SBT 5107 – BIOMOLECULAR INTERACTIONS

CAT

ATTEMPT ALL QUESTIONS

TIME: 1 Hour

(a) Sequence analysis in the Human Genome Project has identified a new class of proteins with hitherto unknown properties. List the different biophysical techniques (at least three) that might be used to investigate the folding stability and interactions of these proteins in solution. In each case describe the theoretical basis of the method and indicate how thermodynamic information may be derived.

[9]

(b) Thermal stability studies of one of the proteins in this family have given the following (partial) thermodynamic data for unfolding of the protein in aqueous solution at pH 7.4 at different temperatures:

t /°C	K	$\Delta G°$ /kJ mol^{-1}	$\Delta H°$ /kJ mol^{-1}	$\Delta S°$ /J K^{-1} mol^{-1}
35	0.28	3.26	75.0	?
40	?	2.02	100.0	?
45	?	0	125.0	392.9
50	2.85	?	150.0	?

(i) Complete this table by supplying the missing data (?) where possible.

(ii) What fraction of the protein molecules would be unfolded at 40, 45 and 50°C, respectively, under these conditions ?

(iii) What does the temperature dependence of the unfolding enthalpy (ΔH°) suggest about the forces responsible for stabilizing the folded protein conformation ?

[10]

(c) What is the "Levinthal Paradox" in the context of protein folding ? Describe how it arises and discuss its implications for the mechanism of protein folding.

[6]

[Gas constant $R = 8.314$ J K^{-1} mol^{-1} ; zero of the Celsius scale = 273.15 K]

(d) Discuss briefly what effects might be relevant in designing a drug for delivery across biological membranes and how this might be studied experimentally with simple model systems. [6]

END