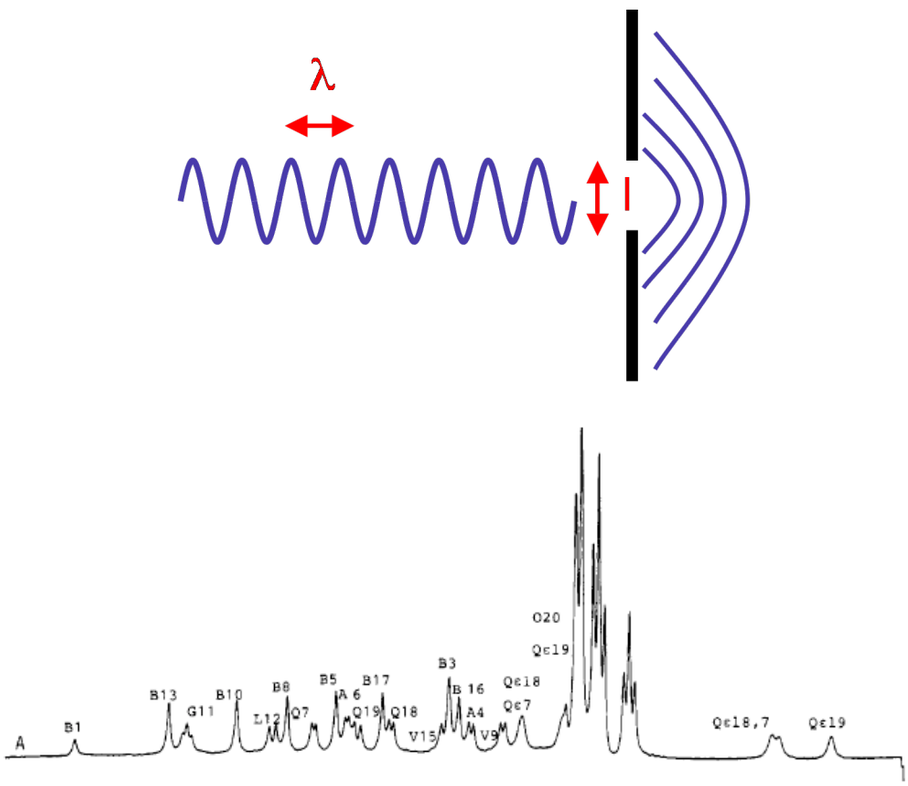

Section 1: *You must answer all of the following questions in* Section 1. *As a guide you can spend up to 2 hours and 30 minutes on this part of the exam. Wherever possible* ***use diagrams and structures*** *to enhance your answers.*

Marks

8 1. Draw the chemical structure of the tetrapeptide Ala-Glu-Ala-Asp at pH 2. Label the backbone dihedral angles that describe the conformation of the peptide. Such a short peptide will exist in dynamic equilibrium between many different conformations. What do you think is the most stable conformation for the backbone of this peptide at pH 2? Explain your reasoning.

6 2. Human Brain contains a *D*-amino acid oxidase that oxidizes all *D*-amino acids except *D*-Glu and *D*-Asp. The enzyme is a flavoenzyme and has been linked to Schizophrenia. It belongs to the (α+β) class of proteins and forms a dimer. Explain what structural features of enzymes in general enable them to distinguish between chiral substrates. Predict the specificity of a synthetic amino acid oxidase made of all *D*-amino acids.

8 3. With the use of **one** the following diagrams, outline how X-ray diffraction **OR** NMR spectroscopy can be used to obtain structural information about proteins and what sort of structural information is obtained.



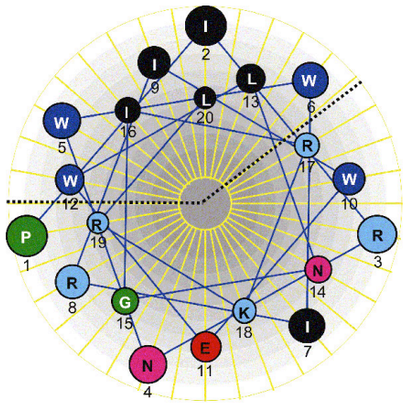
8 4. Name and describe the four levels of protein structure.

8 5. Draw and label a Ramachandran diagram and indicate the location of the left- and right-handed α-helix, parallel and anti-parallel β-sheet, the polyproline helix and the right handed 3_{10} helix.

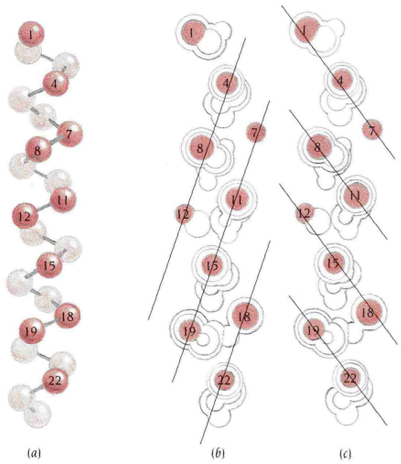
8 6. Give a complete description of the polyproline helix. Briefly describe two different functions of the polyproline helix.

Marks

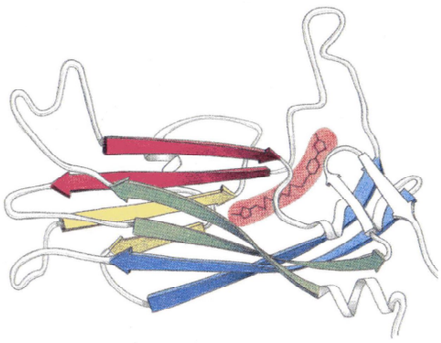
5 7. What features of a protein are depicted in the diagram below and what is the potential use of such a diagram?



6 8. With the use of the following diagram describe two forms of α-helix packing.



6 9. With the aid of the diagram below describe the relationship between the structure of the rhinovirus VP2 coat protein and its interactions with antibodies.



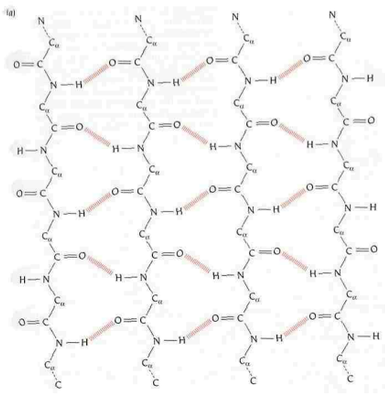
8 10. Explain the concept of Fluorescence Resonance Energy Transfer. Speculate on how it might be used to measure protein *dynamics*.

6 11. With the use of diagrams describe two different types of structure that can be formed from β–α–β motifs.

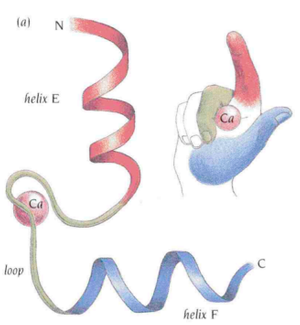
Marks

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

A



B



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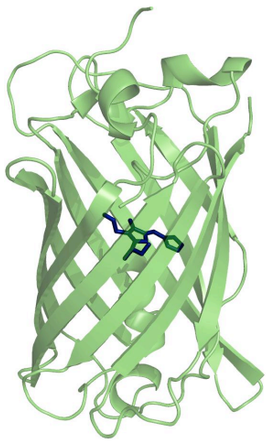

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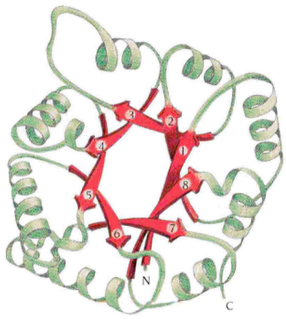

8 13. The Table below shows a measure of the hydrophobicity of the amino acid side-chains. Explain how these values were obtained. Specifically explain why some numbers are large and positive, some are negative, and one measurement is zero. Explain how such values could be used to construct a "*hydropathy*" plot for a protein. What do "*Kyte-Doolittle Hydropathy Plots*" reveal about the structures of some proteins?

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		

1 14. What type of structure surrounds the *special pair* of chlorophylls in the photosynthetic reaction centre?

1 15. What structural feature is shared by the *E. coli* OpmF porin and the soluble retinal binding protein?

8 16. Using diagrams, briefly describe the four classes of membrane protein structures.

Marks

5 17. Over what timescale do biologically important protein conformational changes take place? What range of distances can atoms in proteins move over these times? What is the timescale of Brownian motion? What is the connection between Brownian dynamics and biologically significant conformational changes?

4 18. What is meant by "*Contact Order*" and how is it related to protein folding?

4 19. What is a "*Molten Globule*"?

5 20. A simple model of protein backbone conformation would allow amino acids to exist in only two conformations – the α-helix and β-sheet. According to such a model, how many different backbone conformations are possible for a 200 amino acid protein? How many conformations would be possible if, in addition to the two backbone conformations, each side-chain could exist in two different conformations? Explain the Levinthal Paradox.

6 21. Some *natively unfolded proteins* are biologically active yet disordered. List three possible advantages over folded proteins.

Section 2: *Answer Question 22* ***OR*** *Question 23. You can spend about 10 min. on this question.*

10 22. Outline how combinatorial peptide synthesis can be used to solve problems in drug development.

OR

10 23. Explain how the program ROSETTA was used to design a novel protein.

Section 3: *Answer Question 24* ***OR*** *Question 25. You can spend about 15 min. on this question.*

15 24. Describe the role of the Protein Disulphide Isomerase **OR** the Chaperonin complex in protein folding.

OR

15 25. Describe the factors that contribute to the stability of short α-helices in proteins whereas homopolymers, such as polyglutamic acid, only form stable α-helices if they are composed of hundreds of residues.

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