Protein-urea interactions studied by ^{14}N NMR relaxation and MD simulation of Motilin.

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Abstract

Mixtures of urea- water and a small peptide, Motilin, have been studied using MD simulation techniques as a tool to analyse urea N-14($I = 1$) NMR spin relaxation data. The folded motilin peptide is studied in water and in 8M urea solutions whereas the random coil peptide is studied in 8M urea solution. The description of urea-peptide interactions are discussed in terms of the urea reorientation correlation function and the fraction of perturbed urea. A model for analysing the relaxation enhancement of N^{14} spin relaxation is suggested.

The molecular mechanism whereby urea unfolds proteins has not been established. However, there are many studies which have addressed this problem[1]-[3]. These studies are based on different spectroscopic methods including NMR

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relaxation[1] as well as MD simulations of water/urea/peptide model systems[2]-[3] Is seems as the MD simulations support an indirect and a direct effect of urea with some of the characteristics listed[2]-[3]:

- indirect effect because urea/water mixture appears to better solubilize hydrophobic solutes
- consequently the water/urea solution diminish the hydrophobic interaction thus making proteins more flexible
- new protein sites are hydrated first by water then by urea
- urea residence times around the protein surface is longer than those of water
- urea accumulate around the protein and form more long lived hydrogen bonds with the peptide than water.
- however it is questionable if urea generally act directly by binding to the protein surface

Can N-14 NMR relaxation measurements add anything new to the above points? The accumulated urea display a relatively slow reorientational diffusion and there is an indication of a fraction of invisible urea. That is a fraction of slow exchanging urea molecules which is more tightly bound to the protein. An analysis of the solvent induced perturbing force may shed some new light on the solvent impact on the peptide. We we discuss the NMR relaxation model and the analysis of solvent force correaltion function.

References

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