Physical Chemistry Seminar

Tuesday,
October 20, 2009

11:00 a.m.

Room 1315
Chemistry Building

Long Time Dynamics of Biomolecules by Milestoning: Application to Myosin

Professor Ron Elber

Department of Chemistry and Biochemistry and
Institute of Computational Engineering and Sciences
The University of Texas at Austin

Myosin II is a molecular machine that converts chemical to mechanical energy and enables muscle operations. After a power stroke, which is a step of obvious functional importance, a recovery transition completes the cycle and returns the molecular machine to its pre-stroke state. Atomically detailed simulations in the framework of the Milestoning theory are used to calculate kinetics and mechanisms of the recovery stroke. Milestoning divides the process to transitions between hyper-surfaces (Milestones) along a reaction coordinate. Decorrelation of dynamics between sequential Milestones is assumed which speed up the atomically detailed simulations by a factor of millions. Two hundred trajectories of myosin with explicit water solvation are used to sample transitions between sequential pairs of Milestones. Collective motions of hundreds of atoms are described at atomic resolution and at the millisecond time scale. The experimentally measured transition time of about a millisecond is in a good agreement with the computed time. The simulations support a sequential mechanism. In the first step the P-loop and switch 2 close on the ATP and in the second step the mechanical relaxation is induced via the relay and the SH1 helices. Secondary structure elements are progressing through a small number of discrete states in a network of activated transitions. Transitions between free energy minima at the secondary structure level are assisted by side chain flips between rotameric states. The few-state sequential mechanism is likely to enhance the efficiency of the relaxation since no off-pathway channels were observed.

Refreshments will be available prior to the seminar at 10:45 a.m. outside room 1315

Graduate Students may meet with the speaker at 1:15 p.m. in Room 8305f