T_CSUH Bi-Weekly Seminar

Texas Center for Superconductivity at the University of Houston

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Modulation of Calmodulin Plasticity by the Effect of Macromolecular Crowding

Friday, May 22, 2009
Room 102, University of Houston Science Center
12:00 Noon – 1:00 p.m.

Abstract

In vitro biochemical reactions are most often studied in dilute solution, a poor mimic of the intracellular space of eukaryotic cells which are crowded with mobile and immobile macromolecules. Such crowded conditions exert volume exclusion and other entropic forces that have the potential to impact chemical equilibria and reaction rates. In this article, we used the well characterized and ubiquitous molecule calmodulin (CaM) and a combination of theoretical and experimental approaches to address how crowding impacts CaM's conformational plasticity. CaM is a dumbbell shaped molecule that contains four EF hands (two in the N-lobe and two in the C-lobe) that each could bind Ca^{2+} leading to stabilization of certain substates that favor interactions with other target proteins. Using coarse-grained molecular simulations, we explored the distribution of CaM conformations in the presence of crowding agents. These predictions in which crowding effects enhances the population of compact structures were then confirmed in experimental measurements using fluorescence resonance energy transfer techniques of donor/acceptor labeled CaM under normal and crowded conditions. We further explored the folding energy landscape and examined the structural characteristics of CaM at free energy basins using protein reconstruction methods. We discovered that crowding stabilizes several different compact conformations, which reflects the inherent plasticity in CaM's structure. From these results, we suggest that the EF hands in the C-lobe are flexible and can be thought of as a switch, while those in the N-lobe are stiff as analogous to a rheostat. New combinatorial signaling properties may arise from the product of the differential plasticity of the two distinct lobes of CaM in the presence of crowding. We discuss the implications of these results for modulating CaM's ability to bind Ca^{2+} and target proteins.

Bio

Professor Margaret Cheung joined the University of Houston as a junior faculty member in 2006. Research projects include development of physics principles and application of high-performance computing methods for studying various topics in theoretical biophysics, soft condensed matter, and nano-scale materials.

Professor Cheung received her B.S. in Chemistry from National Taiwan University and her Ph.D. in Physics from the University of California, San Diego. She was a Sloan Postdoctoral Fellow in Computational Biology at the University of Maryland.

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