



# **Modeling, Design, and Engineering of Molecular Motors**

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Molecular motors play crucial roles in diverse biological processes ranging from gene replication, muscle contraction to cell division. They convert chemical energy such as energy from ATP hydrolysis cycle into mechanical work. This talk will use two examples to illustrate how one can use computational methods to complement experimental findings in gaining insight into functions of these enzymes.

T7 DNA helicase is an ATPase molecular motor in bacteriophage T7 separating two strands of DNA. It has been a model system for ring-shaped multimeric proteins. A key question for all these ring-shaped proteins is the coordination of enzymatic functions among their multiple subunits. We developed computational tools to test different hypotheses of coordination mechanisms by comparing simulation results with both steady-state and transient kinetic data. We found that all subunits of T7 DNA helicase are active, and they perform enzymatic functions in a sequential mechanism.

Myosin is a large family of ATPase molecular motors conducting diverse mechanical functions. To identify the coupling step of the mechanical motion and its chemical cycle, we developed an efficient computational method to model dwell-time distributions of single molecule experiments. Comparing with optical trapping data, we found the mechanical motion of myosin V occurs after the phosphate release but before the ADP release. We also studied myosin VI, the only known myosin moving toward a direction opposite to all other myosins. We computationally designed and engineered a series of myosin VI with artificial lever arms and test them with in vitro motility assays and optical traps. We found a short alpha helix of 18 amino acids is enough to change the direction of myosin motion.

**FRIDAY, Sept 26, 2008**

**11:00am-12:00pm 614 Schermerhorn**