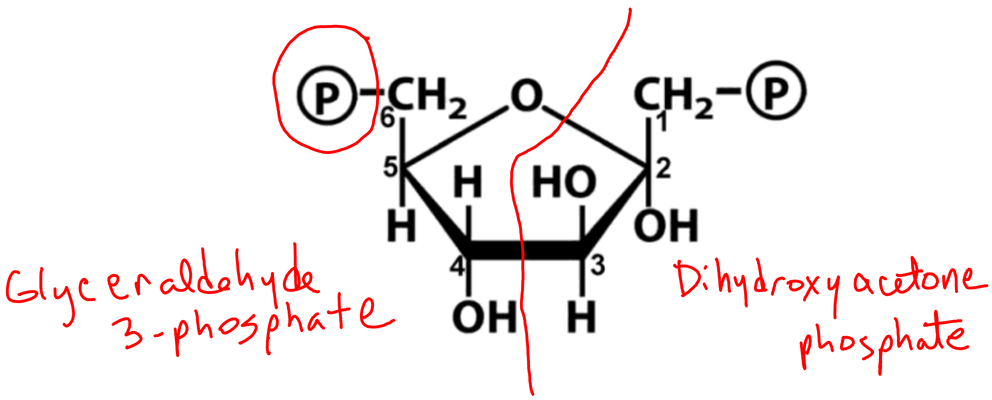
# KEY-PROBLEM SET #1-METABOLISM

Monday, April 21, 2008
3:39 PM

**MCB102 / Metabolism**
**Problem Set #1**
**Spring 2008**

**These are example problems, which are similar to those you may see on the final exam.**

**QUESTION 1: The sugar drawn below is split during glycolysis.**




**(I)** What is the name of the sugar?

FRUCTOSE 1,6-bisphosphate

**(II)** Circle the phosphate group that was added to this sugar by the enzyme hexokinase.

**(III)** Draw a line that bisects the hexose sugar into two pieces according to the enzymatic cleavage performed during glycolysis.

**(IV)** What is the name of the enzyme that performs the cleavage?

Aldolase

**(V)** Label each half of the cleaved hexose on the drawing with the name of the products.

**QUESTION 2: True/False. Circle the correct answer. If you answer false, explain why in one sentence below each part.**

**(I)** Lactate is oxidized by NADH to produce pyruvate, which feeds into gluconeogenesis.

TRUE or FALSE

Lactate is oxidized by $NAD^+$ to make pyruvate, which feeds into gluconeogenesis.

**(II)** It is critical to regulate the reversible steps of glycolysis to prevent "futile cycling."

TRUE or FALSE

It is critical to regulate the irreversible steps of glycolysis to prevent "futile cycling" with competing reactions in the gluconeogenesis pathway.

**(III)** If a cell has excess AMP, then glycolysis is stopped at the pyruvate kinase step.

TRUE or FALSE

If a cell has excess ATP, then glycolysis is stopped at the pyruvate kinase step.

**(IV)** Autotrophs obtain energy from sunlight or minerals and carbon from organic compounds or $CO_2$.

TRUE or FALSE

Autotrophs obtain energy from sunlight or minerals & carbon from $CO_2$.

**(V)** The $\Delta G'^{o}$ of hydrolysis for the removal of a phosphoryl group on phosphoenolpyruvate is greater in magnitude than that for the gamma phosphate of ATP.

TRUE or FALSE

**(VI)** GTP is used in glycolysis at the step in which oxaloacetate is converted to pyruvate.

TRUE or FALSE

GTP is used in gluconeogenesis at the step in which oxaloacetate is converted to phosphoenolpyruvate (PEP).

**QUESTION 3: Multiple Choice. Circle the correct answer.**

**(I)** When a nucleophile attacks the α-phosphorous atom of ATP, what kind of transfer occurs?

**(A)** pyrophosphoryl transfer
**(B)** phosphoryl transfer
**(C)** adenylyl transfer
**(D)** adenosine transfer

**(II)** A chemical reaction is more likely to occur spontaneously if

**(A)** the products of the reaction are more complex than the reactants.
**(B)** the system takes up heat from its surroundings.
**(C)** the products of the reaction are more disordered than the reactants.
**(D)** the system gains free energy.

**(III)** If a chemical reaction starts with 1 M concentrations each of reactants A and B and products C and D, under what conditions of $K'_{eq}$ and $\Delta G'^{\circ}$ will the reaction proceed in the forward direction ~~($\Delta G'^{\circ} = RT \ln K'_{eq}$)~~?

**(A)** If $K'_{eq}$ is greater than 1 and $\Delta G'^{\circ}$ is negative.
**(B)** If $K'_{eq}$ is 0 and $\Delta G'^{\circ}$ is negative.
**(C)** If $K'_{eq}$ is negative and $\Delta G'^{\circ}$ is negative.
**(D)** If $K'_{eq}$ is less than 1 and $\Delta G'^{\circ}$ is positive.

$\Delta G'^{\circ} = -RT \ln K'_{eq}$

NOTE: typo here.

**(IV)** In humans, gluconeogenesis

**(A)** can result in the conversion of protein into blood glucose.
**(B)** helps to reduce blood glucose after a carbohydrate-rich meal.
**(C)** is activated by the hormone insulin
**(D)** is essential in the conversion of fatty acids to glucose.
**(E)** requires the enzyme hexokinase.

**(V)** The steps of glycolysis between glyceraldehyde 3-phosphate and 3-phosphoglycerate involve all of the following *except:*

**(A)** ATP synthesis.
**(B)** catalysis by phosphoglycerate kinase.
**(C)** oxidation of NADH to $NAD^+$.
**(D)** the formation of 1,3-bisphosphoglycerate.
**(E)** utilization of $P_i$.

**QUESTION 4: The hydrolysis reaction of ATP is written as:**

$$ATP + H_2O \leftrightarrow ADP + Pi$$

$$\Delta G^{o\prime} = -31 \text{ kJ mol}^{-1} \text{ (at 300 K)}$$

**(I)** Write the equilibrium constant, $K_{eq}$, for the reaction.

$$K_{eq} = \frac{[ADP][P_i]}{[ATP]}$$

**(II)** Should water be included in the definition of the equilibrium constant above, since it is clearly a reactant? Explain your answer briefly.

Solids or liquids of pure substances, like water, are never included in equilibrium expressions. Water is essentially 55M even after a hydrolysis reaction.

**(III)** A reaction solution contains $1 \times 10^{-9}$ M ATP, $4\times10^{-4}$ M ADP, and 0.9 M Pi. Will the reaction go to the left or to the right under these conditions at 300 K? Circle your answer, and justify your choice with a calculation.

**LEFT** or **RIGHT**

$$\Delta G = \Delta G^{o\prime} + RT \ln Q \qquad Q = \frac{(4\times10^{-4})(0.9)}{(1\times10^{-9})}$$

$$\Delta G = -31 \frac{kJ}{mol} + \left(8.31 \frac{J}{mol\,K}\right)\left(\frac{1\,kJ}{1000\,J}\right)(300\,K)\,($$

$$\Delta G = -31 \frac{kJ}{mol} + 31.8\, kJ/mol = 0.8\, kJ/mol$$

$\Delta G$ is positive so reaction goes to the LEFT.

**QUESTION 5: Cytosol contains a $10^5$ smaller ratio of [NADH] to [NAD+] than in mitochondria.**

**(I)** Using the Nernst equation, $\boldsymbol{E = E^{o\prime} + (RT / nF) \ln[e^- \text{ acceptor}]/[e^- \text{ donor}]}$, calculate the difference in redox potential difference, **Δ*E***, for NADH and NAD+ between the mitochondria relative to the cytosol, where the difference is defined as $\boldsymbol{\Delta E = E_{mitochondria} - E_{cytosol}}$. F = 96,485 C/mol; R = 8.31 J/mol/K. The temperature is 300 K. Show your work.

$$E_{mito} = E^{o\prime} + RT/nF \ln\left[\left(\frac{1}{10^5}\right)\left(\frac{1}{P}\right)\right]$$

$$- \; E_{cyto} = E^{o\prime} + RT/nF \ln\left(\frac{1}{P}\right)$$

P = Cytosolic Ratio of NADH/NAD+

$NAD^+ + 2e^- + H^+ \rightarrow NADH$

$n = 2$

$$\Delta E = -RT/nF \ln 10^5$$

$$= \frac{-(8.31)(300)}{(2)(96485)} \ln 10^5$$

$$\boxed{\Delta E = -150 \text{ mV}}$$

**(II)** With respect to NAD+ and NADH only, which environment is more reducing? Circle your answer and explain your response.

**Cytosol** or **Mitochondria**

NADH is the reduced form of NAD+, and there is a greater ratio of NADH to NAD+ in the mitochondria relative to the cytosol. Notice also that the redox potential is more negative for the mitochondria as well.

**QUESTION 6: Consider the Tables of Standard Redox Potentials, $E^o$, on the following page.**

**(I)** Is FAD~~+~~ a better oxidizer than NAD+? Explain your answer using numbers in the Table.

Consider reaction, $FAD + NADH + H^+ \rightleftharpoons FADH_2 + NAD^+$.

$\Delta E^{o'} = E^{o'}_{FAD} - E^{o'}_{NADH} = -0.219 - -0.320 = +0.101\ V.$

YES, FAD is a better oxidizer, since $\Delta E^{o'}$ is positive and oxidation of NADH will be spontaneous.

**(II)** What is the standard free energy difference, $\Delta G^{o'}$, for the oxidation of $FADH_2$ with $O_2$, where FAD~~+~~ and $H_2O$ are the final products?

$$FADH_2 + \tfrac{1}{2}O_2 \rightleftharpoons FAD + H_2O$$

$$E^{o'}_{O_2} = 0.816 \qquad E^{o'}_{FADH_2} = -0.219$$

$$\Delta E^{o'} = 0.816 - (-0.219) = +1.035\ V$$

$$\Delta G^{o'} = -n\mathcal{F}\Delta E^{o'} = -2(96485)1.035\ V$$

$$\boxed{\Delta G^{o'} = -200\ kJ/mol}$$

**(III)** Using the $\Delta G^{o'}$ value for ATP hydrolysis given in **QUESTION 4**, how many moles of ATP could be produced if this oxidation of $FADH_2$ by $O_2$ described above in part II were perfectly coupled to the formation of ATP from ADP and Pi?

$$\frac{\Delta G^{o'}_{FADH \to FAD}}{\Delta G^{o'}_{ATP \to ADP}} = \frac{-200\ kJ/mol}{-31\ kJ/mol} = \boxed{6.5\ ATP/\text{mole } FADH_2}$$

**TABLE 13–7 Standard Reduction Potentials of Some Biologically Important Half-Reactions, at pH 7.0 and 25°C (298 K)**

| *Half-reaction* | *E′°* (V) |
|---|---|
| $\frac{1}{2}O_2 + 2H^+ + 2e^- \longrightarrow H_2O$ | 0.816 |
| $Fe^{3+} + e^- \longrightarrow Fe^{2+}$ | 0.771 |
| $NO_3^- + 2H^+ + 2e^- \longrightarrow NO_2^- + H_2O$ | 0.421 |
| Cytochrome *f* ($Fe^{3+}$) + $e^-$ ⟶ cytochrome *f* ($Fe^{2+}$) | 0.365 |
| $Fe(CN)_6^{3-}$ (ferricyanide) + $e^-$ ⟶ $Fe(CN)_6^{4-}$ | 0.36 |
| Cytochrome $a_3$ ($Fe^{3+}$) + $e^-$ ⟶ cytochrome $a_3$ ($Fe^{2+}$) | 0.35 |
| $O_2 + 2H^+ + 2e^- \longrightarrow H_2O_2$ | 0.295 |
| Cytochrome *a* ($Fe^{3+}$) + $e^-$ ⟶ cytochrome *a* ($Fe^{2+}$) | 0.29 |
| Cytochrome *c* ($Fe^{3+}$) + $e^-$ ⟶ cytochrome *c* ($Fe^{2+}$) | 0.254 |
| Cytochrome $c_1$ ($Fe^{3+}$) + $e^-$ ⟶ cytochrome $c_1$ ($Fe^{2+}$) | 0.22 |
| Cytochrome *b* ($Fe^{3+}$) + $e^-$ ⟶ cytochrome *b* ($Fe^{2+}$) | 0.077 |
| Ubiquinone + $2H^+$ + $2e^-$ ⟶ ubiquinol + $H_2$ | 0.045 |
| Fumarate$^{2-}$ + $2H^+$ + $2e^-$ ⟶ succinate$^{2-}$ | 0.031 |
| $2H^+ + 2e^- \longrightarrow H_2$ (at standard conditions, pH 0) | 0.000 |

Source: Data mostly from Loach, P.A. (1976) In *Handbook of Biochemistry and Molecular Biology*, 3rd edn (Fasman, G.D., ed.), *Physical and Chemical Data*, Vol. I, pp. 122–130, CRC Press, Boca Raton, FL.

* This is the value for free FAD; FAD bound to a specific flavoprotein (for example succinate dehydrogenase) has a different *E′°* that depends on its protein environments.

**TABLE 13–7 Standard Reduction Potentials of Some Biologically Important Half-Reactions, at pH 7.0 and 25°C (298 K)**

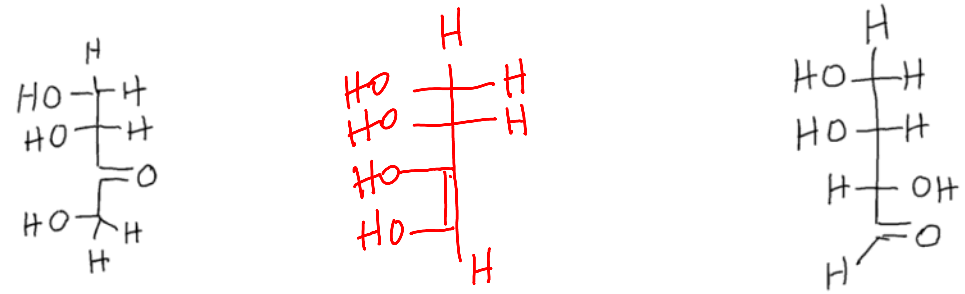
| *Half-reaction* | *E′°* (V) |
|---|---|
| $2H^+ + 2e^- \longrightarrow H_2$ (at standard conditions, pH 0) | 0.000 |
| Crotonyl-CoA + $2H^+$ + $2e^-$ ⟶ butyryl-CoA | −0.015 |
| Oxaloacetate$^{2-}$ + $2H^+$ + $2e^-$ ⟶ malate$^{2-}$ | −0.166 |
| Pyruvate$^-$ + $2H^+$ + $2e^-$ ⟶ lactate$^-$ | −0.185 |
| Acetaldehyde + $2H^+$ + $2e^-$ ⟶ ethanol | −0.197 |
| FAD + $2H^+$ + $2e^-$ ⟶ $FADH_2$ | −0.219* |
| Glutathione + $2H^+$ + $2e^-$ ⟶ 2 reduced glutathione | −0.23 |
| $S + 2H^+ + 2e^- \longrightarrow H_2S$ | −0.243 |
| Lipoic acid + $2H^+$ + $2e^-$ ⟶ dihydrolipoic acid | −0.29 |
| $NAD^+ + H^+ + 2e^-$ ⟶ NADH | −0.320 |
| $NADP^+ + H^+ + 2e^-$ ⟶ NADPH | −0.324 |
| Acetoacetate + $2H^+$ + $2e^-$ ⟶ $\beta$-hydroxybutyrate | −0.346 |
| $\alpha$-Ketoglutarate + $CO_2$ + $2H^+$ + $2e^-$ ⟶ isocitrate | −0.38 |
| $2H^+ + 2e^- \longrightarrow H_2$ (at pH 7) | −0.414 |
| Ferredoxin ($Fe^{3+}$) + $e^-$ ⟶ ferredoxin ($Fe^{2+}$) | −0.432 |

Source: Data mostly from Loach, P.A. (1976) In *Handbook of Biochemistry and Molecular Biology*, 3rd edn (Fasman, G.D., ed.), *Physical and Chemical Data*, Vol. I, pp. 122–130, CRC Press, Boca Raton, FL.

* This is the value for free FAD; FAD bound to a specific flavoprotein (for example succinate dehydrogenase) has a different *E′°* that depends on its protein environments.

**QUESTION 7: Reaction mechanism.**

**(I)** Draw the cis-enediol intermediate of the following reaction in the blank in the center. The reactant and product of the reaction are given at the left and right, respectively.



Reactant

Cis-enediol Intermediate

PRODUCT

**(II)** What type of enzyme mechanism best explains how this transformation occurs?

General acid base