BCHM 463 **Your Name:** _____

Biochemistry and Physiology **ID #:** _____

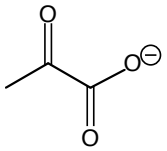
Final Exam, May 19, 2003 **Prof. Jason Kahn**

You have 120 minutes for this exam.

Exams written in pencil or erasable ink will not be re-graded under any circumstances.

You may use a calculator for this exam. No other study aids or materials are permitted.

Generous partial credit will be given, *i.e.*, if you don't know, guess.



Glucose→G6P→F6P→FBP→GAP(+DHAP)→1,3-BPG→3PG→2PG→PEP→Pyruvate

OAA→citrate→isocitrate→αKG→succinyl-CoA→succinate→fumarate→malate→OAA

Hill equation: $Y_{O_2} = \frac{(pO_2)^n}{(p50)^n + (pO_2)^n}$

Explanations should be concise and clear. I have given you more space than you should need.

Honor Pledge: Please write out the following sentence and sign it, or talk to me about it:

"I pledge on my honor that I have not given or received any unauthorized assistance on this examination."

1. Regulation of Metabolism (55 pts):

For each of the questions below, specify the pathway that is activated or inhibited, and explain why the effect makes sense physiologically.

(a; 8 pts) Why does citrate inhibit phosphofructokinase-1 (PFK-1)?

(b; 8 pts) Why does acetyl-CoA activate pyruvate carboxylase?

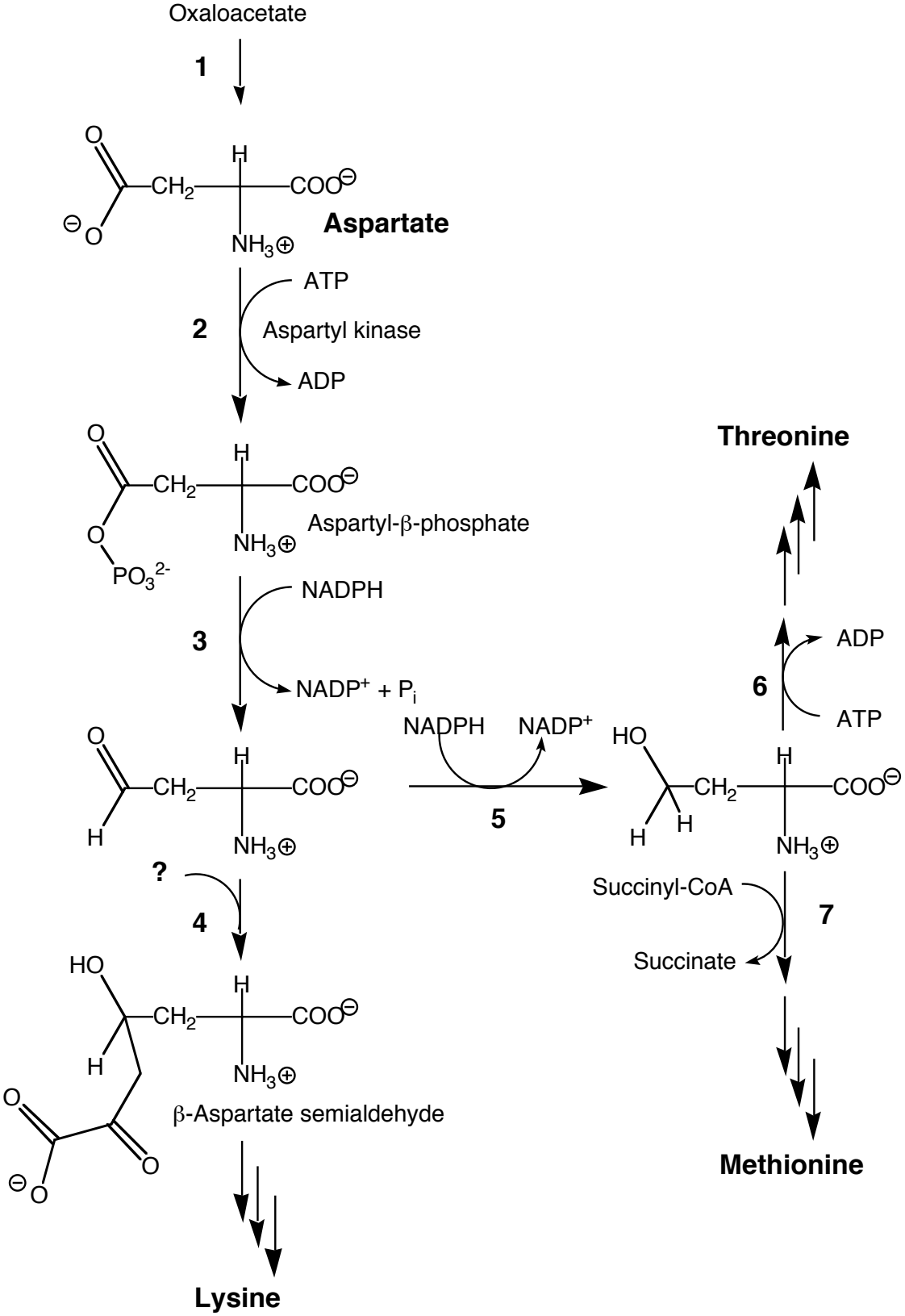
(c; 8 pts) Why does AMP inhibit fructose-1,6-bisphosphatase 1 (FBPase-1)?

(d; 16 pts) Why is pyruvate kinase inhibited upon phosphorylation by cAPK, at least in the liver? What signal is the liver responding to? Why is pyruvate kinase activated by FBP?

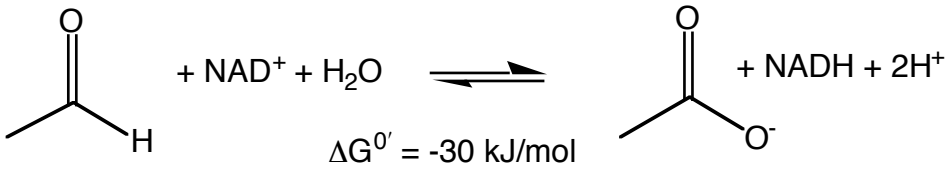
(e; 15 pts) Caffeine blocks cyclic AMP phosphodiesterase, which converts cAMP to 5′-AMP. Would caffeine tend to block or potentiate the action of glucagon, and why? What other example have we seen of a drug that acts by blocking a phosphodiesterase?

2. The Logic of Enzymology and Flux Control (60 pts):

This scheme sketches the biosynthesis of lysine, threonine, and methionine:



(a; 6 pts) Based on the equation below, which is the stronger reducing agent, NADH or acetaldehyde (circle one)? Which of the following three reactions is an aldehyde oxidation (circle one): GAP → 1,3,-BPG citrate → isocitrate F6P → FBP



(b; 8 pts) What features of aspartyl-β-phosphate give the molecule a high phosphate transfer potential? Why is it necessary to phosphorylate aspartate in step 2 when we are just going to remove the phosphate again in the process of making the aldehyde in step 3, thereby hydrolyzing ATP overall? (Hint: part a).

(c; 8 pts) The TCA cycle functions in many ways other than just Acetyl-CoA oxidation. What is the two-word phrase we have used to describe its general role in biochemistry? Which two reactions (give the numbers) in the scheme illustrate this idea?

(d; 8 pts) We discussed two main features common to pathway steps at which flux is usually regulated. What are these two features?

(e; 6 pts) Which step in the synthetic scheme above is allosterically inhibited by high concentrations of methionine, and why?

(f; 6 pts) Identify steps (give one number for each) that illustrate a group transfer reaction_____,

a redox reaction_____, and a C-C bond breakage and formation reaction_____.

(g; 10 pts) It turns out that there are three separate aspartyl kinase isozymes in an E. coli cell. They are regulated differently. Why are there three, and how do you think they are regulated (a correct answer is an oversimplification of the true situation)?

(h; 6 pts) Why is NADPH (as opposed to NADH) generally used as the reducing agent in biosynthetic pathways? The two have essentially identical reduction potentials.

(i; 8 pts) The substrate indicated by the question mark in step 4 is an old friend. Name it, and name the type of reaction.

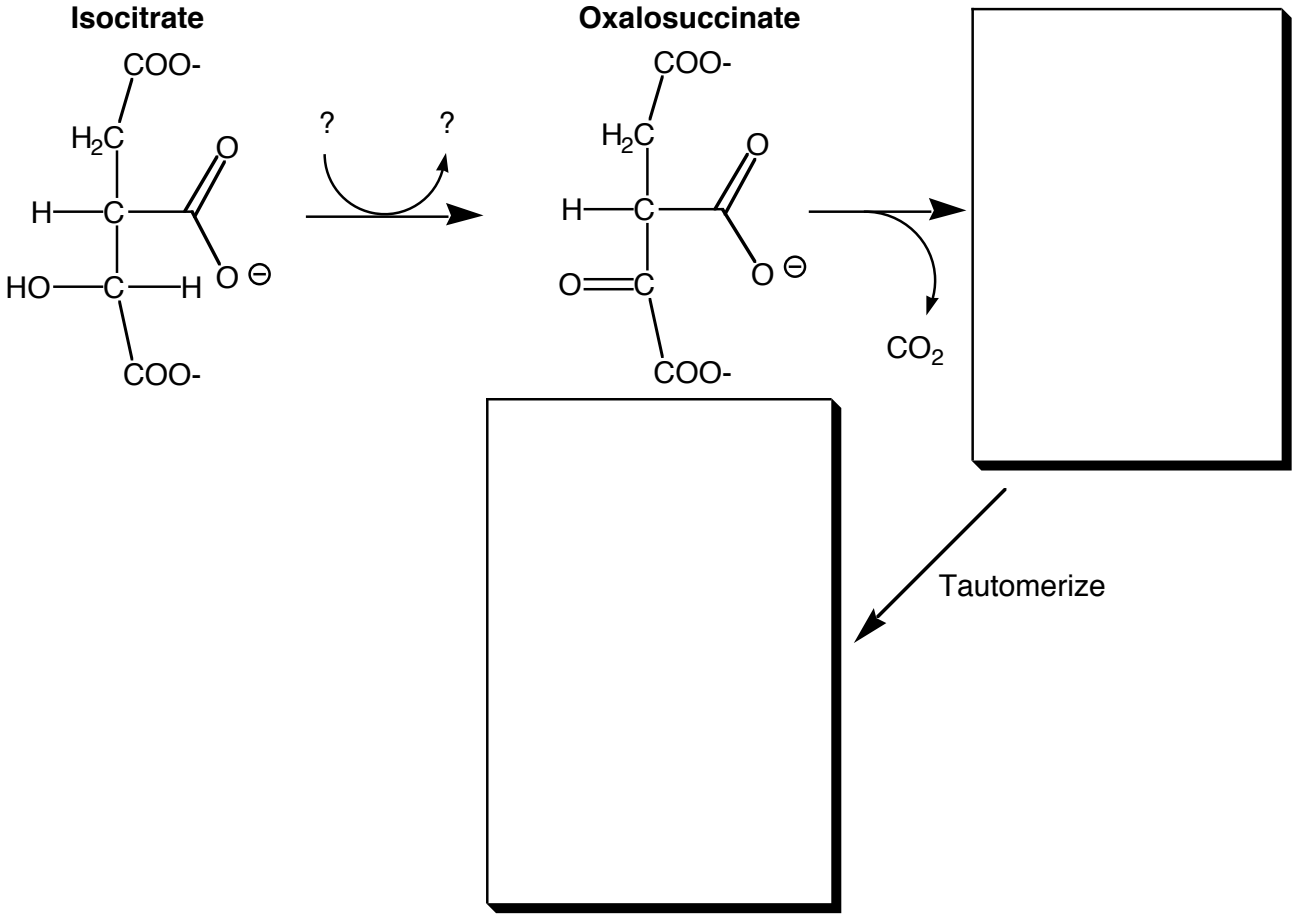
3. Arrow Pushing and Cofactors (40 pts):

The isocitrate dehydrogenase reaction of the TCA cycle is started for you below.

(a; 9 pts) What general kind of reaction is step 1, and what are the cosubstrate and coproduct?

(b; 10 pts) Circle the β-keto carboxylate moiety in the oxalosuccinate intermediate, and draw the electron-pushing arrows for the decarboxylation.

(c; 11 pts) In the box at the right, draw the enolate product of the decarboxylation, and then give the final product in the box below.



(d; 10 pts) Name the cofactor that is used for the decarboxylation of α-keto carboxylic acids, and draw the important functional part of it.

4. Oxidative Phosphorylation (50 pts):

(a; 30 pts) Recall the extended analogy for oxidative phosphorylation in class: A bowling ball is dropped off a high platform, and a worker attempts to use the liberated potential energy to lift many softballs onto a separate platform using spring-loaded seesaws. The softballs run back to the ground through a mill wheel that drives a rotary clamping press. Give the corresponding analogies for each of the following (4 pts each):

(4 pts) The oxidation of NADH

(4 pts) Protons

(5 pts) Using sulfate instead of oxygen as the terminal electron acceptor.

(4 pts) The F0 subunit of the F1-F0 ATPase

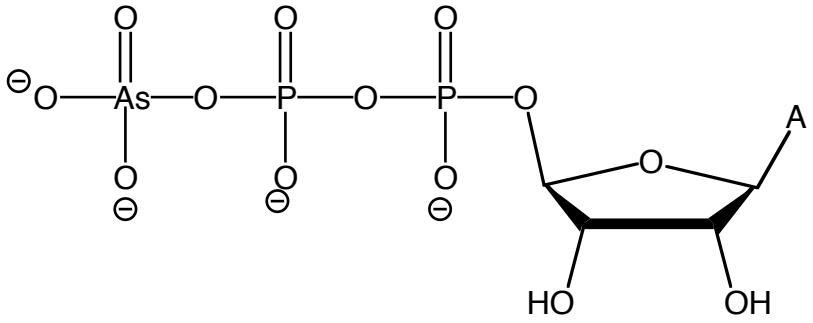
(4 pts) The F1 subunit of the F1-F0 ATPase

(4 pts) Intermediate ledges for the bowling ball

(5 pts) $FADH_2$ (5 pts)

(b; 6 pts) What rationale did we give for the stepwise transfer of electrons?

(c; 14 pts) Arsenic is a poison partly because the F1-ATPase can add arsenate to ADP to make the arsenate ester shown below. The arsenate ester, however, breaks up spontaneously and rapidly. Why is this bad for the cell? What is the general name for this kind of poison? What happens to the victim?



5. Hemoglobin, Altitude, Performance, and Fuel (45 pts)

(a; 10 pts) On a plot of partial saturation vs. pO2, sketch how the increased 2-3-BPG concentration at high altitude increases the efficiency of O2 delivery.

(b; 20 pts) Why is high-altitude training believed to increase athletic performance? (Answer in terms of which pathways will be made to work more efficiently.) Is altitude training likely to be most effective for sprinters or marathoners? Why? There are many adaptations to altitude; consider only BPG for this question.

(c; 15 pts) Draw the disaccharide composed of two D-glucopyranosides linked by a β-1,4 linkage. What abundant polymer is made up of linkages like this? Why is it so stable?

SCORE

1. **Regulation of Metabolism (55 pts):** _____
2. **The Logic of Enzymology and Flux Control (60 pts):** _____
3. **Arrow Pushing and Cofactors (40 pts):** _____
4. **Oxidative Phosphorylation (50 pts):** _____
5. **Hemoglobin, Altitude, Performance, and Fuel (45 pts)**

Total: (Out of 250 points) _____