

MOLECULAR BIOLOGY OF THE CELL, SIXTH EDITION

CHAPTER 3: PROTEINS

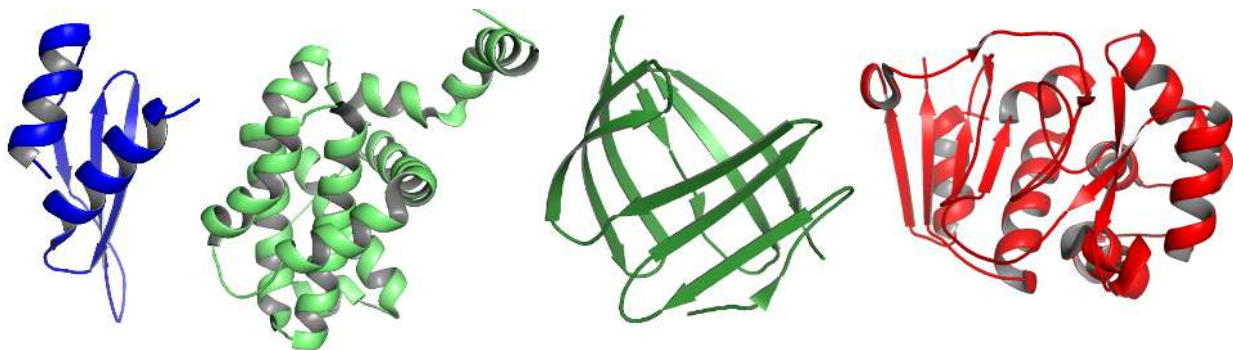
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1. At physiological pH, what is the approximate net charge of a hexapeptide with the following amino acid sequence?

Asp-Val-Ile-Glu-Arg-Ser

- A. -2
 - B. -1
 - C. 0
 - D. +1
 - E. +2
2. Which of the following pairs of amino acid residues would you expect to form ionic bonds?
- A. Glutamic acid and glutamine
 - B. Arginine and lysine
 - C. Lysine and glutamic acid
 - D. Tryptophan and tyrosine
 - E. Tyrosine and glutamine
3. Which of the following stretches of amino acid residues would you expect to find in the interior of protein molecules?
- A. Ala-Asp-Asp-Tyr-Arg
 - B. Gly-Lys-Ser-Pro-Thr
 - C. Phe-Glu-Gln-Glu-Asn
 - D. Ala-Val-Leu-Ile-Trp
 - E. Gly-Tyr-His-Arg-His
4. Which of the following is NOT the role of molecular chaperones in the folding of cellular proteins?
- A. They assist proteins in folding into their correct conformations.
 - B. They help prevent formation of protein aggregates.
 - C. They specify the final three-dimensional shape of proteins.
 - D. They catalyze the folding of proteins in the crowded environment of the cell.

- E. They make the protein-folding process in the cell more reliable.
5. The observation that proteins often *renature* into their original conformations after they have been unfolded by denaturing solvents implies that ...
- A. the information needed to specify the three-dimensional shape of a protein is encoded in its amino acid sequence.
 - B. the cell does not need molecular chaperones for survival.
 - C. the final folded structure of a protein is usually NOT the one with the lowest free energy.
 - D. each protein folds into several different conformations inside the cell.
 - E. All of the above.
6. Imagine a cellular protein composed of 3000 amino acid residues in one continuous polypeptide chain. This protein is almost certainly ...
- A. extracellular.
 - B. globular.
 - C. multidomain.
 - D. composed of mostly α -helical regions.
 - E. intrinsically disordered.
7. For each of the following cartoon representations from left to right, indicate whether the protein structure is composed of only α helices (1), only parallel β sheets (2), only antiparallel β sheets (3), α helices plus parallel β sheets (4), or α helices plus antiparallel β sheets (5) as repetitive secondary structure elements. Your answer would be a four-digit number composed of digits 1 to 5 only, e.g. 5513.

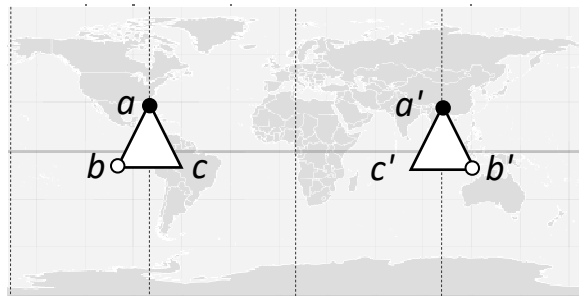


Images created in PyMOL, from PDB entries 1STU, 2LPC, 1SA8, and 3BOB.

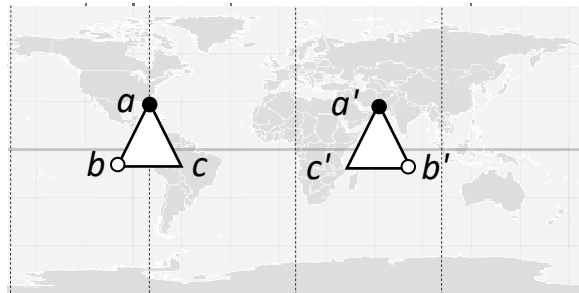
8. Protein secondary structure elements such as α helices and β sheets constitute the major regular folding patterns in proteins. With regard to these elements, ...
- A. hydrogen-bonding between the amino acid side chains defines the type of secondary structure.
 - B. a certain short amino acid sequence always adopts the same secondary structure.
 - C. only a few specific amino acid sequences can adopt these repetitive structures.
 - D. the folding patterns result from hydrogen-bonding between the N-H and C=O groups in the polypeptide backbone.
 - E. All of the above.
9. Which of the following is NOT true regarding the members of a protein family in general?
- A. They have similar three-dimensional conformations.
 - B. They share an ancestry; i.e. they are homologs.
 - C. They can functionally replace each other.
 - D. Their gene sequence is less well conserved than their structure.
 - E. Over evolutionary time scales, the family has expanded mainly through gene duplication events.
10. The number of ways in which protein domains fold in nature is limited. Which of the following is a better estimate of this number?
- A. 200
 - B. 2000
 - C. 200,000
 - D. 2,000,000
 - E. 20 million
11. The human estrogen receptor is a symmetrical dimeric nuclear protein that can regulate gene expression by binding to a DNA sequence called an estrogen response element (ERE) near the promoter of its target genes. Each subunit of the receptor binds to about six base pairs of DNA. Which of the following sequences is a likely candidate for the ERE? The sequences are written in the 5'-to-3' direction. The letter N represents any of the four DNA bases.
- A. AGGTCANNNTGACCT
 - B. AGGTCANNNAGGTCA
 - C. AGGTCANNNACTGGA
 - D. AGGTCANNNATATAT

E. AGGCCTNNNTCATGA

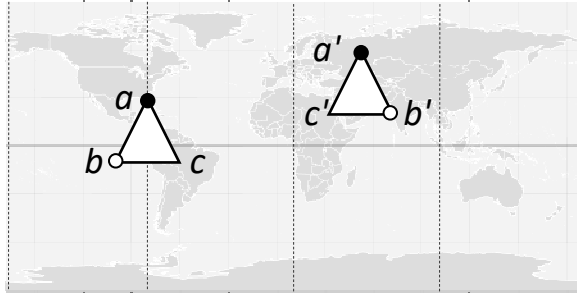
12. We can try to map the surface of a globular protein in two dimensions just like we depict the surface of the Earth in a world map. On such a map, the binding site of a molecule for other molecules of the same protein (for assembly into a multisubunit complex) can be marked. In the following “maps,” two molecules of the protein can bind if the points a , b , and c on the surface of one molecule can align to points a' , b' , and c' in the other molecule, respectively. Which map corresponds to a protein whose assembly gives rise to a helix? Hint: the other maps correspond to a dimer, a ring, and a linear filament.



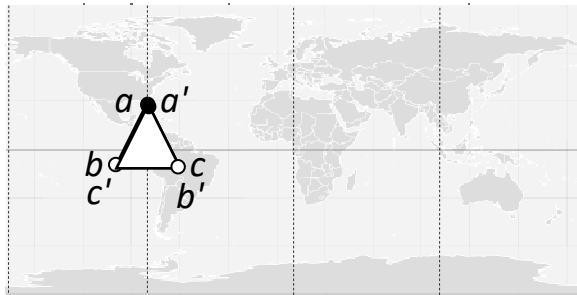
A.



B.



C.



D.

World map from Wikipedia.com, Public Domain

13. Which of the following can be a function for intrinsically disordered protein sequences?
 - A. High-specificity binding to other proteins
 - B. Cell signaling through covalent modification of the protein sequence
 - C. Tethering to hold interacting proteins in close proximity
 - D. Formation of a diffusion barrier from a dense network of such sequences
 - E. All of the above

14. You have purified a multisubunit extracellular protein that has several interchain disulfide bonds. Which of the following chemicals would you add to your purified protein mixture if you wanted to eliminate the disulfide bonds?
 - A. NaCl, a salt
 - B. SDS, an ionic detergent and denaturing agent
 - C. H₂O₂, an oxidizing reagent
 - D. Tris, a buffering agent
 - E. DTT, a reducing agent

15. Many viruses have large capsids in the form of a hollow sphere, made of hundreds of identical protein subunits. What are the advantages of having coats made of several copies of only a few subunits?

- A. Assembly can be readily regulated.
- B. Disassembly can be readily regulated.
- C. It requires a smaller amount of genetic information.
- D. The effect of mistakes in protein synthesis on the overall assembly is minimized.
- E. All of the above.

16. Stable β -sheet aggregates can form from many proteins, forming intertwined cross-beta strands that have the potential to kill cells or damage tissues. Which of the following is NOT true regarding these aggregates?

- A. They form almost exclusively in the cells of the nervous system.
- B. Different types of such aggregates can form from the same protein.
- C. Their formation is associated with conditions such as Parkinson's disease and Kuru.
- D. They can form spontaneously, but also can be triggered to form by an infection with the same aggregate.
- E. Some healthy cells form these aggregates to store their secretory proteins.

17. An amino acid residue that is not part of the active site of an enzyme and does not interact with the ligand is nevertheless critical for ligand binding and is highly conserved. How can this be explained?

- A. This residue is critical for the correct folding and the placement of ligand-binding site residues.
- B. The residue helps with restricting the access of water to the ligand-binding site.
- C. This residue can affect the chemical properties of the residues in the ligand-binding site.
- D. All of the above.

18. Evolutionary tracing has identified clusters of the most invariant amino acids in the SH2 domain family. Which of the following is true regarding these sites?

- A. Mutation in these sites generally keeps the protein functional.
- B. The invariant amino acids generally have negatively charged side chains.
- C. These sites correspond to the binding site for peptides containing phosphorylated tyrosine.
- D. The amino acids at these sites are generally hydrophobic.

E. These sites have evolved fast because they have critical functions.

19. Protein A can bind to each of the proteins B or C. The association rate constants are the same for forming the AB and the AC complexes. However, the dissociation rate constant for AB is 100 times higher than that for AC. Given that every tenfold increase in the equilibrium constant (of the association reaction) corresponds to about -5.9 kJ/mole difference in the standard free-energy change for the reaction (ΔG°), what is the value of ($\Delta G^\circ_{AB} - \Delta G^\circ_{AC}$) in kJ/mole?

- A. -11.8
- B. -5.9
- C. 0
- D. $+5.9$
- E. $+11.8$

20. In interactions between proteins, each hydrogen bond contributes to the free energy of binding by about -4 kJ/mole. If two proteins bind to each other through nine hydrogen bonds, six of which are eliminated when one of these proteins is mutated, how much would you expect the equilibrium constant for their binding to change as a result of the mutation? ($\Delta G^\circ = -5.9 \times \log K_{eq}$)

- A. Increase sixfold
- B. Decrease fourfold
- C. Decrease by six orders of magnitude
- D. Increase 1 million-fold
- E. Decrease by four orders of magnitude

21. The turnover number for an enzyme is equivalent to the number of substrate molecules processed per second per enzyme molecule. To a test tube containing a 100 mM concentration of its substrate, you have added an enzyme at a final concentration of 10 μ M, and have measured the rate of the reaction to be approximately 500 μ M/sec. If the K_m for the binding of the enzyme to this substrate is about 100 mM, what is the turnover number?

- A. 100
- B. 500
- C. 1000
- D. 5000
- E. 10,000

22. Enzymes can catalyze cellular reactions through various mechanisms. Which of the following statements is NOT true regarding enzymes?

- A. They can provide the chemical groups necessary for simultaneous acid and base catalysis.
- B. They have a higher affinity for the transition state of the substrate than for its stable form.
- C. They can form covalent bonds with the substrate during catalysis.
- D. They can strain a substrate to force it toward a specific transition state.
- E. They accelerate a cellular reaction by destabilizing the transition state.

23. An enzyme acts on a tyrosine residue in a target protein to create a binding site for the SH2 domain. This enzyme is most specifically ...

- A. an isomerase.
- B. a nuclease.
- C. a phosphatase.
- D. a kinase.
- E. a synthase.

24. The enzyme lysozyme catalyzes the cutting of a polysaccharide chain through hydrolysis. Which of the following is NOT true regarding the catalytic cycle for this enzyme?

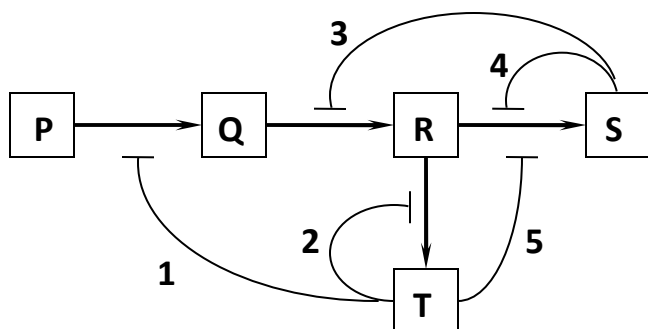
- A. It involves acid catalysis.
- B. It involves base catalysis.
- C. It involves strain catalysis.
- D. It involves covalent catalysis.
- E. It involves metal ion catalysis.

25. How do multienzyme complexes in the cell, such as the fatty acid synthase, enhance reaction rates?

- A. By increasing the diffusion rate of their substrate in the cell
- B. By allowing the channeling of pathway intermediates from one enzyme to the next
- C. By limiting the diffusion of the substrates in membrane-bound compartments
- D. By increasing the intrinsic rate of catalysis for individual enzymes
- E. All of the above

Answer: B Difficulty: 2 Section: Protein Function

26. Which of the regulatory interactions 1 to 5 depicted in the following diagram is NOT an example of a negative feedback regulation?



- A. 1
- B. 2
- C. 3
- D. 4
- E. 5

27. Two ligands, A and B, bind to two different conformations of the enzyme X. The ligand A is the enzyme's substrate, whereas ligand B binds to a remote allosteric site. Which of the following is a consequence of this arrangement?

- A. Binding of A to X does not affect the affinity of X for binding to B.
- B. Binding of B to X does not affect the rate of reaction catalyzed by X.
- C. Binding of A to X increases the affinity of X for B.
- D. Binding of B to X decreases the affinity of X for A.
- E. Binding of B to X has a large effect on the binding of A to X, but binding of A to X has a small effect on X-B binding.

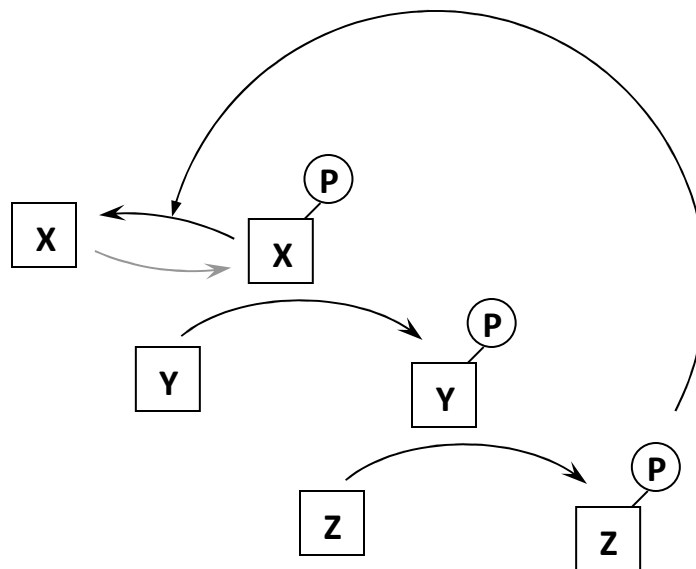
28. The phosphofructokinase (PFK) enzyme is one of the key players in the glycolytic pathway in which glucose eventually breaks down into pyruvate, some ATP is generated, and some NAD^+ is reduced. PFK catalyzes the committed step in the pathway and is under extensive regulation. Which of the following compounds would you expect to activate PFK?

- A. ADP
- B. NADH
- C. Pyruvate

- D. ATP
- E. All of the above

29. Phosphorylation of a protein by a protein kinase ...
- A. adds two positive charges to the protein.
 - B. activates the protein.
 - C. deactivates the protein.
 - D. can create a binding site for other proteins.
 - E. requires the hydrolysis of two molecules of ATP per phosphorylated residue.

30. In the following schematic diagram of a simple signaling pathway, protein Z regulates the activity of protein X, which is an upstream protein kinase, through a negative feedback loop. Which of the following better describes protein Z?



- A. It is a protein kinase that is activated by phosphorylation.
 - B. It is a protein kinase that is inactivated by phosphorylation.
 - C. It is a protein phosphatase that is activated by phosphorylation.
 - D. It is a protein phosphatase that is inactivated by phosphorylation.
31. Most GTPases are present inside the cell at a much higher concentration than their upstream GAP and GEF proteins. Imagine a mutation in a certain GTPase, such as a Rab protein,

resulting in an extremely tight binding between the GTPase and its GEF, and a very slow dissociation. What would you expect to happen in the cell as a result?

- A. Rab proteins will be activated, because the tightly bound GEFs will be unavailable.
- B. Rab proteins will be inactivated, because the tightly bound GEFs will be unavailable.
- C. Rab proteins will be activated, because the Rab-GAPs will become activated.
- D. Rab proteins will be inactivated, because their GAPs will become activated.
- E. Rab proteins will be activated, because there are fewer GAPs available.

32. A viral version of the Src kinase called v-Src is found in some retroviruses. Unlike the cellular Src, the v-Src kinase is constitutively active, and can drive the cell into uncontrolled growth and tumor formation. Which of the following molecular differences between the two versions of Src is more likely to be responsible for this?

- A. v-Src lacks the active-site tyrosine residue.
- B. v-Src lacks a lobe of the kinase domain.
- C. v-Src has multiple inhibitory tyrosine phosphorylation sites in the kinase domain.
- D. v-Src lacks the C-terminal tail that can bind to Src's SH2 domain.
- E. v-Src has a longer C-terminal tail.

33. Switch proteins that bind and hydrolyze GTP are ubiquitous cell regulators in a wide variety of molecular processes. Which of the following statements is NOT true regarding these proteins?

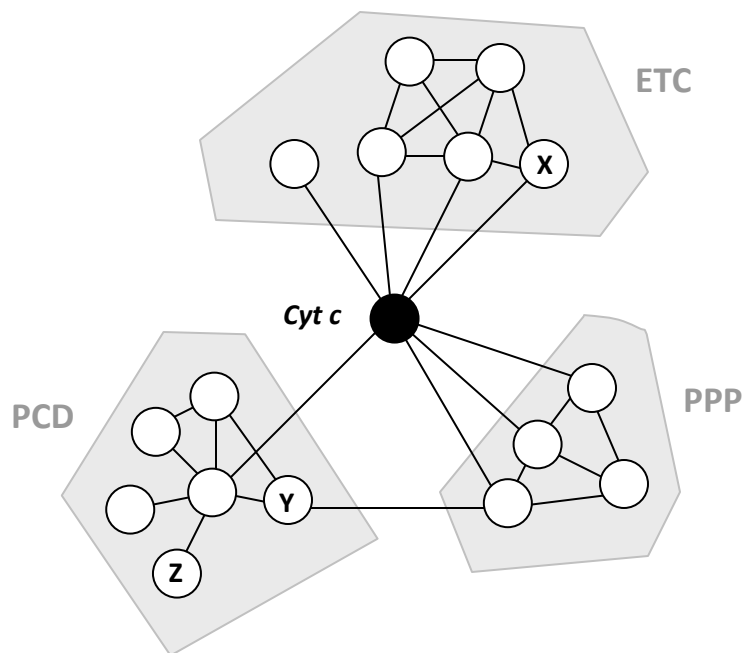
- A. EF-Tu is an example of such proteins.
- B. GTP hydrolysis by the GTPase generally renders it inactive.
- C. Activation of the GTPase involves addition of a phosphate group to its bound guanine nucleotide.
- D. Guanine nucleotide exchange factors generally activate the GTPases.
- E. Guanine nucleotide exchange factors accelerate the release of bound GDP from the GTPases.

34. A polyubiquitin chain has been attached to a protein. The ubiquitin molecules are linked together via isopeptide bonds between Lys48 of one molecule and the carboxyl end of the next one. This protein is expected to ...

- A. be a part of chromatin.
- B. undergo proteasomal degradation.
- C. be involved in DNA repair.
- D. be targeted to endocytic vesicles.

- E. None of the above.
35. The marking of a protein by polyubiquitylation to signify degradation ...
- A. requires the hydrolysis of one ATP molecule to ADP per polyubiquitin chain.
 - B. involves covalent attachment of the target protein to the E1 enzyme.
 - C. is carried out by the proteasome complex.
 - D. is typically done on an arginine residue in the target protein.
 - E. involves the recognition of the target protein by an E2–E3 ligase.
36. The SCF ubiquitin ligase can recognize and mark various target proteins at different stages of the cell cycle. In this complex, ...
- A. different F-box subunits recognize different target proteins.
 - B. the F-box subunit and the E2 ubiquitin-conjugating enzyme are at the opposite ends of the C-shaped molecule.
 - C. a scaffold protein arranges the other subunits such that the two ends of the complex are separated by a gap.
 - D. the use of interchangeable parts such as the F-box subunits makes economical use of the genetic information and allows for rapid evolution of new functions.
 - E. All of the above.
37. In terms of molecular function, what do Ras and myosin have in common?
- A. They normally bind to GTP.
 - B. They couple the hydrolysis of a bound nucleoside triphosphate to protein movements.
 - C. They switch between two distinct conformations controlled by protein phosphorylation and dephosphorylation.
 - D. They are multisubunit proteins and contain a scaffold subunit.
 - E. All of the above.
38. The compound GDPNP is a *GTP analog* that can bind to GTPases in the same way as GTP. However, unlike GTP, it cannot undergo the hydrolysis reaction that normally releases P_i . Therefore, ...
- A. GDPNP and GDP bind to the same conformation of a GTPase.
 - B. a GDPNP-bound Ras is constitutively active.
 - C. a GDPNP-bound EF-Tu cannot bind to tRNA molecules.
 - D. binding of GDPNP to EF-Tu allows multiple cycles of tRNA binding and release without the use of free energy.

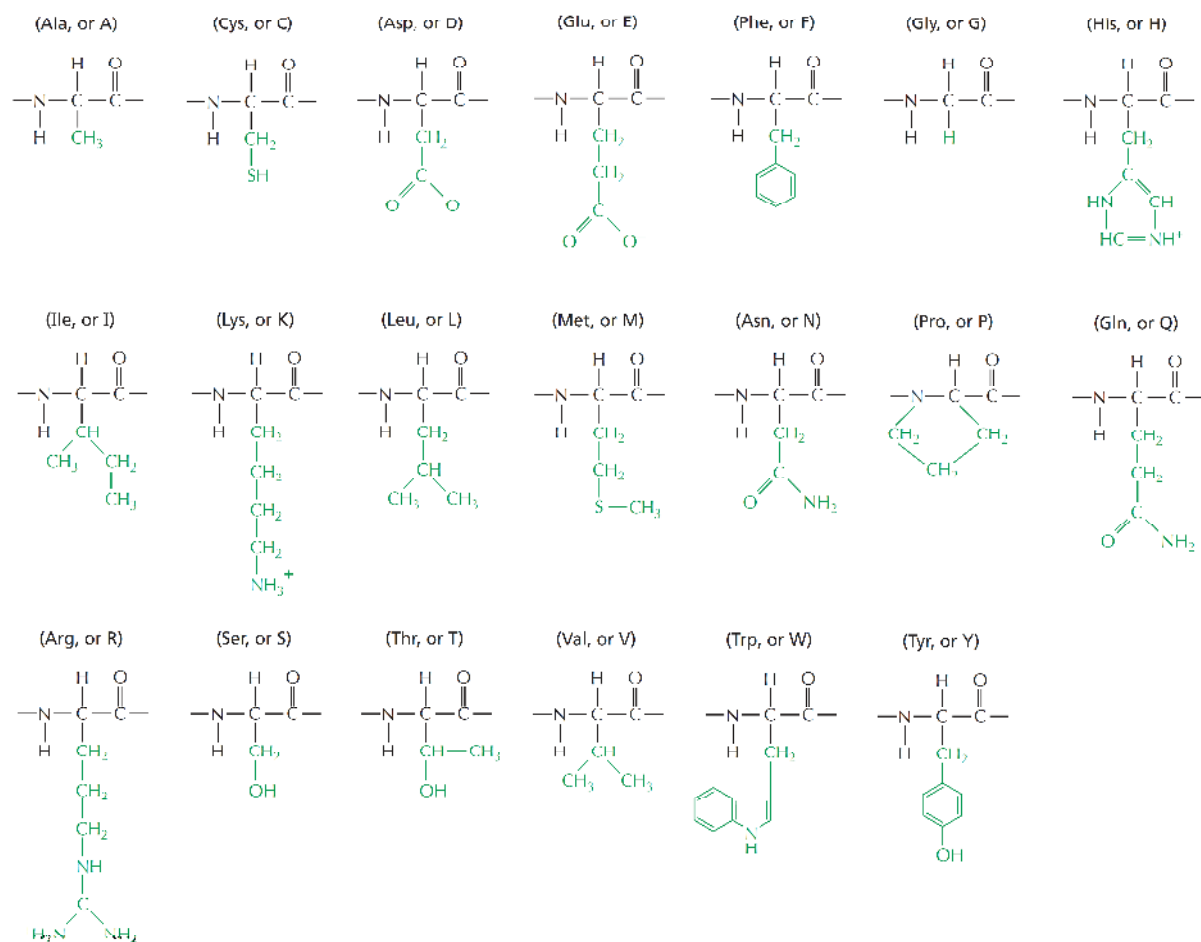
- E. None of the above.
39. Consider the proteins Ras, Src, kinesin, and the ATP synthase pump. All of them ...
- A. are allosteric proteins.
 - B. can have two or more distinct conformations.
 - C. can bind to ATP (or GTP).
 - D. can hydrolyze ATP to ADP (or GTP to GDP).
 - E. All of the above.
40. Many macromolecular complexes in the cell contain scaffold proteins. What do these proteins do that benefits the cell?
- A. They can enhance the rate of critical cellular reactions.
 - B. They can hold the many subunits of a large complex together.
 - C. They can confine and concentrate a specific set of interacting proteins to a particular cellular location.
 - D. They can provide a large macromolecular complex with either flexibility or rigidity.
 - E. All of the above.
41. Imagine a protein that can be independently phosphorylated on any of its 10 tyrosine residues and acetylated on either of its 2 lysine residues. In principle, how many different combinations of these modifications are possible for this protein?
- A. 2^{10}
 - B. 2^{20}
 - C. 10^{10}
 - D. 12^{20}
 - E. 2^{12}
42. A simple protein interaction map is shown below for human cytochrome *c* (Cyt), a heme-containing protein that is normally found inside the mitochondria and is associated with the electron-transport chain (ETC) of the inner mitochondrial membrane. Under special emergency conditions, this protein can also moonlight as a signal transducer for the onset of a pathway leading to programmed cell death (PCD). As shown in the map, it also interacts with a group of phosphoprotein phosphatases (PPP) involved in cell signaling pathways. Assuming that the functions of the proteins labeled as X, Y, and Z are unknown, which of the following points can be reasonably argued from this interaction map?



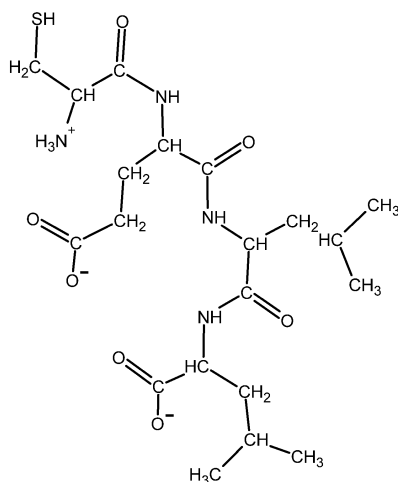
- A. The protein labeled X probably functions in PCD as well as in the ETC, because it interacts with cytochrome *c*, which is known to be closely involved in PCD, and it also interacts with several proteins from the ETC group.
- B. The protein labeled Y probably has a role in PCD, especially if its orthologs in other organisms have such a role and show a similar pattern of interactions.
- C. If the proteins in the PCD group are known to form a large complex, then the protein labeled Z is likely to be the scaffold protein for that complex.
- D. The protein labeled Y probably has a phosphatase function, because it interacts with the proteins of the PPP group.
- E. The protein labeled Z is probably not an essential protein because it only interacts with one other protein in this map.

Reference: The 20 Amino Acid Residues: Questions 43-47

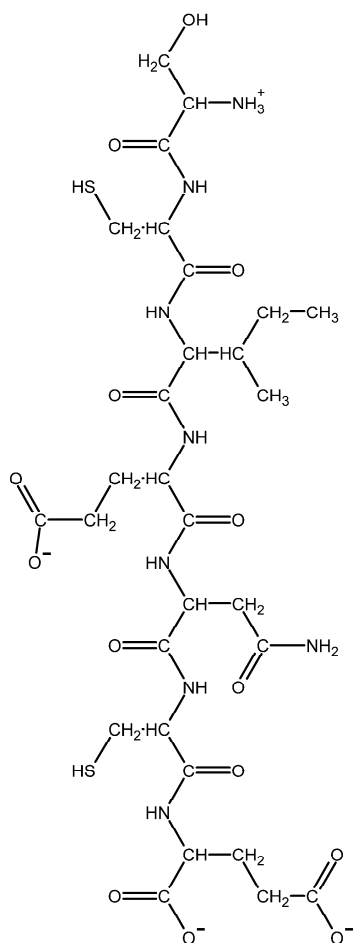
The structural formulas for the 20 naturally occurring amino acid residues are shown in the panel below. Answer the following question(s) with the help of this panel.



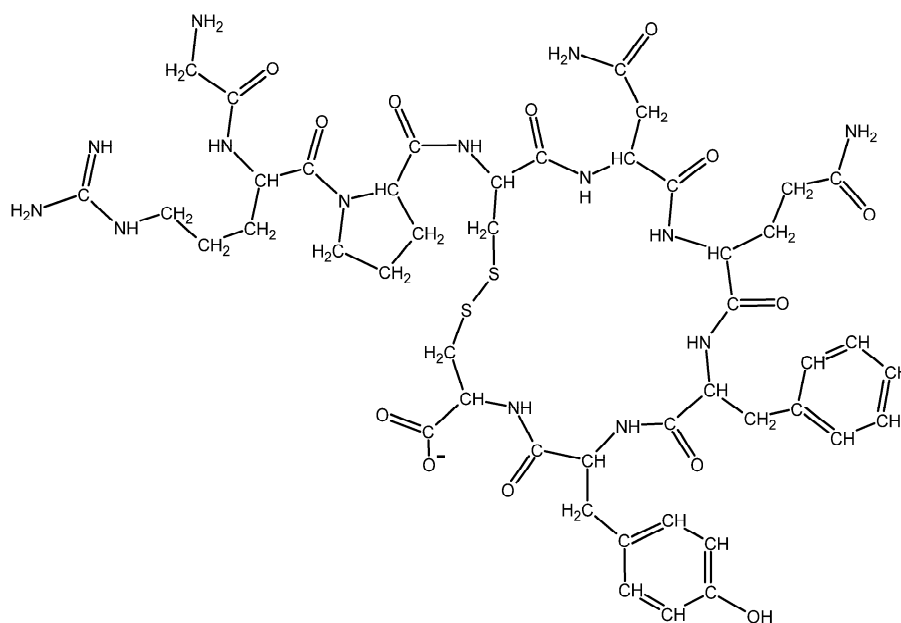
43. Which of the amino acids shown above has the most limited combinations of phi (ϕ) and psi (ψ) angles in its Ramachandran plot? Write down the one-letter abbreviation for it, e.g. A.
44. Which amino acid residues shown above have acidic side chains? Write down the one-letter abbreviations for them, in alphabetical order, e.g. ACGNV.
45. What is the amino acid sequence of the peptide depicted below? Write down the sequence from the N- to the C-terminus, and use only the one-letter abbreviations, e.g. AGCNT.



46. What is the amino acid sequence of the peptide depicted below? Write down the sequence from the N- to the C-terminus, and use only the one-letter abbreviations, e.g. AGCNT.



47. What is the amino acid sequence of the peptide depicted below? Write down the sequence from the N- to the C-terminus, and use only the one-letter abbreviations, e.g. AGCNT.



48. In an α helix, each amino acid residue is rotated by about $+100^\circ$ and raised by about 0.15 nm relative to the previous residue. This means that each full turn of the helix rises by ... nm parallel to the helix's axis.

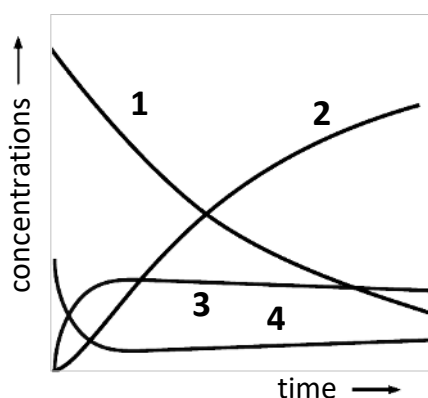
49. There are 3.6 residues per full turn of a (right-handed) α helix. In a typical coiled-coil motif called a leucine zipper, each of the two participating α helices has a leucine residue at every seventh position in the sequence. This places all of these leucine residues roughly on one side of each helix, providing an interaction interface with the leucine side chains of the other helix. Determine the handedness of such a leucine zipper coiled-coil; i.e. do the helices twist around each other in a right-handed (R) or left-handed (L) fashion? Write down R or L as your answer.

50. Imagine that 1 L of a solution containing each of the 20 naturally occurring amino acids at 50 mM concentration each (total concentration of 1 M) is allowed to polymerize in a perfectly stepwise fashion such that at each step, a random amino acid can be incorporated into a growing polypeptide. The steps are repeated, until eventually the solution is only composed of 40-mers

(and virtually all of the monomers have been used). What fraction of all 40-mers can possibly be present in this solution? Round your number to four decimal places. Avogadro's number is 6×10^{23} .

51. Some protein domains are found in many different proteins and have been especially mobile during evolution. A domain of this kind is called a “protein ...”

52. For a simple enzymatic reaction that involves only one substrate and follows Michaelis–Menten kinetics, the changes in the concentrations of substrate, product, free enzyme, and the enzyme–substrate complex over the course of the reaction are depicted by solid curves in the graph below. Which curve (1 to 4) corresponds to [ES]? Write down the number as your answer.



53. A protein is drawn in the following simplified diagram undergoing a set of covalent modifications including the addition of a chain of ubiquitin protein monomers (U) to one of its lysine side chains, a phosphate moiety (P) to its tyrosine side chain, and a lipid farnesyl (F) to its cysteine side chain. Indicate the order of these modifications (1 to 3) in the diagram. Your answer would be a three-letter string composed of letters F, U, and P only, e.g. PFU.



Answers

1. Answer: B

Difficulty: 2

Section: The Shape and Structure of Proteins

Feedback: Each of the acidic amino acids Asp (aspartic acid) and Glu (glutamic acid) carries one negative charge on its side chain at neutral pH, while Arg (arginine) carries one positive charge. The side chains of the other residues shown are not ionized at neutral pH. Additionally, the terminal amine group (one positive charge) and carboxyl group (one negative charge) neutralize each other.

2. Answer: C

Difficulty: 2

Section: The Shape and Structure of Proteins

Feedback: Electrostatic attractions can hold together amino acid residues of opposite charge, i.e. an acidic and a basic residue.

3. Answer: D

Difficulty: 2

Section: The Shape and Structure of Proteins

Feedback: Hydrophobic side chains in a protein—belonging to amino acids such as phenylalanine, leucine, isoleucine, valine, and tryptophan—tend to be buried in the interior of the molecule to avoid the unfavorable contact with water.

4. Answer: C

Difficulty: 1

Section: The Shape and Structure of Proteins

Feedback: The molecular chaperones assist a protein in adopting its correct conformation, which is specified by the protein's amino acid sequence.

5. Answer: A

Difficulty: 2

Section: The Shape and Structure of Proteins

Feedback: This observation indicates that the amino acid sequence of a protein contains all the information needed for specifying its three-dimensional shape.

6. Answer: C

Difficulty: 3

Section: The Shape and Structure of Proteins

Feedback: This large size is about ten times that of an average protein and about thirty times that of an average protein domain. Such a protein is extremely unlikely to constitute a single domain or have an overall globular shape. Although proteins have disordered regions, it is not likely that such a large protein is entirely disordered either. Many large multidomain proteins are mostly made up of β sheets.

7. Answer: 5134

Difficulty: 3

Section: The Shape and Structure of Proteins

Feedback: The first protein (on the left) is composed of α helices and antiparallel β sheet. The second protein is made almost entirely from α helices. The third protein, in contrast, is composed

of antiparallel β sheets only. The protein on the right contains both α helices and parallel β sheets.

8. Answer: D

Difficulty: 1

Section: The Shape and Structure of Proteins

Feedback: It is the repeating hydrogen-bond pattern between backbone atoms that defines each of the secondary structure elements. Many different sequences can adopt each of these structures and, depending on the context, the same sequence may be found in different folding patterns.

9. Answer: C

Difficulty: 2

Section: The Shape and Structure of Proteins

Feedback: Although members of the same family share a similar sequence, ancestry, and three-dimensional conformation, they have nevertheless evolved to have their own specialized functions.

10. Answer: B

Difficulty: 2

Section: The Shape and Structure of Proteins

Feedback: We know the three-dimensional shapes of over 100,000 proteins. However, most of them fold up into conformations that are not entirely novel, and for which known representative proteins already exist. The number of different protein folds is probably not more than about 2000.

11. Answer: A

Difficulty: 3

Section: The Shape and Structure of Proteins

Feedback: Such a symmetrical dimer is expected to recognize a corresponding symmetrical DNA sequence with *inverted repeats*, such that both strands have the same sequence when read in the 5'-to-3' direction. Each subunit recognizes the sequence AGGTCA.

12. Answer: C

Difficulty: 3

Section: The Shape and Structure of Proteins

Feedback: In contrast to dimers (D), rings (B), and straight filaments (A), which require a limited and special arrangement of the subunit binding interfaces, there are many possible arrangements that would give rise to various helical assemblies. The helix formed from this example will be left-handed.

13. Answer: E

Difficulty: 1

Section: The Shape and Structure of Proteins

Feedback: Intrinsically disordered protein sequences are frequent in nature, and many of them are involved in one or more of these four important functions.

14. Answer: E

Difficulty: 2

Section: The Shape and Structure of Proteins

Feedback: A reducing agent such as dithiothreitol (DTT) converts S–S bonds back to SH groups.

15. Answer: E
Difficulty: 1
Section: The Shape and Structure of Proteins
Feedback: Especially for some viruses, small genome sizes confer high evolutionary fitness.
16. Answer: A
Difficulty: 2
Section: The Shape and Structure of Proteins
Feedback: The amyloid fibrils can occur in many tissues, but the nervous system is the most sensitive to their formation and shows the most symptoms when affected. Studies in yeast cells have shown that different types of infectious prions can form from the same type of protein. Although these aggregates are associated with some diseases in humans, healthy cells are known to use them as well, for storage of secretory proteins for example.
17. Answer: D
Difficulty: 2
Section: Protein Function
Feedback: Residues that are far from the binding site can still influence ligand binding by affecting global or local folding of the protein, by controlling the access of water to the binding site, or by changing the chemical properties of other residues.
18. Answer: C
Difficulty: 1
Section: Protein Function
Feedback: The invariant amino acids generally correspond to the conserved binding site for the binding partners of the SH2 proteins.
19. Answer: E
Difficulty: 2
Section: Protein Function
Feedback: The equilibrium constant for complex formation is equal to the ratio of association and dissociation rate constants; thus, it is 100 times higher for AC compared to AB. This makes ΔG°_{AB} more positive than ΔG°_{AC} by a 11.8 kJ/mole difference.
20. Answer: E
Difficulty: 3
Section: Protein Function
Feedback: Elimination of six hydrogen bonds in the interaction increases the ΔG° value by about 24 kJ/mole, which corresponds to a 10,000-fold decrease in the binding equilibrium constant.
21. Answer: A
Difficulty: 3
Section: Protein Function
Feedback: Under these conditions, we have: $[S] = K_m = 100 \text{ mM}$. This means the rate of reaction is: $V = \frac{1}{2} \times V_{\max}$. Thus, $V_{\max} = 2 \times 500 \text{ } \mu\text{M/sec} = 1000 \text{ } \mu\text{M/sec}$. Finally, turnover number is equal to this rate divided by the enzyme concentration; that is: $k_{\text{cat}} = (1000 \text{ } \mu\text{M/sec}) / (10 \text{ } \mu\text{M}) = 100$ per second.
22. Answer: E
Difficulty: 3

Section: Protein Function

Feedback: Transition-state stabilization is a general strategy for enzymes to lower the activation energy and accelerate a reaction.

23. Answer: D

Difficulty: 2

Section: Protein Function

Feedback: This enzyme is a tyrosine kinase.

24. Answer: E

Difficulty: 2

Section: Protein Function

Feedback: Lysozyme uses several mechanisms to accelerate the reaction by several orders of magnitude. The process involves using amino acid side chains that act as acids (donate protons) or bases (accept protons) during the catalytic cycle, straining the substrate to expose the target bonds, and even forming a temporary covalent linkage with one half of the substrate. However, metal ions are not used by this enzyme for catalysis.

25. Answer: B

Difficulty: 2

Section: Protein Function

Feedback: When the diffusion of substrates is limiting the overall rate of an enzymatic reaction or pathway, the use of multienzyme complexes enhances the rate by bringing the various enzymes together and passing the pathway intermediates between them.

26. Answer: E

Difficulty: 2

Section: Protein Function

Feedback: In 5, T is not inhibiting its own production via the regulation of an enzyme that acts earlier in the pathway.

27. Answer: D

Difficulty: 3

Section: Protein Function

Feedback: Due to the negative “linkage” between the two binding events, binding of each of the two ligands to the enzyme reduces the affinity of the enzyme for the other ligand, and this effect is quantitatively reciprocal as well.

28. Answer: A

Difficulty: 3

Section: Protein Function

Feedback: NADH, pyruvate, and ATP are all the products of the pathway and are not expected to activate PFK. On the other hand, a low energy charge in the cell (with a high ADP/ATP ratio) should trigger the activation of the glycolytic and oxidative respiratory pathways to generate more ATP.

29. Answer: D

Difficulty: 1

Section: Protein Function

Feedback: Phosphorylation of a protein (typically coupled to one ATP hydrolysis per reaction) adds negative charges to the protein, potentially changing its surface chemistry and recruiting binding partners that recognize the phosphorylated protein. Some proteins are activated by this modification, while some are not, or are even inactivated.

30. Answer: C

Difficulty: 2

Section: Protein Function

Feedback: Protein Z, when phosphorylated by the protein kinase Y, catalyzes the removal of the phosphate from the protein kinase X, rendering it inactive in a feedback inhibition mechanism.

31. Answer: B

Difficulty: 3

Section: Protein Function

Feedback: The tight binding to the mutant titrates out the available GEFs (guanine nucleotide exchange factors), which are not as abundant as the GTPase itself. Therefore, not enough GEF will be available to activate the rest of the GTPase molecules; thus, compared to the normal situation, the GTPase molecules will become inactivated, with GDP remaining bound.

32. Answer: D

Difficulty: 2

Section: Protein Function

Feedback: By lacking the C-terminal tail that includes the inhibitory tyrosine phosphorylation site, v-Src bypasses the autoinhibitory mechanism mediated by the SH2 domain. Thus it no longer requires the dephosphorylation event to become active.

33. Answer: C

Difficulty: 2

Section: Protein Function

Feedback: Activation of the GTPases involves exchange of a bound GDP for GTP, rather than direct phosphorylation of the bound GDP.

34. Answer: B

Difficulty: 2

Section: Protein Function

Feedback: A polyubiquitin chain with Lys48 linkages generally targets the attached protein to the proteasome for degradation. However, other forms of modification by ubiquitin or related proteins can be involved in a variety of different processes.

35. Answer: E

Difficulty: 2

Section: Protein Function

Feedback: In this pathway, each ubiquitin molecule is activated by linkage to an E1 enzyme via a thioester bond, at the expense of two ATP equivalents. The ubiquitin is then transferred onto an E2 enzyme that is part of an E2–E3 ubiquitin ligase complex. The latter recognizes the target protein and transfers the ubiquitin to a lysine residue in the target protein or to Lys48 of the previous ubiquitin in the chain. A protein marked with this polyubiquitin chain is then recognized and degraded by the proteasome.

36. Answer: E

Difficulty: 1

Section: Protein Function

Feedback: In the SCF complex, the F-box subunit is mainly responsible for substrate specificity, and is separated from the E2 end of the complex by a gap that accommodates the substrate. The use of interchangeable parts in such a complex is obviously advantageous for the cell.

37. Answer: B

Difficulty: 2

Section: Protein Function

Feedback: Through fundamentally similar molecular mechanisms, both myosin and Ras use the free energy of nucleoside triphosphate hydrolysis to perform mechanical work that involves significant conformational changes in a switchlike fashion.

38. Answer: B

Difficulty: 2

Section: Protein Function

Feedback: GDPNP can trap a GTPase in an active conformation, since hydrolysis is not possible.

39. Answer: E

Difficulty: 1

Section: Protein Function

Feedback: Although being as functionally diverse as a switch protein, a protein kinase, a motor, and a pump, these proteins share many structural and mechanistic features.

40. Answer: E

Difficulty: 1

Section: Protein Function

Feedback: Scaffolds can hold the subunits of a large complex together, affecting (enhancing) intersubunit interactions as well as the cellular localization of the whole complex. Scaffolds can confer rigidity or flexibility to large complexes.

41. Answer: E

Difficulty: 1

Section: Protein Function

Feedback: Each modification can have two different states, which therefore doubles the number of combinations.

42. Answer: B

Difficulty: 3

Section: Protein Function

Feedback: Just because two proteins closely interact with each other, it does not mean that they have the same enzymatic activity. For example, a scaffold protein is generally expected to interact with many of the subunits in a complex. Proteins that display similar patterns in maps derived from different organisms are likely to have similar functions—almost certainly if they also have homology. Note that such a map only shows the small subset of interactions from the whole organism that are clustered around cytochrome *c*, and does not reflect all of the interactions for all of the proteins shown.

43. Answer: P

Difficulty: 3

Section: The Shape and Structure of Proteins

Feedback: Proline, being an imino acid, can adopt only a limited set of configurations within a polypeptide chain.

44. Answer: DE

Difficulty: 3

Section: The Shape and Structure of Proteins

Feedback: Aspartic acid and glutamic acid residues have acidic side chains, and are usually negatively charged in cellular proteins.

45. Answer: CELL

Difficulty: 3

Section: The Shape and Structure of Proteins

Feedback: The sequence is cysteine–glutamic acid–leucine–leucine.

46. Answer: SCIENCE

Difficulty: 3

Refer to: The 20 Amino Acid Residues

Feedback: The sequence is serine–cysteine–isoleucine–glutamic acid–asparagine–cysteine–glutamic acid.

47. Answer: GRPCNQFYC

Difficulty: 3

Section: The Shape and Structure of Proteins

Feedback: The sequence is that of the mammalian peptide hormone vasopressin: glycine–arginine–proline–cysteine–asparagine–glutamine–phenylalanine–tyrosine–cysteine. Note the disulfide bond between the two cysteines.

48. Answer: 0.54

Difficulty: 3

Section: The Shape and Structure of Proteins

Feedback: A full (360°) turn in the α helix contains 3.6 residues ($360^\circ/[100^\circ \text{ per residue}]$), and is thus raised by 0.54 nm:

$3.6 \text{ residues per turn} \times 0.15 \text{ nm rise per residue} = 0.54 \text{ nm rise per turn.}$

49. Difficulty: 4

Section: The Shape and Structure of Proteins

Feedback: Seven is slightly short of the number of residues in two full turns of the right-handed α helix (7.2), which places each leucine not perfectly on top of the previous leucine, but slightly rotated in the left-handed sense. Thus, to interact with the leucine residues in the other helix, the helix should twist around it in a left-handed fashion.

50. Answer: 0.0000

Difficulty: 3

Section: The Shape and Structure of Proteins

Feedback: The number of possible 40-mers is equal to 20^{40} or approximately 10^{52} . If every 40-mer in the solution has a unique sequence, there will be 0.025 moles of different 40-mers made in this solution (since the total amount of monomer was 1 mole), which is equivalent to 1.5×10^{22} molecules. Thus, only about one out of every 10^{30} possible 40-mer peptides has been sampled in

this solution. Even the whole universe does not have enough atoms to sample all possible sequences for a protein with 300 amino acid residues in this way.

51. Answer: module

Difficulty: 1

Section: The Shape and Structure of Proteins

Feedback: Protein modules are a subset of protein domains that have been especially mobile during evolution and seem to have particularly versatile structures.

52. Answer: 3

Difficulty: 2

Section: Protein Function

Feedback: After a brief initial period of pre-steady state, the concentration of the formed ES complexes remains more or less constant in the apparent steady-state phase. This assumption allows the derivation of the Michaelis–Menten equation for reaction rate that involves $V_{\max}$, K_m , and $[S]$.

53. Answer: FPU

Difficulty: 2

Section: Protein Function

Feedback: Attachment of lipid compounds such as the farnesyl group to a protein causes it to become membrane-associated. At the right time, a specific phosphorylation can result in recognition of the protein by certain partners, which in this case target the protein for degradation by polyubiquitin addition.