AVVISO DI SEMINARIO

Giovedì 11 febbraio ore 15,00 nell'Aula Seminari del Dipartimento di Scienze e Tecnologie Chimiche, la

Prof. Frans Mulder
Interdisciplinary Nanoscience Center (iNANO), Department of Chemistry, Aarhus University

Terrà un seminario dal titolo:

NMR under pressure – The roles protein cavities play in oxygen binding, water penetration and conformational fluctuations

Proponente: Dott. Marco Sette
Abstract

Proteins often contain completely buried cavities or active sites, which nonetheless can rapidly bind small molecules. Apparently, due to their flexible nature, protein cavities are dynamically accessible to solvent. We used low pressure (up to 10 bar) gas binding experiments to demonstrate directly the penetration and egress of molecular oxygen from the protein interior. This method is highly sensitive, and allows occupancies on the order of 1% to be accurately determined. We believe that this technique may be valuable for various applications, such as detecting transient hydrophobic binding pockets for fragment-based drug design and engineering fluorescent proteins that are less sensitive to quenching. In a second study, we employed hydrostatic pressure (up to 2500 bar) to study protein conformational exchange. As (partially) folded and unfolded states have different molar volumes, the application of pressure acts as a dial that can be used to change the relative populations of protein conformations, and bring ‘hidden conformations’ into view. As these ‘invisible states’ are accessible within a few kcal/mol from the ground state, they may well have been part of the selection process of evolution, as conformational switching is required for a wide variety of biological processes. I will show how, using NMR spectroscopy, we can provide atomic scale insight in these various dynamics processes.

References

Cavity as a source of conformational fluctuation and high-energy state: high-pressure NMR study of a cavity-enlarged mutant of T4 lysozyme.

Detecting O2 binding sites in protein cavities.
Kitahara R, Yoshimura Y, Xue M, Kameda T, Mulder FAA.