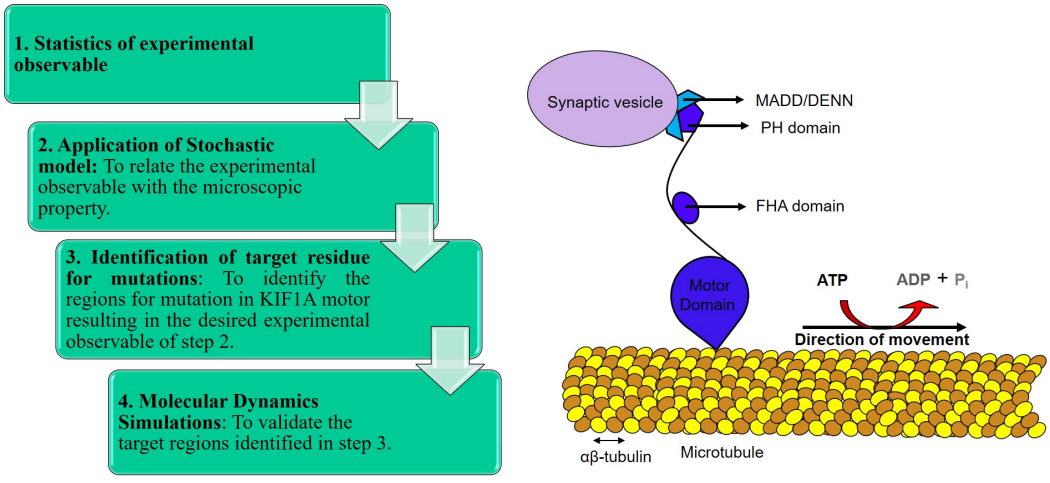
# ABSTRACT

The artificial systems that operate at nanoscales and respond to the changes in their environment can revolutionize several fields, ranging from therapeutics to advanced manufacturing. The critical challenge in rationally designing such nano-machines/nano-engines is to quantitatively relate the phenomena occurring over a broad range of spatial and temporal scales. We are involved in developing computational algorithms to design the above systems rationally. As a step in this direction, we study the biological systems that perform operations similar to the target systems. In the present thesis, we focus on the motor-protein of a Kinesin family that is called KIF1A. Kinesins are microtubule-based motor proteins involved in the transportation of chemical constituents within the cell by using the chemical energy stored in the Adenosine triphosphate (ATP) molecules to translate along the microtubule. Their motion is typically studied via experimental observables like velocity, processivity, and stall-force [28]. We focus on the effect of specific mutations on the translational velocity of the monomeric KIF1A. We start with the application of the stochastic models [49] to determine the response of the motor's translational velocity to the changes in the potential energy (PE) surface of KIF1A. The PE surface of the motor protein is expressed as a function of its position along the microtubule and a suitable reaction-coordinate of the ATP-hydrolysis reaction. We study the response of velocity to the changes in the following features of the PE surface: 1) The maximum possible difference between the PEs at two positions of the motor on the microtubule for a particular stage of ATP-hydrolysis reaction, and 2)

the PE of the transition state that occurs when the ATP bound to KIF1A hydrolyzes to give ADP (Adenosine diphosphate). We observe that the velocity is most susceptible to the PE of the transition state mentioned above, and it is least susceptible to the PE of the motor when it is bound to the ATP. These observations comply with those of the previous theoretical and experimental studies [17]. We then use the structural information of KIF1A to identify the regions in the protein that can be targeted for mutations to validate the above responses experimentally. The study indicates the potential to "tune" the translational velocity of KIFIA by making targeted mutations. Such tunability is very attractive for the development of artificial nanomotors. From an algorithmic perspective, it helps us to identify challenges and to develop methods to quantitatively connect different spatial and temporal scales for the rational design of artificial analogues of biological motors.




(A) (B)

FIGURE 1: a) Schematic representation of the approach to predict mutation on KIF1A motor for desired velocity. b) KIF1A motor-microtubule system