

Name _____

Student number _____

University of Guelph
Department of Chemistry and Biochemistry
19-356
Structure and Function In Biochemistry

Final Exam, April 22, 1998.

Time allowed, 120 min.

Answer questions 1-30 on the computer scoring sheet provided.

Only one option is correct for each of these questions.

Use pencil to fill in the circles representing your chosen answer; and erase cleanly if you make an error. Do not use ink or white-out on the computer scoring sheet.

You may mark your answer on the question paper for your own records, however in case of a discrepancy between question paper and the computer scoring sheet, the choice shown on the computer sheet will be taken as final.

Answer questions 31-34 directly on the question paper.

Questions 1-30 have a weight of 1 mark each

30 marks

Questions 31-34 have marks as indicated

30 marks

=====

60 marks

total

31	32	33	34	
/ 9	/ 6	/ 8	/ 7	/ 30

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Answer questions 1-30 on the computer scoring sheet.

Value 1 mark each

1. Which of the following properties of hemoglobin is **not** part of the Bohr effect?

- A) Decreased O₂ binding at lower pH.
- B) Protonation of histidines near the C-terminus of globin.
- C) Decreased O₂ binding in presence of elevated CO₂ levels.

D) Decreased O₂ binding at high altitude.

E) Formation of carbamate derivatives at the N-terminus of globin.

1) A B C **D** E

Altitude acclimatization is a BPG effect, not a Bohr effect

2. Glycogen phosphorylase is an allosteric enzyme with T and R states; which of the following is **not** true?

- A) Phosphorylase **a** is preferentially in R state without requiring allosteric effectors.
- B) Phosphorylase **b** is preferentially in T state in the presence of Glucose-6-P.

C) Muscle phosphorylase b is preferentially in T state in the presence of 5'AMP

D) Phosphorylase **b** is preferentially in T state in the presence of ATP.

E) Liver Phosphorylase **a** is preferentially in T state in the presence of Glucose.

AMP is a positive effector for phosphorylase *b*

2) A B **C** D E

3. Which enzyme is **not** a component of fatty acid synthase I?

A) Condensing enzyme

B) Acetyl CoA carboxylase

C) Thioesterase

D) Malonyl Transferase

E) Hydroxyacyl dehydratase

3) A **B** C D E

Stryer used the term condensing enzyme for ketoacyl ACP synthase

4. Which of the following **sugar phosphates** is **not** a substrate or product of transaldolase?

A) Sedoheptulose-7-P B) Glyceraldehyde-3-P **C) Ribose-5-P**

D) Erythrose-4-P

E) Fructose-6-P

4) A B **C** D E

Adding 3 carbons to Ribose-5-P would make an octulose-8-phosphate

5. Which of the following is **not** a positive or negative allosteric regulator of phosphofructokinase?

A) Citrate

B) Fructose-2,6-bisphosphate C) ATP

D) 5'AMP

E) Glucose

5) A B C D **E**

6. The balance of various ionic substance inside and outside cells is quite characteristic.

Which of the following ionic conditions would be **abnormal**?

A) [Ca²⁺] lower inside

B) [phosphate esters] lower inside

C) [Na⁺] lower inside

D) [Mg²⁺] higher inside

E) [K⁺] higher inside

This would suggest that the cell contents have all leaked out

6) A **B** C D E

7. Which of the following properties or actions of the pentose phosphate pathway is **untrue**?

A) Causes CO₂ release from glucose without directly consuming O₂.

B) Generates NADPH for reduction in biosynthetic pathways

C) Interconverts different forms of sugar phosphates

D) Generates ribose-5-P for nucleotide synthesis

E) Generates ATP via oxidative phosphorylation of NADPH.

7) A B C D **E**

NADPH is not a substrate of oxidative phosphorylation

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8. Which of the following lipids has **net negative charge**?
- A) Phosphatidyl choline **B) Phosphatidyl serine**
C) Phosphatidyl ethanolamine D) Triacylglycerol
E) Diacylglycerol
- 8) A **B** C D E
- Two negative, one positive charge = net -1
9. The coenzyme generally **required for carboxylation** reactions is:
- A) Thiamine pyrophosphate B) NAD⁺ **C) Biotin**
D) Coenzyme A E) NADPH
- 9) A B **C** D E
10. Which factor is **beneficial if injected within 30 minutes** into a stroke victim?
- A) Vitamin K B) Fibrinogen **C) Tissue plasminogen activator**
D) Factor VIII E) Factor IX
- 10) A B **C** D E
- Converts plasminogen to active plasmin; plasmin breaks down fibrin to dissolve clots
11. Which substance is **beneficial as a preventative** of stroke?
- A) Vitamin K **B) Warfarin** C) Prothrombin
D) Factor VIII E) Factor IX
- 11) A **B** C D E
- Warfarin interferes with Vit K action; clotting factors don't develop as much γ -carboxyglutamate
12. Which of the following substances **can be transported across membranes by simple diffusion**?
- A) Glucose B) ATP C) Simple amino acids
D) CO₂ E) K⁺
- 12) A B C **D** E
- Low mass, neutral, not particularly polar due to molecular symmetry
13. Nitrotyrosine is a modification of natural tyrosine formed by exposure to tetranitromethane, and has the following effect in aspartate transcarbamylase:
- A) Causes breakup of ATCase into c_3 and r_2 components.
B) Allows c_3 and r_2 components to rejoin into c_6r_6 .
C) Causes a shift to the R state.
D) Causes a decrease in sedimentation coefficient.
E) Changes absorbance in response to change from T to R.
- 13) A B C D **E**
- This subject was covered more extensively in Stryer in 1998.
14. During intense physical activity:
- A) the liver synthesizes fatty acids from glucose.
B) the liver recycles lactate from blood into glucose.
C) the liver carries out glycolysis to make ATP which can be sent to the muscles.
D) the liver synthesizes glucose from stored fatty acids.
E) the liver takes up excess glucose from blood.
- 14) A **B** C D E
- The Cori cycle
15. The carrier of carboxylate groups in CoA and ACP is:
- A) phosphopantotheine** B) pyridoxal phosphate C) biotin
D) ATP E) thiamine pyrophosphate
- 15) **A** B C D E
- Pantotheine is the vitamin that is used to make CoA and ACP

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16. Conversion of **pyruvate into PEP** has the following net effect:
(treat ATP and GTP as equivalent for these purposes)
A) Consumes one ATP, makes one NADH
B) Consumes two ATP, makes one NADH
C) Consumes one ATP and one NADH
D) Consumes two ATP and one NADH
E) Consumes two ATP, no net change in overall NADH. 16) A B C D E
17. The body's **primary reserve** of energy is in the form of:
A) ATP
B) proteins
C) triacylglycerols
D) glucose
E) glycogen 17) A B C D E
About 400000 kJ is stored as fats
18. The body's **second reserve** of energy is in the form of:
A) ATP
B) proteins
C) triacylglycerols
D) glucose
E) glycogen 18) A B C D E
About 100000 kJ is available as protein
19. After several hours **without food**:
A) Epinephrine is released to maintain blood glucose levels.
B) Glucagon is released to maintain blood glucose levels.
C) Insulin is released to maintain blood glucose levels.
D) Insulin stimulates fat breakdown to replace glucose.
E) Glucagon stimulates glycolysis rates in liver 19) A B C D E
20. **The brain uses glucose primarily for:**
A) Fatty acid biosynthesis.
B) To store as glycogen.
C) Energy to maintain ion gradients.
D) To make ATP to supply to muscles.
E) Pentose phosphate pathway. 20) A B C D E
21. **Which of the following effects happens after caffeine ingestion:**
A) Persistantly elevated cyclic AMP levels.
B) Protein phosphatase activated.
C) Glycogen synthesis activated.
D) Adenylate cyclase activated.
E) Glycogen phosphorylase activity reduced .
Caffeine inhibits cyclic nucleotide phosphodiesterase 21) A B C D E
22. Isocitrate dehydrogenase is under allosteric control by:
A) Activation by ADP
B) activation by ATP
C) Activation by citrate
D) activation by acetyl CoA
E) Activation by cyclic AMP 22) A B C D E
Higher ADP levels indicate a need for energy metabolism

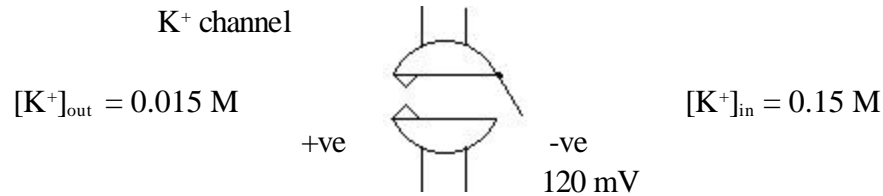
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23. Pyruvate carboxylase is under allosteric control by:
- A) Activation by ADP
B) activation by glucose-6-P
C) Activation by citrate
D) **activation by acetyl CoA**
E) Activation by cyclic AMP
- 23) A B C **D** E

24. The Nernst equation allows one to calculate membrane potential: for any monovalent cation, the predicted equilibrium membrane potential is 60 mV for a concentration ratio of 1 to 10.

The system illustrated below contains an ion selective channel for K^+ .



Predict what happens if the ion channel opens under the conditions shown above:

- A) K^+ does not cross because the potential opposes the concentration gradient.
B) K^+ crosses outwards towards the higher potential.
C) K^+ crosses outwards towards the lower $[K^+]$.
D) **K^+ crosses inwards because of the large membrane potential.**
E) K^+ crosses inwards because of the concentration gradient.
- 24) A B C **D** E

The potential is double the expected equilibrium potential, hence the electrical gradient overrides the concentration gradient.

25. **People who live at altitude adapt to lower pO_2 by:**
- A) Making less 2,3-bisphosphoglycerate to increase O_2 affinity in the lungs.
B) Making more 2,3-bisphosphoglycerate to increase O_2 affinity in the lungs.
C) Making less 2,3-bisphosphoglycerate to enhance O_2 release in capillaries.
D) **Making more 2,3-bisphosphoglycerate to enhance O_2 release in capillaries**
E) By using fetal hemoglobin.
- 25) A B C **D** E

BPG lowers O_2 affinity making it easier to release

26. **Which is the major hemoglobin form made in the embryo during the first month after conception?**
- A) $\alpha_2\beta_2$ B) $\alpha_2\varepsilon_2$ C) **e_2z_2** D) $\alpha_2\delta_2$ E) $\varepsilon_2\beta_2$
- 26) A B **C** D E

27. **Activation of chymotrypsinogen by trypsin involves**
- A) Release of a peptide that blocks access to the active site.
B) Phosphorylation of a critical serine.
C) Binding of calcium to γ -carboxyglutamate.
D) Binding of ATP
E) **Cleavage of a peptide bond to create a positive charged N-terminal Isoleucine**
- 27) A B C D **E**

New N-terminal Ile forms an ion pair with Asp 194 so that the oxyanion hole is correctly aligned

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28. **Fibrinogen** is prevented from clotting by **negative charge in its central region; part of this negative charge is due to the modified amino acid:**
- A) **tyrosine-O-sulfate** B) Serine-O-phosphate C) γ -carboxyglutamate
D) nitrotyrosine E) threonine-O-phosphate

28) **A B C D E**

One of the components of fibrinopeptides A and B responsible for the strong negative charge

29. **The product of 6-phosphogluconate dehydrogenase is**
- A) 6-phosphogluconolactone B) glucose-6-P C) ribose-5-P
D) **ribulose-5-P** E) xylulose-5-P

29) A B C **D** E

30. **The normal final product released by human fatty acid synthase I is**
- A) $C_{16}H_{33}CO_2^-$ **B) $C_{15}H_{31}CO_2^-$** C) $C_{17}H_{35}CO_2^-$
D) $C_{15}H_{31}COSCoA$ E) $C_{17}H_{35}COSCoA$

30) A **B** C D E

This is the formula of palmitate, released from ACP by thioesterase.

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31. Explain what is meant by **symport** and **antiport**, and give an example of a specific **antiport** process in the mitochondrial membrane.

symport:

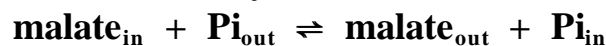
A transport process in which both substrates must bind from one side for the conformation to invert and release both substrates on the opposite side of the bilayer.

antiport:

A transport process in which substrate A binds and induces inversion of conformation so that substrate A can be released on the opposite side of the bilayer. A second substrate B must then bind to restore the original conformation. Substrate B is therefore transported in the opposite direction and in a strict one for one stoichiometry with substrate A.

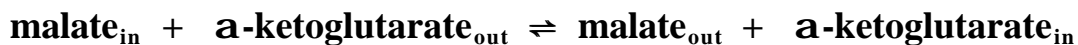
example:

dicarboxylate carrier



or

a-ketoglutarate carrier



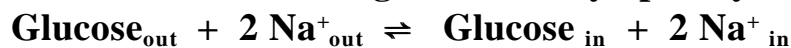
or **tricarboxylate carrier or ATP:ADP translocator or aspartate:glutamate translocator**

4 marks

What process do cells use to import glucose across the cell membrane? What makes it possible to move glucose from low external [glucose] to high internal [glucose]

3 marks

The glucose:Na⁺ symport system



Since [Na⁺]_{out} is about 12× higher than [Na⁺]_{in}, and membrane potential is about -50 mV inwards on intestinal epithelial cells, there is a strong drive inwards for Na⁺. Given these conditions it should be possible to concentrate glucose inside to 10⁴× the outside concentration.

Strictly speaking this applies only to intestinal epithelial cells

Other than transport, give two other roles for membrane proteins:

Any two of

- Structural, e.g. spectrin**
- Identity markers e.g. glycophorin**
- Receptors, e.g. insulin receptor**
- Enzymes, e.g. adenylate cyclase**
- Intracellular signalling, e.g. Ras**

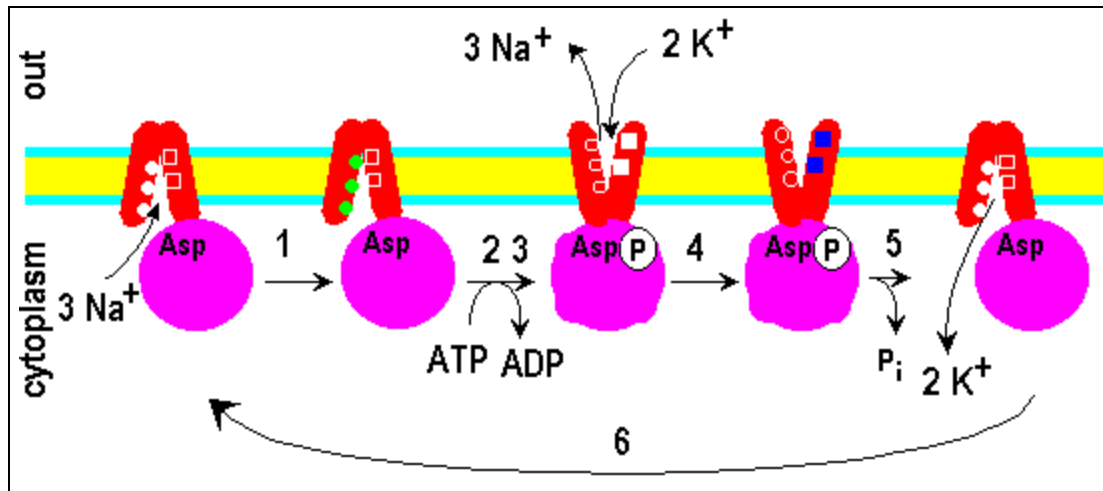
2 marks

32. Your choice:

either **show the cycle of steps involved in the action of the Na/K ATPase pump**

or show the six step reaction sequence of fatty acid synthase I.

6 marks

1) 3 Na⁺ bind to high affinity sites inside

2) ATP binds and phosphorylates Asp 376; this changes the conformation to expose binding sites outside

3) Conformation change has lowered Na⁺ affinity so 3 Na⁺ are released4) conformation change has increased K⁺ affinity so 2 K⁺ bind

5) hydrolysis of aspartyl phosphate occurs so the conformation reverts to the original state

6) The conformation change lowers K⁺ affinity so K⁺ is released inside; Na⁺ sites revert to high affinity.

32. Your choice:
either show the cycle of steps involved in the action of the Na/K ATPase pump

or show the six step reaction sequence of fatty acid synthase I.

6 marks

1) Malonyl transferase attaches malonyl group to ACP using malonyl-CoA as donor

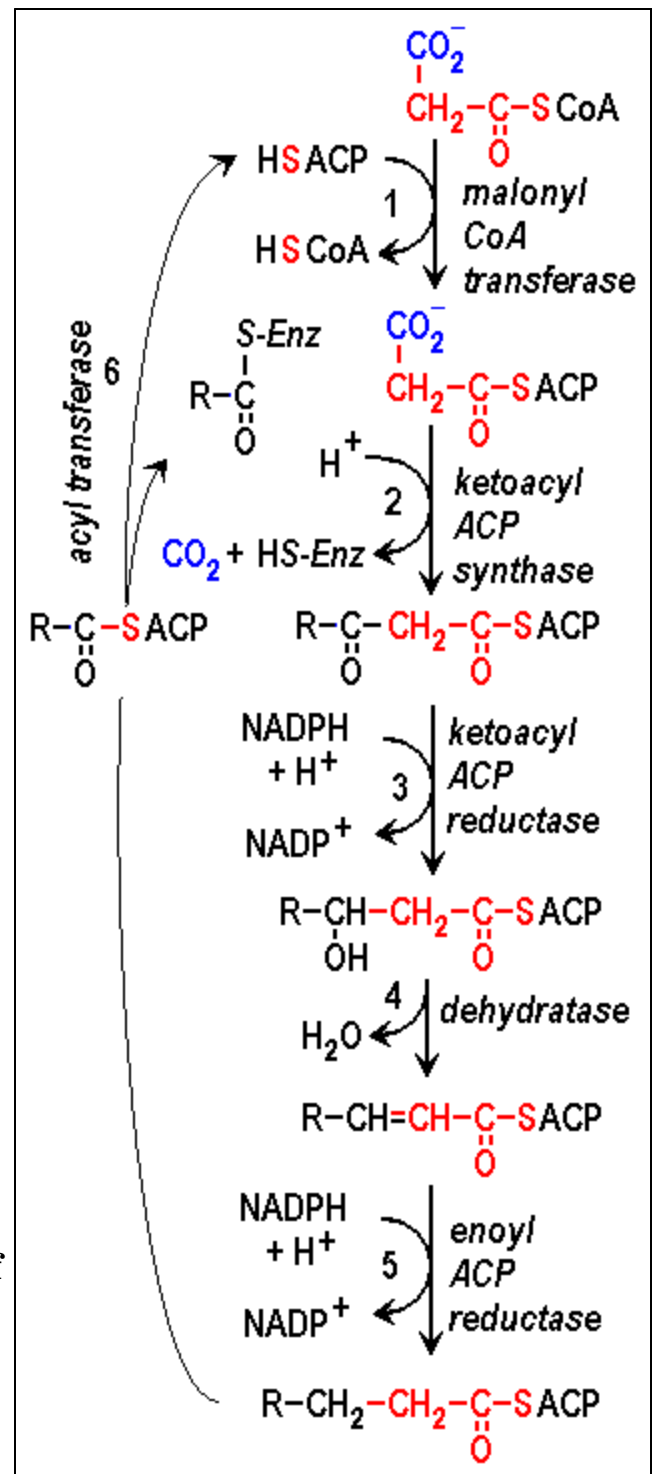
2) Ketoacyl ACP synthase carries the growing acyl chain in its catalytic site (R-CO-S-Enz) from a previous cycle. The synthase condenses the acyl radical to malonyl-ACP, displacing the extra malonyl carboxylate group. This decarboxylation drives the condensation.

3) The ketoacyl-ACP from step 2 is reduced to a hydroxyacyl-ACP

4) Dehydratase eliminates H₂O from the hydroxyacyl-ACP to make enoyl-ACP

5) enoyl-ACP is reduced to the saturated acyl-ACP

6) Acyl transferase moves the saturated acyl chain from ACP to the catalytic site of ketoacyl ACP synthase in readiness for the next cycle, or if the chain has reached its limit leaving ACP empty, an acetyl radical from acetyl CoA can be transferred to the ketoacyl ACP catalytic site HS-Enz.



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33. How is pyruvate converted to phosphoenol pyruvate in animal cells?
Show structures of the principle reactants and products, but cofactors such as ATP etc. can simply be named; name the enzymes, and indicate regulators of the first step.
enzyme reaction 1

pyruvate carboxylase

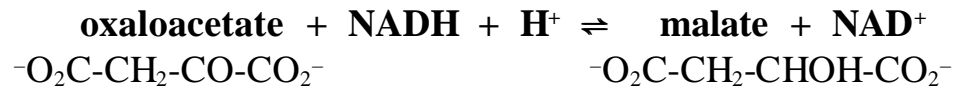
biotin as cofactor



Presence of **acetyl-CoA** is required for activation

enzyme reaction 2

mitochondrial malate dehydrogenase



enzyme reaction 3

cytoplasmic malate dehydrogenase



enzyme reaction 4

PEP carboxykinase



Reactions 2 and 3 may seem a bit redundant.

What other event occurs between reaction 2 and reaction 3?

Malate is exported from the mitochondria to the cytoplasm by the dicarboxylate carrier.

8 marks

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34. Show the sequence of events that lead to activation of glycogen breakdown and deactivation of glycogen synthesis.

7 marks

Initial state: fear or stress

- 1) **Fear or stress lead to release of the hormone epinephrine in anticipation of need for muscular activity (the *fight or flight* response).**
- 2) **Epinephrine binds to its G-protein coupled receptor on muscle cells.**
- 3) **Release of $G_s\alpha$ stimulates adenylate cyclase to produce cyclic AMP**
- 4) **Cyclic AMP activates protein kinase A**
- 5) **Protein kinase A phosphorylates phosphorylase b kinase, increasing its activity.**
- 6) **Phosphorylase b kinase phosphorylates inactive phosphorylase b, converting it to the active phosphorylase a; this leads to an increase in the rate of glycogen breakdown.**
- 7) **Protein kinase A phosphorylates Glycogen synthase I converting it to the less active glycogen synthase D. Glycogen synthase D is a target for further inactivation by glycogen synthase kinase. This shuts down glycogen synthesis**