TEMPLE UNIVERSITY
Department of Mathematics

Applied Mathematics and Scientific Computing Seminar

Wednesday, 13 April 2016, 4:00 p.m.
Room 617 Wachman Hall

(refreshments and social at 3:45 p.m)

Tracing the geometry of water clusters to understand selectivity for drugs

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Abstract. In confined environments such as membrane proteins, water molecules are significantly more ordered than in free solution, and their entropy is not additive. Single water molecules can be tightly bound to a protein, and often essential to its function. However, when a water cluster plays this role, and its constituent molecules are bound to each other, the whole cluster could be easily removed. The M2 proton channel from the influenza virus contains several water clusters within its pore, at least one of which can be replaced by a small-molecule drug. Unfortunately, a direct calculation of the associated free energy cost by molecular dynamics is very challenging. A simple comparison of the three-dimensional shapes of drug and water clusters allows to explain the mechanism of drug recognition and resistance in viral mutants. Using a measure of similarity with protein-bound water clusters can be a useful and inexpensive criterion to search for more potent inhibitors of M2 and similarly-structured viral proteins.