4bc Multi-Scale Modeling of the Actin Filament: from Allostery to the Elasticity of Cytoskeleton

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The success of developing new biotechnologies and medicinal molecules requires a detailed understanding of the underlying biochemical and biophysical processes. These problems, however, are difficult because properties at different length scales and processes at different time scales are intertwined and cannot be separated. For example, microscopic binding events of small molecules could induce conformational changes of proteins and cause different kinds of cellular responses. Allostery of bio-macromolecules is ubiquitous in the biology of the cell. Understanding the mechanism of protein conformational changes and how such changes affect the properties of bio-assemblies is thus essential in developing biophysical models of cellular processes, such as vesicle transportation and fusion, mitosis, endocytosis, and cell signaling. In this poster, the relationship between the conformation of the protein actin and the properties of actin filament is developed via molecular dynamics simulations and coarse-grained analysis. Actin-filaments can be found in all eukaryotic species, and the growth dynamics of the filament are regulated in many ways in order for the cell to maintain its size, shape, and strength. ATP bound protein actin self-assembles under physiological conditions to form helical filament. After binding, the bound ATP is hydrolyzed into ADP and the growth rates and the mechanical properties of the filament are modulated. ATP hydrolysis induces conformational change at the DNase I binding loop of the protein actin and is essential in regulating the growth dynamics of actin filament. However, the connection between the protein conformation and the macroscopic properties of the filament is not well established, and different scenarios have been proposed to describe such a connection. Using molecular modeling techniques, the allostery of the actin filament can be elucidated at the microscopic level and the connection between protein conformation and the elasticity of the filament can be established. Therefore, multi-scale approaches are useful and necessary in developing biophysical models of the cell. These models are essential in understanding the biology of the cell. They are also important in devising systematic approaches in different fields of bioengineering.