The aquaporin family of membrane proteins play an integral part in the transport of water in and out of the cell. They are present in almost all forms of life, from animals to plants to bacteria. In mammals, there are thirteen types of aquaporins numbered 0 - 12. In addition, many aquaporins are associated to diseases, which makes them sought-after drug targets. However, due to a variety of factors progress towards targeted aquaporin drugs has been limited.

The advent of modern high-performance computing has opened new avenues to study biomolecular systems. This, coupled with the quality of the currently available molecular dynamics force-field parameters, allows us to probe drug-protein interactions to ever-higher precision. In this work we will present molecular dynamics simulations of various aquaporins to elucidate their function. We will apply equilibrium and nonequilibrium methods to study the rate of water permeation, the energetic barriers associated with this permeation, as well as the interactions between aquaporins and small-molecule ligands. We will calculate single-channel water permeabilities for various aquaporins and aquaglyceroporins, the latter of which, in addition to water, also transport small uncharged molecules such as glycerol. In the case where no high-quality atomic structures are available, we will employ homology modeling to derive a structure from a well-resolved template. Finally, we will investigate the binding of select aquaporins with small-molecule ligands and describe the atomistic basis for their association.