Lecture 2 Answers

1.

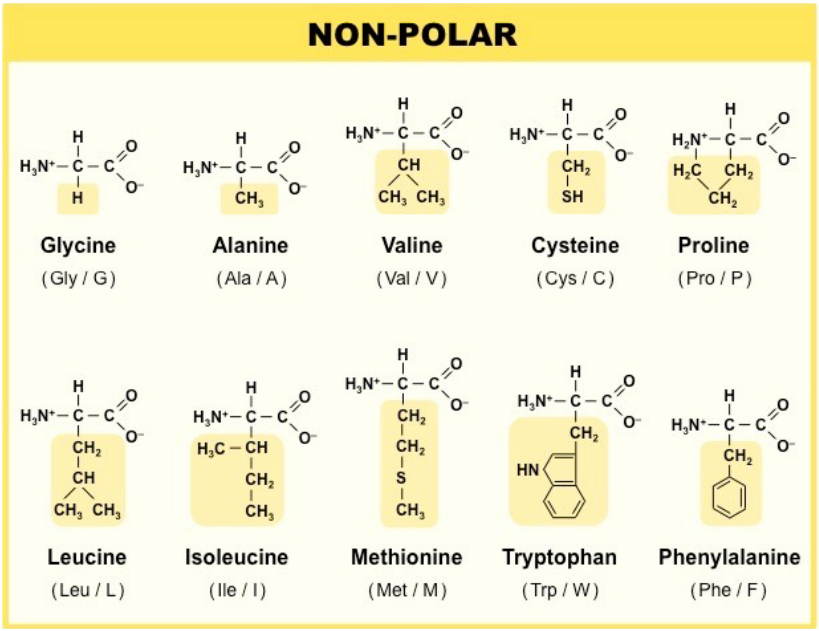
1. Plot A is a plot of a transmembrane domain protein.
2. The transmembrane protein plotted on graph A is likely to have seven

   transmembrane domains because there are seven regions that have a hydropathy index greater than zero, indicating the existence of a stretch of hydrophobic amino acids that could cross the membrane.

3. A window score of 19 is more useful than a window score of 5 because it takes about 20 amino acids to cross the plasma membrane. A stretch of 5 hydrophobic amino acids surrounded by other hydrophilic amino acids would not be sufficient to span the membrane, and thus such a plot would be less informative.

2 N is cytosol, S has a single transmembrane domain toward the end. E is very small with one transmembrane domain and M has probably 3 maybe 4.

3. All amino acids with non-polar hydrophobic side chains can be used. As these are capable of interacting with the fatty acid tails of the cell membrane.



An alpha helix uses ~20 a.a. to cross the membrane, whereas several B-sheets are required to create a B-barrel. Therefore, using many more amino acids.

4. We know that p125 is a transmembrane domain protein. In addition, p50 seems to be tightly associated with the membrane. However, p175 is probably a peripheral membrane protein, because it does associate with the membrane fraction after the first extraction but is removed from the membrane after a treatment with high salt concentrations. This suggests that the association of p175 with the membrane is probably via protein–protein contacts with a membrane protein, because high salt concentrations will disrupt protein–protein interactions. In contrast, p80 is a protein that associates with the membrane only via its interaction with the complex, because in the initial purification it is in the cytoplasmic fraction;

it is likely that p80 associates only weakly with the complex and thus does not co-sediment with the membrane fraction.

5. A. SDS is a strong ionic detergent. When cells are exposed to SDS membrane, proteins are not only extracted from the membrane, they are completely unfolded. After denaturation, they cannot be studied as functional molecules.

B. Triton X-100 has a smaller nonpolar portion and a polar but uncharged end, allowing it to mimic more closely the type of solvation effect of the membrane lipids. Triton X-100 forms a shell around the hydrophobic portion of the protein without disrupting the existing structure. This makes it possible to then place the protein into a new, synthetic membrane bilayer for study.

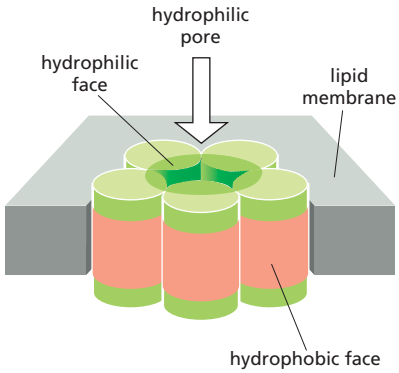
6. Fatty acid chains, prenyl groups, and glycosylphosphatidylinositol (GPI) anchors are the three common lipid anchors for membrane proteins.

7.

A. Lectin
B. Carbohydrate layer
C. Spectrin
D. Multipass transmembrane protein
E. Cortex
F. Glycosylphosphatidylinositol (GPI) anchor

8.
A. Sequence A is the actual membrane-spanning α-helical segment of glycophorin, a transmembrane protein from red blood cells. It is composed predominantly of hydrophobic amino acids, although it does contain the uncharged polar amino acids threonine (T) and serine (S), which are not uncommon in membrane-spanning α helices. Sequence B is unlikely to be a membrane-spanning segment because it contains three prolines (P), which would disrupt an α helix and thereby expose polar groups to the hydrophobic environment of the lipid bilayer.
Sequence C is also unlikely to be a transmembrane segment because it contains three charged amino acids, glutamic acid (E), arginine (R), and aspartic acid (D), whose presence in the hydrophobic lipid bilayer would be energetically unfavorable.

9. The hydrophilic faces of the five membrane-spanning α helices, each contributed by a different subunit, can come together to form a hydrophilic pore across the lipid bilayer that is lined with the hydrophilic amino acid side chains. The hydrophobic amino acid side chains on the opposite sides of the α helices can then interact with the hydrophobic lipid tails in the bilayer.



10. In both an α helix and a β barrel, the polar hydrogen-bonding groups in the peptide bond are fully satisied by internal hydrogen bonds with groups in other peptide bonds. these internal hydrogen bonds dictate the secondary structures known as α helices and β sheets (or β barrels when the edges of a sheet pair to complete the cylinder). By contrast, in a disordered chain, the polar groups in the peptide bonds are not involved in bonding to one another. Such disordered segments can exist in proteins because hydrogen bonds can be made with water molecules or to other polar groups in the protein. In a membrane, however, the hydrophobic hydrocarbon chains of the bilayer provide no hydrogen-bonding partners. As a result, a disordered peptide chain in a membrane is energetically very unfavorable.

11. Proteins can be restricted to specific regions of the plasma membrane in several ways: by attachment to extracellular or intracellular proteins, by attachment to proteins in other cells, and by molecular fences that corral proteins in specific membrane domains. The fluidity of the lipid bilayer is not significantly affected by the anchoring of membrane proteins; the lipid molecules low around anchored proteins like water around rocks in a stream.

12. Cytosolic membrane-binding proteins could induce protrusion of the membrane in several ways. For example, a protein that bound to a concave surface of the membrane, instead of the convex surface shown in B, would bend the membrane to induce a protrusion. Alternatively, a protein that bound phospholipids with small head groups in the cytosolic leaflet of the membrane, instead of large head groups as shown in C, or removed head groups from the phospholipids, would induce a concave curvature of the membrane, giving rise to a protrusion. For the third method of membrane-bending shown in Figure A—inserting a segment of protein into the cytosolic lealet—it is difficult to see how such a mechanism could be used to induce a protrusion.