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Self-assessment quiz for young scientist interested in autumn school "Biomolecular Structure and Function – Computational Approaches"

Answers

1. The second law of thermodynamics predicts for the interior of the isolated box that it will tend to maximize entropy. Organisms on the other hand are typically characterized by high order, i.e. low entropy. Thus, after a long time we should expect that the organisms no longer live.
2. In water, the charges are partially shielded by the water dipoles. This can be roughly described by the dielectric constant εr of about 80. Thus, we have in vacuum the energy Evac=-e2/(4πε0r) and in water Ewat=-e2/(4πε0εrr), with elementary charge e, vacuum permeability ε0 and distance r between the charges. Evac/Ewat=εr=80.
3. Heparin is a strongly O-sulfonated carbohydrate. This means that it is strongly negatively charged. Positively charged patches on heparin binding proteins is therefore a plausible evolutionary solution.
4. Charges are strongly attracted by the highly polar water. Conversely, the inner of soluble proteins usually is unpolar. This means that you slide down a (free) energy hill if you move a charge from the interior to the exterior such a protein.
5. A flexible ligand that moves freely in solution has a high entropy (it can rotate more or less freely around its torsion axes). If the ligand binds to a protein, these rotations will be impeded and entropy lost. This loss of entropy is equivalent to an unfavorable contribution to binding energy. Rigid ligands do not lose this entropy on binding.
6. IENVKAKIQDK follows a pattern of hydrophobic (h) and polar (p) amino acids of hpphppphppp. With 3.6 amino acids per winding of an alpha helix, the 'h' residues could be accommodated on a hydrophobic face of such a helix. For a beta strand, one would expect other patterns, such as hphp... etc.
7. By using protein BLAST to search for sequences, you will find that the sequence may be a part of the amino acid sequence of a ubiquitin protein.
8. A good method to solve this problem is the Smith-Waterman algorithm (or similar algorithms) that performs a optimal local sequence alignment.
9. There are many ways of giving approximate solutions to this problem. If we take e.g. a protein such as Crambin (PDB entry 1crn), we find that it has 327 non-hydrogen atoms in 46 amino acids. This suggests that a protein of 5000 non-hydrogen atoms has about 46*5000/327 = 703 residues. You can check this in the PDB by searching for proteins with chains of about 700 residues and looking at their atom numbers. Pseudo code example:
   xmean = sum over all atoms of (xatom) / Natoms
   ymean = …
   zmean = …
   for all atoms
   rad2atom = (xatom – xmean)^2 + (yatom – ymean)^2 + (zatom – zmean)^2
   proteinradius = sqrt(Max over all atoms rad2atom)

10. By computational modeling you can at best provide plausible predictions. In the end, it is always experiment that has to tell what is real.