Investigating Intermolecular Interactions in Crystalline Aspirin Using CDFT

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Drugs today are widely administered in their crystalline form, namely via tablets and capsules. The crystal structure of a drug molecule affects important drug qualities such as solubility, bioavailability, shelf life, and compaction properties. In order to form a basis for crystal structure prediction, it is necessary to first understand how intermolecular interactions cause molecules to pack in certain ways. Being able to predict and perhaps even control a drug molecule's crystal structure will lead to the development of higher quality drugs that perform more consistently. Scientists and engineers do not fully understand the reasons for a molecule assuming a certain crystal structure. Current methods show that many energetically favorable conformations of a specific molecule are possible, but only a small handful of those are actually observed. Aspirin forms I and II were used as the drug molecules of choice for this study. Employing conceptual density functional theory allowed for the calculation of energy, as well as Fukui functions based on charge densities. CRYSTAL09 was used to optimize coordinates and to conduct single point calculations for neutral and charged aspirin for both the crystal and single molecules. Contacts between molecules were found using Mercury and OpenDX. Mapping charge density, Fukui functions, and electrostatic potential were mapped on a molecule's Hirshfeld surface allowed for the visualization of interactions between molecules in a crystal cell. This was achieved using IBM's OpenDX. Future work will involve calculating the energies of individual interactions in order to determine how influential they are on crystal structure.