C483 Exam 2
Summer 2017

Name Key Seat Number _____

Student ID _____ AI _____

The last page of this exam contains information you might find useful.
This exam contains 110 points. The highest score you may earn on this exam is 100 points.

1 _____/20pts

2. _____/10pts

3. _____/20pts

4. _____/10pts

5. _____/10pts

6. _____/10pts

7. _____/10pts

8. _____/10pts

9. _____/10pts

Total:

Regrading: All requests for regrades must be submitted in writing within 48 hours of the return of the exam. You must explicitly state what has been misgraded and why it is an error. The entire exam will be regraded, which could result in points being added or deducted overall.

Section 1: Short answer (50 points)

1. 20 pts. Fill in the blanks (2 points each.)

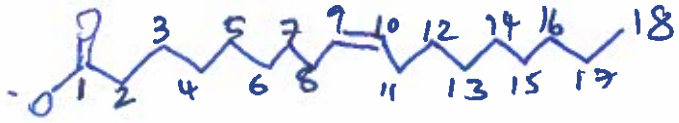
A. What is the relationship of k_{cat} to V_{max}? Explain or write an equation.

$V_{max} = K_{cat}[E]_T$ or it is proportional.

B. A transition state analog binds to an enzyme more tightly than a substrate analog.

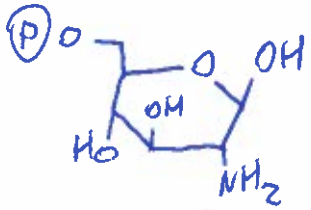
C. K_{cat}/K_m is also known as the specificity constant or enzyme efficiency constant.

D. Draw an 18:1 n-9 fatty acid at physiological pH.



E. A transporter family called the ABC transporters can cause multidrug resistance in microorganisms.

F. Glucosamine is the compound produced when the C-2 hydroxyl of glucose is replaced with an amino group. Draw the β-anomer of D-6-phosphoglucosamine.



G. A ligand that binds to a receptor and inhibits a signal transduction cascade is called antagonist.

H. D-galactose is the C-4 epimer of D-glucose.

I. The part of metabolism involved in breaking down molecules to release free energy is called catabolism.

J. A spontaneous reaction can be used to drive a nonspontaneous reaction only if they are thermodynamically coupled.

2. 10 pts. True or false (1 points each)

A. False The derivation of the Michaelis-Menton equation assumes that the concentration of substrate is held constant in all reactions.

B. True A mechanism-based inhibitor is a type of irreversible inhibitor.

C. True Cholesterol maintains bilayer fluidity over a broad range of temperatures because it is able to increase membrane fluidity at low temperatures and decrease membrane fluidity at high temperatures.

D. True Glycoproteins tend to face the outside of a cellular membrane, exposed to the cellular environment.

E. True The potassium ion channel is able to selectively exclude sodium ion because desolvation of potassium upon entry into the channel is more favorable than sodium desolvation.

F. True Sphingomyelin and phosphoglycerolipids are structurally similar in the sense that they both have a polar head group and two nonpolar tails, but they are different in that they have a different backbone.

G. False When G-protein coupled receptors bind ligands, their autophosphorylation activity is upregulated, leading to signal transduction through recruiting adaptor proteins.

H. True A receptor with a K_D in the nanomolar range will have a higher affinity for its ligand than a receptor with a K_D value in the micromolar range.

I. True There are 16 distinct stereoisomers of aldohexose.

J. True A reaction in which the standard free energy is positive can be either spontaneous, nonspontaneous, or near equilibrium under cellular conditions.

3. 20 pts. Short answer (5 points each)

A. Calculate the free energy change for the movement of Na^+ into a cell when its outside concentration is 150 mM and its cytosolic concentration is 10 mM. Assume 293 K and a -50 mV membrane potential. Is this movement spontaneous or nonspontaneous?

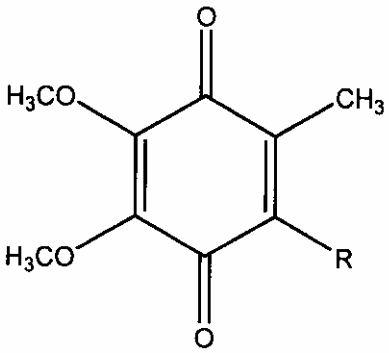
$$\Delta G = 8.314 \frac{J}{mol\,K}(293\,K)\ln\frac{.010}{.150} + (+1)\left(96{,}485 \frac{J}{V_{mem}}\right)(-.05\,V)$$

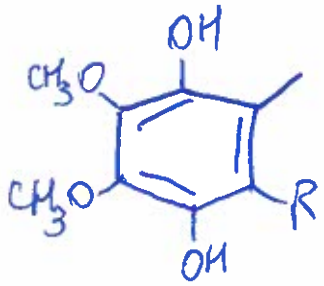
$$= -6.60 \frac{kJ}{mol} + -4.82\ kJ$$

$$= -11.4 \frac{kJ}{mol}$$

spontaneous

B. Below is coenzyme Q in its oxidized form. Draw reduced coenzyme Q. How do NAD^+ and Q differ in their ability to carry electrons?





+2

NAD+: 2 e⁻ carrier, accepts 2 e⁻ at a time

Q: 2 e⁻ carrier, accepts 1 e⁻ at a time (Forms radical)

+3

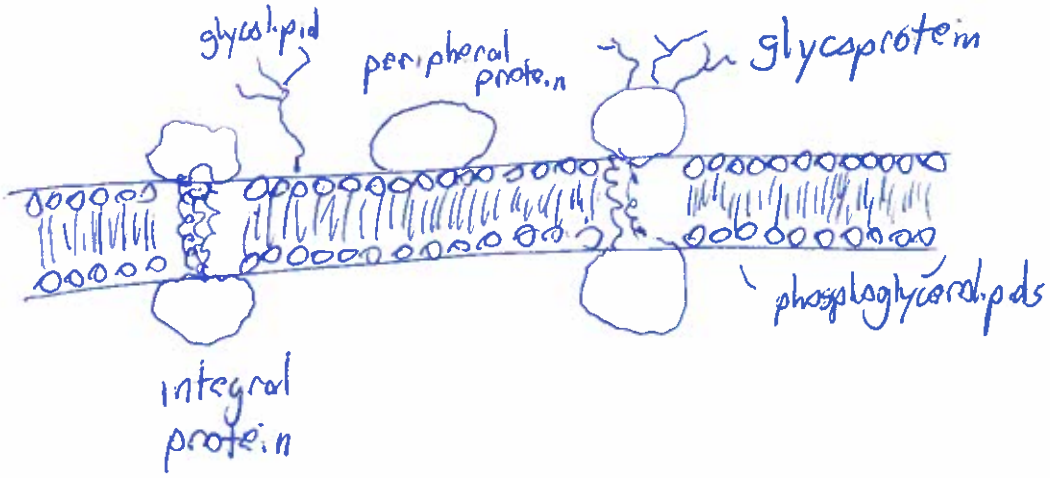
C. Which biomolecule types are put into long term dietary storage? In what form? Fill in the table below:

+1 each

Biomolecule type:	Long term storage: yes/no	Name of long term storage
Amino acids	No	—
carbohydrates	yes	glycogen
Fatty acids	yes	triacylglycerides

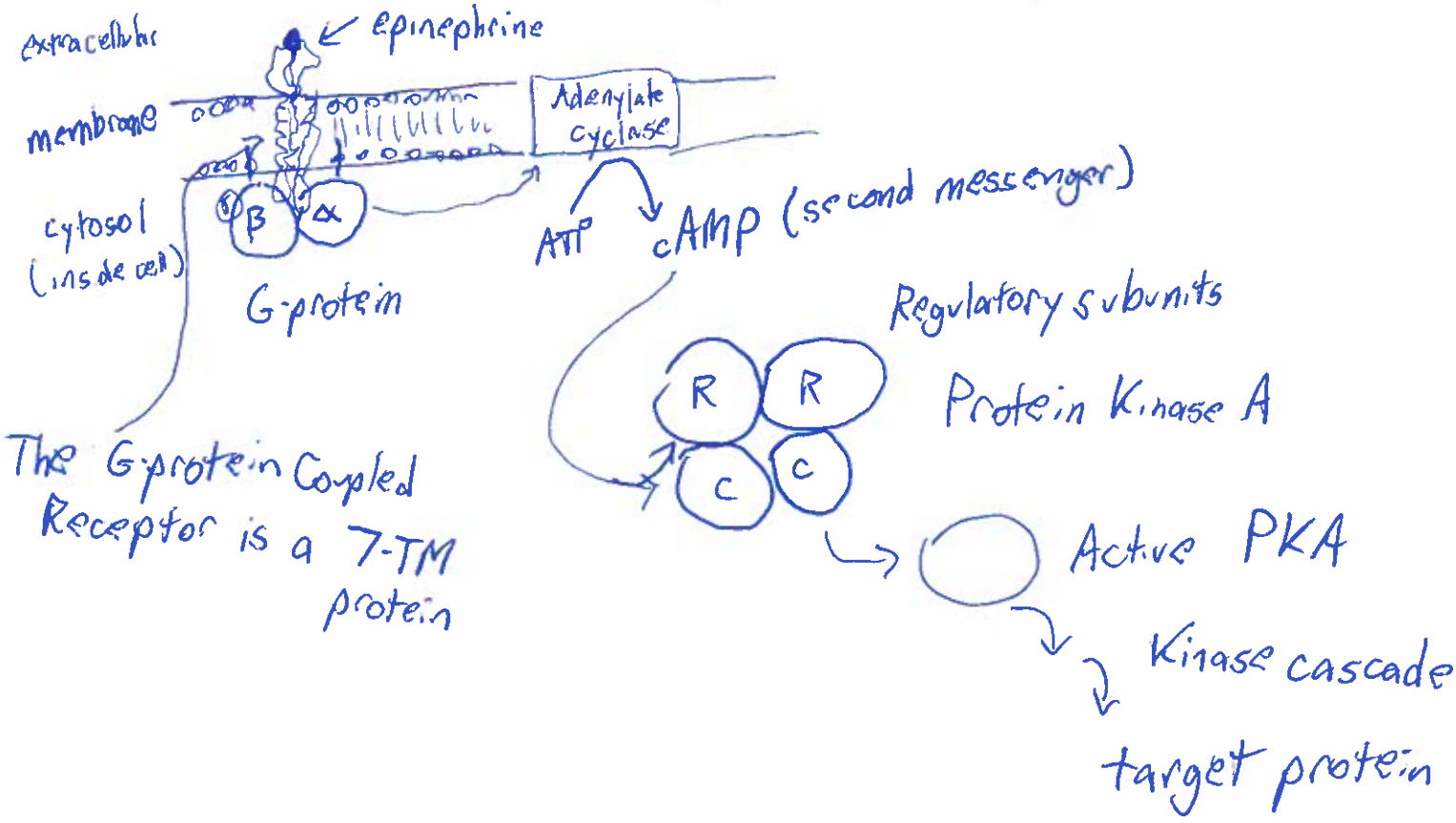
D. Draw a schematic of a portion of a cell membrane and label a peripheral protein, a glycoprotein, an integral protein, phosphoglycerolipids, and glycolipids.

+1 each

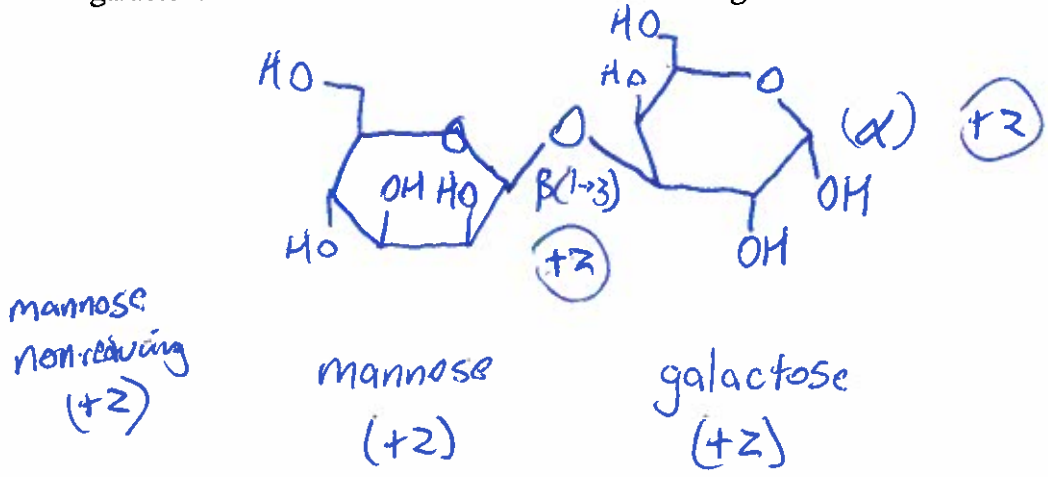


Section 2: Problems (10 points each)

4. Using the β-adrenergic receptor system as an example, draw a schematic of the pathway that leads to a cellular effect such as increased sugar metabolism. Label your schematic with these terms: cAMP, membrane (labelled inside and outside), epinephrine, G-protein, protein kinase A, adenylate cyclase, 7-transmembrane helix, α subunit, G-protein coupled receptor, ligand, regulatory subunit/catalytic subunit, β/γ subunit, phosphorylation cascade, second messenger.



5. Draw the alpha anomer of a disaccharide with a β(1→3) linkage between mannose and galactose in which mannose is on the non-reducing side of the disaccharide.



6. Enzyme catalysis of the cleavage of peptide bonds in small peptides by a proteolytic enzyme is described in the following table. (The arrows indicate the peptide bond that is cleaved in each case.)

Experiment	Substrate	K_m (mM)	k_{cat} (s^{-1})
A	EMTA↓G	4.0	24
B	EMTA↓A	1.5	30
C	EMTA↓F	0.5	18

A. If a mixture of these peptides were presented to the enzyme with the concentration of each substrate being the same, which peptide would be digested most rapidly? Explain.

k_{cat}/K_m ($mM^{-1}s^{-1}$)

A 6

B 20

C 36

The peptide EMTAF. The enzyme has the highest specificity toward that peptide.

+4

B. For the peptide EMTI↓F, K_m = 9 mM and k_{cat} = 18 s^{-1}. What do these data suggest about the specificity of the enzyme?

$\frac{k_{cat}}{K_m} = 2$ for this peptide. The enzyme is significantly slowed when alanine is replaced by the more bulky isoleucine.

+4

C. A mutant enzyme was synthesized, and its enzyme kinetics parameters were determined:

Experiment	Substrate	K_m (mM)	k_{cat} (s^{-1})
D	EMTA↓G	2.0	8

Is the mutant a "better" or "worse" enzyme than the native enzyme? Explain your reasoning.

This mutant has "higher affinity" (smaller K_m) but lower "catalysis" (smaller K_{cat}). Overall, the enzyme is not as efficient. (K_{cat}/K_m = 4 $s^{-1}mM^{-1}$ compared to 6 $s^{-1}mM^{-1}$.)

+3

7. Based on structural principles, would you expect the reaction below to be spontaneous, nonspontaneous, or in between under standard conditions? Explain.

spontaneous- a high energy bond was broken in the reactants

+2

Using data from the last page, calculate the free energy of this reaction under standard conditions.

Glycerol + ATP → glycerol-3-phosphate + ADP

$ATP \rightarrow ADP + P_i$ $\quad \Delta G^{\circ\prime} = -30.5$ kJ/mol

glycerol + Ⓟ → Glycerol-3-P $\quad \Delta G^{\circ\prime} = +9.2$ kJ/mol

-21.3 kJ/mol

+4

Under standard conditions, would the phosphorylation of glycerol using 1,3-bisphosphoglycerate be more favorable, less favorable, or about the same as using ATP? Explain.

1,3-bPG has a higher Ⓟ transfer potential (-49.4 kJ/mol) so it would be more favorable under standard conditions.

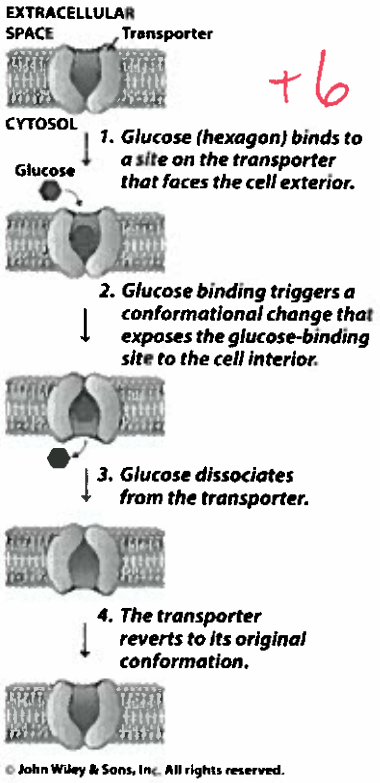
+2

Give one reason why phosphorylation of glycerol using 1,3-bisphosphoglycerate could be less favorable under cellular conditions than under standard conditions.

The concentrations of reactants + pdts might be different in such a way as to make the rxn less spontaneous. (Relatively more pdt than starting material)

+2

8. The scheme below describes the mechanism of the glucose transporter found in the red blood cell:



+6

A. Is this mechanism a thermodynamically reversible or irreversible process? If it is not reversible, explain why. If it is reversible, under what conditions would it reverse its transport?

Either answer is acceptable, depending on explanation. It depends on the reversibility of conformational shift.

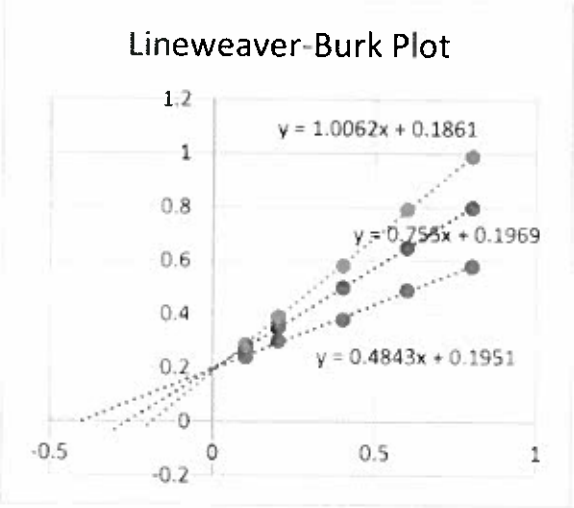
* If conformation isn't favorable in the opposite direction, could be irreversible.

* If reversible, it could be driven back by high [glucose] in cell.

B. If a propyl group is added to the hydroxyl group on C1 of glucose, the modified glucose is unable to bind to its transporter on the extracellular surface. In another experiment, it was shown that if a propyl group is added to the hydroxyl group on C6 of glucose, the modified glucose is unable to bind to its transporter on the cytosolic surface of the membrane. What do these observations tell us about the mechanism of glucose transport?

+4 The conformation change in step 2 changes key contacts with glucose. In the conformation open to the extracellular side, the C-1 hydroxyl makes a key contact. In the conformation open to the cytosolic surface, C-6 hydroxyl makes a key contact.

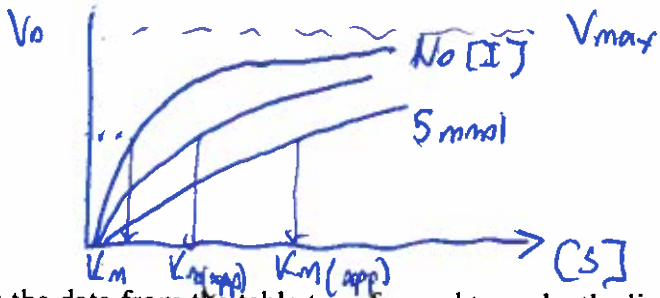
Section 3: Case study (10pts) A new inhibitor of an HIV protease has been investigated under differing concentrations to give the following kinetic data. It was plotted as a Lineweaver-Burk plot, which plots $1/v_o$ as a function of 1/[S].



[S] (mM)	V_o (no I)	V_o (3 mM I)	V_o (5 mM I)
1.25	1.72	1.25	1.01
1.67	2.04	1.54	1.26
2.50	2.63	2.00	1.72
5.00	3.33	2.86	2.56
10.0	4.17	3.70	3.49

A. Plot a rough sketch of these data in a plot of initial velocity vs. substrate concentration.

+2



B. How was the data from the table transformed to make the linear plot shown above?

+2 double reciprocal: $1/V_o$ vs $1/[S]$

+2 C. What type of inhibitor is it? competitive

D. What is the apparent Km when [I] = 5 mM? Why is it different than the apparent Km when [I] = 3 mM?

$y = 1.0062x + 0.1860$

when $y = 0$ $\quad x = -0.185$

$K_m = -\frac{1}{x} = 5.4$ mM

+2

+2 In competitive inhibition, more added [I] requires more [S] to compete. At lower [I], the amount of S required to reach ½ V_{max} is less

Data Tables

[TABLE 12-4]

Standard Free Energy Change for Phosphate Hydrolysis

Compound	$\Delta G^{\circ\prime}$ (kJ · mol^{-1})
Phosphoenolpyruvate	−61.9
1,3-Bisphosphoglycerate	−49.4
ATP → AMP + PP_i	−45.6
Phosphocreatine	−43.1
ATP → ADP + P_i	−30.5
Glucose-1-phosphate	−20.9
PP_i → 2 P_i	−19.2
Glucose-6-phosphate	−13.8
Glycerol-3-phosphate	−9.2

$$\Delta G = RT \ln \frac{[X]final}{[X]initial} + ZF\Delta\psi$$

$R = 8.314$ J/ mol · K

$F = 96{,}485$ J/V · mol

$$\Delta G_{reaction} = \Delta G^{\circ\prime}_{reaction} + RT \ln \frac{[products]}{[reactants]}$$