THE UNIVERSITY OF MANITOBA

Seat # 92 - 128 | E2-229 EITC | Final Examination

CHEM 4630 | Biochemistry of Proteins | Examiner: Dr. J. O'Neil

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*Please put **all** your answers in the exam booklets. There are no optional questions. The total number of marks is 163 so you can spend about 10 minutes on a 10-mark question.*
*Wherever possible **use diagrams and chemical structures** to enhance your answers.*

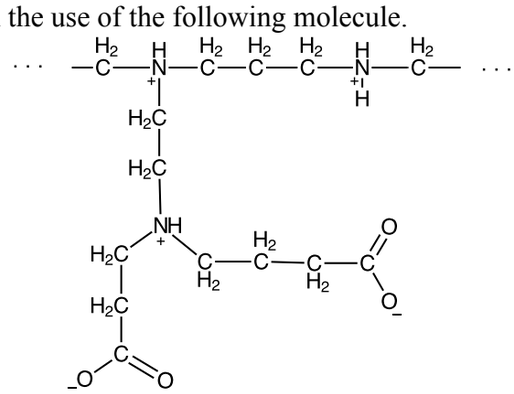
Marks

8 1. With the use of the following table of amino acid masses deduce the sequence of the peptide that generates the following fragment ions in a tandem CID spectrum.

Ala	71	Arg	156	Asn	114
Asp	115	Cys	103	Glu	128
Gln	129	Gly	57	His	137
Ile	113	Leu	113	Lys	128
Met	131	Phe	147	Pro	97
Ser	87	Thr	101	Trp	186
Tyr	163	Val	99		

The mass of the parent ion is 580 Da. The fragment ions have masses of 400 Da, 301 Da and 188 Da. It may be helpful to know the masses of the atoms:
H = 1 Da, C = 12 Da, N = 14 Da, O = 16 Da, S = 32 Da.

5 2. Briefly explain the use of the following molecule.



6 3. What are "*deletion peptides*" in solid-phase peptide synthesis? How do they affect the purity of the final product of a synthesis?

10 4. Describe the structure and function of snow-flea antifreeze protein and explain how solid-phase peptide synthesis contributed to our understanding of the protein.

10 5. What is circular dichroism spectropolarimetry? What are the meanings of the symbols in the following equation? What information does it convey about proteins?

$$\Delta\varepsilon_{protein} = x\Delta\varepsilon_{\alpha} + y\Delta\varepsilon_{\beta} + z\Delta\varepsilon_{t} + r\Delta\varepsilon_{i}$$

8 6. Describe the process by which protein structures are determined by cryoelectron microscopy. What are some benefits of the method in comparison to X-ray diffraction?

4 7. Draw a water molecule and a peptide bond and their associated dipole moments.

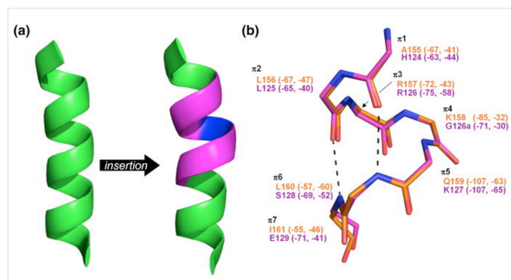
8 8. Draw the chemical structure of the tetrapeptide His-Ala-Asp-Phe at pH 7. Label the backbone and side-chain dihedral angles that describe the conformation of the Ala.
Give a definition of the ϕ dihedral angle.

Marks

8 9. What information did V. N. Ramachandran use to construct his Plot? Draw a Ramachandran Plot and label the locations of the most compact and the most extended conformations for proteins made of *L*-amino acids.

8 10. Define the pitch, rise and repeat of a helix. What are these values for an α-helix?

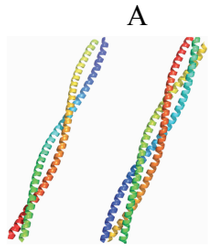
10 11. With the use of the following diagram describe the structure, function and evolution of the π-helix.



3 12. Draw a simple diagram and explain how two α-helices can pack orthogonally.

10 13. With the use of the following diagrams describe the structure and functions of coiled-coils.

A



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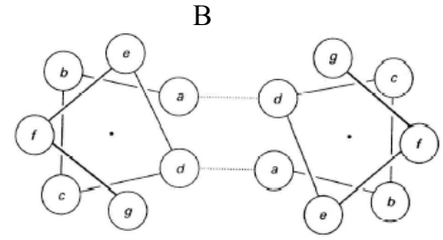
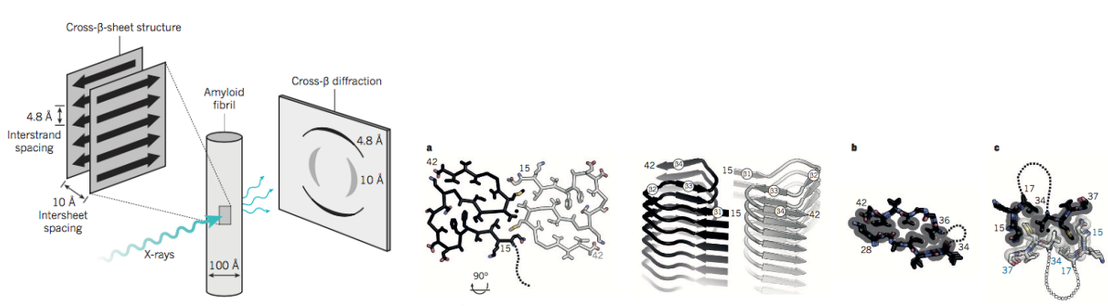
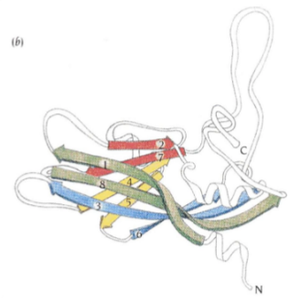


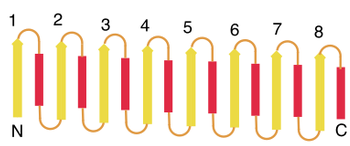
10 14. With the use of the following diagrams comment on the structure of amyloid β-fibrils.

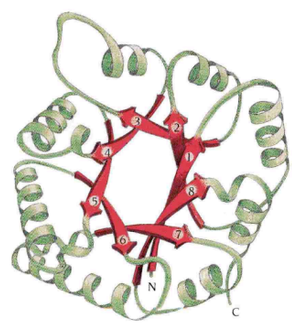


10 15. Draw a Greek Key motif. Draw a diagram and explain the H-bonding partners in a Jelly Roll/Swiss Roll β-barrel. With the use of the following diagram comment on the relationship between drug design, immune evasion and the structure of the icosahedral viral coat proteins.



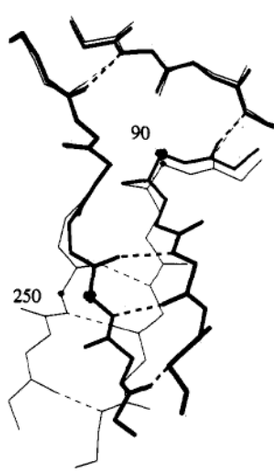
10 16. Describe the structural features and function of one protein with the illustrated motifs, topology and structure:

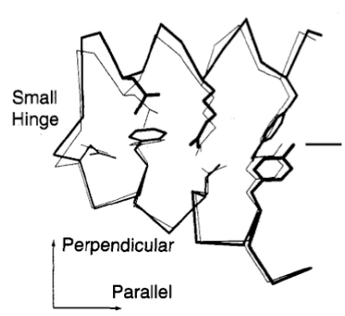




3 17. Describe 3 features that predict proteins to be intrinsically disordered.

5 18. With the use of the following diagrams, describe two mechanisms by which low energy conformational changes can take place in proteins.

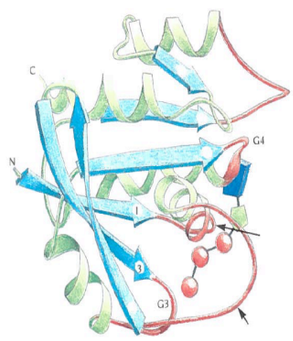




Marks

15 19. With the use of the following diagrams, describe the conformational changes that takes place during the hydrolysis of GTP by the Ras GTPases.

A



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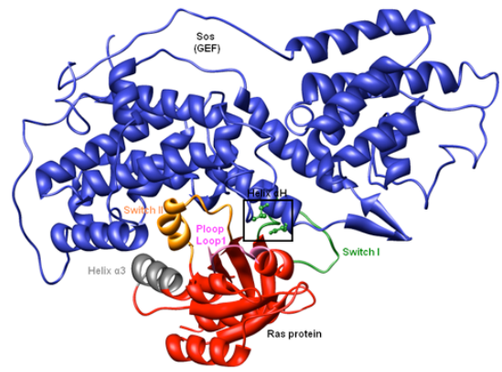

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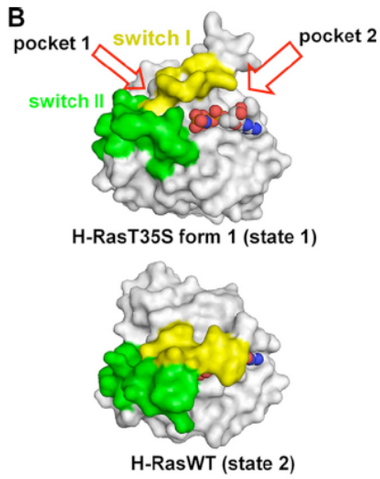

7 20. Briefly outline how classical molecular dynamics calculations are carried out for proteins and what, in general, has been learned from them. You may find the following equation helpful.

$$E = \sum_{bonds} \frac{a_i}{2}(l_i - l_{i0})^2 + \sum_{angles} \frac{b_i}{2}(\theta_i - \theta_{i0})^2 + \sum_{torsions} \frac{Vn}{2}(1+\cos(n\omega - \gamma)) + \sum_{i=1}^{N} \sum_{i \neq j}^{N} 4\varepsilon_{ij}[(\frac{\sigma_{ij}}{r_{ij}})^{12} - (\frac{\sigma_{ij}}{r_{ij}})^6] + \frac{1}{2}\sum_{i=1}^{N} \sum_{i \neq j}^{N} \frac{q_i q_j}{r_{ij}}$$

5 21. What are the meanings of the symbols in the following equation? What are RMSD calculations used for?

$$RMSD = \sqrt{\frac{1}{N} \cdot \sum_{i=1}^{N} \delta_i^2}$$