This exam consists of 6 questions. A maximum of 100 points can be earned. Partial credit will be given. There are a total of 11 pages, including the cover page and one blank sheet at the end for notes. However, do not use the blank sheet for your final answers. If you need more space, use the back of pages 2-10. Write your name on top of each page! Petitions for regarding will be considered only if you have used permanent ink, unless an addition error has occurred.

IT IS YOUR RESPONSIBILITY TO WRITE LEGIBLE! 
No extra effort will be made to decipher your handwriting.

<table>
<thead>
<tr>
<th>Question</th>
<th>Value</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4</td>
<td></td>
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<tr>
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<td>18</td>
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<td>3</td>
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<td>16</td>
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<td>6</td>
<td>20 (+2)</td>
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</tr>
<tr>
<td>TOTAL</td>
<td>100 (+2)</td>
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</tr>
</tbody>
</table>

\[ \Delta G = \Delta G^\circ + RT \ln \left( \frac{\text{Prod.}}{\text{React.}} \right) \]
\[ \Delta G^\circ = -RT \ln K_{eq} \]
\[ \Delta G^\circ = -nF\Delta E^\circ \]
\[ \Delta E^\circ = E^\circ_{\text{Oxidant}} - E^\circ_{\text{Reductant}} \]

I, ____________________________________________, authorize the University to distribute publicly this graded exam (e.g., handed out in class or left in a bin for pick up).

I am aware of the fact that violations of the Academic Code of Conduct\(^1\) may be reported to UC Davis Student Judicial Affairs.

\(^1\)Examples of academic misconduct include: receiving or providing unauthorized assistance on examinations, using unauthorized materials during an examination, altering an exam and submitting it for re-grading, or using false excuses to obtain extensions of time (http://sja.ucdavis.edu/cac.htm).
1. (4 pts) Given below are pairs of reactants and products (the stoichiometry is not necessarily complete or balanced). Use your general understanding of thermodynamics, chemical reactions and metabolism to predict if the reactions as written (\(\rightarrow\)) are thermodynamically favorable (-\(\Delta G^o\)) or unfavorable (+\(\Delta G^o\)) under standard conditions. Circle the correct answer (1 pt for each reaction).

<table>
<thead>
<tr>
<th>Reactants</th>
<th>Products</th>
<th>Standard Free Energy Change ((\Delta G^o))</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADP, Pi</td>
<td>ATP, H(_2)O</td>
<td>positive negative</td>
</tr>
<tr>
<td>Succinyl-CoA, H(_2)O</td>
<td>Succinate, Coenzyme A</td>
<td>positive negative</td>
</tr>
<tr>
<td>Phosphoenolpyruvate, ADP</td>
<td>Pyruvate, ATP</td>
<td>positive negative</td>
</tr>
<tr>
<td>H(_2)O</td>
<td>H(_2), O(_2)</td>
<td>positive negative</td>
</tr>
</tbody>
</table>

2. (18 pts) The first reaction of the TCA cycle is catalyzed by the enzyme citrate synthase (CS). The \(\Delta G^o\) for this reaction is – 32.2 kJ mol\(^{-1}\).

a) Write the CS-catalyzed reaction (do not draw structures, use words or common abbreviations) (2 pts)

\[
\text{Oxaloacetate} + \text{Acetyl-CoA} + \text{H}_2\text{O} \rightarrow \text{Citrate} + \text{Coenzyme A (CoA, CoA-SH)}
\]

b) Calculate the equilibrium constant \(K_{eq}\) for the citrate synthase reaction under standard conditions. For full credit you must show your work and encircle your final answer. (4 pts)

\[
\Delta G^0 = - RT \ln K_{eq}
\]

\[
\ln K_{eq} = \frac{\Delta G^0}{-RT}
\]

\[
K_{eq} = e^{\frac{\Delta G^0}{-RT}}
\]

\[
K_{eq} = e^{(-32,200 \text{ J mol}^{-1} / -8.315 \text{ J mol}^{-1} \text{ K}^{-1} \times 298 \text{ K})}
\]

\[
K_{eq} = 440,221
\]

\[
K_{eq} = 4.4 \times 10^5
\]
c) In heart mitochondria, the following metabolite concentrations were measured: citrate (220 x 10^{-6} M); oxaloacetate (1 x 10^{-6} M); acetyl-CoA (1 x 10^{-6} M); and coenzyme A (65 x 10^{-6} M). Calculate the $\Delta G$ of the citrate synthase reaction under cellular conditions. For full credit you must show your work and encircle your final answer. (8 pts)

\[ \Delta G = \Delta G^\circ + R T \ln Q \]

\[ \Delta G = \Delta G^\circ + R T \ln \frac{[\text{Citrate}][\text{Coenzyme A}]}{[\text{OAA}][\text{Acetyl-CoA}]} \]

\[ \Delta G = -32,200 \text{ J mol}^{-1} + 8.315 \text{ J mol}^{-1} \text{ K}^{-1} \times 310 \text{ K} \ln \left( \frac{220 \times 10^{-6} \text{ M} \times 65 \times 10^{-6} \text{ M}}{1 \times 10^{-12} \text{ M}^2} \right) \]

\[ \Delta G = -32,200 \text{ J mol}^{-1} + 24,663 \text{ J mol}^{-1} \]

\[ \Delta G = -7,537 \text{ J mol}^{-1} \]

\[ \Delta G = -7.5 \text{ kJ mol}^{-1} \]

c) What is the direction of the citrate synthase reaction in heart mitochondria? (2 pts)

Answer: The formation of citrate is favored because $\Delta G$ is negative.

d) Hydrolysis of the intermediate citroyl thioester is part of (or coupled to) the citrate synthase reaction. The $\Delta G^\circ$ for the hydrolysis of thioesters is about –31.5 kJ mol^{-1}. If there would be no coupling of the citroyl thioester hydrolysis to the citrate synthase reaction, what would be the metabolic consequence in heart mitochondria? (2 pts)

Answer: The formation of citrate would NOT be favored because $\Delta G$ is highly positive.
Lactic acid is formed when the bacteria in tooth plaque degrade sugars and carbohydrates from the human diet under anaerobic conditions. Lactic acid exposure destroys the enamel of the teeth causing cavities. Many communities add fluoride ($F^-$) to their drinking water to promote dental health. Fluoride ($F^-$) is a known inhibitor of \textit{enolase}, an enzyme of the glycolytic pathway, and thus inhibits bacterial growth.

a) Write the names of the products of the enolase-catalyzed reaction below the product boxes. (3 pts)

b) Draw the structures of the reactant (2-PGA) and the products into the respective boxes. (5 pts)

\begin{center}
\begin{tabular}{c|c|c}
 \textbf{Reactant} & \textit{For structures, see booklet} & \textbf{Products} \\
2-Phosphoglycerate (2-PGA) & \textbf{Enolase} & +
\end{tabular}
\end{center}

Name: Phosphoenolpyruvate (or PEP) Name: Water

c) Why does inhibition of the enolase reaction effectively inhibit bacterial growth under anaerobic conditions? Briefly discuss \textit{two} metabolic consequences. (8 pts.)

If the enolase reaction is inhibited under anaerobic conditions, substrate-level phosphorylation by the pyruvate kinase reaction is inhibited, which leads to a net production of “zero” ATP during glycolysis.

A second consequence is that pyruvate formation is inhibited, which is necessary to regenerate NAD$^+$ by lactic fermentation (reduction of pyruvate to lactate, coupled to the oxidation of NADH to NAD$^+$). Thus, the entire glycolytic pathway is effectively inhibited, which results in bacterial death as glycolysis is the only pathway that can generate ATP during anaerobiosis.
4. (16 pts) Short questions on co-factors and enzymes.

a) What is the general function of co-factors in enzyme catalysis? (2 pts)

Co-factors are small organic molecules or metal ions that expand the catalytic capabilities of enzymes by providing reactive groups in addition to the limited number of protein amino acid side-chains.

b) Briefly explain the difference between a “co-substrate” and a “prosthetic group”. (4 pts)

Co-substrates are freely diffusible co-factors that are only transiently bound by the enzyme, whereas prosthetic groups are co-factors that are either covalently attached to the enzyme or trapped within the polypeptide chain(s) of the enzyme (non-diffusible co-factors).

c) The table below lists enzymes and co-factors discussed in class (ATP can be considered a co-factor). For each enzyme, indicate all required co-factors by placing an “X” in the appropriate box. Note: Some enzymes may not require a co-factor. You will lose your point if you select additional co-factors that are not required by the enzyme. (1 pt for each enzyme and correct co-factor requirement; 10 pts total)

<table>
<thead>
<tr>
<th>Enzyme</th>
<th>ATP</th>
<th>NAD⁺/NADH</th>
<th>FAD/FADH₂</th>
<th>Lipoic Acid</th>
<th>TPP</th>
<th>CoA-SH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Succinate Dehydrogenase (SDH)</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Hexokinase</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Pyruvate Dehydrogenase (PDH)</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Glycogen Phosphorylase</td>
<td></td>
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<tr>
<td>Pyruvate Decarboxylase (PDC)</td>
<td></td>
<td></td>
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<td></td>
<td>X</td>
<td></td>
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<tr>
<td>Malate Dehydrogenase (MDH)</td>
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<td></td>
<td>X</td>
<td></td>
<td></td>
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<tr>
<td>α-Ketoglutarate Dehydrogenase (α-KGA-DH)</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Glyceraldehyde-3-P Dehydrogenase</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Aldolase</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Isocitrate Dehydrogenase (IDH)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
</tbody>
</table>
5. (26 pts) Short questions on glycolysis.

a) In glycolysis, 2 ATP per glucose are initially consumed, but 4 ATP are finally generated, which equals a net production of 2 ATP per glucose. Why is the initial investment of 2 ATP necessary? Give two reasons. (4 pts)

There are essentially two reasons for the expense of ATP at the beginning of glycolysis:

First, the coupling of ATP hydrolysis to early steps of glycolysis “drives” this pathway forward as the release of energy (-ΔG) converts these steps to essentially irreversible reactions.

Second, the addition of two phosphate groups to the hexose intermediates ensures that the sugars and their cleavage products are negatively charged and thus remain within the cell.

b) The two enzymes that utilize ATP during the initial or “investment” phase of glycolysis belong to what major class of enzymes? Encircle one enzyme class only (no credit otherwise) (2 pts)

Oxidoreductases  Transferases  Hydrolases  Lyases  Isomerases  Ligases

In class?

Oxidoreductases

Transferases

Hydrolases

Lyases

Isomerases

Ligases

No In this case, the actual reaction is:

Pyruvate + NADH + H+ → Lactate + NAD+

or:

Pyruvate + 2H⁺ + 2e⁻ → Lactate (Eº = − 0.18 V)

NAD⁺ + H² + 2e⁻ → NADH + H⁺ (Eº = − 0.32 V)

ΔEº' = Eº' Oxidant − Eº' Reductant

ΔEº' = − 0.18 V − (− 0.32 V)

ΔEº' = 0.14 V

ΔGº' = − nFΔEº'

ΔGº' = − 2 (96.5 kJ mol⁻¹ V⁻¹) (0.14V)

ΔGº' = − 27.02 kJ mol⁻¹
d) Why is it not possible to calculate the ΔG°* value of the aldolase reaction from standard reduction potentials? (2 pts)

The aldolase reaction catalyzes the cleavage of F1,6BP into GA3P and DHAP, which is NOT a redox reaction. Thus, there are no E°* values available to calculate ΔG°*.

e) The enzyme “aldolase” belongs to what major class of enzymes? Encircle one enzyme class only (no credit otherwise) (2 pts)

Oxidoreductases    Transferases    Hydrolases    Lyases    Isomerases    Ligases

f) The degradation of glycogen is an important process that supplies glycolysis with glucose. Briefly explain the major differences between glycogen hydrolysis and glycogen phosphorolysis. (4 pts)

Glycogen hydrolysis is the mechanism to break down the glycogen present in our diet. Water is used to cleave each glycosidic bond, which releases a glucose unit.

On the other hand, a phosphate group is used to cleave the glycosidic bonds of intracellular glycogen reserves (phosphorolysis), which releases glucose-1-P.

g) Mannose is a wide-spread monosaccharide in fruits and vegetables, which is converted by two reactions into an intermediate of glycolysis. Encircle the (three) correct statements. (6 pts)

Mannose is a…   Triose    Aldohexose    Aldoketose

, which is converted to…    Glucose-6-P    Fructose-1-P    Fructose-6-P

by the following pairs of enzymes:    Kinase/    Oxidoreductase    Kinase
                                         Lyase    Isomerase    Isomerase
6. (20 pts) Multiple-choice questions. Circle the best answer. There is only one best answer per question. Each question is worth 2 pts.

a. Which one of the following compounds is NOT a carbohydrate?
   i  Glucose
   ii Galactose
   iii Glycogen
   iv Glycerol
   v Glyceraldehyde

b. The following compounds have a large negative $\Delta G^\circ$ of hydrolysis EXCEPT:
   i  Adenosine triphosphate
   ii Fructose-1,6-bisphosphate
   iii Acetyl-CoA
   iv Phosphoenolpyruvate
   v 1,3-Bisphosphoglycerate

c. Which one of the following co-factors does NOT participate in oxidoreduction reactions?
   i  FAD
   ii NAD
   iii Coenzyme A
   iv Lipoic acid
   v all of the above

d. The essentially irreversible reactions of glycolysis include the one catalyzed by:
   i  phosphoglucoisomerase
   ii Phosphofructokinase
   iii phosphoglycerate kinase
   iv phosphoglycerate mutase
   v aldolase
e. Which one of the following enzymes catalyzes *substrate-level phosphorylation* of ADP to ATP?

i  Succinyl-CoA synthetase  
ii  Triose kinase  
iii  Hexokinase  
iv  Pyruvate dehydrogenase  
v  Glyceraldehyde-3-P dehydrogenase

f. Which of the following statements is NOT true for enzymes:

i  enzymes facilitate a reaction by changing its rate  
ii  enzymes facilitate a reaction by decreasing its activation energy  
iii  enzymes facilitate a reaction by decreasing its free energy change  
iv  enzymes facilitate a reaction by binding to other metabolites  
v  enzymes facilitate a reaction by providing stereospecificity

g. The pyruvate dehydrogenase (PDH) complex is present and functions in the…?

i  Plasma membrane  
ii  Cytosol  
iii  Outer mitochondrial membrane  
iv  Inner mitochondrial membrane  
v  Mitochondrial matrix

h. Under aerobic conditions, the complete oxidation of 1 mole glucose via glycolysis and the TCA cycle yields how many moles of NADH + H⁺ and FADH₂?

i  10 moles NADH + H⁺ and 4 moles FADH₂  
ii  12 moles NADH + H⁺ and 4 moles FADH₂  
iii  14 moles NADH + H⁺ and 2 moles FADH₂  
iv  10 moles NADH + H⁺ and 2 moles FADH₂  
v  16 moles NADH + H⁺ and 0 moles FADH₂
Under anaerobic conditions, skeletal muscles generate lactate from pyruvate in order to:

i. lower the pH for prolonged contraction
ii. promote release of oxygen from hemoglobin
iii. to generate additional ATP via PEP formation
iv. to activate glycogen phosphorolysis
v. to regenerate NAD\(^+\) for further glycolysis

Which of the following is meant by the statement that glucose and galactose are epimers?

i. one is an aldose and the other is a ketose
ii. one is a pyranose and the other a furanose
iii. they are mirror images of each other
iv. they differ only at the configuration at one carbon atom
v. after cyclization, they differ only at the configuration at the carbon atom C-1

**Bonus question (2 extra points)!** The TCA cycle catalyzes the complete degradation of the acetyl unit (CH\(_3\)-CO\(^-\), provided as acetyl-CoA) into two molecules of CO\(_2\). Thus, three additional oxygen atoms must be acquired for generating two CO\(_2\) molecules from acetyl-CoA. What are the compounds that enter the TCA cycle and provide the extra three oxygen atoms?

i. O\(_2\) and H\(_2\)O
ii. 3 H\(_2\)O
iii. 2 H\(_2\)O and Pi
iv. H\(_2\)O and 2 Pi
v. O\(_2\) and Pi
BIS103-001 (Winter 2007)  
Midterm #1 (February 1)  
Name_____________________________________

Use blank sheet as scratch paper.