CIBM SEMINAR SERIES

Computation and **I**nformatics in **B**iology and **M**edicine
Training Program

Qiang Cui, Ph.D.

Assistant Professor
Department of Chemistry
University of Wisconsin-Madison

Molecular Simulations of Mechanochemical Coupling in Myosin

Abstract:

The mechanochemical coupling in the biomolecular motor myosin-II has been analyzed with a combination of simulation methods including a coarse-grained normal mode analysis, molecular dynamics simulations, free energy perturbation and hybrid QM/MM calculations; these methods probed different aspects of the mechanochemical coupling, and the results combined together have yielded new insights into the working mechanism of myosin with atomic level of details.

Both hybrid QM/MM reaction path and classical free energy perturbation calculations indicated that the open-form of the motor domain is not capable of catalyzing ATP hydrolysis, supporting the hypothesis from previous x-ray studies. Energetics based analysis revealed that the activity of hydrolysis is regulated by several residues in the Switch I and Switch II regions; in particular, the conserved salt-bridge between Arg 238 and Glu 459 seems to have both direct influence through electrostatic interactions and indirect effects by modulating the water structure in the active site.

Results from a coarse-grained normal mode analysis including atomic interactions indicated that the large-scale conformational change involved in the Open-Closed transition is highly correlated with the low-frequency normal modes of the motor domain. A remaining question concerns the causal relationship between such elastic type of motion and activities (salt-bridge formation, ATP hydrolysis) at the active site.

Tuesday, September 28th
4:00 p.m.

Genetics/Biotechnology Center Auditorium
425 Henry Mall