Observing the diffusion of oseltamivir into the active and secondary sites of the neuraminidase wild type and the H274Y variant

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Neuraminidase acts catalytically to cleave a terminal sialic acid moiety from host-cell surface receptors enabling the release of nascent influenza viruses and subsequent infection of new cells. Therefore, drugs that function as neuraminidase inhibitors represent an attractive way to combat the proliferation of the virus. The effectiveness of the molecular diffusion of these drugs is highly dependent on the specific configuration of chemical structure of the specific variant of neuraminidase, with oseltamivir being the historically popular drug for the inhibition of the wild type neuraminidase. Brownian dynamics simulations were utilized to compare the surface binding distribution of oseltamivir diffusing to the neuraminidase wild type and diffusing into the mutant H274Y variant of neuraminidase in any of four molecular orientations. Investigations and analysis of these Brownian dynamics results highlight the preferred molecular binding pathways of oseltamivir and highlight the differences that the change in chemical structure provides for the binding process. Furthermore, a conjecture can be made for the effectiveness of oseltamivir treatment on the H274Y mutant.

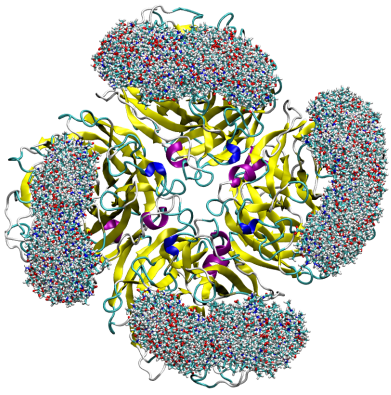

Figure 1: Neuraminidase tetramer with bound oseltamivir