Biochemistry 110 – Final Exam
Fall 2016

• The final exam is open book (see allowed materials in the following bullet point) and the time limit is 5 hours. Please indicate on your exam when you began the exam and when you ended the exam (also indicating if/when you took a break during the exam). If you run out of time, please indicate which questions you completed after the time limit was reached and you can still receive half credit for questions completed after the time limit.

• For the final the exam, you may use the following materials:
  - Your Stryer ‘Biochemistry’ textbook
  - Your lecture notes and homework problem sets
  - Any material that has been posted on the Biochemistry 110 website
  - A calculator, Excel, Mathematica, etc. for calculations/plots

• You may have one break for any amount of time during the exam. During this break you may not consult any Bi/Ch110 materials or talk to other students about the exam.

• Please have each problem of the exam on a separate page with your name on every page of the exam. You may have multiple pages for the same problem but you must have your name on every page.

• The due date for submission of the final exam is at noon in the Bi/Ch110 box located outside of Crellin 268 on Thursday, December 8, 2016. The exam is due at noon sharp and we will begin grading the exam at 12:30pm. You may submit the exam any time before this time/date but not after.

1. _____ /20
2. _____ /34
3. _____ /23
4. _____ /35
5. _____ /25
6. _____ /28
7. _____ /35
8. _____ /15
9. _____ /35
10. _____ /30
11. _____ /20

Total: _____/300
Problem 1: Metabolism (20 points)

Please indicate your answer to each of the following multiple choice questions by circling or writing the letter of the answer you think is correct.

i. (5pts) Dintrophenol is an uncoupler. Which of the following processes does it inhibit first?
   a) Pyruvate decarboxylation by the PDC
   b) TCA cycle
   c) Electron transport
   d) Muscular contraction

ii. (5pts) During a myocardial infarction, the oxygen supply to an area of the heart is dramatically reduced, forcing the cardiac myocytes to switch to anaerobic metabolism. Under these conditions, which of the following enzymes would be activated by increased levels of intracellular AMP?
   a) Succinate DH
   b) PFK-1
   c) Isocitrate DH
   d) Pyruvate DH

iii. (5pts) A patient has been exposed to a toxic compound that increases the permeability of mitochondrial membranes to protons. Which of the following metabolic changes would be expected in this patient?
   a) Increased ATP levels
   b) Increased oxygen utilization
   c) Increased ATP synthase activity
   d) Decreased Pyruvate DH activity

iv. (5pts) Which of the following best explains why cytosolic NADH can yield potentially less ATP than mitochondrial NADH?
   a) Cytosolic NADH loses energy when transferring electrons
   b) Once NADH enters the matrix from the cytosol, it becomes FADH₂
   c) Electron transfer from the cytosol to matrix can take more than one pathway
   d) There is an energy cost for bringing cytosolic NADH into the matrix
Problem 2: (34 points) The citric acid cycle

a. (10 points) Pyruvate, labeled with $^{14}$C as shown below in red with an asterisk (*), was added to cell extracts that contain functioning metabolic enzymes. How many turns of the citric acid cycle does it take to lose all of the $^{14}$C label as $^{14}$CO$_2$? Show your work by tracing the atom through the metabolic reactions in the schematics below.

b. (7 points) Pyruvate is imported into the mitochondria by a specific transporter, the mitochondrial pyruvate carrier. You’re interested in studying this carrier, so you modify cells in culture to express a non-functional mutant. How would you expect the metabolism of these cells to differ from wild type cells? Limit your response to three sentences.
c. (17 points) The glyoxylate cycle is a variant of the citric acid cycle found in plants, bacteria, and fungi. These reactions allow organisms to convert acetyl CoA generated from the breakdown of fats into glucose.

i. (5 points) Why can’t humans make glucose from acetyl CoA? Limit your response to four sentences.

ii. (5 points) Below are the schematics of the citric acid cycle (left) and the glyoxylate cycle (right). How do the reactions of the glyoxylate cycle get around the issues you described in part (a)? Limit your response to four sentences.

iii. (7 points) The bacterium *Mycobacterium tuberculosis*, the cause of tuberculosis, invades the lungs, living in lipid-rich, oxygen-poor environments. Inhibitors of isocitrate lyase are being explored as drug treatments for tuberculosis. Give two reasons why isocitrate lyase is a good drug target for tuberculosis infections in humans. Limit your response to four sentences.
Problem 3: Oxidative Phosphorylation (23 points)

a) (10 points) Consider the energy level of electrons as they travel through the electron transport chain. Draw a graph that shows the free energy of the electrons as they travel through the electron transport chain and to various electron carriers. [Include: Complex I, II, III, IV, as well as Q, Cytochrome c, and O₂]. Also, indicate where proton pumping takes place on the graph with regards to the energy levels.

b) (7 points) Explain the trend that you have graphed, and use it to show how a proton gradient is formed.

c) (6 points) Cyanide is an inhibitor of cytochrome c oxidase. Knowing this information, explain how cyanide kills.
Problem 4: Photosynthesis (35 points)

Please indicate your answer to each of the following multiple choice questions by circling or writing the letter of the answer you think is correct.

1) (5 points) Which of the following sequences correctly portrays the flow of electrons during photosynthesis?
   A) NADPH —> O2 —> CO2
   B) NADPH —> chlorophyll —> calvin cycle
   C) NADPH —> electron transport chain —> O2
   D) H20 —> photosystem I —> photosystem II
   E) H20 —> NADPH —> Calvin cycle

2) (5 points) The light reactions of non-cyclic photophosphorylation supply the Calvin Cycle with:
   A) light energy
   B) sugar and O2
   C) CO2
   D) NADPH
   E) ATP
   F) C and E
   G) D and E
   H) water and sugar

3) (5 points) What three events occur during the light reactions of photosynthesis?
   A) reduction of oxygen, oxidation of NADPH, formation of ATP
   B) oxidation of water, reduction of NADP+, formation of ATP
   C) oxidation of water, reduction of NADP+, hydrolysis of ATP
   D) fixation of carbon dioxide, release of oxygen, synthesis of glucose
   E) release of oxygen, fixation of carbon dioxide, hydrolysis of ATP

4) (5 points) In the basic equation of photosynthesis for the synthesis of one molecule of a sugar such as glucose, how many molecules of carbon dioxide are required and how many molecules of oxygen are produced?
   A. 3, 4
   B. 6, 2
   C. 6, 6
   D. 3, 6
   E. none of these

5) (5 points) What is a property of C4 plants, but not C3 plants?
   A. Initially fix carbon dioxide in mesophyll cells as 4-carbon long compounds.
   B. Initially fix carbon dioxide in bundle sheath cells as 3-carbon long compounds.
   C. Initially fix carbon dioxide in mesophyll cells as 3-carbon long compounds.
   D. Initially fix carbon dioxide in bundle sheath cells as 4-carbon long compounds.
   E. Special leaf anatomy adapted for cold and wet climates.
6) (5 points) Which of the following does not occur in the Calvin Cycle?
A) consumption of ATP
B) release of oxygen
C) regeneration of NADP+
D) carbon fixation
E) oxidation of NADPH

7) (5 points) Which of the following is not true?
A) The light reactions of cyclic photophosphorylation involve redox reactions.
B) The light reactions of cyclic photophosphorylation generate ATP.
C) The light reactions of cyclic photophosphorylation use only photosystem I.
D) The light reactions of cyclic photophosphorylation use chemiosmosis.
E) The light reactions of cyclic photophosphorylation produce NADPH.
Problem 5: Respiration and non-cyclic photophosphorylation (25 points)

Respiration and non-cyclic photophosphorylation both produce ATP using chemiosmosis.

a) (5 pts) In respiration, what molecule donates electrons to the first protein in the electron transport chain?

b) (5 pts) In non-cyclic photophosphorylation, what molecule donates electrons to the first protein in the electron transport chain?

c) (5 pts) In respiration, what molecule accepts electrons from the last protein in the electron transport chain?

d) (5 pts) In non-cyclic photophosphorylation, what molecule accepts electrons from the last protein in the electron transport chain?

e) (5 pts) Non-cyclic photophosphorylation also produces NADPH. In what process is NADPH used, and what role does it perform in this process?
Problem 6: Phototrophic metabolism in purple bacteria (28 points)

Purple sulfur bacteria have photosystem I, but not photosystem II, and thus carry out cyclic photophosphorylation. Plants have both photosystem I and photosystem II, and carry out non-cyclic photophosphorylation.

a) (5 points) Is the Calvin Cycle the same or different in Purple sulfur bacteria and plants? Explain.

b) (5 points) Is the mechanism for producing ATP the same or different in Purple sulfur and plants? Explain.

c) (6 points) What is the initial source of the electrons that are used to convert NADP+ to NADPH for cyclic photophosphorylation?

d) (6 points) What is the source of electrons for the conversion of NADP+ to NADPH for non-cyclic photophosphorylation?

e) (6 points) Explain why the evolution of non-cyclic photophosphorylation was a prerequisite to the evolution of respiration.
Problem 7: Glycolysis/Gluconeogenesis (35 points)

a) (10 points) What are the two major methods of sequestering monosaccharides in cells during catabolic carbohydrate metabolism? Please provide examples of each reaction, including substrate, product, and catalytic enzyme.

b) (15 points) Below is a schematic of the Cori Cycle (or the Lactic Acid Cycle) in which the lactate produced by anaerobic glycolysis is shuttled back into the liver and converted to glucose (which later returns to the muscle and is metabolized back into lactate).

i) Please explain the conditions under which this cycle occurs and why this is advantageous in such circumstances. (5 points)

ii) Is this activity sustainable? And to what extent? Why? (5 points)

iii) Please draw in relevant energy consumption and production. (5 points)

c) Please indicate your answer to each of the following multiple choice questions by circling or writing the letter of the answer you think is correct.

i) (5 points) Ethanol decreases gluconeogenesis by:
   (A) Inhibiting glucose-6-phosphatase
   (B) Inhibiting PEP carboxykinase
   (C) Converting NAD+ into NADH and decreasing the availability of pyruvate
   (D) Converting NAD+ into NADH and decreasing the availability of lactate
ii) (5 points) Excessive intake of ethanol increases the ratio of:
(A) NADH : NAD+
(B) NAD+ : NADH
(C) FADH2 : FAD
(D) FAD : FADH2
Problem 8: Comparing metabolic pathways (15 points)

<table>
<thead>
<tr>
<th>Type of metabolism</th>
<th>Electron Source</th>
<th>Carbon Source</th>
<th>Energy Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>fermentation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>oxygenic photosynthesis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>anaerobic respiration</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>aerobic respiration</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>anoxygenic photosynthesis</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

For each type of metabolism,

a) (10 points = 1 pts/box) Use the following list to fill in Electron source (column 2) and Carbon source (column 3) in the table above.
   - sugar (“sugar” here is a generic term for any organic carbon compound (CH2O)n).
   - Water (H2O)
   - hydrogen sulfide (H2S)
   - methane (CH4)
   - carbon dioxide (CO2)
   - NH3

b) (5 points = 1 pts/box) Fill in Energy source (column 4) in the table above. For this part, you are not limited to the list above.
Problem 9: Fatty Acid Metabolism and Regulation (35 points)

a) (10 points) One micromole of a fully triturated, straight chain saturated fatty acid C\textsuperscript{3}H\textsubscript{3}(C\textsuperscript{3}H\textsubscript{2})\textsubscript{10}COO\textsuperscript{3}H is added to a preparation of disrupted mitochondria, which degrades it completely to acetyl CoA. If 6 micromole of product are re-isolated from the reaction mixture, hydrolyzed to free acetate, and assayed for radioactivity, what will be the overall tritium-to-carbon ratio?

b) (15 points) Explain how each of the following dysfunctional mutants (independently) affect fatty acid metabolism:
   i) (5 points) Dysfunctional isocitrate dehydrogenase
   ii) (5 points) Dysfunctional malic enzyme
   iii) (5 points) Dysfunctional pyruvate kinase

c) (5 points) Explain how the cellular conditions where epinephrine is being synthesized make sense in terms of regulating fatty acid synthesis.

d) (5 points) The fatty acids produced by the fatty acid synthase complex are not substrates for beta-oxidation for what reason?
Problem 10: Enzyme kinetics (30 points)

a) (5 points) How does an enzyme affect the activation energy of a reaction? How does it affect the free energy for the reaction from substrate to product? Explain in three sentences or fewer.

b) (9 points) Given the following $K_M$, $k_{cat}$, and $k_{cat}/K_M$ values, determine the type of inhibition for each of the following enzyme inhibitors. Explain how you determined the inhibitor type for each inhibitor using a maximum of 2 sentences/inhibitor.

<table>
<thead>
<tr>
<th>Enzyme</th>
<th>$K_M$ (mM)</th>
<th>$k_{cat}$ (s$^{-1}$)</th>
<th>$k_{cat}/K_M$ (M$^{-1}$ s$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No inhibitor</td>
<td>2.5</td>
<td>39</td>
<td>1.56*10$^4$</td>
</tr>
<tr>
<td>Inhibitor 1</td>
<td>1.0</td>
<td>15.6</td>
<td>1.56*10$^4$</td>
</tr>
<tr>
<td>Inhibitor 2</td>
<td>10.0</td>
<td>39</td>
<td>3.9*10$^3$</td>
</tr>
<tr>
<td>Inhibitor 3</td>
<td>2.5</td>
<td>15.6</td>
<td>6.24*10$^3$</td>
</tr>
</tbody>
</table>

c) (6 points) You saw in part b that enzymes can both increase and decrease the value of $K_M$. Which of these inhibitors makes enzyme substrate-binding tighter? How can an inhibitor make enzyme-substrate binding tighter? Explain using three sentences or fewer.

d) (6 points) Trypsin us a serine protease whose catalytic triad consists of histidine-57, aspartate-102, and serine-195. Given what you have learned about enzyme mechanisms draw out a mechanism for trypsin cleaving a peptide bond using this catalytic triad.

e) (4 points) In addition to the catalytic triad, proteases sometimes contain a specificity pocket that can limit the types of amino acids that can be cleaved by the enzyme. Trypsin is a protease that cleaves peptide bonds following positively charged amino acids. Given this specificity, what residue(s) would you expect to find in this enzyme’s specificity pocket?
Problem 11: Protein structure (20 points)

a) (5 points) If Anfinsen’s famous protein folding experiment had been performed without removing 2-mercaptoethanol, what would have been the result?

b) (5 points) Name at least two ways peptides can be specifically cleaved and give an example of each type of cleavage.

c) (5 points) Name and describe in two sentences or fewer an experimental method that can be used to obtain a protein structure.

d) (5 points) How is mRNA exported from the nucleus where it is transcribed to the cytoplasm where it is translated into protein? Explain in three sentences or fewer.