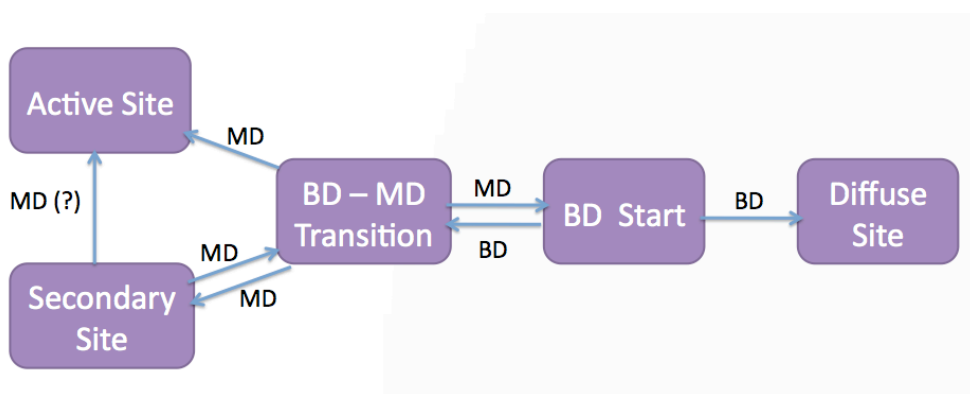


Characterization of the Association between Neuraminidase and Sialic Acid Using Molecular Dynamics Simulations

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Many forms of the influenza virus have been prevalent throughout history, most recently the H1N1 outbreak in 2009. One of the proteins found on the surface of the influenza virus is the tetramer neuraminidase. Neuraminidase is responsible for cleaving sialic acid residues from cellular receptors. This cleavage is an essential role for the success of influenza because it facilitates the release of more viral particles, allowing the infection to spread to neighboring cells. Each neuraminidase monomer contains both an active sialic acid binding and cleavage site and a secondary binding site that has no known function. We are continuously improving upon a comprehensive method to study the association between neuraminidase and its ligands. Our approach utilizes a Markov chain (pictured below), which couples Brownian Dynamics (BD) simulations and Molecular Dynamics (MD) simulations. Our studies are focused primarily on the MD steps between the BD-MD transition surface and the Active Site/Secondary Site. Using input from BD simulations of the ligand approaches, 31 unique starting ligand conformations were selected and simulated using MD. However, the process of generating, simulating, and analyzing MD simulations is extremely labor intensive, so given the large number of simulations required, it was necessary to develop an automated algorithm to handle these tasks. Both our automated algorithm to decrease human intervention as well as our preliminary data produced by this process will be presented.



Markov chain: This figure illustrates the Markov chain. The procedure begins at “BD Start” and ends at either “Diffuse Site” or “Active Site”. The focus of this study is represented by the MD arrows between “BD - MD Transition”, “Active Site”, and “Secondary Site”.