

WEEKLY SEMINAR

Topic: Multi-scale Simulation of Multidrug Transporters

Speaker: Prof. Wenning Wang

Department of Chemistry

Institute of Biomedical Sciences, Fudan University

Time: 15:30-16:30, 4 March, 2014

Venue: Room153, Geography Building, 3663 Zhongshan Road North, Shanghai

(华东师范大学中山北路校区, 地理楼 153 室)

ABSTRACT OF THE TALK

The acquisition of multidrug resistance is a serious impediment to improved healthcare. Multidrug resistance is most frequently due to active membrane transporters that pump a broad spectrum of cytotoxic molecules out of cells. Crystal structures of several families of multidrug transporters have been determined, showing that the transporter proteins undergo large scale conformational changes during the translocation cycles. Here, we explored the conformational dynamics of two families of multidrug transporters, i.e. ATP-binding cassette (ABC) and resistance-nodulation-division (RND) transporters, using multi-scale computational methods. The intrinsic conformational flexibility revealed by coarse-grained normal mode analysis provides the coupling relationships between the conformational changes at different parts of the transporters. The targeted MD simulations revealed the spatio-temporal order of the conformational transitions between different conformational states of the proteins. The timing of the conformational changes depicts allosteric signal transduction pathways across the transporter proteins. Substrate translocation mechanism was also explored by potential of mean force calculation based on all-atom MD simulations.

BIOGRAPHY

Prof. Wenning WANG received her B. Sc. and Ph. D. degrees in the Chemistry Department at Fudan University in 1990 and 1995. She did postdoctoral research at Institute of Molecular Science of Japan and Department of Biochemistry, Hong Kong University of Science and Technology. Now she is a professor at Chemistry Department and Institute of Biomedical Sciences at Fudan University. Prof. Wang's research interests are structural biology and computational biology, including the protein conformational dynamics of large protein complex and membrane proteins, and structural basis of asymmetric cell division and cell polarity.