HW5 Answer Key

Chapter 14

1) No because there is no transporter for a molecule with a phosphate group to enter the cell.

2) In the presence of arsenate, 1,3-bisphosphoglycerate is not formed; instead, this step is essentially skipped. Two moles of ATP per mole of glucose are normally generated at this step. If ATP is not generated at this step, the net ATP yield for the glycolytic pathway is zero, and the cells die because they are unable to meet their energy requirements.

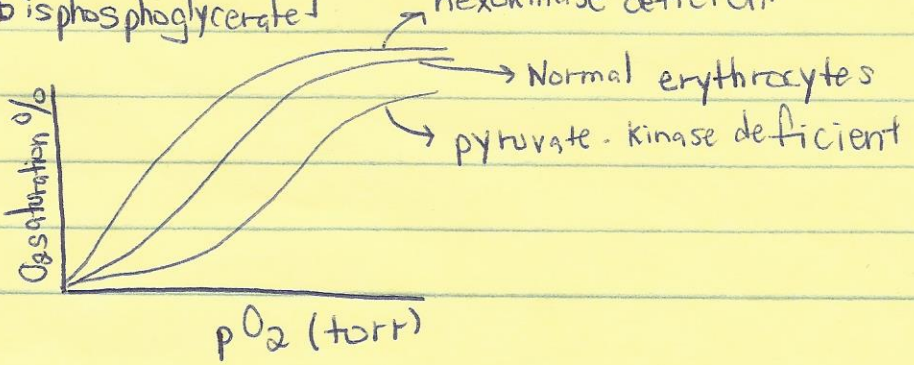
3) Recall ↑[2,3-bisphosphoglycerate], ↓ O_2 binding to hemoglobin

If hexokinase is deficient then you will not produce the glycolysis intermediates and there will be no build up of 2,3-bisphosphoglycerate.

↓[2,3-bisphosphoglycerate]

If pyruvate kinase is deficient then glycolysis intermediates will build-up.

↑[2,3-bisphosphoglycerate]



4) a. ~~For~~ In the brain glucose is present in monomeric form because the brain relies so heavily on it and stores very little glucose as glycogen. Therefore, glucose rather than phosphorylated glucose is the substrate that enters the glycolytic pathway. The first step of glucose catabolism in the brain is catalyzed by hexokinase, so this step is the rate-determining step of the pathway. In other tissues that break down glycogen for glycolysis via phosphorylation, the hexokinase step is bypassed.

b. The low K_M means that the enzyme will be saturated with glucose and will therefore operate at maximum velocity (or close to it). Even if the concentration of glucose were to fluctuate slightly, the brain's ability to catabolize glucose would not be affected.

K_m = [Substrate] @ $\frac{V_{max}}{2}$

blood [glucose] = 5 mM

If [glucose] is 100 x K_m, the enzyme will be saturated.

5) Fructose-1,6-bisphosphatase catalyzes the conversion of fructose-1,6-bisphosphate to fructose-6-phosphate in gluconeogenesis. When the enzyme is deficient, the gluconeogenic pathway is severely impaired and glucose synthesis from smaller metabolites occurs at a low level. At the beginning of a fast, blood glucose levels are maintained at normal levels because the source of blood glucose is glycogenolysis in the liver, which occurs normally. Once liver glycogen has been depleted, a normal individual would rely on gluconeogenesis for endogenous glucose production, but this pathway occurs at a low level in the patient because of the deficient enzyme; therefore, blood glucose levels decrease. Pyruvate levels would increase because it can not be converted to glucose via gluconeogenesis. The deficiency of fructose-1,6-bisphosphatase results in the buildup of the substrate, fructose-1,6-bisphosphate. This would promote the formation of glyceraldehyde-3-phosphate and dihydroxyacetone phosphate since aldolase reaction is reversible. Because glycolysis does not occur during a fast, glyceraldehyde-3-phosphate is not consumed by glyceraldehyde-3-phosphate dehydrogenase, so the ratio of glyceraldehyde-3-phosphate to dihydroxyacetone phosphate which is normally low, increases.

Chapter 16

1. The purpose of steps 4 and 5 is to regenerate the enzyme. In step 3, the product acetyl-CoA is released, but the lipoamide prosthetic group of E_2 is reduced. In step 4, the E_3 reoxidizes the lipoamide group by accepting the protons and electrons from the reduced lipoamide. In step 5, the enzyme is reoxidized by NAD^+. The product NADH then diffuses away.

2. The phosphofructokinase is the major rate-control point for the pathway of glycolysis. Inhibiting phosphofructokinase slows the entire pathway, so the production of acetylCoA by glycolysis followed by the pyruvate dehydrogenase complex can be decreased when the citric acid cycle is operating at maximum capacity and the citrate concentration is high.

3. V_{max} is constant but K_m decreased.
S-acetonyl-CoA is a competitive inhibitor.

4. a. Aconitase is the enzyme that catalyzes the reversible isomerization of citrate to isocitrate. Because this reaction is followed by and preceded by irreversible reactions, the inhibition of aconitase leads to an accumulation of citrate. The concentrations of other citric acid cycle intermediates will be decreased.

b. If the citric acid cycle and mitochondrial respiration are not functioning, the cell turns to glycolysis to produce the ATP required for its energy needs. Consequently, flux through glycolysis increases. The increase in the rate of the pentose phosphate is required to meet the increased demand for reducing equivalents during hyperoxia as it results in the formation of more NADPH.

5. a. $\Delta G = \Delta G^{o\prime} + RT \ln \frac{[\text{malate}]}{[\text{fumarate}]}$

$$0 = -3.4\,\frac{kJ}{mol} + 8.3145\times10^{-3}\,\frac{kJ}{K\,mol}\,(310K)\ln\frac{[\text{malate}]}{[\text{fumarate}]}$$

$$34\,\frac{kJ}{mol} = 2.58\,\frac{kJ}{mol}\ln\frac{[\text{malate}]}{[\text{fumarate}]}$$

$$1.32 = \ln\frac{[\text{malate}]}{[\text{fumarate}]}$$

$$e^{1.32} = \frac{[\text{malate}]}{[\text{fumarate}]}$$

$$3.7 = \frac{[\text{malate}]}{[\text{fumarate}]}$$

b. The ratio of malate to fumarate is 3.7 to 1, indicating that the reaction proceeds in the direction of formation of malate. This is not a control

point for the citric acid cycle because the ΔG is close to zero, indicating it is a near-equilibrium reaction.

6. The substrate is isocitrate, a compound with three carboxylate groups that are negatively charged at physiological pH. Four of the five conserved amino acid residues have positively charged side chains that could form ion pairs with isocitrate. The enzyme-substrate complex should not be too stable, however; it is the role of the enzyme to stabilize the transition state. So it is possible that the positively charged side chains in the binding pocket stabilize the transition state. This stabilization must be important in the conversion of substrate to product, which explains why these residues are highly conserved throughout evolution.

Chapter 19

		$E^{\prime\circ}$ (V)
1) $\frac{1}{2} O_2 + 2H^+ + 2e^- \longrightarrow H_2O$		0.8166
Cyta$_3$ $Fe^{3+} + e^- \longrightarrow Fe^{2+}$		0.35 ↘ lower $E^{\prime\circ}$ ∴ will transfer e^-

	$E^{\prime\circ}$ (V)
~~$2Fe^{3+} + 2e^-$~~	
$2Fe^{2+} \longrightarrow 2Fe^{3+} + 2e^-$	−0.35
$\frac{1}{2}O_2 + 2H^+ + 2e^- \longrightarrow H_2O$	+0.8166
	0.4666V

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

$$= -2\left(96.5 \frac{kJ}{V \cdot mol}\right) \times 0.4666V$$

$$= -90.1 \frac{kJ}{mol}$$ Spontaneous

2. a. $QH_2 \longrightarrow Q + 2H^+ + 2e^-$ $E^{\prime\circ} = -0.045V$

$$E = E^{\prime\circ} + \frac{0.026V}{n} \ln \frac{[Q]}{[QH_2]} \quad \left(= \frac{RT}{F}\right)$$

$$= -0.045V + \frac{0.026V}{2} \ln \frac{1}{10}$$

$$= -0.075V$$

$2\ \text{cyt c}\ (Fe^{3+}) + 2e^- \rightarrow 2\ \text{cyt c}\ (Fe^{2+})\quad E^{0\prime} = 0.235\text{V} \rightarrow 0.254\text{V}$

$$E = E^{0\prime} + \frac{0.026\text{V}}{n} \ln \frac{[Fe^{2+}]}{[Fe^{3+}]}$$

$$= 0.235\text{V} \rightarrow 0.254\text{V} + \frac{0.026\text{V}}{2} \ln 0.2$$

$$= 0.214\text{V} \rightarrow 0.233\text{V}$$

$$QH_2 \rightarrow Q + 2H^+ + 2e^- \qquad E = -0.075\text{V}$$

$$2\ \text{cyt c}(Fe^{3+}) + 2e^- \rightarrow 2\ \text{cyt c}\ (Fe^{2+}) \qquad E = 0.214\text{V} \rightarrow 0.233\text{V}$$

$$QH_2 + 2\ \text{cyt c}(Fe^{3+}) \rightarrow Q + 2H^+ + 2\ \text{cyt c}\ (Fe^{2+}) \qquad \Delta E = 0.139\text{V} \rightarrow 0.158\text{V}$$

b. $\Delta G = -nF\Delta E$

$$= -2\left(96,485\ \frac{\text{J}}{\text{V mol}}\right) 0.139\text{V} \rightarrow 0.158\text{V}$$

$$= -26.8\ \text{kJ/mol} \rightarrow -30.5\ \text{kJ/mol}$$

3. a. Since all of these inhibitors interfere with electron transfer somewhere in the e^- transport chain, oxygen consumption will decrease when any of the inhibitors are added to a suspension of respiring mitochondria. Adding any of these inhibitors prevents electrons from being transferred to the oxygen, the final electron acceptor.

b. In rotenone - or amytal-blocked mitochondria, NADH and Complex I redox centers are reduced while components from ubiquinone on are oxidized. In antimycin A-blocked mitochondria, NADH, Complex I redox centers, ubiquinol, and Complex III redox centers are reduced while cytochrome C and Complex IV redox centers are oxidized. In cyanide-blocked mitochondria, all of the electron transport components are reduced and only oxygen remains oxidized.

4. $\Delta G = RT \ln \frac{C_2}{C_1} + ZF\Delta\Psi = 2.3RT(pH_N - pH_P) + ZF\Delta\Psi$

$= 5.70 \frac{kJ}{mol} \Delta_{pH} + 96.5 \frac{kJ}{V\,mol} \Delta\Psi$

$= 5.70 \frac{kJ}{mol}(0.4) + 96.5 \frac{kJ}{mol}(0.2V)$

$= 21.6 \frac{kJ}{mol}$ Endergonic

5. In ATP synthase, the rotation of the γ subunit results in changes in interactions with the αβ trimer subunits. A direct contact between the γ subunit and αβ paired subunit induces a conformational change that results in release of ATP. The energy that drives this process is the proton-motive force due to protons moving into the matrix via the F_o unit of the synthase.

6. 1 NADH : 2.5 ATP : 10 H^+

1 $FADH_2$: 1.5 ATP : 6 H^+

	Direct Product	Final ATP	Final H^+
a. Glycolysis	2 NADH	5	20
	2 ATP	2	8
Pyruvate oxidation	2 NADH	5	20
Acetyl-CoA oxidation	6 NADH	20	80
in citric acid cycle	~~2 NADH~~	2	8
	2 ATP	34	136

	Direct Product	Final ATP	Final H^+
b. Glycolysis	2 $FADH_2$	3	12
	2 ATP	2	8
Pyruvate oxidation	2 $FADH_2$	3	12
Acetyl-CoA oxidation	8 $FADH_2$	12	48
in citric acid cycle	2 ATP	2	8
		22	88