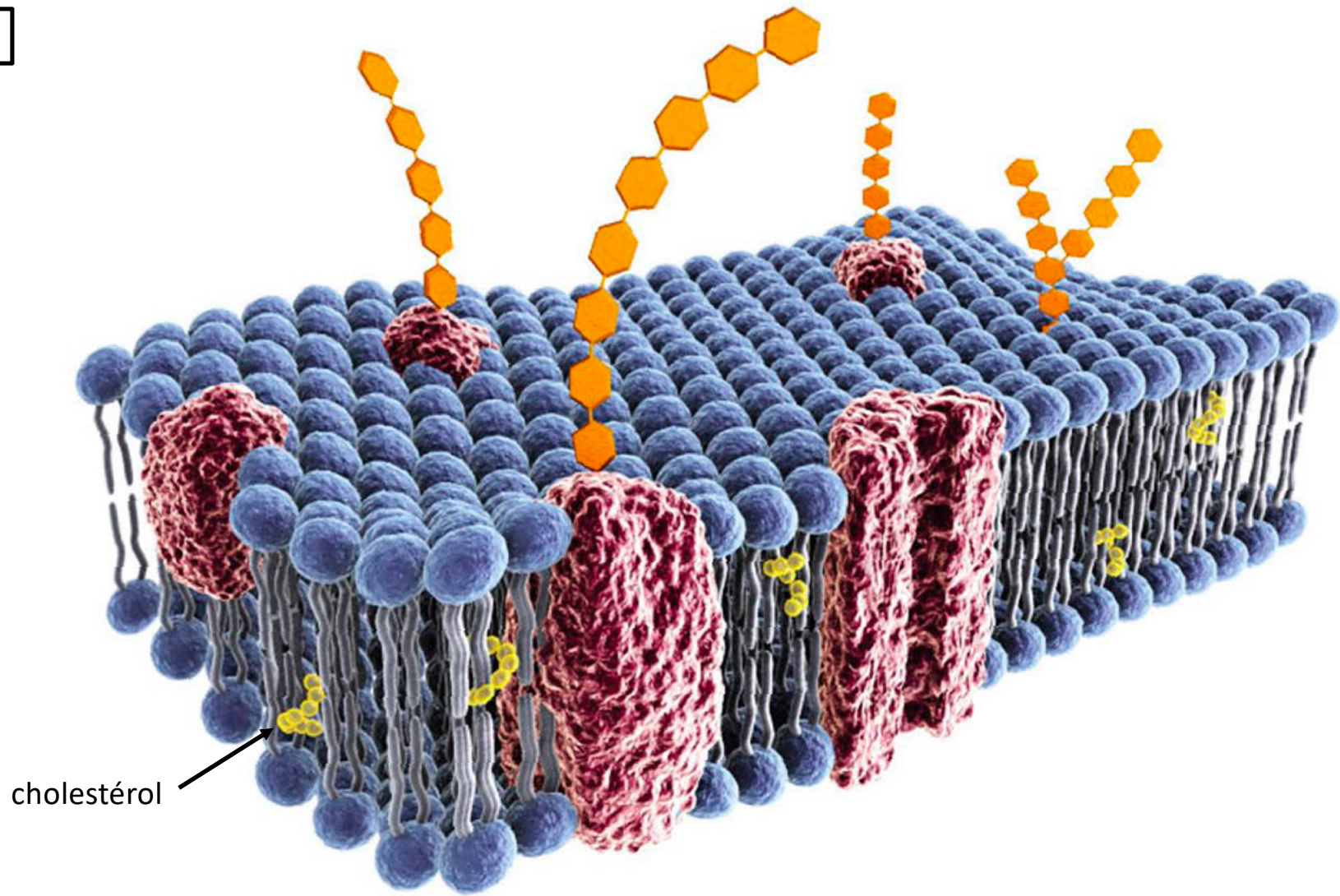


Figure 11-29a
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Membrane



Hydropathy scale

Quantitative scale

Table 6-2 Hydropathy Scale for Amino Acid Side Chains

Side Chain	Hydropathy
Ile	4.5
Val	4.2
Leu	3.8
Phe	2.8
Cys	2.5
Met	1.9
Ala	1.8
Gly	-0.4
Thr	-0.7
Ser	-0.8
Trp	-0.9
Tyr	-1.3
Pro	-1.6
His	-3.2
Glu	-3.5
Gln	-3.5
Asp	-3.5
Asn	-3.5
Lys	-3.9
Arg	-4.5

How does one get experimentally such a number ?

Source: Kyte, J. and Doolittle, R.F., *J. Mol. Biol.* **157**, 110 (1982).

Hydropathy scale

Table 1.2 A hydrophobicity scale for amino acids

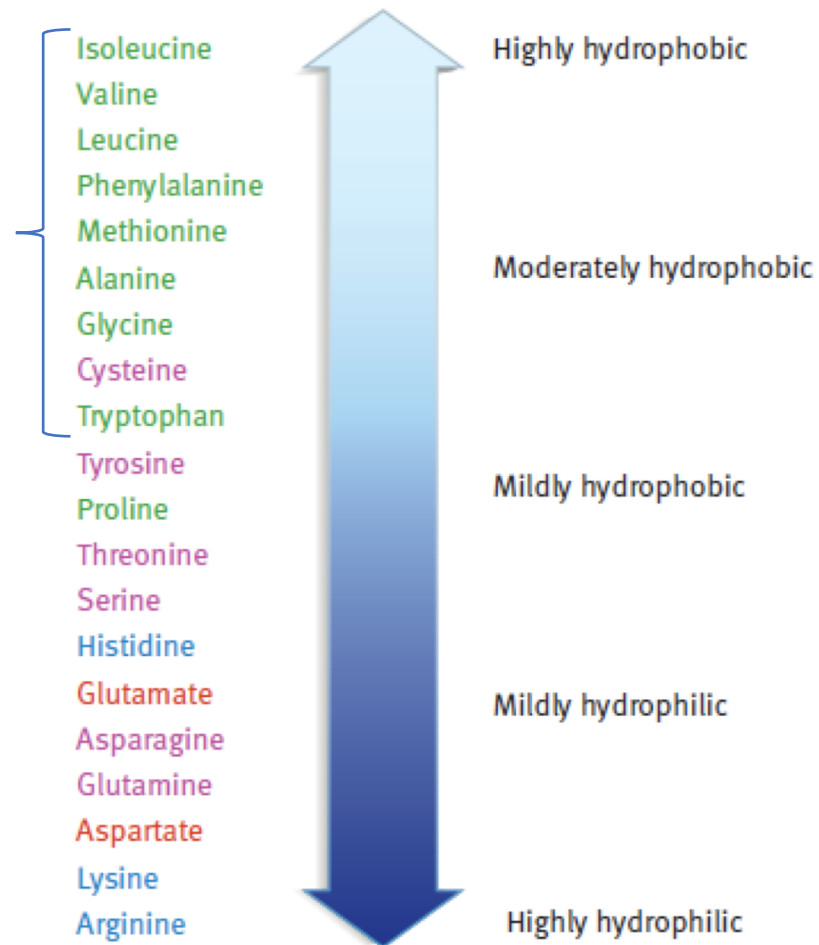
Amino acid	Transfer free energy (kJ mol ⁻¹)
Phe (F)	15.5
Met (M)	14.2
Ile (I)	13.0
Leu (L)	11.7
Val (V)	10.9
Cys (C)	8.4
Trp (W)	7.9
Ala (A)	6.7
Thr (T)	5.0
Gly (G)	4.2
Ser (S)	2.5
Pro (P)	-0.8
Tyr (Y)	-2.9
His (H)	-12.5
Gln (Q)	-17.1
Asn (N)	-20.1
Glu (E)	-34.3
Lys (K)	-36.8
Asp (D)	-38.5
Arg (R)	-51.4

Hydropathy scale

Purely qualitative

TABLE 3.1 **How Amino Acids Interact with Water**

20 amino acids are ranked according to how likely they are to interact with water. Color codes are based on Figure 3.3.



Transbilayer disposition of glycophorin in an erythrocyte

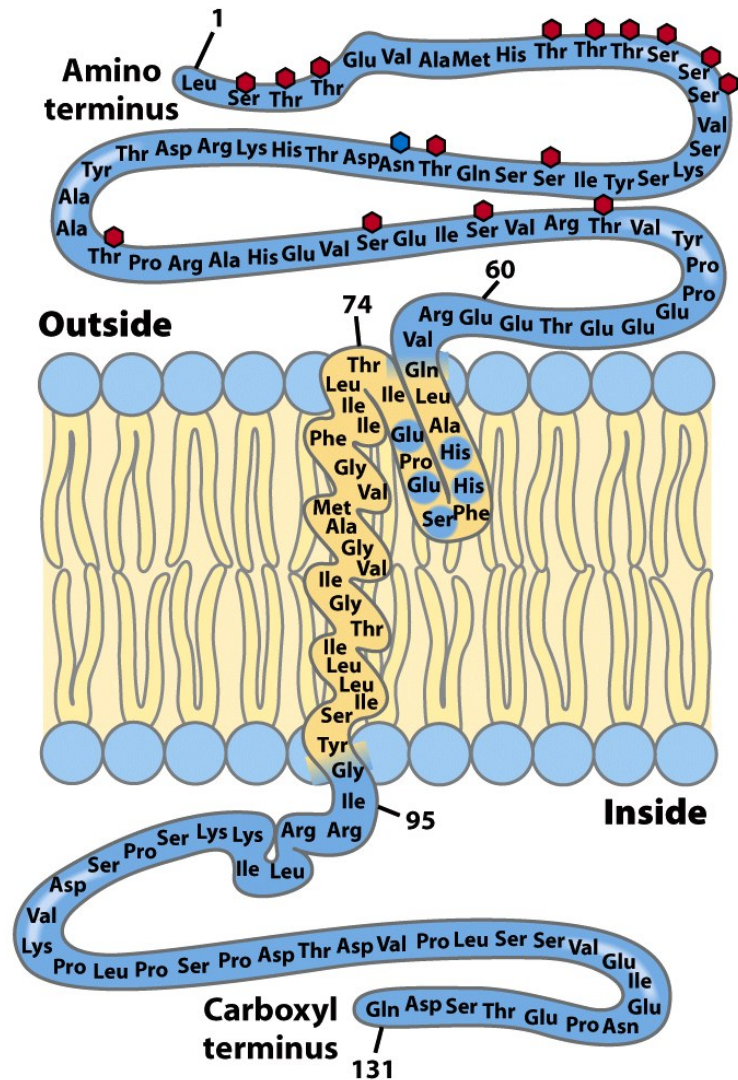


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Hydropathy profile

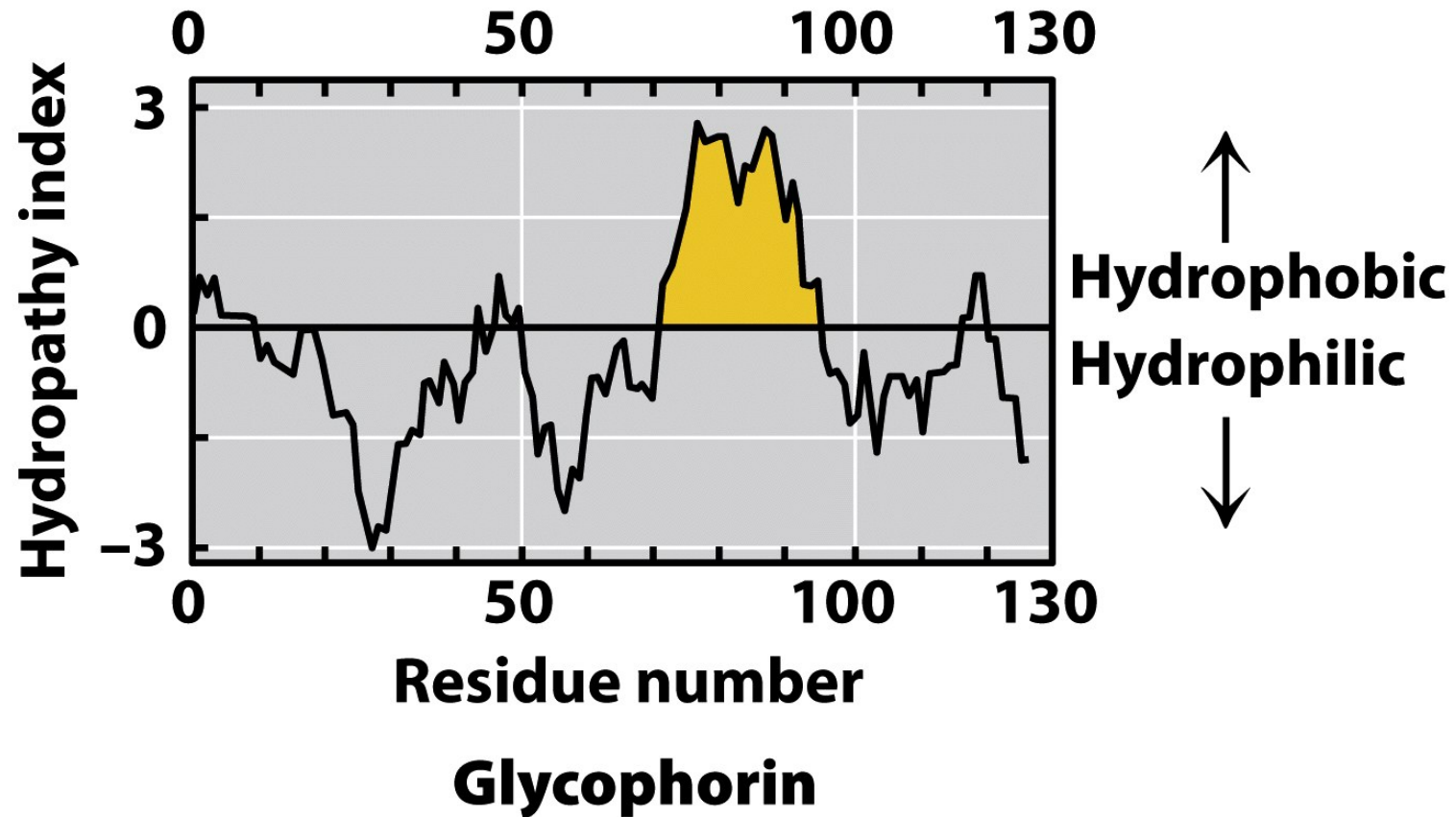
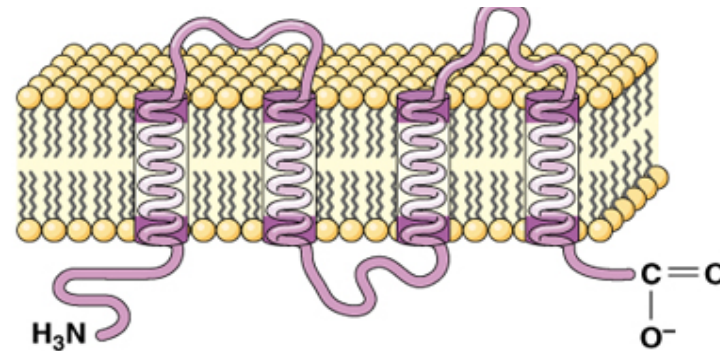
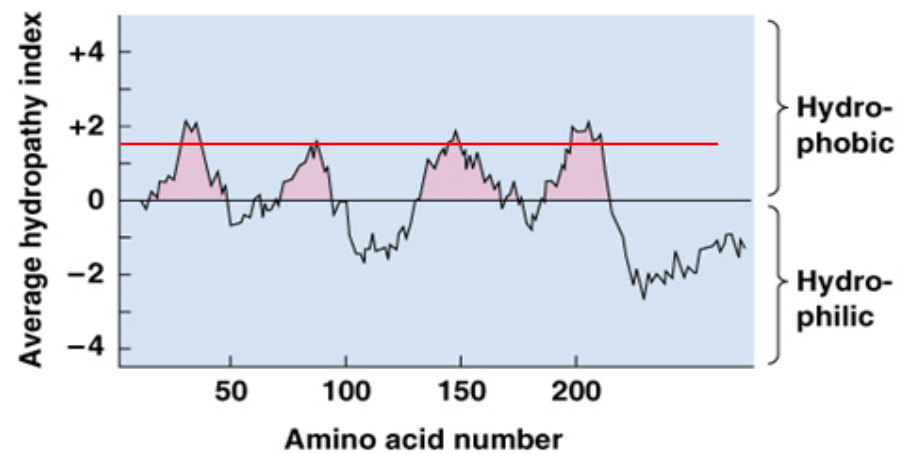


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Hydropathy profile

Textbook examples are oversimplified.



(b)

Example of **connexin**: 4 positive peaks from hydropathy analysis predicts the protein has 4 transmembrane domains.

Hydropathy profile

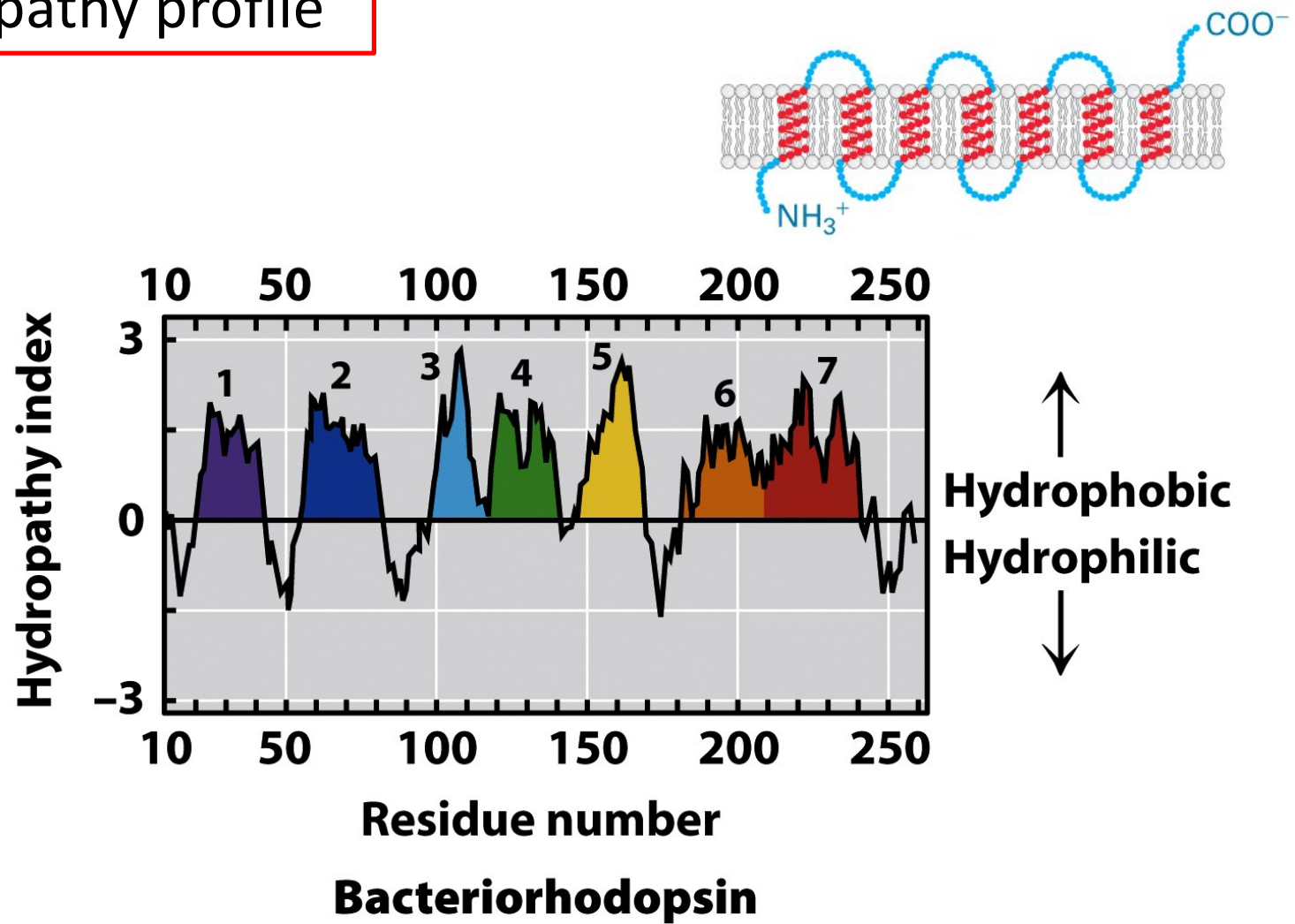


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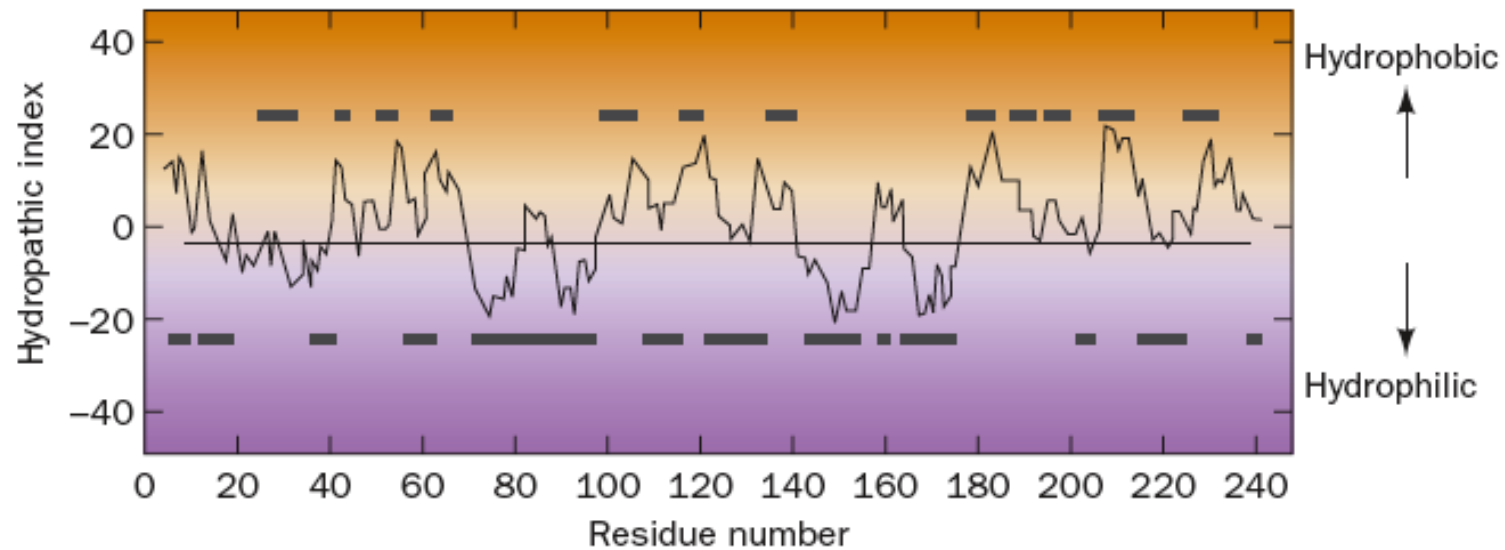
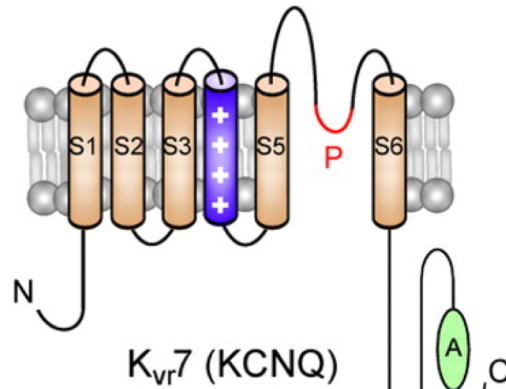
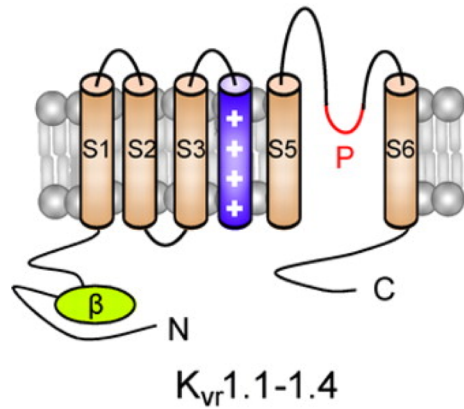
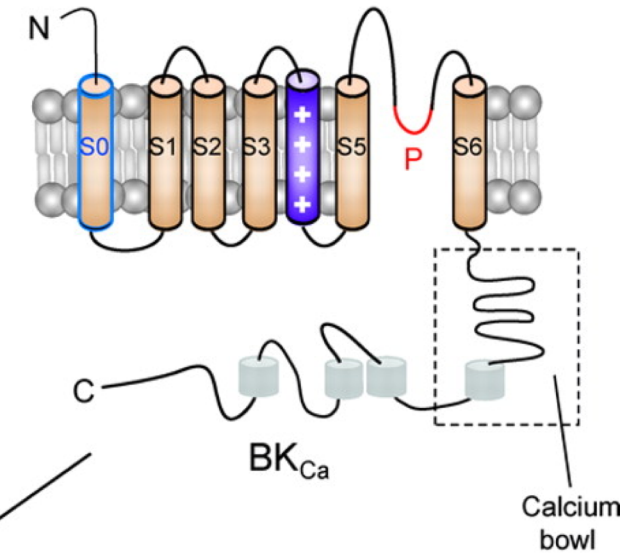


Figure 6-35 A hydropathic index plot for bovine chymotrypsinogen. The sum of the hydropathies of nine consecutive residues is plotted versus residue sequence number. A large positive hydropathic index indicates a hydrophobic region of the polypeptide, whereas a large negative value indicates a hydrophilic region. The upper bars denote the protein's interior regions, as determined by X-ray crystallography, and the lower bars denote the protein's exterior regions. [After Kyte, J. and Doolittle, R.F., *J. Mol. Biol.* **157**, 111 (1982).]

Voltage-gated K^+ channels (K_{ir})

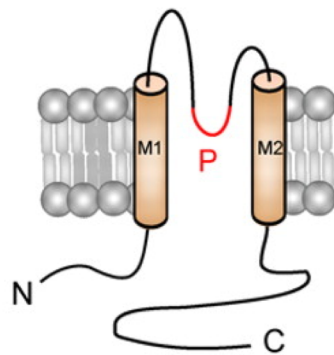


Calcium-activated K^+ channels (K_{Ca})

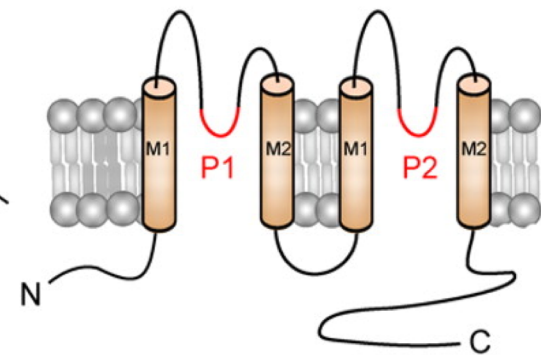
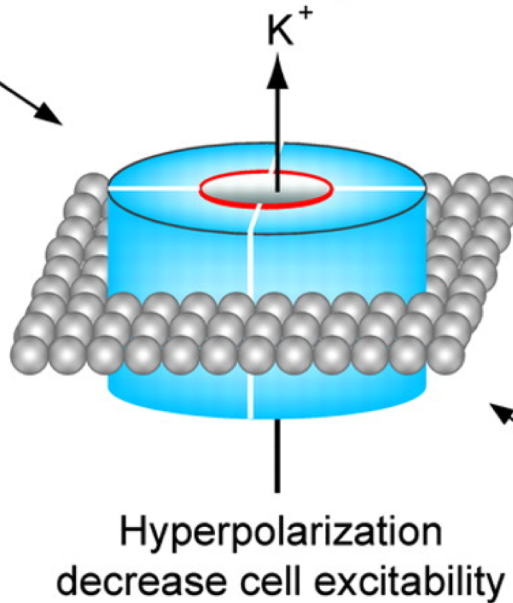


4 families

(75 genes)

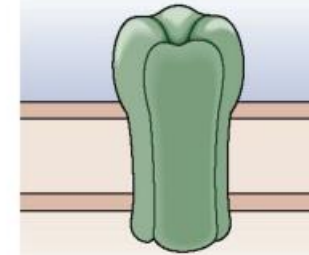
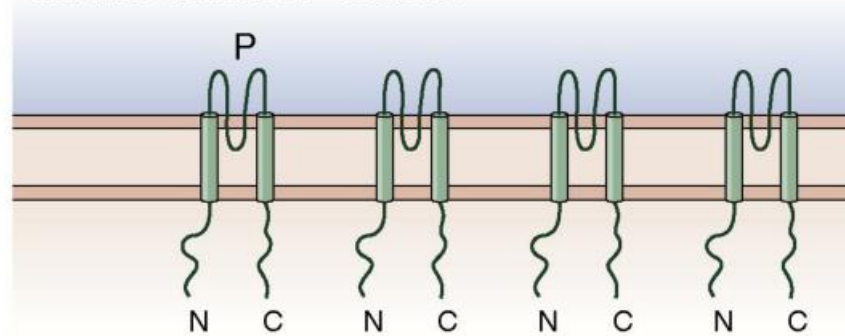


Inward rectifier K^+ channels (K_{ir})



Leakage K⁺ Channels Are Dimers of Subunits With Two P-Loops Each

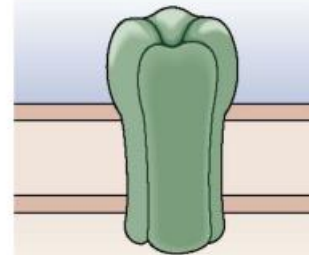
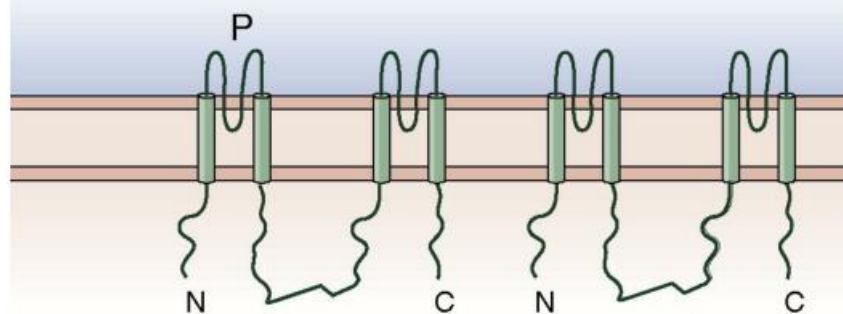
Inward rectifier K⁺ channel



tetramer

4 x 2 = 8 TM

Leakage K⁺ channel



dimer

2 x 4 = 8 TM

Leakage channels
are “almost always”
open

Potassium leakage

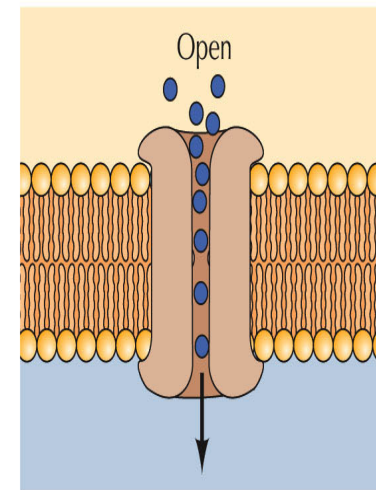
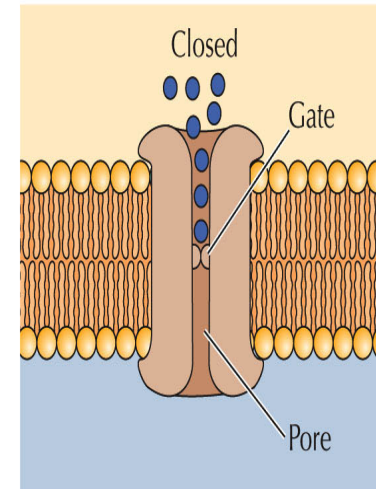


Ion channels

Ions **never** diffuse through the plasma membrane

- **Porins** permit the free passage of ions and small polar molecules through the outer membranes of bacteria.
- **Ion channels** mediate the passage of ions across plasma membranes.
- ◊ **Ligand-gated channels** open in response to the binding of neurotransmitters or other signaling molecules.
- ◊ **Voltage-gated channels** open in response to changes in electric potential across the plasma membrane.

Leakage channels are “almost always ” open



The structure of a bacterial K⁺ channel.

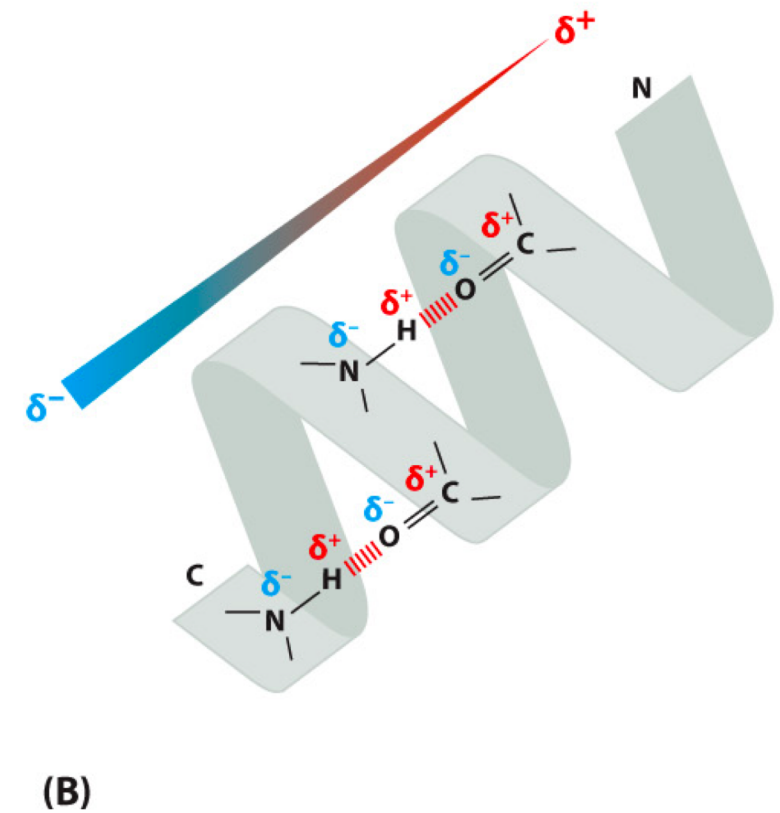
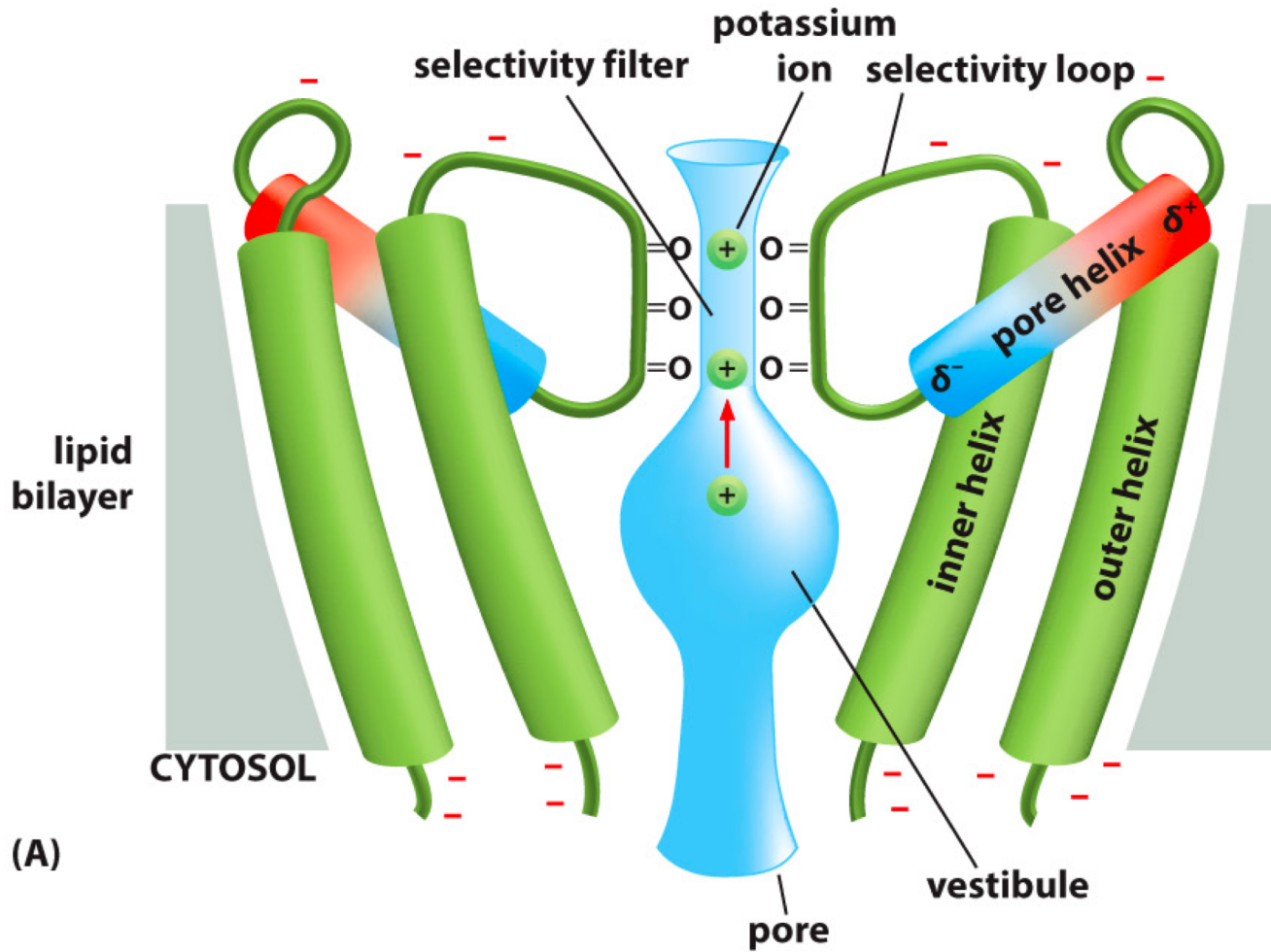
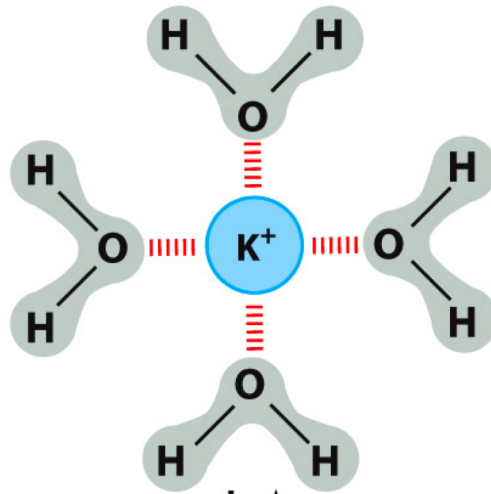


Figure 11-24 Molecular Biology of the Cell 6e (© Garland Science 2015)

(A) ion in vestibule



K^+ specificity of the selectivity filter in a K^+ channel.

(B) ion in selectivity filter

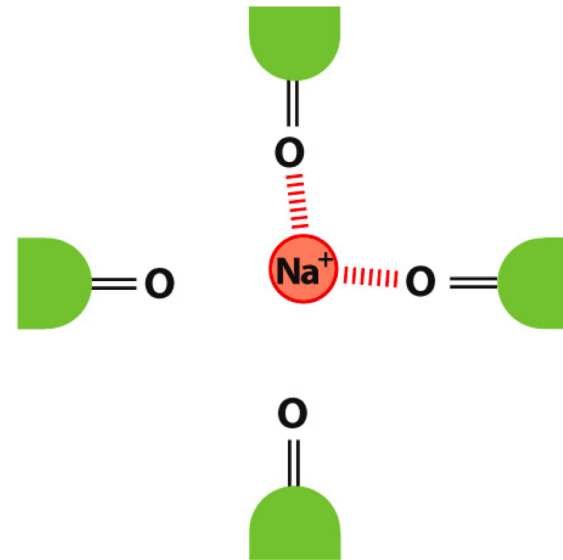
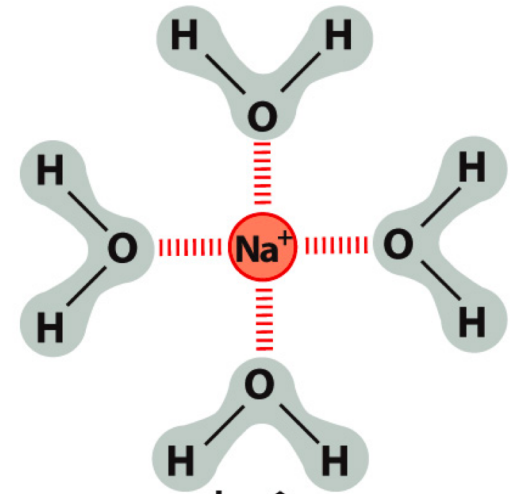
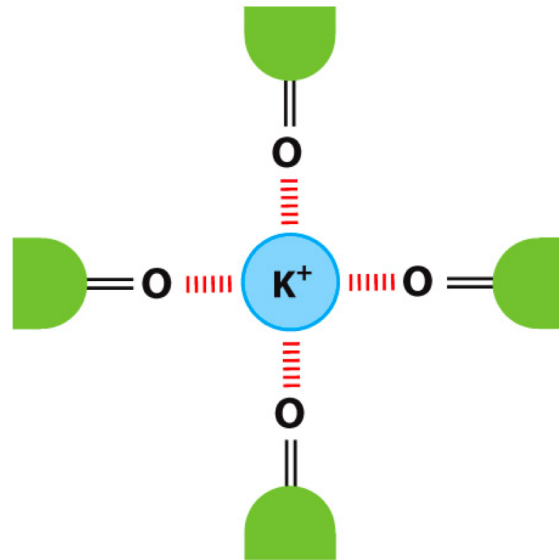
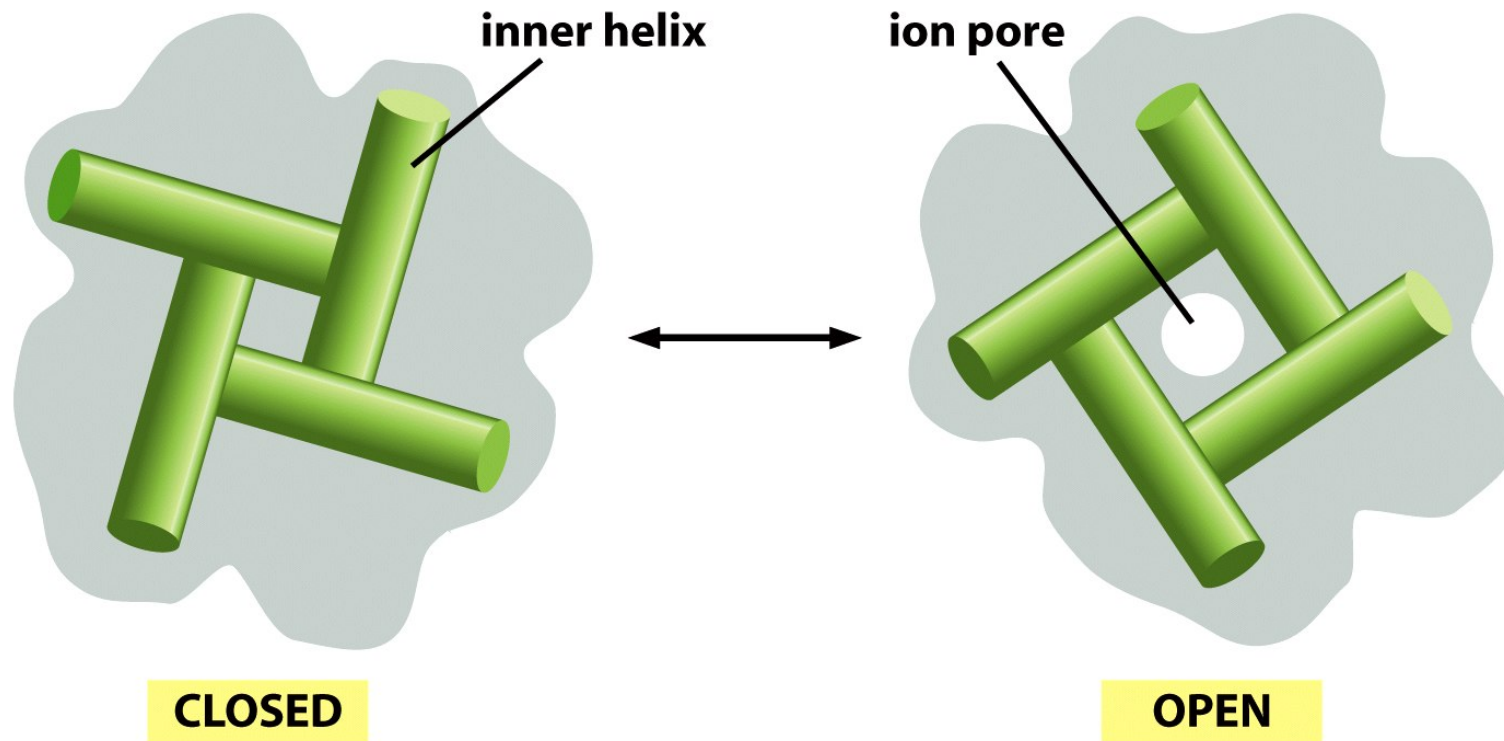
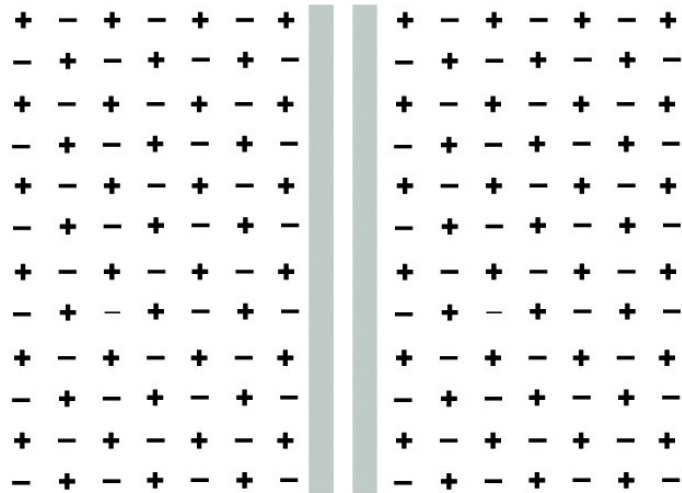


Figure 11-25 Molecular Biology of the Cell 6e (© Garland Science 2015)

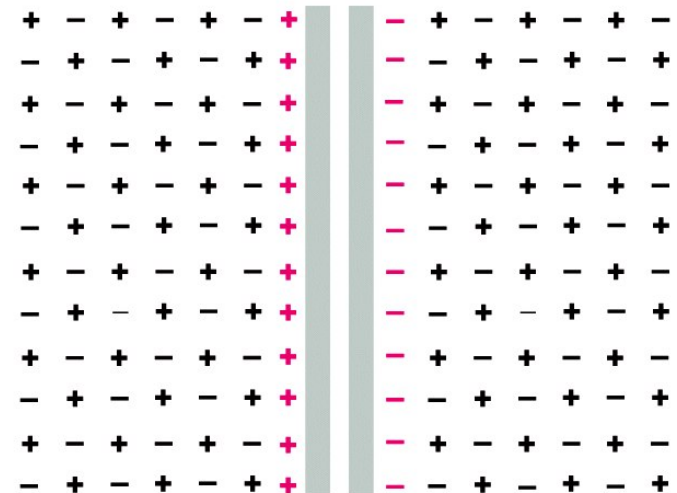
A model for the gating of a bacterial K^+ channel



The ionic basis of a membrane potential



exact balance of charges on each side of the membrane; membrane potential = 0



a few of the positive ions (*red*) cross the membrane from right to left, leaving their negative counterions (*red*) behind; this sets up a nonzero membrane potential