

C483 Exam 3
Spring 2016

Name Key _____ Seat Number _____

Student ID _____ Discussion section: Tues 3:35 Tues 4:40

The last page of this exam contains equations and scratch area.

This exam contains 110 points. The highest score you may earn on this exam is 100 points.

- 1. _____/20pts
- 2. _____/10pts
- 3. _____/20pts
- 4. _____/10pts
- 5. _____/10pts
- 6. _____/10pts
- 7. _____/10pts
- 8. _____/10pts
- 9. _____/10pts

Total:

Regrading: All requests for regrades must be submitted in writing within 48 hours of the return of the exam. You must explicitly state what has been misgraded and why it is an error. The entire exam will be regraded, which could result in points being added or deducted overall.

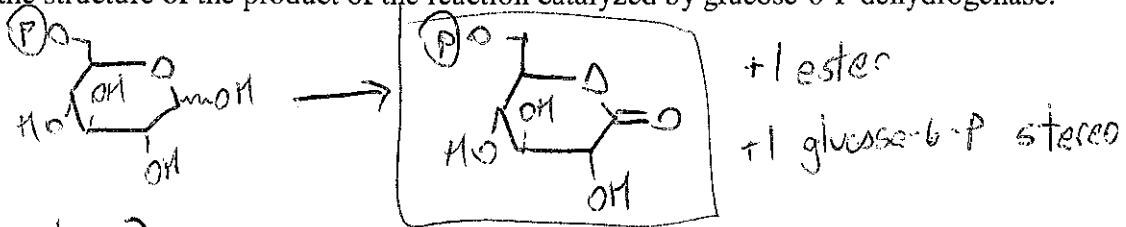
Section 1: Reading guides (50 points)

1. 20 pts. Fill in the blanks (2 points each.)

A. In addition to acetyl CoA, odd chain fatty acids produce Succinyl CoA as the product of beta-oxidation through the action of cobalamine (vitamin B₁₂.)

B. The molecule malonyl CoA is an inhibitor of beta-oxidation of fatty acids.

C. Draw the structure of the product of the reaction catalyzed by glucose-6-P dehydrogenase.



acyl CoA DH)
(succinate)
DH

D. Complex 2 is a membrane bound enzyme that carries out a redox reaction that contributes to the Q-pool but does not contribute to the proton gradient.

E. The formation of oxaloacetate from pyruvate is an example of an anaplerotic, or "filling up" reaction.

F. The binding mechanism of ATP synthase uses the energy stored in a proton gradient to power a molecular motor.

G. Cholesterol synthesis is regulated at the enzyme HMG-CoA reductase, which is the target of a class of drugs called statins.

H. Fructose can be fed into glycolysis by being transformed into fructose-6-phosphate. Under anaerobic conditions, one molecule of fructose can be used to produce how many net ATP using this pathway? 2

I. The coenzyme needed in both the first step of gluconeogenesis from pyruvate and the activation of acetyl CoA for fatty acid synthesis is biotin.

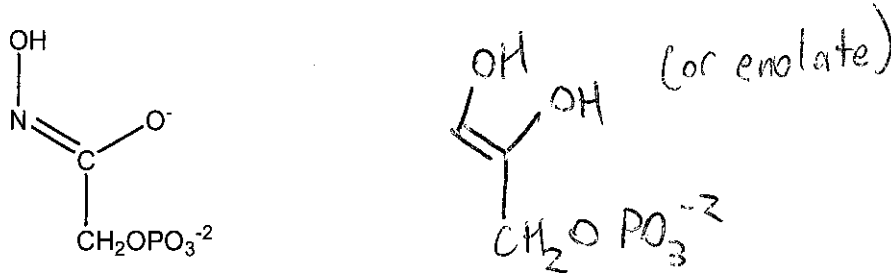
J. Glucose-1-phosphate is released in glycogen degradation when the glycosidic bond is broken not by hydrolysis, but rather phosphorylation.

2. 10 pts. Write True or False (1 point each)

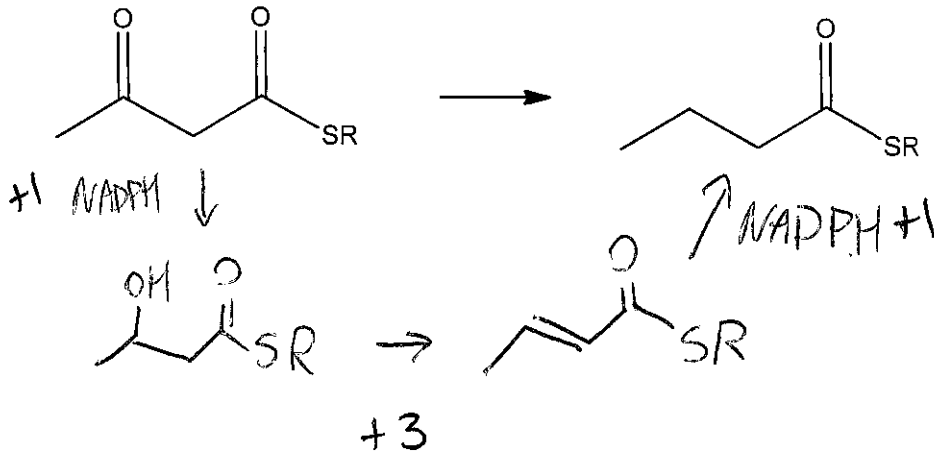
- A. True The committed step of glycolysis is the second thermodynamically irreversible step of the pathway starting from glucose.
- B. False In the pentose phosphate pathway, the reaction of ribulose-5-phosphate to ribose-5-phosphate is catalyzed by a transketalase.
- C. False α -ketoglutarate dehydrogenase is more like isocitrate dehydrogenase than pyruvate dehydrogenase.
- D. True Citrate is an activator of fatty acid synthesis by promoting the carboxylation of acetyl CoA.
- E. True Increasing the concentration of citric acid cycle intermediates increases flux through the cycle.
- F. False (Refer to the table at the end of the exam.) NAD^+ has a greater tendency to be reduced than does coenzyme Q.
- G. False The formation of pyruvate from phosphoenolpyruvate is so energetically favorable that, once pyruvate is formed, the cell can never transform it back into PEP.
- H. False Genetic defects in HDL receptors can lead to high levels of "bad cholesterol" in the blood.
- I. False Iron-sulfur clusters and Q are similar in that they can accept or donate either one or two electrons at a time.
- J. False Phosphofructokinase and glycogen synthase are reciprocally regulated with each other.

3. 20 pts. Short answer (5 points each)

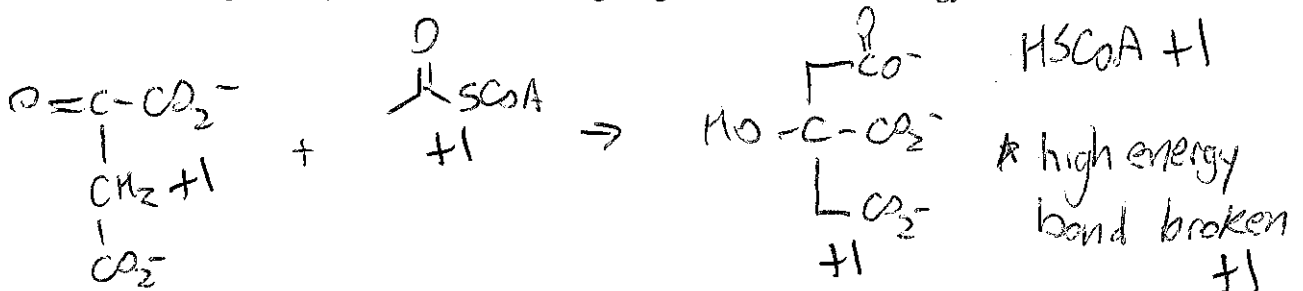
A. Phosphoglycohydroxamate binds 150 times tighter than dihydroxyacetone phosphate to triose phosphate isomerase. Based on this information, propose a structure for the intermediate of the triose phosphate isomerase reaction.



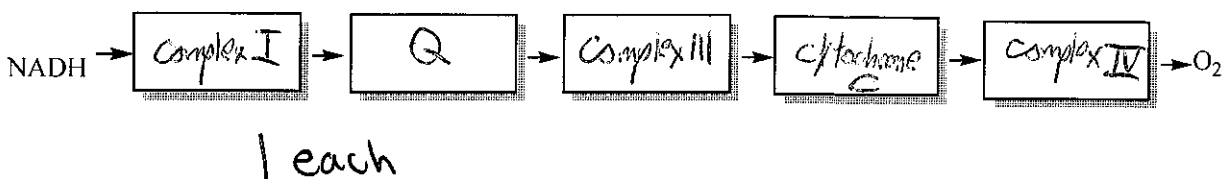
B. Show the steps involved in reduction of the ketone in fatty acid synthesis. Include any cofactors necessary for each step.



C. Draw the starting materials and products of the reaction catalyzed by citrate synthase, the first step of the citric acid cycle. Explain why this reaction has a large negative standard free energy.

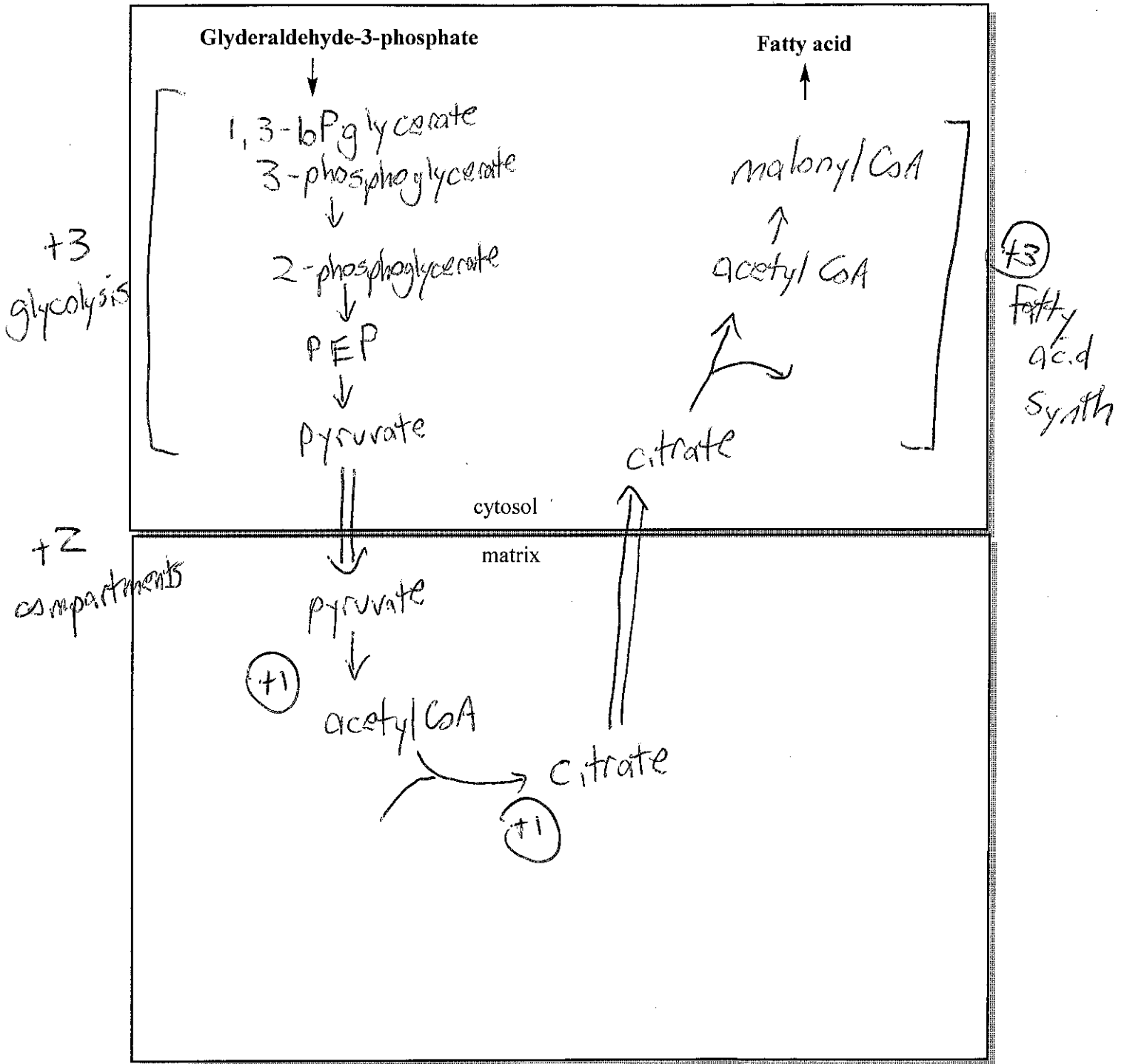


D. List the protein complexes and mobile carriers, in order, that carry electrons from NADH to molecular oxygen in the electron transport chain.

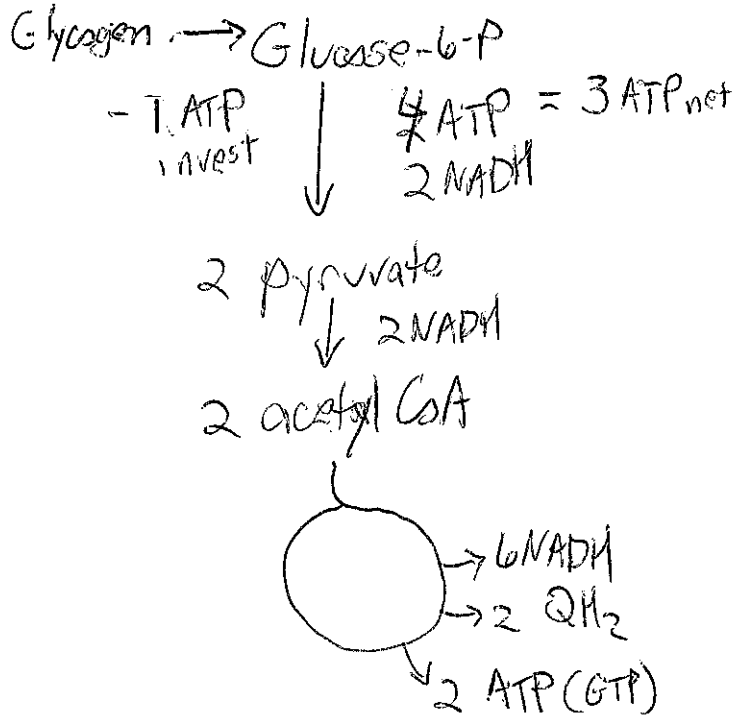


Section 2: Problems (10 points each)

4. Carbon atoms originating in glyceraldehyde-3-phosphate can end up incorporated into fatty acids under conditions of abundant metabolic fuel. Name or draw structures for ALL the intermediates along this pathway, including them in the correct compartment.



5. Give a full accounting of how many ATP can be net produced starting from EITHER one molecule of glucose stored in glycogen OR one molecule of palmitate (16-carbon fatty acid) in the cytosol. Assume that the catabolism is conducted under aerobic conditions. Your full accounting should be detailed—including the number of substrate-level phosphorylations and where reduced cofactors are produced.



total

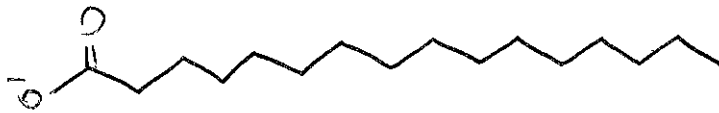
5 substrate level ATP

2 NADH_(cytosol) = 3 or 5

8 NADH_(matrix) = 20 ATP

2 QH₂ = 3 ATP

total = 31 - 33 ATP



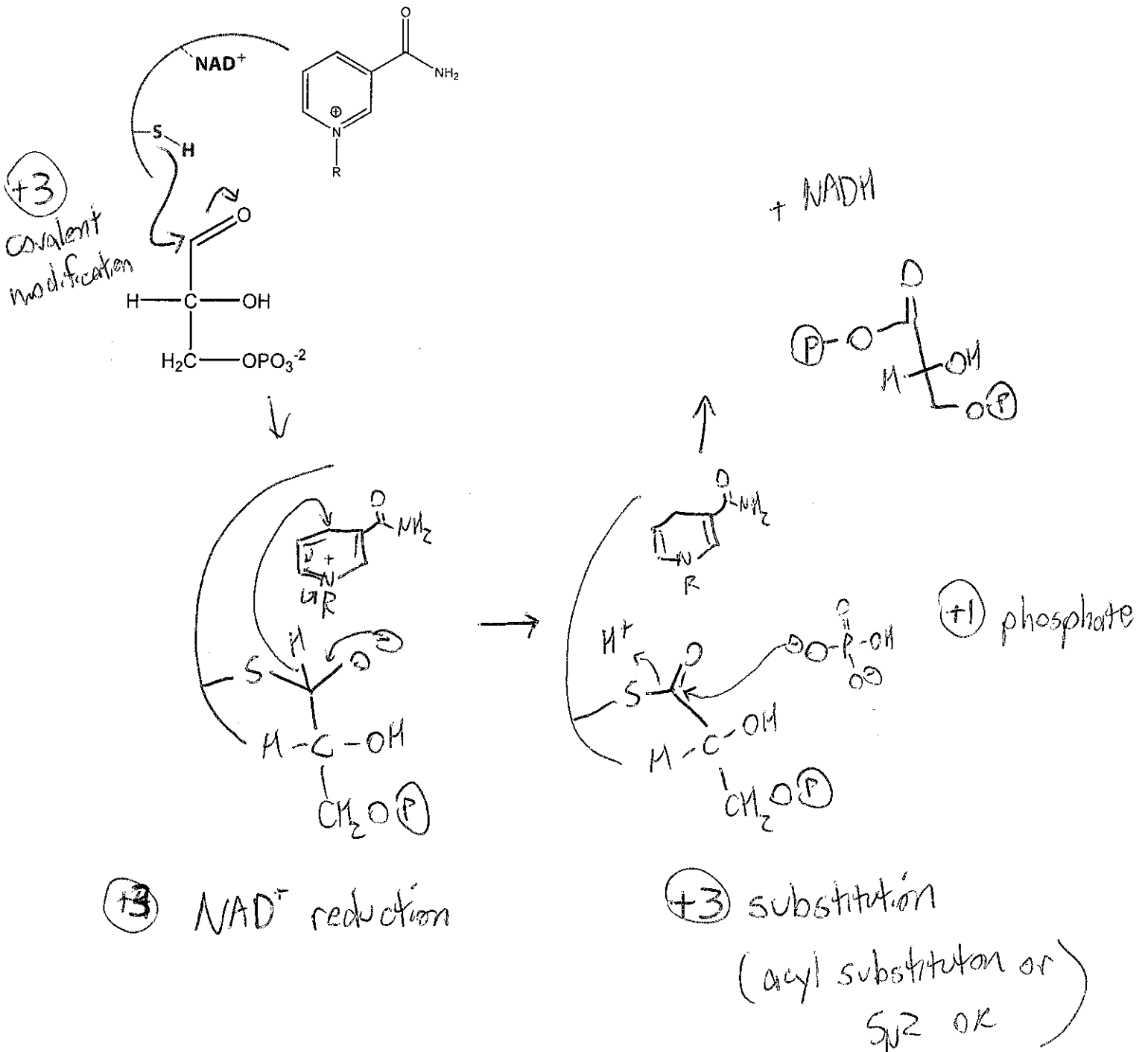
-2 ATP
activate to
acyl CoA

7 Oxidations = 7 QH₂ $\times 1.5 = 10.5$
7 NADH $\times 2.5 = 17.5$

8 Acetyl CoA $\times 10$ ATP = 80
(3 NADH, QH₂, ATP) 108 ATP
- 2 invest

106 ATP

6. Provide a full, enzyme-catalyzed arrow mechanism of glyceraldehyde-3-P dehydrogenase, including the role of the active site cysteine residue. What is the source of phosphate? Use the structure of NAD⁺ is provided.



7. Is net synthesis of glucose in mammals possible from the following compounds?

A. an 18:1 fatty acid

No

B. a 15:0 fatty acid

yes

C. glyceraldehyde-3-phosphate

yes

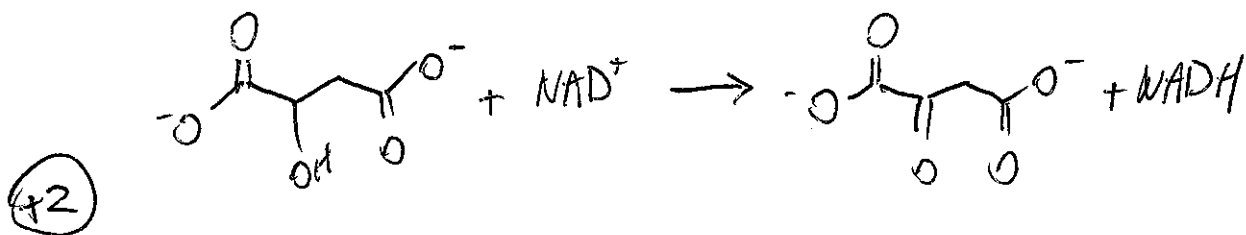
D. Leucine, which is degraded into acetyl CoA and acetoacetate

No

E. phenylalanine, which is degraded into fumarate and acetoacetate

yes

8. Write out the reaction (structures) for the oxidation of malate by NAD^+ .



Calculate the standard free energy change for the oxidation of malate by NAD^+ .

malate	→	Oxaloacetate	$\mathcal{E}^{\circ} = +0.166 \text{ V}$	(+3)
NAD^+	→	NADH	$\mathcal{E}^{\circ} = -0.315 \text{ V}$	
			$\Delta \mathcal{E}^{\circ} = -0.149 \text{ V}$	

(+3)

$$\Delta G^{\circ} = -nF\Delta \mathcal{E}^{\circ}$$

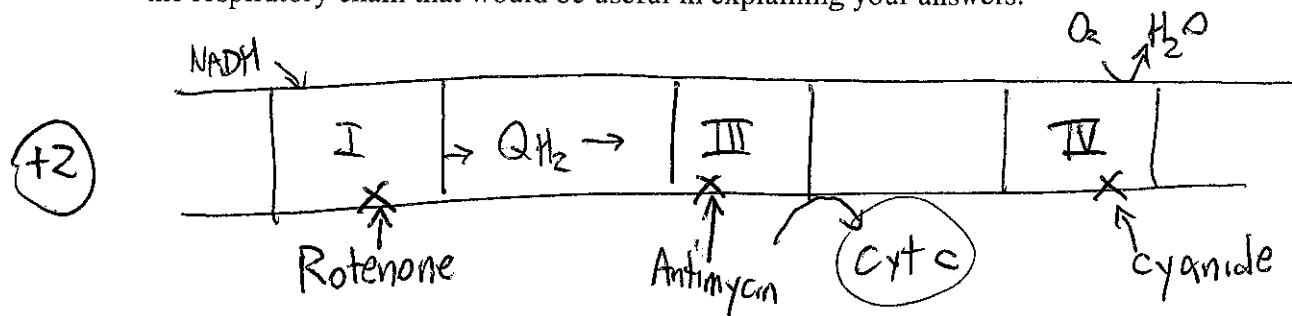
$$= -2 \left(96,485 \frac{\text{J}}{\text{molV}} \right) (-0.149 \text{ V}) = +28.8 \frac{\text{kJ}}{\text{mol}}$$

Is this reaction spontaneous under standard conditions?

No (+2)

9. Section 3: Case study (10pts) A series of respiratory poisons have recently been studied. Rotenone is known to block electron transport in Complex I. Antimycin (an antibiotic) is known to block electron transport in Complex III, and cyanide binds to Complex IV in the oxygen binding center. Nigericin and valinomycin are used together as antibiotics because they insert into the inner membrane of the mitochondria and act as a K^+/H^+ antiporter and a K^+ channel, respectively.

A. Ascorbate (vitamin C) is being investigated as a remedy for these poisons because it is able to donate a pair of electrons to cytochrome c. Would an infusion of vitamin C be able to bypass rotenone-blocked, antimycin-blocked, or cyanide blocked mitochondria? Draw a schematic of the respiratory chain that would be useful in explaining your answers.



(+2) - Vitamin C can bypass rotenone + Antimycin because it dumps e^- further down the chain.

(+2) - Cyanide blocks the very end, so vitamin C cannot bypass it.

B. Explain how nigericin/valinomycin acts as a respiratory poison and why vitamin C is unable to overcome its effects.

(+2) Acting together, Nigericin and valinomycin disrupt the proton gradient by allowing the membrane to become permeable.

(+2) Vitamin C cannot overcome it because, even though the ETC continues + pumps protons, the gradient is dissipated.