ABSTRACT

Kinesins are motor proteins associated with the intracellular transport phenomena. They translate over protein filaments called Microtubule by the hydrolysis of Adenosine Triphosphate (ATP). Mutations in the kinesin motors are directly linked to neurological disorders. The complex protein structures and broad range of Spatio-temporal scales trigger the requirement of a multiscale approach for a computationally efficient analysis of these mutations.

In our present work we describe our efforts to develop an algorithm to relate the Site-specific mutagenesis of Kinesin 3 and its velocity by using Stochastic Models[1] and Molecular Simulations. The Stochastic Models form the macroscopic base for predicting the Spatio-Temporal potential energy landscape corresponding to the experimental velocities. Molecular simulations[2] form the microscopic basis of the algorithm. They predict the spatial distribution of residues at selected positions of the motor in a particular chemical state. The Generalized Ensembles and the Information Theory based approach called MaxEntropy are used to bridge the macroscopic and microscopic approach. The above strategy helps us to identify the *target residue* and to predict the change in the chemical nature of the target residue that can result in a desired change in the motor velocity. We have demonstrated the algorithm using results for monomeric kinesin KIF1A.The methodology is robust enough to be used for mutagenesis study of other biological systems which could help in various fields ranging from therapeutic application[5] to the development of biologically inspired nanoscale machines[6].