Life on Arsenic?
Towards the Thermodynamic, Kinetic, and Dynamic Modeling of an Arsenatidylcholine Membrane System

Kendra Marcus
Advisor: Dr. Stephen Cartier

In December 2010, Dr. Felisa Wolfe-Simon et al published a study in Science claiming to have isolated a “bacterium (GFAJ-1) that can grow by using arsenic instead of phosphorus.” Current research is being conducted in the theoretical chemistry community to investigate the stability of arsenic-based biological molecules. The objective of this study was to determine the kinetic, thermodynamic and dynamic consequences of an arsenatidylcholine membrane system through molecular modeling. Two modeling programs were primarily used in this study. Spartan Essentials ’08 was employed for semi-empirical (PM3) and ab initio calculations to observe the thermodynamic and kinetic stress of hydrolysis on both a single arsenatidylcholine polar head and an arsenate diester. Dynamic consequences of the arsenate substitution within a hydrated, dipalmitoylphosphatidylcholine (DPPC) membrane system are currently being studied using GROMACS. Semi-empirical calculations suggest that both phosphate-ester and arsenate-ester bonds are thermodynamically favored to undergo acid-catalyzed hydrolysis. In identical conditions, arsenate-ester bonds undergo hydrolysis more readily than phosphate-based esters, suggesting lower stability. A hydrated DPPC membrane was fully parameterized and simulated over a time frame of 2 ns. Time lapsed simulation data shows full exposure of phosphate groups within the polar heads of the phospholipids to water. This exposure, coupled with Spartan data, indicates that the heads of the arsenolipids system may hydrolyze and cause the disassociation of the membrane system. Novel parameterization of arsenate-ester bonding patterns for GROMACS must be executed before an arsenatidylcholine lipid system can be simulated. If arsenate is truly integrated into the biomolecules of GFAJ-1, unstudied biochemical pathways to prevent the hydrolysis of arsenate esters may be utilized by the organism.


