Investigation of Differences in Desolvation Energy Between Ligands

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The spread of the Influenza A virus between cells in the human body is dependent on the viral enzyme neuraminidase. Neuraminidase binds and cleaves terminal sialic acid moieties on cell surface receptors releasing the virus from the infected cell. Many drugs targeting Influenza work by inhibiting the binding of these sialic acids to neuraminidase through direct competition for the active site. The main focus of research in our lab has been to investigate the pathways and kinetics of ligands binding to the active site of neuraminidase. Our previous work showed that oseltamivir had unique reaction kinetics compared to zanamivir, peramivir, and sialic acid, despite similarities in their chemical structures. Surprisingly, the difference in reaction kinetics was shown to be caused by the desolvation energy of each ligand. The desolvation energy is the free energy required to remove the solvent (water) from between the two molecules as they approach each other. This experiment focused on determining differences in desolvation energies for each ligand as a function of distance from the active site of the neuraminidase. In addition, multiple different orientations of the ligands were used in order to identify any changes in energy caused by the approach of the molecule. The main focus was analyzing both the actual value of the desolvation energies for each ligand, as well as the trends that occurred in regard to distance from the enzyme.