Revision Übung GST

1 Feb 2011

Look for anything that is difficult.

Make sure you can do a simple derivation (Herleitung) for questions like 6.

Check that you have short and correct answers to questions like 14 and 15.

1. As a chemist, you would expect ΔG to refer to some reaction. What is the relevant reaction in protein folding ?
2. I define ΔH as the enthalpy change upon a protein folding. Name and explain two different energetic terms which would contribute to this.
3. In the reaction above, I imagine there is something called the "unfolded state". Why is this a simplification ?
4. I can measure the stability of a protein. I change the pH of the system and the protein becomes more stable. Give 2 examples of contributions to the ΔG which could explain this.
5. I have a small molecule which causes a protein to unfold. According to all evidence, the small molecule does not interact with the native protein. How could the small molecule be causing a change in stability ?
6. Given the coordinate of a particle in a harmonic oscillator is $x(t) = A\cos(\omega t + \delta)$ and given that kinetic energy is ½ mv^2, write an expression for the kinetic energy of a harmonic oscillator. Is the energy constant ? If not, is energy still conserved ?
7. I consider the motions within a protein, treating them as harmonic oscillators. I claim that most particles in a protein have similar kinetic energy. Consider the expression for kinetic energy. The relationship of kinetic energy, frequency and amplitude is given by

$$E_{kin} = \frac{1}{2}mv^2 = \frac{1}{2}mA^2\omega^2\sin^2(\omega t + \delta)$$

   Is the kinetic energy really a constant with time ?

   Are the larger amplitude motions associated with the low or high frequencies ?

   Explain.

8. In a harmonic oscillator, the force depends on the coordinates x as in $m\frac{d^2x}{dt^2} = -kx$

   Show that $x(t) = A\cos(\omega t + \delta)$ is a valid solution.
9. If I have a two-state system, what does the frequency of the motions mean ?
10. Why does the frequency of motions increase with increasing temperature in a two-state model ?

11. Why does the frequency of the motions not increase in a harmonic oscillator model ?
12. A crystallographer does not usually speak about harmonic oscillators. They normally use a wave equation, $y(x) = F\cos\left(\frac{2\pi}{\lambda}x + \alpha\right)$. How does this correspond to the harmonic oscillator equation give above ? What are the meanings of α and λ ?
13. Over the course of evolution, which changes faster – protein sequence or structure ? Give a reason why this may be the case.
14. Some protein structure classifications impose a hierarchy on proteins. Why may this be a reasonable thing to do ?
15. Give an argument why a hierarchical classification may not be appropriate for many proteins.
16. Why is it fundamentally difficult to superimpose two protein structures if they are not the same size ?
17. I have two models of one protein, but they are rather different. Describe an algorithm with pseudo-code to find the more similar regions of the structures.
18. You would like to align protein structures of different sizes and you would like to turn the problem into a classic dynamic programming formulation. Describe one method for this.
19. Similarity of protein structures is often measured using the root mean square difference of coordinates. Draw an example to show why this may not be a good measure.
20. Describe a measure of protein similarity which is quantitative (in Å), but is not the root mean square difference (*rmsd*) of Cartesian coordinates. Why may it be better than *rmsd* of Cartesian coordinates.
21. You have built an initial structural model for a sequence. You have a very simple model for the energy of the system. Describe a method to find a reasonable arrangement of side-chains.
22. You want to use distance geometry to generate possible conformations of a loop in a protein. You have endpoints for the loops. Describe how you would cast this into a problem suitable for the metric matrix method.