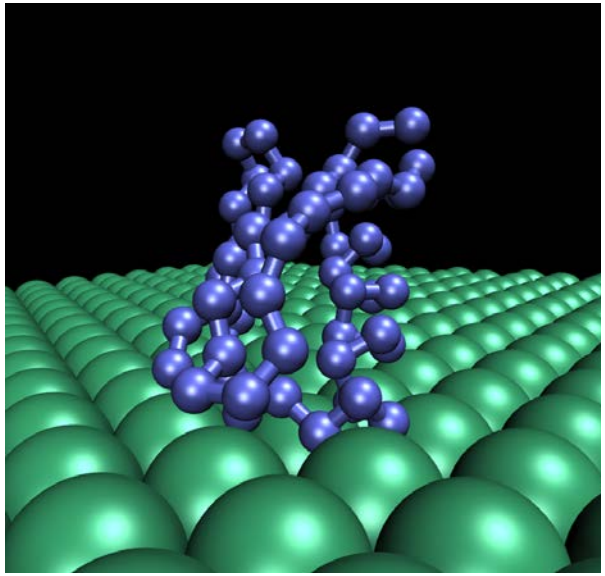

We design and characterize new materials at the nanoscale through the use of theory and computation. Our research focuses include drug design through prediction of physical properties and binding affinities and the design of novel biomimetic materials. We are especially interested in the development of computational tools that can fundamentally change molecular design by making searches through chemical and configurations space much more predictive, reliable, and efficient.

Shirts Research Group

Michael Shirts

Assistant Professor
michael.shirts@virginia.edu
faculty.virginia.edu/shirtsgroup/

Department of Chemical Engineering
University of Virginia
Charlottesville, VA
434.243.1821

"Developing atomistic simulation of molecular materials in order to create fundamentally new ways to design novel pharmaceutical and other nanoscale products."

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Computer-aided drug design

Drug resistance is one of the biggest challenges in the pharmacological treatment of infectious diseases, and current informatics based drug discovery methods are not well suited to rapidly develop new drug variants that can successfully overcome resistance. Our research has demonstrated that statistical mechanical methods can predict ligand binding affinities to within 1 kcal/mol in simple atomistically detailed systems. We are developing new, highly accurate computational methods to enable screening of thousands to millions of new drug affinities simultaneously.

Design of protein/surface interactions

Tailoring protein adsorption and desired conformational variations is central to the purification of therapeutic proteins such as monoclonal antibodies, the development of engineered biomaterials and biosensors, and assembly of nanoscale devices. We must design purification processes that prevent proteins from misfolding or otherwise aggregating during chromatographic purification, as one of the largest costs in therapeutic biologics is the purification process. In collaboration with experimental researchers at UVa., we are using multiscale modeling to investigate the detailed transport and thermodynamics of protein interactions with chromatographic and other purification surfaces.

Improvements in molecular simulation and property prediction

The most pressing problem in the atomic-level simulation of polymers, macromolecules, and other complicated dense fluids is the lack of sufficient sampling to accurately measure and observe physical phenomena. Without sufficient conformational sampling, it is impossible even to verify if models are sufficiently faithful to experiment, let alone explore behavior of either long time scales or of larger molecular systems. It is currently only possible to simulate the equivalent of a few microseconds of all but the smallest biological systems, with some heroically expensive extensions to milliseconds with large supercomputers. We are making important contributions to efficient analysis of free energy calculations and other thermodynamic data and our current research focus on methods for sampling both chemical and configuration space of heteropolymers and complex fluids to design new nanoscale materials and understand biophysical phenomena.

RECENT RESEARCH DEVELOPMENTS

- A new, more efficient approach to computationally transforming molecules in order to compute the difference in thermodynamic properties between them
- Better understanding of the mechanics of enzymatic degradation of cellulose for biofuel production.
- New methods to greatly accelerate thermodynamic parallel simulation techniques
- Biophysical characterization of novel biomimetic cancer suppressant drugs

RECENT GRANTS

- NSF – Integrated Program for Conformational Effects in Protein Chromatography
- NSF – Highly Multidimensional Thermodynamics Property Prediction for Chemical Design Using Atomistic Simulations

SEAS Research Information
Pamela M. Norris, Associate Dean
University of Virginia
Box 400242
Charlottesville, VA 22903
pamela@virginia.edu
434.243.7683

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