

QUANTUM EFFECTS OF PROTON TRANSFER IN BIOLOGICAL SYSTEMS

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EXECUTIVE SUMMARY

Quantum effects of nuclei have been shown to affect chemical reactions in a variety of condensed-phase chemical systems, including certain biological enzymatic reactions. In this study, we investigate how the quantum effects of hydrogen and its isotopes affect the rate of charge transfer in a model biological system in which a water molecule acts as an intermediary between the donor and acceptor molecule. Our calculations show an abnormally high kinetic isotope effect, which is indicative of a quantum mechanical tunneling mechanism, and we see dramatically different behavior when these quantum effects are turned off. This study makes a strong case for examining larger, more realistic biological systems using this approach in the future.

RESEARCH CHALLENGE

In most chemical dynamics calculations, it is assumed that all nuclei are classical particles and all electrons are quantum particles represented by molecular orbitals. This approach is typically quite good, especially for high-temperature chemistry and heavy nuclei, or basically anything other than hydrogen. There are certain cases, however, where the quantum mechanical effects

of nuclei become important. Such cases include condensed-phase chemistry in which a hydrogen/proton transfer is the rate-limiting step. There is evidence to suggest that many biological chemical systems fit into this category, and we examine a model system in this study to determine how these quantum effects influence the mechanism of charge transfer.

These quantum effects can potentially impact both the efficiency and overall mechanism of charge transfer. The primary challenges in this field revolve around how exactly one should include the quantum effects of nuclei, but also how the electronic structure should be evaluated as the chemical system evolves from a reactant to a product state. In this particular study, we chose a model that we believe will capture the important physics of the proton transfer mechanism, but it is also simple enough that we can extract the important properties of this mechanism before examining larger, much more complicated systems.

Our calculations can give us a close look at exactly how this charge transfer process occurs, and we can use this information to improve our fundamental understanding of how nature has taken advantage of quantum mechanics in a way that has a profound influence on the chemistry of living organisms.

METHODS & CODES

We employed the ring polymer molecular dynamics (RPMD) method to include quantum effects of proton motion in our system. This method was chosen because it has been shown to be accurate for a wide range of applications, it scales linearly with respect to the system size, and the calculations can be done in parallel across many cores. Our code primarily simulates the physics of our chemical system as it evolves from a reactant state to a product state. To this end, many simulations containing many particles need to be performed in a highly parallel computing environment. Our group developed a Fortran-based code, which was highly scalable and well-suited for supercomputing environments such as Blue Waters.

RESULTS & IMPACT

Our calculations show an abnormally high kinetic isotope effect (KIE) for proton transfer in this model system. The kinetic isotope effect, in this case, is a measure of how much faster the reaction occurs when a proton, rather than a deuteron, is the charge carrier. In standard classical chemical dynamics calculations we observe a KIE of approximately 1.4 for all temperatures. In our quantum mechanical calculations we see a KIE of 35 at room temperature,

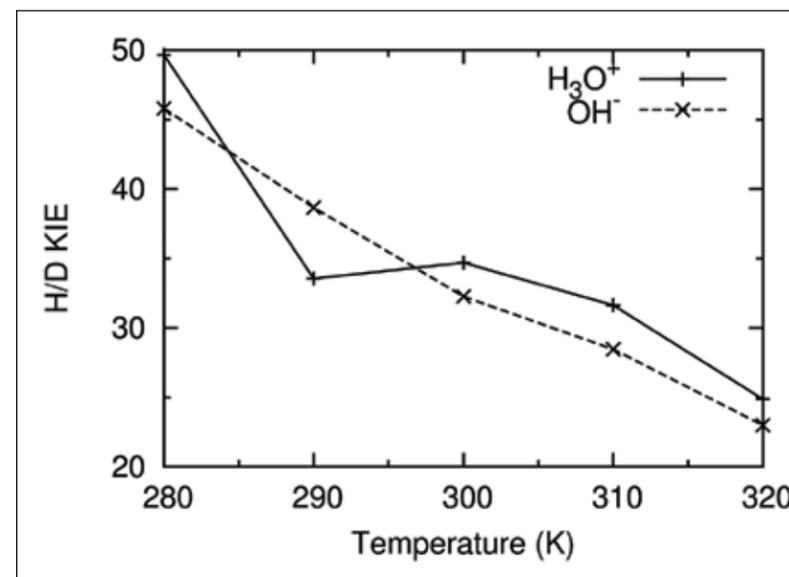


Figure 2: The inclusion of quantum effects in the proton transfer mechanism shows an extremely high kinetic isotope effect when the rate of proton transfer is compared to the rate of deuteron transfer, and this points to the importance of quantum effects in this process. Image from *J. Phys. Chem. A*, 121, pp. 819–826, 2017.

and an even higher KIE at lower temperatures. This indicates that quantum tunneling of nuclei plays an important role in this charge transfer mechanism, and a physically correct picture of this process depends on the inclusion of these quantum effects.

These calculations have provided us with a very close and detailed view of a physical phenomenon that plays an important role in many biological systems and would not have been possible without highly parallel supercomputing resources. The seemingly obscure phenomenon of quantum mechanical tunneling has been shown, in this study, to profoundly impact the rate of charge transfer in a simple model biological system, and this has similar implications for more complicated but fundamentally similar systems that are found in many different natural biological systems.

WHY BLUE WATERS

The RPMD method relies on taking averages among many chemical dynamics simulations with different initial conditions. Often, we need to perform hundreds of thousands of calculations in order to see converged results. Fortunately, these jobs can be run in parallel with one another, and a supercomputing environment in which we can run massively parallel jobs over thousands of cores is ideal. Additionally, the scalability of this method typically means that if enough compute cores are available, no job should take more than 30 minutes. The efficient parallelization, short job queues, and responsiveness of the system made Blue Waters a perfect platform for our code development and job submission. Additionally, the Blue Waters Student Internship Program provided a perfect gateway into using these resources while funding an undergraduate student's research experience on Blue Waters.

PUBLICATIONS AND DATA SETS

Mazzuca, J. W., and C. P. Schultz, Quantum Mechanical Enhancement of Rate Constants and Kinetic Isotope Effects for Water-Mediated Proton Transfer in a Model Biological System. *J. Phys. Chem. A*, 121 (2017), pp. 819–826.

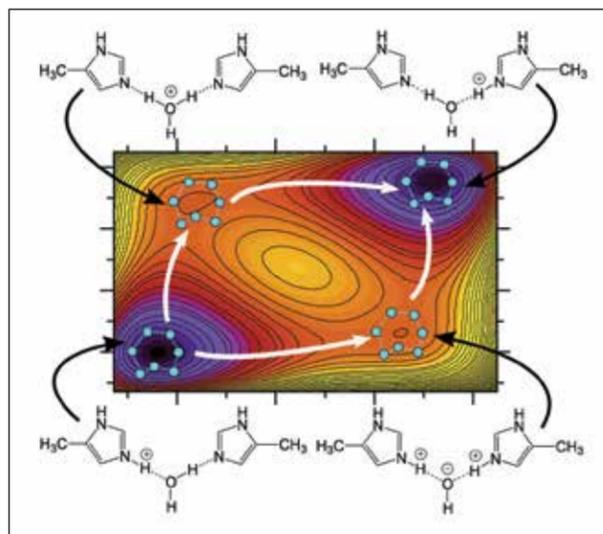


Figure 1: This image shows how potential energy changes as a proton is passed from a donor to acceptor molecule, with the help of an intervening water. The arrows represent two paths that the proton may travel to reach the product state, and quantum effects of this phenomenon were included using the ring polymer molecular dynamics (RPMD) method. Image from *J. Phys. Chem. A*, 121, pp. 819–826, 2017.