Metabolic Biochemistry Midterm
Thursday Oct 31, 2013; 12:30-1:50

Happy Halloween. One reason for this exam is to solidify your knowledge of
the commonly used ideas and information that describe the chemical
language of metabolism. The other is to estimate how much you know. We
can best serve these two distinct purposes by making the scoring the
midterm so that it can only help you: if averaging in the midterm helps you at
the end of the quarter (meaning if it is a higher percentage score than the
final), we will use it in calculating the scoring. If it hurts you (meaning you got a
better percent grade on the final than the midterm)... it is not used! So the course score it
is more about what you end up learning rather than exactly when you learned it.

Our only advice: Please please pretty please read the whole question before you start your
answer. And please don’t hesitate to ask questions. That is why we are circulating around like
glycolytic Coelacanths who must answer questions to survive...

We are not about tricking you or trying to be crafty and fooly. This is a very straightforward
exam, and what we ask for is what we want. Period. Enjoy, to the extent that this is possible in
a midterm...

Summation

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Total __________(out of 100)
1 (7 pts) My plate is full… Hey look! Yet another license plate for practice of the amino acid one letter code. This is one of those lucky plates where every letter is an amino acid. First, match up the letters on the license plate to the correct full amino acid names. For those names that are not represented on the plate, put “none”.

a) Aspartate D________
b) Lysine none
 c) Serine S______
d) Tryptophan none
e) Arginine R_____
f) Histidine none
g) Alanine A_____ 
h) Asparagine YN 
i) Tyrosine ________

j) Which AAs on the license plate have a net negative charge at normal cell pH? _______
k) Which AAs on the license plate participate in the chymotrypsic catalytic triad? _____
l) Which AAs on the license plate have an aromatic ring in the R group? _______
m) 1pt) How does Histidine (His) function in the chymotrypsin catalytic triad? (one sentence)

2 (5 pts) Bonobase kinetics… You and a lab mate are studying two versions of the same enzyme. One comes from humans, the other comes from the bonobo (see pic). Each catalyzes the same reaction, converting X into Y. (This is a very popular reaction to study). You are each working with the purified proteins from these sources. You perform rate vs. [X] plots and discover that both enzymes follow Michaelis-Menten kinetics. Furthermore, you discover that both enzymes have the SAME Km value, but the kcat of the bonobo enzyme is twice as large as the human enzyme. Answer the following questions:

a) What concentration of X will show ½ maximal saturation with the human and the bonobo enzymes: human ______ bonobo ______

a) You run experiments with exactly the same amount of each enzyme. Which (if either) sample shows a higher Vmax in that particular experiment? Decide and explain why:

For a given sample of each enzyme (Etot)
the bonobo enzyme will have the higher Vmax, by a factor of two; VmaxBonobo = kcatBonobo.Etot = 2kcat.Human.Etot = 2 Vmax.Human

A Lineweaver-Burke plot is shown to the right.

b) What does the vertical axis represents in this type of plot? ______

c) What does the horizontal axis represent in the LB plot? ______

d) Are the lines on this LB plot a reasonable depiction of the two enzymes you and your lab mate are working with? Why (one sentence)

Yes. The shared x intercept indicates same Km (−1/4 Km) and the Vmax’s are different (the lower line would be the bonobo enzyme, but I didn’t ask that... should have...)
3 (4 pts) What's in a name; an acid by any other... For the following dicarboxylic acid names (you have seen this before I suspect) write the correct number of carbons.


b) Now, we are going to draw a structure, using the name game. Krebs cycle molecule oxaloacetate could also be called alpha-keto-succinate, although (unfortunately) no one does call it that. Draw the structure of this molecule in the space to the right.

4 (3 pts) The Fate of Fructose, Gamename Style When fructose is ingested, one of two things can happen to it. It can be phosphorylated on the 6 position, which makes it a glycolytic intermediate. OR, in the liver, it can be phosphorylated on the 1 carbon, giving fructose-1-phosphate. Then a unique enzyme called aldolase B converts it into two three-carbon molecules.

a) One of the products of the aldolase B reaction of Fr1P is glyceraldehyde. Draw glyceraldehyde either from what you know about glycolysis or the name game. Use the box on the right.

b) What is the other product of the aldolase B reaction? ____________________

5 (6 pts) In it for the long haul... This is a picture of an early molecule in glycolysis, called fructose-6-phosphate (ring form).

a) Using this structure, write the reaction catalyzed by phosphofructokinase (PFK), which involves this molecule in the space below. Include other needed substrates or products.

b) What would you expect to happen to the activity of PFK if cellular ATP levels were low and AMP levels were high in the cell

The activity of PFK would be elevated due to allosteric activation of the enzyme caused by the AMP...
6 (12.5 pts) Parts and labor (this is a greatest hit) Often glycolytic intermediates are simply mentioned as abbreviations. The box on the left is a "parts list" of molecules in glycolysis.

a) Using these abbreviations, and arrows for each enzyme-catalyzed step, draw a reasonable depiction of glycolysis. I provided glucose. Use all the parts. It helps to remember which things have six carbons and which have three. Make sure to include NAD and ATP where needed, using curved arrows to reduce clutter. Include "Lac" even though it is technically after glycolysis. Remember there is a branched reaction...

b) Using the abbreviations in the list, and any other reactants or products needed, write the reaction catalyzed by pyruvate kinase. No structures needed.

\[
\text{PEP} + \text{ADP} \xrightarrow{\text{PK}} \text{pyruvate} + \text{ATP}
\]

7 (4 pts) Lac-luster performance… The enzyme lactate dehydrogenase plays a very important role in glucose metabolism.

a) First, write out the complete reaction of lactate dehydrogenase, including structures of the pathway metabolites. (If this is challenging perhaps reciting this soothing word will help: “Chi-co-co”.)

\[
\text{CH}_3\text{C(OH)CO}_2^- + \text{NADH} \xrightarrow{\text{LDH}} \text{CH}_3\text{CHOHCO}_2^- + \text{NAD}^+
\]

b) What is the function of this reaction in terms of the glycolytic pathway?

LDH reaction regenerates NAD^+, allowing continued flow of glycolysis.

c) An anaerobic organism is treated with a potent inhibitor of LDH, and the organism dies very quickly. Why?

Since glycolysis is, in anaerobiosis, the main source of ATP, LDH inhibition would cause a block of this critical energy source; no NAD^+ availability = no glycolysis.
8 (6 pts) **Pumpkin Pie-ruvate** The pyruvate dehydrogenase (PDH) complex is a multi-activity enzyme that converts pyruvate into a useful source of carbon. Answer these questions about this amazing molecular device.

a) Write out the net reaction of the PDH. What goes in, what comes out. No need for structures or internal cofactors.

\[ \text{Pyr} + \text{CoA} + \text{NAD}^+ \xrightarrow{\text{PDH}} \text{AcCoA} + \text{NADH} + \text{CO}_2 + \text{H}^+ \]

b) A key cofactor of the PDH is the lipoic acid cofactor, tightly anchored to E2. The structure of the “business end” of the lipoic acid cofactor at the start of the catalytic cycle looks like on the left. Draw the same business end when it is fully loaded with the group it carries during the PDH reaction. No need for a reaction. Just the structure of the lipoic acid when it is carrying the things in carries.

![Diagram of lipoic acid cofactor]

\[ \text{CH}_3 - \text{C} - \text{S} \quad \text{(Note: it is reduced!)} \]

\[ \text{HS} \]

\[ \text{(HS)} \]

**c)** The reaction that modifies lipoic acid in PDH is one of a group called “reductive acetylation.” Why does this name make sense? One sentence

**The lipoic acid is in its reduced form (−SH) and it is acetylated.**

**d)** The activity known as E3 in the PDH uses the cofactor FAD. What is the function of this FAD in returning lipoic acid to its original status (like in the picture above) in the complete catalytic cycle of PDH?

**The FAD returns the reduced lipoic acid (HS) to its original oxidized (S) form**
9 (11 pts) Circle Up, Young Metabolites…. This year, we number the metabolites of the Krebs cycles, rather then the enzymes (if this picture looks familiar). For each question answer with the molecule number that is the best answer. You can use a single number, more than one, or put “none” if none apply:

a) Which metabolite is a product of PDH? 1
b) Which metabolite has CO₂ removed by a Krebs cycle reaction 3,4
c) Which metabolite is produced by an enzyme that is similar to PDH? 5

d) Which metabolite is created by gaining H₂O? 8

e) Which **metabolite** is oxidized by FAD? 6

f) Which metabolite has 6 carbons and 3 –CO₂ groups? 2,3

g) Which 4-carbon metabolite reduces NAD⁺? 8

h) Aconitase uses 2 as a substrate

i) Isocitrate dehydrogenase uses 3 as a substrate

j) Citrate synthase uses 1,9 as a substrate

10 (4 pts) Metabolites of the Krebs Persuasion The picture shows a Krebs cycle molecule. The carboxyl groups are numbered for ease in answering. These are not the carbon numbers, they are just labels for the carboxyl groups.

a) What is the name of the Krebs cycle molecule shown? ISOCITRATE

b) Indicate with an arrow the carbon the OH was bound to when it was part of the substrate molecule used to make this.

c) Which carboxyl group will be lost in the very next next Krebs cycle reaction (1,2,3)

d) Which carboxyl group will be lost in the reaction after the one in d? (1,2,3)

e) Which carboxyl group was most recently part of AcCoA? (1,2,3)

f) If a **lone** Krebs cycle turns 100 times, how many acetyl groups are fed into it?

g) ...and how many CO₂ exit the cycle during the lone cycle’s 100 turns?

h) ...and how many oxaloacetate molecules will be available for the 101th turn of that lone Krebs cycle?
11 (5.5 pts) **The other Kreb-ish cycle** Continuing with the “ghost of questions past” theme, we will use the metabolite-labeled schematic from the last question to talk about the variation of the Krebs cycle known as the glyoxylate cycle.

a) Which Krebs molecules (use numbers) are NOT made in the glyoxylate cycle:

b) What four carbon molecule is released with each turn of the GC?

c) How many acetyl groups enter per turn of the GC?

d) How many CO₂ are released during one turn of the GC?

e) And how many OAA are present after 100 turns?

f) The pictures on the left are two molecules of the glyoxylate cycle. Glyoxylate (duh) and L-malate, which we will abbreviate G or M. Answer the following questions to about these two molecules:

1) Which (G or M) is part of the Krebs cycle also ________

2) Which (G or M) one is generated by isocitrate lyase ________

3) What molecule reacts with G to make M? ________

4) Which two carbons in M were contributed by G, numbering from the top of M (eg. 2,3): ________

12 (8 pts) **That other glucose pathway** Glucose is also metabolized by the pentose phosphate pathway (PPP). This pathway is not for energy so much as to make stuff.

a) What are the two main products of the pentose phosphate pathway?

b) What two major classes of macromolecules are built from a product of the PPP?

c) How many reduction reactions occur in this pathway?

d) 5.5pt) This is a molecule of the PP pathway. Write the name of the molecule below it, and the reaction that consumes this hapless carboxylic acid during the PP. Include cofactors, structure of the resulting molecule, and other products.
13 (17 pts) Swimming pools, movie stars… We often joke about the mitochondrion being depicted as a “so cal swimming pool” and you can see I am not lying. This was Peter Mitchell’s own swimming pool, which he had filled with a strong solution of ATP, using his nobel prize money. I hear that in Berkeley they use a natural pond...

a) Draw the classic swimming pool/kidney bean model of the mitochondrion, and label the parts we talked in class. Label the IM, OM, IMS, and matrix, and indicate where the cytosol is in relation to your mito. Then use K, E, P, and G to label where Krebs, ETC, PDH, and Glycolysis occur in your diagram. Finally, draw an arrow to show the direction the proton motive force pushes protons to make ATP. Use the box below, to promote TAs sanity...

b) Complexes I-IV, comprise the Electron Transport Chain. The biochemistry of each can each be described by a simple net chemical reaction involving an initial electron donor and acceptors, such as NADH, or cytc, as examples. PICK TWO, (any two) and next to the complex name (I, II, III, or IV) write the balanced NET reaction that that complex catalyzes (no need for Q cycles and such nonsense). Don’t worry about the proton gradient in this question.

\[
\begin{align*}
\text{I} & : 2\text{NADH} + 2\text{H}^+ + \text{Q} & \rightarrow & \text{NAD}^+ + \text{QH}_2 \\
\text{II} & : \text{succinate} + \text{Q} & \rightarrow & \text{fumarate} + \text{QH}_2 \\
\text{III} & : \text{QH}_2 + 2\text{cytc}_{\text{ox}} & \rightarrow & \text{Q} + \text{cytc}_{\text{red}} + 2\text{H}^+ \\
\text{IV} & : 2\text{cytc}_{\text{red}} + 2\text{H}^+ + \frac{1}{2}\text{O}_2 & \rightarrow & 2\text{cytc}_{\text{ox}} + \text{H}_2\text{O}
\end{align*}
\]
14 (7 pts) Keep it Real, Yo! (T/F)
Write T or F for each question

a) ______ If a reaction’s activation energy drops by L, the rate is multiplied by $e^{L/RT}$

b) ______ Enzymes increase the reverse reaction of a metabolic reaction by the same multiplicative factor as the forward reaction

c) ______ Ingested fructose is eventually converted into molecules that can be metabolized by glycolysis

d) ______ There are individual endergonic reactions in the pathway of glycolysis

e) ______ The Krebs cycle is used both for catabolism and anabolism

f) ______ The Krebs cycle does not employ oxygen as a substrate

g) ______ The Krebs cycle performs numerous oxidation reactions

h) ______ Mammals can covert AcCoA into carbohydrates with the Krebs cycle

i) ______ Mammals can convert AcCoA into carbohydrates with the glyoxylate cycle

j) ______ Plants can convert AcCoA into carbohydrates with the glyoxylate cycle

k) ______ If isolated, normally functioning mitochondria are given ADP and succinate, both electron transport and ATP synthesis will occur.

l) ______ If isolated, normally functioning mitochondria are giving only succinate, and no ADP, electron transport will occur, but ATP synthesis will not occur.

m) ______ If isolated normally functioning mitochondria are given succinate, ADP and a weak organic acid like DNP, electron transport will occur, but ATP synthesis will not

n) ______ Randy knows powerful people high in the UCSD bureaucracy