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On the application of molecular simulation tools in studies of organic molecular crystals (i.e., modeling disorder and other crystalline properties)

Eric J Chan
Bristol Myers Squibb, USA

Analysis and prediction of physical properties of crystalline materials is of crucial importance. For example, a pharmaceutical crystal form must satisfy a target profile with respect to process-ability as well as bioavailability. In the material development arena, undesirable physical phenomena offer non-trivial challenges. Such phenomena include polymorphism, disorder, solvation/de-solvation, disproportionation and variation in the crystal particle size shape; because these phenomena impact the physical structure and related properties of a material, challenges also exist analytical and characterization perspective. Nowadays varieties of atomistic simulation techniques are useful to support analysis, provide further chemical/physical insight and for risk assessment/predictive capabilities. The once active laboratory chemical crystallographer may be forced to seek refuge *in silico*. Such computational activities are facilitated by a plethora of commercial and community software tools and codes. However, in some cases workflows and tools are not as streamlined and options are limited, the former experimentalist then takes the role of a computer scientist. We discuss a selection of case studies where such former mentioned novel molecular simulation hackwork is applied to small molecule crystallography, the majority being pharmaceutically relevant. Example workflows include atomistic simulation methods (MC or MD) useful for interpreting supplementary scattering features like diffuse and satellite intensities from single crystal X-ray diffraction. One study demonstrates insight into de-solvation processes. For understanding the interplay between different solvents within the crystal structure, a Grand Canonical Monte Carlo (GCMC) model was developed combining crystal structure, molecular mechanics models and SSNMR data. This was useful to estimate site occupation parameters for solvent bound to a crystal. We argue the supplementary knowledge of molecular level interactions provides a simple means for prediction of the corresponding thermodynamic properties such as the solvent activities and temperatures required to remove or replace unwanted lattice solvent. Another example includes s*ilico* screening for solvent effect on crystal morphology.

Biography

Eric J Chan has completed his graduate studies in Organic Chemistry/Biochemistry, PhD in coordination chemistry of metal-organic complexes and chemical crystallography and Post-doctoral study in X-ray single crystal diffuse scattering interpretations, molecular models, and Monte Carlo methods for molecular simulation, solid state organic chemistry and analysis of organic solids. He has expertise in crystallography, solid-state or materials chemistry and molecular simulations. He has interest in computational physics approaches used in chemistry. Graduate in organic chemistry/biochemistry, PhD: coordination chemistry of metal-organic complexes and chemical crystallography.

Eric.Chan@bms.com

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