Medical Biochemistry Examination I
October 7, 1998
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 99 questions on 21 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 0.50 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. The answer sheet for questions 1-98 is a computer graded form. **Use a No. 2 pencil only.** 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. One question (99) should be answered within the exam booklet itself.**

5. When you are finished with the exam, return both the test booklet and the answer sheet. 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 hours (until 11:30 am)** to complete this exam. Good luck.
Questions 1-10 are True or False. **Darken either T or F on the answer sheet.**

1. (1 point) During agarose gel electrophoresis, DNA migrates toward the negative electrode because of the negative charges on the phosphate backbone.

2. (1 point) As the complexity of the genome increases, the value of $\text{Cot}_{1/2}$ increases.

3. (1 point) Bacteriophage and plasmids both enter into bacteria by the transformation process.

4. (1.5 points) A cDNA library represents the transcripts which are generated in a specific tissue/organ at a particular time.

5. (1 point) PCR (polymerase chain reaction) is a series of reactions whereby double-stranded DNA is denatured, followed by renaturation to specific oligonucleotide primers and synthesis of the intervening nucleotides using a heat-stable polymerase enzyme.

6. (1.5 points) In muscle, dystrophin functions as a bridge linking the extracellular matrix with the cytoskeleton.

7. (1 point) A single bacterium can be infected by many different phage which replicate and eventually lyse the bacterium.

8. (1.5 points) In the human genome, the reassociation kinetics of most genes and transcribed sequences would be found in the intermediate component.

9. (1 point) When “chromosome walking”, it is necessary to know the precise nucleotide sequence of the probe.

10. (1.5 points) To isolate the promoter region of a gene, one would screen a genomic library.

**Questions 11-27 are multiple choice. Unless explicitly stated, there is only one correct answer for each question.**

11. (2 points) The addition of SDS to a protein homogenate allows the separation of proteins during SDS-PAGE based on which one of the following?

   A. purity of the protein preparation  
   B. isoelectric point  
   C. molecular weight  
   D. phosphorylation status
12. (2 points) A Northern blot provides information about which one of the following?

A. the size of the corresponding cDNA
B. the size of the corresponding gene
C. the size of the corresponding unspliced RNA
D. the size of the corresponding protein

13. (2 points) Plasmids are useful as cloning vectors because they

A. may have polylinker cloning sites
B. may encode antibiotic resistance genes
C. act as self-replicating extrachromosomal elements
D. two of the above
E. Answers A, B and C are correct

14. (1 point) Familial hypertrophic cardiomyopathy is associated with mutations in proteins associated with which one of the following?

A. sarcomere
B. sarcolemma
C. nucleus
D. extracellular matrix

15. (2 points) Which of the following fragment(s) would you expect to generate a signal when used as a probe in a genomic Southern blot? Pick the one best answer.

A. promoter sequence fragment
B. exon sequence fragment
C. intron sequence fragment
D. 3’ untranslated sequence fragment
E. two of the above
F. Answers A, B, C and D are correct
G. none of the above

16. (2 points) During dideoxy sequencing, DNA synthesis stops because of which one of the following?

A. a limiting amount of dideoxynucleotides in the reaction mixture
B. a hydroxyl group is missing from incorporated dideoxynucleotides
C. the DNA polymerase I (Klenow fragment) randomly stops chain elongation
D. the radioactive nucleotide induces mutations which disrupt chain elongation
17. (1 point) Dystrophin protein is associated with which one of the following?

A. the sarcolemma
B. the sarcomere
C. patients having muscular dystrophy
D. the neuromuscular junction

18. (2 points) Which one of the following DNA sequences would most likely be a recognition sequence for a type II restriction enzyme?

A. (5’) GAGTAT  (3’)
   CTCATA

B. (5’) CTGNTG  (3’)
   GACNAC

C. (5’) CAGGAC  (3’)
   GTCCTG

D. (5’) CTGCAG  (3’)
   GACGTC

19. (1 point) In constructing a typical cDNA library, which one of the following cloning vectors would you use?

A. plasmids
B. phage
C. cosmids
D. PERTs

20. (1 point) Myotonic dystrophy is caused by which one of the following processes?

A. missense mutations within sarcomeric protein genes
B. missense mutations within a protein kinase gene
C. trinucleotide expansion within a protein kinase gene
D. trinucleotide expansion within sarcomeric protein genes

21. (2 points) A Cot_{1/2} value depends upon all of the following EXCEPT for which one?

A. the DNA sequence
B. the number of the base pairs being analyzed
C. the amount of salt in the solution
D. Answers A, B, and C are correct
E. none of the answers are correct
22. (2 points) Which one of the following terms correctly completes the following analogy?

oligonucleotide is to Southern blot as __________ is to Western blot

A. protein
B. antibody
C. Northern blot
D. DNA

23. (1 point) Restriction enzymes which recognize identical target sequences are called which one of the following?

A. polymerases
B. ligases
C. isoschizomers
D. kinases

24. (2 points) Which single cloning vector would you use to obtain a gene spanning 120 kb in one contiguous piece of DNA? Choose the one best answer.

A. plasmid
B. cosmid
C. bacteriophage
D. YAC

25. (2 points) Which of the following TWO fragments would you expect to detect a hybridizing band when used as a probe in a Northern blot? This question requires TWO answers.

A. promoter sequence fragment
B. exon sequence fragment
C. intron sequence fragment
D. 3’ untranslated sequence fragment

26. (1 point) The principle cause of Duchenne’s muscular dystrophy is which one of the following?

A. the inability of transcription factors to successfully bind to the DMD promoter
B. an expansion of a trinucleotide repeat sequence
C. missense point mutations resulting in changes in amino acid sequence
D. deletions resulting in an absence of protein
27. (2 points) The most likely explanation for detecting multiple bands on a genomic Southern blot is due to which one of the following?

A. the common bands having the same number of G’s and C’s in their DNA
B. the common bands have similar DNA sequence
C. the common bands encode proteins located in the same region of the cell
D. the common bands occurred by random chance

For questions 28-48 choose the ONE best answer.

28. (1 point) Which one of the following statements is FALSE?

A. Collagen contains proline at every third residue.
B. Collagen fiber formation requires prolyl hydroxylase.
C. Collagen formation requires lysyl oxidase.
D. Collagen has triple helical structure.
E. Interchain cross-linking in collagen involves modified lysine residues.

29. (1 point) Under physiological conditions, which one of the following amino acid side-chains can be either positively charged or uncharged, depending on its local environment in the protein?

A. Lysine.
B. Histidine.
C. Arginine.
D. Glutamine.
E. Asparagine.

30. (1 point) Which one of the following statements is CORRECT?

A. The interior of a protein consists almost entirely of nonpolar residues such as leucine, valine, methionine, and phenylalanine.
B. Protein folding is driven by the strong tendency of hydrophilic residues to hydrogen bond with water.
C. Peptide-chain entropy favors the folded state of a protein.
D. Van der Waals interactions are too weak to contribute to the stability of the folded protein.
E. Hydrogen bonding is the driving force for protein folding in water.
31. (1 point) Which one of the following statements about hemoglobin subunit-subunit interactions is FALSE?

A. The T form is stabilized by additional ionic bonds between subunits.
B. The contacts or bonds between the $\alpha_1 \beta_1$ (or $\alpha_2 \beta_2$) subunits are the same in the R and T forms of hemoglobin.
C. The shift from the T to R conformation in hemoglobin will cause bond changes between $\alpha_1 \beta_2$ (or $\alpha_2 \beta_1$) subunits.
D. Hydrogen bonds and hydrophobic interactions stabilize the T but not the R quaternary forms of Hb.
E. Oxygenation of Hb causes a conformational change such that one $\alpha \beta$ dimer ($\alpha_1 \beta_1$) rotates relative to the other.

32. (2 points) Which one of the following statements is CORRECT? The entropy of a reaction refers to:

A. The heat given off by the reaction.
B. The energy of the transition state.
C. The effect of temperature on the rate of the reaction.
D. The tendency of the system to move toward maximal randomness.
E. None of the above.

33. (2 points) Which one of the following is TRUE about the Bohr effect?

A. The Bohr effect refers to the tendency of medical students to sleep during lectures on hemoglobin.
B. The Bohr effect involves the protonation and deprotonation of His 146 in the beta subunit of hemoglobin.
C. Both myoglobin and hemoglobin exhibit the Bohr effect.
D. The Bohr effect refers to the effect of bisphosphoglycerate on the affinity of hemoglobin for oxygen.
E. The Bohr effect is important for the transport of carbon dioxide from the lungs to the peripheral tissues.

34. (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$_2$. 
35. (1 point) Which one of the following statements concerning water is INCORRECT?

A. Water is a substance with a high dielectric constant.
B. Most of the physical properties of water can be attributed to a network of hydrogen bonding.
C. Water itself is dipolar in nature mainly due to the electronegativity of oxygen.
D. There is a large change in hydrogen bonding in the conversion of water to ice.
E. The high heat of vaporization makes water an effective thermal buffer.

36. (1 point) Which one of the following groups of amino acids would be characterized as entirely hydrophobic?

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

37. (1 point) Which one of the following statements concerning hemoglobin is INCORRECT?

A. The valence of iron in normal hemoglobin is +2.
B. The valence of iron in methemoglobin is +3
C. The protoporphyrin ring in hemoglobin is stabilized by noncovalent ionic bonds.
D. In normal hemoglobin there is a coordinate covalent bond to iron by a histidine.
E. The exterior or surface of hemoglobin is characterized by mainly hydrophilic amino acids.

38. (1 point) Which one of the following statements concerning the heme moiety in hemoglobin is INCORRECT?

A. Heme binding to the protein is mediated by hydrophobic interactions.
B. When iron is in its Fe$^{3+}$ valence state, it will bind H$_2$O instead of O$_2$.
C. The proximal histidine forms one of six ligands to the iron.
D. The iron atom is directly in the plane of the protoporphyrin ring when hemoglobin is in the deoxy form.
E. Carbon monoxide binding to the iron atom is reduced due to the presence of a distal histidine.
39. (1 point) Which one of the following statements concerning sickle cell hemoglobin is INCORRECT?

A. Sickle cell formation occurs due to a point mutation in the β-subunit of hemoglobin.
B. Sequence studies have shown that a substitution of Val for Glu in the β-6 position can lead to sickle-cell disease.
C. Substitution of a hydrophobic amino acid for a hydrophilic one creates a new-tetramer-tetramer binding site.
D. Sickle cell formation is favored by the high O₂ found in the lungs.
E. The solubility of the deoxy sickle-cell hemoglobin is significantly less than that of normal oxygenated hemoglobin.

40. (1 point) All of the following statements concerning the conversion of deoxy to oxy hemoglobin are true EXCEPT for which one?

A. This conversion can be described as a taut (T) to relaxed (R) form of the hemoglobin molecule.
B. BPG is sterically excluded from the central binding cavity.
C. Several inter- and intra-ionic bonds are broken in the process.
D. The iron atom moves into the plane of the protoporphyrin IX ring.
E. A tyrosine residue (Tyr 145) forms a hydrogen bond with an asparate (Asp 94).

41. (1 point) In comparing myoglobin to hemoglobin, all of the following statements are correct EXCEPT for which one?

A. Both myoglobin and hemoglobin use the Fe²⁺ of iron to bind oxygen.
B. The amino acid sequence of myoglobin is identical to that of the β-subunits of hemoglobin.
C. Myoglobin lacks cooperative oxygen binding due in part to its lack of quaternary structure.
D. If hemoglobin were entirely removed from the presence of BPG, it would look similar to myoglobin in oxygen binding.
E. The protoporphyrin ring in both myoglobin and hemoglobin is bound non-covalently by hydrophobic interactions.

42. (1 point) High altitude adjustment to oxygen deprivation in hemoglobin is accomplished by all of the following EXCEPT for which one?

A. Increased number of red blood cells in the blood.
B. Increased number of hemoglobin molecules within the red cell.
C. Higher local concentrations of BPG in the tissues.
D. Lower local concentrations of BPG in the lungs.
E. Turning on of the gene which expresses fetal hemoglobin.
43. (1 point) Sickle Cell Anemia persists in populations for which one of the following reasons?

A. The mutation involved is not sufficiently destructive to quaternary structure to be lethal.
B. It confers upon heterozygotes a resistance to malaria infection.
C. The mutation occurs on the surface of the molecule and is therefore not functionally significant.
D. The mutation only affects a small fraction of the hemoglobin even for the homozygote.

44. (1 point) The major structural feature of the collagen molecule is which one of the following?

A. Tandem α-helical and β-subunits.
B. Extended β-pleated sheets wound into a super helix.
C. Three left-handed polyproline helices wound into a right-handed superhelix.
D. Three right-handed α-helices wound into a right-handed superhelix.
E. Three 3_10-helices wound into a right-handed superhelix.

45. (1 point) All of the following amino acids are found in mature collagen EXCEPT for which one?

A. Pro
B. Hyp (hydroxyproline)
C. Gly
D. Hyl (hydroxylysine)
E. Cys

46. (1 point) Prolyl and Lysyl hydroxylase share all of the following cofactors EXCEPT for which one?

A. ascorbic acid
B. Fe^{3+}
C. Molecular oxygen
D. α-ketoglutarate
E. ferrous iron

47. (1 point) A major problem caused by a lack of vitamin C in collagen biosynthesis is which one of the following?

A. Improper folding of collagen subunits.
B. Reduction of stabilizing disulfide bridges to form cysteine.
C. Lack of a pre-pro sequence thus inhibiting membrane transport.
D. Oxidation of iron from Fe^{2+} to Fe^{3+}.
E. Inhibition of the peptidases required for collagen production from procollagen.
48. (2 points) Which one of the following statements concerning collagen is **INCORRECT**?

A. Proline and hydroxyproline can constitute up to one third the number of residues in collagen
B. Proline is incompatible with any type of helix formation
C. Glycine is present at every third amino acid residue
D. Proline is hydroxylated by prolyl hydroxylase
E. Collagen is synthesized as a prepro-protein

For questions 49-52 ONE or MORE of the lettered options is/are correct. On the answer sheet, fill in the circles containing ALL of the correct answers. You will be penalized 0.25 points for each incorrect answer selected, although the lowest possible score on a question will be zero.

49. (2 points) Which of the following properties are common to both \( \alpha \)-helix structure and \( \beta \)-pleated sheet structure?

A. Hydrogen bonds form between main-chain carbonyl and NH groups.
B. Both structures are maintained by hydrogen bonding between amino acid side-chains.
C. The peptide bond in both structures is planar and trans.
D. All twenty amino acids can be found in both structures.

50. (2 points) Which of the following statements is (are) **TRUE** about the pentapeptide Asp-Leu-Arg-Ala-Ser?

A. there are four charged groups at pH=7
B. the carboxyl-terminal residue is Ser
C. the net charge at pH=7 is 0.
D. the net charge at pH=7 is –1.

51. (2 points) Which of the following treatments decrease(s) the oxygen affinity of hemoglobin A \textit{in vitro}?

A. increase in pH from 7.2 to 7.4
B. dissociation of \( \alpha_2-\beta_2 \) into monomer subunits.
C. Decrease in [BPG]
D. Increase pCO\(_2\) from 10 to 40 torrs.
52. (2 points) Which of the following is (are) correct about collagen?

A. The role of the pro sequence of collagen is to initiate triple helix formation.
B. Desmosine is commonly found in collagen.
C. Hydroxylation of lysine is necessary for stability of collagen fibers.
D. Tropocollagen molecules are found in a head-to-tail arrangement with an organized spacing between each molecule.
E. The pre sequence of collagen is necessary to get the newly synthesized collagen across the endoplasmic reticulum.

Questions 53 - 84 have a defined number of answers, as indicated in the questions.

53. (2 points) The current definition of a gene would encompass which one of the following?

A. A complete regulatory/transcriptional unit
B. The segment of DNA between the initiator and stop codons
C. A segment of DNA greater than 1 kilobase in length
D. The segment of DNA corresponding exactly to the mRNA, tRNA or rRNA
E. Any segment of DNA encoding a polypeptide

54. (1 point) In DNA, the bond between the deoxyribose sugar and the phosphate is which one of the following?

A. a polar bond
B. an ionic bond
C. a hydrogen bond
D. a covalent bond
E. a van der Waals bond

55. (1 point) How many double stranded DNA molecules 8 base pairs long are theoretically possible? Choose the one best answer.

A. 32
B. 12
C. 65,536
D. 64
E. 256

56. (1 point) The backbone of a DNA strand is composed of which one of the following?

A. sugars and bases
B. phosphates and sugars
C. bases and phosphates
D. nucleotides and sugars
E. phosphates and nucleosides
57. (1 point) If a 1000 kilobase fragment of DNA has 10 evenly spaced and symmetrical replication origins and DNA polymerase moves at 1 kilobase per second, how many seconds will it take to produce two daughter molecules (ignore potential problems at the telomeres)? There is only one answer to this question.

A. 100  
B. 20  
C. 30  
D. 40  
E. 50  

58. (2 points) You are studying the replication of a virus. After isolating the genome of purified virus, an analysis of the nucleotide content gave the following result. A= 32%, T= 32%, C= 20%, G=16%. Which one of the following statements would be consistent with this result?

A. The genome is made of RNA  
B. The genome is a circular double stranded DNA molecule  
C. You made a mistake in your calculations  
D. The genome is single stranded DNA  
E. None of the above  

59. (1 point) Primase is not required during DNA repair processes because of which one of the following?

A. All of the primase is associated with replication origins  
B. RNA would be highly mutagenic at a repair site  
C. DNA polymerase can use any 3' -OH end for elongation  
D. DNA polymerase I does not require a primer  
E. All of the above  

60. (2 points) The concept of genetic complementation is best described by which one of the following statements?

A. The ability of one strand of DNA to recognize its partner  
B. The inheritance of a mutant copy of a gene from one generation to the next  
C. The repairing of a mistake in the genetic code during replication  
D. The ability of a functioning copy of a gene to rescue a cellular defect caused by a mutant copy of that gene  
E. The ability of the products of two different genes to form a functioning complex
Questions 61 - 70 are TRUE/FALSE Questions (1 point each). Answer by darkening either T or F on the answer sheet.

61. Bacteria and other organisms that grow in hot springs or thermal vents would be expected to have a high percentage of A/T base pairs in their genomic DNA.

62. DNA polymerase I is the primary replication enzyme in bacteria

63. Semi-conservative replication implies a pair of daughter DNA molecules is produced, each one of which contains one parental DNA strand and one newly synthesized strand

64. DNA ligase is always required during either DNA replication or DNA repair processes

65. Proofreading requires the movement of RNA polymerase in the 3' to 5' direction

66. Reverse transcriptase is error-prone because it is an RNA polymerase

67. A nonsense mutation is a specific kind of missense mutation

68. All codon-anticodon interactions involve a wobble component

69. Without the sigma factor RNA polymerase is unable to transcribe DNA

70. Translation of ribosomal RNA gives a peptidyl transferase enzyme

71. (2 points) Consider the following segment of DNA from within the protein coding portion of a gene

\[ 5' \text{ GGAACTCTAGGGGCTG } 3' \]
\[ 3' \text{ CCTTGAGATCCCCGAC } 5' \]

Which one of the following statements is true?

A. Either strand could be the transcribed strand
B. The lower strand must be the transcribed strand
C. The upper strand must be the transcribed strand
D. Both could be transcribed simultaneously
E. Neither can be transcribed because both contain stop codons
72. (2 points) In chromosomal DNA, which one of the following statements is true?
   A. The RNAs of all genes are synthesized 5' to 3' off the same DNA strand
   B. The RNAs of all genes are synthesized 3' to 5' off the same DNA strand
   C. RNAs of different genes can be synthesized off different strands, but always 5' to 3'
   D. RNAs of different genes can be synthesized off different strands, but always 3' to 5'
   E. Different genes can be synthesized off either strand, some 3' to 5', and some 5' to 3'

73. (1 point) In the read-out of the genetic code in prokaryotes, which one of the following processes acts before any of the others?
   A. tRNA alignment with mRNA
   B. termination of transcription
   C. movement of the ribosome from one codon to the next
   D. recruitment of termination factors to the A site
   E. export of mRNA from the nucleus

74. (1 point) Choose the one best answer: In the translation of the lac structural genes ribosomes come off the mRNA:
   A. After the β-galactosidase and transacetylase genes only
   B. Only at the end of the operon
   C. After every protein coding cistron
   D. At the operator
   E. Only when there is a mutation

75. (1 point) A null repressor mutation (I) results in which one of the following?
   A. Constitutive transcription
   B. Inducible transcription
   C. Transcription but no translation
   D. No translation
   E. No transcription

76. (1 point) A promoter mutation (P) results in which one of the following?
   A. Constitutive transcription
   B. Inducible transcription
   C. Transcription but no translation
   D. No translation
   E. No transcription
77. (2 points) Which one of the following is not involved in transcription initiation of eukaryotic genes?
   A. TATA binding protein
   B. RNA polymerase II
   C. Enhancer sequences
   D. Cap binding protein
   E. ATP

78. (2 points) During mutagenic exposure to nitrous acid an adenine base in DNA deaminates to form a base that hydrogen bonds like guanine. Which TWO of the following statements are true?
   A. The altered base is identical to the one found in the nucleoside inosine
   B. The new base now has a keto group at the C-2 position
   C. The mutational event after replication would be A-T to T-A
   D. The mutational event after replication would be A-T to C-G
   E. The mutational event after replication would be A-T to G-C
   F. The new base can now take part in wobble base pairing

79. (2 points) You are studying the molecular biology of the hormone receptor class of transcription factor. These proteins consist of two connected, but independent, domains, one of which can bind to the hormone in question, while the other binds to the regulatory sequences of the gene to be induced (but only after hormone has caused a conformational change in the protein). If a gene was constructed in which the DNA-binding domain of the thyroid hormone receptor was replaced by the DNA binding domain of the estrogen receptor, and then introduced into cells, which one of the following would you anticipate to occur?
   A. The introduced receptor would respond to thyroid hormone, and activate thyroid hormone-responsive genes
   B. The introduced receptor would respond to estrogen, and activate estrogen-responsive genes
   C. The introduced receptor would respond to estrogen, and activate thyroid hormone-responsive genes
   D. The introduced receptor would respond to thyroid hormone, and activate estrogen-responsive genes.
   E. All of the above
80. (2 points) tRNA charged with cysteine can be chemically treated so that the amino acid changes its identity to alanine. If some of this charged tRNA is added to a protein synthesizing extract that contains ALL the normal components required for translation which ONE of the following statements represents THE MOST LIKELY OUTCOME after adding a mRNA that has both cys and ala codons in the normal reading frame?

A. Cysteine would be added each time the alanine codon was translated  
B. Alanine would be added each time the cysteine codon was translated  
C. The protein would have a deficiency of cysteine residues  
D. The protein would have a deficiency of alanine residues  
E. The protein would be entirely normal

81. (1 point) Choose the one best answer: Synthesis of translatable mRNA:

A. in eukaryotes involves more enzymes than in prokaryotes.  
B. starts at the same initiation codons used during protein synthesis.  
C. in prokaryotes involves a different RNA polymerase than is used for tRNA synthesis.  
D. stops at the same termination codons used during protein synthesis.  
E. Both B and D are true.

82. (1 point) Which ONE of the following is true concerning the structure of tRNA?

A. Many chemically modified bases are found at the 3’ end of the molecule  
B. Base pairs containing G-U are often encountered  
C. The anticodon loop is near the amino acid binding site. 
D. It is a linear structure with no H-bonding between bases.  
E. Contains a CCA sequence at its 5’ end.

83. (1 point) All of the following statements about the beta-like globin genes are correct EXCEPT for which one?

A. There are two closely related fetal globin genes.  
B. Synthesis of delta globin occurs only during the first trimester of pregnancy.  
C. The genes are arranged 5’-->3’ along the chromosome in the order that they are expressed during development.  
D. The embryonic globin genes are expressed very soon after fertilization of the egg.  
E. They all contain three exons and two introns.

84. (2 points) In the gene for a protein containing 300 amino acids, which one of the following mutations would be the LEAST LIKELY to result in a faulty protein?

A. Insertion of a single base in the codon for amino acid 12.  
B. Deletion of two bases from the codon for amino acid 19.  
C. A nonsense mutation in the codon for amino acid 37.  
D. A single base change such that amino acid 12 is now leucine rather than isoleucine.  
E. A single base change such that glutamic acid at position 205 is changed to lysine.
For questions 85 - 92 (2 points each) use the list provided on the right column (A through T) for the answers. Please select the most appropriate answer(s) from the list for each question. A question may have more than one correct answer, and an answer may be used more than once. No question will have more than three correct answers, if that many. You will be penalized one-half point for each incorrect answer listed, although the lowest value for any question will be zero.

85. Sequence at the 5' end of an exon
   A. Splice acceptor site
   B. Splice donor site
   C. Intron-exon junction
   D. GU

86. Sequence near (not at) the 3' end of an intron
   A. Splice acceptor site
   B. Splice donor site
   C. Intron-exon junction
   D. GU

87. Catalytic component of the splicing machinery
   A. Splice acceptor site
   B. Splice donor site
   C. Intron-exon junction
   D. GU

88. Linkages present on adenosine at the lariat 3′ way junction
   A. AU
   B. GU
   C. AG

89. Trans acting components whose presence is required for efficient splicing
   A. Cap binding protein
   B. Poly A binding protein
   C. snRNP
   D. Spliceosome

90. Cis acting components at the splice acceptor site and the splice donor site
   A. Splice acceptor site
   B. Splice donor site
   C. Intron-exon junction
   D. GU

91. A large particle consisting of numerous RNA and protein species
   A. Splice acceptor site
   B. Splice donor site
   C. Intron-exon junction
   D. GU

92. Result of a cryptic splice acceptor occurring in an intron
   A. Splice acceptor site
   B. Splice donor site
   C. Intron-exon junction
   D. GU

Questions 93-98 have one or more correct answers. Indicate all correct answers on the answer sheet. You will be penalized one-half point for each incorrect answer selected, although the lowest score awarded per question is zero.

93. (2 points) An apparently healthy patient presented with no detectable β-globin mRNA in her circulating red blood cells, yet analysis of her DNA showed the β-globin gene to be present and its sequence to be normal. Which of the following statements would be consistent with these observations?

   A. She could have deletional HPFH
   B. The far upstream "locus activation region" could have been deleted.
   C. β-globin gene-proximal sequences could be mutated
   D. She could have non-deletional HPFH
   E. There is a problem with only one of her two chromosome 16's.
   F. The γ-globin genes could be responding to the wrong enhancer
94. (2 points) The c-myc gene is a human proto-oncogene that contains three exons and two introns - interestingly the first exon contains no information that is encoded in the final protein. A single nucleotide mutation within the c-myc gene led to a change in the splicing pattern of the RNA produced. Which of the following results could NOT be a possible outcome from such a change?

A. There is no alteration in the resulting protein
B. The reading frame of the resulting message is altered from beginning to end
C. The reading frame of the resulting message is altered up until the aberrant splice is encountered
D. Both the normal protein and an aberrant protein are produced in similar amounts
E. No protein product of any kind is found
F. The reading frame of the resulting message is altered beyond the aberrant splice site
G. The capping reaction would fail
H. An aberrant protein is produced that is smaller than the normal protein
I. An aberrant protein is produced that is larger than the normal protein

95. (2 points) Frequently observed features in specific DNA-protein interactions (e.g. those that occur at regulatory elements) include:

A. The insertion of amino acid side chains between the stacked base pairs of the DNA helix
B. The interaction of \( \alpha \)-helical regions of protein with DNA through the major groove
C. The disruption of DNA base pair hydrogen bonds in favor of amino acid side chain-base hydrogen bonds
D. The interaction of \( \alpha \)-helical regions of protein with DNA through the minor groove
E. Metal ion-dependent unwinding of the minor groove
F. The presence of protein heterodimers at certain sequences

96. (2 points) In the lac operon, which regions do not code for protein?

A. Z and Y
B. O and Z
C. P and O
D. P and Z
E. O and Z
97. (2 points) In double stranded DNA which of the following statements is true?

A. \( A+G=T+C \)
B. \( T=G \)
C. \( G=C \)
D. \( A+C=G+T \)
E. \( G+C=A+T \)
F. \( A=G \) and \( C=T \)
G. \( A+T=G+C \)

98. (2 points) Which of the following is/are a component of DNA? Indicate all correct answers on the answer sheet.

A. Arginine
B. Alanine
C. Adenine
D. Asparagine
E. Cysteine
F. Cytosine
G. Guanidinium
H. Thiamine
I. Thymine

The essay question is on the next page.
99. (8 points) Describe, in terms of the molecular structure of hemoglobin, why oxygen binding to hemoglobin is cooperative. Limit your answer to this page only and write very clearly for full credit. An outline form for the answer may be used.

1. O₂ binds to heme FE
2. Fe moves into plane of porphyrin ring pulling on helix F via coordinate covalent bond with HIS-92
3. Hydrogen bond between Tyr-145 in helix H and backbone carbonyl of Val-98 broken by movement by helix F
4. Ionic bond between His-146 imidazole and carboxyl of Asp-94 broken by movement of helix F
5. Breaking carbonyl of His-146 on β-subunit and Lys amino group on side-chain from α-subunit tells α-subunit that β-subunit has bound molecular O₂.
1. F 31. D or B 61. F 91. H, L
3. F 33. B 63. T 93. C, D, F
4. T 34. C 64. T 94. C, G
5. T 35. D 65. F 95. B, F
10. T 40. E 70. F
11. C 41. B 71. A
12. A 42. E 72. C
13. E 43. B 73. A
15. F 45. E 75. A
17. A 47. D 77. D
21. E 51. D 81. A
22. B 52. A, C, D, E 82. B
24. D 54. D 84. D
25. B, D 55. C 85. DELETE
26. D 56. B 86. Q
27. B 57. E 87. K, L
30. A 60. D 90. D, F