LLNL-TR-401371

LAWRENCE
LIVERMORE
NATIONAL
LABORATORY

Heterogeneous processes at the intersection of chemistry and biology: A computational approach

I.-F. W. Kuo, C. J. Mundy

February 14, 2008

Disclaimer

This document was prepared as an account of work sponsored by an agency of the United States government. Neither the United States government nor Lawrence Livermore National Security, LLC, nor any of their employees makes any warranty, expressed or implied, or assumes any legal liability or responsibility for the accuracy, completeness, or usefulness of any information, apparatus, product, or process disclosed, or represents that its use would not infringe privately owned rights. Reference herein to any specific commercial product, process, or service by trade name, trademark, manufacturer, or otherwise does not necessarily constitute or imply its endorsement, recommendation, or favoring by the United States government or Lawrence Livermore National Security, LLC. The views and opinions of authors expressed herein do not necessarily state or reflect those of the United States government or Lawrence Livermore National Security, LLC, and shall not be used for advertising or product endorsement purposes.

Auspices Statement

FY07 LDRD Final Report

Heterogeneous processes at the intersection of chemistry and biology: A computational approach

LDRD Project Tracking Code: 05-ERD-021

I-Feng W. Kuo, Principal Investigator

Abstract

Heterogeneous processes hold the key to understanding many problems in biology and atmospheric science. In particular, recent experiments have shown that heterogeneous chemistry at the surface of sea-salt aerosols plays a large role in important atmospheric processes with far reaching implications towards understanding of the fate and transport of aerosolized chemical weapons (*i.e.* organophosphates such as sarin and VX). Unfortunately, the precise mechanistic details of the simplest surface enhanced chemical reactions remain unknown. Understanding heterogeneous processes also has implications in the biological sciences. Traditionally, it is accepted that enzymes catalyze reactions by stabilizing the transition state, thereby lowering the free energy barrier. However, recent findings have shown that a multitude of phenomena likely contribute to the efficiency of enzymes, such as coupled protein motion, quantum mechanical tunneling, or strong electrostatic binding. The objective of this project was to develop and validate a single computational framework based on first principles simulations using tera-scale computational resources to answer fundamental scientific questions about heterogeneous chemical processes relevant to atmospheric chemistry and biological sciences.

Summary of work

Whether your interest is in atmospheric science or biological science, it has become more evident recently that heterogeneous reactions play many vital roles.[1-6] For atmospheric science, the heterogeneity occurs at the liquid-vapor interface where the surface layer acts as a catalyst on which chemistry can occur. Chemistry at the liquid-vapor is often more complex then homogenous chemistry because at the interfacial, properties of reactants can be drastically modified from those in the gas- or condensed-phase. It has been shown in both a laboratory setting and in the field that the heterogeneous reaction is possible and play dominant roles.[4-6] Similarly, in biological systems such as enzymes, the heterogeneity being referred to occurs within the protein whereby particular configuration of atoms can stabilize transition state and accelerate different reaction by many orders of magnitude.[3,7] Although atmospheric science and enzymology appears to be on opposite spectrum from each other, for this proposal, we showed that we can use the same technique based on first principles simulation to answer fundamental scientific questions related to each. By using the same computational framework to tackle a wide variety of scientific fields, it increases our confidence in using computers for predictive simulations where experiments cannot be carried out either due to cost or safety concerns.

The computational framework that was employed during this project has been incorporated into the simulation code CP2K.[8] In particular, the computational framework adopted is based on first principles technique where we solved Kohn-Sham formulation of density functional theory[9] as implemented in the QuickStep module of the simulation package CP2K.[8,10,11] CP2K is an ideal tool for this project because it is a molecular dynamics (MD)/Monte Carlo (MC) simulation software suite that utilizes an $O(N)$ electronic structure algorithm[10] and contains both mixed quantum mechanics/molecular mechanics (QM/MM) and *metadynamics* methods.[12-16] The QM/MM method is especially suitable for large heterogeneous systems as it allows one to treat the degrees of freedom that are involved in explicit chemistry within an accurate framework using first principles based potential while less relevant degrees of freedom can be treated using classical empirical potential to save computational costs. A dual basis set formulism[10,11] (Gaussian type orbitals plus plane-wave basis sets) was used where the core states are described by analytical pseudopotentails.[17] For studies carried out in this project, a triple zeta with double polarization Gaussian type orbitals was used in addition to plane-waves expanded up to 280 Ry cutoff. Wavefunctions are quenched to a tolerance of 10^{-7} Hartree using an $O(N)$ orbital transformation method.[18] This combination was found to produced highly precise results but at the same time maximize computational efficiency.[11]

Results from this project has being published in peer reviewed journal and are attached as is with this report. Overall, the manuscripts attached with this report can be classified into three domains. The first part relates to validation of first principles simulation technique. The second part are studies related to atmospheric science using aforementioned computational framework. The last part deals with the most heterogeneous and complex system studied in this project, namely enzymes.

To validate the accuracy of first principles simulation technique, we chose to focus our studies on water because it is ubiquitous in nature and often a necessity to many relevant chemical processes with amble amounts of literature data for comparison. We performed a series of studies to look at the accuracy of first principles water when compared to experiments so as set a confidence level for predictability when working with unknowns.[19,20] The most sensitive measure of the quality of water is to compute the vapor-liquid coexistence curve since this requires the interplay of many subtle intermolecular forces over a wide thermodynamic region.[21-24] Furthermore, we have also looked at other dynamical and structural properties of water as well as reproducibility of our simulation results to gain a great deal of confidence in that we believe this computational framework can be used in more complex systems.[25,26]

Understanding heterogeneous reactions at the liquid-vapor interface of aerosols is one of our main goal. It was found that using first principles based simulation to study the aqueous liquid-vapor interface can successfully reproduce experimental (NEXAS and SFG) results but requires large amount of computer time.[27,28] Unfortunately, large amount of computer time are not always available and thus we determined certain interfacial properties can be reproduced using cheaper empirical potentials.[29,30] It was also found that unlike bulk water, polarization effects are very important at the interface.[30] In fact, it was discovered that not all polarizable models are adequate, only highly expensive polarization model that allows for out of plane motion of charges are necessary. Though polarizable model are less demanding then first principles based methods, they are still quite expensive computationally. But the biggest problem with polarizable model like normal empirical models is that bond breaking and forming is not possible and the necessary parameters to accurately describe polarization effects are not readily available. Therefore use of polarizable models as a predictive tool still seems out of reach. Last, little is known about chemical stabilities of key species that populate the interfacial region. Two key species that are known to populate interfacial regions are hydroxide radicals and chloride ions.[2,4] It has been hypothesized elsewhere that a combination of hydroxide radicals with chloride ion can lead to the formation of chlorine gas. Chlorine gas can then be converted to highly reactive chlorine radicals via

photolysis. For our study, we looked at the stability of hydroxide-chloride ion complex both in bulk as well as in the more relevant interfacial surface environment.[31] We then postulated from our results that a charge transfer process occurs at the interface which leads to formation of neutral chlorine gas via a hydrogen-bonded complex involving a second chloride ion species as the likely chemical mechanism that leads to formation of highly reactive chlorine radicals in the atmosphere.

The most complex heterogeneous system studied within this project is the enzyme ODCase.[32] ODCase was selected as a representative biological system because it catalyzes a key biological reaction pathway via an unknown mechanistic pathway.[32] ODCase catalyzes the conversion of OMP to UMP, which is a precursor to synthesis of RNA nucleotides.[3,33] Since enzymatic activities are highly localized to a small region and a subset of atoms, we employed QM/MM techniques where only relevant atoms in this interconversion process are treated by first principles techniques. From this study, it was found that first principles simulation technique can be used to study biological systems and answer pertinent questions regarding mechanistic pathways as well as compute activation barriers for different reaction pathways.[33]

Conclusion

This project has produced many publications towards validating the accuracy of first principles simulation as well as topic related to atmospheric sciences and enzymology. With know accuracy and confidence in the predictability of first principles techniques, we are looking toward applying this same methodology to area of threat agent science strategically aligned with on-going efforts in Global Securities.

References

(1)   Gard, E.; Kleeman, M.; Gross, D.; Huges, L.; Allen, J.; Morrical, B.; Fergenson, D.; Dienes, T.; Galli, M.; Johnson, R.; Cass, G.; Prather, K. *Science* **1998**, *279*, 1184.

(2)   Knipping, E. M.; Lakin, M. J.; Foster, K. L.; Jungwirth, P.; Tobias, D. J.; Gerber, R. B.; Dabdub, D.; Finlayson-Pitts, B. J. *Science* **2000**, *288*, 301.

(3)   Lee, J. K.; Houk, K. N. *Science* **1997**, *276*, 942.

(4)   Finlayson-Pitts, B. J.; Hemminger, J. C. *J. Chem. Phys.* **2000**, *104*, 11463.

(5)   Ghosal, S.; Hemminger, J. C. *J. Phys. Chem.* **1999**, *103*, 4777.

(6)   Gard, E. E.; Kleeman, M. J.; Gross, D. S.; Hughes, L. S.; Allen, J. O.; Morrical, B. D.; Fergenson, D. P.; Dienes, T.; Galli, M. E.; Johnson, R. J.; Cass, G. R.; Prather, K. A. *Science* **1998**, *279*, 1184.

(7)   Warshel, A. *Annu. Rev. Biophys. Biomol. Struct.* **2003**, *32*, 425.

(8)   CP2K. http://cp2k.berlios.de.

(9)   Kohn, W.; Becke, A. D.; Parr, R. G. *J. Phys. Chem.* **1996**, *100*, 12974.

(10)   Lippert, G.; Hutter, J.; Parrinello, M. *Mol. Phys.* **1997**, *92*, 477.

(11)   VandeVondele, J.; Krack, M.; Mohamed, F.; Parrinello, M.; Chassaing, T.; Hutter, R. *Comput. Phys. Commun.* **2005**, *167*, 103.

(12)   Laino, T.; Mohamed, F.; Laio, A.; Parrinello, M. *J. Comput. Theo. Chem.* **2005**, *1*, 1176.

(13)   Laino, T.; Mohamed, F.; Laio, A.; Parrinello, M. *JCTC* **2006**, *2*, 1370.

(14)   Laio, a.; VandeVondele, J.; Rothlisberger, U. *J. Chem. Phys.* **2002**, *116*, 6941.

(15)   Laio, A.; Parrinello, M. *PNAS* **2002**, *99*, 12562.

(16)   Laio, a.; Rodriguez-Fortea, A.; Gervasio, F. L.; Ceccarelli, M.; Parrinello, M. *J. Phys. Chem. B* **2005**, *109*, 6714.

(17)   Goedecker, S.; Teter, M.; Hutter, J. *Phys. Rev. B* **1996**, *54*, 1703.

(18)   VandeVondele, J.; Hutter, J. *Journal of Chemical Physics* **2003**, *118*, 4365.

(19)   Mcgrath, M. J.; Siepmann, J. I.; Kuo, I. F. W.; Mundy, C. J.; VandeVondele, J.; Hutter, J.; Mohamed, F.; Krack, M. *Chemphyschem* **2005**, *6*, 1894.

(20)   Kuo, I. F. W.; Mundy, C. J.; McGrath, M. J.; Siepmann, J. I.; VandeVondele, J.; Sprik, M.; Hutter, J.; Chen, B.; Klein, M. L.; Mohamed, F.; Krack, M.; Parrinello, M. *J. Phys. Chem. B* **2004**, *108*, 12990.

(21)   McGrath, M. J.; Siepmann, J. I.; Kuo, I. F.; Mundy, C. J.; VandeVondele, J.; Mohamed, F.; Krack, M. *J. Phys. Chem. A* **2005**, *110*, 640.

(22)   Mcgrath, M. J.; Siepmann, J. I.; Kuo, I. F. W.; Mundy, C. J. *Mol. Phys.* **2006**, *104*, 3619.

(23)   Mcgrath, M. J.; Siepmann, J. I.; Kuo, I. F. W.; Mundy, C. J.; VandeVondele, J.; Hutter, J.; Mohamed, F.; Krack, M. *J. Phys. Chem. A* **2006**, *110*, 640.

(24)   Mcgrath, M. J.; Siepmann, J. I.; Kuo, I. F. W.; Mundy, C. J.; VandeVondele, J.; Sprik, M.; Hutter, E.; Mohamed, F.; Krack, M.; Parrinello, M. *Comp. Phys. Comm.* **2005**, *169*, 289.

(25)   Kuo, I. F. W.; Mundy, C. J.; McGrath, M. J.; Siepmann, J. I. *J. Chem. Theo. Comput.* **2006**, *2*, 1274.

(26)   Mcgrath, M. J.; Siepmann, J. I.; Kuo, I. F. W.; Mundy, C. J. *Mol. Phys.* **2007**, *105*, 1411.

(27)   Kuo, I. F. W.; Mundy, C. J. *Science* **2004**, *303*, 658.

(28)   Mundy, C. J.; Kuo, I. F. W. *Chem. Rev.* **2006**, *106*, 1282.

(29)   Kuo, I. F. W.; Mundy, C. J.; Eggimann, B. L.; McGrath, M. J.; Siepmann, J. I.; Chen, B.; Vieceli, J.; Tobias, D. J. *J. Phys. Chem. B* **2006**, *110*, 3738.

(30)   Wick, C. D.; Kuo, I. F. W.; Mundy, C. J.; Dang, L. X. *J. Comput. Theo. Chem.* **2007**, *3*, 2002.

(31)   D'Auria, R.; Kuo, I. F. W.; Tobias, D. J. *J. Phys. Chem. A* **submitted**.

(32)   Borman, S. *Chem. Eng. News* **2004**, *82*, 35.

(33)   Stanton, C. L.; Kuo, I. F. W.; Mundy, C. J.; Laino, T.; Houk, K. N. *J. Phys. Chem. B* **2007**, *111*, 12573.