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Title:
Concerted neutron scattering and molecular dynamics simulation studies of membrane protein structure and dynamics

Abstract:

Membrane proteins perform a wide variety of important physiological functions, including energy production and signal transduction. High-resolution structures of membrane proteins determined by crystallographic techniques provide some clues to their function, but they generally do not provide information on the surrounding membrane. This is unfortunate because it is becoming increasingly evident from a growing body of evidence that specific protein-lipid interactions play an important role in membrane protein structure and function. In the first part of this lecture, I will show how neutron diffraction experiments employing selectively deuterated samples can be used in conjunction with molecular dynamics simulations to gain insight into the structure of membrane proteins in lipid bilayers, as well as protein-lipid and protein-water interactions, using the voltage-sensing domain from a voltage-gated ion channel as an example.

Protein motions occur over many decades of time, from femtoseconds to seconds and longer. It is well established that fast (picosecond to nanosecond) atomic fluctuations are usually required for protein function. A large number of experimental and simulation studies have led to the conclusion that the environment of a protein has a profound influence on its dynamics. In the second part of this lecture, I will describe how temperature-dependent neutron spectroscopic measurements on selectively deuterated samples, combined with molecular dynamics simulations, can be used to unravel the coupling between the motions of proteins and their environment on picosecond-nanosecond timescales. Using the maltose binding protein as an example, I will show that soluble protein motions are directly coupled to their aqueous solvent. Using the protein bacteriorhodopsin in its native purple membrane as an example, I will show that the situation is more complicated in membranes, where protein dynamics couple directly to both water and lipid motions.

Suggested reading:

1. D. Krepkiy, M. Mihailescu, J. A. freites, E. V. Schow, D. L. Worcester, K. Gawrisch, D. J. Tobias, S. H. White, K. J. Swartz. Nature 462, 473-479 (2009).
2. D. J. Tobias, N. Sengupta, M. Tarek. Faraday Discuss. 141, 99-116 (2009).
3. K. Wood, A. Frölich, A. Paciaroni, M. Moulin, M. Härtlein, G. Zaccai, D. J. Tobias, M. Weik. J. Am. Chem. Soc. 130, 4586-4587 (2008).
4. K. Wood, M. Plazanet, F. Gabel, B. Kessler, D. Oesterhelt, D. J. Tobias, G. Zaccai, M. Weik. Proc. Natl. Acad. Sci. 104, 18049-18054 (2007).