C483 Exam 3
Fall 2017

Name Key Seat Number ____________

Student ID ____________________

Page 11 of this exam contains equations and other helpful information. You may remove page 12 from the exam for scratch paper.

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. The committed step of glycolysis is catalyzed by the enzyme PFK.

B. Of the ten steps of glycolysis, four of them are catalyzed by which type of enzyme?
Kinase

C. The chemical driving force that gives a large standard free energy change to the reaction of phosphoenolpyruvate with ADP to form ATP and pyruvate is Enol tautomerization

D. A futile cycle in which glucose-6-P were incorporated into glycogen and then released from glycogen to reform glucose-6-P would cost a total of one ATP equivalent(s).

E. Under starvation conditions, ketone bodies are produced from excess acetyl CoA because of the low available concentration of the citric acid cycle intermediate OAA.

F. Of all the citric acid cycle reactions, only succinylCoA synthetase performs a substrate-level phosphorylation.

G. High levels of acetyl CoA can activate the enzyme pyruvate carboxylase, which can lead to greater flux through the citric acid cycle.

H. The glyoxylate pathway can be used by plants and some bacteria to make net glucose from acetyl CoA.

I. According to the chemiosmotic theory, it is the protonmotive force that couples the electron transport chain to oxidative phosphorylation.

J. The molecule malonyl CoA is made in the regulated step of fatty acid synthesis, and is an inhibitor of fatty acid oxidation.

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

A. True There are three thermodynamically irreversible reactions in both the glycolysis pathway and in the citric acid cycle.

B. True Of the eight steps of the citric acid cycle, four of them are catalyzed by dehydrogenases.

C. False Transaldolases use no cofactor when they transfer a two-carbon fragment from one carbohydrate to another.

D. True Glycogen is degraded using phosphorolysis in both liver and muscle tissue.

E. True Although radiolabeled carbon atoms from acetyl CoA can end up in glucose through metabolic pathways, no net glucose can be made from acetyl CoA in humans.

F. False An artificial ATP synthase that had 11 subunits in its *c* ring would be more efficient than human ATP synthase.

G. True One of the distinctions between fatty acid synthesis and degradation is cellular location of the pathway.

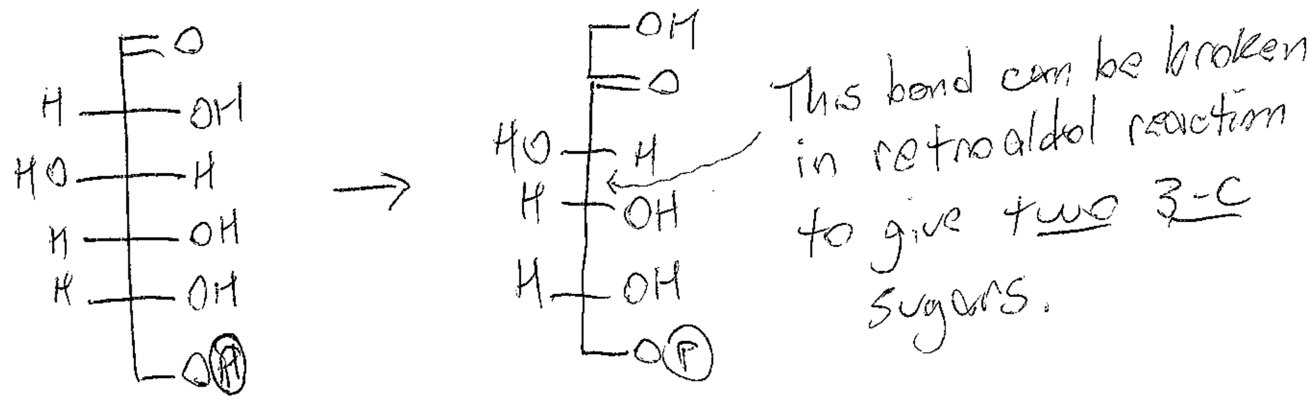
H. False Acetyl CoA is transformed into squalene in the committed step of cholesterol synthesis.

I. True The transformation of three 5-carbon sugars into two 6-carbon sugars and a 3-carbon sugar requires no input of ATP.

J. True A portion of an odd chain fatty acid can be used to make net glucose in humans..

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

A. Draw the straight chain structures of the reactants and products in the reaction catalyzed by phosphoglucose isomerase, and explain why this reaction is necessary prior to the reaction catalyzed by aldolase.



B. Calculate the change in standard reduction potential for the oxidation of succinate by NAD^+. How does your answer explain why this cofactor is not used physiologically?

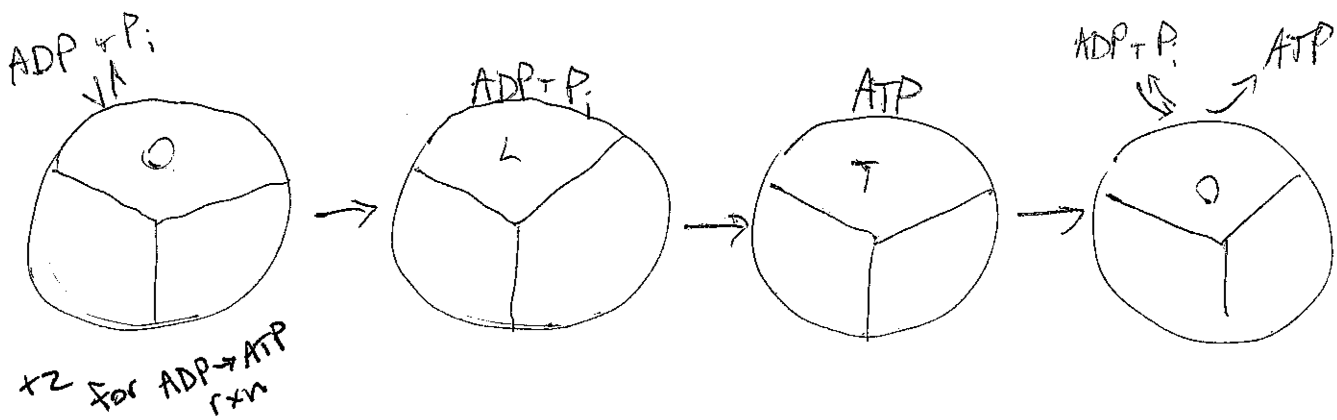
succinate → fumarate $\varepsilon^\circ = -0.031\ V$

NAD^+ → NADH $\varepsilon^\circ = -0.315\ V$ +2

$\Delta\varepsilon^\circ = -0.346\ V$ +1

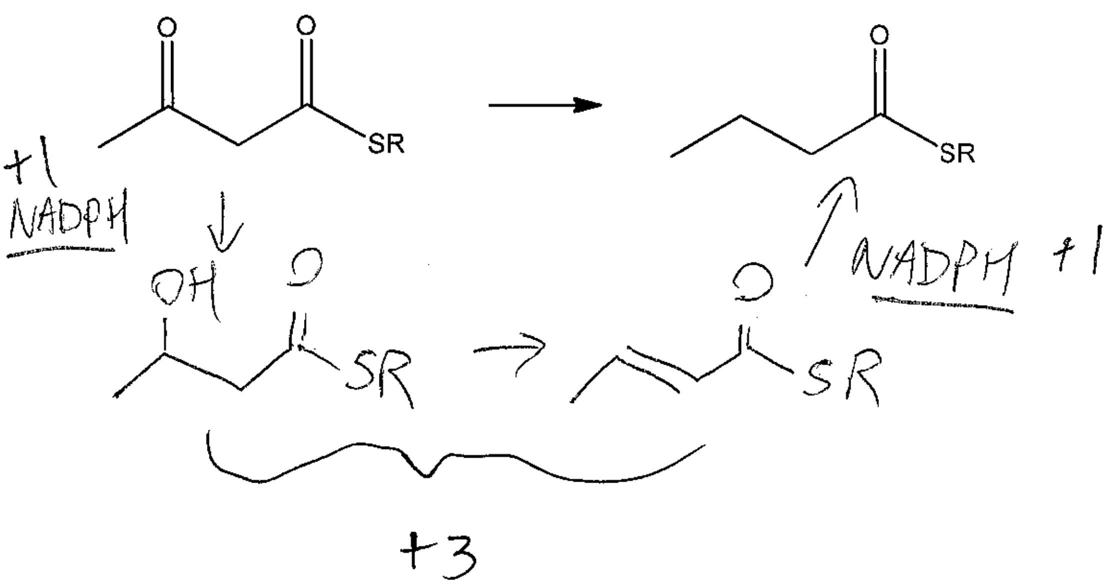
The reduction potential for NAD^+ is too low – a nonspontaneous rxn under standard conditions. +2

C. Draw a schematic of the binding change mechanism for ATP synthesis in oxidative phosphorylation.



+3 for O/L/T trimer

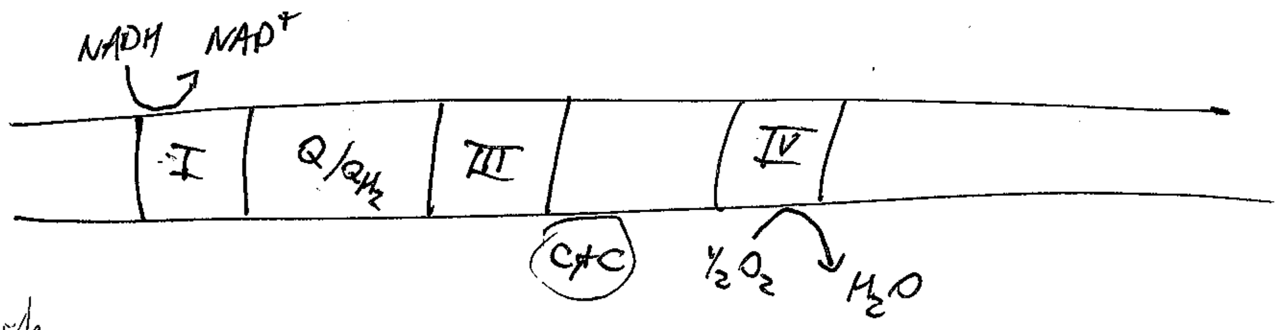
D. Show the intermediates of the steps involved in reduction of the ketone in fatty acid synthesis. Indicate which redox cofactor(s) are involved in each step.



Section 2: Problems (10 points each)

4. A. Draw a schematic of the electron transport chain, including complexes and mobile carriers, to show the flow of electrons from NADH in the matrix onto O_2.

+4



-1 each mistake

B. Calculate the theoretical P:O ratio of NADH in the matrix. Show all work.

+4

$$\left(\frac{10\ H^+}{NADH}\right)\left(\frac{3\ ATP}{8\ H^+}\right) = 3.7\ \frac{ATP}{NADH}$$

or

$$\frac{3\ ATP}{8\ H^+}\left(\frac{10\ H^+}{NADH}\right)\left(\frac{NADH}{\frac{1}{2} O_2}\right) = 3.7\ \frac{ATP}{\frac{1}{2} O_2}$$

C. The Q-cycle doubles the proton pumping efficiency of Complex III. Calculate the P:O ratio of the electron chain without the Q-cycle.

+2

- Complex 3 would pump 2 H^+ rather than 4 H^+
- Total = 8 H^+ per NADH

$$\left(\frac{3\ ATP}{8\ H^+}\right)\left(\frac{8\ H^+}{NADH}\right) = 3.0\ \frac{ATP}{NADH}$$ rather than 3.7

5. Draw all intermediates of the gluconeogenesis pathway from two molecules of lactate to form one molecule of glucose. Label each step that requires or uses NADH or ATP.

8 pts for intermediates

-1/error

How many ATP equivalents would be need to transform one molecule of phosphoenolpyruvate and one molecule of dihydroxyacetone phosphate into a molecule of glucose? Explain.

DHAP

→ Glc

PEP → → → GAP

1 ATP

1 NADH (2.5 or 1.5)

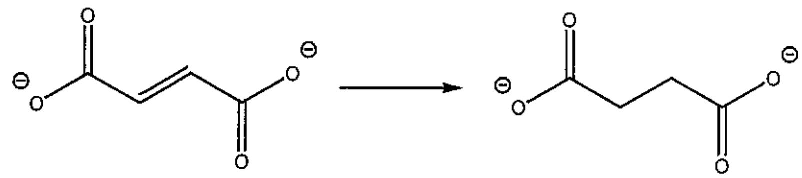
total of 3.5 eq. ATP

(also accept 2.5 eq)

6. For each of the following enzymes or reactions, list each of the following cofactor(s) that are necessary: $NAD^+/NADH$, $NADP^+/NADPH$, biotin, TPP, $FAD/FADH_2$, CoA. You many write more than one of these cofactors. If no cofactor is necessary, write "no cofactor."

A. acetylCoA carboxylase biotin

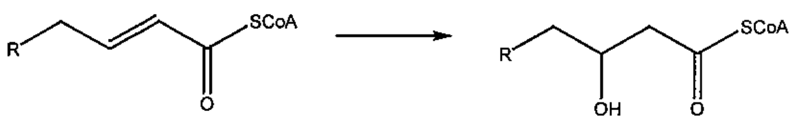
B.



$FAD/FADH_2$

C. aldolase none

D.

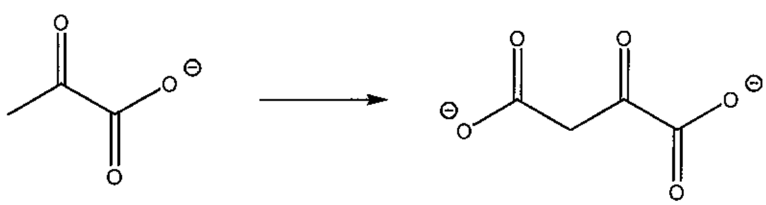


none

E. Glucose-6-phosphatase none

F. isocitrate dehydrogenase $NAD^+/NADH$

G.



biotin

H. pyruvate → lactate $NAD^+/NADH$

I. Glucose-6-phosphate dehydrogenase $NADP^+/NADPH$

J. transketalase TPP

7. Draw an arrow mechanism for the reaction of glyceraldehyde-3-phosphate with inorganic phosphate and NAD^+ to produce 1,3-bisphosphoglycerate and NADH. The enzyme, glyceraldehyde-3-phosphate dehydrogenase (GAPDH), uses a cysteine sidechain in covalent catalysis. Draw the full structure of NAD^+, as given on page 11, in your mechanism.

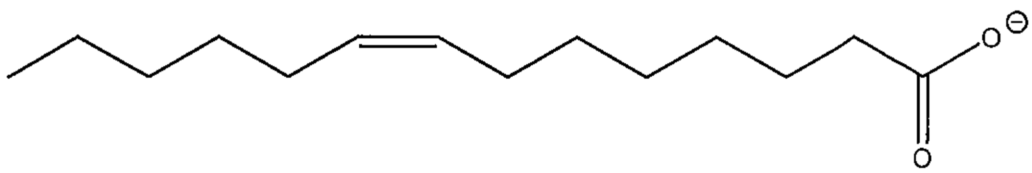
+2 GAP, 1,3 bPG

+2 NAD^+/NADH

see Ch13 mechanism

+6 arrows/intermediates

8. What is the NET amount of ATP that can be produced by full oxidation of the following fatty acid assuming oxidative phosphorylation is fully active? Show your work, including the number of reduced cofactors produced in this process.



14 C required   6 β-oxidation steps

(+2) 6 NADH ×2.5

(+2) 5 QH_2 (because of unsaturation) ×1.5   } 22.5 ATP

(+2) 7 Acetyl CoA

(+2) { 3 NADH, 1 QH_2, 1 substrate level }   70 ATP

92.5 ATP

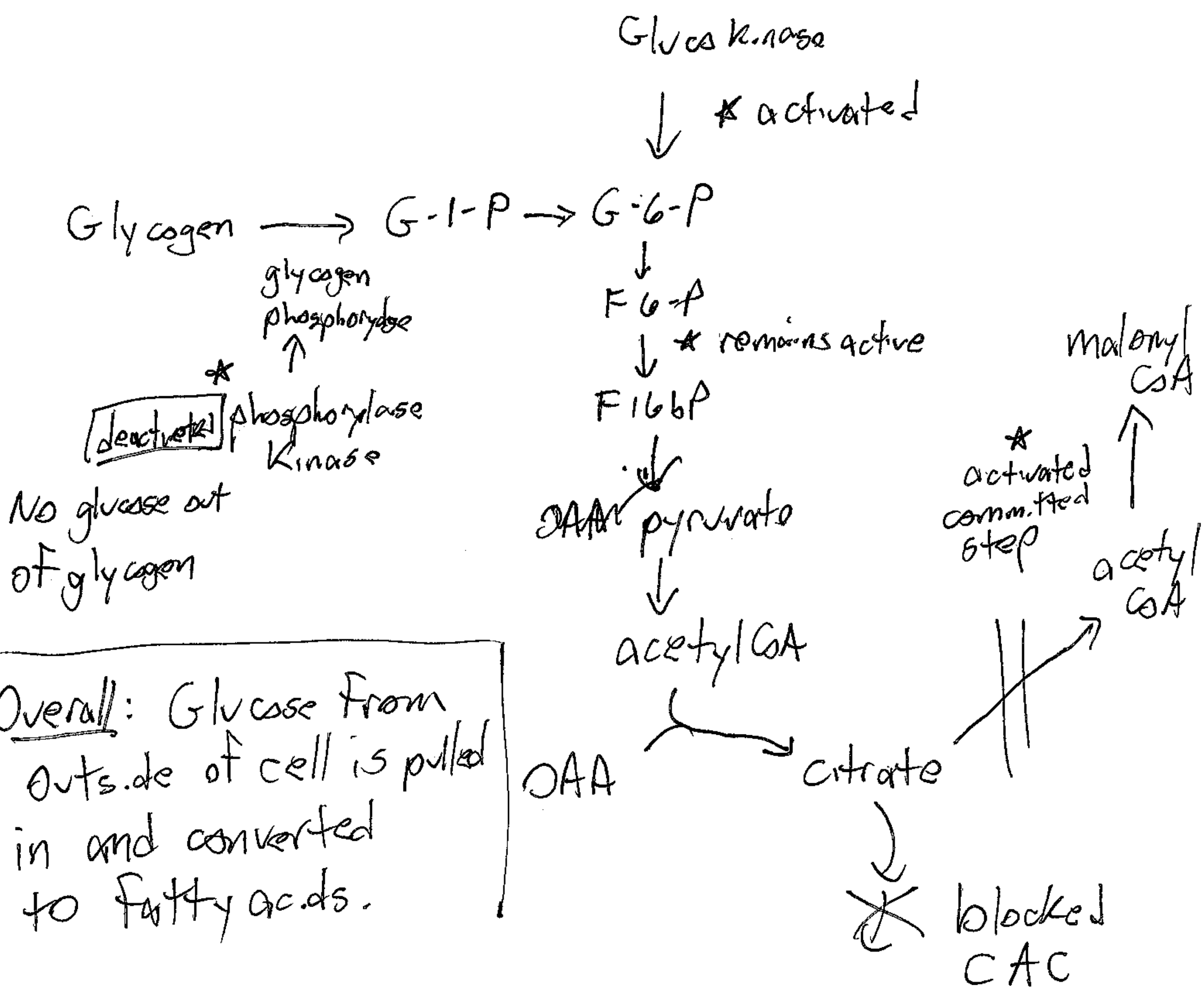
(+2) −2 ATP for activation   90.5 ATP

9. Section 3: Case study (10pts) Compound X has been administered to mouse liver cell tissue and has been found to have the following effects:

- +1 Fructose-2,6-bisphosphatase is inactivated
- +1 The activity of phosphorylase kinase is decreased by 80% through inhibition of a signal transduction pathway
- +2 Glucokinase and hexokinase are both activated by 50%
- +2 Isocitrate dehydrogenase activity is significantly lowered.
- +2 Levels of acetylCoA carboxylase rise through over-expression.

+2 Overall

What is the net effect metabolic effect of Compound X when the liver tissue is presented with high levels of glucose? Incorporate each piece of data into your answer.



Overall: Glucose from outside of cell is pulled in and converted to fatty acids.

Data Tables and equations:

Standard Free Energy Change for Phosphate Hydrolysis

Compound	$\Delta G^{\circ\prime}$ (kJ · mol^{-1})
Phosphoenolpyruvate	−61.9
1,3-Bisphosphoglycerate	−49.4
ATP → AMP + PP_i	−45.6
Phosphocreatine	−43.1
ATP → ADP + P_i	−30.5
Glucose-1-phosphate	−20.9
$PP_i \rightarrow 2\,P_i$	−19.2
Glucose-6-phosphate	−13.8
Glycerol-3-phosphate	−9.2

[TABLE 15-1] Standard Reduction Potentials of Some Biological Substances

Half-Reaction	$\mathcal{E}^{\circ\prime}$ (V)
	0.815
	0.48
	0.42
Cytochrome a_3 (Fe^{3+}) + e^- ⇌ cytochrome a_3 (Fe^{2+})	0.385
Cytochrome *a* (Fe^{3+}) + e^- ⇌ cytochrome *a* (Fe^{2+})	0.29
Cytochrome *c* (Fe^{3+}) + e^- ⇌ cytochrome *c* (Fe^{2+})	0.235
Cytochrome c_1 (Fe^{3+}) + e^- ⇌ cytochrome c_1 (Fe^{2+})	0.22
Cytochrome *b* (Fe^{3+}) + e^- ⇌ cytochrome *b* (Fe^{2+})(*mitochondrial*)	0.077
Ubiquinone + 2 H^+ + 2 e^- ⇌ ubiquinol	0.045
$Fumarate^-$ + 2 H^+ + 2 e^- ⇌ $succinate^-$	0.031
FAD + 2 H^+ + 2 e^- ⇌ $FADH_2$ (*in flavoproteins*)	~0.
$Oxaloacetate^-$ + 2 H^+ + 2 e^- ⇌ $malate^-$	−0.166
$Pyruvate^-$ + 2 H^+ + 2 e^- ⇌ $lactate^-$	−0.185
Acetaldehyde + 2 H^+ + 2 e^- ⇌ ethanol	−0.197
S + 2 H^+ + 2 e^- ⇌ H_2S	−0.23
Lipoic acid + 2 H^+ + 2 e^- ⇌ dihydrolipoic acid	−0.29
NAD^+ + H^+ + 2 e^- ⇌ NADH	−0.315
$NADP^+$ + H^+ + 2 e^- ⇌ NADPH	−0.320
$Acetoacetate^-$ + 2 H^+ + 2 e^- ⇌ 3-$hydroxybutyrate^-$	−0.346
$Acetate^-$ + 3 H^+ + 2 e^- ⇌ acetaldehyde + H_2O	−0.581

Source: Mostly from Loach, P. A., In Fasman, G. D. (ed.), *Handbook of Biochemistry and Molecular Biology* (3rd ed.), Physical and Chemical Data, Vol. I, pp. 123 - 130, CRC Press (1976).

$$\Delta G = RT \ln\frac{[X]final}{[X]initial} + Z F \Delta\psi \qquad \Delta G^{\circ\prime} = -nF\Delta\,\mathcal{E}^{\circ\prime} \qquad \Delta G = -nF\Delta\,\mathcal{E}$$

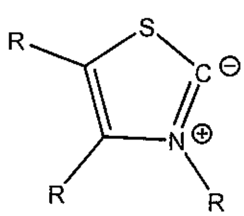
$$R = 8.314 \text{ J/ mol} \cdot \text{K} \qquad \mathcal{E} = \mathcal{E}^{\circ\prime} - \frac{RT}{nF}\ln\frac{A(reduced)}{A(oxidized)}$$

$$F = 96{,}485 \text{ J/V} \cdot \text{mol}$$

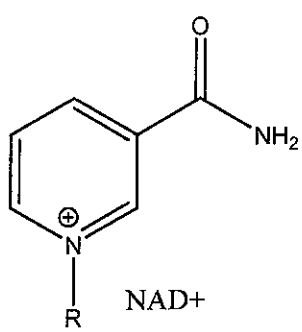
$$\Delta G^{\circ\prime} = -RT \ln K_{eq}$$

$$\Delta G_{\text{reaction}} = \Delta G^{\circ\prime}_{\text{reaction}} + RT \ln\frac{[\text{products}]}{[\text{reactants}]}$$

Cofactor Structures:

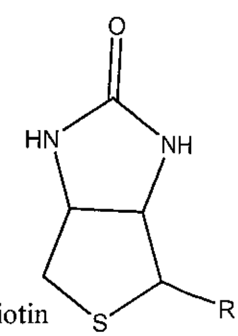


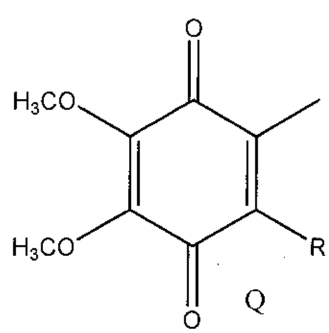
TPP



NAD+

biotin





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Scratch paper: Nothing on this page will be graded. You can remove this page, but please turn it in with your exam.