DEPARTMENT OF MATH PHYSICS & COMPUTER SCIENCE
UNIVERSITY OF CINCINNATI BLUE ASH COLLEGE

SUMMER RESEARCH OPPORTUNITIES FOR UNDERGRADUATE students

FOR APPLICATION YEAR: 2025

PROJECT TITLE: Investigating the Human Ca^{2}? Ion Pump (SERCA) and Drug Development Potential using Computer Simulation Methods.

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Project Description

The human Ca^{2}? ion pump, SERCA, is a critical transmembrane protein responsible for transporting calcium ions into intracellular storage compartments. It plays a vital role in physiological processes, including skeletal muscle contraction, relaxation, and signal transduction. SERCA's ion transport activity can be effectively inhibited by several compound classes, including 2,5-di-tert-butylhydroquinone (BHQ) derivatives.

In recent research, we developed a computational protocol leveraging Free Energy Perturbation Molecular Dynamics (FEP-MD) simulations combined with restraining potentials to compute the absolute binding free energy of BHQ derivatives to SERCA. Our method integrates the Generalized Born Solvent Boundary Potential (GBSBP) and the Spherical Solvent Boundary Potential (SSBP) techniques. This hybrid approach focuses explicitly on the active binding site while modeling the remainder of the system implicitly.

We evaluated distinct contributions to the standard binding free energy, including electrostatic, repulsive, dispersive, and restraining potentials, computed separately. Our results demonstrated that the absolute binding free energy of BHQ (11.63 kcal/mol) closely aligns with experimental measurements (10.56 kcal/mol).

Building on this success, our proposed research aims to apply this protocol to study a variety of drug-like small molecules with potential medicinal applications targeting SERCA.

Student Involvement and Learning Opportunities

Participants in this project will gain:

- Expertise in molecular docking and dynamics simulations.
- Proficiency in free energy calculation methods.

- Hands-on experience with high-performance computing (HPC) environments.
- Skills in using Visual Molecular Dynamics (VMD) software.
- Opportunities for technical writing and scientific presentations.

Students will also carry out independent computational simulation projects, with potential co-authorship opportunities in scientific journal publications. This experience is designed to provide valuable skills for careers in computational biophysics, drug discovery, or related fields.