The first molecular dynamics simulation of a protein in 1977 [1]. The choice of the larger protein SHP2 for the next part of our study was due to the fact that large biologically important protein conformational changes monitored in this molecule by FRET have much more rapid kinetics in vivo than in vitro [2]. We will seek to understand this computationally.

We expect this work to make a large contribution towards bridging the gap between structure and dynamics of proteins in vivo and in vitro.

METHODS & RESULTS

In the current study we explored a native and mutant BPTI in which the mutation confers added flexibility to the protein [3]. We confirmed that our molecular dynamics in bulk replicates the reported experimental results in solution, and then explored the effects of confinement on both the native and the mutant strains.

Confinement (encapsulation in silica cavity) has a large effect on the dynamics of BPTI. The mutant of BPTI (G37A) exhibits large flexibility compared to its wild type. Both wild type and mutant BPTI’s RMSD drops when placed in confinement. The water structure is dramatically changed due to confinements and density layering is observed near silica wall. The peak density of water in density layering is augmented due to the overlap of the protein hydration shell and near-wall ordering.

WHY BLUE WATERS

Our largest simulations so far involve just under 100,000 atoms and all our simulations involve much conformational sampling because we are interested in significant deviations from crystal structure. In the next stage of the project, the systems involving the complete SHP2 protein, including fluorescent probes, will be significantly larger. These expensive computations are not possible to perform in reasonable time without a petascale supercomputer.