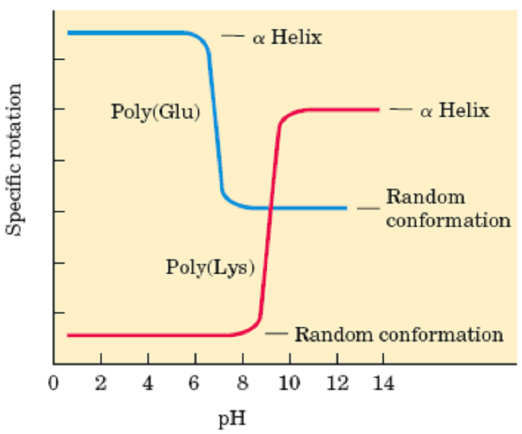
BIRLA INSTITUTE OF TECHNOLOGY AND SCIENCE, PILANI
BIO C331, BIOPHYSICS
FIRST SEMESTER 2009 – 2010
COMPREHENSIVE EXAMINATION (CLOSED BOOK)
Full marks: 120 (Weightage: 30%) DATE: 02.12.09 DURATION: 3 Hrs.

- **Answer to the point**
- **Irrelevant answer may attract penalty**
- **Steps in each calculation carry marks**
- **Answer PART-A and PART-B in separate answer paper**

PART-A

1. a) Hair grows at a rate of ~20 cm/yr. All this growth is concentrated at the base of the hair fiber, where α-keratin filaments are synthesized inside living epidermal cells and assembled into rope-like structures. The fundamental structural element of α-keratin is the α-helix. Assuming that the biosynthesis of α-helical keratin chains is the rate-limiting factor in the growth of hair, calculate the rate at which peptide bonds of α-keratin chains must be synthesized (peptide bonds per second) to account for the observed yearly growth of hair. **[4]**

b) The unfolding of the α-helix of a polypeptide to a randomly coiled conformation is accompanied by a large decrease in a property called its specific rotation, a measure of a solution's capacity to rotate plane-polarized light. Poly-glutamate, a polypeptide made up of only L-Glu residues, has the α-helical conformation at pH 3. When the pH is raised to 7, there is a large decrease in the specific rotation of the solution. Similarly, poly-lysine (L-Lys residues) is an α-helix at pH 10, but when the pH is lowered to 7 the specific rotation also decreases, as shown by the following graph. What is the explanation for the effect of the pH changes on the conformations of poly-(Glu) and poly-(Lys)? Why does the transition occur over such a narrow range of pH? **[3]**



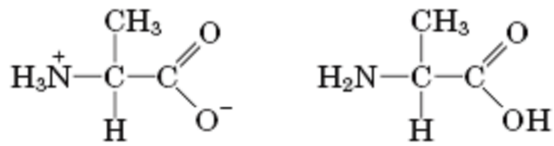
c) Draw Ala-Val-Ala with LDL configuration on C-alpha atoms, with all *cis* peptide bonds and *trans* phi (ϕ) and psi (ψ) torsion angles. **[4]**

d) If you conduct a database analysis of DNA binding proteins, which type of residues would you expect to be in the vicinity of DNA backbone and which residues would you expect to interact with DNA bases? Justify your answer. **[2]**

e) Comment on the nature of α-helix formed by following sequence. Justify your answer**.** **[3]**
ASP VAL ALA GLY HIS GLY GLN ASP ILE LEU ILE ARG LEU PHE LYS SER

f) Compare the stability and instability factors of α-helices and β-sheets. **[4]**

2. a) At a pH equal to the isoelectric point of alanine, the *net* charge on alanine is zero. Two structures can be drawn that have a net charge of zero, but the predominant form of alanine at its pI is zwitterionic.



Zwitterionic Uncharged

(i) Why is alanine predominantly zwitterionic rather than completely uncharged at its pI?
(ii) What fraction of alanine is in the completely uncharged form at its pI? Justify your assumptions. **[2+3]**
b) Write notes on weak interactions within biomolecules. **[5]**
3. a) What could be the reasons for the occurrence of more frequent β-turns than γ-turns in nature? **[3]**
b) The cells of many eukaryotic organisms have highly specialized systems that specifically repair G–T mismatches in DNA. The mismatch is repaired to form a G≡C (not A=T) base pair. Can you suggest why cells might repair a G-T mismatch to form a G≡C? **[3]**
c) Draw the preferred path of conversion of C2'-endo sugar to C3'-endo sugar in DNA. Why this path is preferred? Justify your answer with proper diagram. **[5]**
d) Why do you think C2'-endo and C3'-endo sugar pucker does not appear in the same DNA molecule very frequently? **[3]**
e) Write short notes on following
(i) Keto-enol tautomerism in nucleic acid bases **(ii)** Hoogsteen pairing **(iii)** DNA supercoiling **[6]**

4. a) Bacteriorhodopsin is a very common membrane-spanning protein. The single polypeptide chain of Bacteriorhodopsin folds into seven hydrophobic α- helices, each of which traverses the lipid bilayer roughly perpendicular to the plane of the membrane (~4.5 nm in thickness). What could be the minimum number of amino acid residues required to form a single chain of Bacteriorhodopsin. Comment on the folding mechanism of this membrane protein. **[2+3]**
b) Lipid bilayers formed between two aqueous phases have this important property: they form two-dimensional sheets, the edges of which close upon each other and undergo self-sealing to form liposomes. **(i)** What properties of lipids are responsible for this property of bilayers? Explain. **(ii)** What are the consequences of this property for the structure of biological membranes? **[2+2]**
c) What is the major driving force of micelle formation? **[1]**

5. a) What is protein folding problem ? Why it is not solved in last 30 years? **[2]**
b) Why do you think hydrogen bond and disulphide bond formation could not possibly be the driving forces of protein folding? What do you think the driving force of protein folding and why? **[2+3]**
c) Write notes on
(i) Molten globule states **(ii)** Kinetically Trapped protein **(iii)** Levinthal's Paradox **[6]**
d) In different protein folding theories, how is short range interactions accounted for? **[4]**
e) Draw and explain folding funnel in context of "new view" of protein folding theory. **[3]**
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PART-B

1. a) Discuss the basic features of Porod-Kratky model. If the end-to-end distance vector is related with the persistence length as

$$\frac{\langle r^2 \rangle}{L_c} = 2aL_c\left[1-\frac{a}{L_c}\left(1-\exp\left\{-\frac{L_c}{a}\right\}\right)\right]$$

Then discuss the behavior of this chain in the limit large L_c and for the case $L_c << a$.

b) What is the relation between the radius of gyration with end-to-end distance vector.

c) What is the probability of forming a helix from a chain containing 3 peptides? Justify your answer. **[1+6+2+1]**

2. (a) State two differences and similarities between the zipper model for helix-coil transition in polypeptide and dsDNA. **[2+2]**
(b) Discuss the Zipper model (mention three major points/assumptions) for dsDNA and find out the partition function of dsDNA. **[3+3]**

3. a) How the optical tweezers are useful in studying the various physics properties of biopolymers? Discuss two major points**.**
b) Using proper diagram**,** discuss (*three major points*) the unzipping (Y-shape) of dsDNA chain.
c) What is the minimum X-ray wavelength produced by 40 keV electrons if

$$h = 6.64 \times 10^{-34}\ \text{Js}$$

[2+6+2]

4. Define the persistence length. If l is the bond length and C_∞ is the characteristic ratio of the chain, prove that the persistent length, a, is

$$a = \frac{l}{2}(C_\infty + 1)$$

[2+8]

pK_a Table for natural amino acid

Amino acid			**pK_a of α-CO_2H**	**pK_a of α-NH_3^+**	**pK_a of side chain**
Alanine	Ala	A	2.4	9.9	
Arginine	Arg	R	1.8	9.0	12.5
Asparagine	Asn	N	2.1	8.7	
Aspartate	Asp	D	2.0	9.9	3.9
Cysteine	Cys	C	1.9	10.7	8.4
Glutamate	Glu	E	2.1	9.5	4.1
Glutamine	Gln	Q	2.2	9.1	
Glycine	Gly	G	2.4	9.8	
Histidine	His	H	1.8	9.3	6.0
Isoleucine	Ile	I	2.3	9.8	
Leucine	Leu	L	2.3	9.7	
Lysine	Lys	K	2.2	9.1	10.5
Methionine	Met	M	2.3	9.8	
Phenylalanine	Phe	F	2.2	9.3	
Proline	Pro	P	2.0	10.6	
Serine	Ser	S	2.2	9.2	
Threonine	Thr	T	2.1	9.1	
Tryptophan	Trp	W	2.5	9.4	
Tyrosine	Tyr	Y	2.2	9.2	10.5
Valine	Val	V	2.3	9.7	