

Today's class:

Structural motifs and membrane proteins

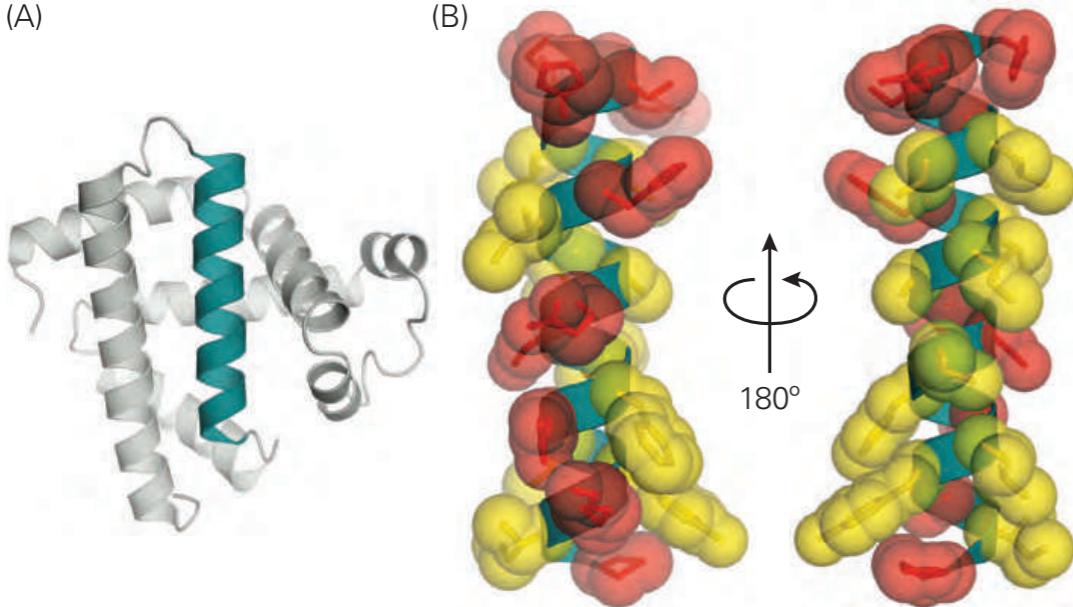
*This lecture follows the chapter 4 in the book
'The Molecules of Life' by Kuriyan, Konforti & Wemmer, 1st Ed, 2013*

α helices and β strands are often amphipathic

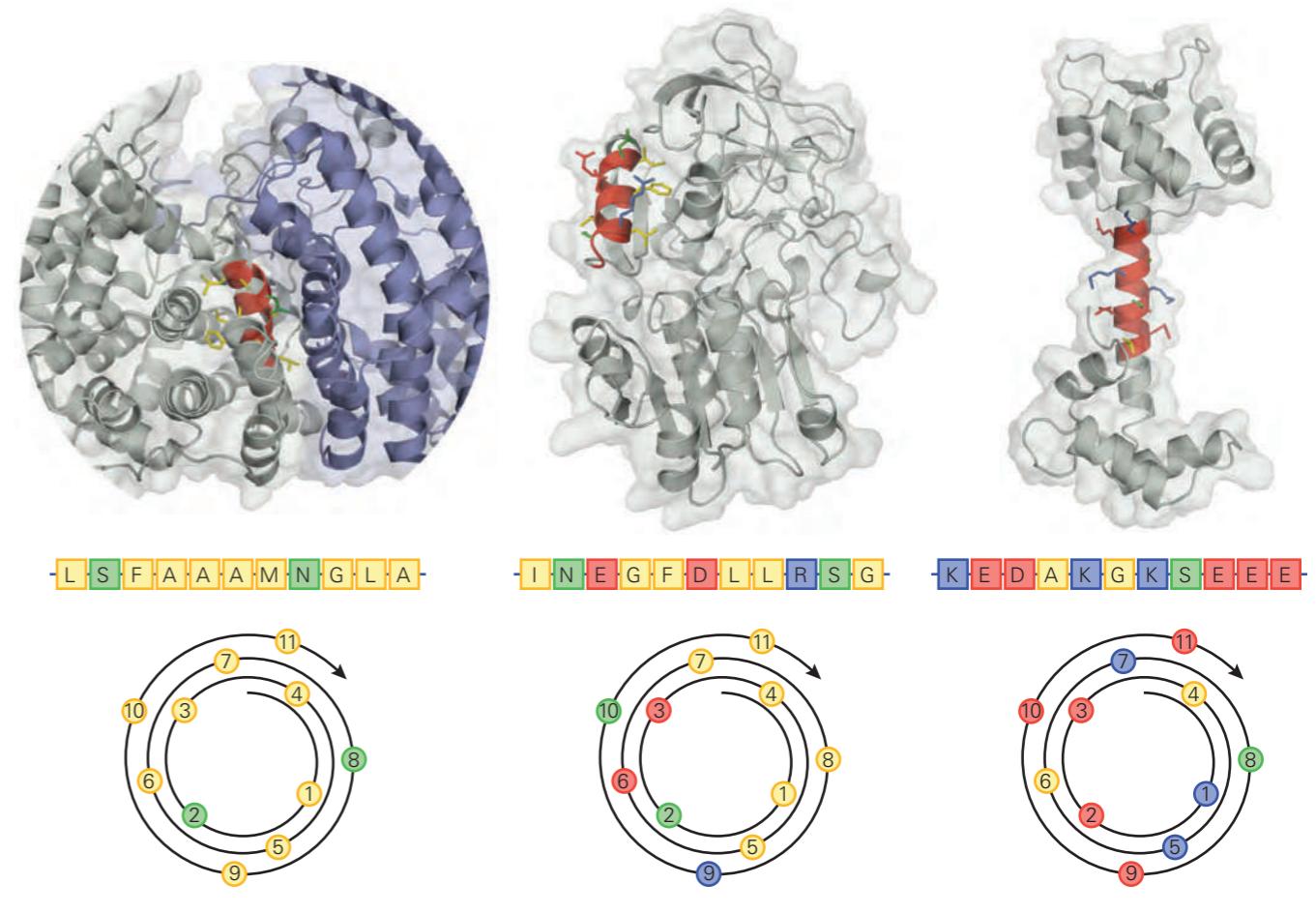
One face hydrophobic & other face hydrophilic

(A)

(B)



Amphipathic α helices



Residue identities of α helices change based on water exposure

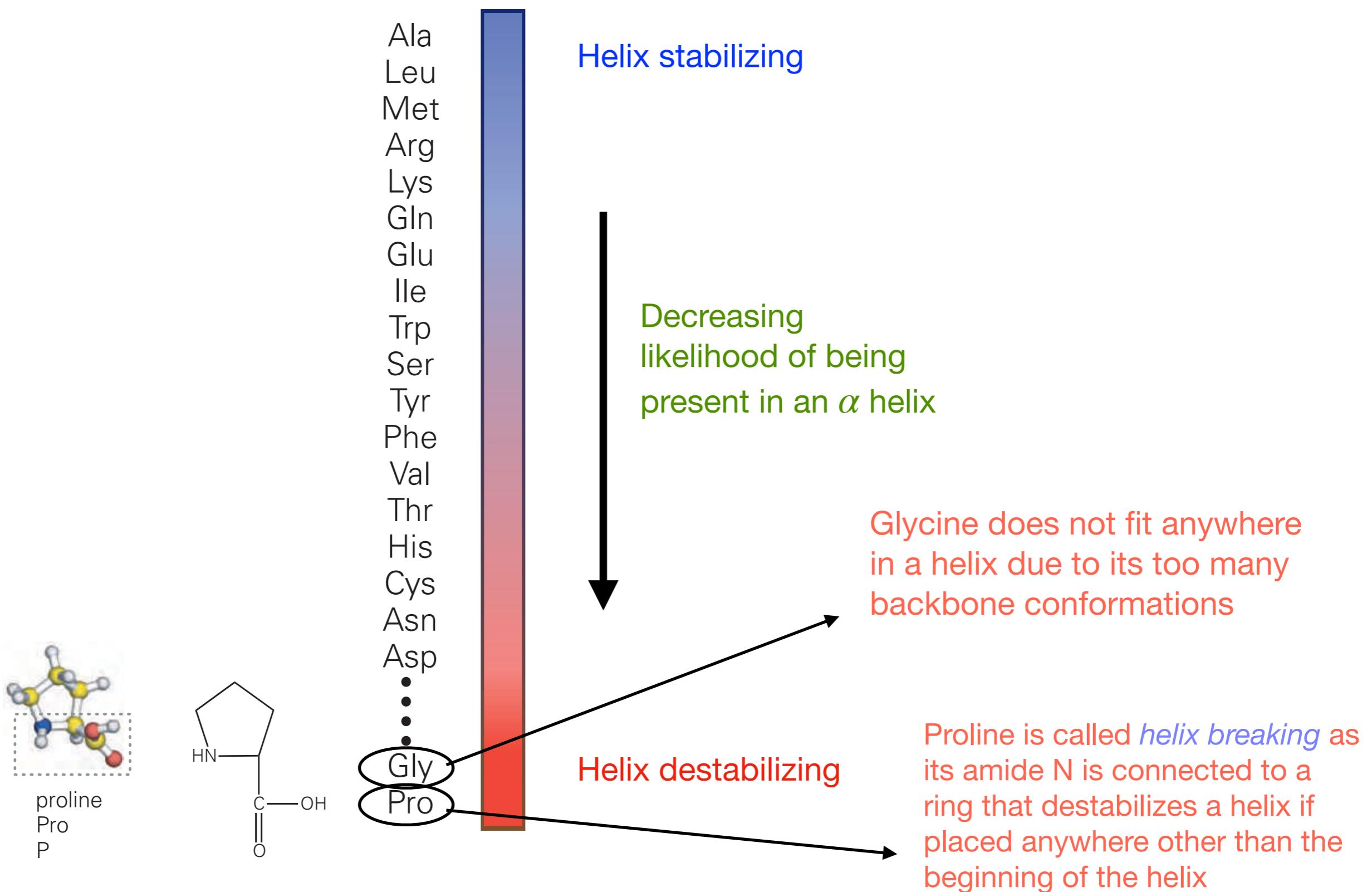
(A)

(B)



Thr - Ile - Lys - Phe - Val - Ala - Asp -

Some amino acids are more preferred in α helices than others



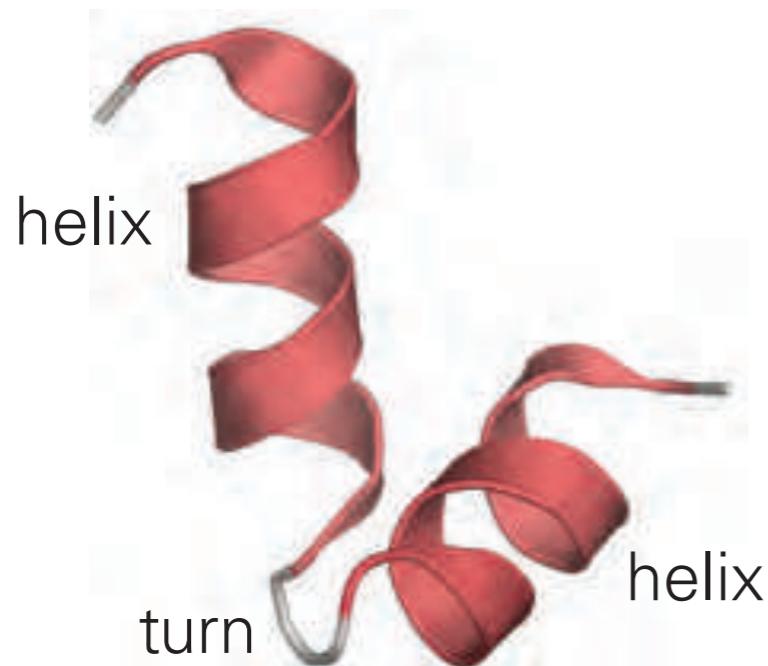
Secondary structure elements connect to form protein structural motifs

Structural motif

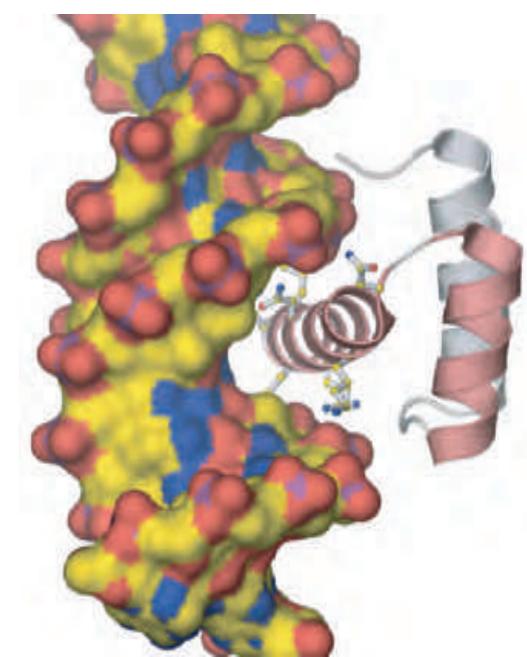
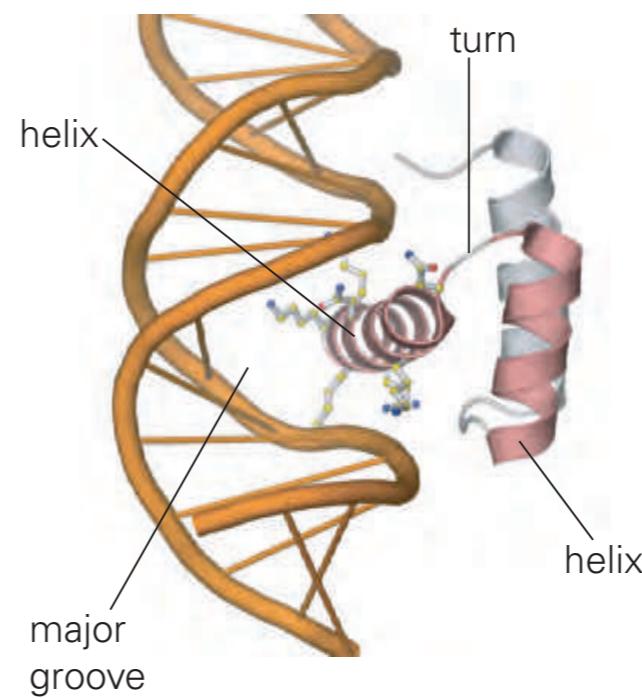
A three-dimensional arrangement of two or more secondary structural elements that is commonly found in many proteins is called a structural motif. Motifs are typically components of larger domains, and more than one motif may be found in a protein domain.

Some motifs can be associated with a particular function, such as binding to DNA, metal ions, or small molecules

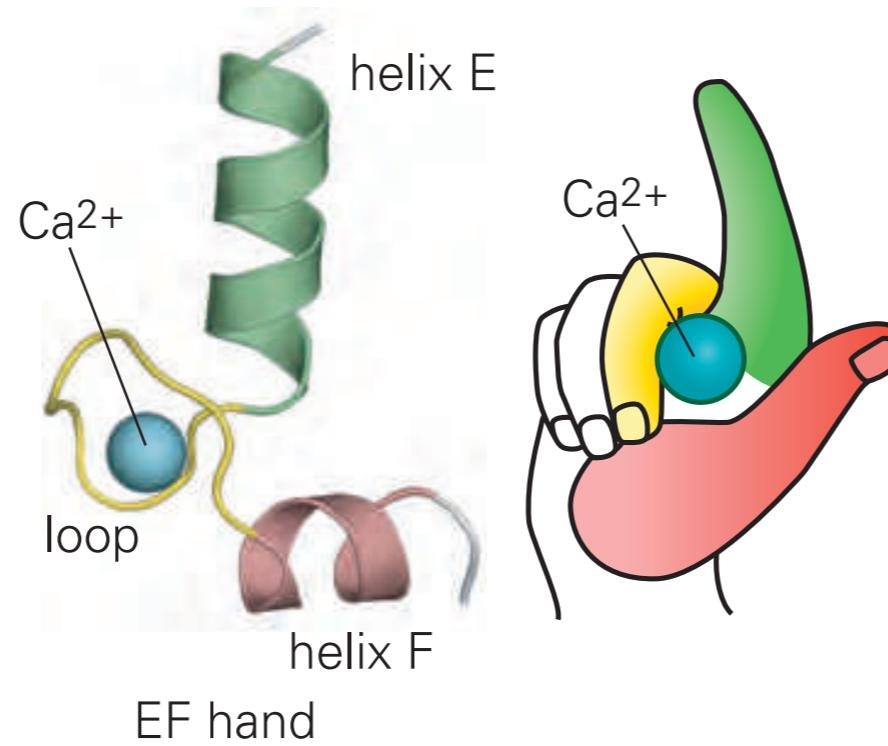
Helix-turn-helix motif



Usually binds to DNA



EF hand motif



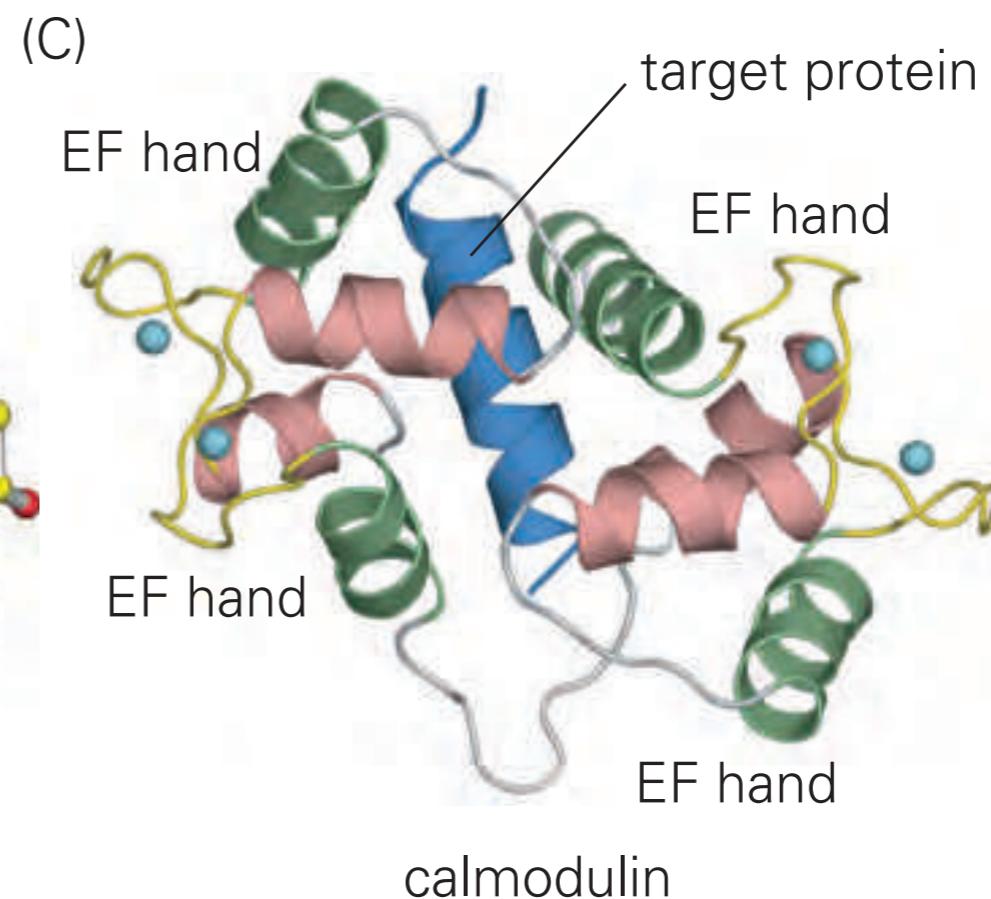
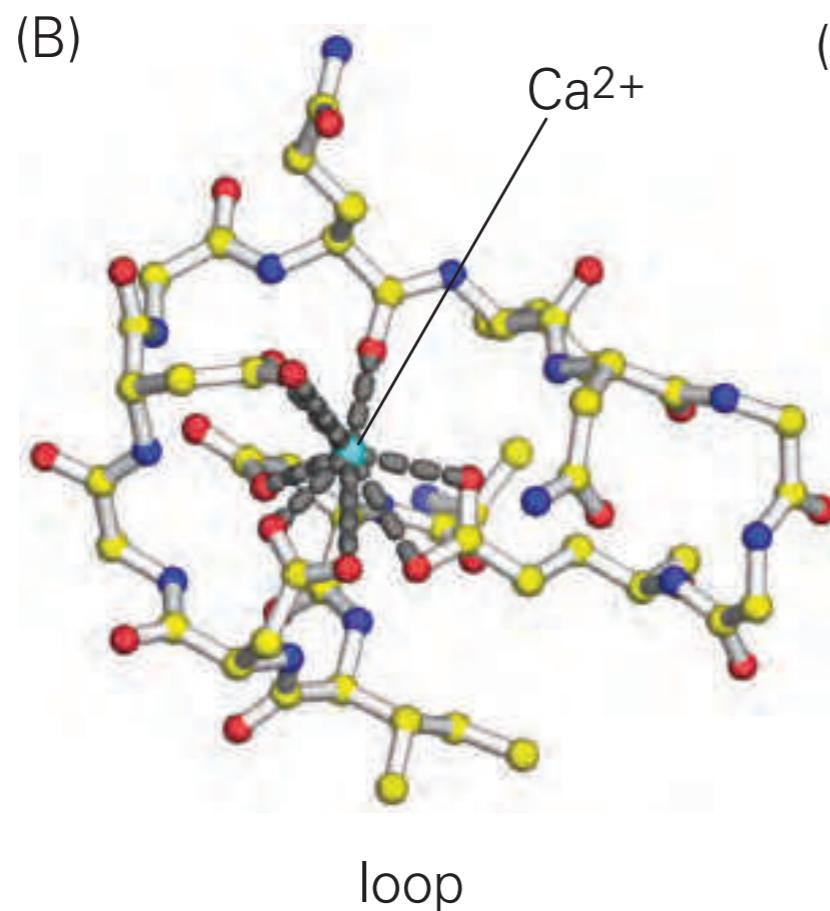
Helix-loop-helix motif

States of Calmodulin in cell

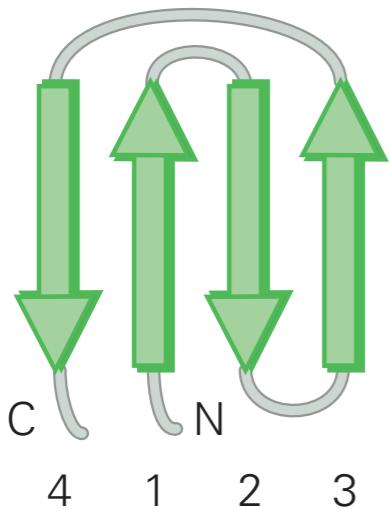
Ca^{2+} - free state = closed

Ca^{2+} - saturated state = open

Ready to bind target proteins



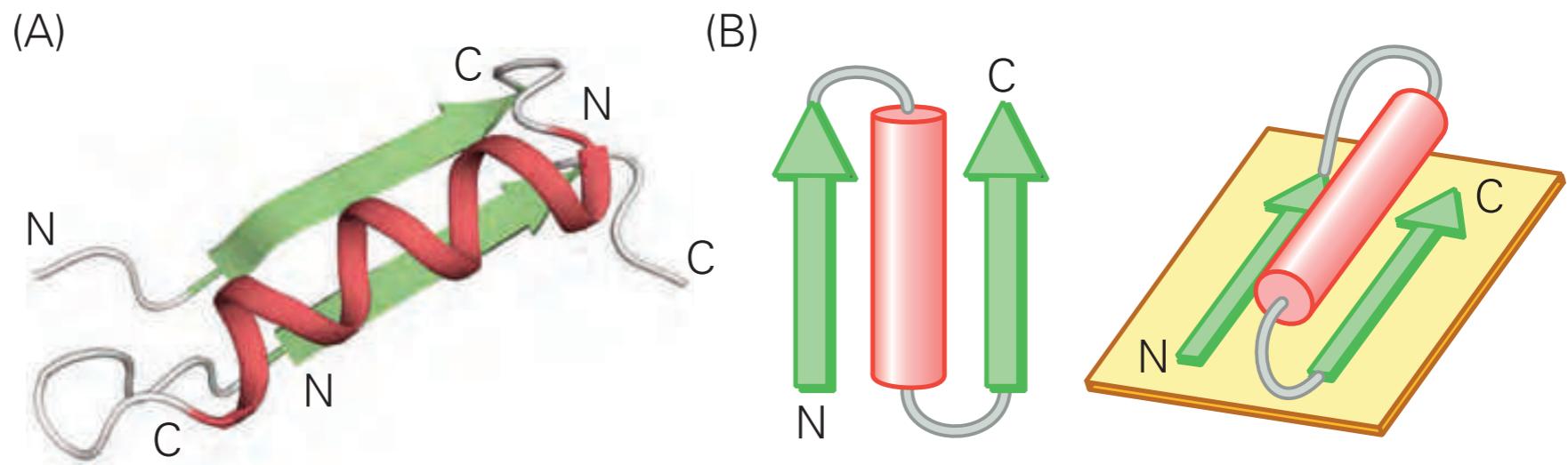
Structural motifs involving β strands



Greek key motif

No specific function

Observed in many protein structures



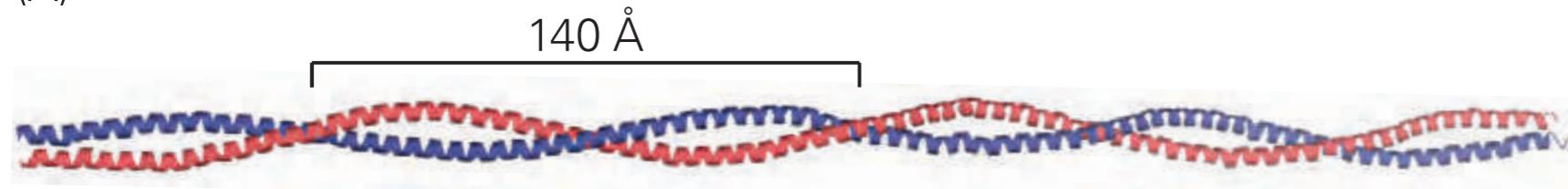
$\beta - \alpha - \beta$ motif

Occurs in proteins with parallel β strands

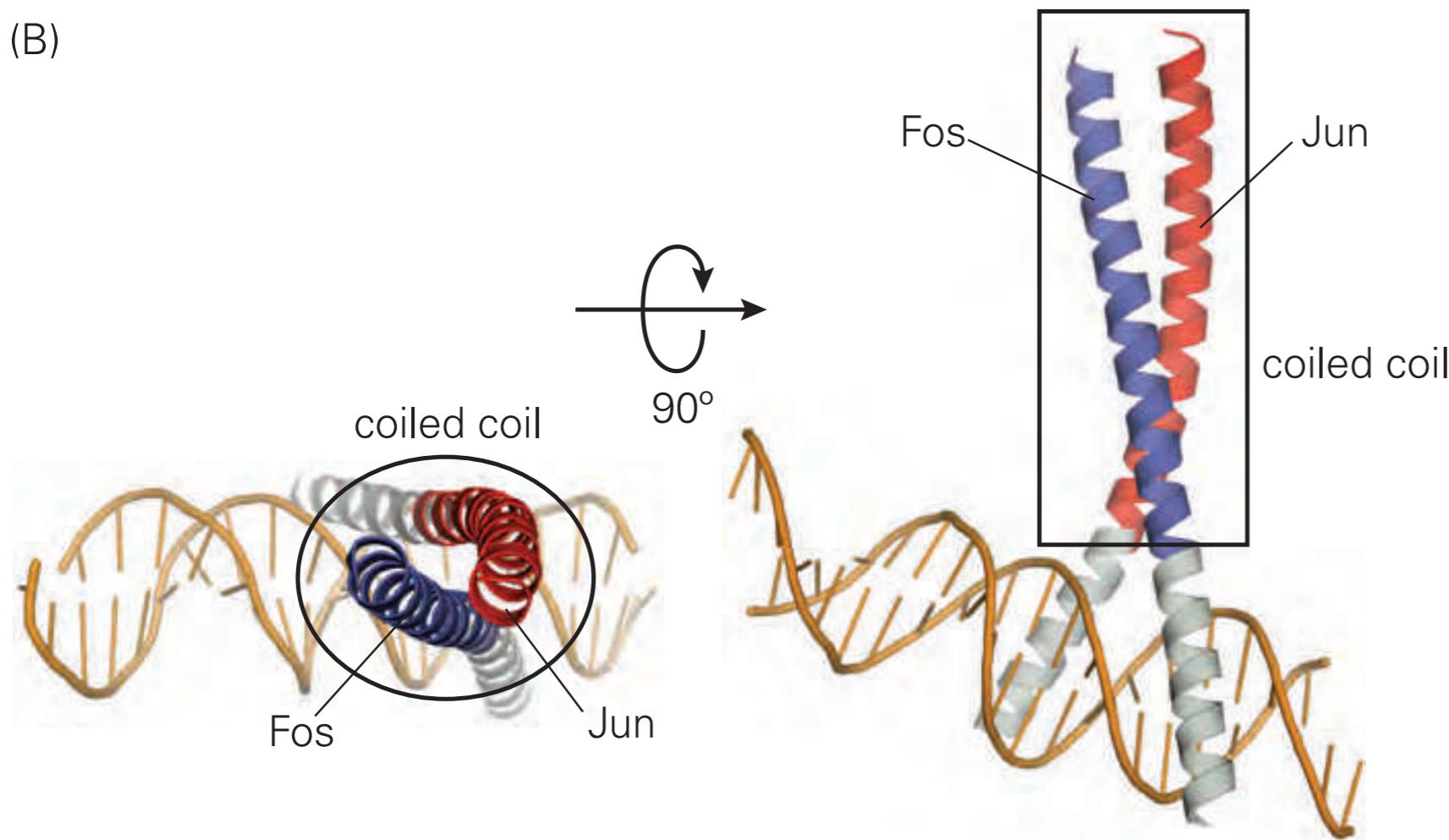
E.g. the enzyme triosephosphate isomerase is entirely built up by repeated combinations of this motif, where two successive motifs share one β strand

Amphipathic α helices can form dimeric structures called coiled coils

(A)



(B)

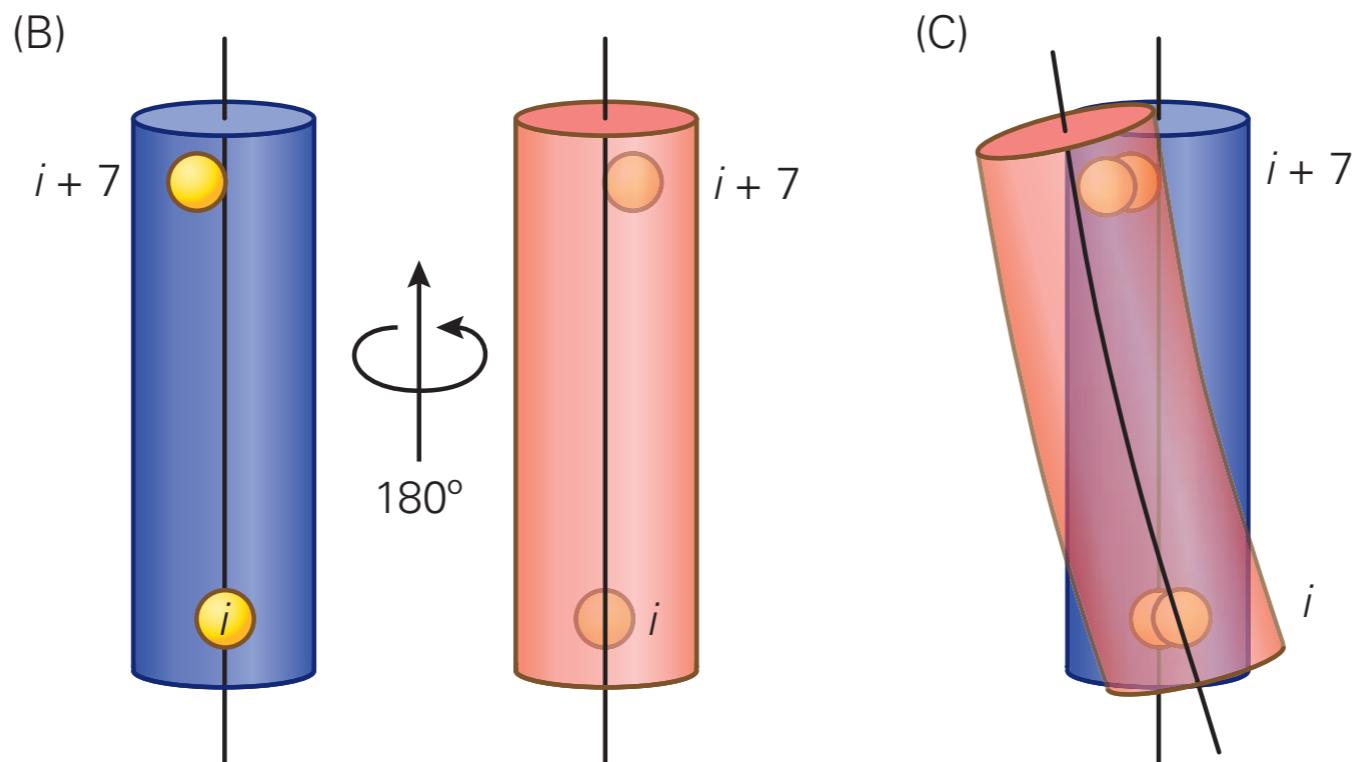
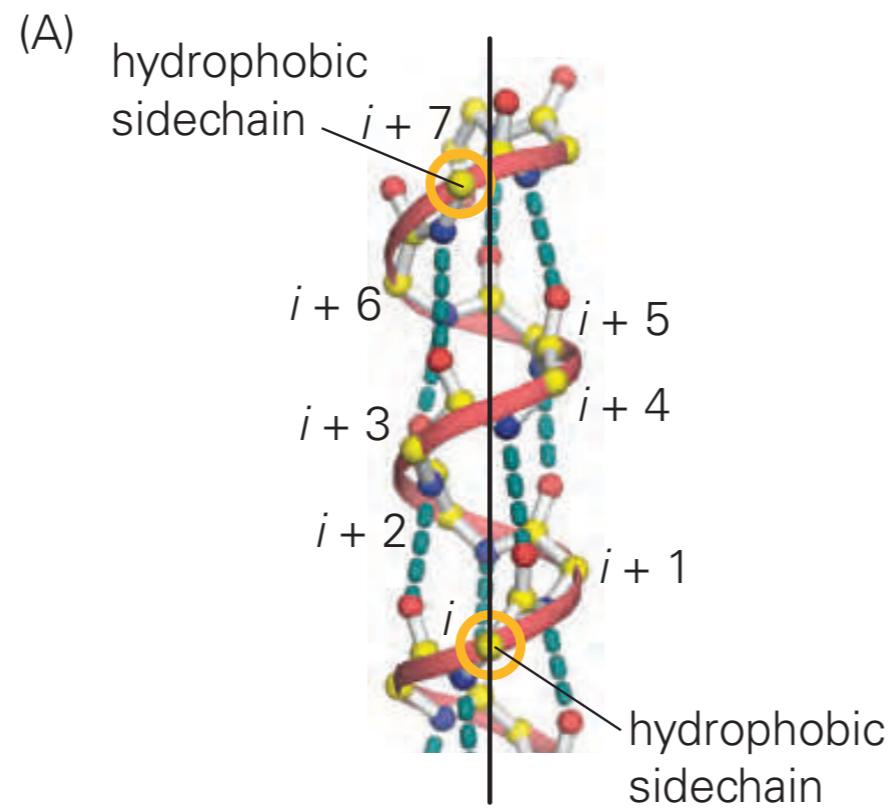


Such coiled coil helices are the basis of fibrous proteins. e.g. muscle fibers. They can be hundreds amino acids long and provide durability.

Supercoil

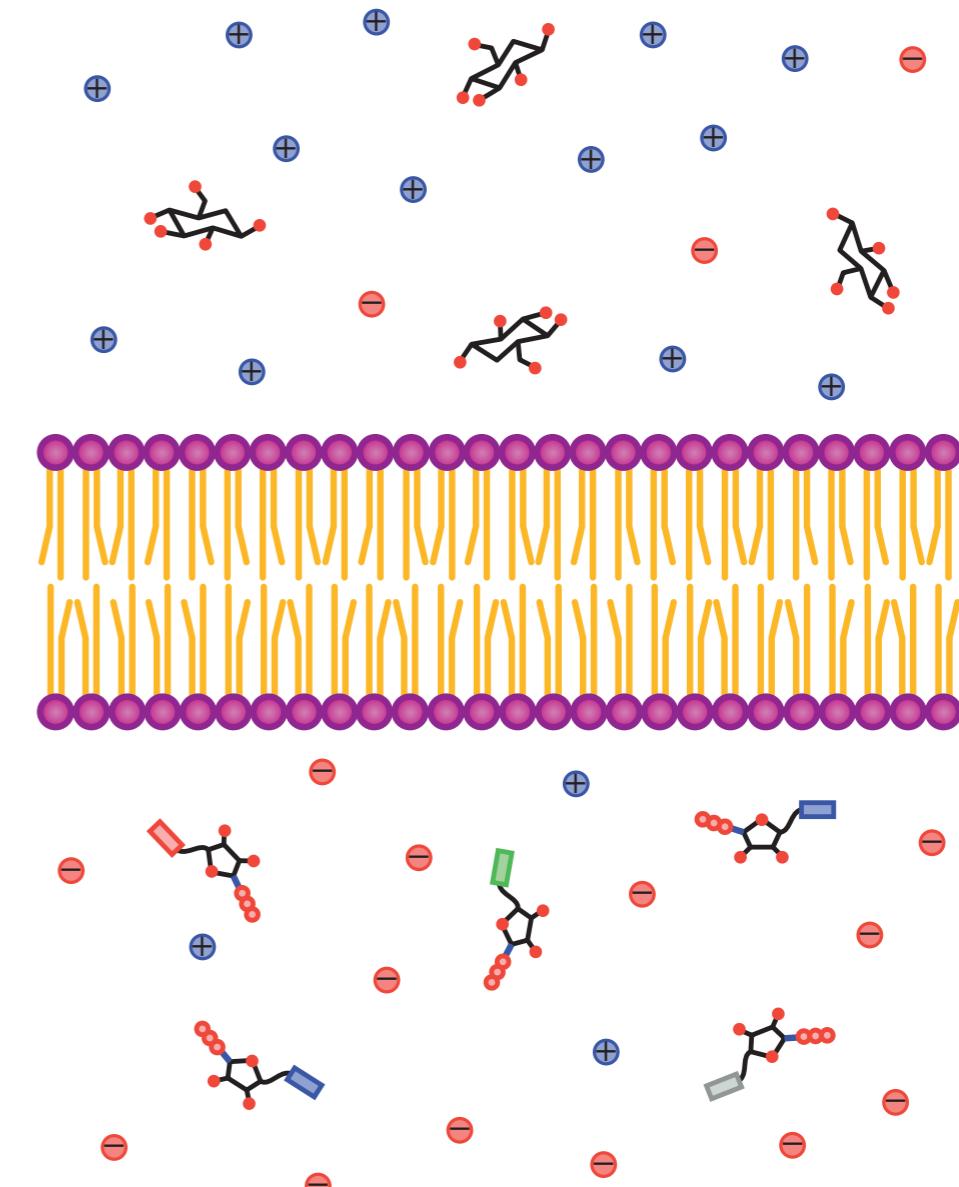
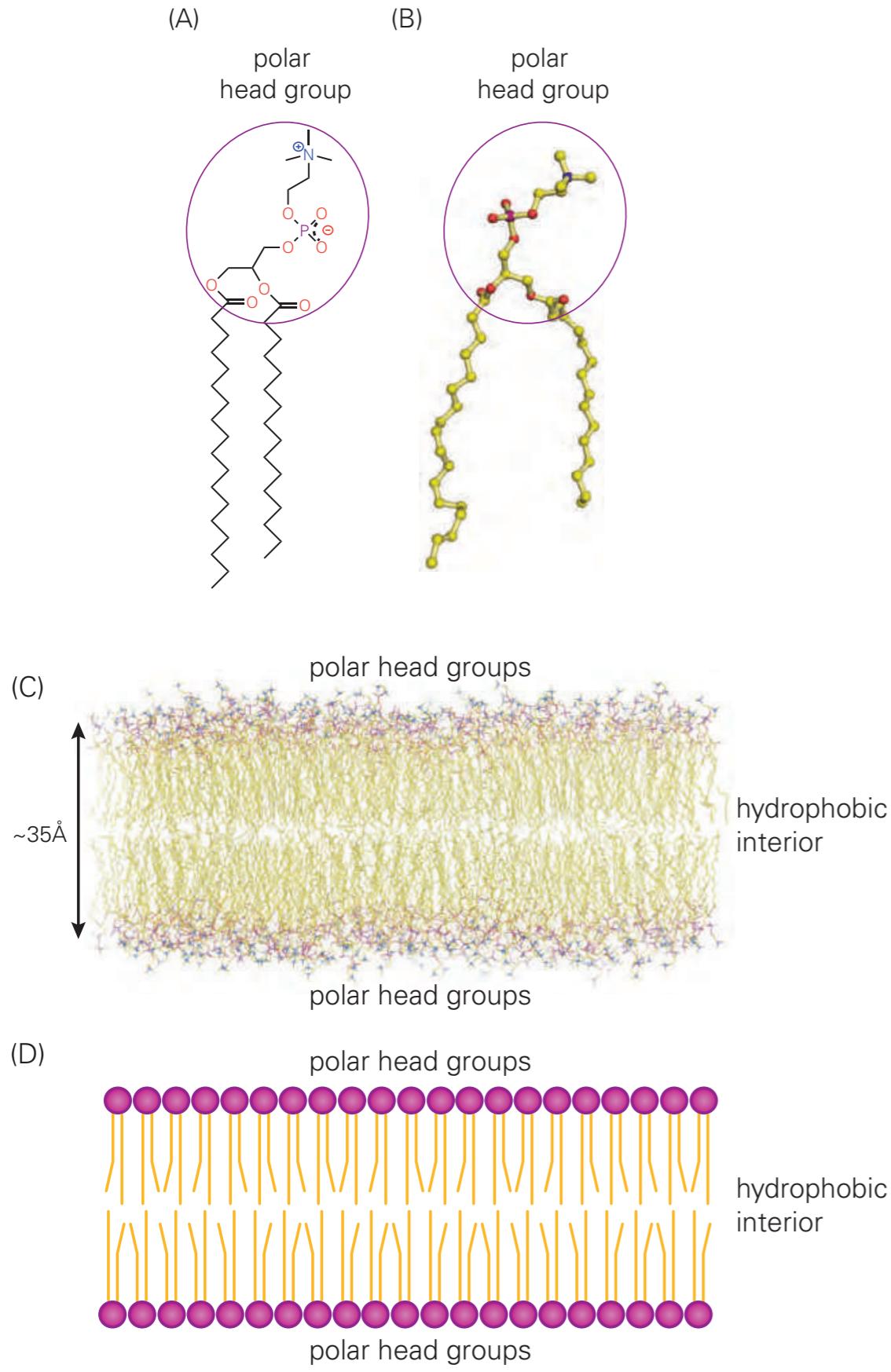
When the axis of a helix is coiled rather than straight, the resulting structure is called a supercoil or a superhelix.

Coiled coil super helices are always left-handed



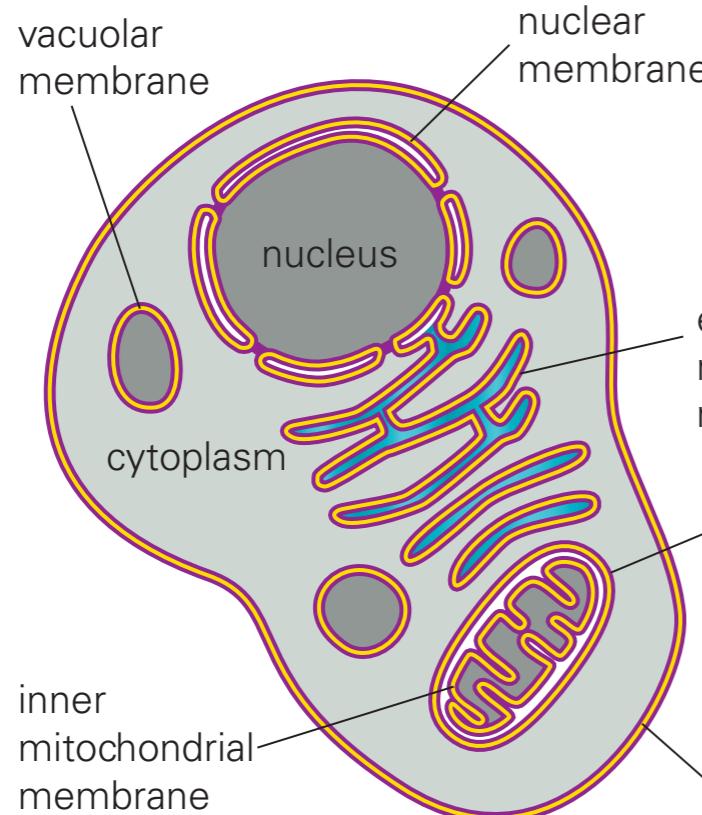
Structural principles of membrane proteins

Lipid bilayers form nearly impermeable barriers to polar molecules



The hydrophobic center of the lipid bilayer cannot form hydrogen bonds, and so polar molecules do not readily pass through membranes. Loss of H-bonds lead to a large energy penalty!

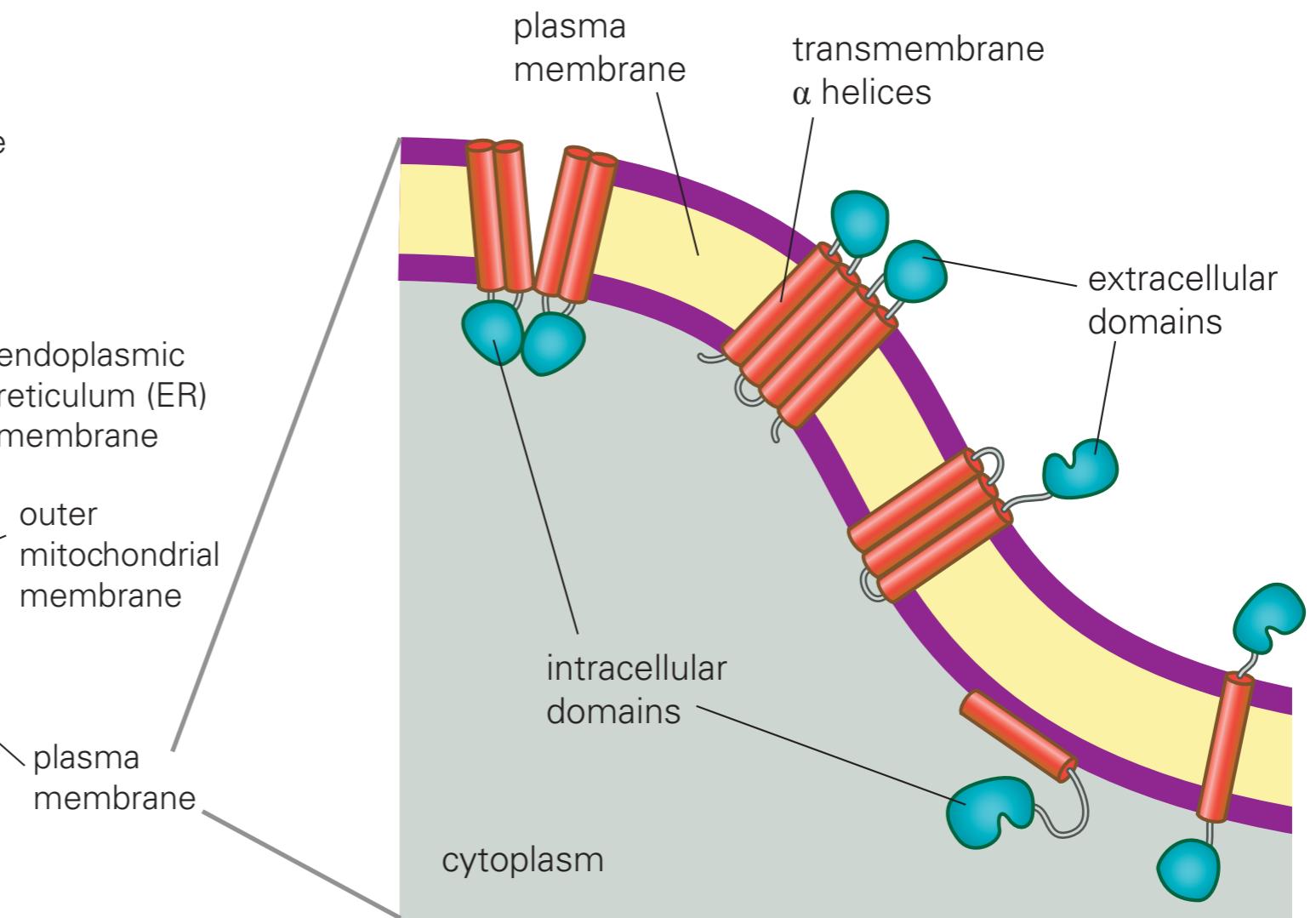
Cellular membranes keep stuff separated but exchanges needed for life



Membranes efficiently maintain compartments inside the cell

But exchanges are necessary for cellular functions -

how do they happen?

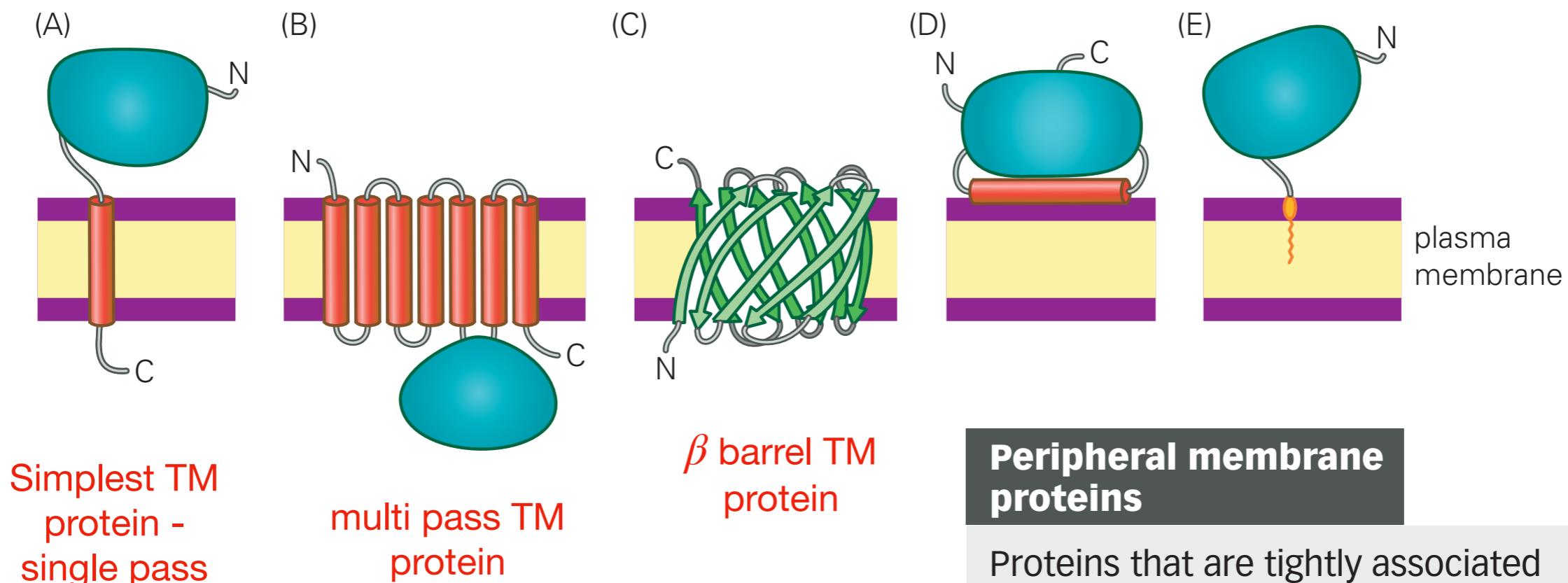


Integral membrane proteins

Proteins that are associated with the membrane for the entirety of their lifespan are known as integral membrane proteins. The three-dimensional structure of these proteins depends on interactions with the lipids in the membrane. Proteins with at least one peptide segment that crosses the membrane bilayer are transmembrane proteins.

Exchanges are mediated by integral membrane proteins

Membrane proteins have distinct regions that interact with the lipid bilayer



Simplest TM
protein -
single pass

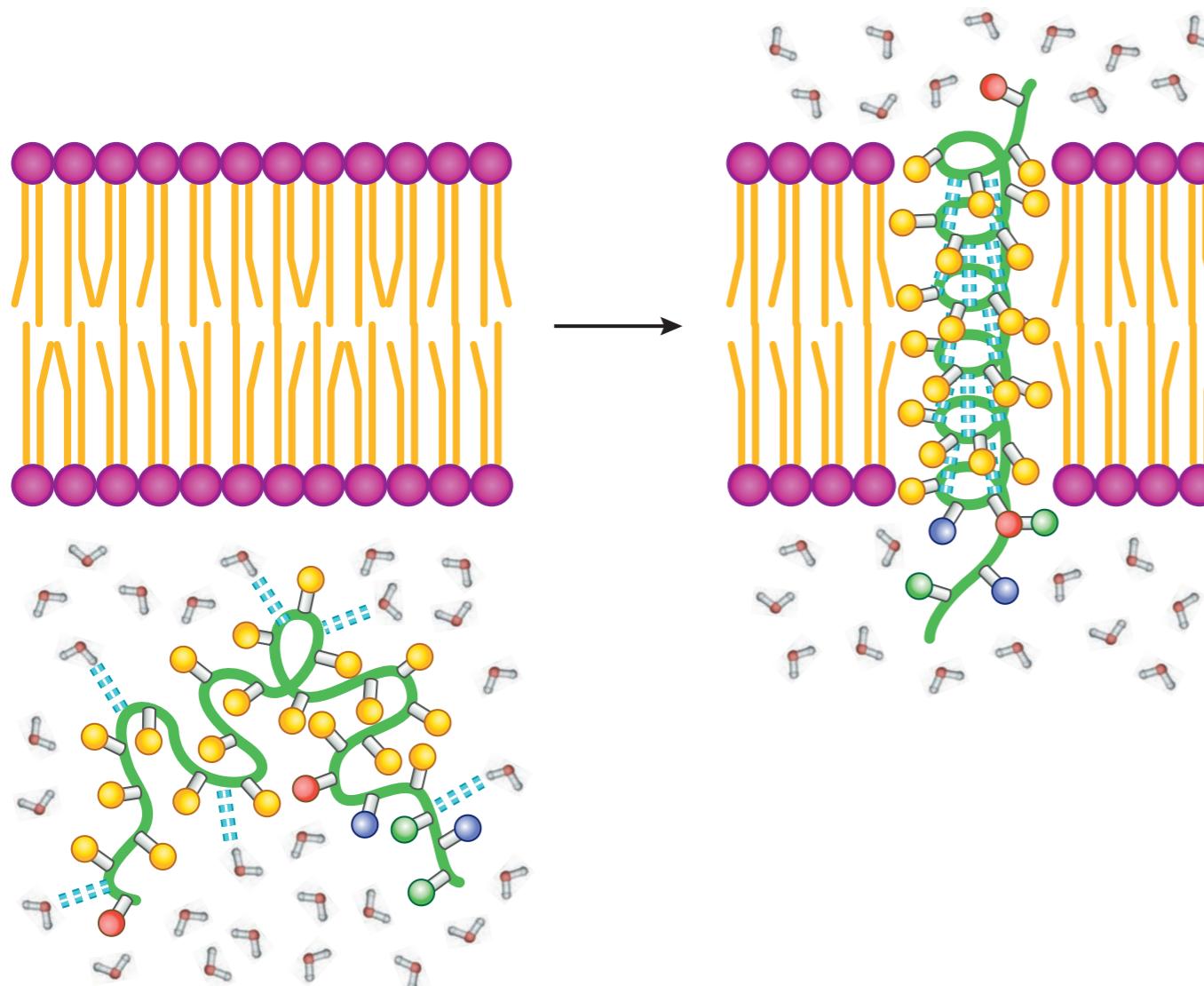
multi pass TM
protein

β barrel TM
protein

Peripheral membrane proteins

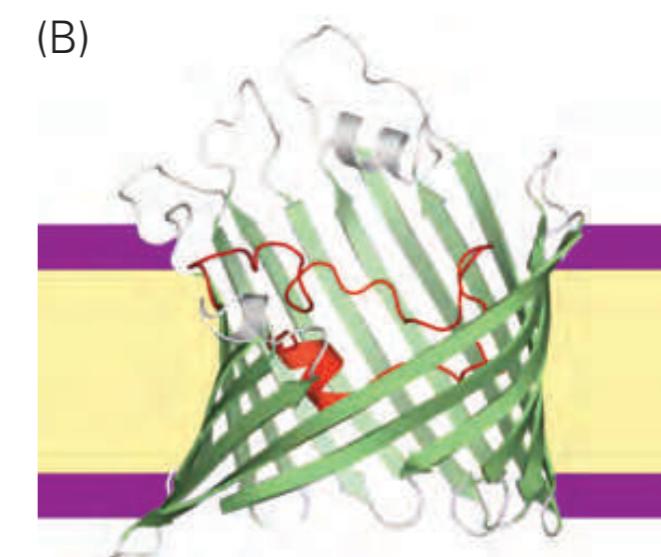
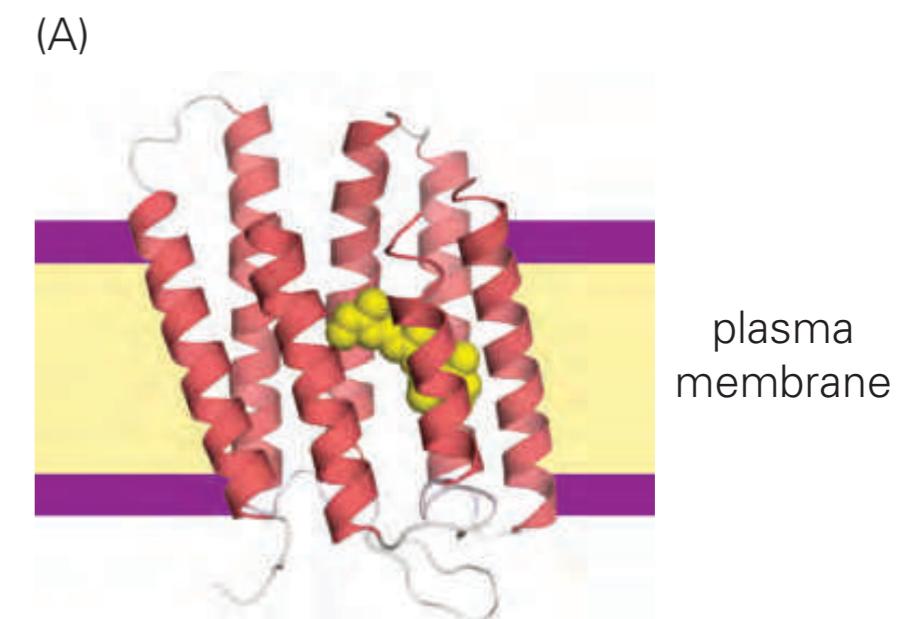
Proteins that are tightly associated with membranes, but do not traverse the membrane, are known as peripheral membrane proteins. Such proteins may be bound to the membrane by noncovalent interactions or covalently attached to a membrane lipid.

Hydrophobicity dictates the structure of the transmembrane domains

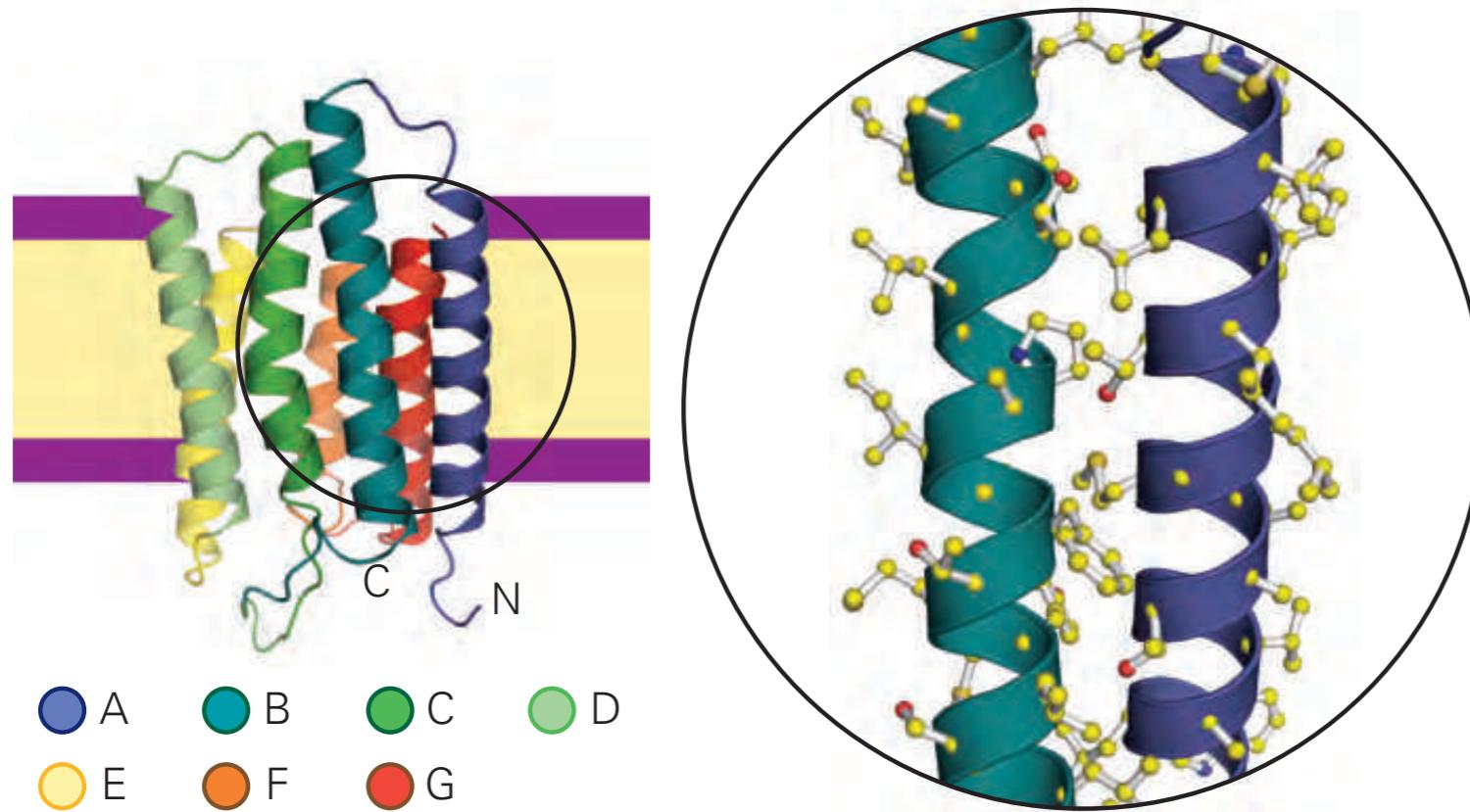


Transmembrane α helices satisfy the hydrogen- bonding requirements of the peptide backbone

This is why most TM domain have well-defined secondary structure



Hydrophilic residues are rarely found in the transmembrane domains



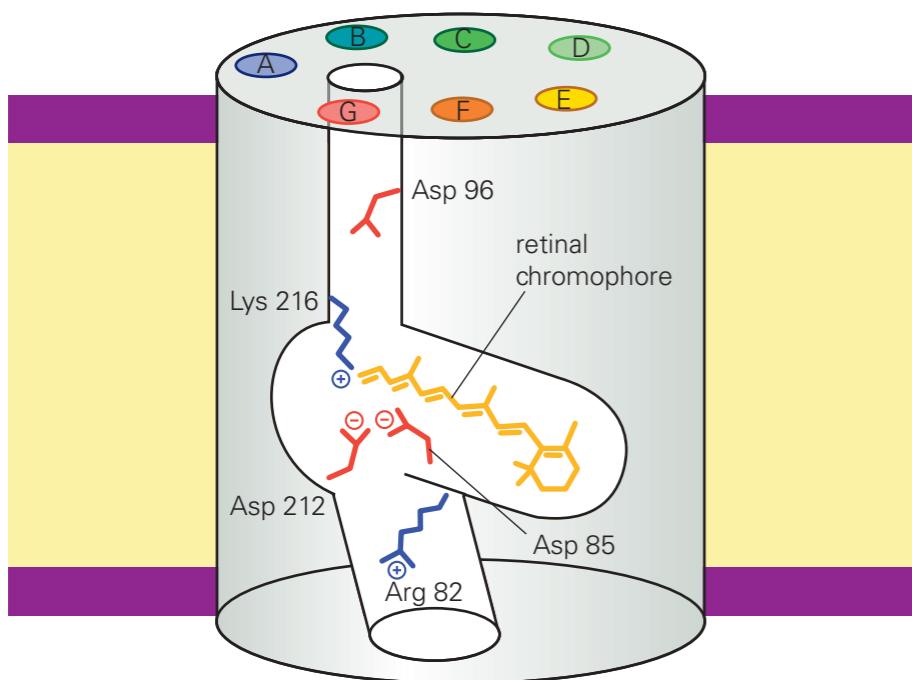
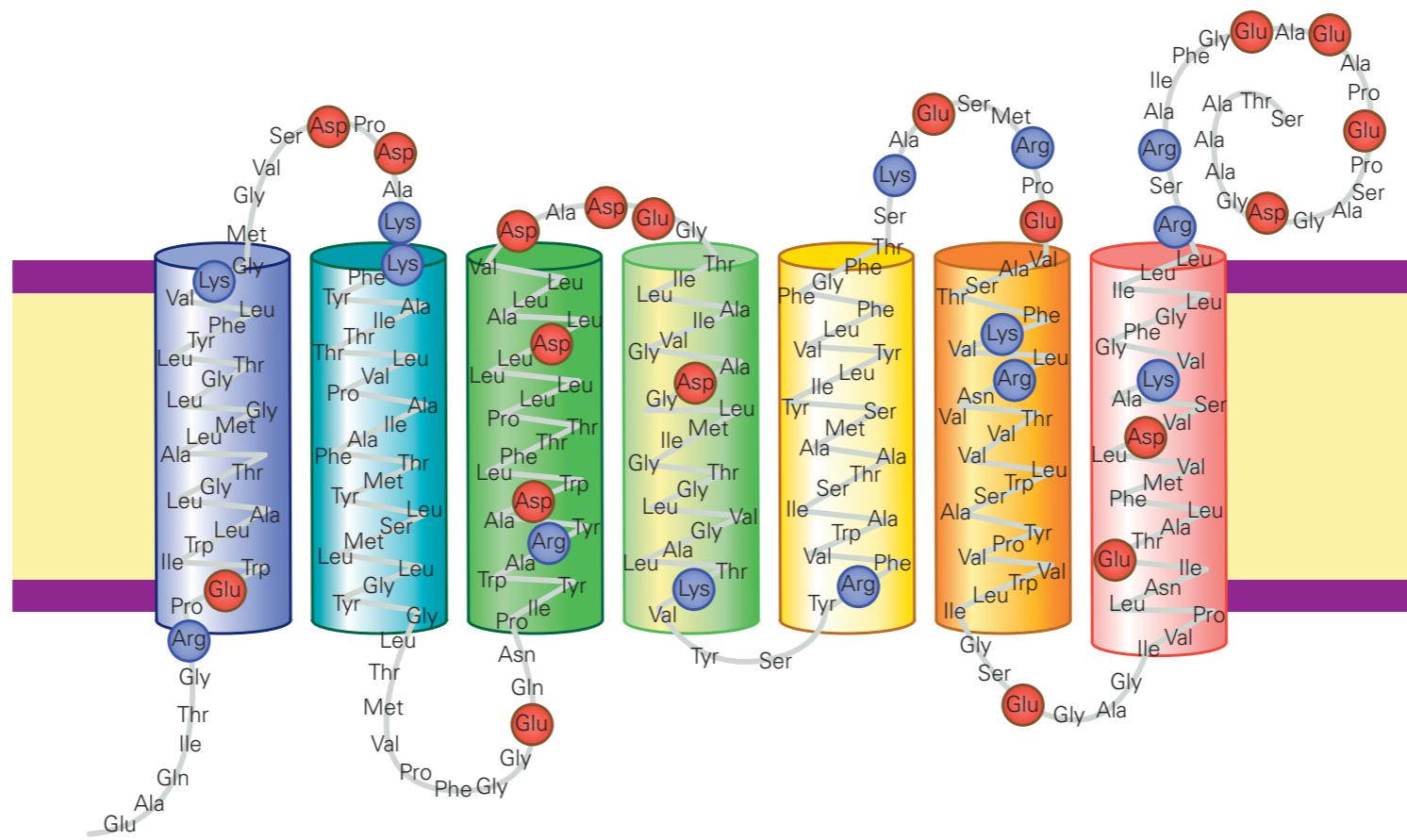
most of the residues at the interfaces between the helices are hydrophobic, as are the residues on the outer surface that faces the membrane.

Hydrophilic residues are typically not part of such construction because

- H-bonding partners would be hard to find
- Any mutations will destabilize the TM domain

That's why any mutations on the TM domain happen in hydrophobic residues

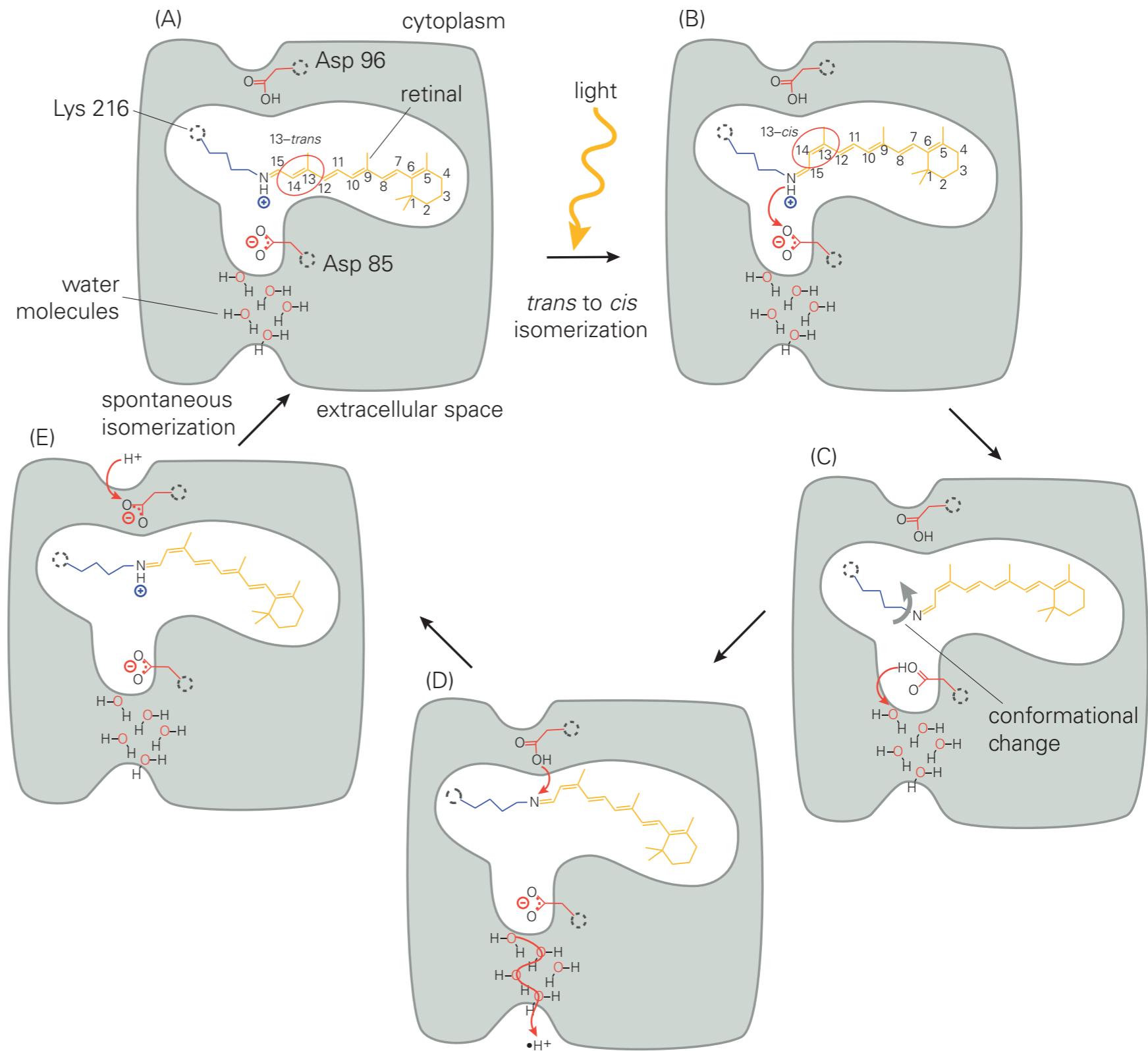
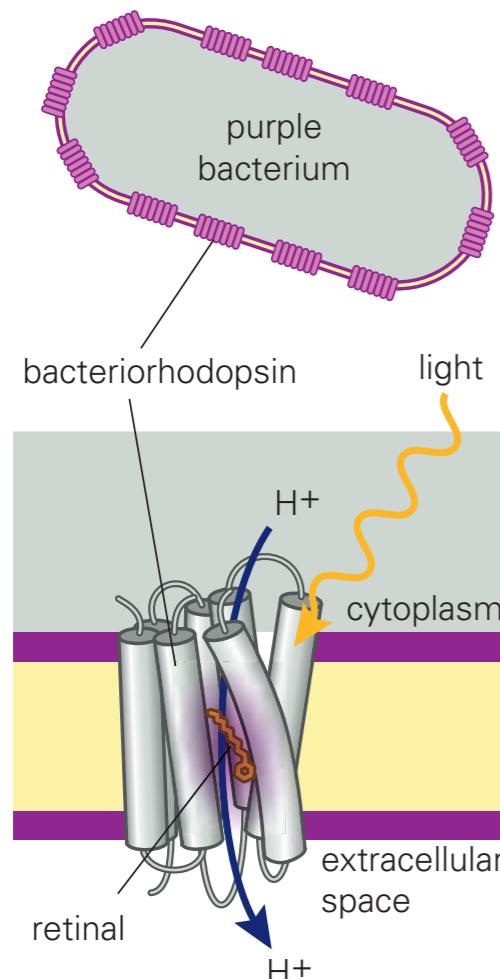
Hydrophilic residues in the transmembrane domains have specific functions



Charged residues in bacteriorhodopsin

A proton conducting network within the protein is created. Charged residues line this pathway and interact with the retinal chromophore

Bacteriorhodopsin acts as a light-driven proton pump



The membrane of the purple bacterium, *Halobacterium halobium*, is densely packed with molecules of bacteriorhodopsin. Light causes isomerization of the retinal chromophore bound to bacteriorhodopsin, which is coupled to the movement of protons out of the cell.