Name: ___**Key**_____ Key_____

Chem 4512/6502 Exam 1 February 16, 2016

by Dr. A. Oyelere

Please put your name at the top of every page.

There are **8 multi-part questions** to this exam.
Please look over the whole exam before you start answering questions. The maximum points for each question are indicated. There are 100 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

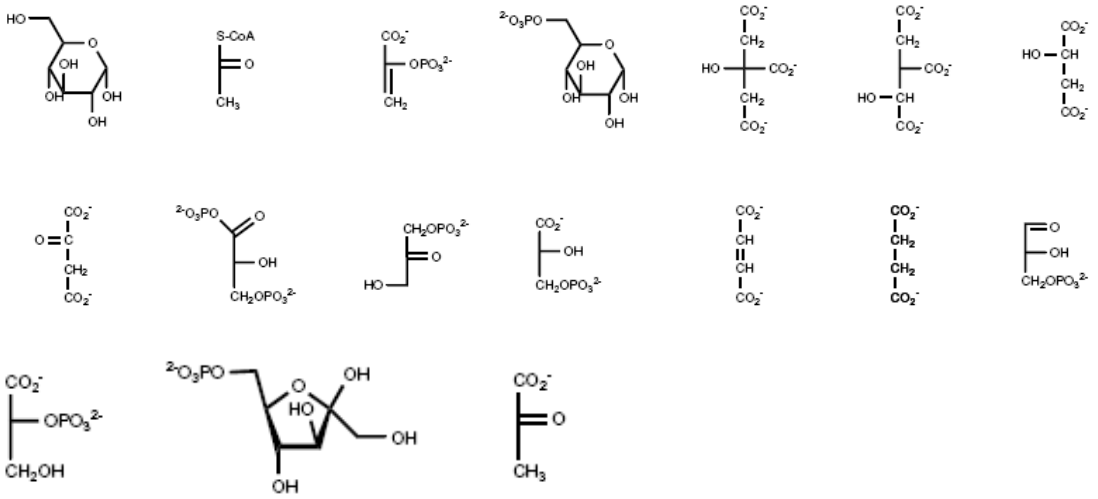
You are expected to strictly adhere to Georgia Institute of Technology Honor Code.

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

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.)

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

I. Heterotrophs are organisms that

a. Produce food form inorganic molecules or sunlight.
b. Can survive without energy.
c. Must consume other organisms to get energy.
d. None of the above

II. Which of the following is an enzyme?

a. ribulose
b. sucrose
c. dehydrogenase
d. NADH

III. When a phosphate group is removed from an ATP molecule,

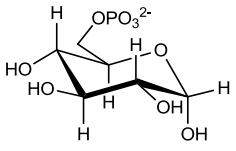
a. a substantial amount of energy is released.
b. an enzyme is formed
c. energy is stored
d. activation energy is increased

IV. Glycolysis takes place in

a. mitochondria
b. golgi apparatus
c. endoplasmic reticulum
d. cytosol
e. none of the above

V. Which of the following compounds is not a glycolytic metabolite?

A.



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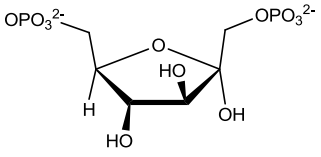

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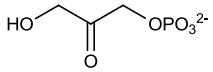

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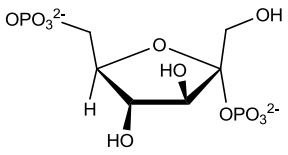
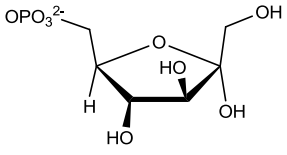


E.



Ans:D

VI. When the free energy of the products is higher than the free energy of the reactants; such a reaction is referred to as an _____ reaction.

a. entropy
b. endergonic
c. exergonic
d. activation
e. thermo neutral

VII. Anabolism is best described as

a. degradative pathways
b. biosynthetic pathways
c. mechanical pathways
d. energy producing pathways
e. none of the above

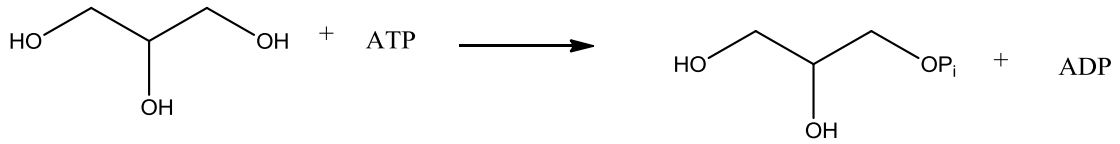
VIII. The steps of glycolysis between glyceraldehyde 3-phosphate and 3 phosphoglycerate involve all of the following except:

a. ATP synthesis.
b. Catalysis by phosphoglycerate kinase.
c. Oxidation of NADH to NAD^+.
d. The formation of 1,3-bisphosphoglycerate.
e. Utilization of Pi.

IX. During glycolysis in the liver, glucose is converted to glucose-6-phosphate by the enzyme(s):

a. glucokinase.
b. fructokinase.
c. hexokinase.
d. all of the above.
e. none of the above.

X. What type of enzyme catalyzes the reaction below?



a. kinase
b. isomerase
c. mutase
d. aldolase
e. dehydrogenase

XI. In which of the following metabolic conversions is ATP "consumed" during glycolysis?
a. 1,3-Bisphosphoglycerate → 3-phosphoglycerate
b. Glucose → glucose-6-phosphate
c. 2-Phosphoglycerate → 3-phosphoglycerate
d. Fructose-1,6-bisphosphate → dihydroxyacetone phosphate + glyceraldehyde-3-phosphate
e. Glucose-6-phosphate → fructose-6-phosphate

XII. The pentose phosphate pathway is an anabolic reaction that generates NADPH and pentose. This biochemical pathway provides the cell with _____ for nucleotide and nucleic acid synthesis.

a. **Ribose-5-phosphate**
b. Erythose-4-phosphate
c. NADPH
d. Hydrogen peroxide

XIII. When the pentose pathway metabolizes glucose, the C-1 of glucose ends up mostly in:

a. CO_2
b. glycogen
c. 3-phosophoglycerate
d. pyruvate
e. ribulose-5-phosphate

XIV. There is an oxidative and a non-oxidative phase in the pentose phosphate pathway. Which of the following is produced during the oxidative phase?

a. Glucose-6-phosphate
b. $NADP^+$
c. **NADPH**
d. Both A and C

XV. The metabolic basis of fructose intolerance is:

a. Deficiency of Glucokinase
b. Deficiency of Fructokinase
c. **Deficiency of Fructose-1-phosphate aldolase**
d. Deficiency of Hexokinase
e. Deficiency of Enolase

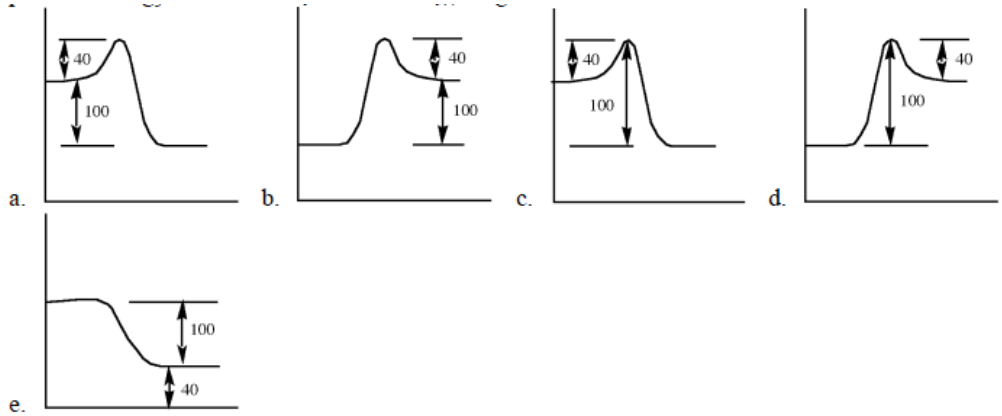
XVI. In most tissues, an increase in the following ratio directly causes an increase in glycolysis activity:

a. $FADH_2/FAD$
b. ATP/ADP
c. GTP/GDP
d. $NADH/NAD^+$
e. $NAD^+/NADH$

XVII. What thermodynamic parameter is a measure of randomness or disorder in a system?

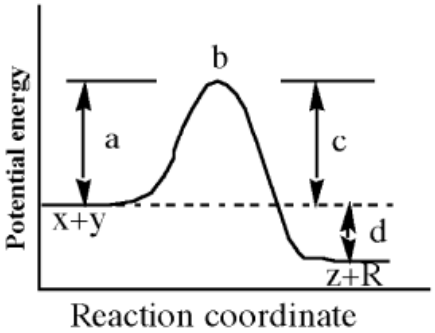
a. entropy
b. enthalpy
c. free energy
d. potential energy
e. activation energy

XVIII. A reaction has an activation energy of 40 kJ and an overall energy change of reaction of -100 kJ. In each of the following potential energy diagrams, the horizontal axis is the reaction coordinate and the vertical axis is potential energy in kJ. Which potential energy diagram best describes this reaction?



Ans: A

XIX. Given the following potential energy diagram for the one-step reaction
X + Y → Z + R The arrow "d" represents the _____.



a. energy content of products
b. activation energy for the forward reaction
c. energy content of reactants
d. activation energy for the reverse reaction
e. the net change in energy for the reaction

XX. Enzymes accelerate thermodynamically possible reactions by:

a. systematically removing one of the products
b. lowering the overall free energy change for the reaction
c. reducing the temperature coefficient
d altering the equilibrium constant
e. lowering the activation energy of the reaction

Section 2: Answer <u>all</u> questions in this section.

2 (10 pts). Pick the correct answer from the list (A-P) and fill in the blank. *NOTE*: answers may be used more than once or not at all.

i. One of the products of glycolysis under aerobic or anaerobic conditions is **<u>NADH/ATP</u>**.

ii. Organisms that require oxygen are called **<u>Aerobes</u>**.

iii. Redox reactions of nicotinamide cofactors (*e.g.* NAD^+) involves transfer of a **<u>Hydride</u>**.

iv. 1,3-Bisphosphoglycerate is a type of **<u>Acyl phosphate</u>**.

v. The coenzyme **<u>NAD+</u>** is the oxidizing agent in glycolysis.

vi. Enzyme that imposes an equilibrium-like condition on reaction catalyzed by PFK **<u>FBPase</u>**.

vii. The phenomenon which accounts for rapid glucose consumption by tumor cells **<u>Warburg effect</u>**

viii. A loss of electrons from a substance is known as **Oxidation**.

ix. Enzyme that splits Fructose-1,6-bisphosphate, a six carbon sugar, into two three carbon sugars is called **<u>Aldolase</u>**.

x. The process by which ATP is formed from ADP in glycolysis is referred to as **<u>Substrate level</u>** phosphorylation.

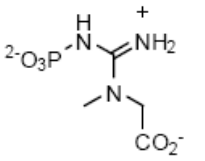
Possible answers:

A) acyl phosphate	B) FBPase
C) hydride	D) Aldolase
E) proton	F) oxidation
G) NAD+	H) ATP
I) Pasteur effect	J) Warburg effect
K) NADH	L) aerobes
M) substrate-level	N) NADPH
O) reduction	P) NADP+

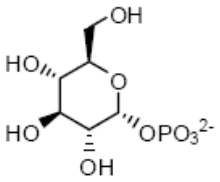
3 (2 pts). Briefly distinguish between a holoenzyme and an apoenzyme. (Hint: compare them on the basis of activity).

Ans: Holoenzyme (catalytically active) = apoenzyme (catalytically inactive) + a prosthetic group

4 (3 pts). Explain why the ΔG°' of hydrolysis of phosphocreatine (-43.1 kJ/mol) is greater than that for glucose-1-phosphate (-20.9 kJ/mol). Draw structures or mechanisms to help explain your argument.

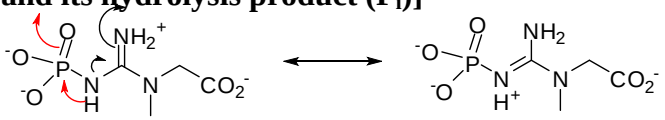


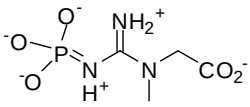
Phosphocreatine



Glucose-1-Phosphate

Due to competing resonances in the guanidine group [or the resonance stabilization of phosphoguanidine bond in phosphocreatine is much less than that of its hydrolysis product (P_i) compared to resonance stabilization of glucose-1-phosphate and its hydrolysis product (P_i)]



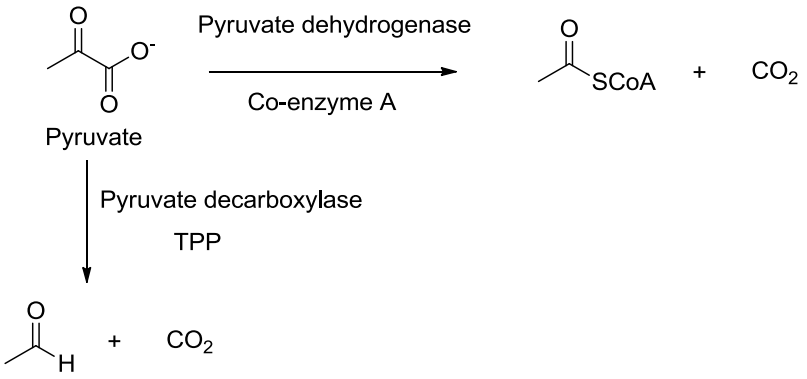


Unfavorable

5a (2 pts). You have provided ATP containing a radioactively labeled terminal phosphate to a system undergoing glycolysis. Which of the glycolytic intermediates will <u>not</u> be radioactively labeled?

Ans: The phosphate added to glucose in step 1 of glycolysis is removed in step 10. As a result all intermediates in glycolysis, except <u>pyruvate</u> (and glucose), will contain radioactive phosphate.

5b. Pyruvate dehydrogenase and pyruvate decarboxylase are two enzymes in yeast which facilitate further metabolism of pyruvate.

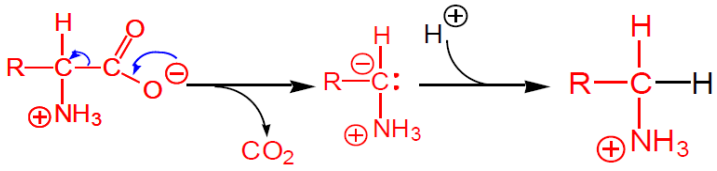


A) **(2 pts)** Provide the products of pyruvate dehydrogenase and pyruvate decarboxylase reactions in the schemes above.

B) **(1 pt)** Comment on the redox outcome of each reaction.
Ans: Pyruvate dehydrogenase reaction is an oxidative decarboxylation reaction while there is no apparent change in the oxidation state in pyruvate decarboxylase reaction.

Section 3: Questions 6 through 8. Answer <u>any two</u> questions in this section. Each question is worth 20 points

6 (20 points)
6a. Shown below is a plausible mechanism for an uncatalyzed decarboxylation of amino acids.



i (3 pts). Why is the uncatalyzed reaction energetically costly (thermodynamically unfavorable)?

Ans: The need for charge separation at transition state

ii (2 pts). What is the enzyme's likely cofactor?

Ans: Pyridoxal phosphate (PLP)

6bi (2 pts). What is the committed step (reaction) of glycolysis? [Note – name of the substrates and products will suffice]

Ans: F-6-P + ATP → F-1,6-P + ADP

6bii (2 pts). Name the enzyme that catalyzes the committed step in glycolysis.

PFK

6biii (2 pts). Name one activator and one inhibitor of this enzyme

Ans: Activator: AMP (ADP acceptable)
Inhibitor: ATP

6biv (2 pts). Why is the reaction catalyzed by hexokinase *not* the committed step of glycolysis?

Ans: The reaction catalyzed by hexokinase, i.e. the conversion of glucose to glucose-6-phosphate (G-6-P), is not unique to glycolysis. Hence, G-6-P can be injected into glycolysis through sources other than hexokinase. Also hexokinase has multiple substrates.

6c. The following reaction represents the last step of Glycolysis

PEP + ADP → Pyruvate + ATP

i) (3 pts). Calculate the equilibrium constant K based on the following cellular concentrations of the reactants

[PEP] = 1 mM
[Pyruvate] = 0.9 mM
[ADP] = 0.8 mM
[ATP] = 3.0 mM

Ans:

$$K = \frac{[Pyruvate] \cdot [ATP]}{[PEP] \cdot [ADP]}$$

$$= \frac{0.0009 \cdot 0.003}{0.001 \cdot 0.0008} = 3.375$$

ii) (3 pts). Calculate ΔG at 25 °C assuming that $\Delta G^{o'}$ = -23.0 kJ•mol^{-1}. (note: R = 8.314 J•K^{-1}•mol^{-1})

$$\Delta G = \Delta G^{o'} + RT \ln K$$
$$= -23{,}000 \frac{J}{mol} + (8.314 \cdot 298.15) \frac{J}{mol} \ln(3.375)$$
$$= -23{,}000 \frac{J}{mol} + 3015 \frac{J}{mol} = -19985 \frac{J}{mol} = -20 \frac{kJ}{mol}$$

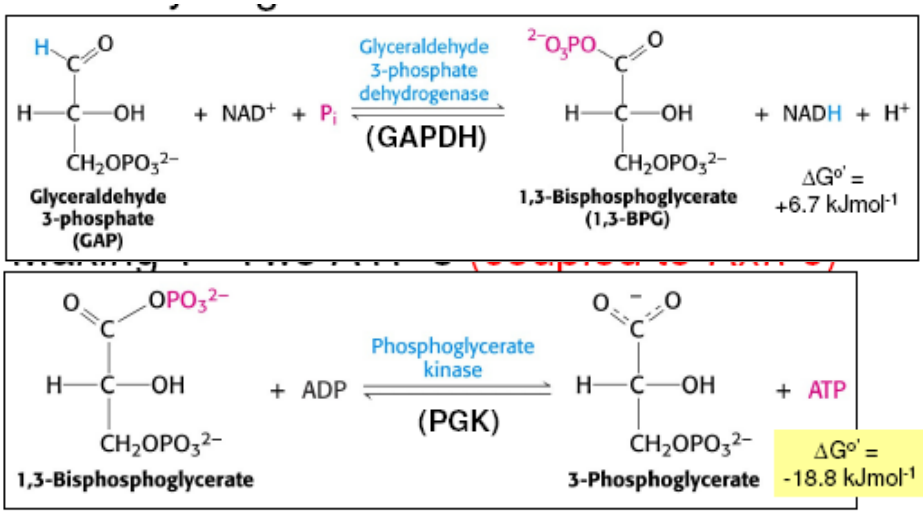
iii) (1 pt). Is the reaction endergonic or exergonic at cellular conditions?

Ans: Exergonic

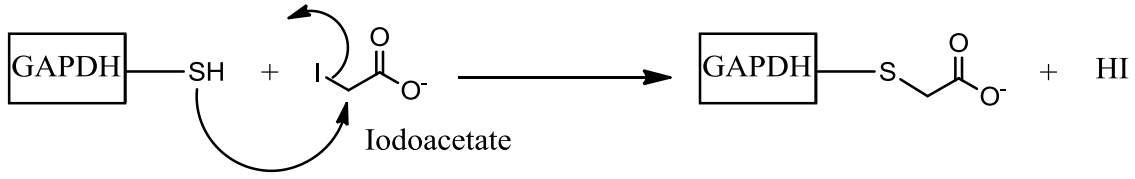
7 (20 points)

7a (4 pts). Conversion of GAP (+ a source of Pi) to 1,3-BPG (catalyzed by glyceraldehyde-3-phosphate dehydrogenase) is an energetically unfavorable reaction. However, the reaction still takes place in glycolysis. What drives this reaction forward? (**Note: Appropriate reactions are required for full points**)

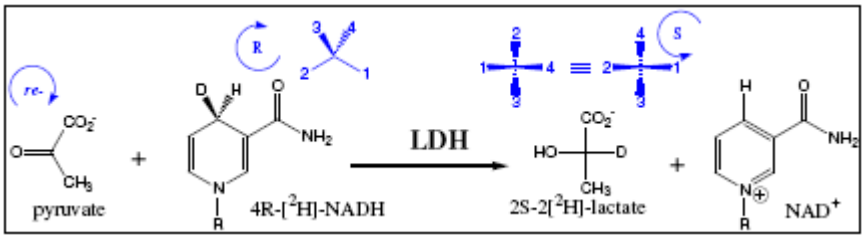
Ans: The reaction is coupled to the next glycolytic reaction, i.e., Phosphoglycerate Kinase



7b (3 pts). Using appropriate illustration, describe the mechanism of iodoacetate inhibition of glyceraldehyde-3-phosphate dehydrogenase (GAPDH).



7c (3 pts). What is the importance of lactic acid fermentation in multicellular organisms such as humans? (Use chemical equation to illustrate your point)



Sustenance of glycolysis through generation of NAD^+

7d. (4 pts) What is the metabolic purpose of the Cori Cycle?

Ans: The Cori cycle salvages (reclaims) the chemical potential of lactate produced by fermentation reactions in skeletal muscle by converting two 3-C acids back to glucose in liver which then supplies the muscle tissue with glucose.

7e (2 pts). The phosphoglucose isomerase reaction interconverts glucose-6-phosphate and fructose-6-phosphate. Write the reaction catalyzed by phosphoglucose isomerase (structures or words) in the direction in which it would occur in glycolysis.

glucose-6-P --> fructose-6-P

7fi (2 pts). In the overall reaction describing glycolysis, $2H_2O$ are released. Which enzyme(s) are responsible for the dehydration reaction(s)?

Enolase

7fii (2 pts). F^- ion is a potent inhibitor of the enzyme(s) responsible for the dehydration reaction(s) in glycolysis. What is the mechanism of inhibition of the enzyme(s) activity by F^- ion?

F^- forms complex with Mg^{2+} at enzyme active site

8 (20 points)

8a (4 pts). Metabolic pathways are highly regulated such that there is rarely unsatisfied need for reactants or unnecessary buildup of products. Give 4 general methods of control of metabolic pathways in the cell. **Ans:**

1. Control of amount of enzymes present 2. Control of activity of enzymes

3. Control of accessibility of substrate molecules 4. Separation of Biosynthetic and degradative pathways (compartmentation)

8bi (2 pts). Give the overall reaction of the Pentose Phosphate Pathway (PPP).

$3G6P + 6NAD(P) + 3H_2O \rightarrow$
$6NAD(P)H + 6H^+ + 3CO_2$ +2F6P + glyceraldehyde-3-phosphate

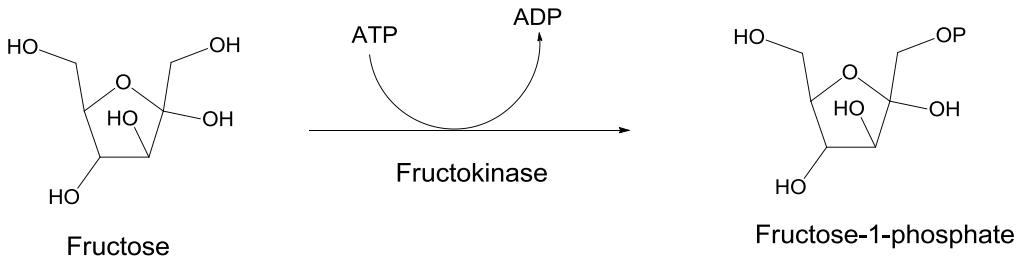
8bi (3 pts). A deficiency in glucose-6-phosphate (G6P) dehydrogenase leads to which condition? How can this be a good thing?

Favism (Hemolytic anemia acceptable);

Resistance to the malaria parasite (due to decrease in glutathione production)

8c (3 pts). What is the enzyme that transfers a phosphate group to fructose in glycolysis in liver? What is the product of the reaction catalyzed by this enzyme?

Fructokinase



Fructose

Fructose-1-phosphate

8d (2 pts). Give the names of the two enzymes, both found in liver but not in most other body cells, which allow the liver to control blood glucose concentration.

Ans: Glucokinase & Glucose-6-phosphatase

8e (6 pts). Very briefly define the following terms or concepts (Your answer can contain **no more** than 20 words):

i. The role of TIM in glycolysis

Catalyzes the inter-conversion between DHAP and GAP (thus supplying the pathway with GAP which moves down the pathway.)
(2 points)

ii. Role of Mg++ in ATP dependent reactions

(Substrate binding and) electrostatic stabilization of negative charges to facilitate nucleophilic attack on electrophilic phosphate group.
(2 points)

iii. The biochemical basis of Tarui disease

Deficiency of PFK-1
(2 points)