BIRKBECK COLLEGE

(University of London)

Advanced Certificate in Principles in Protein Structure

MSc Structural Molecular Biology

Date: Thursday, 1st September 2011

Time: 3 hours

You will be given a start time with your exam instructions

Students will be required to answer 10 out of 15 questions.
All questions carry 10 marks each.

Each question must start on a new page and the question number written at the top of each sheet.

1. Proteins have many functions. Give a brief overview of this diversity using five different proteins. {2 Marks each}.

2. Answer all parts;

   a) What is the CORN law? {2 Marks}.

   b) Name the two sulphur containing amino acids. {1 Mark}.
   How can one of these form a covalent bond? {1 Mark}.

   c) Name three aromatic amino acids. Where would you expect to find them located in a globular protein structure? {3 Marks}.

   d) Describe the peptide bond. Indicate the difference between trans and cis peptide bonds. {3 Marks}.

3. a) Draw a Ramachandran plot and indicate secondary structure regions. {5 Marks}.

   b) Use this Ramachandran plot to explain why glycine and proline are structurally important in globular proteins. Indicate a possible location for a Gly and Pro residue in a polypeptide chain. {5 Marks}.

4. For each of the following;

   a) Describe a reverse turn. What is the feature that distinguishes a type I from a type II turn. {4 Marks}.

   b) Indicate in detail the properties of an alpha helix. What can cause an alpha helix to be bent? {4 Marks}.

   c) How are the Greek key motifs arranged in gamma crystallin? {2 Marks}.

5. Discuss the eight headings you would consider while undertaking critical reading of a research paper. {10 Marks}.

6. a) Describe the main difference in tertiary structure between a beta-barrel domain and a beta-sandwich domain. {6 Marks}.

   b) Describe the structure of an enzyme that has a TIM beta/alpha barrel. {4 Marks}.

7. How can the modular architectures of polypeptide chains be exploited for cell signalling? {10 Marks}.

8. Explain how the similarity scores for amino acids in the BLOSUM matrices are used in calculating the best alignment of a pair of protein sequences. {4 Marks}.

   For each of the below give one reason why you would expect:

   A much higher score in any given BLOSUM matrix for matching a pair of Trp residues than for matching a pair of Ala residues. {2 Marks}.

   A high score for matching Phe with Tyr in the same matrix. {2 Marks}.

   A negative score for matching Leu with Asp in the same matrix. {2 Marks}.

9. a) Illustrate how an anti-parallel beta sheet can form both sides of the interface region of a protein homodimer. {3 Marks}.

   b) Draw a diagram of an asymmetric object organized as a trimer with cyclic symmetry. {3 Marks}.

   c) In general terms, what is the main difference between interface regions in dimers and trimers? {4 Marks}.

10. a) List four steps between the production of the primary RNA transcript and the synthesis of a eukaryotic protein. {2 Marks}.

b) What determines the stability of a cytoplasmic protein? {4 Marks}.

c) How does a cell respond to a misfolded cytoplasmic protein? {4 Marks}.

11. Draw or describe the geometry of each of the following inter-atomic interactions as they are found in protein structures, and explain how each arises in simple chemical terms:

a) Hydrogen bonds. {4 Marks}.

b) Van der Waals interactions. {3 Marks}.

c) Ion pairs. {3 Marks}.

12. What, in the most general terms, is the type of reaction that is catalysed by a protease? Which top-level class in enzyme classification includes the proteases? {2 Marks}.

Describe the catalytic mechanism of action of a serine protease such as trypsin. Include in your answer the function of the following parts of the enzyme active site:
The catalytic triad
The oxyanion hole
The specificity pocket
{8 Marks}.

13. a) Draw an oxygen dissociation curve for haemoglobin. {2 marks}.

b) Describe how the molecular structure of haemoglobin causes this kind of binding. {8 Marks}.

14. Describe in detail, or draw, the structures of **any two** of the three membrane proteins listed below. Describe the function of your two selected proteins briefly. {5 Marks each}.

a) The photosynthetic reaction centre of a purple bacterium such as *Rhodopseudomonas.*

b) The potassium leak channel (a voltage-gated potassium channel).

c) A porin from *E. coli.*

15. a) Draw or describe the interaction between a MHC class I molecule, a peptide and the co-receptor that leads to the binding of a T cell to an antigen presenting cell. Indicate the positions of the cell membranes and name the co-receptor involved. {8 Marks}.

b) Name the fold that occurs in each of the proteins in this complex. What type of super-secondary structure does it contain? {2 Marks}.