THE UNIVERSITY OF MANITOBA

April 26, 2003 FINAL EXAMINATION

PAPER NO: 621 LOCATION: U. College Great Hall PAGE NO: 1 of 4

DEPARTMENT & COURSE NO: Chemistry 2.463 TIME: 3 HOURS

EXAMINATION: Biochemistry of Proteins EXAMINER: J. O'Neil

Section 1: *You must answer all of the following questions in* Section 1. *As a guide you can spend up to 2 hours and 10 minutes on this part of the exam. Wherever possible* ***use diagrams*** *to enhance your answers.*

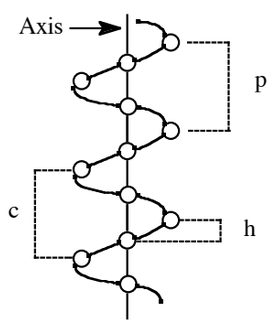
Marks

8 1. Explain in words what is a dihedral angle and give a definition of the angle ϕ. Draw the chemical structure of the peptide Val-Phe-Asp at pH 7 and label all the side-chain and backbone dihedral angles with Greek letters or names.

4 2. How many different conformations can a 3 amino acid peptide form if each amino acid can adopt 6 different conformations? What is the Levinthal Paradox/

10 3. What information did V. N. Ramachandran use to construct his Plot? Draw a Ramachandran Plot and label the locations of the right and left-handed α-helices, parallel and antiparallel β-sheets, the right-hand 3_{10} helix, and the collagen triple helix.

8 4. With the use of the following diagram define and explain the parameters that are used to distinguish different types of helix?



6 5. Draw the following sequence on a helical wheel: L-N-R-A-Y-E-I-L-D-T-A. What does your diagram indicate about the helix?

9 6. Use a 7 residue moving window and the table below to calculate and graph a hydropathy plot for the sequence R-T-S-E-G-A-V-L-V-I-M-V-F-Q-E-K

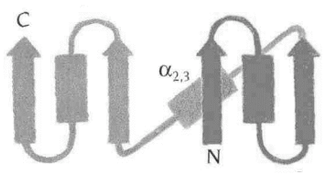
R	15.86	D	9.66	E	7.75	N	7.58
K	6.49	Q	6.48	H	5.60	S	4.34
T	3.51	Y	1.08	G	0.00	C	-0.34
A	-0.87	W	-1.39	M	-1.41	F	-2.04
V	-3.10	I	-3.98	L	-3.98		

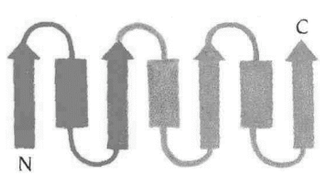
In general, what information does a hydropathy plot convey?

Marks

12 7. Identify the following structures. Describe the main features using examples wherever possible.

A **B**





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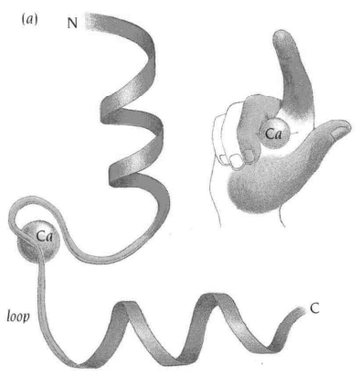
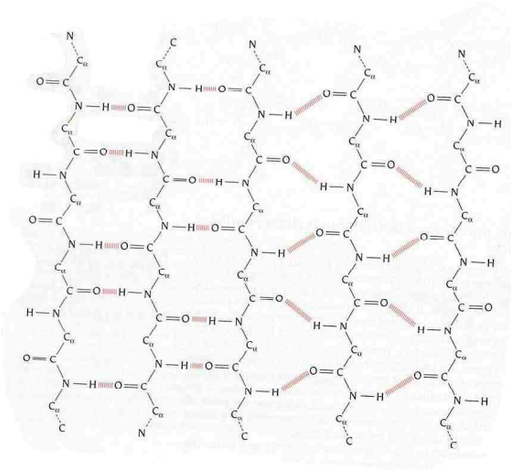
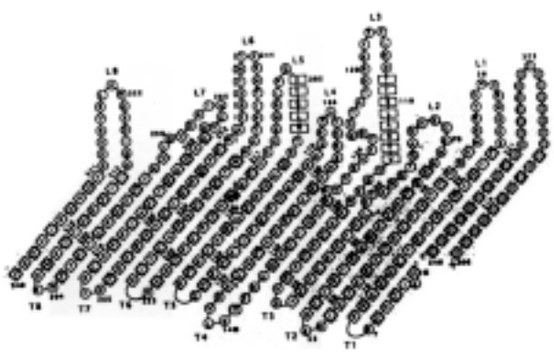
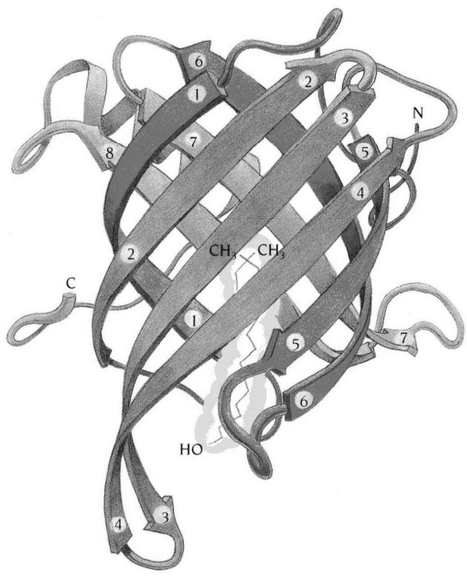




16 8. With the use of the following diagrams compare and contrast the water-soluble β-barrels with those that form integral membrane proteins. Be sure to relate function to structure.

A **B**





Marks

5 9. X-ray diffraction is used to obtain the atomic structures of proteins. One measure of the quality of these structures is their "resolution". Explain what is meant by "resolution".

6 10. Explain the meanings of the symbols in the following equation. Explain how the equation is used with respect to protein structures.

$$R = \Sigma||F_{obs}|-|F_{calc}|| \; / \; \Sigma|F_{obs}|$$

3 11a. An IgG molecule can undergo a major conformational change upon binding an antigen molecule. What is the timescale over which this change takes place? Molecular dynamics programs (algorithms) simulate the motions of atoms on "long" timescales by calculating atom trajectories over "short" timescales and adding them together. What is the timescale of these "short" trajectories? With present day computers how "long" can protein dynamics be simulated?

6 11b. What conclusions have been reached so far about the nature of protein dynamics based on molecular dynamics simulations?

2 12. What did you observe and learn from viewing the protein dynamics movies that were available on the course web site?

6 13. What are Chameleon sequences? What do they tell us about the protein folding problem?

6 14. The large subunit of GroE undergoes a massive conformational change upon binding ATP and the GroEs. Three of the 4 amino acids involved in the two hinge regions of GroEl are Gly and one is Pro. Using structural arguments explain the roles of Gly and Pro in protein structure and dynamics.

Section 2: *Answer 1 of the following questions in* Section 2. *You can spend about 25 min. on this question.*

20 15. Describe helix formation in poly-L-Proline and poly-L-Glutamic acid. Explain why the helix<-->coil transition is highly cooperative in long homopolymers.

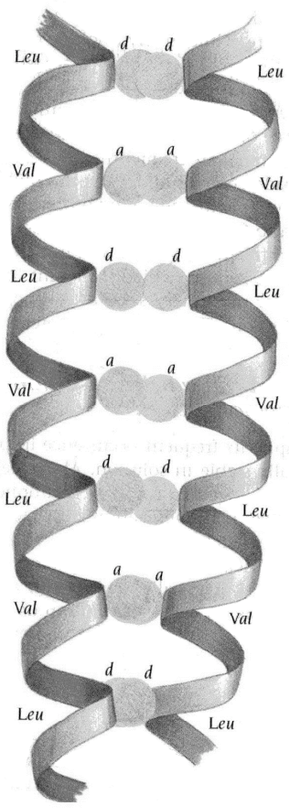
20 16. Describe the "protein folding problem". Explain the concept of *cooperativity* and indicate its relevance to protein folding.

Section 3: *Answer 1 of the following questions in* Section 2. *You can spend about 25 min. on this question.*

Marks

20 17. With the use of the following diagrams explain the different ways in which helices can pack in proteins. Give an example of each type.

A



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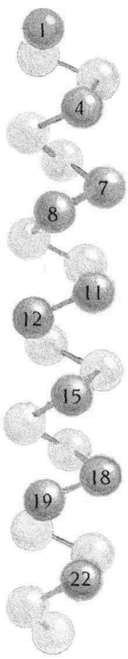
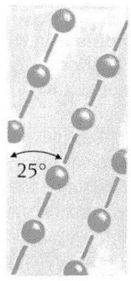


(a)



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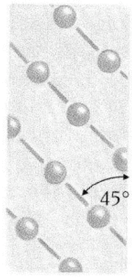

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B **C**

20 18. Cells have evolved a number of mechanisms to assist protein folding. Describe 6 such mechanisms and name the factors involved in the process.