

Name _____

Student number _____

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

Final Exam, April 21, 1997.

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 31-39 directly on the question paper.

Questions 1-30 have a weight of 1 mark each

Questions 31-39 have marks as indicated

30 marks

30 marks

=====

60 marks

total

31-32	33-34	35	36-37	
/ 7	/ 8	/ 7	/ 8+1	/ 30 + 1

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Answer questions 1-30 on the computer scoring sheet.

Value 1 mark each

1. Which of the following **sugar phosphates** is **not** a substrate or product of transketolase?

A) Ribulose-5-P

B) Xylulose-5-P

C) Ribose-5-P

D) Erythrose-4-P

E) Fructose-6-P

1) **A B C D E**

Ribulose-5-P is isomerized or epimerized before proceeding to the rearrangement reactions of the pentose phosphate pathway.

2. The carrier of the 3-carbon **aldol group in transaldolase** is:

A) Thiamine pyrophosphate

B) A lysine side chain of the enzyme

C) Pyridoxal phosphate

D) Biotinyllysine

E) A thioester bond

2) **A B C D E**

3. **NADH for gluconeogenesis can be provided by:**

A) Mitochondrial malate dehydrogenase.

B) Cytoplasmic malate dehydrogenase.

C) Mitochondrial pyruvate dehydrogenase.

D) Cytoplasmic glucose-6-phosphate dehydrogenase.

E) Mitochondrial isocitrate dehydrogenase.

3) **A B C D E**

When amino acids are used as initial substrate, malate is exported from mitochondria

4. **The potential futile cycle of hexokinase and glucose-6-phosphatase is prevented by:**

A) Cyclic AMP activation.

B) ATP inhibition.

C) AMP activation.

D) Fructose-2,6-bisphosphate

E) Release of glucose product into the endoplasmic reticulum. 4) **A B C D E**

This keeps the product of gluconeogenesis away from hexokinase.

5. **How many ATP molecules are made per glucose** in the second half of the gluconeogenesis pathway?

A) None

B) One

C) Two

D) Three

E) Six

5) **A B C D E**

“Second half” is irrelevant, since no ATP is made at any point of the gluconeogenesis pathway

6. Given the condition **[ATP] low in muscle**, which of the following states is **highly unlikely**?

A) Phosphorylase b active.

B) Phosphofructokinase 1 active.

C) Pyruvate kinase active.

D) Isocitrate dehydrogenase active.

E) PEP Carboxykinase active.

6) **A B C D E**

PEP carboxykinase is a gluconeogenesis enzyme, part of an energy consuming pathway that will be inactive if ATP is needed

7. After the **liver**, which organ is **next most active in gluconeogenesis**?

A) Kidney

B) Muscle

C) Adipose tissue

D) Brain

E) Heart

7) **A B C D E**

Kidneys recover “waste” amino acids from urine and use them for gluconeogenesis

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8. Given the condition of **no recent food input, moderate energy demand**, e.g. easy walking, and **acyl CoA levels high**, which of the following metabolic states is **most likely**?

A) Pyruvate carboxylase active.

B) Citrate lyase active.

C) Glucose-6-phosphate dehydrogenase active.

D) Acetyl CoA carboxylase active.

E) Pyruvate dehydrogenase active.

8) **A B C D E**

Metabolic state is right for gluconeogenesis: energy demands relatively low, blood glucose falling because no recent input.

9. **Which of the following is not a part of the fatty acid synthase I complex?**

A) Hydroxyacyl dehydrogenase.

B) Enoyl reductase.

C) Dehydratase.

D) Thioesterase.

E) Malonyl transferase.

9) **A B C D E**

Strictly speaking some of these names should include ACP or CoA, but that might give the game away!

β -oxidation has dehydrogenases, fatty acid synthase has reductases.

10. **Biotin is linked to its carrier protein by:**

A) An amide link to lysine.

B) A phosphate diester bond to serine.

C) An amide bond to glutamate.

D) An amide bond to asparagine

E) Non-covalent bonding.

10) **A B C D E**

Biotin has a hydrocarbon side chain ending in a carboxylate group. This forms an amide with lysine creating the long "arm".

11. At **moderate working rates**, the **major glucose consumer** in the body is:

A) Adipose tissue

B) The liver

C) Muscle

D) The heart

E) The brain

11) **A B C D E**

The brain is a major glucose consumer; when the rest of the body is inactive, the brain always keeps busy.

12. **Hemoglobin S protein can be detected easily by observing:**

A) The increased size of the S-mutant β -globin on SDS-polyacrylamide gels.

B) The increased binding affinity of Hemoglobin-S for O_2 .

C) The decreased binding affinity of hemoglobin-S for O_2 .

D) The reduced negative charge and higher isoelectric point of hemoglobin-S.

E) Increased polarity of the peptide fragment containing the mutation.

12) **A B C D E**

Neutral valine replaces negative glutamate, hence loss of charge and decreased polarity

13. **β^0 Thalassemia is not always lethal because:**

A) α_4 hemoglobin functions adequately.

B) The other β globin gene takes over.

C) γ -globins continue to be expressed in adult life.

D) The body makes do with myoglobin provided no strenuous activity is undertaken.

E) It is never observed.

13) **A B C D E**

γ -globin is in the same group as β -globin and the $\alpha\alpha\gamma\gamma$ hemoglobin-F is reasonably functional

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14. **The Cori cycle can be described as:**

- A) **Gluconeogenesis in liver coupled to anaerobic glycolysis in muscle.**
- B) Glycolysis in the liver coupled to gluconeogenesis in muscle.
- C) Anaerobic glycolysis in muscle coupled to aerobic glycolysis in liver.
- D) Glycolysis in muscle coupled to TCA cycle in liver
- E) Glycogen synthesis in liver coupled to glycolysis in muscle.

14) **A B C D E**

15. **The negatively charged polysaccharide heparin is an anticoagulant because:**

- A) It is a serine protease inhibitor.
- B) .It is a plasmin activator.
- C) It inhibits antithrombin III.
- D) **It promotes action of antithrombin III.**
- E) It binds to phospholipid membranes.

15) **A B C D E**

16. Which of the following is **most likely** to be able to cross a membrane without help of a transporter protein?

- A) **Ethanol**
- B) acetyl-SCoA
- C) Glyceraldehyde-3-phosphate
- D) Glucose
- E) Na⁺.

16) **A B C D E**

Ethanol is small, uncharged and relatively less polar than the other options

17. **The Bohr effect is the reduced affinity of hemoglobin for O₂**

- A) Due to binding of 2,3-bisphosphoglycerate
- B) Due to high altitude.
- C) **Due to lower pH**
- D) In fetal hemoglobin.
- E) Resulting from the hemoglobin S mutation.

17) **A B C D E**

The Bohr effects are the decreased affinity resulting from acidification and presence of HCO₃⁻ or CO₂. BPG was not discovered until 60 years after Bohr.

18. **ATP acts on aspartate transcarbamoylase:**

- A) By providing energy for the reaction.
- B) By phosphorylating the substrate.
- C) As a homotropic effector
- D) As a feedback inhibitor.
- E) **By binding and stabilizing the R state of the enzyme.**

18) **A B C D E**

ATP is not a substrate and is not involved in the catalytic reaction; it is a positive heterotropic effector

19. **The normal human adult expresses:**

A) **Four a-globin and two b-globin genes**

B) Two **a**-globin and two **b**-globin genes.

genes.

- C) Two **a**-globin and four **b**-globin genes.
- D) Two **a**-globin and one **b**-globin gene.
- E) One **a**-globin and two **b**-globin genes.

19) **A B C D E**

Chromosome 16 has 2 α genes, chromosome 11 has 1 β gene and you should have two of each chromosome

20. **Glucose transport into animal cells is the result of:**

- A) An ATP driven glucose transporter.
- B) **Symport with Na⁺.**
- C) Antiport in exchange for Na⁺.
- D) Symport with K⁺.
- E) Antiport in exchange for K⁺.

20) **A B C D E**

Strictly speaking the symport is for intestinal cells; other cells use various simple uniports

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21. **The brain consumes glucose primarily for:**

- A) Fatty acid biosynthesis. B) Glycogen synthesis.
 C) Pentose phosphate pathway. D) Energy supply to muscles.

E) Energy to maintain ion gradients.

21) **A B C D E**

Intense electrical activity requires constant maintenance of the Na⁺ and K⁺ gradients

22. **Which of the following would be an abnormal ionic condition in the cell?**

(‘High’ implies higher than outside, ‘low’ implies lower than outside.)

- A) Low intracellular Na. B) High intracellular K⁺
 C) High intracellular Mg²⁺ D) **High intracellular Ca²⁺**
 E) High intracellular phosphates

22) **A B C D E**

Cytoplasmic Ca²⁺ is kept at about 10⁻⁷ M

23. **Which of the following effects or states is not a consequence of caffeine ingestion:**

- A) Persistantly elevated cyclic AMP levels. B) Active glycogen phosphorylase.
 C) Inactivated Glycogen synthase. D) **Activated adenylate cyclase.**
 E) Elevated blood glucose.

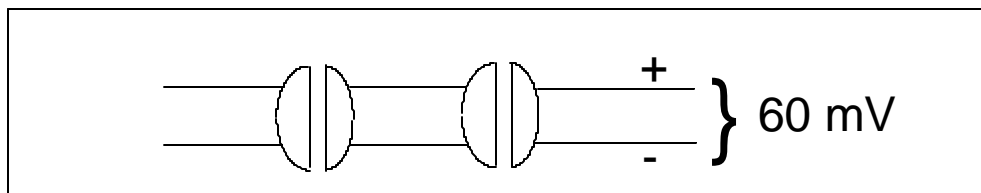
23) **A B C D E**

Caffeine prevents cyclic AMP breakdown; it does not stimulate adenylate cyclase (and may cause desensitization of the GPCR that activate adenylate cyclase)

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 two kinds of ion selective channel, one for Na⁺ and one for K⁺.

K⁺ channel Na⁺ channel
 [K⁺]_{out} = 0.015 M [Na⁺]_{out} = 0.15M



[K⁺]_{in} = 0.15 M [Na⁺]_{in} = 0.015 M

Predict what happens if both ion channels open together under the conditions shown above:

- A) **Na⁺ crosses inwards, K⁺ does not cross.**
 B) K⁺ crosses outwards, Na⁺ does not cross.
 C) Both ions cross, K⁺ outwards and Na⁺ inwards.
 D) Neither cross because the concentration ratios are in equilibrium with membrane potential.
 E) Neither ion can cross without ATP hydrolysis.

24) **A B C D E**

The potential shown has the polarity of the equilibrium potential for K⁺; therefore if both channels open simultaneously, the membrane potential exactly opposes the K⁺ concentration gradient so K⁺ does not move even if its channel is wide open. The potential has the value of the equilibrium potential for Na⁺ but the opposite polarity, so it reinforces the Na⁺ gradient.

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25. Which of the following is a bilayer-forming amphipathic molecule? (R is $-C_{17}H_{35}$)

- A) CH_2-CO-R B) CH_2-CO-R C) **CH_2-CO-R**
 $CH-CO-R$ $CH-CO-R$ **$CH-CO-R$**
 CH_2-CO-R $CH_2-O P^{2-}$ **$CH_2-OP^- OCH_2CH_2NH_3^+$**

- D) $R-CO_2^-$ E) $R-CO-SCoA$ 25) A B **C** D E

C) is phosphatidyl serine, a bilayer forming phospholipid; A) is totally nonpolar triacylglycerol B) is micelle forming phosphatidic acid

26. Which of the following is not a protease of some kind?

- A) Thrombin **B) Fibrin** C) Plasmin.
 D) Pepsin E) Elastase 26) A B C D E

Fibrin is the fibre-forming protein that actually makes up a blood clot

27. Under normal conditions, the body's energy needs are met primarily by:

- A) Oxidation of fatty acids in muscles** B) Pentose phosphate pathway in the liver.
 C) Oxidation of glucose in the brain. D) Gluconeogenesis in the liver
 E) Anaerobic glycolysis in the muscle. 27) A B C D E

"Normal" slow steady energy demands rely on fatty acid oxidation (except in the brain, but brain accounts for 20% of total energy needs)

28. After a starch-rich meal we expect to find:

- A) Elevated blood glucagon. B) High rates of gluconeogenesis in liver.
 C) Active glycogen phosphorylase in liver. **D) Elevated cytoplasmic citrate in liver.**
 E) High activity of protein kinase A in liver. 28) A B C **D** E

All other options are characteristic of low blood glucose

29. Serine proteases of the chymotrypsin family have an active site based on the catalytic triad consisting of :

- A) Serine, Glycine and Aspartate. B) Serine, Glycine and Methionine.
 C) Serine, Histidine and Glycine. **D) Serine, Histidine and Aspartate**
 E) Phenylalanine, Tryptophan and Tyrosine. 29) A B C **D** E

Ser195, Gly193 Asp194 make up the oxyanion hole, not the catalytic triad, which is Asp102, His57, Ser195. Phe Tyr Trp are the substrates, not the catalytic triad.

30. The blood clotting factor that is activated by both intrinsic and extrinsic pathways is:

- A) Factor VIII B) Factor IX C) Factor VII
 D) Factor XI **E) Factor X.**

30) A B C D **E**

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31. The net cost of making **one glucose** from pyruvate is **6 ATP or GTP**. Identify the reactions that use ATP or GTP. (Name reactants, enzyme and products of these steps; structures not required).

5 marks

i)

Pyruvate carboxylase (1/2)



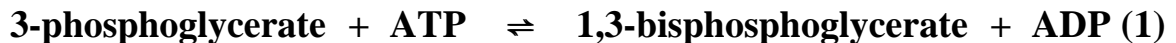
ii)

PEP carboxykinase (1/2)



iii)

phosphoglycerate kinase (1/2)



Which of the above steps is a **glycolysis reaction in reverse**? **i** **ii** **(iii)** (1/2)
(circle as appropriate)

32. State the **purpose(s) of the pentose phosphate pathway** in metabolism;
in which organ is this pathway most active?

2 marks

The pentose phosphate pathway is a major source of NADPH required as a reducing agent for biosynthetic reactions (1)

it is also a source of ribose-5-phosphate for nucleotide synthesis (1/2)

The liver is responsible for much of the pentose phosphate activity (1/2)

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33. i) How does TCA cycle regulation lead to appearance of citrate in the cytoplasm? State which TCA cycle enzyme is regulated, what the regulating factors are, and briefly explain why it's citrate that accumulates in large quantities rather than another TCA cycle intermediate.
2 marks

TCA cycle is regulated by the level of ADP(1/2), which is needed to activate isocitrate dehydrogenase (1/2)

Because aconitase has an unfavourable equilibrium, citrate accumulates at much higher levels than isocitrate (1/2)

The tricarboxylate carrier then moves citrate into the cytoplasm (1/2)

- ii) What is citrate converted to when it reaches the cytoplasm? State the immediate product of the first reaction (enzyme, any other reactants and products by name, structures not required). State the final product of the pathway. 2 marks

citrate lyase (1/2)

citrate + HSCoA + ATP → acetyl CoA + oxaloacetate + ADP + P_i
(1)

Most acetyl-CoA appearing in the cytoplasm is destined for fatty acid biosynthesis (1/2)

- iii) Name an enzyme that is regulated by the presence of cytoplasmic citrate; state whether it is positive or negative regulation.

Acetyl CoA carboxylase (1/2) is positively regulated by citrate (1/2)

1 mark

34. Glycogen is broken down to glucose-1-phosphate by glycogen phosphorylase in one step. Identify the reactions required for the synthesis of glycogen starting from glucose-1-phosphate. (Name enzymes, additional substrates/cofactors and products, as appropriate; structures not required.) 3 marks

UDP-Glucose pyrophosphorylase or UTP:glucose-1-phosphate uridylyl transferase (1/2)

requires UTP as additional substrate (1/2) and makes UDP glucose (1/2)

Glycogen synthase (1/2) uses UDP glucose as substrate (1/2) and makes glycogen (1/2)

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35. Nerve action depends on **ion selectivity and voltage sensitivity** of ion channels in the membrane.

How is ion selectivity determined?

State the basis for **excluding ions that are too large**, and for **excluding ions that are too small**.

2 marks

Ions must pass through selectivity filter that strips off hydration layer (1/2)

amino acid side chains must provide ligands of equal energy to hydration (1/2)

Ions that are too large won't fit (1/2)

Ions that are too small don't align with all ligands so energy is too weak to replace hydration (1/2)

The key events of the **action potential** are illustrated at right.

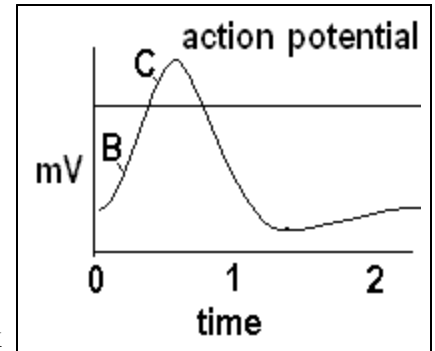
What are the time units? **(milliseconds)**

(circle one)

seconds

minutes

1 mark



What are the typical voltages at the resting potential **-60 mV**

and at the peak (just after (C) in the figure),
mark

+ **25-30 mV**

(1/2 each)

1

A) **How does the process get started?**

presence of action potential just upstream raises local potential to about -40 mV

B) **What happens at (B)?**

Na⁺ voltage gated channels open, increasing permeability to Na⁺, and this makes the local potential rise rapidly

C) **What happens at (C)?**

Potential approaches its peak so that K⁺ channels open, while Na⁺ channels start to be inactivated.

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36. Pyruvate Carboxylase is a three-component enzyme. There are two catalytic components:

Reaction at first catalytic component:

(Show structures of the principal reactant and product; name the prosthetic group.)

2 marks

Biotin carboxylase



Reaction at second catalytic component:

(Name the reactants and product.)

2 marks

pyruvate carboxyltransferase



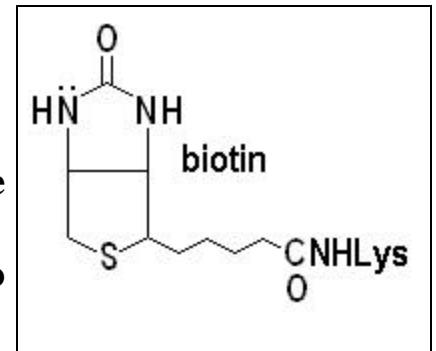
What is the function of the third component:

Structure of the prosthetic group is a **bonus mark**:

1 mark + 1

Biotin carrier domain holds the biotin by an amide bond to lysine.

The lysine allows sufficient mobility for biotin to move between the catalytic centres



37. Your choice: show the **structures (reactants and products)** of either the **oxidative stages of the pentose phosphate pathway** or of the **transaldolase reaction** (including enzyme bound intermediate).

3 marks

