Biology 5357

Chemistry & Physics of Biomolecules

Examination #3

Glycobiology, Membranes
& Membrane Proteins Module

December 9, 2022

Name: ______________________________

Question 1. (12 points; A-C, 4 pts each)

"Lectin" is a generic term for glycan-binding domains or proteins. Enzymes with sugar substrates, and sugar-binding antibodies, are usually not classed as lectins.

(A) Glycans tend to bind on the surface of lectins, instead of in a hydrophobic pocket as typical of many other ligands and substrates. Explain.

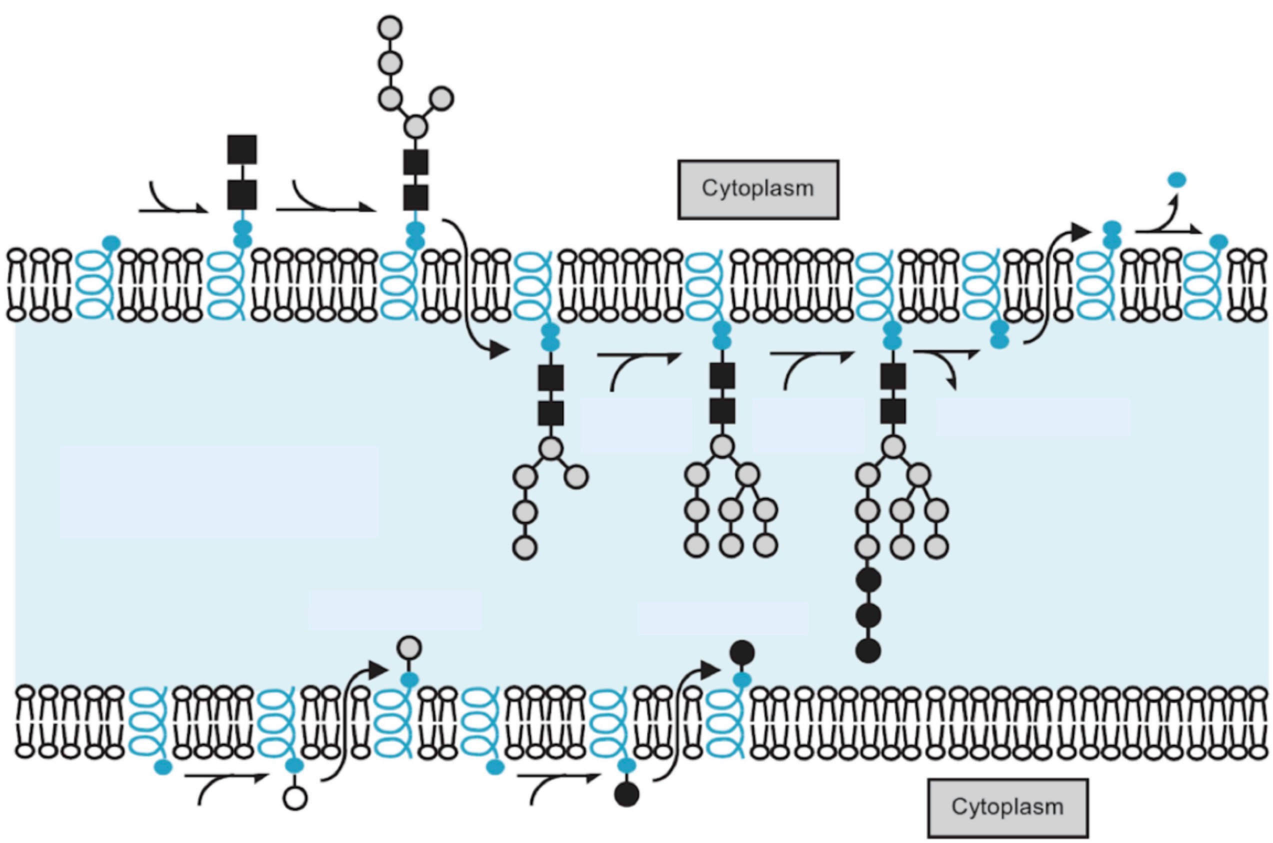
(B) Many glycan-binding proteins contain multiple lectin domains. Explain why might this be the case?

(C) Mannose binding protein (MBP) contains a trimeric cluster of three similar carbohydrate recognition domains (CRDs). If each CRD-glycan interaction is independent and has a free energy of 4 kcal/mol, then what would the overall dissociation constant be for MBP with a multivalent glycan ligand?

Question 2. (15 points; A, 5 pts; B 10 pts)

(A) What biological structure and what overall process is depicted in the diagram below?

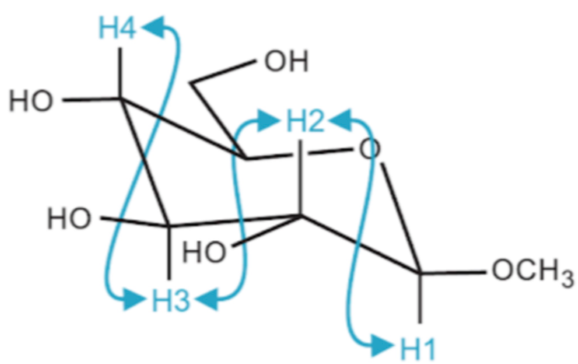
(B) Identify each of the following symbols in the diagram: black squares, black circles, blue ovals, blue coils and grey circles.

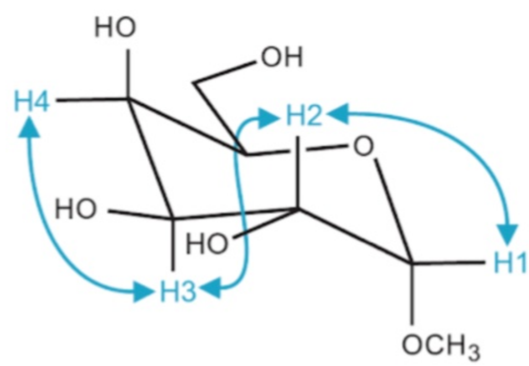


Question 3. (15 points; A-E, 3 pts each)

(A) Briefly, describe how glycans are involved in determination of blood type, *i.e.,* A, B, AB or O.

(B) Explain how NMR coupling constants would differentiate β-methyl-glucose (below on left) from α-methyl-galactose (below on right).





(C) Given the monosaccharides in part (B), draw the structure of Galβ1-4GlcNAc.

(D) Glycosidic bond formation has a ΔG of about +3.5 kcal/mole, while hydrolysis of ATP into ADP plus phosphate has a ΔG of -7.3 kcal/mol. Thus, one might expect hydrolysis of a single ATP would be sufficient to form one glycosidic linkage. However, two ATPs are generally required. Explain.

(E) Two major classes of O-linked glycoproteins are mucins and proteoglycans. Very briefly, where can these two classes of proteins be found, how are they similar, and how do they differ?

Question 4 (6 points)

Describe three hypotheses that were proposed in Singer & Nicolson's "*The Fluid Mosaic Model of the Structure of Cell Membranes*." Provide a rationale for each hypothesis by describing the experimental evidence that supported each idea.

Question 5 (8 points)

What are the eight major sub-classes of lipoidal molecules found in cellular membranes?

Question 6 (6 points; A-C, 2 pts each)

A sample of an *E. coli* bacterial culture was grown at 37°C and then transferred to 4°C. Over time, the bacteria continue to grow, but its inner membrane composition changes as a result of *homeoviscous adaptation*. Explain the molecular reasons why the following changes in membrane composition would lead to increased membrane fluidity at colder temperatures:

(A) Lipid saturation decreases

(B) Lipid chain length decreases

(C) Decrease in PE and increase in PG phospholipids

Question 7 (10 points; A-E, 2 pts each)

Draw an example of each of the following amphiphile states/phases and describe the chemical species or conditions where the following phases are likely to be observed.

(A) Monolayer at the air-water interface

(B) Spherical micelle

(C) Lipid bilayer

(D) Free monomer in water

(E) Hexagonal phase

Question 8 (4 points)

Rank the following lipid and membrane dynamic behaviors from fastest to slowest:

(A) Acyl-chain isomerization

(B) Lipid flip-flop

(C) Lateral diffusion

(D) Axial rotation

Question 9 (8 points; A-D, 2 pts each)

The amino acid sequence of the first half of the S4 transmembrane helix in a voltage-gated K^+ channel is as follows:

AILRVIRLVRV

Consider the amino acid partitioning data in the following table:

Amino Acid	**Radzicka Scale** (*i.e.,* cyclohexane) ΔG, kcal/mole	**Hessa Scale** (*i.e.* translocon) ΔG, kcal/mole
A	-1	1
I	-4	-1
L	-3	-1
R	9	2
V	-2	-2
F	-2	-1
K	14	3
S	3	1
H	2	1

(A) Calculate the free energy of partitioning of this helix segment using the Radzicka scale.

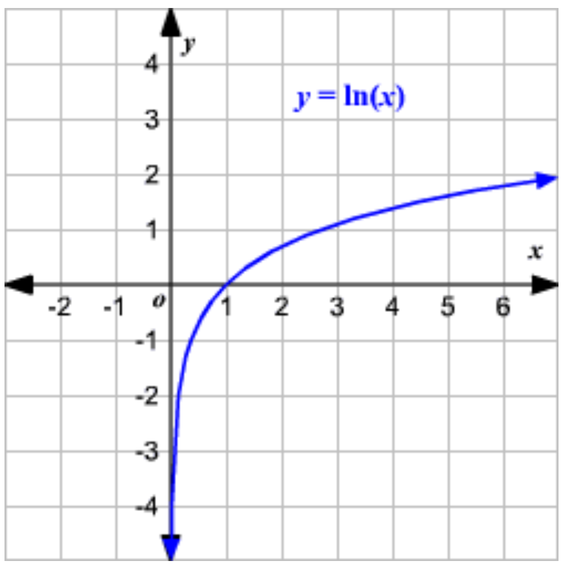
(B) Calculate the free energy of partitioning of this helix segment using the Hessa scale.

(C) Explain why one scale predicts a more favorable partitioning free energy than the other scale.

(D) Explain what other considerations, not reflected in these individual amino acid partitioning free energies, that would further stabilize this helix in the lipid bilayer environment.

Question 10 (8 points; A, 4 pts; B-C, 2 pts each)

The giant algae *Chara corallina* is an organism that lives in pond water and generates action potentials in response to touch stimulation. The resting membrane potential of the cell is -175 mV, and the action potential reaches a peak depolarization of 0 mV. The main ionic components in the cell are $[K^+]_{int}$ = 110 mM, $[Na^+]_{int}$ = 5 mM, $[Ca^{2+}]_{int}$ = 0.001 mM and $[Cl^-]_{int}$ = 22 mM. The concentrations of ions in the pond water environment are $[K^+]_{ext}$ = $[Na^+]_{ext}$ = $[Ca^{2+}]_{ext}$ = 0.1 mM and $[Cl^-]_{ext}$ = 0.4 mM. Note at room temperature, RT/F is approximately 25 mV.



X	ln(x)
0.001	-7
0.01	-5
0.018	-4
0.02	-4
50	4
55	4
100	5
1100	7

(A) What are the equilibrium potentials for each of the component ions?

(B) Which two types of leak channels could be responsible for establishing the resting membrane potential?

(C) Which two types of channels could be responsible for the upstroke of the action potential?

Question 11 (8 points; A-B, 4 points each)

Consider the protein-dependent mechanisms of membrane transport.

(A) Describe two different types of active transport. Give an example of each.

(B) Describe two different types of protein-dependent passive transport. Give an example of each.

Bonus Question (2 points !)

Describe an area of membrane or membrane protein research that requires further study and rationalize why.