ID No.: _____

Medical Biochemistry Examination I

October 5, 2001
Kresge Auditorium
Please follow these directions:

1. Do not begin the exam until all students have received a copy of the exam. You will be instructed as to when to break the seal.

2. The exam consists of **125** questions on **33** pages, with this title page considered page 1. There are 150 points on this exam. The point value for each question is indicated by the question. For multiple answer questions without a defined number of answers 0.25 points will be deducted for each incorrect answer, although the lowest point value assigned for a question is 0. **No multiple answer question will have more than 4 correct answers.** *If a question has a defined number of answers, there is no penalty for guessing.*

3. Place your ID number on every page of the exam booklet and on the answer sheet you will hand in. Also, print your name on the line provided on the answer sheet.

4. There are two answer sheets for this exam. The first answer sheet should be used for questions 1-82 on pages 2-21. The second answer sheet should be used for questions 1-43 on pages 22-33. Fill in the circle for the correct answer(s) completely. If you believe that a question has more than one correct answer fill in all answers for that question completely. If you wish to change an answer, be sure to erase cleanly. Make sure that you use your biochemistry ID number to fill in the ID box. **You should use the three leftmost boxes to insert your number.**

5. When you are finished with the exam, return both the test booklet and the answer sheets. The test booklet will be returned to you when the grading is complete. **Be sure to pick up the next section of the course syllabus as you leave.**

6. Questions will not be allowed during the exam. If you believe there is a typographical error do the best you can with the information available. Do not spend extra time on the question. If it is determined that the information presented is ambiguous, or in error, then the question will not be counted in the final scoring.

7. Following the last page of the exam are two blank pages for your use, and a third page which can be used by you to list your answers. You can take this sheet with you from the exam, and use it to check your answers against the posted answers (outside of room 3109 MSB). **You will not be given extra time to fill out this answer sheet.** Answers will be posted on October 9th, at 2:00 pm, assuming that all students attend the exam at its scheduled time.

8. You will have **3.5 hours (until 5:00 pm)** to complete this exam. Good luck.

ID No.: _____

THIS IS PART ONE OF THE EXAM. QUESTIONS 1-82 SHOULD BE ANSWERED ON ONE ANSWER SHEET. PART II OF THE EXAM SHOULD BE ANSWERED ON THE OTHER ANSWER SHEET

1. (1 point) Which **ONE** of the following is most responsible for the maintenance of protein secondary structure?

   A. Hydrophobic interactions
   B. van der Waals forces
   C. Hydrogen bonds
   D. Disulfide cross-links
   E. Salt bridges

2. (1 point) Which **ONE** of the following statements concerning the properties of heme is **CORRECT**?

   A The heme in sickle cell hemoglobin is unable to bind O_2.
   B. Fe has six coordination positions, four of which are occupied by the nitrogen atoms of the porphyrin ring.
   C. In deoxyhemoglobin, the sixth coordination position of heme is occupied by water.
   D. The fifth coordination position of the Fe^{+2} is occupied by the distal histidine residue.
   E. The heme iron is oxidized as it binds O_2.

3. (2 points) Which **ONE** of the following statements concerning 2,3 bisphosphoglycerate (BPG) is **INCORRECT**?

   A. BPG binding increases the oxygen affinity of hemoglobin.
   B. The stoichiometry of BPG is one molecule per hemoglobin tetramer.
   C. BPG stabilizes the T form of hemoglobin through ionic bonds.
   D. In the complete absence of BPG, hemoglobin and myoglobin are observed to have identical oxygen binding properties.
   E. The binding of BPG is weaker to fetal hemoglobin than to the adult form.

4. (2 points) Concerning sickle cell anemia and the structure of hemoglobin S, which **ONE** of the following statements is **INCORRECT**?

   A. The molecular consequence of sickle cell anemia results from the mutation of glutamate 6 to valine in the β-chain of hemoglobin.
   B. The complementary hydrophobic pocket at the EF corner of the β-chain is inaccessible in the T form of hemoglobin S.
   C. Sickle cell formation is favored by low oxygen tension in the tissues.
   D. The solubility of deoxy-hemoglobin S is greatly reduced compared to the oxygenated form.
   E. Sickle cell anemia does not result from oxidation of the heme iron to the ferric form.

5. (2 points) Conversion of the T form of hemoglobin to the R form is **INCORRECTLY** described by which **ONE** of the following statements?

   A. Subunit interface displacement occurs resulting in a smaller central cavity.
   B. BPG binding is reduced by a factor of 100 fold.
   C. The iron atom moves into the plane of the protoporphyrin IX ring.
   D. Movement of the proximal histidine pulls several other residues in the F helix along with it.
   E. Tyrosine 145 forms a hydrogen bond with aspartate 94 in the β-chain.

6. (1 point) Which **ONE** of the following groups of amino acids would be characterized as entirely hydrophobic?

   A. His, Gly, Ala
   B. Phe, Ile, Val
   C. Trp, Glu, Val
   D. Asn, Glu, Arg
   E. Asp, Ser, Phe

7. (1 point) Under which **ONE** of the following conditions would hemoglobin have the highest affinity for oxygen?

   A. High bisphosphoglycerate and high pH
   B. High bisphosphoglycerate and low pH
   C. Low bisphosphoglycerate and high pH
   D. Low bisphosphoglycerate and low pH
   E. Low bisphosphoglycerate and low pH and high CO

8. (1 point) Choose the **SINGLE** best answer concerning the amino acid cysteine.

A. It is required for the formation of tertiary structure in proteins.
B. It can be present within the active site of enzymes and function as a nucleophile.
C. It forms disulfide bonds in secreted proteins.
D. The side-chain thiol has a pK of 6.5.
E. Both A and C
F. Both B and C

9. (1 point) Collagen contains large amounts of which **ONE** of the following?

A. Inter-chain hydrogen bonds
B. Intra-chain hydrogen bonds
C. ß-sheet
D. α-helix
E. 3_{10} -helix

10. (1 point) Which **ONE** of the following enzymes is required for formation of cross-links in collagen?

A. pro-collagen peptidase
B. protein disulfide isomerase
C. elastase
D. lysyl oxidase
E. protein desmosine oxidase

11. (2 points) Which **ONE** of the following is directly responsible for initiation of triple helix formation during procollagen biosynthesis?

A. deamination of lysine residues to form an aldehyde group and formation of crosslinks.
B. intra-peptide disulfide bond formation in the N- terminal pro-peptide of procollagen.
C. hydroxylation of lysine residues in the procollagen protein.
D. inter-peptide disulfide bond formation between C- terminal pro-peptides of procollagen.
E. removal of cross-linked C- terminal pro-peptides in mature collagen.

12. (1 point) Hydroxylation of prolyl residues of procollagen chains by prolyl hydroxylase requires all of the following **EXCEPT** for which **ONE**?

A. prolyl residue
B. ascorbate
C. CO_2
D. O_2
E. α-ketoglutarate

13. (1 point) At their isoelectric point proteins exhibit which **ONE** of the following?

A. no ionized groups.
B. no positively charged groups.
C. no negatively charged groups.
D. all of their acidic groups protonated.
E. no tendency to migrate in an electric field.

14. (1 point) Which **ONE** of the following statements is **TRUE** for proline and hydroxyproline in collagen?

A. Hydroxylation occurs on the collagen protein after synthesis on the ribosome
B. Proline in native collagen results from dehydroxylation of hydroxyproline
C. Collagen is not synthesized on ribosomes permitting direct insertion of hydroxyproline
D. Hydroxylation of proline occurs on the prolyl-tRNA
E. There are separate codons for hydroxyproline and proline

15. (1 point) Which **ONE** of the following statements is **TRUE** for collagen?

A. The fundamental collagen polypeptide is an alpha-chain that forms alpha-helices.
B. Collagen fibrils are formed by the self-assembly of procollagen molecules.
C. The carbohydrate residues are bound to hydroxyproline.
D. Glycine makes up nearly one third of the amino acid residues.
E. Arrangement of collagen fibrils is determined by the presence of alanine.

16. (1 point) At physiological pH, lysine (pK amino group = 9.0; pK carboxylate group = 2.2; pK of ionizing side-chain = 10.5) would exist mainly as a species with a net charge of which **ONE** of the following?

A. -2
B. -1
C. 0
D. +1
E. +2

17. (1 point) When fatty acids are added to water, they aggregate to form micelles. Which **ONE** of the following is the most important driving force for aggregation?

A. Hydrogen bonding between the adjacent carboxy groups.
B. Reduction of the hydrocarbon surface area exposed to water.
C. Van der Waals interactions between carboxyl groups and water.
D. Electrostatic interactions between the carboxyl groups and water.
E. Hydrogen bond formation between fatty acids in the micelle.

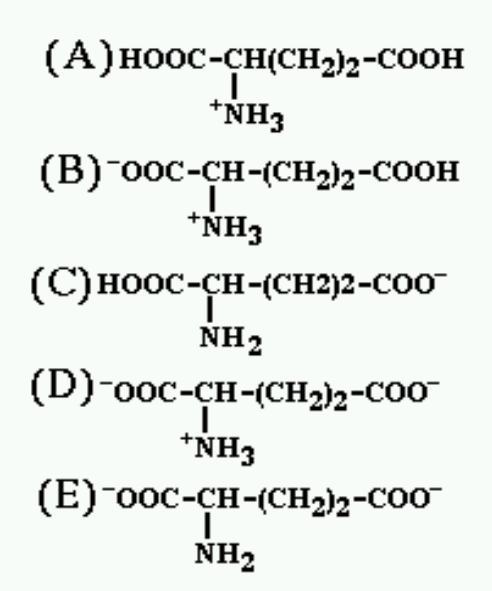
18. (1 point) Given the following 5 amino acids, which **ONE** has the bulkiest side chain?

A. alanine
B. valine
C. tyrosine
D. histidine
E. tryptophan

19. (1 point) Given the following 5 amino acids, which **ONE** of them is the most hydrophilic at pH 7.0?

A. serine
B. asparagine
C. methionine
D. arginine
E. glycine

20. (1 point) Which **ONE** of the following ionic species of glutamate is predominant at pH 10.5?



21. (1 point) Which sequence of atoms can be found in the backbone of polypeptides? Choose the **ONE** best answer.

A. C-C-N-C
B. N-C-C-C
C. C-O-C-N
D. C-N-N-C
E. C-C-C-N

22. (1 point) In a multisubunit protein such as hemoglobin, the individual polypeptide chains are usually bound to one another by all of the following **EXCEPT** for which **ONE**?

A. hydrogen bonds
B. electrostatic interactions
C. hydrophobic interactions
D. peptide bonds

23. (1 point) Which **ONE** of the following amino acid substitutions most likely causes a change in a protein's tertiary structure?

A. Isoleucine to arginine
B. Arginine to lysine
C. Valine to leucine
D. Threonine to serine
E. Asparagine to glutamine

24. (1 point) How does fetal hemoglobin (Hb F) differ from normal adult hemoglobin (Hb A)? Choose the **ONE** best answer.

A. A histidine residue in Hb A is replaced with a neutral amino acid in Hb F.
B. An alpha chain lysine residue in Hb A is replaced with a neutral amino acid in Hb F.
C. Hb F has a greater tendency to associate in the deoxygenated state.
D. Hb F has a greater affinity for CO.
E. Hb F exhibits enhanced oxygen unloading versus Hb A at the same pO_2.

25. (1 point) The O_2 binding affinity of hemoglobin decreases when there is a decrease in which **ONE** of the following?

A. ionic strength
B. 2,3 -bisphosphoglycerate concentration
C. carbon dioxide concentration
D. pH
E. vitamin C

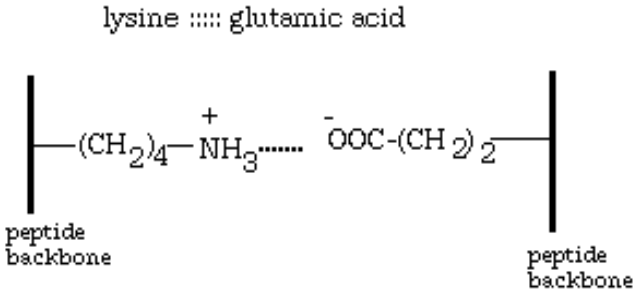
26. (1 point) Which **ONE** of the following is an important difference between hemoglobin (Hb) and myoglobin (Mb)?

A. Hb is a heterotetramer containing 2 alpha and 2 beta chains
B. Hb binds oxygen more tightly than Mb
C. Each chain in Hb contains a heme prosthetic group
D. Hb does not bind CO
E. The polypeptide chains of Hb are folded mostly into α-helices

27. (1 point) In oxygenated myoglobin, the oxygen molecule does which **ONE** of the following?

A. becomes the sixth coordinating link to the heme iron.
B. causes the reversible oxidation of Fe^{2+} to Fe^{3+}.
C. forces a change in conformation of one alpha-helix to a beta-strand.
D. is coordinated to the imidazole side-chain of the distal histidine.
E. replaces a histidine side chain in the iron coordination system.

28. (2 points) Ionic bonds between positively and negatively charged amino acid side chains, sometimes called salt bridges, often stabilize protein tertiary structures. Given the salt bridge:



Over what range of pH will this salt bridge be stable? (Assume that the side chains must be at least 50% charged in order for the salt bridge to be stable and the pK for $-NH_3$ is ~10.5 and the pK for -COO- is ~4.0). Choose the **ONE** best answer.

A. between pH 3.0 and 9.5
B. between pH 4.0 and 10.5
C. between pH 5.0 and 11.5
D. between pH 4.0 and 11.5
E. between pH 3.0 and 10.5

29. (1 point) The primary structure of the collagen alpha-chain is best represented by which **ONE** of the following? X, Y, and Z represent any amino acid and n=250-400.

A. (X-Gly)n
B. (Pro-Y-Z)n
C. (Lys-Pro-Z)n
D. (X-Y-Gly)n
E. (Gly-X-Y-Pro)n

30. (1 point) The genetic cause of most cases of alpha thalassemia is which **ONE** of the following?

A. A point mutation of the alpha globin gene
B. Mutations affecting the transcriptional regulation of the beta globin gene
C. Mutations causing structurally abnormal hemoglobin
D. Deletion of one or more alpha globin genes

31. (1 point) Which **ONE** of the following mutations of the beta globin gene would **NOT** be expected to produce beta thalassemia?

A. A point mutation that results in premature chain termination
B. A point mutation that results in abnormal splicing of pre-mRNA
C. A point mutation that results in defective assembly of the complex required for transcription
D. A point mutation that results in substitution of valine for glutamic acid at position 6

32. (1 point) Which **ONE** of the following statements is **TRUE** concerning sickle cell anemia (hemoglobin SS)?

A. It's inheritance follows an autosomal dominant pattern
B. It's patients have an elevated level of hemoglobin A2
C. Premature red cell breakdown leads to anemia
D. Heart attacks are common among children with the disease

33. (1 point) Why does sickle cell anemia **NOT** cause problems for fetuses that carry the genetic defect (hemoglobin SS)?

A. The synthesis of hemoglobin SS does not begin until around the time of birth
B. The imbalance of globin chain synthesis is less during fetal life
C. Maternal oxygen affinity differs from that of the fetus
D. Stillborn infants with sickle cell anemia are common

34. (2 points) Nucleic acids are composed of which of the following component parts? This question may have more than one correct answer; indicate all correct answers on the answer sheet.

A. Nitrogen-containing heterocyclic bases
B. Diphosphate linkages
C. Sugars with 6 carbon atoms comprising the ring structure
D. 5' to 3' phosphodiester linkages
E. Deoxyglucose sugars
F. 2' hydroxyl or 2' deoxy substituents
G. Peptide linkage between sugar and base

35. (1 point) A typical purine base may be identified by which **TWO** of the following characteristics?

A. 4 carbons and 2 nitrogens in the ring structure
B. At least one oxygen atom linked to the ring structure
C. 5 carbons and 4 nitrogens in the ring structure
D. A nitrogen atom in the 9 position
E. 6 carbons and 3 nitrogens in the ring structure
F. A carbon atom in the 1 position

36. (1 point) Typical anti-HIV drugs like AZT are toxic to humans because of which **ONE** of the following reasons?

A. Inhibition of the poly A polymerase enzyme
B. Incorporation into mRNA
C. Completely inhibits the polymerizing ability of DNA polymerase
D. Incorporation into full-length viral DNA and thus enhance mutation frequency
E. Incorporation into cellular DNA causing termination of replication

37. (1 point) The reason there are 64 possible codons is which **ONE** of the following?

A. There are 64 aminoacyl tRNA synthetases
B. Each base is able to participate in wobbling
C. All possible reading frames can be used in this way
D. There are 4 possible bases at each of three codon positions
E. The more codons, the faster protein synthesis can be accomplished

38. (1 point) Resistance of HIV to nucleoside analogs commonly arises because of which **ONE** of the following?

A. Human cells become impermeable to their uptake
B. The virus produces a specific enzyme to degrade the analogs
C. Error-prone replication of the viral genome leads to a reverse transcriptase with altered properties
D. Reverse transcriptase is no longer needed by resistant viruses
E. Viral components inhibit phosphorylation of the nucleoside

39. (2 points) In comparing DNA and RNA which features are **UNIQUE** to one or the other molecule? This question may have more than one correct answer; indicate all correct answers on the answer sheet.

A. Contain phosphodiester linkages
B. Are synthesized in the 5' to 3' direction
C. Can participate in G-C base pairs
D. Usually contain both single stranded and double stranded regions
E. Are created from nucleoside triphosphates
F. Can participate in G-U base pairs
G. May undergo post-synthetic modification of bases
H. Frequently have a 3' poly A tail
I. Are considered informational macromolecules
J. Are typically repaired in vivo

40. (1 point) Repeating dinucleotide sequences are very common in eukaryotic genomes, e.g. .....ACACACACACACACACACACAC..... Based on what you know, which **ONE** of the following statements is likely to be correct?

A. When occurring within genes they will give rise to a monotonous run of a single amino acid
B. depending on the reading frame they will give rise to repetitive runs of 1, 2 or 3 amino acids
C. Irrespective of reading frame they will produce a run of the same two alternating amino acids
D. Ribosomes will rapidly dissociate from mRNAs containing such sequences
E. If located within introns they will precipitate alternative splicing events

41. (1 point) The stop codons in mRNA are UAA, UAG and UGA. Considering only the 3rd position of the codon, how many other codons are subject to sustaining a nonsense mutation that would lead to the production of one of these? Choose the **ONE** best answer.

A. 1
B. 2
C. 3
D. 4
E. 5
F. 6

42. (1 point) All of the following components except for which **ONE** are necessary for replicating a prokaryotic chromosome?

A. DNA polymerase III
B. DNA primase
C. RNA polymerase I
D. DNA ligase
E. Ribonucloside triphosphates

43. (2 points) Which of the following characteristics of proof-reading are essential to maintain fidelity in DNA replication? This question may have more than one correct answer; be sure to indicate all correct answers on the answer sheet.

A. Degrading DNA in the 5' to 3' direction
B. Using wobble pairing to increase efficiency
C. Using methylation differences to determine parent vs daughter strand
D. Always having a free 3'-OH end on the strand being synthesized
E. Having both a nuclease and a polymerase activity on the same molecule
F. Ensuring the correct amino acid is bound to its cognate tRNA

44. (2 points) Which of the following enzymatic activities are **NOT** contained within DNA polymerase I? This question may have more than one correct answer; be sure to indicate all correct answers on the answer sheet.

A. Making internucleotide linkages in the 5' to 3' direction
B. Destroying internucleotide linkages in the 5' to 3' direction
C. Having an exonuclease activity specific for RNA but not DNA
D. Making internucleotide linkages in the 3' to 5' direction
E. Destroying internucleotide linkages in the 3' to 5' direction

45. (1 point) Okazaki fragments show all of the following characteristics except for which **ONE**?

A. Are mixed DNA/RNA polymers
B. Are typically 1000 nucleotides long in prokaryotes
C. Are joined together by DNA primase
D. Are formed as part of the lagging strand
E. Allow a replisome to move in one direction on double stranded DNA

46. (1 point) Bidirectional replication is a phenomenon which is best described by which **ONE** of the following?

A. Allows bacteria to grow in two directions at once
B. Requires at least two replication origins
C. Requires no more than two replisomes
D. Cannot occur on linear chromosomes
E. Is purely theoretical since it cannot be visualized

47. (1 point) DNA replication requires primers in order to proceed because of which **ONE** of the following?

A. DNA primase cannot work de novo
B. DNA polymerases need a template from which to copy DNA
C. Replication origins cannot be melted in their absence
D. DNA polymerases require free 3' ends in order to both make DNA and check it
E. DNA primase only works at replication origins

48. (2 points) Which of the following processes would **NOT** increase the chances of causing mutations in DNA? This question may have more than one correct answer; be sure to indicate all correct answers on the answer sheet.

A. Exposure to UV light
B. Incorrect charging of tRNA
C. Loss of 3' to 5' exonuclease activity in DNA polymerase
D. Translational frameshifting by ribosomes
E. Deamination of cytosine bases
F. Eating large quantities of wild mushrooms

49. (1 point) The Ames test attempts to identify potential mutagens in which **ONE** of the following ways?

A. By converting Salmonella into E. coli
B. By selecting for a "back mutation" to convert an inactive gene to an active one
C. By using chemically exposed bacteria to infect human cells
D. By killing Salmonella bacteria
E. By creating mutations in the histidine codon

50. (1 point) Telomere shortening might be expected to occur in all of the following situations **EXCEPT** for which **ONE**?

A. A down-regulation of telomerase activity
B. Elimination of the telomerase RNA-encoding gene
C. Highly differentiated mammalian cells
D. Very old bacterial cells
E. Enhanced 3' to 5' exonuclease activity in the cell

51. (1 point) When cytosine deamination occurs in DNA all of the following activities are needed to repair the lesion except for which **ONE**?

A. DNA ligase
B. AP endonuclease
C. Uracil DNA glycosylase
D. DNA primase
E. DNA polymerase I

52. (1 point) Mismatch repair is characterized by each of the following observations **EXCEPT** for which **ONE**?

A. Recognition of a mismatch site by a specialized "mut" protein
B. The presence of 5-methyl cytidine in the sequence GATC
C. The existence of a mismatch within 1 kb of a GATC sequence
D. Endonuclease cleavage at the 5' side of GATC
E. A high incidence of cancer when one of the "mut" proteins is lacking

53. (1 point) 5-methyl cytidine is present in high quantities in mammalian DNA, so it is likely to be a hot-spot for mutation because of which **ONE** of the following?

A. It is unable to base pair with G, hence creating a distortion in DNA
B. It is hydrolyzed to give 5-methyl uracil, which is removed by uracil DNA glycosylase to leave an unrepaired gap in DNA
C. It is deaminated to thymine, which results in a G:T mismatch
D. It should not be there in the first place
E. It causes DNA polymerase to utilize incorrect bases when encountering it on the template strand

54. (1 point) The enzyme telomerase synthesizes DNA strands at the end of chromosomes through which **ONE** of the following mechanisms?

A. By converting DNA polymerase into a continuously cycling mode
B. By adding each of the 4 nucleotides in turn to produce a repetitive sequence
C. By extending the leading strand via instructions from its own internal template
D. By violating the usual rule and synthesizing DNA 3' to 5'
E. By adding long poly A tails to the leading strand

55. (1 point) The key mechanistic failure in Xeroderma Pigmentosum patients involves which **ONE** of the following?

A. Mutation in the photolyase gene
B. Inability to excise a section of UV damaged DNA
C. Mutation on one of the mismatch repair components
D. Inability to synthesize DNA across the damaged region
E. Loss of proofreading capacity

Questions 56-61 (0.5 point each) are either **TRUE or FALSE**. **Answer T or F on the answer sheet.**

56. Cancer is a common consequence of mutation in DNA repair genes
57. Chemically damaged bases are usually removed and repaired by nucleotide excision repair rather than base excision repair
58. Double stranded regions in RNA occur by parallel base pairing rather than the antiparallel base pairing characteristic of DNA
59. Uracil is not found in DNA because it would base pair with G
60. G-C base pairs require less energy to disrupt than A-T base pairs
61. Retroviruses are the only known source of dogma-violating reverse transcriptases

62. (1 point) Transcription in prokaryotes requires all of the following components except for which **ONE**?

A. DNA
B. tRNA
C. Mg^{2+} ions
D. rNTP's
E. RNA polymerase

63. (1 point) Several different proteins can be synthesized from a typical prokaryotic mRNA because of which **ONE** of the following?

A. Any of the 3 reading frames can be used
B. There is redundancy in the choice of codon/tRNA interactions
C. The gene contains several operator sequences from which to initiate translation
D. Alternative splicing events are commonly found
E. Many mRNAs are organized in a series of consecutive translational cistrons

64. (1 point) In order for prokaryotic transcription to be initiated all of the following have to occur except for which **ONE**?

A. The promoter needs to be recognized by holoenzyme
B. DNA downstream of the promoter has to be "melted"
C. Sigma factor has to accompany the polymerase to the promoter
D. The DNA strand that acts as template is the one that reads 5' to 3'
E. Two molecules of rNTP are condensed to form the first phosphodiester bond

65. (2 points) mRNAs in prokaryotes and eukaryotes have differences in all of the following features except for which **TWO**?

A. Structure at the 5' end of the mRNA
B. Structure at the 3' end of the mRNA
C. Temporary existence of lariat structures
D. Require transport to the site of translation
E. Are translated 5' to 3'
F. Are transcribed in the nucleus
G. Require initiation factors to be assembled with ribosomes for translation

66. (1 point) Each of the following features are characteristics of introns except for which **ONE**?

A. 100% conservation of a dinucleotide sequence at both their 5' and 3' ends
B. Contain a poly purine sequence directly adjacent to their 3' end
C. Always form a lariat through an A residue about 30 nt from the 5' end
D. Bind to protein/RNA complexes called snRNP's to facilitate splicing
E. Are not present in prokaryotes

67. (2 points) Most eukaryotic genes produce mRNAs that are processed. Which of the following are correct statements regarding this process? This question may have more than one correct answer; indicate all correct answers on the answer sheet.

A. All processing occurs before the mRNA is fully synthesized
B. Capping of the 5' end occurs as soon as the 5' end emerges from the polymerase
C. The capping machinery uses methylated GTP to create the cap
D. Polyadenylation occurs after the repeated sequence AUUUA is produced at the 3' end
E. All processing is completed before transport of the mature mRNA to the cytoplasm
F. Alternative splicing only occurs when mutations in or around the intron sequences have been sustained

68. (2 points) Promoters are ubiquitous elements for all eukaryotic genes. Which **TWO** of the following statements regarding eukaryotic promoters are **INCORRECT**?

A. Many, but not all, promoters contain a TATAA consensus at ca. -30 bp
B. The TATAA sequence is on the sense strand, thereby defining the other strand as the template for transcription
C. Many genes need only a TATAA sequence for efficient transcription
D. Upstream regulatory elements within 200 bp of the TATAA sequence bind to TFII initiation factors (such as TFIIA and B) and help to recruit TFIID
E. Enhancers are typically not considered part of the promoter, though they can affect transcription rates
F. Many of the factors that bind at a TATAA promoter are themselves complexes of several individual proteins

69. (2 points) In comparing protein synthesis in eukaryotes and prokaryotes there are many similarities. Which **TWO** of the following are clearly different between these two groups of organisms?

A. Number of GTP molecules consumed per peptide bond completed during elongation
B. Presence of polyribosomes on individual mRNA molecules
C. Requirement of a chemically modified form of methionine at initiation
D. Requirement for a capped mRNA in order to get efficient translation
E. Requirement for two species of methionine-specific RNA
F. Large numbers of ancillary proteins in both the small and large ribosomal subunits

70. (2 points) tRNA s have several unique features which distinguish them from other types of RNA. From what you have learned in this course, which of the following features are **NOT UNIQUE** to tRNA? This question may have more than one correct answer; be sure to indicate all correct answers on the answer sheet.

A. Ability to form a 3D structure by virtue of intramolecular base pairing
B. Modification of the 3' end by non-templated bases
C. Presence of inosine residues
D. Presence of a methylated G base (or bases)
E. Presence of thymine base(s)
F. Existence of covalent links to amino acids

71. (1 point) Lac repressor displays each of the following characteristics except for which **ONE**?

A. Binds to a specific dyad symmetric DNA sequence
B. Typically functions in a tetrameric complex at the lac operon
C. Blocks passage of RNA polymerase
D. Requires allolactose to inhibit its ability to bind to DNA
E. Regains its ability to bind to DNA in the absence of glucose

72. (1 point) Complementation in trans signifies which **ONE** of the following molecular scenarios?

A. DNA in one strand is complementary to DNA in the other strand
B. It is a technical term for referring to coupled transcription and translation
C. The ability of DNA sequences on different chromosomes to hybridize to one another
D. The protein product of a gene on one piece of DNA is able to compensate for a mutant, non-functional version of the protein encoded on another
E. The transport of proteins from the cytoplasm to the nucleus, or vice-versa

73. (1 point) Finely tuned gene transcription levels in cells are typically controlled by which **ONE** of the following?

A. Unique combinations of positively or negatively acting transcription factors
B. A combination of messenger half-life and transport of mRNAs
C. Presence of either σ factor or TFIID
D. The presence or absence of mutations in promoters or other regulatory regions
E. The relative concentration of glucose versus lactose in the cells

74. (1 point) Frequently seen features among DNA binding proteins include all of the following **EXCEPT** for which **ONE**?

A. The existence of a specific α helix that lies across the major groove of DNA
B. The ability to form dimers between identical or non-identical partners
C. The ability to form multiple hydrogen bonds between amino acid side chains and the edges of base pairs in the double strand
D. The ability to interact with small molecule effectors to alter DNA binding ability
E. The ability to recognize RNA molecules with the same sequence

Questions 75-82 (0.5 point each) are either **TRUE or FALSE. Answer T or F on the answer sheet.**

75. Enhancers can only work from positions upstream of genes
76. Where proteins form multimeric complexes, one non-functional subunit can have a dominant negative effect on the whole complex
77. Splicing is one way to increase the diversity of the protein population in an organism starting with a fixed number of genes
78. The concentration of mRNA in the cell is necessarily proportional to its rate of transcription
79. Cellular aging may well be related to the lack of telomerase in the cells
80. Combinatorial regulation of gene expression allows many unique regulatory patterns to evolve from a relatively small number of proteins
81. Mg^{2+} is needed for replication and transcription but not for translation
82. Eukaryotes and prokaryotes use a universal genetic code

THIS ENDS PART I. ANSWER SHEET ONE SHOULD HAVE 82 ANSWERS ON IT. SWITCH TO ANSWER SHEET II FOR THE REST OF THE EXAM.

THIS BEGINS PART II OF THE EXAM. USE THE SECOND ANSWER SHEET FOR QUESTIONS 1-43 OF PART II

1. (2 points) Glucagon release by the pancreas will result in the phosphorylation and inhibition of which of the following enzymatic activities? There may be more than one correct answer to this question; be sure to indicate all correct answers on the answer sheet.

   A. Citrate synthase
   B. Glucokinase
   C. Hexokinase
   D. Liver phosphofructokinase-1
   E. Muscle phosphofructokinase-1
   F. Liver phosphofructokinase-2
   G. Muscle phosphofructokinase-2
   H. Liver pyruvate kinase
   I. Muscle pyruvate kinase
   J. Succinate dehydrogenase

2. (2 points) The major roles of glycolysis are which of the following? This question may have more than one correct answer; be sure to indicate all correct answers on the answer sheet.

   A. To synthesize glucose
   B. To generate energy
   C. To produce FADH2
   D. To synthesize glycogen
   E. To provide precursors for other biosynthetic pathways
   F. To utilize ATP to generate heat

3. (2 points) A type I diabetic, upon receiving an overdose of insulin, will exhibit which of the following metabolic changes? This question may have more than one correct answer; be sure to indicate all correct answers on the answer sheet.

   A. Hyperglycemia
   B. Hypoglycemia
   C. Lactic acidosis
   D. Elevated levels of pyruvate in the blood
   E. Reduced oxygen binding to hemoglobin
   F. Increased glycosylation of hemoglobin

4. (1 point) A biochemist has placed in a test tube all of the enzymatic machinery and cofactors necessary to convert glucose to pyruvate. The scientist than places within the test tube a sulfhydral reagent which forms covalent bonds with free sulfhydral groups in proteins. After adding the inhibitor, glucose was added to the test tube. Which **ONE** metabolite would initially accumulate within the test tube under these conditions?

   A. 1,3 bisphosphoglycerate
   B. Citrate
   C. Fructose 1,6 bisphosphate
   D. Fructose-6-phosphate
   E. Glucose-6-phosphate
   F. Glyceraldehyde-3-phosphate
   G. Glycogen
   H. Pyruvate

5. (1 point) In the same experiment as described in the previous question, instead of adding a sulfhydral reagent a reagent targeted against free amino groups is added to the test tube. This reagent forms a covalent bond with free amino groups in proteins. Under these conditions, in the presence of glucose, which **ONE** metabolite would initially accumulate within the test tube?

   A. 1,3 bisphosphoglycerate
   B. Citrate
   C. Fructose 1,6 bisphosphate
   D. Fructose-6-phosphate
   E. Glucose-6-phosphate
   F. Glyceraldehyde-3-phosphate
   G. Glycogen
   H. Pyruvate

6. (1 point) Which **ONE** of the following is **NOT** required for glucagon to elevate cAMP levels in liver cells?

   A. Glucagon receptor
   B. GTP
   C. Adenylate cyclase
   D. G-proteins
   E. IRS-I

7. (1 point) Starting with fructose and synthesizing two molecules of pyruvate, the net yield of ATP and NADH would be which **ONE** of the following?

A. 1 ATP, 1 NADH
B. 1 ATP, 2 NADH
C. 1 ATP, 4 NADH
D. 2 ATP, 1 NADH
E. 2 ATP, 2 NADH
F. 2 ATP, 4 NADH
G. 3 ATP, 1 NADH
H. 3 ATP, 2 NADH
I. 3 ATP, 4 NADH

8. (2 points) Elevated levels of ATP will lead to the direct inhibition of which of the following enzymes? This question may have more than one correct answer; be sure to indicate all correct answers on the answer sheet.

A. Adenylate kinase
B. Hexokinase
C. Isocitrate dehydrogenase
D. Phosphofructokinase-I
E. Phosphofructokinase-II
F. Pyruvate carboxylase
G. Pyruvate dehydrogenase
H. Pyruvate kinase

9. (2 points) A decrease in blood glucose levels will, in the liver, lead to the inhibition, either directly or indirectly, of which of the following enzymatic activities? This question may have more than one correct answer; be sure to indicate all correct answers on the answer sheet.

A. Aldolase
B. Cyclic-AMP dependent protein kinase
C. Enolase
D. Glyceraldehyde-3-phosphate dehydrogenase
E. Phosphofructokinase-II
F. Pyruvate kinase

Questions 10-14 (2 points each) are matching questions concerning diseases associated with carbohydrate metabolism. Match the **ONE** best enzyme defect (lettered choices) with the disease or condition listed in the question. An answer may be used once, more than once, or not at all.

10. Hereditary fructose intolerance
11. Lactose intolerance
12. Galactosemia
13. Type I diabetes
14. Type II diabetes

A. Aldolase
B. Galactose-1-phosphate uridyl transferase
C. β-galactosidase (or β-glucosidase)
D. Glucose-6-phosphatase
E. Insulin receptor
F. Phosphofructokinase-I
G. Pyruvate kinase
H. UDP-galactose C4 epimerase
I. None of the above

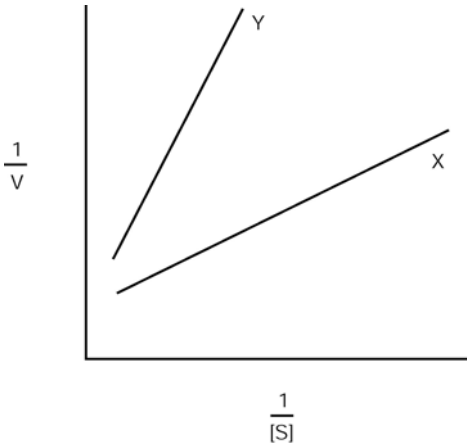
15. (1 point) Starting with glucose labeled in either position 1, 2 or 3 with ^{14}C, which labeled molecule will be the first to lose the radioactive carbon as $^{14}CO2$ if the glucose is used exclusively for the glycolytic and TCA cycles? Choose the **ONE** best answer.

A. 1-[^{14}C]-glucose
B. 2-[^{14}C]-glucose
C. 3-[^{14}C]-glucose
D. Both 1 and 2-[^{14}C]-glucose would lose it at the same time
E. Both 1 and 3-[^{14}C]-glucose would lose it at the same time
F. Both 2 and 3-[^{14}C]-glucose would lose it at the same time

16. (1 point) Arsenate will block the formation of ATP by all of the following enzymes (or combination of enzymes) except for which **TWO**?

A. Adenylate kinase
B. ATP synthase
C. Glyceraldehyde-3-phosphate dehydrogenase/Phosphoglycerate kinase
D. Pyruvate kinase
E. Succinate thiokinase

Questions 17-20 (1 point each) are based on the figure to the right. The data shown in the figure are based on measuring the enzyme kinetics of an enzyme in the absence (curve X) or presence (curve Y) of an allosteric modifier. Answer each question based on this graph.



17. The allosteric modifier is acting as which **ONE** of the following?

    A. An activator of the enzyme
    B. A competitive inhibitor of the enzyme
    C. A non-competitive inhibitor of the enzyme
    D. Insufficient data to make a determination

18. The K_m of the enzyme in the presence of the modifier is which **ONE** of the following as compared to the absence of the modifier?

    A. Greater
    B. The same
    C. Less than
    D. Insufficient data to make a determination

19. The V_{max} of the enzyme in the presence of the modifier is which **ONE** of the following as compared to the absence of the modifier?

    A. Greater
    B. The same
    C. Less than
    D. Insufficient data to make a determination

20. The type of plot used to display the data is which **ONE** of the following?

    A. Eadie-Hofstee plot
    B. Hill plot
    C. Lineweaver-Burk plot
    D. Michaelis-Menton plot
    E. Scatchard plot

21. (2 points) An inhibitor of the Na^+, K^+-ATPase of the intestinal epithelial cell would be expected to block which **TWO** of the following events?

A. Facilitated sugar transport across the brush border membrane
B. Facilitated sugar transport across the serosal membrane
C. Active sugar transport across the brush border membrane
D. Active sugar transport across the serosal membrane
E. The generation of a sodium gradient, interior positive, across the brush border membrane
F. The generation of a sodium gradient, interior negative, across the brush border membrane

22. (2 points) ΔG^o is the free energy change of a reaction under standard conditions. In which **ONE** of the following ways does $\Delta G^{o\prime}$ differ from ΔG^o?

A. $\Delta G^{o\prime}$ is determined when the temperature is 273 degrees Kelvin
B. A positive value for $\Delta G^{o\prime}$ indicates a favorable reaction
C. $\Delta G^{o\prime}$ ignores the concentration of water, and allows it to be treated as a constant
D. $\Delta G^{o\prime}$ is calculated by dividing ΔG^o by two
E. $\Delta G^{o\prime}$ is calculated assuming the $[H^+] = 5 \times 10^{-7}$ M

23. (2 points) Which of the following muscle enzymes will **NOT** be allosterically inhibited under conditions of high glucose levels in a normal individual? Consider the case of someone who has eaten a large carbohydrate-rich meal, and then gone to vegetate in front of the TV for the next two hours. This question may have more than one correct answer; indicate all correct answers on the answer sheet.

A. Citrate synthase
B. Fumarase
C. Isocitrate dehydrogenase
D. Phosphofructokinase-I
E. Phosphoglycerokinase
F. Pyruvate dehydrogenase

Questions 24-27 (1 point each) are based on the following scenario. A medical student, too nervous to eat for 24 hours due to upcoming exams, decides to go for a jog before the morning biochemistry exam. During the jog, indicate the phosphorylation and activity state of the following enzymes. Choose the **ONE** best answer for each enzyme.

24.	Liver phosphofructokinase-I	A.	Phosphorylated and active
25.	Liver phosphofructokinase-II	B.	Phosphorylated and inactive
26.	Liver pyruvate kinase	C.	Not phosphorylated, and active
27.	Muscle pyruvate dehydrogenase	D.	Not phosphorylated, and inactive

28. (1 point) The ATP yield from the complete oxidation of one mole of oxaloacetate to carbon dioxide and water will yield how many moles of ATP, assuming that the malate/aspartate shuttle is used for all cytoplasmic reduced cofactors? Choose the **ONE** best answer.

A. 8.5
B. 10.5
C. 12.5
D. 14.5
E. 16.5

29. (1 point) Transport molecules exist for all of the following compounds to cross the inner mitochondrial membrane except for which **TWO**?

A. Citrate
B. α-ketoglutarate
C. Malate
D. NADH
E. Oxaloacetate
F. Pyruvate

30. (1 point) FADH2 donates its electrons to coenzyme Q in the electron transfer chain from which of the following enzymes? This question may have more than one correct answer; indicate all correct answers on the answer sheet.

A. Glyeraldehyde-3-phosphate dehydrogenase
B. Glycerol-3-phosphate dehydrogenase (mitochondrial)
C. Malate dehydrogenase
D. NADH dehydrogenase
E. Pyruvate dehydrogenase
F. Succinate dehyrogenase

31. (2 points) A novel organism has been found with a unique electron transfer chain. The

ΔE^o values for the individual components are as follows:

Component A = + 1.004 mv
Component B = -0.027 mv
Component C = +0.321 mv
Component D = -0.064 mv
Component E = -0.457 mv

What is the likely order of the transfer of electrons in this chain? Choose the **ONE** best answer.

A. E transfers to D, which transfers to B, which transfers to C, which transfers to A
B. E transfers to B, which transfers to D, which transfers to A, which transfers to C
C. E transfers to D, which transfers to A, which transfers to C, which transfers to B
D. A transfers to C, which transfers to B, which transfers to D, which transfers to E
E. C transfers to A, which transfers to D, which transfers to B, which transfers to E
F. B transfers to C, which transfers to A, which transfers to D, which transfers to E

32. (1 point) Using the information from the previous question, what is the maximum amount of energy (in kcal/mole) which can be obtained from transferring one pair of electrons through all of the components of the electron transfer chain. Assume that a pair of electrons is transferred, and the Faraday constant equals 23,000 calories per mole-volt. Choose the **ONE** answer closest to your calculated answer.

A. -23
B. -46
C. -69
D. -92
E. Cannot be determined from the data given

33. (1 point) Consider the following experiment. Carefully isolated liver mitochondria are incubated in the presence of a limiting amount of succinate and malonate, an inhibitor of malate dehydrogenase. Three minutes after adding the substrates cyanide is added, and the reactions allowed to proceed for another seven minutes. At this point in time, which of the following components of the electron transfer chain will be in an oxidized state? There may be more than one correct answer to this question; indicate all correct answers on the answer sheet.

A. Complex I
B. Complex II
C. Complex III
D. Coenzyme Q
E. Cytochrome C

34. (1 point) Consider the following experiment. Carefully isolated liver mitochondria are placed in a weakly buffered solution. Malate is added as an energy source, and an increase in oxygen consumption confirms that the electron transfer chain is functioning properly within these organelles. Valinomycin and potassium are then added to the mitochondrial suspension. Valinomycin is a drug which allows potassium ions to freely cross the inner mitochondrial membrane. What will the effect of the valinomycin addition do to the proton-motive force which had been generated by the oxidation of malate? Choose the **ONE** best answer.

A. The proton-motive force will be reduced to a value of zero
B. There will be no change in the proton-motive force
C. The proton-motive force will be increased
D. The proton-motive force will be decreased, but to a value greater than zero

35. (1 point) A form of diabetes can result from all of the following abnormalities **EXCEPT** for which **ONE**?

A. Decreased insulin receptor number
B. Increased insulin receptor number
C. Production of antibodies directed against the insulin receptor
D. Lack of tyrosine kinase activity of the insulin receptor
E. Inability to autophosphorylate the insulin receptor
F. Inability of insulin receptor substrates to bind to the activated insulin receptor
G. Inability to produce insulin

36. (1 point) Which **ONE** of the following vitamins is not required to produce or be a cofactor necessary for an oxidative decarboxylation reaction to occur?

A. Biotin
B. Lipoic acid
C. Niacin
D. Phosphopantothenic acid
E. Riboflavin
F. Thiamine

37. (1 point) The energy required to synthesize one mole of glucose from two moles of lactate is best represented by which **ONE** answer?

A. 1 mole
B. 2 moles
C. 3 moles
D. 4 moles
E. 5 moles
F. 6 moles
G. 7 moles
H. 8 moles

38. (2 points) Elevated levels of blood and tissue lactic acid can result from which of the following conditions? There may be more than one correct answer to this question; indicate all correct answers on the answer sheet.

A. Anaerobic muscle glycolysis
B. Aerobic muscle glycolysis
C. Intravenous galactose infusions
D. Intravenous glucose infusions
E. Intravenous fructose infusions
F. Pyruvate carboxylase deficiency
G. Hexokinase deficiency
H. Alcohol intoxication

39. (1 point) In the conversion of α-ketoglutarate to glucose, which of the following compounds are **NOT** obligatory intermediates in this pathway? This question may have more than one correct answer; indicate all correct answers on the answer sheet.

A. 1,3 bisphosphoglycerate
B. Citrate
C. Fructose 1,6 bisphosphate
D. Malate
E. Oxaloacetate
F. Pyruvate
G. Succinate

40. (1 point) A G_s protein has been mutated such that the intrinsic GTPase activity is destroyed. If glucagon was to activate this mutated G protein in liver cells, which **ONE** of the following would be the most likely to occur?

A. Prolonged elevation of cAMP levels
B. No change in cAMP levels
C. Prolonged decrease in cAMP levels
D. Transient increase in cAMP levels
E. Transient decrease in cAMP levels

41. (1 point) High energy thio-ester bonds are created or produced during the reaction sequence for which of the enzymes listed below? There may be more than one correct answer to this question; indicate all correct answers on the answer sheet.

A. Glyceraldhyde-3-phosphate dehydrogenase
B. Isocitrate dehydrogenase
C. α-ketoglutarate dehydrogenase
D. Lactate dehydrogenase
E. Malate dehydrogenase
F. Pyruvate dehydrogenase
G. Succinate dehydrogenase

42. (2 points) Hypoglycemia can result from severe alcohol intoxication due to which **ONE** of the following reasons?

A. Biotin deficiency
B. Lactate accumulation due to reduced oxygen uptake in the presence of ethanol
C. An increased ratio of NAD^+/NADH due to alcohol metabolism
D. A decreased ratio of NAD^+/NADH due to alcohol metabolism
E. None of the above

43. (2 points) A deficiency of which of the following vitamins would be expected to hinder the activity of the enzymes involved in gluconeogenesis? Ignore energy considerations in answering this question; concentrate only on the enzymes of gluconeogenesis. This question may have more than one correct answer; indicate all correct answers on the answer sheet.

A. Biotin
B. Lipoic acid
C. Niacin
D. Phosphopantothenic acid
E. Riboflavin
F. Thiamine
G. Vitamin C

Medical Biochemistry Exam I, October 5, 2001, Answer Key

Part 1 (Q 1-82)

1. C
2. B
3. A
4. B
5. E
6. B
7. C
8. F
9. A
10. D
11. D
12. C
13. E
14. A
15. D
16. D
17. B
18. E
19. D
20. E
21. A
22. D
23. A
24. A
25. D
26. A
27. A
28. B
29. D
30. D
31. D
32. C
33. A
34. A, D, F
35. C, D
36. E
37. D
38. C
39. D, F, H, J
40. C
41. E
42. C
43. D, E
44. C, D
45. C
46. C
47. D
48. B, D, F
49. B
50. D or E
51. D
52. B
53. C
54. C
55. B
56. T
57. Deleted
58. F
59. F
60. F
61. F
62. B
63. E
64. D
65. E, G
66. B or C
67. B, E
68. C, D
69. C, D
70. A, B, D
71. E
72. D
73. A
74. E
75. F
76. T
77. T
78. F
79. T
80. T
81. F
82. Deleted

PART II (1-43)

1. F, h
2. B. E
3. B
4. F
5. C
6. E
7. E
8. C, D, G, H
9. E, F
10. A
11. C
12. B or H
13. I
14. E
15. C
16. A, D
17. B
18. A
19. B
20. C
21. C, F
22. C
23. B, E
24. D
25. B
26. B
27. C
28. C
29. D, E
30. B, F
31. A
32. C
33. A
34. D
35. B
36. A
37. F
38. A, E, F
39. B, F
40. A
41. A, C, F
42. D
43. A, C