CHEM-643 Biochemistry Name ______________________________

Mid-term Examination

8:00 – 10:00 AM, Friday, 4 November 2011

Dr. H. White - Instructor

This examination will assess your learning, problem-solving skills, and ability to communicate clearly. Parts are intended to be challenging even to the best students in the class. Some of the questions will deal with material you have not seen before and is not in your text; however, those questions can be answered by applying basic principles discussed in the course.

There are 11 pages to this examination including this page.

- **Write your name on each new page**.
- Read every question so that you understand what is being asked. If you feel any question is unclear or ambiguous, clearly explain your answer or interpretation. Please call my attention to any errors you encounter.
- This is examination is closed book until 9:15AM. You may refer to your assignments and your lecture notes, but not textbooks at that time. You may also refer to the hand-drawn metabolic pathway sheets available from the course website.
- Do not expose your answers to the scrutiny of your neighbors. Please fold under each page before you go on to the next.

Breakdown of the examination by sections:

| | |
|---|---|
| I. Basic Vocabulary | 15 Points |
| II. Problems | 105 Points |
| Total | 120 Points |

Exam Statistics

| | |
|---|---|
| Class Range | 45-102(2)/120 |
| Class Mean | 72.1/120 |

N = 21

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**Part I - Basic Vocabulary and Working Knowledge** (1 point each)

______________________________ 1. Expected cofactor(s) for the decarboxylation of an alpha amino acid.

______________________________ 2. Expected cofactor(s) for the decarboxylation of an alpha keto acid.

______________________________ 3. Expected cofactor(s) for the carboxylation forming a beta keto acid.

______________________________ 4. Class of acids that readily decarboxylate.

______________________________ 5. Name of bicyclic ring system found in NAD.

______________________________ 6. Vitamin precursor for FAD.

______________________________ 7. Coenzyme involved in interconverting methylmalonyl CoA and succinyl CoA.

______________________________ 8. Common name for a five-carbon, straight-chain dicarboxyllic acid.

______________________________ 9. Vitamin recommended to reduce the incidence of neural tube defects, e.g. spina bifida.

______________________________ 10. Class of molecules that give color to butterfly wings.

______________________________ 11. Term for organisms that require specific nutrients, e.g. vitamins, amino acids, that they cannot make.

______________________________ 12. Generic name for enzymes that require biotin.

______________________________ 13. Metal ion found in nitrogenase other than iron.

______________________________ 14. Has about the same $-\Delta G^{o\prime}$ for hydrolysis as $ATP \rightarrow ADP + Pi$.

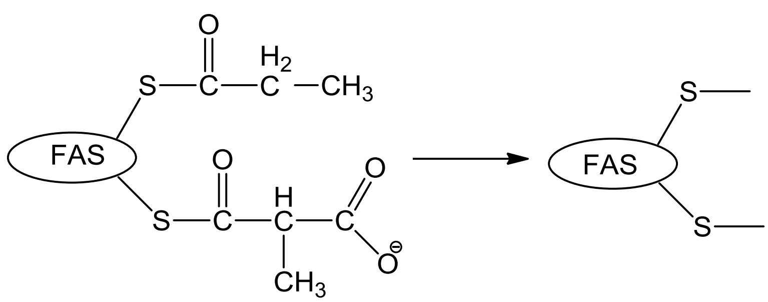
______________________________ 15. Pyruvate dehydrogenase and glycine cleavage enzyme have this sulfur-containing prosthetic group in common.

**Part II: Problem Solving/ Competency**

1. (14 Points Total) The Dipper Duck produces unusual methyl-branched fatty acids that are incorporated into the waxes produced by its preen gland. The diagram below depicts the arrangement of precursors on fatty acid synthase just prior to the formation of the first carbon-carbon bond.

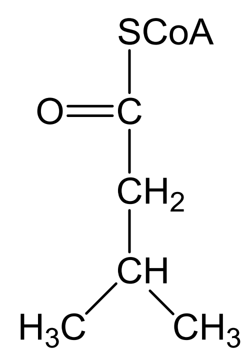
   a. (4 points) Indicate on the left figure how this carbon-carbon bond is formed by "pushing arrows".

   b. (4 points) Complete the structure on the right as it would be on the enzyme after the reaction has occurred.




   c. (6 points) The above reaction would be on the path to synthesize 2,4,6-trimethyl nonanoate, a fatty acid found in the hydrolysate of waxes from the Dipper Duck. Waxes are lipids that contain a hydrophobic acid in ester linkage to a hydrophobic alcohol. In an aqueous environment, the ΔG for ester hydrolysis is favorable. Show by drawing chemical reactions, how biosynthetic ester formation is coupled to other reactions so that it also is a favorable reaction.

2. (8 points) In *Bacillus spp*, leucine can be converted to a precursor (primer below) for the biosynthesis of fatty acids with a penultimate methyl branch. Without generating mythical reactions, show how leucine can be converted to the primer shown. Indicate any and all cofactors involved in the reactions that you use.



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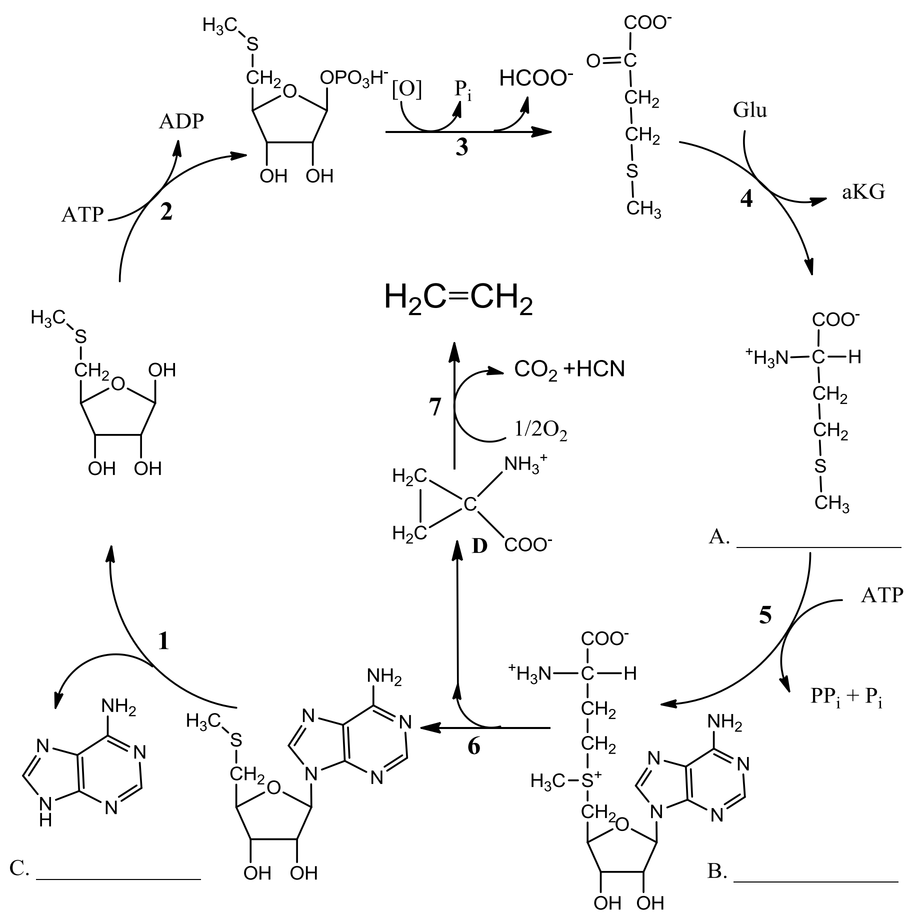
3. (22 Points Total) Plants produce ethylene as a gaseous hormone that induces ripening in fruit. The metabolic pathway for ethylene synthesis is shown below and the questions that follow refer to this figure.




a. (6 points) Identify by name compounds A, B, and C.

b. (3 points) With carbons leaving the cycle as compounds such as $C_2H_4$, $CO_2$, HCN, and $HCOO^-$, the cycle's carbon must be replenished. Draw a circle around the source of all carbon coming into the cycle.

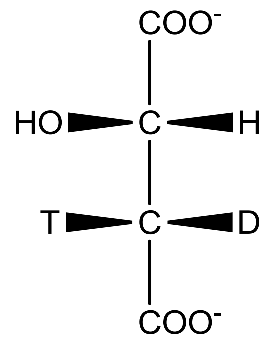
c. (4 points) For reactions 2 and 4, identify the generic name for enzymes catalyzing that type of reaction.

2. ____________________________, 4. ______________________________

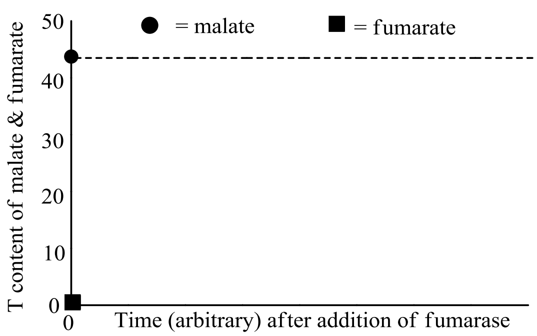
d. (5 points) The two adjacent methylene groups in compound B are converted in two steps to ethylene via D, a cyclopropanyl amino acid intermediate. Would an enzyme be able to distinguish between the methylene groups in compound D? Explain your answer.

e. (4 points) Identify two aspects of Reaction 7 that would make it a favorable reaction.

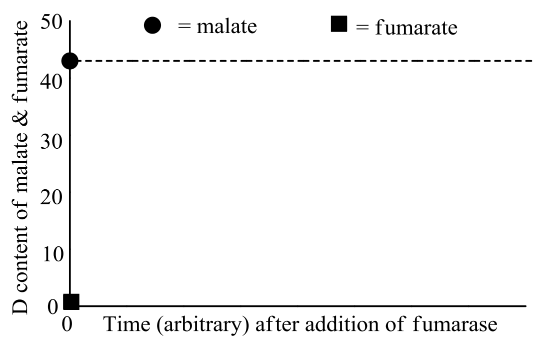
4. (16 Points Total) In two of your problem sets, your attention was focused on the TCA cycle enzyme fumarase that catalyzes the interconversion of malate and fumarate via a trans elimination of water. Hans Krebs determined the $K_{eq}$ for fumarase to be 4.4 (= [malate]/[fumarate]) at pH 7.0 [*Biochem. J*. **54**, 78-82 (1953)]. Consider an aqueous ($H_2O$) solution containing 44mM malate and 10mM fumarate with the malate molecule labeled with tritium and deuterium (indicated as T and D) as shown at the right.




a. (6 points) On the graph below, plot the amount of **T** in malate and in fumarate as a function of time after the addition of fumarase. (Dashed line represents the total T in the system.)




b. (6 points) On the graph below, plot the amount of **D** in malate and in fumarate as a function of time after the addition of fumarase. (Dashed line represents the total D in the system.)




c. (4 points) Draw the structure of malate after full equilibration has occurred showing the location of any remaining isotopes.

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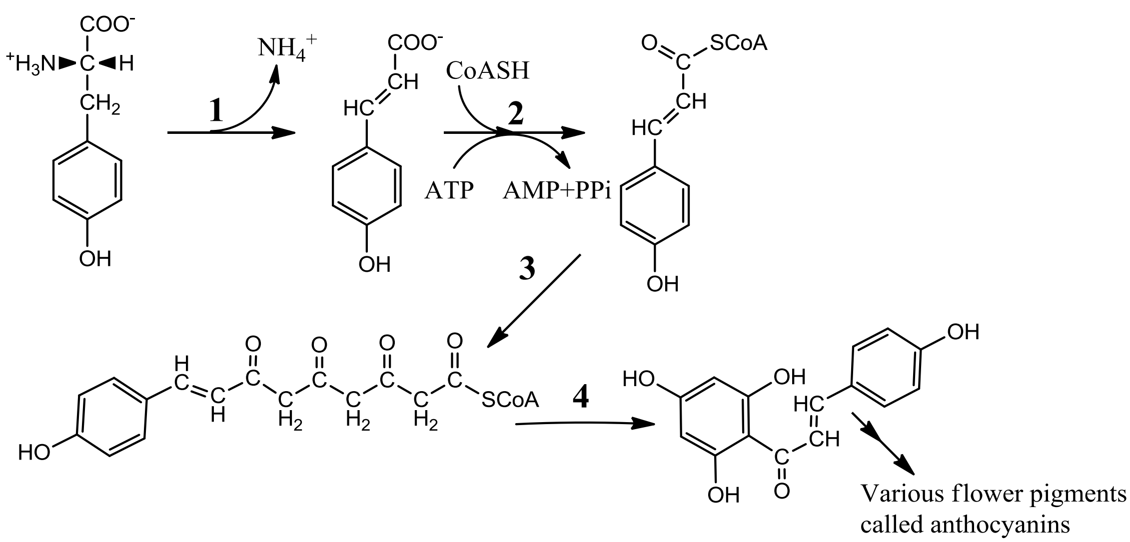
5. (19 Points Total) A trip to Longwood Gardens reveals the great variety of yellows, reds, and blues plants produce in their flowers. Most of those pigments are due to anthocyanins and flavones derived from the pathway sketched out below.

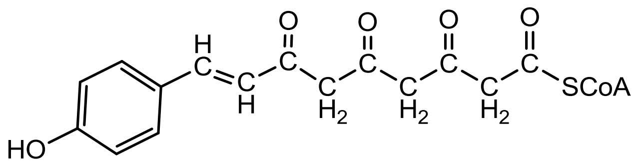



a. (3 points) Reaction 1 involves a *trans* elimination of ammonia. This is not a reaction observed in nature for more than a few amino acids. Chemically, what makes this a favorable reaction for tyrosine?

b. (5 points) Formation of a thioester bond between a carboxylic acid and CoASH is not favorable by itself and so it is coupled to the hydrolysis of ATP to AMP and PPi. Show how ATP is used in this reaction by drawing the intermediate and how electrons move in the formation and reaction of this intermediate.

c. (5 points) By analogy to things we have discussed in class, indicate what happens in Reaction 3.

d. (6 points) Show a chemically reasonable sequence of reactions with arrow pushing that shows how the trihydroxyphenyl group is generated in Reaction 4 from the compound below containing the six carbons added in Reaction 3.




6. (16 Points Total) Enzymes, like people, are not perfect. Sometimes they make mistakes we have to live with, i.e. they don't always do what they are supposed to. Take for example the TCA Cycle enzyme L-malate dehydrogenase (MDH) that catalyzes the NAD-dependent interconversion of malate and oxaloacetate. Every once in a while (~$10^{-7}$) it mistakes α-ketoglutarate (αKG) for oxaloacetate and produces L-2-hydroxyglutarate, a compound that has no metabolic function.

a. (4 points) Draw out the chemical structures of the reactants, products, and coenzyme involvement in this mistaken reaction.

b. (4 points) Because MDH is an abundant enzyme, L-2-hydroxyglutarate would accumulate if it were not for a "metabolic repair enzyme", the FAD-linked L-2-hydroxyglutarate dehydrogenase (LHGDH). Draw out the chemical structures of the reactants, products, and coenzyme involvement in this "repair" reaction.

c. (4 points) Given the function of the enzyme and the way natural selection operates, predict what property of FAD would make it nature's choice for this reaction rather than NAD or NADP?

d. (4 points) About 100 people world-wide have been diagnosed with L-2-hydroxyglutaric aciduria [*J. Inherit. Metab. Disease* **32**, 135-142 (2009)]. This autosomal recessive disease results in progressive neurologic problems (ataxia) that usually develop in infancy. Pretend you were a physician specializing in metabolic diseases. Propose two hypotheses to explain the metabolic defect in this disease.

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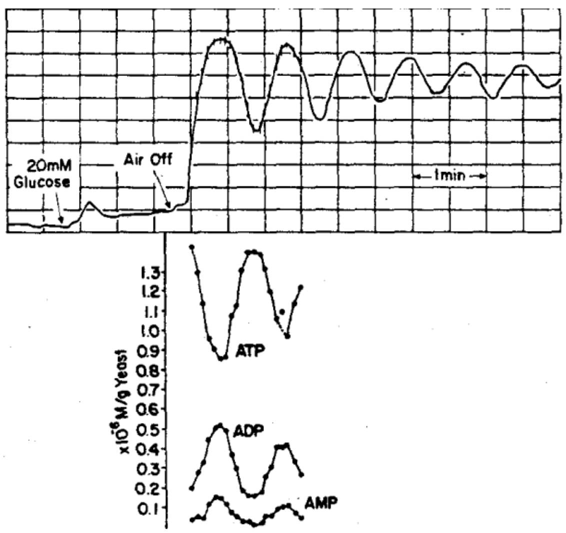
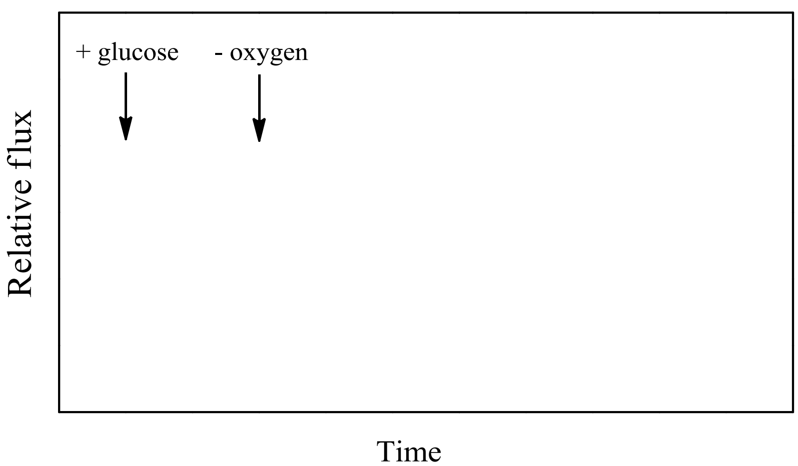
Answer **one** of the two following questions.

7. (10 Points) The oscillations of metabolites following a transition from oxygenated to deoxygenated observed in yeast cells growing on glucose medium indicate there are changes in the flow of carbon through glycolysis.

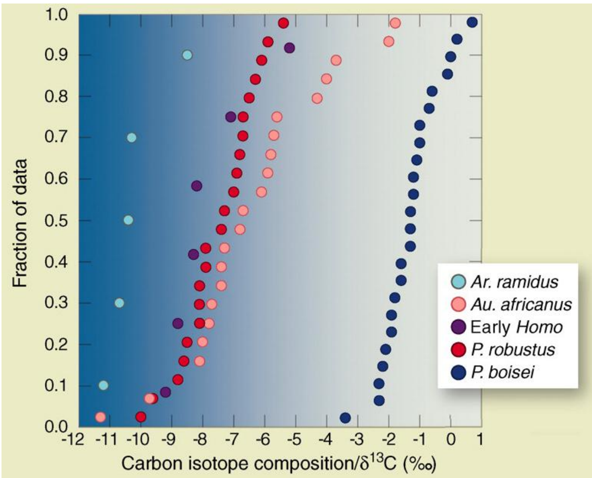



a. Draw a graph in the box provided that represents the flux of metabolites in the tail end of glycolysis after the phosphofructokinase reaction.

b. Explain your reasoning.



8. (10 points) An article in the Oct. 14 issue of *Science* [**334**, 190-193 (2011)] includes the following figure in which the $\delta^{13}C$ value was determined for tooth enamel from 75 specimens representing 5 species of fossil hominoids that lived in Africa between 0.8 and 4.4 million years ago. Each point represents a tooth from one fossil. The data are grouped by species and normalized so that data from each species can be compared.




Based on what you have learned in this course:

a. What was the research question being asked by the scientists who did this work?

b. Based on these data, what conclusions can one make?