Observing the inter- and intramolecular events of sialic acid binding to the active site of neuraminidase

Bryon J. Banman, Jeremy E. Adelman, Alvin R. Wu, Adam W. Van Wynsberghe

Department of Chemistry, Hamilton College, Clinton, NY 13323

The tetramer neuraminidase is an important part of the influenza virus' replication cycle. Terminal sialic acid residues on host cell surface receptors bind to and are cleaved by neuraminidase, facilitating nascent viral release and allowing subsequent infection. Several competitive inhibitors of neuraminidase, including peramivir, zanamivir, and oseltamivir are currently used as antiviral treatment. To better understand the mechanism by which small molecules bind to the active site we used molecular dynamics (MD) simulations to observe the inter- and intramolecular event that occur upon binding. Trajectories of sialic acid ligands were initiated from six different starting positions with a variety of spatial orientations relative to the active site. Throughout the trajectories, we investigated the specific interactions between active site residues and the functional groups of sialic acid. In addition we looked at which interactions are strongest and thus most important to sialic acid binding.