THE UNIVERSITY OF MANITOBA

April 22, 1995 FINAL EXAMINATION

PAPER NO: 891 LOCATION: Engineering 447 (1-43) PAGE NO: 1 of 4

DEPARTMENT & COURSE NO: CHEMISTRY 2.463 TIME: 3 HOURS

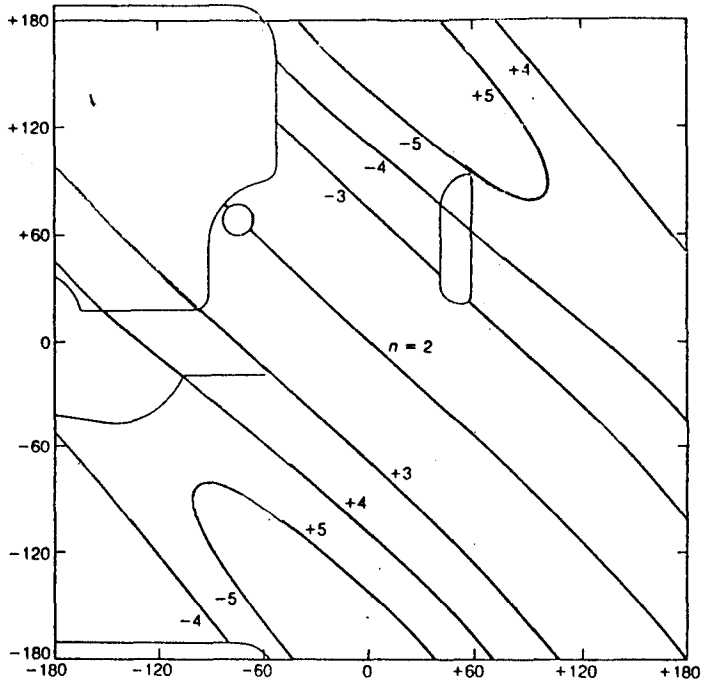
EXAMINATION: Biochemistry of Proteins EXAMINER: J. O'Neil

Section 1: *You must answer all of the following questions in* Section 1. *You can spend up to 2.5 hours on this part of the exam. Wherever possible use* ***diagrams*** *to enhance your answers.*

Marks

4 1. Draw the peptide Ile-Met and label all the dihedral angles ϕ, ψ, ω χ.

9 2. Explain what is a Ramachandran Plot and the information it presents. In the diagram below label the locations of the right and left-handed α-helices, parallel and antiparallel β-sheets, the right-handed 3_{10} helix, and the collagen triple helix.



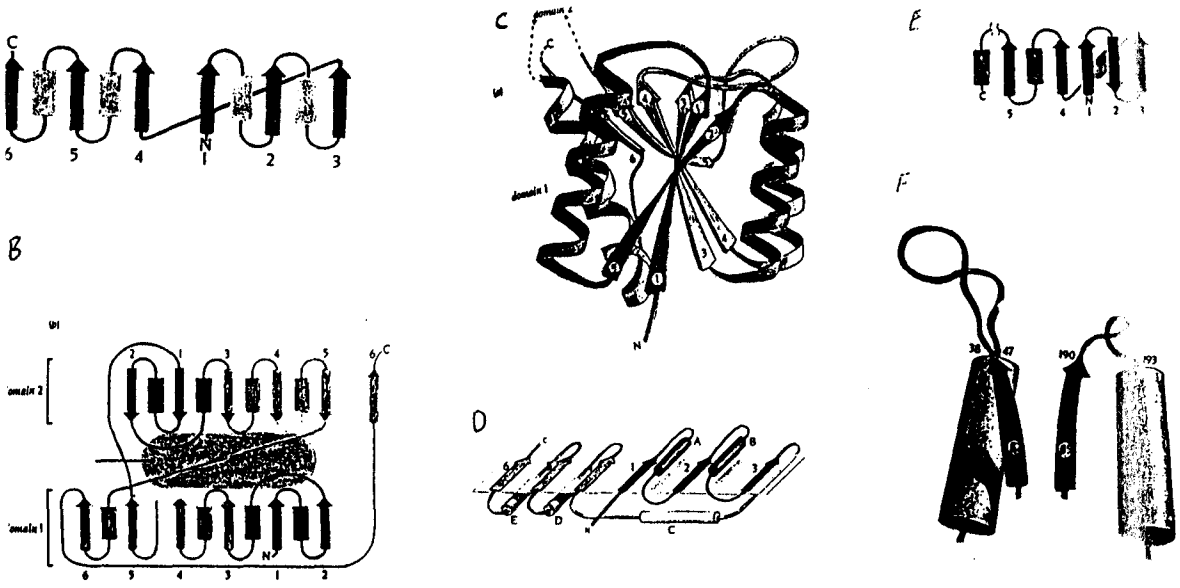
2 3. What is the biological significance of the polyproline helix?

6 4. Different types of helical secondary structure are possible including α–, 3_{10}, and π–helices. Give a full description of an α-helix including parameters such as the helical repeat.

2 5. Give a reason why it might be misleading to describe *loop structures* as secondary structure.

1 6. Is it possible for a β-strand to occur as an isolated ribbon or must it always occur paired with another β-strand?

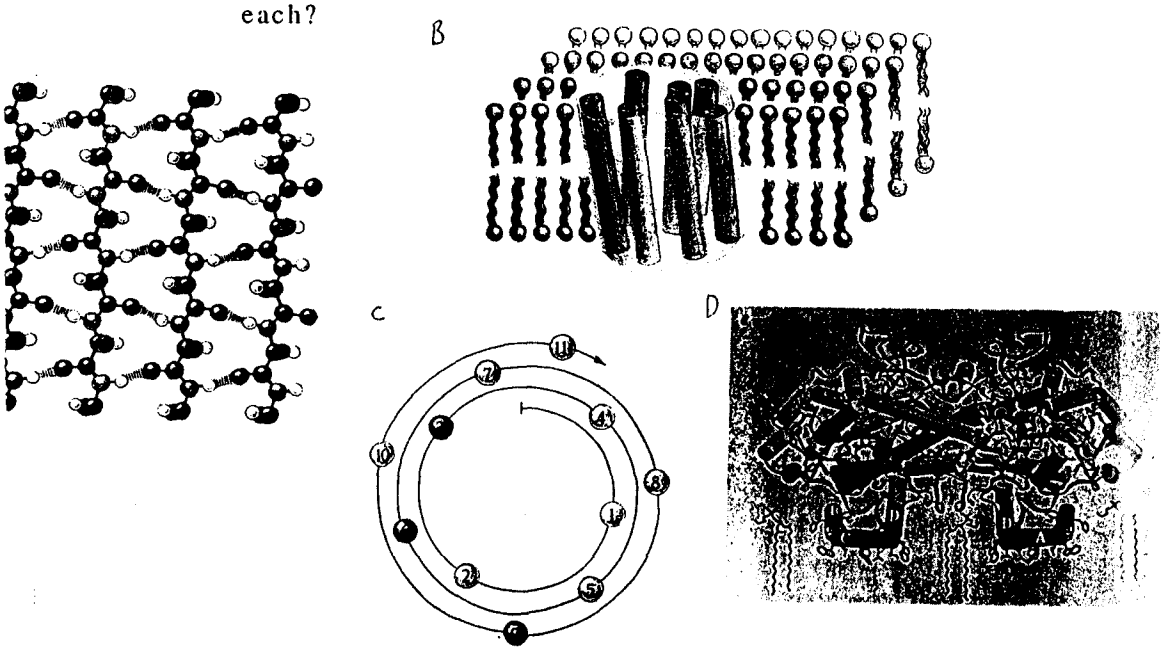
9 7. Identify the *topological switch points* in the following structures: What is the significance of *topological switch points*?



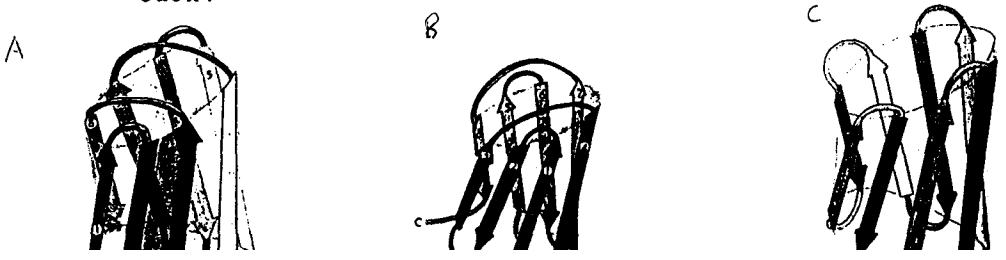
3 8. Describe the "globin fold".

7 9. The globin fold occurs in nearly all living cells with amino acid sequence homologies ranging from 16% to 99%. The 3D structures of these molecules are virtually identical. Discuss.

12 10. Identify the following structures. What are the main features of each?



12 11. Identify the following structures. What are the main features of each?



3 12. Explain the advantage of using molecules such as H_2 and CH_4 as analogues of amino acids in the measurements of side chain hydrophobicity.

5 13. In attempts to understand the origin of introns explain why it is important to distinguish between *ancient* and *modern* proteins.

5 14. Is it possible for a 200 amino acid protein to search all possible conformations until it reaches its global energy minimum?

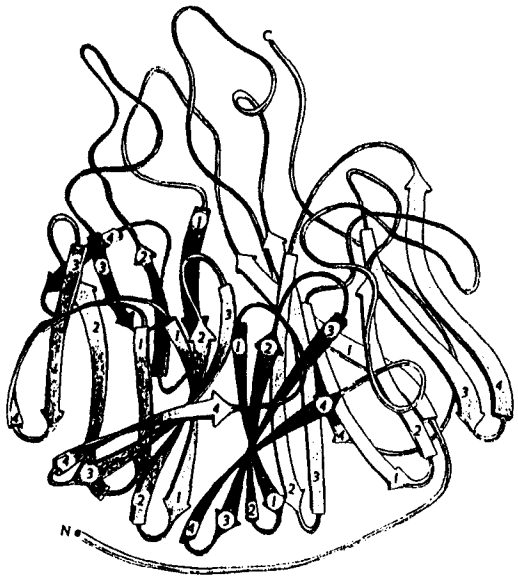
5 15. Explain the hydrophobic effect and its role in protein folding.

5 16. Describe the *biased random search* mechanism of protein folding. Explain how this proposal relates to the *hydrophobic zipper* and *molten globule* hypotheses for protein folding.

8 17. Explain how a "stopped-flow" apparatus is used to measure protein folding / unfolding kinetics. What is the main conclusion about protein folding that this method has uncovered?

5 18. Explain how proline isomerization may complicate the kinetics of protein folding.

10 19. The structure of the enzyme neuraminidase from influenza virus is shown below. Give a full description of the structure, including the secondary structure, motifs, and quaternary structure. Use your own diagrams where appropriate.

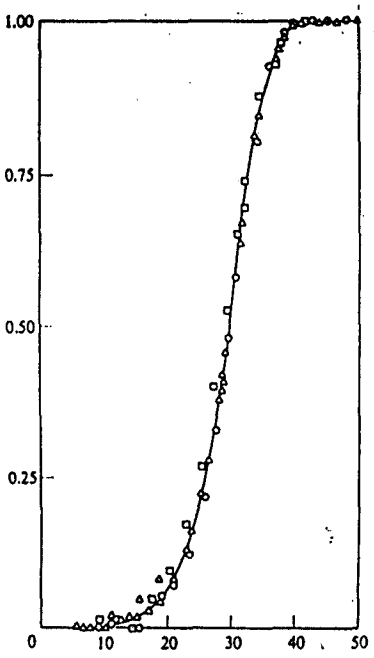


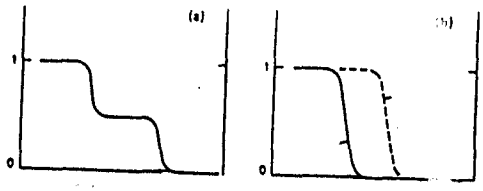
Section 2: *Answer 1 of the following questions in* Section 2. *You can spend about 1/2 hour on this question.*

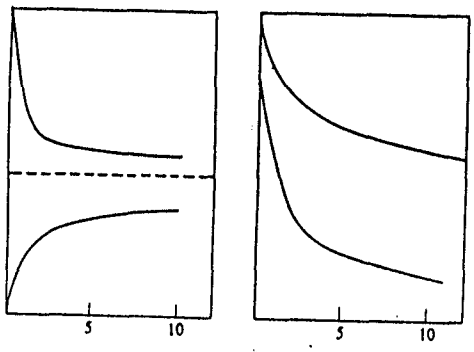
20 20. Describe the molten globule hypothesis **and** the hydrophobic zipper models of protein folding. Discuss the evidence which suggests that each model may correctly describe protein folding.

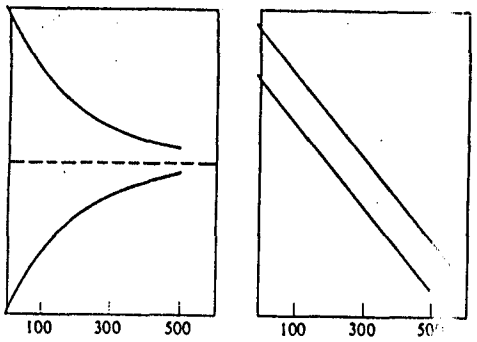
OR

20 21. Using the graphs below describe several methods for the detection of equilibrium and kinetic intermediates in the folding pathway of a protein. To make proper use of the graphs you must label them. Show examples of experiments which would support the *frame work model* and others which would support folding by *modular assembly.*









133