BIOC*2580 Fall 2007 Final Examination
Friday December 7, 2007; 8:30 a.m. Instructor: Dr. David Josephy

Instructions: No written aids or programmable calculators may be brought into the exam. Electronic communication devices (such as cellular telephones) are strictly prohibited. This exam. determines 45% of the final course grade. Total marks for this paper = 80. Time allotted = 2 hours (120 minutes).

Section A: True/False questions. Please mark your answers on the "Scantron" card. Answer **A** if the statement is **true**; answer **B** if the statement is **false.** One mark each × 11 questions = 11 marks. (No marks will be deducted for wrong answers.)

1. Enzymes are biochemical catalysts.
2. Phosphatidylglycerol is a form of "storage fat".
3. The conversion of an aldehyde to an acid is an oxidation reaction.
4. Thymine is a normal base constituent of both DNA and RNA.
5. The two strands of the DNA double helix are *anti-parallel*.
6. Glucose is a reducing sugar.
7. Succinic acid is a tricarboxylic acid.
8. Lester B. Pearson won the Nobel Prize for explaining the significance of ATP in bioenergetics.
9. Each of the first three reactions of glycolysis consumes one molecule of ATP.
10. "GLUT" proteins are transporters that catalyze the import of glucose into cells.
11. Oxidative phosphorylation occurs in eukaryotic cells but not in bacterial cells.

Section B: Multiple-choice questions. Please mark your answers on the "Scantron" card. One mark each × 25 questions = 25 marks. (No marks will be deducted for wrong answers.)

12. The activities of many proteins are regulated by <u>phosphorylation</u>: the enzyme-catalyzed addition of phosphate groups to specific amino acid residues in the protein. The most likely donor of these phosphate groups is:

A) ATP; B) phosphatidylcholine; C) acetyl CoA;
D) NADH; E) NADPH.

13. Phosphorylation of proteins (see previous question) can occur on either serine, threonine, or tyrosine residues. These amino acids share the property that their side chains are ...

A) very hydrophobic; B) negatively (-) charged at physiological pH;
C) positively (+) charged at physiological pH; D) alcohols; E) aromatic rings.

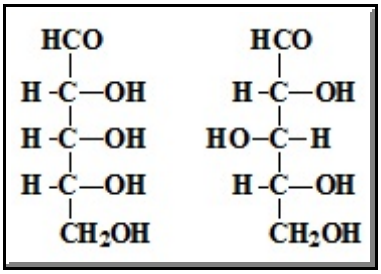
14. The complete hydrolysis of one mole of phosphatidylglycerol yields the components glycerol, fatty acid, and inorganic phosphate, in which of the following respective molar ratios?

A) 1 : 1 : 1 B) 1 : 2 : 1 C) 2 : 2 : 1
D) 2 : 1 : 2 E) 1 : 2 : 2

15. The linkage between the alpha and beta phosphate groups in ATP is best described as a ...

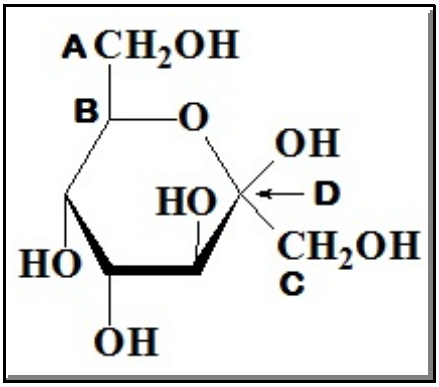
A) thioester linkage; B) glycosylic linkage; C) phosphate ester linkage;
D) phosphodiester linkage; E) phosphoanhydride linkage.

16. The Fischer structures shown at right represent ...
A) two different representations "on paper"
of the same sugar molecule;
B) a pair of epimeric aldopentoses;
C) a pair of anomeric aldopentoses;
D) a pair of anomeric ketopentoses;
E) none of the above answers is correct.



17. The sugar known as *sedoheptulose* is shown at right.
The anomeric carbon atom is atom:

A) **A** B) **B** C) **C** D) **D** E) none of the above.



18. Melibiose, a disaccharide, is designated "galactose α(1→6) glucose".
In the structure of melibiose, a glycosidic bond links (via an O atom), the ...
A) anomeric C atom of galactose, in the beta configuration, to the C6 atom of glucose;
B) anomeric C atom of galactose, in the alpha configuration, to the C6 atom of glucose;
C) anomeric C atom of galactose, in the alpha configuration, to the anomeric C atom of glucose;
D) C6 atom of galactose to the anomeric C atom of glucose;
E) C6 atom of galactose to the C6 atom of glucose.

19. A chemical reaction has a positive enthalpy change and a positive entropy change.
This reaction ...
A) will always be spontaneous;
B) will always be non-spontaneous;
C) could be either spontaneous or non-spontaneous, depending on the temperature;
D) must be an oxidation-reduction reaction;
E) can only occur in the presence of a catalyst.

20. A biosynthetic metabolic pathway functions in the following manner:

$$A \xrightarrow{\rho} B \xrightarrow{\sigma} C \xrightarrow{\tau} D \xrightarrow{\upsilon} E$$

where A, B, C, D, and E are metabolites, and ρ, σ, τ, and υ are the enzymes that catalyze the indicated steps in the pathway. In order to maintain a steady level of operation of the pathway, which of the following regulatory mechanisms would be most appropriate?
A) Synthesis (*i.e.*, gene expression) of the four enzymes occurs only in the presence of metabolite E;
B) Metabolites B, C, and D are inhibitors of enzyme υ;
C) Metabolite E is an inhibitor of enzyme ρ;
D) Metabolite A is an inhibitor of enzyme υ;
E) Metabolite A is also converted into metabolite E by a different, ATP-dependent pathway.

21. The following thermodynamic data are available for the conversion of A to B:

(uncoupled reaction) $A \rightleftarrows B$ $K_{eq} = 10^{-3}$

(ATP-coupled reaction) $A + ATP \rightleftarrows B + ADP + P_i$ $K_{eq} = 200$

In the living cell, the steady state ratio of [ATP] / ([ADP] [P_i]) = 5×10^3. By approximately what factor will the coupling to ATP hydrolysis increase the ratio of [B] / [A], relative to the value for the uncoupled reaction?

A) 10^9 B) 2×10^8 C) 10^8 D) 2×10^5
E) 1 (*i.e,* the ratio will be unchanged)

22. The glycosylic (also called "glycosidic") bonds in nucleic acids ...
A) connect bases to one another; B) connect sugars to bases;
C) connect sugars to one another; D) are also known as "phosphodiester linkages";
E) none of the above statements is true.

23. All of the following enzymes would be found in the mitochondria of a human intestinal epithelial cell, <u>except</u>:
A) succinate dehydrogenase; B) carnitine acyltransferase;
C) enoyl-CoA hydratase; D) pyruvate dehydrogenase; E) pyruvate kinase.

24. The mechanism of the reaction catalyzed by the beta-oxidation enzyme enoyl-coA hydratase is similar to that of the citric acid cycle enzyme ...
A) malate dehydrogenase; B) alpha-ketoglutarate dehydrogenase; C) aconitase;
D) fumarase; E) citrate synthase.

25. Within the cell, ATP exists mainly as a complex with:
A) K^+; B) Na^+; C) Ca^{++}; D) Mg^{++}; E) Fe^{++}.

26. All but one of the following metabolic transformations can be accomplished without making or breaking any carbon-carbon bonds. The one exception is:

A) glutamate ⇌ glutamine;
B) alpha-ketoglutarate ⇌ glutamate;
C) oxaloacetate ⇌ aspartate;
D) citrate ⇌ isocitrate;
E) isocitrate ⇌ alpha-ketoglutarate.

27. Fatty acids are usually transported across the inner mitochondrial membrane in the form of:

A) coenzyme A thioesters; B) glycerol esters; C) carnitine esters;
D) mixed anhydrides with ATP; E) none of the above answers is correct.

28. The complete oxidation of *arachidic acid* requires X rounds of beta oxidation and Y rounds of the citric acid cycle, where X and Y =

A) 9 and 10; B) 8 and 9; C) 9 and 9;
D) 10 and 10; E) none of the above; ... respectively.

29. Considering the metabolic processes we have discussed in this course, which one of the following molecules is a substrate for an oxidation reaction?

A) fructose-1,6-bisphosphate; B) dihydroxyacetone phosphate;
C) glyceraldehyde-3-phosphate; D) phosphoenol pyruvate;
E) glucose-6-phosphate.

30. Oxidative phosphorylation and electron transport are said to be "coupled". By this, we mean that, in the mitochondrion:

A) neither process can occur without the other;
B) oxidative phosphorylation requires electron transport, but not vice versa;
C) electron transport requires oxidative phosphorylation, but not vice versa;
D) the same proteins catalyze both processes;
E) chemical "uncouplers" stop both processses.

31. Which one of the following statements concerning electron transport and ATP synthesis in the mitochondrion is false?

A) Electron transfer by the electron transport chain is coupled to H^+ transport out of the matrix.
B) Reduced coenzymes donate electrons to the electron transport chain.
C) ATP synthesis occurs on the matrix side of the membrane.
D) Oxygen is reduced to water by the respiratory electron transport chain.
E) Cytochrome c carries e^- between Complexes I and III, and also between Complexes III and IV.

32. The "half-channel" structures, which allow protons to move from the inter-membrane space into the ATP synthase, and from the ATP synthase into the mitochondrial matrix, are located in the ...
A) a; B) b; C) c; D) γ; E) ε ... subunit(s) of the enzyme.

33. A vintner (winemaker), wishing to get his wine into the liquor stores sooner after the grape harvest, tries bubbling oxygen gas into the fermentation vats. To his satisfaction, he finds that this change to the winery's standard operating procedures makes the yeast cultures multiply much more rapidly. The final product (*i.e.*, the wine) would be ...

A) produced more quickly, bringing commercial advantage to the winery;
B) undrinkable, and almost alcohol-free;
C) unacceptably high in alcohol;
D) unacceptably sweet;
E) little different from the standard product, making the process change a waste of effort.

34. The oxidation of a fatty acyl CoA to an enoyl CoA, catalyzed by *acyl CoA dehydrogenase*, uses the oxidizing agent: A) FAD; B) NAD^+; C) $NADP^+$; D) O_2; E) H_2O_2.

35. According to the mechanism of ATP synthase catalysis proposed by Paul Boyer, the energy released by the proton motive force is used mainly to promote the ...

A) binding of the alpha subunits to the beta subunits, to form the catalytic active sites;
B) binding of ADP to the enzyme;
C) condensation of ADP with inorganic phosphate to form ATP;
D) release of ATP from the enzyme;
E) none of the above.

36. Which of the following statements about glucose is false?

A) The glucose concentration in the blood plasma of a well-nourished human is about 5 mM;
B) Glucose enters human cells readily, by passive diffusion across the cell membrane;
C) Upon entry into most cells, glucose is rapidly phosphorylated;
D) Glucose can be catabolized under either aerobic or anaerobic conditions;
E) Glucose can bind covalently to some proteins in the blood.

	1	2	3
	123456789	0123456789	0123456789	0123456
CORRECT ANSWERS:	121211222	1214352423	3125445313	1512142

Student name: ID number:

Section C: Short answers. 20 marks total for Section C.
Note: Sections C and D are reproduced here twice - first without the answers, and then with the answers filled in.

1. Next to the name of the substrate shown on the left, write the name of the enzyme which catalyzes its metabolism (catabolism). 5 marks.

substrate	**enzyme name**
fructose 1,6-*bis*phosphate	
3-phosphoglycerate	
2-phosphoglycerate	
malate	
citrate	

2. "*Pas de deux*". Each of the catabolic enzymes listed below acts on two substrates. One of the substrates is given; name the other substrate. (Do not name the products of the reaction; do not draw any chemical structures.) The first question is completed for you, as an example. 4 marks.

enzyme	**substrate 1**	**substrate 2**
hexokinase	*glucose*	*ATP*
pyruvate kinase	ADP	
fumarase	fumarate	
thiolase	CoASH	
lactate dehydrogenase	pyruvate	

Student name: ID number:

3. *"Sweet success"*. Fill in the six missing entries in the following table, accounting for the ATP yield of aerobic glucose oxidation (beginning with one molecule of glucose). Assume the use of the malate-aspartate shuttle for transfer of reducing equivalents into the mitochondrion. 6 marks.

Metabolic process	**Immediate product**	**ATP yield**
glycolysis (glucose to pyruvate)	2 NADH	
	2 ATP	2
pyruvate oxidation	2 NADH	
acetyl CoA oxidation	6 NADH	
		3
	2 ATP	
SUM (TOTAL NET YIELD OF ATP) =		

4. "*Bits and pieces*". The chemical components listed in the first column are constituents of the biomolecules listed in the third column. Mix and match, by writing the appropriate letters (corresponding to the biomolecule) in the middle column. The first answer is given as an example. (No answer appears twice.) 5 marks.

component	*letter*	***biomolecule***
deoxyribose	D	**A**: trehalose
porphyrin		**B**: coenzyme Q
pantothenic acid		**C**: cytochrome c
glucose		**D**: DNA
N,*N*,*N*-trimethylethanolamine		**E**: coenzyme A
isoprenoid side chain		**F**: phosphatidylcholine

Student name: ID number:

Section D: **Structures and written answers.**
Answer any **three (3)** of the **four (4)** questions in part D.
Each question is worth 8 marks; 24 marks total for Section D.

1. Draw the complete chemical structure of NAD^+.

2. Lipids, which are poorly soluble in water, can spontaneously form several different types of aggregates (assemblies of many molecules) when they are dispersed in water. Briefly discuss at least three types of lipid aggregates; one of these types should be the lipid *micelle*.

For each type of aggregate: (i) provide a simple sketch indicating its size and geometry; (ii) identify the kinds of lipids that tend to form the aggregate; (iii) discuss any practical uses or biological roles of the aggregate. (It is not necessary to draw any detailed chemical structures.)

3. Inherited disorders of pyruvate metabolism are rare human metabolic diseases. Many of these cases result from mutations in genes encoding the protein sub-units of the pyruvate dehydrogenase complex. In the affected individuals, pyruvate dehydrogenase enzyme activity is greatly diminished. Briefly explain each of the following clinical observations about this disease. (2 marks for each part.)

a) Lactic acidosis (*i.e.*, elevated levels of lactic acid in the blood, and lowered blood pH) is a common clinical finding in this disease; why? (Hint: What is the metabolic relationship between pyruvate and lactate?)

b) In addition to lactate, blood levels of the amino acid alanine ($HOOC\text{-}CH(CH_3)\text{-}NH_2$) are often elevated. Why? (Hint: What is the structural and metabolic relationship between alanine and pyruvate?)

c) Mental retardation is a common symptom of the disease. Why? (Hint: The brain's energy supply is particularly dependent on the catabolism of one substrate - which one?)

d) A common strategy for clinical management of this disease is administration of a special high-fat diet. In this diet, fat accounts for 80% of total caloric intake, while protein and carbohydrates each account for only 10%. (In diets recommended for healthy persons, typical caloric intake values are 20% fat, 20% protein, and 60% carbohydrate.) Why is the high-fat diet beneficial?

4. Explain, with simple diagrams, the mechanism by which the proton gradient across the inner mitochondrial membrane powers the rotation of the F_o portion of the ATP synthase.
(You do not need to discuss the mechanism of ATP synthesis by the F_1 portion of the ATP synthase.)

Student name: ID number:

Section C: Short answers. 20 marks total for Section C.

1. Next to the name of the substrate shown on the left, write the name of the enzyme which catalyzes its metabolism (catabolism). 5 marks.

substrate	**enzyme name**
fructose 1,6-*bis*phosphate	**aldolase**
3-phosphoglycerate	**phosphoglycerate mutase**
2-phosphoglycerate	**enolase**
malate	**malate dehydrogenase**
citrate	**aconitase**

2. "*Pas de deux*". Each of the catabolic enzymes listed below acts on two substrates. One of the substrates is given; name the other substrate. (Do not name the products of the reaction; do not draw any chemical structures.) The first question is completed for you, as an example. 4 marks.

enzyme	**substrate 1**	**substrate 2**
hexokinase	*glucose*	*ATP*
pyruvate kinase	ADP	**PEP (phospho*enol*pyruvate)**
fumarase	fumarate	**H_2O (water)**
thiolase	CoASH	**β-ketoacyl-CoA**
lactate dehydrogenase	pyruvate	**NADH ($+H^+$)**

Student name: ID number:

3. *"Sweet success"*. Fill in the six missing entries in the following table, accounting for the ATP yield of aerobic glucose oxidation (beginning with one molecule of glucose). Assume the use of the malate-aspartate shuttle for transfer of reducing equivalents into the mitochondrion. 6 marks.

Metabolic process	**Immediate product**	**ATP yield**
glycolysis (glucose to pyruvate)	2 NADH	**5**
	2 ATP	2
pyruvate oxidation	2 NADH	**5**
acetyl CoA oxidation	6 NADH	**15**
	2 $FADH_2$	3
	2 ATP	**2**
SUM (TOTAL NET YIELD OF ATP) =		**32**

4. "*Bits and pieces*". The chemical components listed in the first column are constituents of the biomolecules listed in the third column. Mix and match, by writing the appropriate letters (corresponding to the biomolecule) in the middle column. The first answer is given as an example. (No answer appears twice.) 5 marks.

component	*letter*	***biomolecule***
deoxyribose	D	**A**: trehalose
porphyrin	**C**	**B**: coenzyme Q
pantothenic acid	**E**	**C**: cytochrome c
glucose	**A**	**D**: DNA
N,*N*,*N*-trimethylethanolamine	**F**	**E**: coenzyme A
isoprenoid side chain	**B**	**F**: phosphatidylcholine

Student name: ID number:

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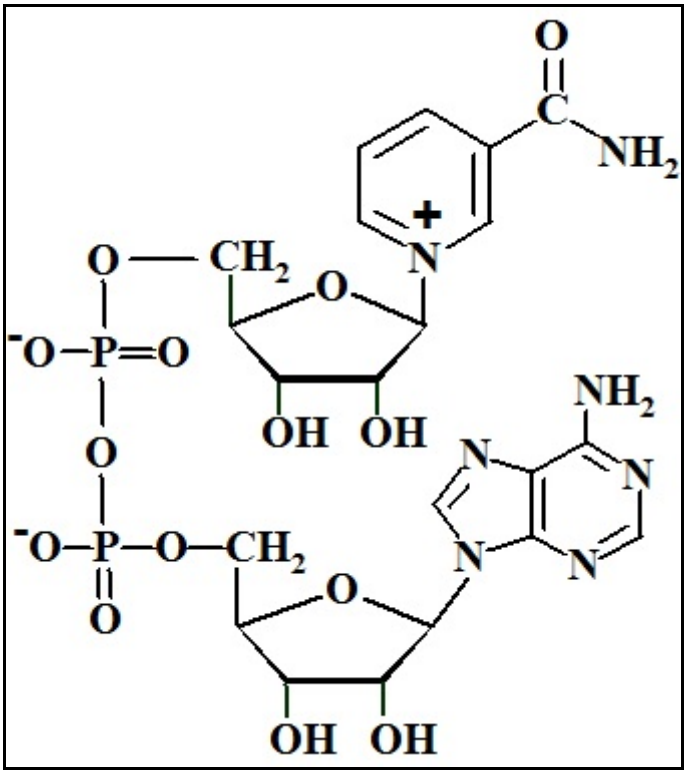
1. Draw the complete chemical structure of NAD^+.



Student name: ID number:

2. Lipids, which are poorly soluble in water, can spontaneously form several different types of aggregates (assemblies of many molecules) when they are dispersed in water. Briefly discuss at least three types of lipid aggregates; one of these types should be the lipid *micelle*.

For each type of aggregate: (i) provide a simple sketch indicating its size and geometry; (ii) identify the kinds of lipids that tend to form the aggregate; (iii) discuss any practical uses or biological roles of the aggregate. (It is not necessary to draw any detailed chemical structures.)

For sketches - see the textbook and the lecture manual

Micelle

(i) roughly spherical; polar groups on surface; usually small (approx. 3-10 nm diameter) but may be up to 100 nm.

(ii) fatty acids; soaps (salts of fatty acids) and detergents.

(iii) soap; casein (milk micelles);
emulsification of lipids in the g.i. tract.

Vesicle *or* Liposome

(i) roughly spherical; encloses aqueous core;
100 nm - microns diameter;
may be *unilamellar* or *multilamellar* (concentric "onion-skins")

(ii) many membrane lipids, *e.g.*, PC.

(iii) "artificial cell" (model system); drug delivery vehicle

Bilayer

(i) planar; polar head groups on surface; **hydrophobic interior; approx. 3 nm thickness but surface area may be very large**

(ii) many membrane lipids, *e.g.*, PC (same as for vesicles)

(iii) the lipid component of all biological membranes.

Student name: ID number:

3. Inherited disorders of pyruvate metabolism are rare human metabolic diseases. Many of these cases result from mutations in genes encoding the protein sub-units of the pyruvate dehydrogenase complex. In the affected individuals, pyruvate dehydrogenase enzyme activity is greatly diminished. Briefly explain each of the following clinical observations about this disease. (2 marks for each part.)

a) Lactic acidosis (*i.e.*, elevated levels of lactic acid in the blood, and lowered blood pH) is a common clinical finding in this disease; why? (Hint: What is the metabolic relationship between pyruvate and lactate?)

Pyruvate dehydrogenase catalyzes metabolism of pyruvate to acetyl CoA; when the enzyme activity is diminished, sugar catabolism (*e.g.*, in the muscles) leads to pyruvate accumulation. Some of the excess pyruvate is reduced (by NADH, catalyzed by lactate dehydrogenase) to give lactate. Tissue lactate is exported to the liver via the blood. Lactic acid causes lowering of blood pH.

b) In addition to lactate, blood levels of the amino acid alanine ($HOOC\text{-}CH(CH_3)\text{-}NH_2$) are often elevated. Why? (Hint: What is the structural and metabolic relationship between alanine and pyruvate?)

Alanine is the alpha-amino acid with the same carbon skeleton as the alpha-keto acid pyruvate. Some of the excess pyruvate is converted to alanine (by transamination).

c) Mental retardation is a common symptom of the disease. Why? (Hint: The brain's energy supply is particularly dependent on the catabolism of one substrate - which one?)

The brain relies on glucose for energy. Diminished pyruvate dehydrogenase activity lowers production of acetyl CoA, so the ATP yield of glucose catabolism is greatly lowered (effectively, from the aerobic approx. 30 ATP to the anaerobic 2 ATP). The brain is starved of energy and does not develop normally.

d) A common strategy for clinical management of this disease is administration of a special high-fat diet. In this diet, fat accounts for 80% of total caloric intake, while protein and carbohydrates each account for only 10%. (In diets recommended for healthy persons, typical caloric intake values are 20% fat, 20% protein, and 60% carbohydrate.) Why is the high-fat diet beneficial?

Most metabolic energy is derived from acetate catabolism (Krebs cycle, oxidative phosphorylation). Pyruvate dehydrogenase deficiency prevents acetyl CoA production from sugars (via pyruvate) but it does not affect acetyl CoA production from fatty acids (via beta-oxidation), so fats are the preferable energy sources.

Student name: ID number:

4. Explain, with simple diagrams, the mechanism by which the proton gradient across the inner mitochondrial membrane powers the rotation of the F_o portion of the ATP synthase.
(You do <u>not</u> need to discuss the mechanism of ATP synthesis by the F_1 portion of the ATP synthase.)

(see textbook Fig. 19-25 (f) and the lecture manual)