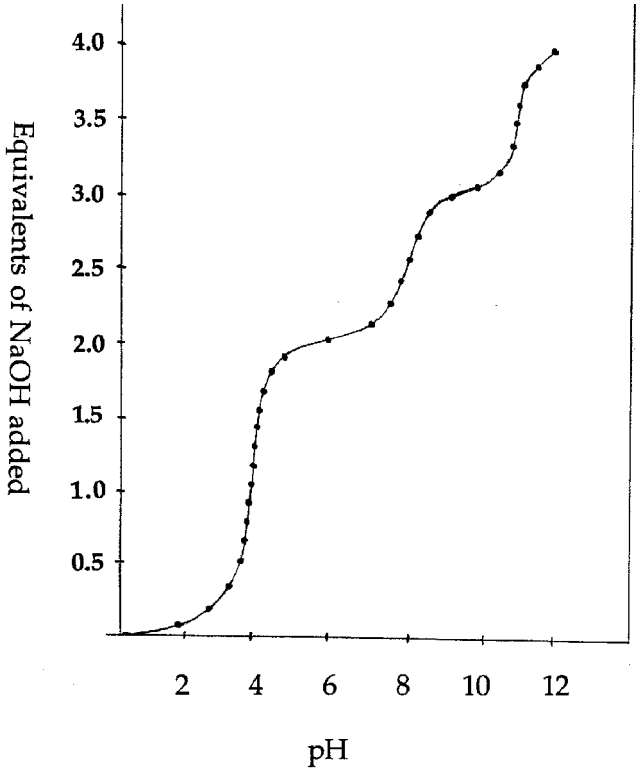
The following table may be used in answering some of the questions.

Functional Group	pK' (or range)
alpha-carboxyl in a free amino acid	1.8 to 2.4
alpha-carboxyl in a peptide	4.0
alpha-amino group in a free amino acid	9.0 to 10.8
alpha-amino group in a peptide	8.0
beta-carboxyl group of aspartate	3.9
gamma-carboxyl group of glutamate	4.3
ring nitrogen of histidine	6.0
sulfhydryl of cysteine	8.3
phenolic hydroxyl of tyrosine	10.9
epsilon-amino group of lysine	10.8
guanidino-group of arginine	12.5

Choose the single best answer for the following questions.

1. Identify the dipeptide that would provide the titration curve shown below



A. YN

B. DS

C. KH

D. QY

E. KD

2. The maximal concentration of the isoelectric form of isoleucyl-lysyl-arginine will occur at a pH value of

A. 6.0

B. 8.0

C. 9.4

D. 10.8

E. 11.65

3. On the basis of your understanding of the properties of the individual amino acids found in proteins, such as their charge, polarity and steric bulk, which of the following mutations is likely to be the most disruptive of the tertiary structure of the protein in which it occurs? (Acknowledging that any change might be disruptive depending on where it occurs)

A. A glu replaces an asp

B. An asn replaces a gln

C. A lys replaces an ile

D. A leu replaces a val

E. A ser replaces a thr

4. The following type of amino acid residue in proteins is formed by a posttranslational modification

A. Tryptophanyl

B. Prolyl

C. Glutaminyl

D. Hydroxyprolyl

E. Ornithinyl

5. Which statement concerning the 27-residue peptide shown below is true?

ANELE - GANTN - EWTHE - MEHAS - EMERG - ED

A. If the molecule were subjected to three cycles of Edman degradation, a residue each of alanine, glutamine and aspartic acid would be released

B. Exhaustive digestion with trypsin will produce three peptides

C. Residue 20 is a serine

D. The C-terminal residue is glutamic acid

E. None of the above statements is true

Choose the single best answer for the following questions.

6. Which statement concerning the properties of a right-handed alpha helix is true?

A. Proline residues are frequently seen in the C-terminal half of the structure

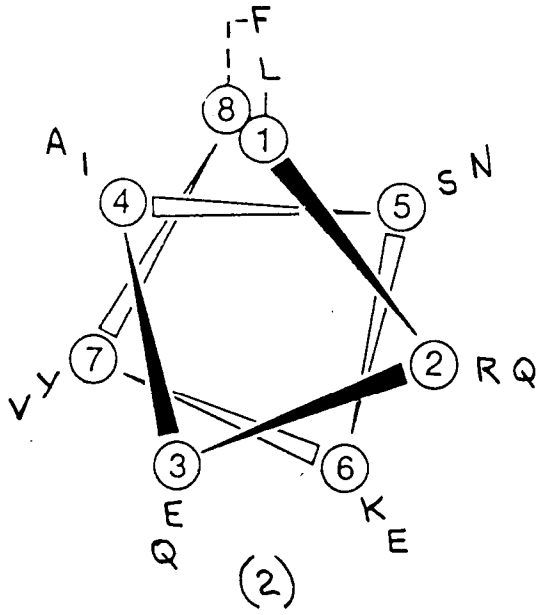
B. The structure will be disrupted by exposure to sodium dodecylsulfate

C. There is a translation along the axis of the helix of 3.5 Angstroms per residue

D. The macrodipole generated by the helix results in a positive potential at the C-terminal end of the structure

E. None of the above statements is true

7. The amphipathic nature of the helix depicted below would be reduced if residue 4 were replaced by



A. W

B. Q

C. L

D. F

E. None of the above replacements would reduce the amphipathic nature of the helix

8. A mixture of four proteins, A, B, C, and D is subjected to fractionation on a preparative scale by ion-exchange chromatography on a column containing a cation exchanger. The pI values of the four proteins are 7.1, 6.4, 7.3, and 5.2, respectively. The application of a pH gradient from pH 4.0 to pH 7.5 should result in the elution of the proteins in the following order:

A. D, then B, then A, then C

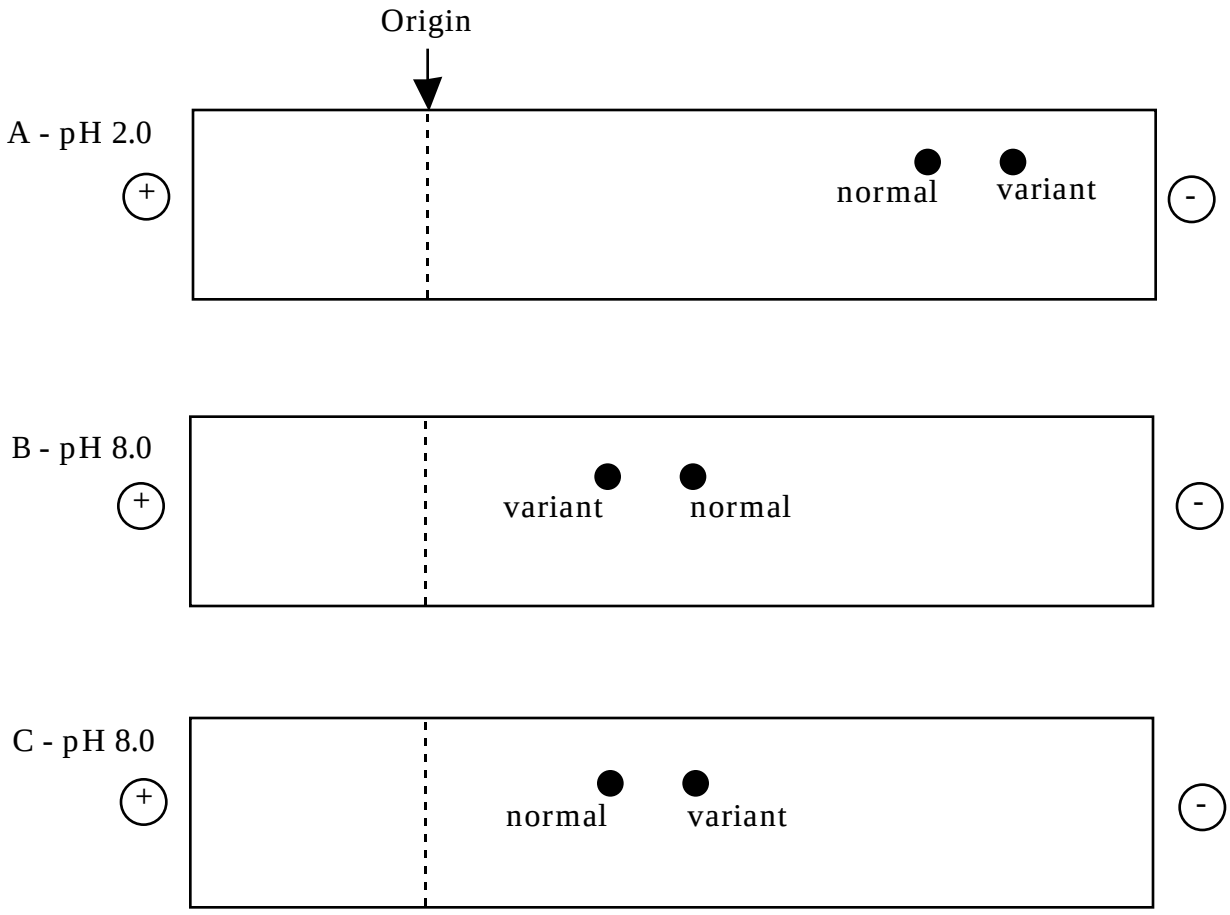
B. A, then C, then D, then B

C. C, then A, then B, then D

D. C, then A, then D, then B

E. D, then B, then C, then A

9. In an electrophoretically detectable variant of Hb F, a lysine was found to have replaced an isoleucine residue at position 92 in the gamma chain. Which of the patterns shown below would be predicted for electrophoretic experiments at the indicated pH values for the gamma chains of normal Hb F and of the variant?



A. Pattern "A" only

B. Pattern "B" only

C. Pattern "C" only

D. Both patterns "A" and "B"

E. Both patterns "A" and "C"

10. Myoglobin differs from hemoglobin in the following ways

A. The iron atom (or atoms) remain in the ferrous (+2) state in the presence of oxygen

B. Carbon monoxide binds less tightly than it does to a simple heme molecule

C. It utilizes an iron-protoporphyrin IX complex as a prosthetic group

D. It binds oxygen reversibly

E. Myoglobin does not differ from hemoglobin in any of the above ways

11. In the normal course of human development, this hemoglobin will <u>not</u> be seen

A. $Zeta_2epsilon_2$

B. $Alpha_2epsilon_2$

C. $Zeta_2delta_2$

D. $Alpha_2delta_2$

E. $Zeta_2gamma_2$

Choose the single best answer for the following questions.

12. Hemoglobin F differs from hemoglobin A in the following way:

A. One of its subunits comes from chromosome 11 and the other comes from chromosome 16

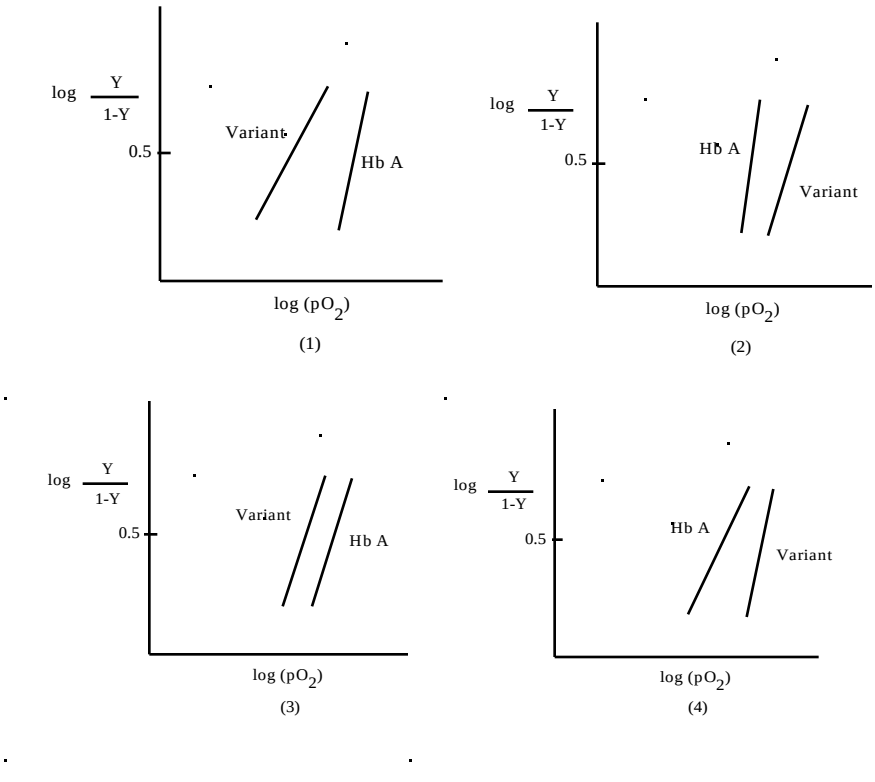
B. Its Hill coefficient is greater than one

C. Under normal physiological conditions it has a higher oxygen affinity than hemoglobin A

D. It has a higher affinity for BPG than does hemoglobin A

E. Hemoglobin F does not differ from hemoglobin A in any of the above ways

13. A variant of hemoglobin A was found to have an increased oxygen affinity and a reduced cooperativity with respect to normal hemoglobin A. Which Hill plot corresponds to this situation?



A. (1)

B. (2)

C. (3)

D. (4)

14. Amino acid analysis of the alpha chain of a variant hemoglobin has revealed that one of its seven phenylalanine residues has been replaced by a tyrosine. To determine where along the chain this replacement has occurred, a sample of the variant chain was digested with trypsin and the resulting mixture of peptides was fractionated by HPLC. A peptide seen in the variant, but not found in a tryptic digest of the normal alpha chain, was composed of 1 asp, 1 asn, 1 pro, 2 val, 1 tyr, and 1 lys. Using the amino acid sequence of the alpha chain of <u>normal</u> hemoglobin given below, determine the location of the phenylalanine to tyrosine replacement.

					5					10				15
1	VAL	LEU	SER	PRO	ALA	ASP	LYS	THR	ASN	VAL	LYS	ALA	ALA	TRP	GLY
16	LYS	VAL	GLY	ALA	HIS	ALA	GLY	GLU	TYR	GLY	ALA	GLU	ALA	LEU	GLU
31	ARG	MET	PHE	LEU	SER	PHE	PRO	THR	THR	LYS	THR	TYR	PHE	PRO	HIS
46	PHE	ASP	LEU	SER	HIS	GLY	SER	ALA	GLN	VAL	LYS	GLY	HIS	GLY	LEU
61	LYS	VAL	ALA	ASP	ALA	LEU	THR	ASN	ALA	VAL	ALA	HIS	VAL	ASP	ASP
76	MET	PRO	ASN	ALA	LEU	SER	ALA	LEU	SER	ASP	LEU	HIS	ALA	HIS	LYS
91	LEU	ARG	VAL	ASP	PRO	VAL	ASN	PHE	LYS	LEU	LEU	SER	HIS	CYS	LEU
106	LEU	VAL	THR	LEU	ALA	ALA	HIS	LEU	PRO	ALA	GLU	PHE	THR	PRO	ALA
121	VAL	HIS	ALA	SER	LEU	ASP	LYS	PHE	LEU	ALA	SER	VAL	SER	THR	VAL
136	LEU	THR	SER	LYS	TYR	ARG									

A. Tyrosine has replaced phe-33

B. Tyrosine has replaced phe-36

C. Tyrosine has replaced either phe-33 or phe-36

D. Tyrosine has replaced phe-98

E. Tyrosine has replaced phe-128

15. A small sleep-inducing peptide was found to have the following primary structure:

N-acetyl-asparginyl-glycyl-tyrosyl-valyl-leucyl-glutamyl-lysyl-tryptophanylamide

Assuming that the pK values of the side chains in this peptide are the same as those found in the corresponding amino acids, what is the pH of a 2 mM solution of this peptide if there are ten molecules of peptide with the gamma carboxyl of the glutamyl residue protonated for every molecule of peptide with the gamma carboxyl unprotonated?

A. 3.3

B. 3.9

C. 4.1

D. 4.3

E. 5.3

16. Which set of conditions guarantees that the standard free energy change as determined by the Gibbs equation below MUST be positive?

$\Delta G = \Delta H - T\Delta S$.

A. ΔH is positive and ΔS is negative

B. ΔH is negative and ΔS is negative

C. ΔH is positive and ΔS positive

D. ΔH is negative and ΔS is positive

E. none of the above

Choose the single best answer for the following questions.

17. A mixture of pyruvate and NADH in a buffered solution at pH 7.0 is treated with lactate dehydrogenase and allowed to attain equilibrium.

pyruvate + $NAD_{reduced}$ <-> lactate + NAD_{oxid}

A portion of this solution is removed and diluted 10-fold in the same buffer. What does the equation below predict about the composition of the dilute solution with respect to the original equilibrium mixture?

$\Delta G = \Delta G^0 + RT \ln ([lactate][NAD_{oxid}] / [pyruvate][NAD_{reduced}])$

A. the dilute solution will also be at equilibrium

B. the dilute solution will come to a new equilibrium by converting lactate and NAD_{oxid} into pyruvate and $NAD_{reduced}$

C. the dilute solution will come to a new equilibrium by converting NADreduced and pyruvate into NAD_{oxid} and lactate

D. no conclusions can be drawn from the equation about the composition of the dilute mixture with respect to the original equilibrium mixture

E. none of the above

18. Which statement is correct about the energetics of fatty acid activation by the following process?

fatty acid + ATP = fatty acyl-AMP + pyrophosphate (1)

pyrophosphate + H_2O = 2 phosphate (2)A. reaction (1) is irreversible and reaction (2) is reversible

B. reaction (1) is reversible and reaction (2) is irreversible

C. both reactions are irreversible

D. both reactions are readily reversible

E. reaction (2) is catalyzed by a ligase

19. Which statement about NAD is INCORRECT?A. it is a dinucleotide

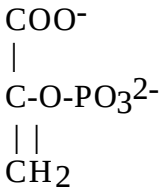
B. a dietary insufficiency of niacin can lead to impairment of NAD biosynthesis and cause pellagra

C. it is a substrate for many enzymes that catalyze oxidation-reduction reactions

D. it contains a pyridine ring system

E. it participates in 1-electron transfers

20. All of the following are true for the compound shown below EXCEPT



A. it is formed from its precursor by the splitting out of H_2O

B. the phosphoryl group can be transferred to ADP

C. the $\Delta G^{0'}$ for hydrolysis is about -14 kcal/mol

D. it is a precursor of pyruvate

E. a glycolytic enzyme hydrolyzes it to pyruvate and phosphate

Choose the single best answer for the following questions.

21. A deficiency of which glycolytic enzyme in red blood cells could lead to hemolytic anemia?

A. hexokinase

B. glyceraldehyde 3-phosphate dehydrogenase

C. pyruvate kinase

D. lactate dehydrogenase

E. any one of the above

22. Galactosemia is a serious inborn error resulting from an inability to metabolize galactose normally. How does galactose differ from glucose?

A. it is a disaccharide

B. it is the α-anomer of glucose

C. it is 2-deoxy glucose

D. it is the 4-epimer of glucose

E. it is a pentose not a hexose

23. Which glycolytic enzyme catalyzes a reaction that is essentially irreversible?

A. aldolase

B. phosphoglucose isomerase

C. glyceraldehyde 3-phosphate dehydrogenase

D. enolase

E. pyruvate kinase

24. The oxidation of pyruvate by pyruvate dehydrogenase requires coenzymes derived from all of the listed vitamins EXCEPT

A. niacin

B. thiamine

C. ascorbate

D. pantothenate

E. riboflavin

25. All of the following are correct regarding pyruvate dehydrogenase EXCEPT

A. it is inhibited by acetyl CoA and NADH

B. it is located in the mitochondrial outer membrane

C. it contains covalently-bound lipoate which acts as an acyl carrier and as an oxidant-reductant

D. it catalyzes an essentially irreversible reaction

E. it is inhibited by phosphorylation when energy-rich signals are high

26.
The first reported genetic disorder of the TCA cycle was recently described for two individuals with fumarase deficiency. What reaction does fumarase catalyze?

A. the formation of malate

B. the formation of oxaloacetate

C. the formation of isocitrate

D. the hydrolysis of citryl CoA

E. the formation of succinate

27.
It is reported that one of the commonest causes of lactic acidosis in infants is a defect in the E1 subunit of the pyruvate dehydrogenase complex. What reaction does this subunit catalyze?

A. the formation of acetyl lipoamide

B. the oxidation of reduced flavoprotein by NAD^+

C. the formation of hydroxyethyl thiamine pyrophosphate

D. the reoxidation of reduced lipoate by a flavoprotein

E. none of the above

28.
Glucagon is involved in all of the following EXCEPT

A. opposing the effect of insulin

B. triggering a phosphorylation cascade that affects many cytoplasmic proteins

C. turning off hepatic pyruvate kinase activity

D. shutting off hepatic glycolysis

E. elevating the hepatic levels of fructose 2,6-bisphosphate

29.
Glucose toxicity

A. has been attributed to the ability of glucose to modify proteins covalently

B. is likely to be enhanced in individuals with hyperglycemia

C. is implicated in damage to blood vessels and nerves

D. is implicated as a cause of circulatory disorders in diabetes

E. all of the above

30.
The protein of the pancreatic β-cells that is believed to sense a rise in blood glucose and set in motion events leading to insulin release is

A. gluconin

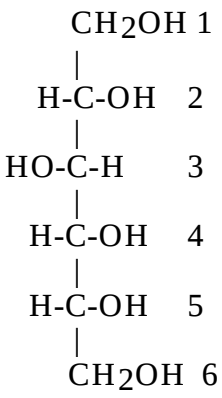
B. blood insulin release protein (BIRP)

C. hexokinase

D. glucokinase

E. phosphofructokinase

31.
The sugar D-sorbitol (shown below) is sometimes used as a substitute for glucose. The first step in its metabolism is its conversion into fructose (which can subsequently enter the glycolytic pathway). A 2-electron oxidation at which carbon would produce fructose from sorbitol?



D-sorbitol

A. 1

B. 2

C. 3

D. 4

E. none of the above

32. An enzyme has a K_M of 0.1 mM and a V_{MAX} of 100 units per mg protein. What is the velocity of the enzyme-catalyzed reaction when the substrate concentration is equal to 0.1 mM?

A. 0.1 units / mg protein

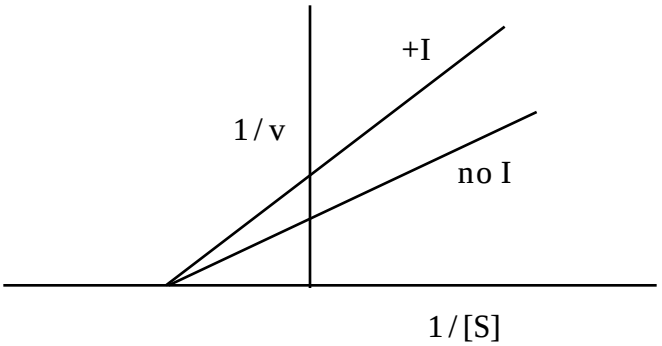
B. 10 units / mg protein

C. 25 units / mg protein

D. 50 units / mg protein

E. 100 units / mg protein

33. The following plot shows the activity of an enzyme in the absence (no I) and presence (+I) of an inhibitor that binds reversibly to the enzyme. Which statement is correct?



A. The inhibitor can bind to the enzyme-substrate complex

B. The inhibition can be overcome by the addition of more substrate

C. V_{MAX} can be attained eventually in the presence of the inhibitor

D. The inhibitor must look like the substrate to inhibit the enzyme

E. The K_M for the enzyme is increased in the presence of the inhibitor

34. The following statements refer to the relationship between the substrate concentration [S] and the K_M for an enzyme. Which statement is correct?

A. At [S] > K_M, initial velocity increases linearly with increasing [S]

B. At [S] < K_M, initial velocity is independent of [S]

C. When [S] = K_M, the enzyme is operating at maximal velocity

D. At [S] < K_M, an enzyme can be saturated with substrate provided that the [S] is in molar excess over the [E]

E. None of the above

35. Which of the following amino acids would least likely participate as either a proton donor or as a proton acceptor during catalysis?

A. Cysteine

B. Asparagine

C. Serine

D. Histidine

E. Tyrosine

36. Velocity measurements are made over a range of substrate concentration in the absence and in the presence of an inhibitor that binds covalently at the active site of an enzyme. The data are analyzed using a double reciprocal plot. With respect to this analysis, which of the following statements is correct?

A. The K_M for the enzyme is increased in the presence of the inhibitor

B. The numerical value of the Y intercept is larger for the slope determined in the presence of the inhibitor

C. V_{MAX} is reduced in the presence of the inhibitor

D. Statements A and B are correct

E. Statements B and C are correct

37. With respect to the active sites of enzymes, which of the following statements is true?

A. The active site amino acids, which participate in catalyzing the reaction, are always immediately adjacent to each other in the protein primary sequence

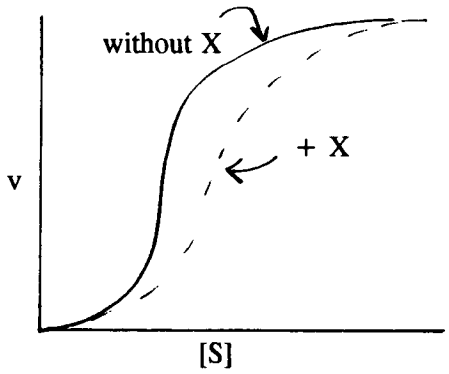
B. Active site amino acids never react covalently with reaction intermediates during the course of catalysis

C. A substrate and a cofactor can both be bound in the active site at the same time

D. The binding of substrate cannot influence the conformation of an enzyme active site

E. Inducing substrate strain in the active site always leads to a decrease in the rate of a chemical reaction

38. From the plot of initial velocity versus substrate concentration shown below, which of the following statements is correct?



A. There is positive cooperativity in substrate binding

B. Compound X increases the enzyme affinity for substrate

C. Compound X must resemble the structure of the substrate to exert its effect

D. X decreases V_{MAX}

E. None of the above statements are correct

In each group, for each numbered question select the best lettered answer. Each lettered answer may be selected once, more than once, or not at all.

39. Possess the smallest and the largest of the side chains of the common amino acids

40. The side chains of both of these amino acids have hydrogen bonding capacity

41. Both side chains contain aromatic rings

42. Both side chains carry a negative charge at physiological pH values

A. P and Y

B. A and W

C. F and Y

D. C and I

E. G and F

F. G and Y

G. E and D

H. M and F

I. Q and L

J. G and W

In each group, for each numbered question select the best lettered answer. Each lettered answer may be selected once, more than once, or not at all.

43. Binds to hemoglobin, but not myoglobin

44. An increased concentration of CO_2 will decrease the affinity of hemoglobin for this substance

A. Protons (H^+)

B. 1, 3-bisphosphoglycerate (BPG)

C. Oxygen (O_2)

D. Proximal histidine F8

E. Fe-protoporphyrin IX (heme)

45. A normal, if minor, form of adult human hemoglobin

46. A hemoglobin variant in which the replacement of a phe by a ser in the beta chain weakens heme binding

A. Hb M Iwate

B. Hb Bart's

C. Hb A_2

D. Hb Portland

E. Hb Hammersmith

In each group, for each numbered question select the best lettered answer. Each lettered answer may be selected once, more than once, or not at all.

47. A coenzyme used in the activation of carboxyl groups48. A coenzyme derived from pantothenate

A. thiamine pyrophosphate

B. nicotinamide adenine dinucleotide phosphate

C. thorazine

D. coenzyme A

E. lipoate

F. flavin mononucleotide

49. A glycolytic enzyme that uses phosphate as a substrate50. A glycolytic enzyme that releases water as a product

A. enolase

B. hexokinase

C. pyruvate kinase

D. glyceraldehyde 3-phosphate dehydrogenase

E. triosephosphate isomerase

F. aldolase

G. phosphofructokinase

In each group, for each numbered question select the best lettered answer. Each lettered answer may be selected once, more than once, or not at all.

51. A TCA enzyme that uses phosphate as a substrate

52. A TCA enzyme that adds water across a double bond

A. citrate synthase

B. isocitrate dehydrogenase

C. α-ketoglutarate dehydrogenase

D. succinate thiokinase

E. succinate dehydrogenase

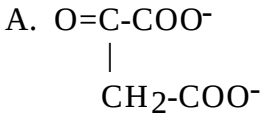
F. fumarase

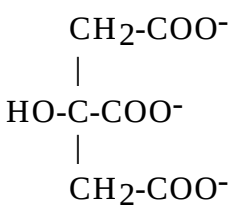
G. malate dehydrogenase

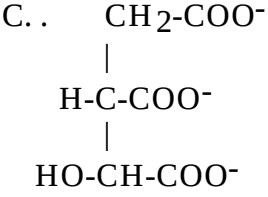
In each group, for each numbered question select the best lettered answer. Each lettered answer may be selected once, more than once, or not at all.

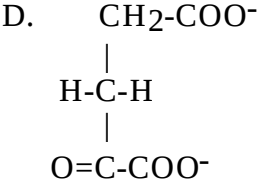
53. A compound that might logically be expected to be elevated in the blood or urine of an individual who had a deficiency in aconitase

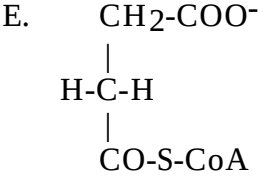
54. A compound that requires a flavoprotein for its further oxidation

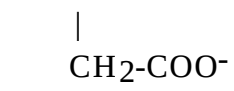
A.


B.


C. .


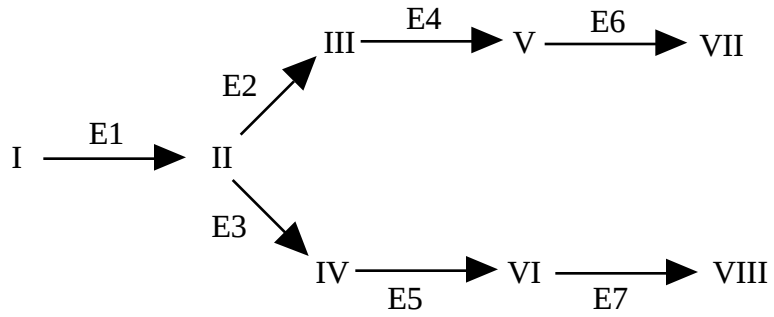
D.


E.


F.


A branched metabolic pathway is shown below in which the Roman numerals indicate the metabolites formed at each step in the pathway. The enzymes that catalyze each of the steps are indicated (E1-7).

In each group, for each numbered question select the best lettered answer. Each lettered answer may be selected once, more than once, or not at all.



Choose from the following scenarios (A-E) to answer the following two questions

55. Which scenario is an example of product inhibition in this pathway?56. Which scenario would lead to a decrease in the production of both metabolites VII and VIII?

A. Metabolite VII inhibits enzyme E1

B. Metabolite VIII inhibits enzyme E5

C. Metabolite VII inhibits enzyme E6

D. Metabolite VII inhibits enzyme E2

E. Metabolite VIII inhibits enzyme E3