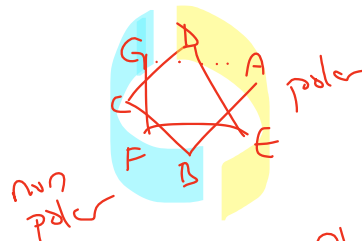
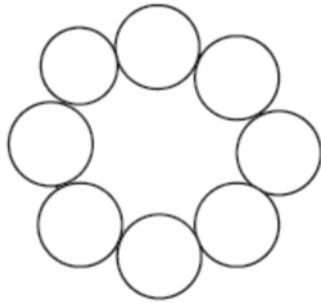


## Membrane Proteins

Integral membrane proteins often contain helical segments of appropriate length to span the lipid bilayer. In a protein that has a single segment that spans the membrane, the helix usually only contains hydrophobic residues and is called a single-span membrane protein. In transmembrane proteins with multiple segments that span the membrane, hydrophilic residues are often found in sequences of the helices.

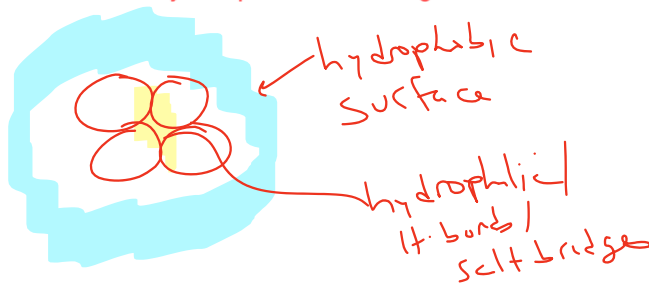
1. Why are hydrophobic residues favored in single-span membrane proteins? **They need to interact with the nonpolar hydrocarbon chain of lipids.**
2. The model below shows the arrangement of helices in a multi-spanning transmembrane protein that serves as a passive pore for glucose (so glucose can move freely from one side of the membrane to the other). Using the heptad repeat pattern, propose a 14 amino acid sequence that might form one of the helices in this protein.

**You need to give the outside of the helix a nonpolar surface and the inside of the helix (in the pore opening) hydrophilic residues. If you really want to think critically about the sequence, you could propose side chains with a hydrophobicity score around zero at the interface region. This would ensure that they are able to interact with the polar and nonpolar parts of the protein.**



Gln Trp Phe Asn Ser Val Ile  
QWFNSVIQWFNSVI

3. Propose a structural orientation for multiple hydrophilic residues of the helices of a multi-span protein that does NOT form a pore. Why did you choose to hydrophilic residues in those positions? **This is kinda the opposite of the hydrophobic effect. You want to have hydrophobic side chains exposed to the lipids, but you want to have hydrophilic side chains that can come together to interact through dipole-dipole or H-bonding interactions. This would also be a very nice place for salt bridges.**



4. Only ~2% of the proteins in the Protein Data Bank are transmembrane proteins. From what you know about how the structure of proteins are determined, explain this observation. **Membrane proteins are hard to crystallize. They have regions that really want to interact with a nonpolar solvent but typical crystallization solutions don't provide this. In some cases, structural biologists are able to add small amounts of detergent (typically non-ionic detergents) to the solution to all membranous proteins to remain in the proper conformation. This is a very difficult task to accomplish.**