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JOURNAL Highlight

Chemical Engineers Advance Molecular Simulation

Molecular simulation is a powerful tool for understanding the relationships between molecular structure and the properties of matter. It provides valuable insight for the development of bottom-up design strategies for processes ranging from petroleum refining to pharmaceutical formulation. Aided by advances in computing hardware and algorithm design, molecular simulation has become widely adopted in academia and industry over the last few decades. Conservative estimates suggest that such advances have effectively increased modeling capabilities by at least nine orders of magnitude since the late 1970s.

In the February *AIChE Journal* Perspective article, "Recent Advances in Molecular Simulation: A Chemical Engineering Perspective," Jeremy Palmer of the Univ. of Houston and Pablo Debenedetti of Princeton Univ. discuss the state of molecular simulation, challenges that need to be addressed, and contributions made by chemical engineers to expand the use of molecular simulation.

As engineers and scientists attempt to tackle increasingly more-complex problems, however, major challenges arise at the frontiers of molecular simulation, the authors say. The most formidable challenge is overcoming the computational demands of modeling physical systems and processes governed by meso- and macro-scopic length and time scales. Although significant progress has been made in addressing this challenge, researchers continue to push the limits of molecular simulation by choosing to study systems whose structural complexity and/or dynamical sluggishness make them increasingly difficult to model, they say.

Chemical engineers have played a key role in advancing molecular simulation by developing strategies to overcome the length and time scale limitations of conventional approaches. One important strategy advanced by chemical engineers is coarse-graining. While it is common practice in molecular simulation to treat individual atoms as the fundamental building blocks of matter, this level of detail is unnecessary to accurately capture the physical properties of many systems. It is often possible to develop accurate coarse-grained models in which two or more atoms on the same molecule are replaced by a single pseudo-atom. This simplifies the model and reduces the computational cost associated with simulating over large length and long time scales.

The accuracy of a coarse-grained model depends on several factors, including how the structure of the molecule is represented and how the model parameters are determined. Chemical engineers have been successful in developing sophisticated approaches that help address the latter issue. Erich A. Müller and George Jackson at Imperial College London, for example, have developed a method in which parameters for coarse-grained models are directly extracted from equations of state that have been fitted to experimental data. This saves much computational effort; fitting an equation of state to experimental data is much easier than performing a large number of simulations to optimize model parameters by trial and error. So far, Müller and Jackson's approach has proven successful in developing accurate coarse-grained models for several compounds, including linear alkanes, polyethylene surfactants, and carbon dioxide.

Other advanced computational strategies are often necessary to study activated processes — *i.e.*, infrequent events that cause a system to transition between two well-defined states separated by a free-energy barrier, such as nucleation. The time scales of such processes are too long to simulate even with coarse-grained models. In such cases, rare-event simulation techniques can be used to characterize the kinetics and molecular-level mechanisms governing these processes. In addition, methods designed to compute free energy can be used to identify metastable and equilibrium states and calculate free-energy barriers that control the rate of activated processes.

Many rare-event and free-energy simulation techniques were originally developed by physicists and chemists, but chemical engineers have been instrumental in advancing their development and application to industrially relevant problems. Bernhardt Trout's team at MIT, for example, has recently used rare-event techniques to study the crystallization of benzene from a melt. The molecular-level insight into the crystal nucleation mechanism gained from this work could have implications for developing new strategies to control the formation and stability of pharmaceutically active crystalline compounds.

Chemical engineers have also led the charge in other important areas, including the design of publicly available software to perform molecular simulation on advanced computational hardware (*e.g.*, graphical processing units), the development of algorithms to screen massive libraries of materials for carbon sequestration and natural gas storage, and the application of quantum chemistry methods to improve catalyst design, the authors say. Because chemical engineers have made sustained efforts over the last few decades to make molecular simulation an integral part of the discipline, they are in a unique position to play an important role in future developments in this field. CEP