Atomistic Modeling of Solute Precipitate Nucleation

Modeling the nucleation of molecular crystals, and particularly nucleation from solution, is critical to many applications in the food, chemical, construction, and pharmaceutical industries, among others. Despite its apparent simplicity, however, understanding this process poses major challenges both to experimental and theoretical studies. Critical nuclei often comprise only a handful of molecules, and the stochastic nature of nucleation makes it extremely hard to design experiments to observe such small aggregates. On the other hand, simulation approaches are limited due to the slow nature of nucleation compared to molecular relaxation times.

In this work, we present recent results for the nucleation of drug molecules from solution, and show the effect of different solvents on the nucleation rates. We use a unique approach where order parameters for the crystal are constructed directly from the crystal structure, and construct a minimum free energy path for nucleation on this order parameter space using the String Method in Collective Variables. We will also discuss some of the current challenges to overcome in studying heterogeneous nucleation processes, as well as dealing with solution depletion effects in simulations.

Erik E. Santiso

Erik E. Santiso received his Ph.D. in Chemical Engineering at NC State University in 2007, worked as a postdoctoral associate at MIT and Imperial College London, and joined the faculty at NC State University in 2013, where he works as an Assistant Professor in the Department of Chemical and Biomolecular Engineering. His interests include the modeling of complex activated processes such as nucleation and chemical reactions in solution, developing tools to predict the properties of biomimetic polymers, and using machine learning techniques in combination with molecular simulation to discover new materials.