

C - 2020 Rickards Protein Modeling - Rickards Invitational Div. C - 12-05-2020

Welcome to Rickards Protein Modeling!

General Biochemistry

1. (1.00 pts) What type of bond joins carbohydrate molecules to one another?

- ☒ A) Glycosydic Linkage
- ☐ B) Peptide Bond
- ☐ C) Ester linkage
- ☐ D) Ionic bond
- ☐ E) Phosphodiester bond

2. (1.00 pts) What type of bond links the pentose sugars of nucleic acids together?

- ☐ A) Ionic bond
- ☐ B) Glycosidic linkage
- ☒ C) Phosphodiester bonds
- ☐ D) Dative bond
- ☐ E) Ester linkage

3. (1.00 pts) What type of bond links amino acids together to form proteins?

- ☐ A) Coordinate covalent bond
- ☐ B) Ester linkage
- ☒ C) Peptide bonds
- ☐ D) Glycosidic linkage
- ☐ E) Ionic bond

4. (1.00 pts) Which of the following bonds would you find in a lipid?

- ☐ A) Ionic bond
- ☐ B) Coordinate covalent bond
- ☐ C) Dative bond
- ☒ D) Ester linkage
- ☐ E) Phosphodiester bond

5. (1.00 pts) Select all of the following levels of protein structure that are incorrectly matched with its description.

(Mark **ALL** correct answers)

- ☐ A) Primary Structure: Sequence of amino acids
- ☐ B) Secondary Structure: Hydrogen bonding of backbone
- ☒ C) Tertiary Structure: Formation of alpha helices and beta sheets
- ☒ D) Quaternary Structure: 3-D folding due to side chain interactions
- ☐ E) All of the above are correctly matched

6. (1.00 pts) Sickle cell anemia is caused by a point mutation that leads to the replacement of a _____ residue with a _____ residue.

glutamic acid

valine

7. (1.00 pts) Which of the following best explains why the peptide bond is relatively inflexible?

- ☒ A) Peptide bonds have partial double bond character
- ☐ B) Steric hindrance due to bulky substituents on either side of the bond
- ☐ C) The carbon-nitrogen bond is a polar covalent bond
- ☐ D) Peptide bonds do not exhibit abnormal inflexibility

8. (1.00 pts) The increased favorability of which of the following interactions accounts for the stability of antiparallel beta sheets relative to parallel beta sheets?

- ☐ A) Geometry
- ☐ B) Ionic bonds
- ☒ C) Hydrogen bonds
- ☐ D) Steric interactions
- ☐ E) Pi stacking interactions

9. (3.00 pts)

Disulfide bonds are generally formed [intracellularly/extracellularly] because the extracellular environment is [oxidizing/reducing] while the intracellular environment is [oxidizing/reducing].

extracellularly

oxidizing

reducing

10. (2.00 pts)

On a Ramachandran plot, left-handed alpha helices would be found in the [top left/top right/bottom left/ bottom right] while right-handed alpha helices would be found in the [top left/top right/bottom left/ bottom right].

top right

bottom left

11. (1.00 pts) The final shape of a folded protein sequence is called its _____.

- ☐ A) Transition state
- ☐ B) Molten globule
- ☐ C) Activated complex
- ☐ D) Parent conformation

☒ E) Native conformation

12. (1.00 pts) Which of the following best describes the structure of collagen?

- ☐ A) Alpha helix
- ☐ B) Double helix
- ☒ C) Triple helix
- ☐ D) Amorphous
- ☐ E) Globular

13. (1.00 pts) What set of rules accounts for the 1:1 ratio of purines to pyrimidines?

Expected Answer: Chargaff's rules

14. (2.00 pts) What two radioisotopes were used in the Hershey-Chase experiment?

Expected Answer: P-32 and S-35

15. (3.00 pts) What experiment demonstrated that, in bacteria, genetic mutations arise in the absence of selection, rather than being a response to selection?

Expected Answer: Luria-Delbruck

Amino Acids

For questions 16-25, name the amino acid(s) that matches the given description.

16. (1.00 pts) The two amino acids that are almost never found in alpha helices.

Expected Answer: Proline and glycine

17. (1.00 pts) The only achiral amino acid.

Expected Answer: Glycine

18. (1.00 pts) The two amino acids that contain sulfur.

Expected Answer: Cysteine and methionine

19. (1.00 pts) Coded for by the UAG codon.

Expected Answer: +1 Pyrrolysine +0.25 Stop

20. (1.00 pts) Coded for by the UGA codon.

Expected Answer: Selenocysteine

21. (1.00 pts) Forms disulfide bridges.

Expected Answer: Cysteine

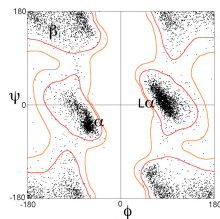
22. (1.00 pts) Most acidic amino acid.

Expected Answer: Aspartic acid

23. (1.00 pts) Most basic amino acid

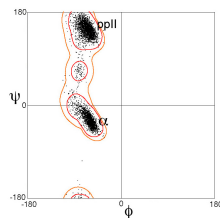
Expected Answer: Arginine

24. (1.00 pts) The one with this Ramachandran plot:



Expected Answer: Glycine

25. (1.00 pts) The one with this Ramachandran plot:



Expected Answer: Proline

Structural Motifs

For questions 26-35, name the structural motifs that matches the given description.

26. (1.00 pts) Connecting these motifs laterally makes a beta sheet.

Expected Answer: Beta strand

27. (1.00 pts) DNA binding motif that binds to the major groove of DNA.

Expected Answer: Helix turn helix or HTH

28. (1.00 pts) Also called a 3_613 -helix.

Expected Answer: Alpha helix

29. (1.00 pts) Can be identified as a ~7 residue "bulge" within an alpha helix.

Expected Answer: Pi helix

30. (1.00 pts) 4th most common secondary structural motif. Each residue corresponds to a 120 degree turn.

Expected Answer: 3_{10} helix

31. (1.00 pts) HLH domain found in Ca-binding proteins.

Expected Answer: EF hand

32. (1.00 pts) Highly conserved motif found in aquaporins.

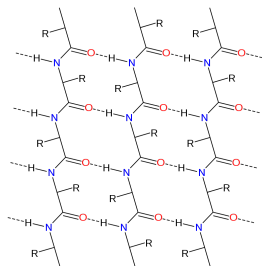
Expected Answer: NPA motifs

33. (1.00 pts) The one in this picture:



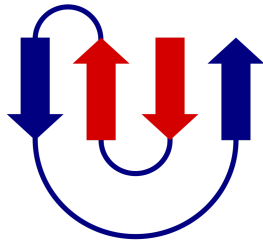
Expected Answer: Beta hairpin

34. (1.00 pts) The one in this picture:



Expected Answer: Alpha sheet

35. (2.00 pts) The one in this picture:



Expected Answer: Greek Key

Protein Folding

Questions 36-40 are about protein folding.

36. (4.00 pts) Explain how hydrophobic interactions help drive protein folding.

Expected Answer: +2 Hydrophobic residues cluster inside while hydrophilic stay on the outside +2 They do this because of entropy (be generous, if they say entropy and they're not wrong this is fine)

37. (4.00 pts) Explain the function of chaperonins in protein folding and how they aid in protein folding.

Expected Answer: +2 Provide favorable conditions for folding to happen +1 Prevent aggregation +1 Can tag misfolded proteins for degradation

38. (4.00 pts) State what Anfinsen's dogma is and the three conditions it uses to define the native structure.

Expected Answer: +1 Native structure determined solely by primary structure +3 Uniqueness, stability, kinetically accessible

39. (10.00 pts)

Outline the experimental procedure Anfinsen used to investigate his theory. What protein did he use? What parts of this protein did he target and what reagents did he use to target them? How did this support his theory?

Expected Answer: +2 Ribonuclease A +1 Disulfide bonds +2 Urea and 2ME to break the bonds +1 When he removed the urea and 2ME the protein spontaneously refolded! +1 Shows that refolding happens in vitro +1 Just removing 2ME gives back 1% activity +1 Note that recovery is never 100%, because mistakes always happen +1 any mention of PDI

40. (4.00 pts) State what Levinthal's paradox is and explain how it relates to Anfinsen's dogma. Provide an explanation that resolves this paradox.

Expected Answer: +1 Levinthal's relates to how proteins reach their native state +1 Says that trying every possible conformation would take way way too long +2 Local sequences stabilize, serving as a nucleation point in folding, i.e. there are partially folded intermediates first

Acid-Base Chemistry of Amino Acids

41. (2.00 pts)

Because all amino acids have amine and carboxylic acid groups, they can act as both an acid and a base. What is the chemical term for molecules that can act as both acids and bases?

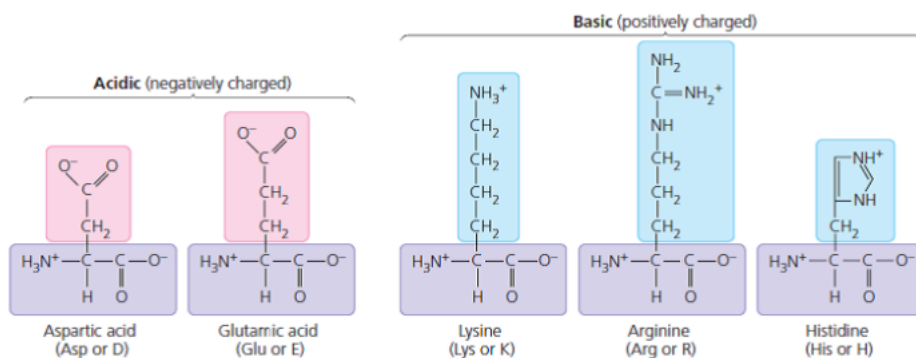
Expected Answer: Amphoteric

42. (2.00 pts)

The amine and carboxyl groups of amino acids also mean they simultaneously have a negative and positive charge. What is the chemical term for molecules that simultaneously have both ionic states?

Expected Answer: Zwitterion

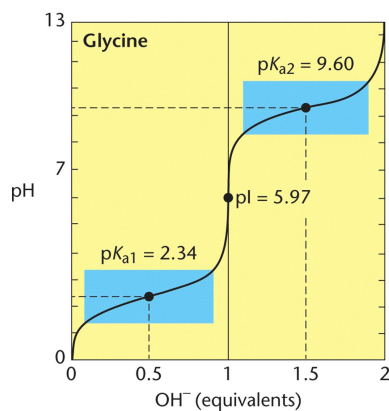
43. (8.00 pts)



The amino acids shown above have side chains with acidic or basic properties. Which of these amino acids has the most acidic side chain? Why? Which has the most basic side chain? Why? [Hint: Compare the relative stability of their conjugate acids/bases in your argument.]

Expected Answer: +1 - Identifying aspartic acid as the most acidic. +2 - Any reasonable explanation mentioning induction. +1 - Explanation makes comparison to glutamic acid. Does not have to be explicit (e.g. "Asp's longer carbon chain" is fine). +1 - Identifying arginine as the most basic. +2 - Any reasonable explanation mentioning resonance. +1 if mentions induction but not resonance. +1 - Explanation makes comparison to lysine and histidine.

Questions 44-46 refer to the following titration curve:



44. (1.00 pts) Above is the titration curve for glycine. What is the net charge on glycine at pK_{a1} , pI , and pK_{a2} ?

Expected Answer: [+1] [0] [-1]

45. (1.00 pts) True or False: Glycine acts as a good buffer at the pH of blood.

☐ True ☒ False

46. (1.00 pts) The pI of glycine is equal to the arithmetic mean of its pK_{a1} and pK_{a2} . Is this true for all amino acids?

- ☐ A) Yes
- ☒ B) No

Laboratory Methods

47. (2.00 pts)

The Edman degradation is a method for _____ polypeptides by removing residues one at a time from the _____ and identifying each residue as it is removed.

sequencing

N-terminus

48. (2.00 pts) Outline the procedure for performing an Edman degradation. Make sure you name the specific reagents you would use at each step.

Expected Answer: Phenyl isothiocyanate then trifluoroacetic acid

49. (2.00 pts) The Bergmann degradation is the predecessor of the Edman degradation. Briefly explain how the Edman degradation improved on the Bergmann degradation.

Expected Answer: +2 Easier to do sequentially, Edman retains structure of polypeptide, as opposed to making an amide. +0.5 for point out differences but not explaining how that's an improvement (e.g. cleaves a different end)

50. (2.00 pts) Gel electrophoresis may be used in the separation and characterization of proteins. Briefly describe the working principle behind gel electrophoresis.

Expected Answer: +1 size separation +0.5 electric field moves charged molecules +0.5 larger moves slower

51. (2.00 pts)

Sodium dodecyl sulfate or SDS is a reagent commonly used to measure the atomic mass of protein samples in gel electrophoresis. Give a reason why SDS is used in gel electrophoresis.

Expected Answer: +2 for any of these: it denatures the proteins; gives proteins similar charge so it separates by size only; forces peptides into a rod shape, removes shape variable etc.

52. (2.00 pts) Name four variants of chromatography used in biochemistry and/or biology.

Expected Answer: Many possible answers

53. (2.00 pts) What two properties does 2D gel electrophoresis separate molecules by?

(Mark **ALL** correct answers)

- ☒ A) Molecular mass
- ☐ B) Molecular size
- ☒ C) Isoelectric point
- ☐ D) Ionic radius
- ☐ E) Charge density

Questions 54-56 require you to give your answer as a list of amino acids. The common name, chemical name, three letter abbreviation and one letter abbreviation are all acceptable. (These will be manually graded).

54. (2.00 pts) Trypsin cleaves on the carbonyl side of which amino acids?

Expected Answer: Lys, Arg

55. (2.00 pts) Chymotrypsin cleaves at the carbonyl side of what residues?

Expected Answer: Phe, Trp, Tyr

56. (2.00 pts) Cyanogen bromide cleaves at the carbonyl side of what residues?

Expected Answer: Met

CRISPR

For questions 57-61, state what the given acronym stands for.

57. (1.00 pts) CRISPR

Expected Answer: Clustered Regularly Interspaced Short Palindromic Repeats

58. (1.00 pts) NHEJ

Expected Answer: Non homologous end joining

59. (1.00 pts) SSB

Expected Answer: Single stranded break. I'll generously give you points for single-stranded binding protein.

60. (1.00 pts) BER

Expected Answer: Base excision repair

61. (1.00 pts) HDR

Expected Answer: Homology directed repair

62. (9.00 pts) Name the three stages of the CRISPR-Cas9 immunity pathway and briefly describe what happens during each stage.

Expected Answer: +1 Spacer acquisition +2 processed DNA (protospacer) is integrated into CRISPR array locus +1 crRNA biogenesis +2 transcription of CRISPR locus into single pre-CRISPR RNA (pre-crRNA) and processing into mature cr-RNA +1 target interference +2 single Cas protein (or complex) uses crRNA as guide to cleave phage sequence complementary to crRNA spacer sequence

63. (8.00 pts) Name the two nuclear domains of Cas9 along with their function, then describe the mechanism of operation for each domain.

Expected Answer: +1 RuvC +1 Carboxylate-chelated two-metal-ion cleavage mechanism +2 Binding of divalent cations move scissile phosphate on nontarget strand towards the cation +1 HNH +1 exists in equilibrium between active and inactive states +2 metal ions drive the active site towards the target strand

Exploration

Questions 64-83 require you to investigate the protein at the following link: <https://www.rcsb.org/3d-view/jsmol/4ia4> (<https://www.rcsb.org/3d-view/jsmol/4ia4>) (<https://www.rcsb.org/3d-view/4IA4>)

You're free to click around the various tabs for this protein as you'd like, but you should refrain from visiting any other pages or websites.

Note: There's a lot of background questions. If you want to skip to the actual JSmol part go to question 74.

64. (1.00 pts) In what organism was this protein isolated? Give the species name.

Expected Answer: *Spinacia oleracea*

65. (1.00 pts) What is the weight of this protein, in kilodaltons?

Expected Answer: 122.13

66. (1.00 pts) How many mutations does this sample have?

Expected Answer: 0

67. (8.00 pts) This experiment used X-ray diffraction to elucidate the structure of the protein. Outline the procedure for XRD.

Expected Answer: No credit for blatantly plagiarized answers off of Google/Wikipedia/etc. Otherwise, we're pretty generous here: +2 mention Bragg's law +1 mention crystallizing the sample +1 mention hitting sample with x-rays +1 x-rays interact with the electrons +1 mention an interference pattern in any way +1 specify pattern is caused by phase difference +1 mention a Fourier transform +8 auto get full points if they give any correct/relevant equations, e.g. protein scattering density -1 if they say the x-rays interact with photons

68. (1.00 pts) At what resolution was the XRD procedure conducted?

Expected Answer: 3.10 angstroms

69. (1.00 pts) What ligand species, if any, were observed in this sample?

Expected Answer: Hg²⁺

70. (2.00 pts) What method was used to crystallize this sample?

Expected Answer: Hanging drop vapor diffusion

71. (10.00 pts) Select ANY of the terms from the list below and define it as well as you can.

- Hanging drop vapor diffusion
- Matthews coefficient
- Solvent content
- Space group
- Molecular replacement

Expected Answer: Many possible answers (key doesn't fit here)

72. (10.00 pts) Using as many terms from the list below as you can, outline the computational/data science aspect of this experiment.

- Data refinement
- Data reduction
- Data scaling
- Data phasing

Expected Answer: Many possible

73. (10.00 pts) Using as many of the terms from the list below as you can in your response, describe the experimental procedure of this diffraction experiment.

- Synchrotron
- Monochromator
- CCD
- Beamline

Expected Answer: Many possible

74. (1.00 pts) How many ligands are there in each bioassembly?

Expected Answer: 12

75. (1.00 pts) What amino acid is at residue 39 of this protein?

Expected Answer: Arginine

76. (1.00 pts) What amino acid is at residue 264?

Expected Answer: Leucine

77. (1.00 pts) How many hydrophobic atoms are in this structure?

Expected Answer: 5096

78. (1.00 pts) How many hydrophilic atoms are in this structure?

Expected Answer: Any of these (depends on which ones you consider hydrophilic): 2181 from (arg,lys,his,glu,asp,asn,gln,thr,ser,cys) 2085 from (asn, gln, ser, thr, lys, arg, his, asp, glu) 1893 from (ser,thr,asp,glu,cys,asn,gln,arg,his) 1708 from (gln, ser, thr, asn, met, his, tyr)

79. (1.00 pts) How many charged atoms are in this structure?

Expected Answer: 1089

80. (1.00 pts) How many atoms are in sheets?

Expected Answer: 142

81. (1.00 pts) How many hydrogen bonds are in the entire protein?

Expected Answer: 194

82. (1.00 pts) How many hydrogen bonds are there from residues 59-172?

Expected Answer: 44

83. (1.00 pts) When the structure is restricted to water molecules, how many atoms are listed in the jsmol console?

Expected Answer: 1

END OF EXAM