Name: _____

Chem 4512/6502 Sample Final Exam

by Dr. A. Oyelere

Please put your name at the top of every page.

There are **3 multi-part Sections** to this exam.
Please look over the whole exam before you start answering questions. The maximum points for each question are indicated. There are **150** points possible. Your whole answer **MUST** be written in the spaces provided. All programmable calculators must be **cleared** of any memory of previous work related to this class.

Potentially helpful information is provided

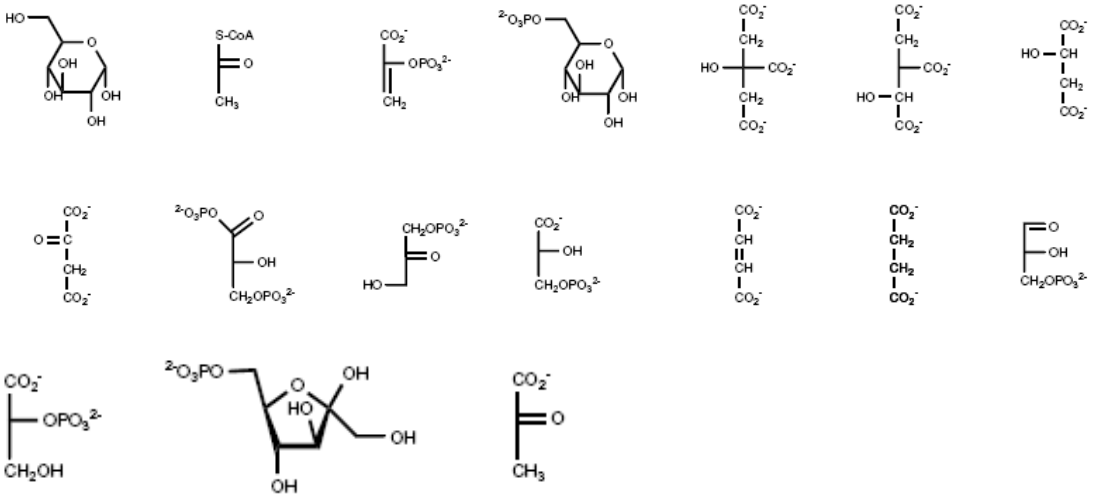
You are expected to strictly adhere to Georgia Institute of Technology Honor Code.

Georgia Institute of Technology Honor Code.

I have neither given nor received help on this work.

Signature **date**

Potentially helpful information:



Energy Charge (EC):	Change in Free Energy:
$\frac{[ATP]+0.5[ADP]}{[ATP]+[ADP]+[AMP]}$	$\Delta G' = \Delta G^{o'} + RT \ln \frac{[product]_{actual}}{[substrate]_{actual}}$ *At equilibrium (when $\Delta G' = 0$):* $\Delta G^{o'} = -RT \ln \frac{[product]_{equilibrium}}{[substrate]_{equilibrium}}$

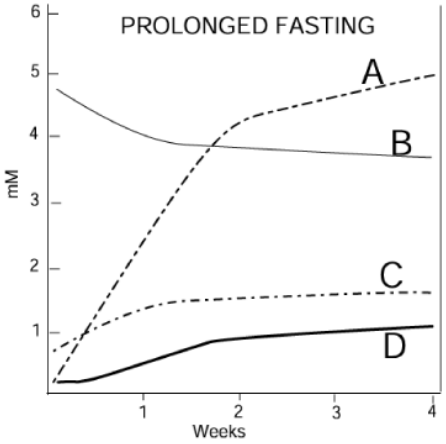
USEFUL CONSTANTS:
R (gas constant) **= 8.315 J•mol^{-1}•Kelvin^{-1} = 8.315 x 10^{-3} kJ•mol^{-1}•Kelvin^{-1}**
F (Faraday Constant) **= 96.48 kJ•V^{-1}•mol^{-1}**

If temperature = 25 °C, absolute temperature T = 298 K (Assume this temperature unless problem states otherwise.)

ATP $\rightleftharpoons$ ADP + Pi $\quad \Delta G^{o'} = -30.5$ kJ/mol

Section 1: Answer <u>all</u> questions in this section. Each question is worth 2 points.

I. The following graph shows the increase of blood acetoacetate, beta-hydroxybutyrate, glucose and free fatty acids during a fast.



Which of the following is CORRECT?

A) Curve A represents glucose
B) Curve B represents free fatty acid
C) Curve B represents acetoacetate
D) Curve C represents glucose
E) **Curve A represents beta-hydroxybutyrate**

V. Fill in the blank in the following sentence. In the catabolism of isoleucine the carbon skeleton enters the citric acid cycle as acetyl-CoA. Isoleucine is therefore called a _____ amino acid.

A) aminogenic
B) diabetic
C) ketogenic
D) glucogenic

VIII. Uric acid is the end product of purine as well as protein catabolism in

A) Man
B) Fish
C) Birds
D) None of these

XIV. Products of the light reactions of photosynthesis that are required by the dark reaction are

A) oxygen and ATP
B) ATP and NADPH
C) water and oxygen
D) oxygen and NADPH

XV. The Calvin Cycle is dependent on the light reactions for a supply of

A) water.
B) carbon dioxide.
C) RuBP.
D) NADPH.

XVI. Which sequence accurately reflects the flow of electrons in photosynthesis?

A) H_2O → Photosystem I → Photosystem II → NADP
B) Photosystem II → Photosystem I → NADP →H_2O
C) H_2O → Photosystem II → Photosystem I → NADP
D) Photosystem I → Photosystem II → NADP → H_2O

XVII. Inner mitochondrial membrane does not allow the free movement of one of the following compounds.

A) O_2
B) ATP
C) CO_2
D) H_2O

XVIII. Which of the following is not a part of the electron transport chain?

A) cytochrome
B) $FADH_2$
C) coenzyme Q
D) NADH
E) coenzyme A

XIX. If the mitochondria cannot pump hydrogen across the intermembrane space, the immediate consequence is that

A) ATP synthesis will not occur.
B) lactate will accumulate.
C) pyruvate will not form.
D) sugar will not be hydrolyzed.

XX. During electron transport, protons are NOT pumped out of the mitochondrion at this site:

A) Complex I
B) Complex II
C) Complex III
D) Complex IV

XXI. Which of the following enzymes is **not** involved in decarboxylation?

A) Pyruvate dehydrogenase complex
B) Isocitrate dehydrogenase
C) Malate dehydrogenase
D) α-ketoglutarate dehydrogenase

XXII. The only reaction in the citric-acid cycle in which a carbon-carbon bond is formed is catalyzed by

A) citrate synthase
B) isocitrate dehydrogenase
C) succinyl-CoA synthetase
D) fumarase

XXIII. Which one of the following enzymatic activities would be decreased by thiamine deficiency?

A) Fumarase
B) Isocitrate dehydrogenase
C) α-Ketoglutarate dehydrogenase complex
D) Succinate dehydrogenase

XXIV. Which of the following pathways in the liver are stimulated by insulin?

A) gluconeogenesis
B) glycogen synthesis
C) beta oxidation of fatty acids
D) all of the above

XXV. Which molecule is a substrate for glycogen synthesis?

A) glucose-6-phosphate
B) ADP-glucose
C) UDP-glucose
D) glucose 1,6-bisphosphate

XXVI. Which of the following best describes the Cori cycle?

A) Glycolysis in the liver is coordinated with gluconeogenesis in the muscle.
B) It involves anaerobic catabolism in the liver.
C) The liver synthesizes glucose from lactate produced in the muscle
D) Alanine is used to carry amino groups to the liver.

XXVIII. Concerning the fatty acid synthase complex, all of the following are true EXCEPT

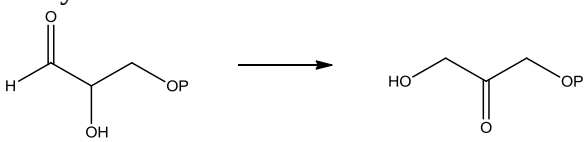
A) Products include $NADP^+$ and CoA
B) Products include stearate (C18:0) and CO_2
C) Substrates include acetyl CoA
D) Substrates include malonyl CoA
E) Substrates include NADPH

XXIX. Acyl carrier protein and CoA have all of the following in common EXCEPT

A) Both incorporate ADP into their structure
B) Both incorporate pantothenic acid into their structure
C) Both have a functional SH group (thiol group)

D) Both form thioester bonds with fatty acids
E) Both form high-energy bonds with fatty acids

XXX. What type of enzyme catalyzes the reaction below?



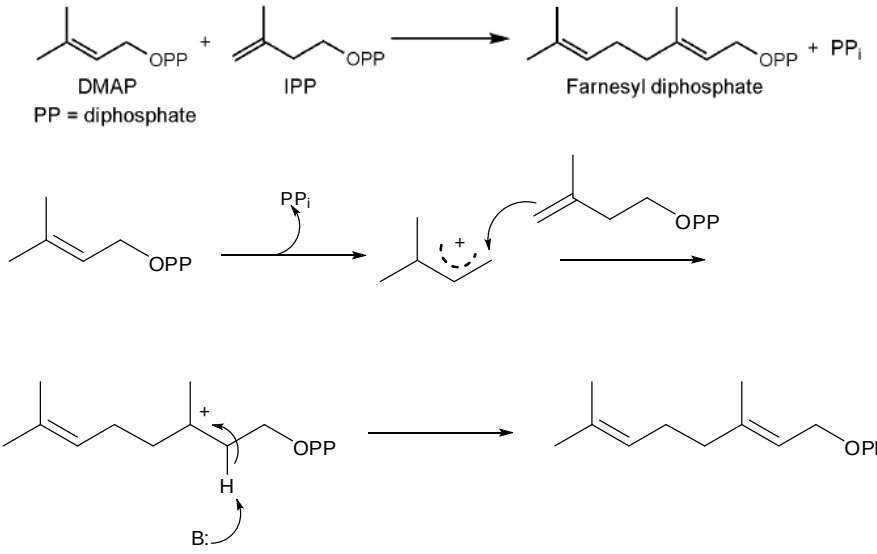
A) Kinase
B) Isomerase
C) Mutase
D) Aldolase
E) Dehydrogenase

Section 2 (30 points): Answer <u>all</u> questions in this section.

2 (10 points)
a (2 pts). An aliquot of $H_2{}^{18}O$ is added to a suspension of chloroplasts capable of photosynthesis. Where does the label appear when the suspension is exposed to light?

Ans: The majority of the label appears as $^{18}O_2$.

b (4 pts). Prenyl transferase catalyzes the following reaction. Provide a reasonable mechanism for this reaction.



3 (10 points)

Answer True or False

II. The “light reactions” of photosynthesis can occur only under light conditions, and the “dark reactions” occur only during the dark hours.

A) True, **B) False**

IV. During electron transfers as part of oxidative phosphorylation Fe-S clusters can undergo two-electron redox reactions.

A) True, **B) False**

VI. Carboxylation of acetyl CoA to malonyl CoA is the committed step in fatty acid synthesis

A) True B) False

VIII. LDL particles are "bad" cholesterol that are associated with increased disease risks.

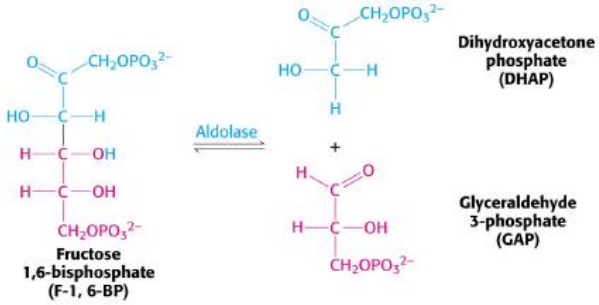
A) True B) False

IX. HDL particles are responsible for delivering cholesterol to peripheral tissues.

A) True, **B) False**

4 (10 points)

a (3 pts). Give the structures of the substrate(s) and the products of glycolysis enzyme aldolase



b (3 pts). $\Delta G^{o'}$ for the aldolase reaction is 22.8 kJmol^{-1}. In the cell at 37^{o}C, [DHAP]/[GAP] = 5.5. Calculate the equilibrium ratio of [FBP]/[GAP] when [GAP] = 10^{-4} M.

Ans:

When [GAP] = 10^{-4} M, [DHAP] = 5.5 x 10^{-4} M

Recall, $\Delta G^{o'} = -RTlnK$

$K = e^{-\Delta Go'/RT}$

Recall from the Aldolase reaction,

K = [DHAP] [GAP] /[FBP]
Therefore,
$K = [DHAP][GAP]/[FBP] = e^{-\Delta Go'/RT}$
$K = [DHAP][GAP]/[FBP] = e^{-(22,800)/(8.3145 \times 310)}$
$K = [5.5 \times 10^{-4}\ M][10^{-4}\ M]/[FBP] = e^{-(22,800)/(8.3145 \times 310)}$
$K = [5.5 \times 10^{-4}\ M][10^{-4}\ M]/[FBP] = 1.4 \times 10^{-4}$
$[FBP] = 3.8 \times 10^{-4}$
Therefore, $[FBP]/[GAP] = 3.8 \times 10^{-4} / 10^{-4} = 3.8$

c (2 pts). Explain why the degradation of odd-chain fatty acids can boost the activity of the TCA cycle.

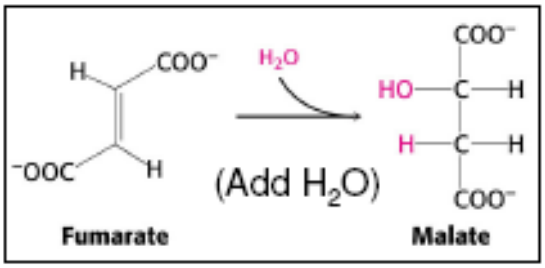
Ans: Supplies succinyl-CoA and this increases the catalytic activity of the cycle

d (2 pts). Peroxisomes (the cytoplasmic organelle containing enzymes, especially catalase) shorten very long chain fatty acids via β-oxidation and thus prepare them for complete degradation by the mitochondrial β-oxidation system. The first enzyme in the pathway is peroxisomal fatty acyl-CoA oxidase. Give the overall reaction for this enzyme.
Ans:
Overall reaction: **Fatty acyl-CoA + O_2 → *trans*-Δ^2-enoyl-CoA + H_2O_2**

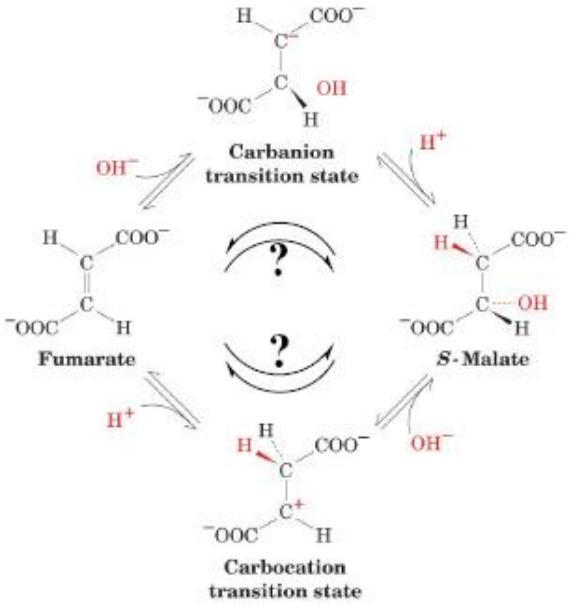
Section 3: Answer <u>any two</u> questions in this section. Each question is worth 30 points

5 (30 points)

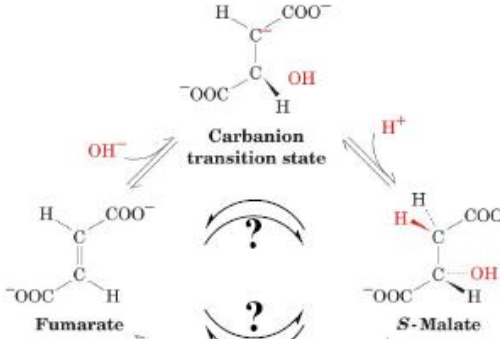
a. The citric acid pathway enzyme fumarase facilitates the highly stereospecific hydration of fumarate to give malate as shown below:



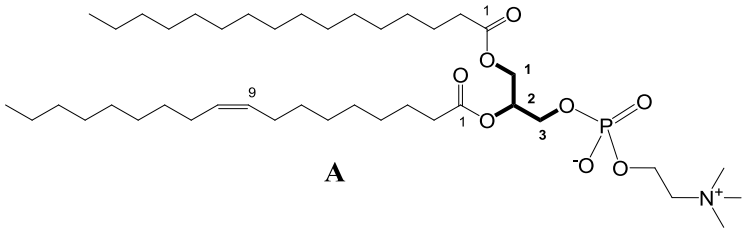
i (4 pts). Provide the two possible mechanistic pathways for the hydration of fumarate as catalyzed by fumarase. Be sure to clearly identify the transition state of either pathway.



ii (2 pts). Based solely on the principles of organic chemistry, which of these pathways is preferable?

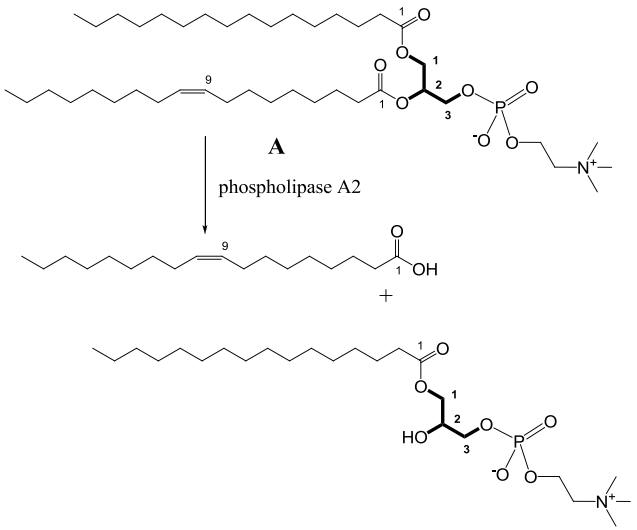


b. Lipid A is subjected to hydrolysis by phospholipase A2,



A

(i) (2 pts). Write the products of hydrolysis of lipid A by phospholipase A2.

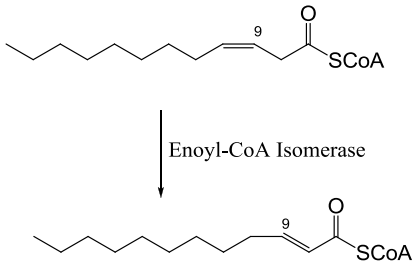


(ii) (2 pts). What problem(s) are likely to be encountered during the β-oxidation of the FA product in **5b(i)**?

The presence of cis double bond at the β, γ position of the Carboxy-CoA group

(iii) (3 pts). Using chemical illustrations, describe enzymatic activit(ies) that are required to solve these problem(s).

The problem is easily solved thru the action of enoyl-CoA isomerase:



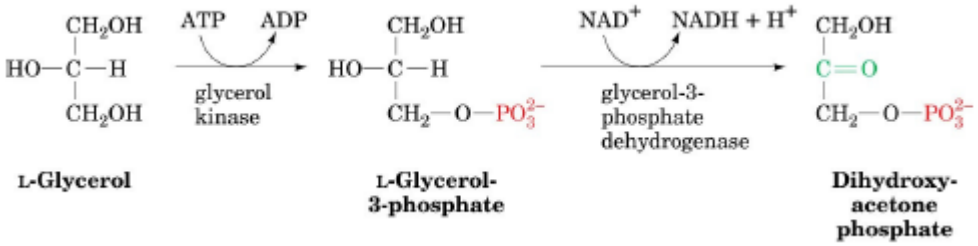
c (6 pts). Koop and Lehninger are pioneering scientists whose work led to the elucidation of fatty acid catabolism. Succinctly describe Knoop's and Lehninger's experiments and the conclusions from these studies (limit to four sentences for each experiment).

Koop's Experiment: Fed dog with even- and odd-chain fatty acids (FAs) with ω-phenyl group and analyzed urine sample collected from these dogs for metabolites. Concluded that FAs are metabolically oxidized at their β-carbon atom (hence β-oxidation), resulting in the release of a C-2 specie per β-oxidation cycle.

Lehninger's Experiments: Added FAs to homogenized rat liver in the presence and absence of ATP. He observed that the FAs are metabolized only in the presence of ATP. Concluded that FA has to be activated to commence β-oxidation

d (3 pts). Using appropriate chemical illustrations, explain why degradation of triacylglycerols in humans can be used to generate glucose via the gluconeogenic pathway even though fatty acid degradation does not result in net glucose production.

Triacylglycerol contains glycerol which can be converted to a gluconeogenic intermediate and used for glucose synthesis:

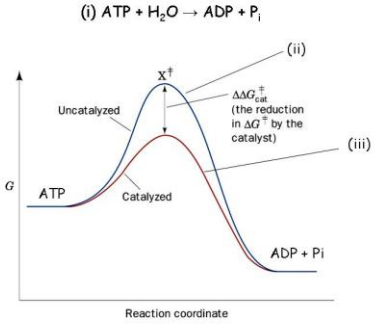


e. Hydrolysis of high energy phosphate compounds such as ATP is thermodynamically favorable. However, ATP does not hydrolyze to any appreciable extent in water unless appropriate enzyme is included in the solution.

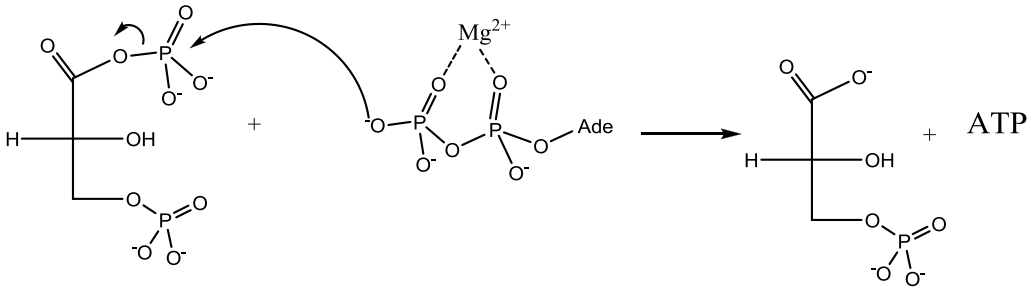
(i) (2 pts) Give the equation of the hydrolysis of ATP in water, clearly indicating the substrates and products

(ii) (3 pts) Using appropriate diagram (illustration), give a plausible explanation why ATP does not hydrolyze spontaneously in water despite the large negative ΔG of the reaction.

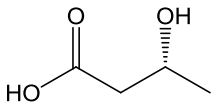
(iii) (3 pts) (Preferably on the same illustration in ii) illustrate how an enzyme might facilitate ATP hydrolysis.
Ans:



6 (30 points)
a (3 pts). Write a detailed mechanism for 1,3-bisphosphoglycerate kinase (in the direction of ATP formation) (include all products)



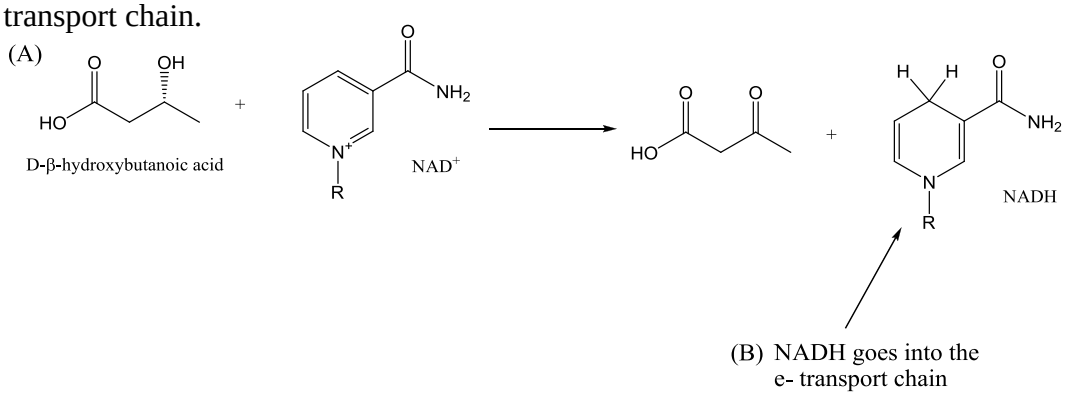
b. It has been observed that the infusion of the ketone body D-β-Hydroxybutyrate (DβHB) in mice confers partial protection against dopaminergic neurodegeneration through a mechanism that involves the electron transport chain.



D-β-hydroxybutanoic acid

(i) (2 pts). Propose a plausible transformation of DβHB that may jump-start electron transport.

(ii) (2 pts). Identify the product resulting from the transformation of DβHB that goes into the electron transport chain.



ci (3 pts). Give the name of the molecule that serves as the template molecule in the Calvin cycle.

Ans: Either Ribulose-5-phosphate (R-5-P) or Ribulose-1,5-diphosphate (RDP, R-1,5-DP) is acceptable. Technically, Ribose-5-P and Xylulose-5-phosphate are acceptable but only partial credit (2 pts)

cii (2 pts). What explains the dependence of the Calvin cycle enzyme Rubisco on light activation of PSII?

Ans: Light activated electron transport through PSII is required for proton pumping into the thylakoid space from the stroma. This results in an increase in stromal pH and efflux of Mg^{2+} to the stroma to balance the charge. Rubisco activity is stimulated by this increase in pH and elevated [Mg^{2+}] in the stroma.

ciii (2 pts). Explain why adding cyanide to a suspension of mitochondria blocks ATP synthesis.

Ans: Cyanide blocks electron transfer in the ETS at complex IV, resulting in the loss of the proton motive force that is required to drive ATP synthesis.

d (4 pts). What is the effect of uncoupler molecules such as dinitrophenol on the production of (i) NADPH) and (ii) ATP in a chloroplast?

Ans:

(i) No Effect

(ii) Reduction in ATP production

e (2 pts). How many ATP molecules are needed to fix a molecule of CO_2 in (i) C3 plant (normal plant) and (ii) in a C4 plant?

Ans:

(i) 3 ATPs

(ii) 5 ATPs

f (2 pts). The net reaction for oxidative phosphorylation can be written as:

$$2NADH + 2H^+ + O_2 \rightarrow 2H_2O + 2NAD^+$$

Write an analogous equation for the light reactions of photosynthesis.

$$2H_2O + 2NADP^+ \rightarrow 2NADPH + 2H^+ + O_2$$

Partial credit for $2H_2O + 2NAD^+ \rightarrow 2NADH + 2H^+ + O_2$

g. A recently discovered bacterium carries out ATP synthesis coupled to the flow of electrons through a chain of carriers to some electron acceptor. The components of its electron transfer chain differ from those found in mitochondria; they are listed below with their standard reduction potentials.

Electron carriers in the newly discovered bacterium:

Oxidant	Reductant	E'° (V)
NAD^+	NADH	–0.32
flavoprotein *b* (FP_b) (oxidized)	flavoprotein *b* (reduced)	–0.62
cytochrome *c* (Fe^{3+})	cytochrome *c* (Fe^{2+})	+0.22
Fe-S protein (oxidized)	Fe-S protein (reduced)	+0.89
flavoprotein *a* (FP_a) (oxidized)	flavoprotein *a* (reduced)	+0.77

(i) (2 pts) Place the electron carriers in the order in which they are most likely to act in carrying electrons.

FPb→ NAD+ → cyt c → FPa → Fe-S

(ii) (2 pts) Is it likely that O_2 (for which E'° = 0.82 V) is the final electron acceptor in this organism? Why or why not?

No; Fe-S has a larger E'°, so will probably be the terminal acceptor.

(iii) (2 pts) Using inhibitors and artificial electron donors, you find that the pathway is inhibited by CN^- ion but inhibition is overcome by the addition of NADH. What is the actual sequence of electron transport in this system?

FPb→ cyt c → NAD+ → FPα → Fe-S

(iv) (2 pts) What is the major factor explaining why your prediction in (a) turned out to be incorrect?

intracellular concentrations greatly affect the actual E values and can alter the order of electron transfer.

7 (30 points)

a (2 pts). What is the biochemical basis of maple syrup urine disease?

Ans: Deficiency of branched chain α-keto acid dehydrogenase

bi (2 pts). Which intermediates of the urea cycle must cross the mitochondrial memberane?

Ans: Ornithine and citrulline

bii (2 pts). Aspartame, a widely used non-sugar sweetening in diet soft drinks, is a dipeptide comprising of Asp and Phe-methyl ester. Why do food products containing aspartame bear warning labels for phenylketonurics (patients with PKU)?

Ans: aspartame hydrolysis will generate Phe, therefore a potential dietary source of Phe which cannot be efficiently metabolized by PKU patients.

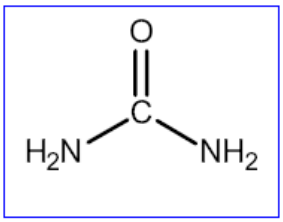
c (3 pts). Ubiquitin is a small protein of 76 amino acids that plays an important role in protein degradation by the proteasome, a multisubunit complex called the cellular "garbage disposal". What is the biochemical function of ubiquitin, i.e., *how* does it mediate protein degradation by the proteasome?

Ans:Ubiquitin serves as a molecular tag that identifies proteins targeted for degradation by the proteasome (ubiquitin subunits on proteins bind to the proteasome entry site).

d (5 pts). Write the overall equation for the urea cycle. Draw the structure of urea and indicate where all of its non-hydrogen atoms come from as derived from the urea cycle.

Ans:

$Asp + NH_3 + HCO_3^- + 3ATP \rightarrow Urea + Fumarate + 2ADP + 2P_i + AMP + PP_i$

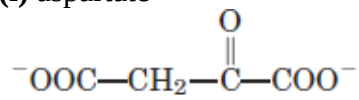


The C and O atoms are from CO_2 (carbonate).
One NH_2 group is from ammonia (NH_3).
One NH_2 group is from Asp.

e (3 pts). Using appropriate chemical illustrations to identify the key intermediates, justify why "Substrate Channeling" is essential for the reactions catalyzed by the Urea Cycle enzyme Carbamoyl Phosphate Synthetase
Ans: Increases the rate of rxn by preventing the loss of NH3 and protecting high energy intermediates – carboxyphosphate and carbamate – from degradation

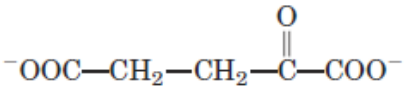
f (8 pts). Name and draw the structure of the a-keto acid resulting when each of the following amino acids undergoes transamination with a-ketoglutarate:

(i) aspartate



Oxaloacetate

(ii) glutamate



α-Ketoglutarate