Computational Tools to Address Multiscale Problems in Biophysics

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My seminar will present my ongoing research in the field of computational physical chemistry.
The overarching aim of my work is to understand the relationship between structure and function in complex chemical and biological systems using state-of-the-art computational chemistry, modelling, and simulation techniques. These investigations are designed to advance our understanding of molecular mechanisms underlying important chemical processes in Nature. I will highlight three areas of research, [1] biocatalysis, [2] sterol homeostasis, [3] SARS-CoV-2 polymerase.

[1] Biocatalysis refers to catalysis accomplished by enzymes that contain complex transition-metal catalytic centers. The mechanisms of substrate binding and electron transfer are not yet fully understood. Working together with biologists who provide us with structural data, we model these complex enzymes using hybrid quantum mechanical/molecular mechanical (QM/MM) methodologies.

[2] Sterol homeostasis is regulated by a wide range of cellular components, including lysosomal proteins. Failure of these proteins to perform their function can have severe physiological consequences, in some cases leading even to organism death. In humans, several lysosomal storage disorders have been identified, and many of these are fatal, killing the patients in early age, frequently before adulthood. My research has focused on the Niemann Pick Type C (NPC) disease, characterized by a disrupted transport of cholesterol and lipids out of cellular compartments. Molecular dynamic (MD) simulations, together with insight from machine learning, reveal cholesterol trafficking mechanisms.

[3] MD simulations combined with machine learning have revealed the atomic details of mutations in the SARS-CoV-2 polymerase, the enzyme responsible for RNA polymerization. We have identified "fitness cores" in the enzyme that are driving the rapid evolution of the SARS-CoV-2 polymerase.