Part A:

1. d: The molecule shown is not normally found in nature because it contains ether linkages, instead of esters. In addition, it has on acyl chain too many for a phospholipid and one phosphate group too many if it were a triglyceride.
2. d
3. b
4. d Remember that α means the anomeric OH group is pointing down, β-means the group is pointing up.
5. d Activation of fatty acids, to from the Acyl-CoA occurs in the cytoplasm, but the oxidation occurs in the matrix.
6. d
7. d was the best answer, since both cAMP and caffeine can stimulate protein kinase A. Full points were given for b) since it is the normal second messenger.
8. c This is a ketose, so the second carbon (c) is the anomeric. The carbon that was bearing the C=O group *always* becomes the anomeric carbon.
9. d The total free energy associated with a concentration gradient is:$\Delta G = +RT\ln[X]_{IN}/[X]_{OUT} + ZF\Delta\psi$. Fructose is not charged, so the second term does not contribute to the Gibb's free energy. Therefore $\Delta G = (2.5)\ln(1000) = (2.5)(2.3)(3) = 17.25$ kJ/mol.

   This is sufficient to drive the synthesis of G-6-P (ΔG for hydrolysis < 17 kJ/mol) but insufficient to drive the synthesis of ATP which would require ~30 kJ/mol.
10. Since the activity increases F-2.6-P is an allosteric activator of PFK.

B 1.

Choice A: The correct answer is Gly-Phe-Gly-Phe, since the electron density off of the β-carbon is large and similar for both residues. The density is too small for Trp and too large for Ser.

Choice B:

i) Either molecular weight (gel-filtration chromatography) or difference in charge (ion-exchange chromatography) could be use to separate lysozyme from hexose kinase.

ii) Hexose kinase and hemoglobin have the same size and charge therefore neither gel-filtration or ion-exchange chromatography cannot be used. The following two options exist:

- Change the pH and hope it changes the charge, since you don't know the number of charged groups on these proteins this may not work. Therefore only +3 pts were given.
- Use affinity chromatography. Hexose kinase would be the best enzyme to target here, attaching hexose, ATP, ADP, etc to the column beads. It would be more difficult to develop an affinity column for hemoglobin, both the heme and Fe^{2+} are bound too tightly to the protein. However, BPG could be used.

B2.

Choice A: The major force that drives the self-assembly of bilayers is the hydrophobic effect: the release of ordered water molecules from the non-polar acyl chains when the bilayer forms leads to a large increase in entropy of the system. Van der Waals forces also stabilize the bilayer, but do not contribute greatly to self-assembly.

Integral membrane proteins present a non-polar surface to the acyl chains, in addition they must satisfy all hydrogen bonds, since there are no donors or acceptors in the bilayer.

Choice B: Curve A is lipid 1 curve B is lipid 2. The presence of a cis-double bond leads to a large disruption of the packing of the acyl chains, leading to a loss of van der Waals interactions (ΔH). This reduces T_M and also broadens the transition since the width of the transition depends on ΔH. The trans double bond (lipid 3) would be similar in properties to lipid 1.

B3.

Choice A: Both have α(1-4) and α(1-6) linkages between glucose. However glycogen is more highly branched, thus producing more ends in the polymer. This is an advantage for animals because glucose can be released at a rapid rate if it is necessary to flee a dangerous situation.

Choice B: These are composed of polymers of alternating NAM-β(1-4)-NAG (n-acetyl muramic, N-acetyl-glucose) residues. The sugar polymers are crosslinked with peptide. Lysozyme specifically recognizes the N-acetyl group and cleaves the β-(1-4) linkage. Although cellulose also has a β(1-4) linkage, it does not contain an N-acetyl group and therefore is not a substrate for lysozyme.

B4.

Choice A: Protein from tofu would first be broken down into amino acids that would then enter the TCA cycle. Triglycerides would be broken down to glycerol and fatty acids, the fatty acids would undergo β-oxidation.

Choice B: Feedback inhibition occurs when a metobolite later on in the pathway inhibits a step, e.g. citrate is a feedback inhibitor of PFK in glycolysis.
Product inhibition occurs when the direct product of the reaction inhibits the enzyme that created the product, e.g. hexose kinase is inhibited by G-6-P.

B5.

i) Reduction of a carboxylic acid to an aldehyde	$NADH \rightarrow NAD^+$	Dehydrogenase
ii) Removal of a phosphate group	P_i produced	Phosphatase
iii) Addition of water to double bond (no redox)	H_2O required	Enolase/fumarase/hydratase
iv) Addition of a phosphate group to Serine	$ATP \rightarrow ADP$	Protein Kinase

B6.

Choice A: Electrons are transferred in the following path:

Succinate→FAD in complex II→CoQ→Complex III→one electron transfers via cytochrome C→complex IV→4 e^- to O_2 to produce $2H_2O$. Protons are pumped from the inside of the membrane to the outside in complexes III and IV.

Choice B: The key concept was that the ATP synthase has three β-subunits**,** which can assume three different conformations, depending on the position of the γ subunit: one that binds neither ADP+P_i or ATP, one that binds ADP+P_i tightly, and one that binds ATP tightly. The pumping of three protons across the membrane causes a rotation of γ, changing the conformation of the β-subunit. The complete cycle is as follows:

ADP+P_i load → ATP formed → ATP released → ADP+P_i load

ATP synthesis occurs when the bound ADP+P_i finds itself in a β-subunit whose conformation favours ATP, thus the lower energy state of ATP results in the formation of ATP from ADP+P_i.

B7.

Choice A:

i) The $ZF\Delta\psi$ gives the contribution of moving a particle of charge Z, through a voltage difference of $\Delta\psi$ as it is transported across the membrane. It is important in ATP synthesis since charged particles are transported (protons) and a membrane potential, or voltage difference, exists across the membrane.

ii) There will be no flow of [X] since the system is at equilibrium and is already at the lowest energy state. If [X] is charged and $\Delta\psi \neq 0$ then there will be a difference in the concentration of [X] across the membrane, however the free energy associated with this concentration difference will be *exactly* balanced by the electrostatic contribution. So no flow will occur under these conditions as well.

Choice B: Thermodynamic coupling is used to produce B from A. If the ΔG^o for the A→B reaction is positive, but it's still spontaneous, then the ΔG must be less than zero. The only way for this to occur is if the concentration of B is much less than the equilibrium amount. Consequently the reaction from B→C must have a large negative ΔG, such that any B that is produced from A is converted to C, thus keeping the [B] low.

B8.

Choice A: Most of our initial energy is derived from glucose and glycogen. A high carbohydrate diet will cause glucose to be stored a glycogen and thus be readily available for activity.

Choice B: Marathon runners run at a slow pace for an extended period of time. They will deplete their glycogen stores early in the race (after about 2 hours based on the homework problem) and will have to rely on the oxidation of fats via β-oxidation and the TCA cycle to generate energy. Under extreme conditions, proteins will also be broken down to oxidize amino acids.

B9.

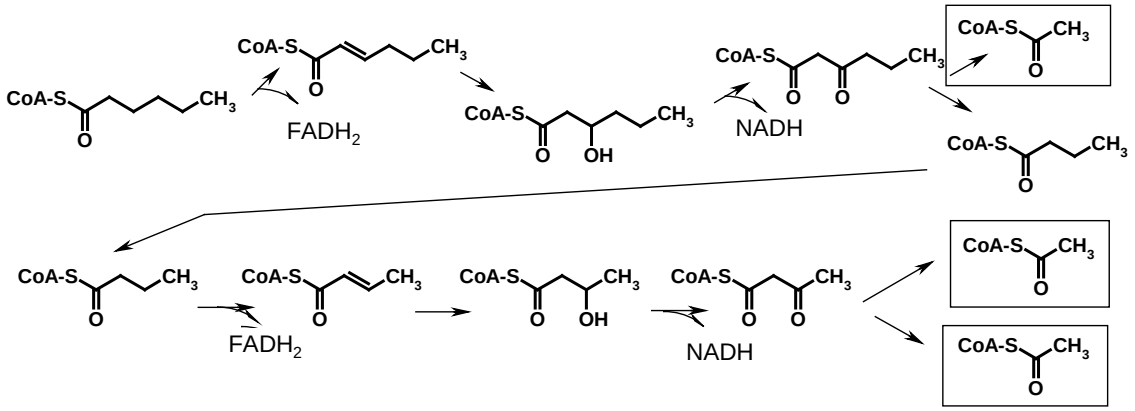
Choice A: In all cases the energy derived from oxidation is stored as "high-energy" electrons on $FADH_2$ or NADH. These electrons are then used in oxidative phosphorylation to produce ATP. It was necessary to give at least one redox reaction for either pathway, however partial credit was given for a discussion of kinase reactions in glycolysis.

Redox Reaction in glycolysis: glyceraldehyde-3-P→1,3 phosphoglycerate +NADH

Redox Reactions in TCA cycle: Pyruvate dehydrogenase, isocitrate dehydrogenase, α-ketoglutarate dehydrogenase, succinate dehydrogenase, malate dehydrogenase.

Choice B: It was necessary to show the complete oxidation of the C6- fatty acid to three acetyl-CoAs. It was not necessary to show the activation step. The net yield is 2 $FADH_2$ and 2 NADH.

Note that the C2 units are removed from the *carboxylic acid (thioester) end*, two at a time.



B10:

Choice A:

Key concept: High concentrations of ATP and NADH indicate that the cell has lots of energy, therefore you would expect glycolysis and the TCA cycle to be off under these conditions. Conversely, high concentrations of ADP/AMP and NAD^+ would indicate low energy reserves and glycolysis and the TCA cycle should be turned on. This is indeed the case, as illustrated below. This regulation prevents the cell from wasting energy synthesizing ATP when it has plenty, and provides a means of generating energy when it is required.

Note the ATP/ADP/AMP regulate glycolysis/gluconeogenesis while both ATP and NADH regulate the TCA cycle.

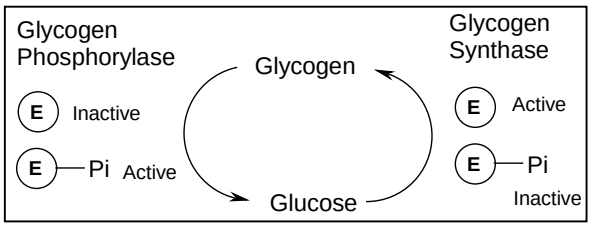
Glycolysis: PFK: Activated by ADP, AMP, inhibited by ATP.

TCA Cycle: Pyruvate dehydrogenase, Citrate syn, isocitrate dehydrogenase, α-ketoglutarate are all inhibited by ATP and NADH. Isocitrate dehydrogenase is activated by NAD^+ and ADP.

Choice B:

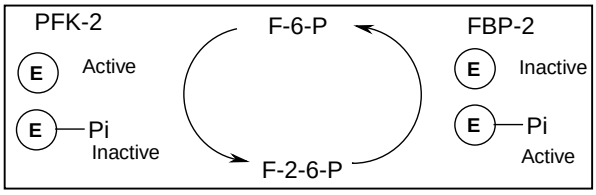
Key concept: HELP -<u>H</u>igh <u>E</u>nergy (glucose) means <u>L</u>ow protein <u>P</u>hosphoryation. Unfortunately, this is just the way nature designed it so you have to memorize this. You should (for the final) understand the relationship between hormonal signaling and levels of protein phosphorylation.

The regulation can be derived from the above concept. Since high glucose levels ought to lead to storage of glycose in glycogen, glycogen synthase should be active when dephosphorylated and glycogen phosphorylase should be inactive under these conditions. The reverse should occur when glucose levels are low. Low glucose levels imply high protein phosphorylation, hence glycogen synthase should be inactive when phosphorylated while glycogen phosphorylase should be active. This is summarized in the cartoon to the right. This regulatory mechanism insure that excess glucose is stored in glycogen and provides a means to release glucose from glycogen when glucose is needed by the organism.



Choice C:

Key concept: F-2-6-P levels follow glucose levels. Again, this is just the way nature is, so you have to memorize this. This fact, when combined with HELP allows your to derive how F-2,6-P levels are controlled by protein phosophorylation (see right). PFK-2 must be active when dephosphorylated (HELP), making more F-2-6-P.



With respect to glycolysis, high glucose levels turn on glycolysis so that energy is obtained for biosyntheis. Low glucose levels prompt the liver to make glucose from pyruvate. Hence F-2,6-P should activate glycolysis (PFK) and inhibit gluconeogenesis (F-1,6-bisphosphatase), as indicated to the right