NAME:
SID:

Chemistry 135, Third Exam
November 15, 2019
Please only turn this page once asked to do so by the instructor.

This exam will be worth 15% of your overall grade. Please read all of the instructions/questions carefully and answer the question in the space provided or indicated. There should **12** total pages containing **7** multi-part questions. Be sure to transfer any answers you wish to receive credit for to the space provided. No calculators, phones, electronic devices, etc. may be used during this exam. Good luck!

Please do not make any marks on this coverpage except for writing your name and student ID.

Questions

Question	Points	Question #	Points
1	12	**5**	48
2	47	**6**	18
3	10	**7**	35
4	12		
	Total	**182**	

Remember that whenever you take an exam, you are really taking *two* tests. The first is a test of your knowledge from the class. The second, and more important, is a test of integrity: that the answers you put down represent your answers and not someone else's. Please make sure to pass the more important test!

You will not need any calculators, phones, electronic devices, headphones, etc. to complete this exam (indeed, they will slow you down), so please make sure these are put away.

Please do not make any marks on this coverpage except for writing your name and student ID.

1. Please carefully evaluate the following statements. If the statement is correct, please mark it as "True." If the statement is false, please provide the correction(s) that renders the statement true. (4 points each)

For example:
The chemical biology program at Stanford is the best!
This would be marked as "FALSE" and could be corrected in the following way:
The chemical biology program at ~~Stanford~~ *Cal* is the best!

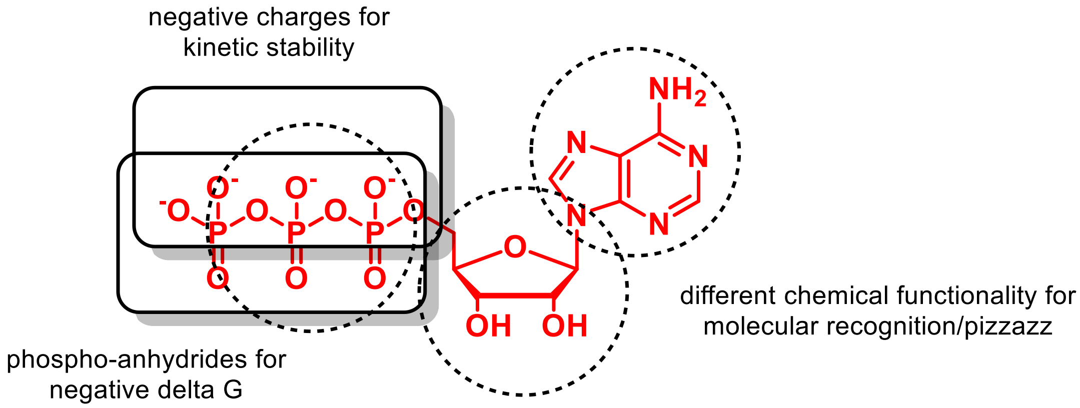
a. _____ The thermodynamic property of $\Delta G'^{\circ}$ refers to the amount of free energy required or released to go from standard conditions ~~equilibrium concentrations~~ to ~~actual~~ equilibrium position or equilibrium concentrations.

b. _TRUE In order for ATP to be used to drive unfavorable reactions, ATP hydrolysis must be involved in the bond forming and breaking steps of the reaction mechanism.

c. FALSE Generally speaking, anabolic ~~catabolic~~ reactions use high energy intermediates to construct biomolecules, while catabolic ~~anabolic~~ reactions break down biomolecules to extract high energy intermediates.

2. In class, we discussed some of the features that make ATP, adenosine triphosphate, an excellent universal cellular energy source.

a. In the space below, please provide the structure of ATP (6 points).



b. We also discussed three characteristics of ATP that make it such an excellent cellular energy source. In the space below, please provide three characteristics of ATP that make it an excellent universal cellular energy source (1 sentence per reason, 9 points).

Characteristic 1- ATP has a large, negative ΔG'° of hydrolysis.

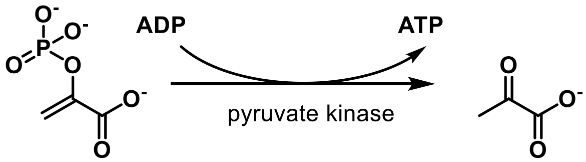
Characteristic 2- ATP is kinetically stable, or has a high activation barrier for reaction.

Characteristic 3- ATP possesses molecular diversity, or a wide range of different chemical functionalities.

c. For the structure you provided in part (a), please indicate by circling and labeling the molecule which portions of ATP account for the three characteristics you provided in part (b) (6 points).

see part (a)

d. The equation below depicts the final step of glycolysis. This step is an example of (circle one, 4 points)



Equation 1

oxidative decarboxylation	oxidative phosphorylation	**substrate level phosphorylation**	thioester hydrolysis

e. If the standard free energy change for the overall reaction shown in **Equation 1** is -7.5 kcal/mol, calculate the standard free energy change associated with the hydrolysis of PEP. Please write out the two relevant half-reactions that allow you to make this estimate. (10 points)

Overall reaction:
PEP + ADP → pyruvate + ATP $\Delta G'^\circ$ = -7.5 kcal / mol

Two half-reactions:
PEP + H_2O → pyruvate + P_i $\Delta G'^\circ$ = ?

ADP + P_i → ATP + H_2O $\Delta G'^\circ$ = +7.3 kcal/mol
overall:

7.3 + X = -7.5; X = -14.8 kcal / mol

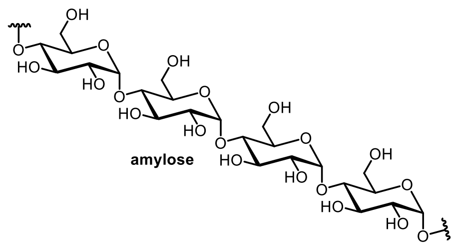
f. What two factors help explain the large, negative standard free energy change associated with PEP hydrolysis? (6 points)

-hydrolysis of the phosphate group or phosphate ester (~ -3 to -4 kcal)
-enol to keto tautomerization of pyruvate (~ -11 to -12 kcal)
*students do not need to provide these numbers

g. Although PEP possess a large and negative standard free energy change associated with hydrolysis, it is less than an ideal choice as a universal cellular energy source. Speculate as to why PEP is not as good of a choice for a universal cellular energy source as ATP. (6 points) (**Hint**: the best answers will consider the characteristics that make ATP a great universal energy source and compare and contrast this with PEP).

Although PEP has a large, negative $\Delta G'^\circ$, unlike ATP, it does not possess a wide range of diverse functionalities (i.e. no nucleobase, no cyclic sugar, no hydroxyls, etc.).
It is also probably not very kinetically stable, since the kinetic stability of ATP comes from the 4 negative charges on the phosphoanhydrides, and PEP does not have a phosphoanhydride.

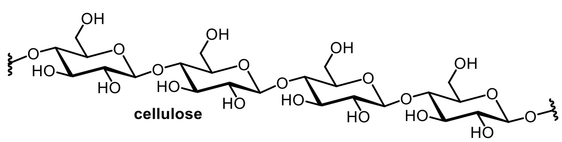
3. Cornstarch is a polymeric carbohydrate isolated from corn. It is commonly used in cooking as a thickener for sauces, soups, and glazes. Chemically speaking, cornstarch is composed of a mixture of amylose and amylopectin (see structure, below).



a. Amylose is readily digested in humans by the enzyme salivary amylase. Provide the name of the monosaccharide produced when salivary amylase hydrolyzes the glycosidic bonds of amylose. (3 points)

glucose

b. In contrast, the polysaccharide cellulose (below) is the primary component of vegetable fibers, like cotton, and is not digestible by humans. What is the monosaccharide that makes up cellulose? (3 points)



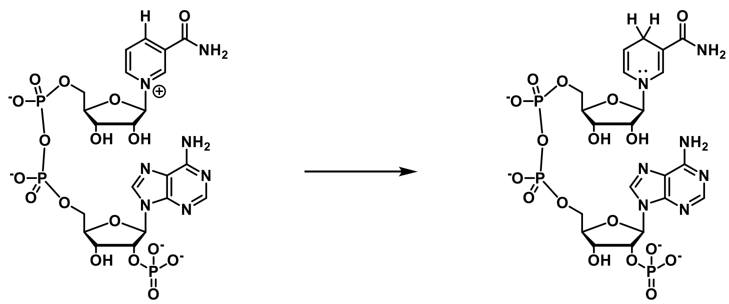
glucose

c. What is the main difference between the polysaccharide amylose and cellulose? (4 points)

They have different configurations around their glycosidic bonds. Amylose is α and cellulose is β.

4. For the following equilibrium expressions, provide an estimate of ΔG'°. Provide a name or abbreviation for the indicated molecules. (12 points)

a.

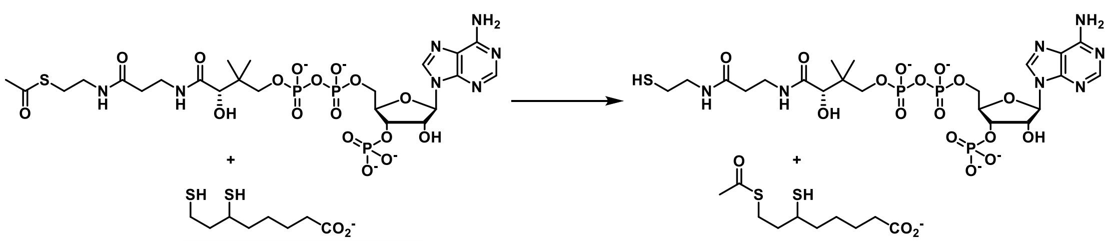


NADPH

ΔG'° is +14.8 kcal/mol

NADPH

b.



CoA-SH
or Coenzyme A

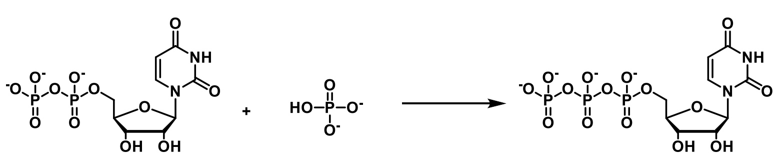
lipoate/lipoic acid
or dihydrolipoate/-ic acid

lipoate/lipoic acid or dihydrolipoate/-ic acid

Coenzyme A.

ΔG'° is approximately 0 kcal / mol.

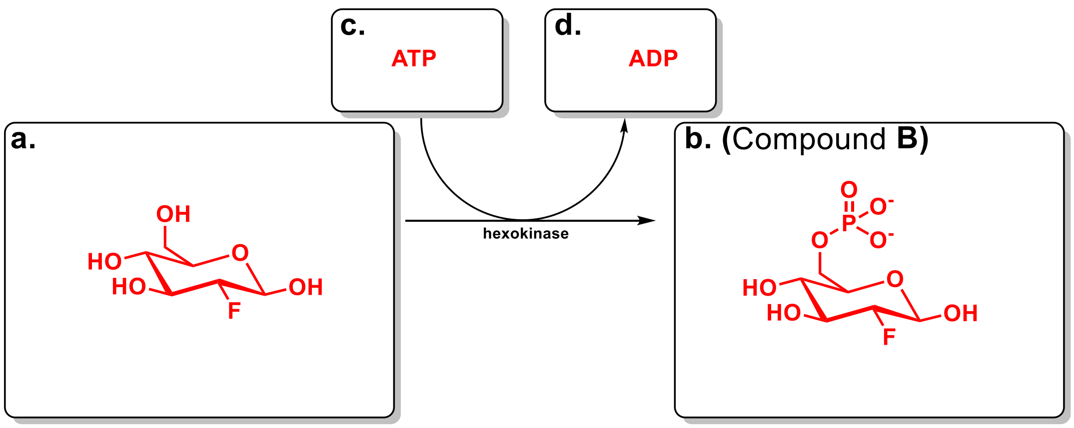
c.



ΔG'° is approximately + 7.3 kcal/mol

5. The molecule 2-fluorodeoxyglucose, or FDG, is an important molecule used today in clinical diagnostics. When FDG is synthesized with a radioactive isotope of fluorine (^{18}F), it can be used, in combination with a medical imaging technique called positron emission tomography, or PET, to image cancerous tumors in patients. FDG is retained inside cancer cells, where FDG is a substrate for some, but not all of the enzymes in the steps of glycolysis. FDG has a fluorine atom instead of the typical hydroxyl group on the C2 carbon of glucose. In the space below, please complete the balanced equation for the reaction catalyzed by hexokinase (step 1 of glycolysis), including

a. a detailed structural drawing of the starting material, FDG,
b. the product of this reaction (Compound **B**),
c. the additionally required reagent (abbreviation okay), and
d. its byproduct (abbreviation okay). (2 points each)



Normally, glucose (and FDG) is allowed to enter the cell through the transporter GLUT 1, which allows glucose to pass through the plasma membrane in a concentration-dependent fashion (i.e. it does not use ATP to power this movement). Shown below is the equilibrium expression that describes the transport of glucose into the cell.

$$\textbf{glucose (outside cell)} \rightleftharpoons \textbf{glucose (inside cell)}$$

Equation 2

e. What is the standard free energy (ΔG'°) associated with this expression? What is the value of K_{eq}? (8 points)

The ΔG'° for this expression is 0 kcal/mol. K_{eq} is 1.

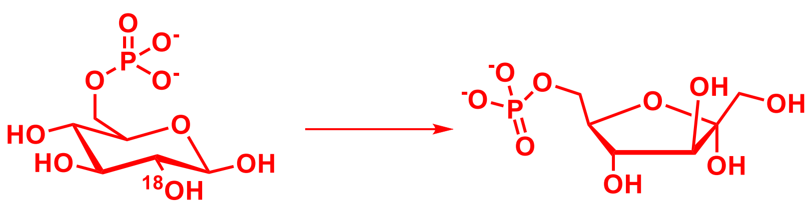
f. In the first step of glycolysis, glucose is converted into glucose 6-phosphate by hexokinase. Does this affect the standard free energy (ΔG'°) associated with **Equation 2** (above)? Does this affect the actual free energy (ΔG) associated with **Equation 2** (above)? Explain your answer in 1-2 sentences. (6 points)

No effect on ΔG'°. It does change the actual free energy (ΔG), making ΔG negative by consuming Glc (in). This changes Q and pushes the reaction towards the right.

g. Although FDG is readily incorporated into the first step of glycolysis, the product of this reaction (Compound **B**, above) cannot act as a substrate for the second step of glycolysis. Briefly explain this observation. (1-2 sentences, 4 points)

The isomerization of glucose to fructose requires the presence of an OH group on C2. FDG does not have an OH group on C2, so cannot be a substrate.

h. FDG containing radioactive ^{18}F decays with a half-life of about 2 hours. The decay of ^{18}F within compound **B** eventually results in the generation of a positron and emission of two gamma rays, which are detected to compute a map of tumor cells within a patient's body. In addition to these high-energy particles, the decay of ^{18}F-compound **B** also generates an oxygen (^{18}O) at the C2 position. This new compound now resembles the natural substrate in every way, except for the inclusion of a heavy oxygen at the C2 hydroxyl group. In the space below, please show the reaction of this new compound (compound **B**, with C2-oxygen) in the 2nd step of glycolysis. (6 points)

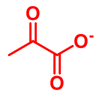


i. For the metabolism of FDG (and its decay product) through glycolysis, what is the net production of ATP, per glucose molecule? (2 points)

2 ATP per glucose molecule.

j. What is the carbohydrate that is produced at the end of glycolysis? Provide a name and structure. (4 points)

pyruvate



k. One of the key steps in glycolysis is the splitting of sugar to generate two fragments each containing 3 carbons. This reaction is catalyzed by the enzyme aldolase, which uses a lysine reside as a critically important amino acid residue. Explain why a mutation of the active site lysine to alanine would have disastrous consequences for the catalytic efficiency of aldolase. (6 points)

Aldolase uses lysine as a covalent catalyst to split 1,6-bisphosphofructose. Lysine must be able to form a Schiff base/imine/iminium with fructose. Alanine would not be able to form the required covalent intermediate

l. Conceptually, the role of lysine in aldolase is similar to the role that thiamine pyrophosphate (TPP) plays in the reactions catalyzed by pyruvate dehydrogenase and pyruvate decarboxylase. In these transformations, TPP acts as a/an (circle one) (4 points)

HEEP carrier	**electron sink**	phosphoanhydride	general acid

to help facilitate the (circle one)

production of lactate.	interconversion of an anomic carbon.	generation of ATP from a mixed anhydride.	**removal of CO_2 from pyruvate.**

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6. We have covered several different metabolic pathways during this third section of Chem 135.

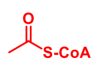
a. While studying for exam 3, a classmate of yours asserts that glycolysis is the most important catabolic pathway for glucose, because glycolysis effectively captures all of the chemical energy contained in the bonds of glucose, by fully oxidizing glucose. Do you agree with your classmate? Briefly explain your answer. (8 points)

No. Most of the chemical energy of glucose remains in the 2 molecules of pyruvate. There are 12 reducing equivalents, or HEEPs in glucose, and there are 5 HEEPs / pyruvate, for a total of 10. So, most of the HEEPs/chemical energy/reducing equivalents remain; it has not been fully oxidized.

b. In a different study group, you encounter a different classmate who was extoling the virtues of the tri-carboxylic acid cycle. This classmate was impressed by the fact that the reducing equivalents and free energy content of acetyl CoA are completely captured by the overall reactions of the citric acid cycle. Do you agree with the assessment of your classmate? Fill out the missing information about the TCA cycle, below and use this information to briefly defend your answer. (10 points)

acetyl-CoA

(please provide structure of the "business end")



citric acid cycle →

please list the net products of the TCA cycle, per equivalent of acetyl-CoA

2x CO2

3x NADH

1x FADH2

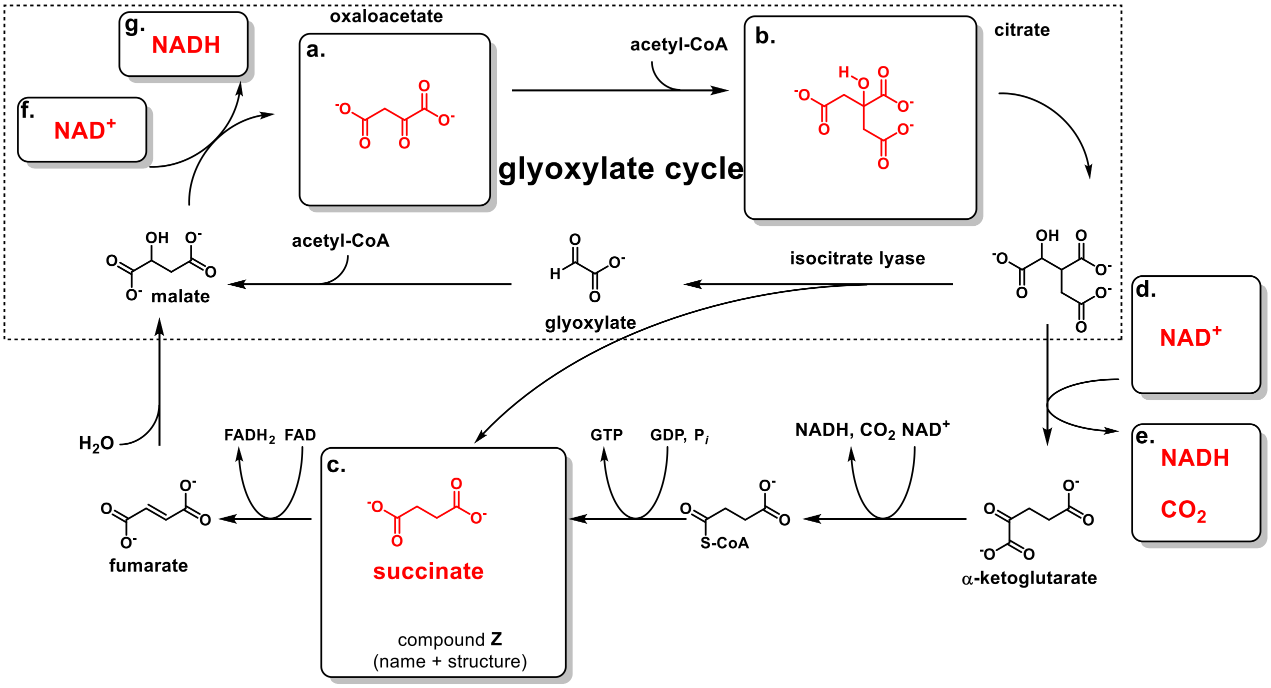
1x GTP

The 4 HEEPs in acetyl CoA are transferred into 4 HEEP carriers, 3 NADH and 1 $FADH_2$.

The high free energy containing thioester is converted to GTP, another high free energy containing molecule.

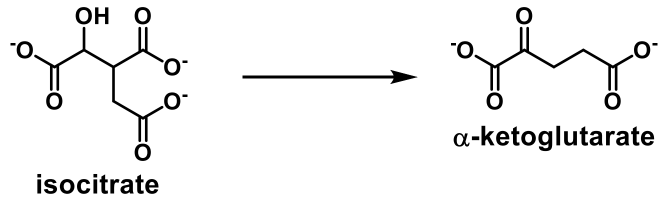
The 2 carbons of Ac-CoA are fully oxidized to CO_2.

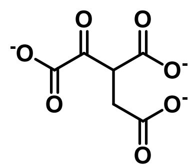
7. In plants and some microorganisms, an additional cycle – the glyoxylate cycle – operates alongside the citric acid cycle. The glyoxylate cycle shares several of the same steps as the TCA cycle, but diverges in a key way: isocitrate is converted by isocitrate lyase into glyoxylate and another compound (compound **Z**, in the diagram below). Then, glyoxylate is combined with acetyl CoA to generate the TCA intermediate, malate. Shown below is a diagram that combines glyoxylate cycle reactions with TCA cycle reactions that we have learned from class. Provide the following information.



a. Structure of oxaloacetate. (3 points)
b. Structure of citrate. (3 points)
c. Structure and name of "Compound **Z**". (6 points)
d. Cofactor required for synthesis of α-ketoglutarate (abbreviation okay). (1 point)
e. Additional byproducts produced during generation of α-ketoglutarate (there are 2. Abbreviations okay). (3 points)
f. Cofactor required for synthesis of oxaloacetate (abbreviation okay). (1 point)
g. Additional byproduct produced during generation of oxaloacetate (abbreviation okay). (1 point)

h. In the space below, provide a detailed arrow-pushing mechanism for the transformation of isocitrate into α-ketoglutarate (reproduced for your convenience, below). Be sure to indicate how the cofactors and byproducts you indicated in parts **d** and **e** are consumed and/or generated. (18 points)





NOTE: Prof. Miller mistakenly provided this structure as "isocitrate" in the original exam.
The key below shows the correct answer, with isocitrate as the starting material