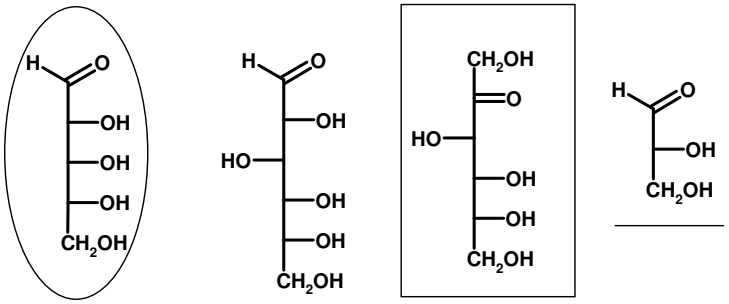
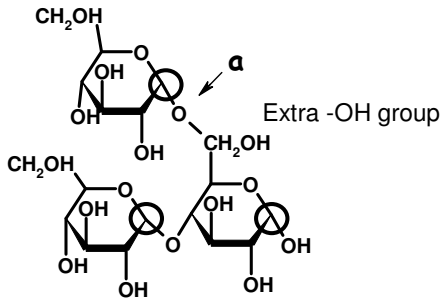
This exam consists of 7 pages and 12 questions. Total points = 100. Allot 1 min/2 points. Note: The last two questions account for 24 points.

1. (3 pts) Using the structures on the right:
   i) Place a box around the carbohydrate that is a ketose.
   ii) Circle the aldose that is found in nucleic acid.
   iii) Underline the aldose that will ***not*** form ring structures in solution.



2. (9 pts) A trisaccharide is shown on the right.
   i) This trisaccharide could have been produced from which of the following polysaccharides (1 pt)?
      a) cellulose **c) glycogen**
      b) bacterial cell walls
   ii) Briefly justify your choice (4 pts).



a) Cellulose is not branched, (and also consists of β 1-4 linkages.)
b) Bacterial cell walls are crosslinked with peptides and contain modified glucose.
c) Glycogen is branched and contains glucose monomers, so this is the correct choice.

Bonus Question: There is an additional OH group on C5 of the monosaccharide at the reducing end (+1 pt).

iii) Circle one anomeric carbon in the trisaccharide and indicate its chirality (α or β) (2 pts).
All three are circled – note that these are the only carbons attached to two oxygens. All are in the α-configuration.
iv) Describe the linkage labeled with 'a' (e.g. β (1-3)) (2 pts).

The linkage is between C1 and C6, so the linkage is α(1-6).

3. (8 pts) Please do ***one*** of the following three choices. Please indicate your choice.

Choice A: Draw any **one** of the following three lipids (be certain to indicate your choice).

i) dibutyric phosphatidyl choline

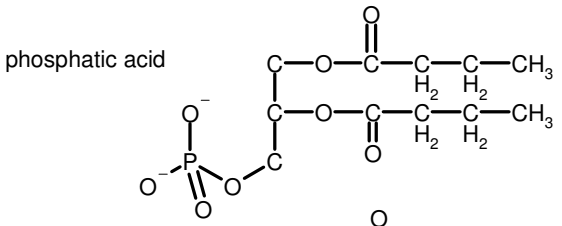
ii) dibutyric phosphatic acid

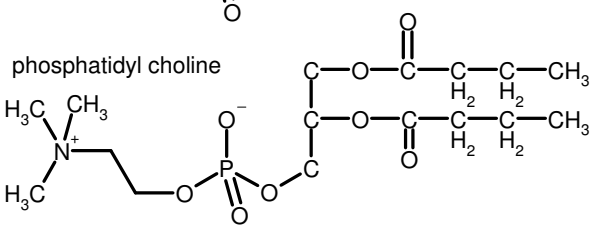
iii) dibutyric phosphatidyl serine

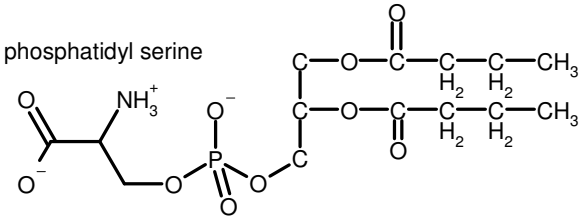
(Butyric is a four carbon fatty acid.)

Choice B: Briefly explain why fatty acids form micelles in water while phospholipids form bilayers.

Choice C: Define the critical micelle concentration (CMC) and then briefly explain why the CMC would be lower for palmitic (16 carbons) than for butyric acid (4 carbons).







B. A fatty acid is cone shaped, with a larger headgroup than its non-polar tail. So they pack together to form a sphere. Phospholipids are more like a cylinder. The area of the head group is similar to that of the two acyl chains, thus they pack to form an extended two-dimensional array of molecules.

C. The CMC is the highest concentration of free fatty acids that can be obtained in solution before micelles form (+4 pts). Palmitic acid is more non-polar than butyric acid, so it will be less soluble in water and from micelles at a lower concentration.

4. (10 pts) Bacteria can successfully grow over a large temperature range by changing the chemical structure of the lipids in their membrane to maintain a fluid membrane.

i) Why is it important for the bacteria to maintain a fluid membrane (2 pts)?

Electron transport requires a fluid membrane for the diffusion of non-polar electron carriers (2 pts)

Membrane proteins require a fluid environment for proper function (2 pts)

ii) Assuming that the growth temperature of the bacteria was shifted from 30 C to 10 C, describe the changes in the fatty acid composition that you might observe in the bacterial membranes after the temperature decrease. You should clearly state which molecular interaction(s) will be affect by this change (8 pts).

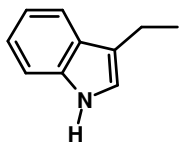
- The drop in temperature would decrease the fluidity of the membrane by increasing van der Waals interactions (4 pts)
- To compensate, the bacteria could either synthesize shorter chain fatty acids or fatty acids with cis-double bonds (+ 2 pts)
- Either would reduce the van der Waals contacts, decreasing the melting temperature of the membrane lipids (+ 2 pts)

5. (6 pts) Please do one of the following two choices. Please indicate your choice.

Choice A: Briefly explain why all integral membrane proteins are either α-helical or in a β-barrel conformation?

There are no hydrogen bond donors or acceptors within the non-polar part of the membrane. Therefore the mainchain hydrogen bonds, that were originally to water, must be satisfied internally. In an α-helix they are satisfied within the same polypeptide segment, in the case of a β-barrel they are between strands.

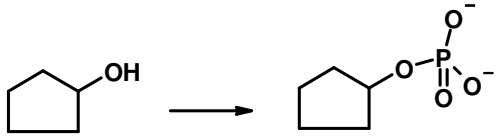
Choice B: Tryptophan, whose sidechain is shown to the right, is commonly found in membrane proteins. Where would you expect this amino acid to be found? In the middle of the bilayer or at the interface between the lipid and the aqueous solvent? Briefly justify your answer.



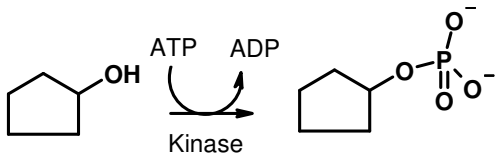
At the interface. Although Trp is largely non-polar, its N-H group is a hydrogen bond donor. So it would have to find a suitable acceptor – usually water or the phosphate group of the lipid.

6. (10 pts) The reaction shown on the right occurs in a metabolic pathway. The standard free energy, ΔG^o, of this reaction is +15 kJ/mol.

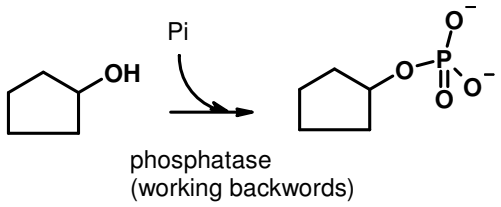
i) (6 pts) *Briefly* describe how ***either*** direct ***or*** indirect coupling could be used to make the reaction proceed in the indicated direction (left to right) during the normal operation of the metabolic pathway.



Direct: A kinase would directly couple the energy of ATP hydrolysis (-30 kJ/mol) to the phosphorylation. Giving an overall standard energy change of -15 kJ/mol.



Indirect: A subsequent reaction in the pathway must be favorable such that the concentration of the product (the phosphorylated compound) is kept well below its equilibrium concentration. Since no ATP is involved in the addition of phosphate – the reaction would be catalyzed by a phosphatase.



ii) (2 pts) What is the sign of ΔG for the *coupled* reaction?

Since the pathway is flowing from left to right, the Gibbs energy must be negative.

iii) (2pts) Give the *general* name of the enzyme that would catalyze the reaction. (Note that the name will depend on the type of coupling you elected to discuss.)

Answered in part i.

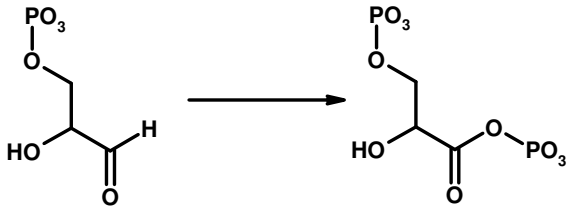
7. (8 pts) The principle source of energy in metabolism arises from **oxidation** of organic compounds. Select ***one*** oxidation reaction from those shown on the right. Please indicate your choice (A, B, C, or D).

i) State the general name of the enzyme that catalyzes reactions of this type (2 pt).

The key word is "oxidation". All redox reactions are catalyzed by dehydrogenases.
(loss of hydrogen = loss of electron)

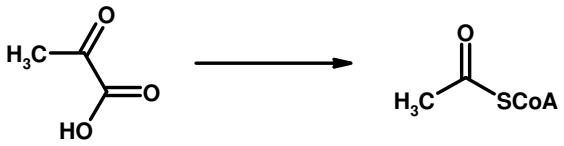
(For part A: if you stated kinase you were given +1 pt)

A



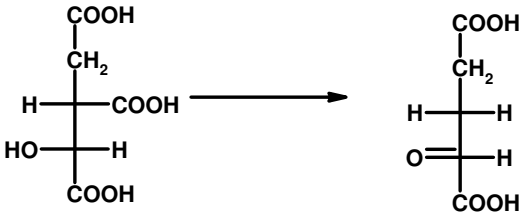
ii) State the pathway(s) in which your selected reaction(s) occurs (2 pt).

B



A: glycolysis
B: Entry to TCA cycle (TCA ok)
C: TCA cycle
D: TCA cycle & fatty acid oxidation.

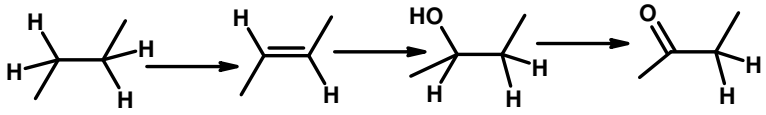
C



iii) Draw (or list) any cofactors/cosubstrates and products that are involved in your chosen reaction(s) if they are not already shown (2 pts).

It was only necessary to give the redox cofactors.

D



In reactions A-C, NAD^+ accepts electrons and is converted to NADH.

In reaction D, the conversion of the alkane to the alkene generates $FADH_2$ from FAD. The conversion of the alcohol to the ketone generates NADH from NAD^+

iv) Briefly discuss how the energy released from the oxidation is stored for subsequent conversion to ATP (2 pts).

Both NADH and FADH are "high energy" compounds, i.e. their synthesis is associated with a large positive change in standard energy, i.e.:

$$NAD^+ \xrightarrow{\Delta G^0 = +60\,kJ/mol} NADH$$

8. (12 pts) Please do **one** of the following two choices. Please indicate your choice.

Choice A: Protein phosphorylation is used to control glycogen/glucose levels in liver cells. Selecting ***either*** the hormones glucagon ***or*** insulin, briefly discuss how protein phosphorylation is used to regulate glycogen/glucose levels. *Briefly* discuss why this regulatory scheme is of benefit to the organism.

Glucagon:

- This is a signal for low blood sugar, indicating that the liver should release glucose from glycogen to increase blood sugar levels.
- glucagon binding to the receptor leads to the phosphorylation of enzymes by protein kinases.
- The enzyme that degrades glycogen (glycogen phosphorylase) is therefore active when phosphorylated. Consequently the enzyme that converts glucose to glycogen must be inactive when phosphorylated.

Insulin:

- This is a signal for high blood sugar. Therefore the liver should remove glucose from the blood and store it in glycogen.
- Insulin binding to its receptor caused dephosphorylation of enzymes. Therefore the enzyme that synthesizes glycogen from glucose must be active when dephosphorylated. Consequently, the enzyme that breaks down glucose must be inactive when dephosphorylated.

The net result of the above is homeostasis – maintaining blood glucose levels.

Choice B: PFK-1 in glycolysis and fructose-bis-phosphatase-1 in gluconeogenesis are regulated both by energy sensing as well as by hormones. Briefly explain how these two pathways are regulated by ***one*** of these regulatory methods. You need not discuss *how* the levels of F2,6P are regulated, by you should state the levels of F2,6P under different conditions. *Briefly* discuss why this regulatory scheme is of benefit to the cell/organism.

In energy sensing, high levels of ATP inhibit glycolysis by inhibition of PFK-1. This prevents the generation of more ATP than is needed. High levels of AMP or ADP activate PFK-1, causing glycolysis to occur to replenish the ATP. The bis phosphatase is regulated in an inverse manner, except that it is not sensitive to ADP, i.e. high ATP levels turn on gluconeogenesis.

In hormonal regulation, F26P levels control these pathways. High blood glucose causes high levels of F26P which activate PFK-1, allowing glycolysis to occur if needed. Low blood glucose decreases the F26P levels, inhibiting PFK-1 so the liver doesn't reduce it glucose levels further by trying to run glycolysis.

The bisphosphatase is regulated in the opposite way, such that low F26P levels activate gluconeogenesis, such that glucose is synthesized since the levels are low.

The net result of the above is homeostasis – maintaining blood glucose or cellular ATP levels.

9. (6 pts) Electron transport reactions occur in the mitochondrial inner membrane (state location). In this pathway, electrons from $FADH_2$ would pass through complex __II__ and would be carried on coenzyme Q__ to complex III. The electrons would then be carried on cytochrome C to complex IV where they would be deposited on ___oxygen_____ to give _____water_____. The energy released during electron transport is stored as a ___proton gradient_____.

10. (4 pts) Please select ***one*** of the following three questions.

Choice A: Using succinate dehydrogenase ***or*** cytochrome C as an example, briefly discuss how metal ions are utilized in the electron transport process.

The iron undergoes one electron oxidations, cycling between Fe^{2+} and Fe^{3+}. (3 pts)

In cytochrome C, the iron is on the heme (1 pt).
In succinate dehydrogenase, the iron is held in iron-sulfur centers (1 pt)

Choice B: In anaerobic metabolism, lactate is generated from __pyruvate__ in the muscles to regenerate _____NAD+_____ for use in _____glycolysis_____ (name of a metabolic pathway). The lactate is usually converted to glucose in the _____liver_____ (organ).

Choice C: In the reaction that involves the conversion of pyruvate to acetyl-CoA. Acetyl-CoA would be called a _____product_____ inhibitor of the enzyme while citrate would be called a _____feedback_____ inhibitor of the enzyme.

11. (12 pts) Please do ***one*** of the following two questions. Clearly indicate your choice.

Choice A: Mr. Couchpotato eats principally potato chips. *Briefly* describe how the carbon atoms contained within the starch of the potato chips end up as triglycerides on Mr. Couchpotato's waist. Your answer should state which pathways are involved, giving key intermediates.

The carbohydrates would be converted to pyruvate by glycolysis (+6 pts)
The pyruvate is converted to acetyl-CoA (+ 4 pts)
The acetyl-CoA is then used to make fatty acids (+2 pts)
The fatty acids go into triglycerides for storage.

Choice B: Ms. Couchpotato begins a *high intensity* aerobics exercise program to lose weight. She also begins a high protein diet at the same time. Is it likely that she will be able to maintain her intense exercise program on this diet. Yes or No? *Briefly* support your answer by stating which pathways are involved, giving key intermediates.

No.

She will deplete her glycogen stores during the high intensity aerobics (+4 pts). Since she is eating mostly protein, she will have difficulty replacing the glycogen since only a few amino acids can provide carbon for glucose synthesis (+4 pts)

The low glycogen stores will make it difficult to get quick energy from glycolysis since glucose will be limiting (+4 pts).

12. (12 pts) Please do ***one*** of the following ***two*** choices. Please indicate your choice:

Choice A: A fictitious enzyme can utilize the energy associate with a glucose gradient across the cell membrane to synthesize ATP from ADP and P_i. The standard free energy for hydrolysis of ATP is -30 kJ/mol.

i) What *fundamental* property of all phospholipid bilayers would allows the persistence of the glucose gradient (2 pts)?

Polar or charged molecules cannot cross the membrane.

ii) Assuming that the intracellular concentration of glucose is 1 mM, determine the smallest concentration of glucose outside the cell that will provide sufficient energy to generate *one* ATP molecule. The voltage across the membrane is 0.1 V, inside positive. ($\Delta G = RT \ln \{[B]/[A]\} + Z\,F\,\Delta V$) (10 pts).

The membrane voltage difference can be ignored – glucose has no charge.

ΔG has to be at least -30 kJ/mol to overcome the energy for the addition of Pi to ADP.

Assuming the direction is from outside to in ("outside"=reactant, "in"=product)

$-30\ kJ/mol = 2.5\ kJ/mol \ln (1\ mM/x\ mM)$

$-12 = \ln (1 / x)$

$e^{12} = x$

$1.6 \times 10^5\ mM = x$

This answer underscores the importance of the voltage difference across a membrane in generating significant Gibbs energy.

Choice B: Discuss how ATP synthesis is coupled to proton transport. Your answer should include a discussion of the mechanism (a suitable diagram is quite acceptable) and a *brief* discussion of the energetics involved.

The enzyme ATP synthase allows protons to flow from the high concentration outside the mitochondrial matrix to the inside (2 pts).

The important parts of the synthase are three β-subunits whose **conformation is made to be asymmetric by the interaction with the γ subunit** in the center of the three β-subunits. Depending on the orientation of the gamma subunit, the β-subunit will have one of three states (6 pts):

i) no affinity for ADP & Pi or ATP.
ii) High affinity for ADP and Pi
iii) High affinity for ATP (this conformation causes ADP + Pi → ATP)

The movement of three protons through the synthase causes the γ subunit to rotate 120°.

This rotation causes a change in the conformation of the β-subunits.

A β-subunit will undergo the following series of changed due to the rotation of the gamma subunit (2 pts):

No affinity → ADP & Pi → ATP → No affinity (ATP released).

Energetics: The movement of three protons provides about 60 kJ/mol of energy, sufficient to make one ATP (2 pts).