MCB110
Final Midterm

May 8, 2012

_____.
Your name and student ID

QUESTION	POINTS
1 (5 points)	
2 (15 points)	
3 (10 points)	
4 (10 points)	
5 (10 points)	
6 (20 points)	
7 (20 points)	
8 (10 points)	
9 (15 points)	
10 (15 points)	
11 (20 points)	

TOTAL (150 points)
WARNING: Due to the time constraints of assigning grades, **there are no regrades for the last exam. The assigned letter grade is final.**
WARNING: Cheating of any sort is an extremely serious offense. In addition to resulting in an F for the course, cheating may result in further punishment including suspension from the University at the recommendation of the Student Conduct Officer.
WARNING: Your exam will be taken apart and each question graded separately. Therefore, if you do not put your name and ID# on every page or if you write an answer for one question on the backside of a page for a different question, you are in danger of irreversibly LOSING POINTS!

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Q1 – Which lipid will more easily flip-flop in the lipid bilayer, a phosphatidylethanolamine or a ganglioside? Why? (5 points)

PE because it has a small polar head group relative to the oligosaccharides present in gangliosides. This makes it very difficult for the latter to cross the hydrophobic center of the bilayer

If they understand that a ganglioside has a larger head group than PE, give partial credit?

Q2 – What kind of lipid regions do sphingolipids and cholesterol make in the plasma membrane. Name two properties, one concerning fluidity and one concerning dimensions, that make them distinct. How do they affect integral membrane proteins concerning their localization and diffusion? (15 pts)

They form lipids rafts with less fluidity than the rest of the plasma membrane and with a thicker bilayer. Integral membrane proteins with longer transmembrane regions tend to concentrate/localize in these regions, where their diffusion is reduced.

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Q3 – State one thermodynamic difference between the mode of operation of a glucose facilitative transporter and the Na+/Glucose cotransporter. State a similarity in their molecular mechanisms of transport concerning the link between conformational states of the transporter and ligand movement (10 pts)

While the facilitative transporter lets glucose diffuse down its concentration gradient, the Na/glucose co-transporter pumps glucose against a concentration gradient.

They both need to go through a full conformational change cycle in order to move one glucose molecule across the bilayer.

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Q4 – Use thermodynamics to deduce the resting potential in cells containing potassium leaking channels, assuming a concentration of potassium 10 times bigger inside of the cell than outside, and no other leaking channels (10 pts).

What come below is the answer key – Not given at the exam.

$$\Delta G = 0$$

$$2.3RT \log_{10} \frac{[C_i]}{[C_o]} = - zF\Delta E$$

At equilibrium:

$$\Delta G = 0$$

$$2.3RT \log_{10} \frac{[C_i]}{[C_o]} = -zF\Delta E$$

$$1.4 kcal/mol \log_{10} \frac{10}{1} = - 23.06 kcal/molVz\Delta E$$

$$\Delta E @ - 1.4/23 @ - 66 mV$$

The sign of this voltage should be negative for credit!

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Q5 –Describe the steps taking place during a cycle of ATP hydrolysis in the P-type Ca++ pump in the plasma membrane, concentrating on protein conformational states and calcium affinities, and their consequences (10 pts).

The initial state of the pump is E1, where the pump is open to the cytosol (where Ca concentration is low). In this state the pump has high affinity for Ca++, so calcium ions bind. The pump then binds ATP and then hydrolizes it and transfers the Pi to the phosphorylation domain. This results in a conformational change to the state E2. In this state the pump is open to the outside and has very low affinity for Calcium so Ca++ is released. The pump is then dephosphorylated, changing back to the E1 state and restarting the cycle.

Q6 – Describe the order of events in the activation of a postsynaptic cell, starting with the arrival of the action potential at the presynaptic cleft and ending with the activation of a new action potential at in the postsynaptic cell. How can the signaling at the synapse be terminated (two distinct ways) (20 pts)?

Upon arrival of the action potential, voltage-gated calcium channels open. This leads to the fusion of synaptic vesicles loaded with neurotransmitter to the presynaptic membrane, and thus to the release of the neurotransmitter to the synaptic cleft. The neurotransmitter then binds to and opens ligand-gated ion channels on the postsynaptic cell. If these are Na+ channels, this leads to the activation of an action potential in the postsynaptic cell. The neurotransmitter is cleared from the synaptic cleft either by degradation or by reuptake into the presynaptic cell.

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Q7 – What kind of **phenotype** will temperature-sensitive mutants will cause in budding yeast for these different proteins in the membrane trafficking pathways and why (20 points):

- SRP – **failure to reach the ER would result in release of secretory proteins into the cytosol. Class A**
- Sec23 – **Failure to bud will result in enlarged ER. Class B**
- V-snare in CopII vesicles – **failure to fuse will result in accumulation of vesicles in the cytosol. Class C**
- dynamin – **Fission failure will lead to accumulation of clathrin coated vesicles that remain attached to the membrane. If they say class D and they explain why, I'm fine with it. But I specifically went over the detailed molecular effect of this mutation in class.**

GRADERS: Just stating a class is not enough for full credit. They need to be descriptive.

Q8 – Describe how resident proteins of the rough ER are retrieved from the Golgi if accidentally incorporated into CopII vesicles. What distinct physical property between the Cis Golgi and the rough ER makes this possible and how? (10 points)

They contain KDEL sequences that bind to a receptor enriched in COPI vesicles budding from the Cis Golgi and destined to the ER. The system works because the pH of the Golgi and ER are different and the affinity of the KDEL receptor for its target sequence is higher at the pH of the Cis Golgi.

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Q9 – Describe the molecular players and steps resulting in the activation of the MAP kinase cascade by EGF (15).

Growth hormone binding results in the activation of RTKs. Phosphotyrosines are recognized by the adaptor Grb2, which then brings to the site SOS, which is a GEF for Ras. Activated Ras then activates MAPKKK, which phosphorylates and activates MAPKK, which then phosphorylates MAPK. The active MAPK then enters the nucleus where it phosphorylates its targets resulting the transcriptional activation of gene involved in cell cycle progression.

Q10 – Explain, starting with the activation of phospholipase C, the molecular events leading to the phosphorylation of PKC substrates (15 points)

Activated phospholipase C cleaves PIP2 into DAG and IP3. Binding of IP3 to ligand-gated Ca++ channels in the ER releases Ca++ into the cytosol. PKC binds Ca++ leading to its localization to the plasma membrane, where interaction with DAG results in its full activation.

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Q11 – What kind of receptor (type/activity) is responsible for insulin signaling? Describe the role of extracellular and intracellular domains in the receptor? What are IRSs? What protein motifs recognize IRSs? (20 points)

RTK (receptor tyrosine kinase)
The extracellular alpha subunits binds to insulin. The cytosolic domains of the beta subunits have tyrosine kinase activity.
IRS stands for Insulin receptor substrates which are examples of adaptor proteins. They get phosphorylated by the insulin receptor and act to recruit other proteins to the plasma membrane.
SH2 domains recognize the phosphorylated IRSs by binding to phosphor-tyrosin motifs.