Computational Design of HIV-1 Protease Inhibitors

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Computational chemistry methods are used with a focus on drug design to inhibit certain proteins that are imperative to the HIV lifecycle. There are a few well known points during the lifecycle at which drugs can inhibit the maturation of the virus. One of these points occurs after translation of the viral RNA. The protein HIV protease hydrolyzes the preprocessed viral peptide chains into smaller strands which are then assembled to create more new viruses. This study saw the molecular dynamics simulation of five derivatives of the Polyoligomeric Silsesquioxanes (POSS) molecule in the active site of the HIV Protease to test the effectiveness of POSS as an inhibitor. Using the Maestro graphical user interface, the POSS molecules were manually docked into the active site of the protease. The simulations were all run for 100 nanoseconds using Desmond in an explicit water solvent model (tip3p) and the amber99SB force field, modified to accommodate the silicon molecules of the POSS molecule. Inhibitory effects are visualized using VMD. Flap motion, time spent in the active site, hydrogen bonding, and the time the POSS exits (which has shown to be different depending on the side chains) are utilized in the analysis of inhibitor effectiveness.