XVIIIth International Workshop on Quantum Atomic and Molecular Tunneling in Solids and other Phases

The Madison Concourse Hotel
Madison, Wisconsin

May 20 - 24, 2017

Scientific Organizers
Jürgen Eckert
Amnon Kohen

Local Organizer
Robert McMahon
QAMTS 2017 Program

Saturday May 20

18:00-20:00  Registration and Welcome Reception

Sunday May 21

8:00-8:45  Breakfast

9:00  Welcome, Bob McMahon

9:15  Hydrogen Bond Network Rearrangement Dynamics in Water Clusters: Implications for the Liquid, Richard Saykally, Berkeley

10:00  The Use of the Bell-Limbach Tunneling Model for the Calculation of Arrhenius Curves of Hydrogen Transfer in Liquids and Solids, Hans Limbach, Berlin

10:45-11:15  Coffee

11:15  Hydride Transfer Probed using Mass-Modulated Enzymes and Coenzyme Biomimetics, Nigel Scrutton, Manchester

12:00  Influence of Conformation and Environment on Tunnelling Reactions, Tim Schleif, Joel Mieres Perez, Paolo Costa, and Wolfram Sander, Bochum

12:45-14:00  Lunch

14:00  Quantum Correlations in Molecular Rotor Systems, Thomas Halverson and Pierre-Nicholas Roy, Waterloo

14:45  Including Tunneling in Semiclassical Simulations, Rubén Meana-Pañeda, Jingjing Zheng, Xuefei Xu, and Donald G. Truhlar, Bethesda

15:15-15:45  Coffee

15:45  Lipoxygenase as a Model for Vibronically Non-Adiabatic Proton-Coupled Electron Tunneling Near Room Temperature, Judith Klinman, Berkeley

16:30  General Algorithm Implementation for Thermal Rates: the Galitherra Software, David Ferro-Costas and Antonio Fernández-Ramos, Santiago de Compostela

18:00  Dinner
Monday May 22

8:00-8:45 Breakfast

9:00 Symmetrical Quasi-Classical Model for Classical Molecular Dynamics Simulations of Electronically Non-Adiabatic Processes, William Miller, Berkeley

9:45 Translation-rotation Dynamics of Clathrate-confined Dihydrogen Clusters, Peter Felker, Los Angeles

10:30-11:00 Coffee

11:00 Manipulating and Probing the Polarisation of a Methyl Tunnelling System by Field-cycling NMR, Anthony J Horsewill, Bo Zhang, Sabah M.M. Abu-Khumra, and Abdellah Aibout, Nottingham

11:30 Empirical Valence Bond Studies of Decomposition of Neurotransmitters Catalyzed by Monoamine Oxidases, Jernej Stare and Janez Mavri, Ljubljana

12:00 -13:00 Lunch

13:15 Excursion – shuttle bus leaves promptly at 13:15

15:00-17:00 Tour of Frank Lloyd Wright’s Taliesin, Spring Green, WI

http://www.taliesinpreservation.org/

18:15 Approximate time of return to conference hotel

18:30 Dinner

Tuesday May 23

8:00-8:45 Breakfast

9:00 Proton Tunneling in Proteins, Paul M. Champion, Boston


10:30-11:00 Coffee

11:00 Tunnelling and Parity Violation in Chiral Molecules: From Theory towards Spectroscopic Experiment and the Evolution of Biomolecular Homochirality, Martin Quack, Zürich
11:45  On the use of Quantum Dynamics to Unveil the Complex Photochemistry of Green Fluorescent Protein, Miguel Moreno, Marc Nadal-Ferret, Ricard Gelabert, and José M. Lluch, Barcelona

12:30-14:00  Lunch

14:00  Neutron Spectroscopy of Water under Ultra-confinement, Alexander I. Kolesnikov, Knoxville

14:45  Molecular Dynamics of Large Systems with Quantum Corrections for Selected Nuclei, Sophya Garashchuk, Columbia, SC

15:30  Rovibrational Quantum Dynamics of the Methane-water Dimer, János Sarka, Attila G. Császár, and Edit Mátyus, Budapest

16:00-16:30  Coffee

16:30  Isotopically Different Tunneling-Ready-State Structures in Hydride Transfer Reactions in Solution, Yun Lu, Edwardsville

17:15  H-Tunneling-Ready-State Structures Obtained from Adjusting Hessian Matrices of Donor-Acceptor Complexes, Nader Sakhaee and Yun Lu, Edwardsville

18:30  Conference Banquet

   Pyle Center, University of Wisconsin-Madison
   Approximately 15-minute walk from conference hotel

Wednesday May 24

8:00-8:45  Breakfast

9:00  The Mechanism of Double-Proton Transfer at Very Low Temperatures, Antonio Fernández-Ramos, Santiago de Compostela

9:45  Quantum Transition State Theory, Timothy J. H. Hele, Ithaca

10:30-11:00  Coffee

11:00  The last word: How Important is Quantum Tunneling in Enzyme Reactions? Dan T. Major, Ramat-Gan

11:45  Concluding Remarks, Bob McMahon and Juergen Eckert

12:00  Lunch and departure
Hydrogen Bond Network Rearrangement Dynamics in Water Clusters: Implications for the Liquid

Richard J. Saykally

Department of Chemistry
University of California; Berkeley, CA, 94705
saykally@berkeley.edu

Theoretical studies of the hydrogen bond network rearrangement (HBNR) dynamics in liquid water have indicated that librational motions initiate the HB breaking/formation processes. We present the results of using a simple time evolution method to extract and compare the hydrogen bond lifetimes for the water dimer, trimer, and pentamer from the experimentally measured tunneling splittings in the ground and excited intermolecular vibrational states. We find that the specific nature of the intermolecular vibrational excitation does not significantly influence the hydrogen bond lifetime of the dimer, and that only excitations to a librational vibration affect the water trimer or pentamer lifetimes. Hence, observing and quantifying the enhanced hydrogen bond breaking dynamics for these types of vibrations in water clusters serves as support for theoretical predictions. The specific enhancement of bond breaking in larger clusters relative to the dimer also indicates that hydrogen bond cooperativity is a vital element of these dynamics.


The Use of the Bell-Limbach Tunneling Model for the Calculation of Arrhenius Curves of Hydrogen Transfer in Liquids and Solids

Hans-Heinrich Limbach

Institut für Chemie und Biochemie, Freie Universität Berlin, Takustr. 3, 14195 Berlin, limbach@chemie.fu-berlin.de

For the calculation of Arrhenius curves of hydrogen transfer reactions and the corresponding kinetic H/D isotope effects various theories have been proposed. (1) First principle theories: Redfield-type, Variational Transition State or Instanton Theory. (2) Empirical models depending on experimental parameters: Siebrand model, the Dogonadze-Kusnetzov-Ulstrup-Knapp-Klinman-model, Bell tunneling model. The latter has been modified in my laboratory and will be discussed here in particular using a number of examples. Six parameters are required for the calculation of a single H and D transfer reactions, which can all be obtained experimentally if a large temperature range is covered (Fig. 1). Important new parameters are the minimum energy $E_m$ for tunneling to occur and a contribution $\Delta m$ of heavy atom motions to the tunneling mass. Different sources of $E_m$ and $\Delta m$ and their influence on the Arrhenius curves are discussed. Hydrogen bond compression is implicitly taken into account in the model. In addition, pre-equilibria leading to or away from the reacting configuration are easily included. Several applications are discussed and literature cases are addressed where the Bell tunneling model had been considered as not able to represent experimental results. In conclusion, the Bell-Limbach model can serve in a first analysis of Arrhenius curves and prepares for subsequent first principle studies.

![Fig. 1. Typical Arrhenius curves of H and D transfer calculated using the six parameters of the Bell-Limbach tunneling model.](image-url)
Hydride transfer probed using mass modulated enzymes and coenzyme biomimetics

Nigel S. Scrutton

Centre for Synthetic Biology of Fine and Speciality Chemicals, Manchester Institute of Biotechnology and School of Chemistry, University of Manchester, Manchester, United Kingdom

The flavoenzyme pentaerythritol tetranitrate reductase (PETNR) catalyses the reduction of a wide range $\alpha,\beta$ unsaturated carbonyl compounds, some of biotechnological interest, through oxidation of the coenzyme NAD(P)H. Over the years we have investigated the mechanism of hydride transfer from both forms of the reducing nicotinamide coenzyme and more recently a number of non-natural nicotinamide biomimetics. In all cases hydride transfer from the coenzyme/biomimetics is by quantum mechanical tunneling. The enzyme–coenzyme/reactant complex involves $\pi-\pi$ stacking of the NAD(P)H nicotinamide and flavin mononucleotide (FMN) isoalloxazine moieties, which form a charge-transfer (CT) complex. In addition to FMN, there are 16 “local” active site residues within 5 Å of the bound coenzyme. To investigate whether “heavy enzyme” isotope effects in PETNR arise through local and/or global perturbations, we have used specific labeling of the protein and/or FMN to untangle their individual contributions to “heavy enzyme” effects [1]. Ultrafast fluorescence spectroscopy was then used to probe the time scales of vibronic coupling between protein and FMN to infer likely time scales of those vibrations involved in the “heavy enzyme” effect in PETNR. Isotope effects specifically arising from the FMN suggests that vibrations local to the active site play a role in the hydride transfer chemistry, while the protein-only “heavy enzyme” effect demonstrates that protein vibrations contribute to catalysis in PETNR. With selected biomimetics hydride transfer is faster than with the natural coenzymes [2,3]. The temperature dependence of kinetic isotope effects (KIEs) for hydride transfer between these “better than nature” biomimetics is consistent with transfer by quantum mechanical tunneling. A strong correlation between rate constants and temperature dependence of the KIE ($\Delta\Delta H^\ddagger$) for H/D transfer implies that faster reactions with biomimetics are associated with enhanced donor–acceptor distance sampling suggesting this is (partly) responsible for the observed rate enhancements. This emphasizes the need to optimize donor–acceptor distance sampling to obtain high catalytic performance from H-transfer enzymes. Combined, our work with mass modulated enzymes and coenzyme biomimetics is providing deeper insight into mechanisms of hydride transfer and the potential importance of dynamics in assisting these tunneling reactions.

References
The kinetics of tunneling reactions strongly depend on the molecular environment. Weak interactions with solvents, organic glasses, or matrices slightly change geometries and charge distributions in molecules which frequently results in drastic changes in tunneling rates.

We will discuss several examples from our laboratory which show variations in tunneling rates in matrices such as parahydrogen, argon, or xenon.\textsuperscript{1,2} One example is 1,5-dimethylsemibullvalene, which rapidly undergoes a degenerate Cope rearrangement. Borden et al. predicted that carbon tunneling allows the degenerate Cope rearrangement of semibullvalene to occur rapidly at cryogenic temperatures and suggested an experiment based on isotopic substitution to verify this hypothesis.\textsuperscript{3} We could verify this prediction using matrix isolation spectroscopy.

\begin{figure}[h]
  \centering
  \includegraphics[width=0.8\textwidth]{reaction_diagram.png}
  \caption{Reaction diagram of 1,5-dimethylsemibullvalene.}
\end{figure}

\textbf{References}

Quantum entanglement is one of the least intuitive properties of quantum systems. Regardless of whether or not actual quantum computing devices, based on quantum entanglement, have been realized, the field of entanglement has proven to be a robust landscape from which many new and innovative research areas have arose. The most prevalent of which is the study of quantum spin systems, which are seen as the most viable candidates for quantum devices, due to the relative ease with which Bell pair states can be achieved. However, what they owe in simplicity, they may lack in versatility, and some have sought an alternative system that would provide more flexibility than that of basic, two-level spin systems. In this vein, we present here an overview of the work done in the field of quantum rotors. In particular, we showcase exact dynamics calculations done on both quadrupolar (hydrogen clusters) and dipolar (hydrogen fluoride chains) molecular rotor systems. With regards to the former, we explore the importance of many-body effects on the vibrational spectra. As for the latter, the entanglement entropy is computed as a function of various geometric parameters. To date, the limiting factor of this field, like most in exact quantum dynamics, has been the exponential scaling of exact basis set solutions to the full rovibrational Schrodinger Equation. One way to directly circumvent this, is to utilize Quantum Monte Carlo approaches where one forgoes full eigenstate resolution. Rather, statistical estimates of properties such energy expectation values and correlation functions are obtained. However, full basis set calculations are necessary for proper benchmarking of these types of methods. That is not to say that exact calculations are one-dimensional in scope. On the contrary, modern computational technology, coupled with smart theoretical techniques, allow for the exploration of systems sizes beyond that of the simple proof-of-concept ranges.
Including tunneling in semiclassical simulations

Rubén Meana-Pañeda\textsuperscript{a}, Jingjing Zheng\textsuperscript{b}, Xuefei Xu\textsuperscript{c}, and Donald G. Truhlar\textsuperscript{d}

\textsuperscript{a}Laboratory of Computational Biology, National Heart, Lung and Blood Institute, National Institutes of Health, Bethesda, Maryland, USA ruben.meana-paneda@nih.gov, \textsuperscript{b}Gaussian, Inc., Wallingford, Connecticut, USA zheng@gaussian.com \textsuperscript{c}Center for Combustion Energy and Department of Thermal Engineering, Tsinghua University, Beijing, PR China, xuxuefei@tsinghua.edu.cn, \textsuperscript{d}Department of Chemistry, Chemical Theory Center, and Supercomputing Institute, University of Minnesota, Minneapolis, Minnesota, USA, truhlar@umn.edu

Tunneling is a quantum mechanical effect by which a particle can pass through a classically forbidden region of space, i.e., by which a particle goes through a barrier that it classically it could not surmount. This effect is especially important for reactions that involve light particles, such as proton transfer or hydrogen-atom transfer reactions that are important in biochemistry, combustion, atmospheric chemistry, and catalysis.

The classical trajectory method is a powerful tool that has been used to study complex dynamical systems; when applied to complex systems it is often just called “molecular dynamics.” However one drawback is that tunneling is neglected. Over the years various attempts have been made to include tunneling in classical simulations, but none of these have led to a successful practical method. Here we present a practical algorithm to include tunneling in molecular dynamics simulations. The essential features that make the new method successful are that it uses the army ants algorithm for quantum mechanical rare event sampling and partially optimized semi-classical tunneling paths based on internal coordinates.
Lipoxygenase as a Model for Vibronically Non-Adiabatic Proton-Coupled Electron Tunneling Near Room Temperature

Judith P. Klinman

Department of Chemistry and Department of Molecular and Cell Biology
University of California, Berkeley, CA 94720
klinman@berkeley.edu

The enzyme soybean lipoxygenase (SLO) catalyzes a proton coupled electron transfer reaction from C-11 of its substrate linoleic acid to an active site ferric-hydroxide reactive center:

This reaction is characterized by a family of distinctive kinetic parameters that include: a highly inflated kinetic deuterium isotope effect, a low energy of activation and a small difference in energy of activation for transfer of deuterium vs. protium, \( \Delta E_a = E_a(D) - E_a(H) \). These properties have been further explored via the introduction and characterization of a series of site specific mutants. Perhaps the most startling outcome is a double mutant, in which two active site hydrophobic residues have been reduced in size, referred to as DM-SLO. The DM-SLO shows the highest kinetic deuterium isotope effect reported for any condensed phase reaction near room temperature, \( k_H / k_D = 661\pm27 \). Biophysical probes have been combined with kinetic analyses using both WT and mutant enzymes; these probes include ENDOR spectroscopy, the application of high pressure, and hydrogen deuterium exchange into the protein backbone. A model that is consistent with the aggregate data invokes a multi-dimensional process in which the heavy atoms of the protein tune the enzyme active site for efficient electron and proton tunneling. The different classes of stochastic motions within the protein backbone include global motions that are independent of the pattern of labelling of substrate (referred to as conformational sampling) and local motions that allow for a rapid sampling of families of H-donor acceptor distances; the latter are sensitive to the isotope undergoing transfer. This enzyme system provides a unique opportunity to tease apart the physical parameters that underlie enzyme catalyzed C-H activation processes.

(Supported in part by funds from the NIGMS)
The theoretical calculation of accurate thermal rate constants is essential in Chemistry and the comparison with experimental data has allowed the chemical community to get insight into the mechanistic of chemical systems. The well-known Transition State Theory (TST) is, probably, the most famous approach to estimate thermal rate constants with almost no computational cost. Unfortunately, as a counterpart to its simplicity, these rate constants may not be good enough to satisfactorily reproduce the experimental values. For this reason, different corrections should be introduced to obtain accurate values, which can be achieved using Variational Transition State Theory (VTST) [1] and its multi-path analogue (MP-VTST) [2].

Here we present Galitherra [3], a new software developed in our Research Group, which is able to calculate VTST and MP-VTST thermal rate constants in all type of systems. Among the different features of this program, we highlight: (i) calculation of the minimum energy path (MEP) by the Page-McIver algorithm [4], (ii) automatic definition of redundant internal coordinates followed by the corresponding projection of the force constant matrix along the MEP [5], (iii) calculation of the canonical variational transition state [1], (iv) estimation of tunneling effects using Small-Curvature Tunneling (SCT) [6], (v) incorporation of anharmonicity in torsional degrees of freedom [7], and (vi) possibility of dealing with conformational reaction channels [8].

In relation to the calculation of molecular properties, such as energies, gradients and force constants, Galitherra can readily interact with Gaussian and Orca through a simple script. It can also be easily modified by the user to introduce additional electronic structure packages or analytical potential energy surfaces.

[3] From “General ALgorithm Implantation for THERmal Rates”.
A recently described symmetrical windowing methodology [J. Phys. Chem. A 117, 7190 (2013)] for quasi-classical (SQC) trajectory simulations has been applied to the Meyer-Miller (MM) [J. Chem. Phys. 70, 3214 (1979)] model for the electronic degrees of freedom in electronically non-adiabatic dynamics. The approach treats nuclear and electronic degrees of freedom (DOF) equivalently (i.e., by classical mechanics, thereby retaining the simplicity of standard molecular dynamics), and provides ”quantization" of the electronic states through the symmetrical quasi-classical (SQC) windowing model. The approach is seen to be capable of treating extreme regimes of strong and weak coupling between the electronic states, as well as accurately describing coherence effects in the electronic DOF (including the de-coherence of such effects caused by coupling to the nuclear DOF). A survey of recent applications to a variety of problems is presented to illustrate the performance of the approach. Also described is a newly developed variation on the original SQC model (found universally superior to the original) and a general extension of it to obtain the full electronic density matrix (at no additional cost/complexity). It has also been pointed out that even though the MM classical vibronic Hamiltonian generates ‘Ehrenfest dynamics’, when this is processed via the SQC windowing methodology detailed balance is described correctly. A full review of much of this work is given in W. H. Miller and S. J. Cotton, Classical Molecular Dynamics Simulation of Electronically Non-Adiabatic Processes, Faraday Discuss. 195, 9-30 (2016).
We describe computational approaches to the elucidation of the quantal translational-rotational dynamics of entrapped molecular clusters. The focus is on dihydrogen clusters entrapped in clathrate hydrate cages. We discuss nuclear-orbital/configuration-interaction methods applied to the dynamics of (H$_2$)$_4$ entrapped in the large cage of type-II clathrate hydrate. We also discuss an approach in which the correlated translation motion of the two H$_2$ moieties in clathrate-entrapped (H$_2$)$_2$ is solved for first, the results of which are then used to build up a translation/rotational basis for the solution of the full dynamics of the entrapped cluster. We find that the dynamics of the encaged clusters is well modeled by taking them to be semi-rigid molecules composed of spherical H$_2$ pseudo-atom moieties.
Manipulating and probing the polarisation of a methyl tunnelling system by field-cycling NMR

Anthony J Horsewill, Bo Zhang, Sabah M.M. Abu-Khumra, & Abdellah Aibout

School of Physics & Astronomy, University of Nottingham, Nottingham, NG7 2RD, UK
A.Horsewill@nottingham.ac.uk

In NMR the polarisation of a Zeeman system may be routinely probed and manipulated by applying resonant rf pulses. At low temperature, like spin-½ nuclei, the quantum tunnelling states of a methyl (CH₃) rotor are characterised by two energy levels and it is interesting to consider how these tunnelling states might be probed and manipulated in an analogous way to nuclear spins in NMR. In this presentation, magnetic field-cycling NMR experiments will be described where, by irradiating methyl tunnelling sidebands, the polarisation of the CH₃ tunnelling system is measured and manipulated in a prescribed fashion. At the heart of the technique is a phenomenon that is analogous to dynamic nuclear polarisation and the solid effect where forbidden transitions mediate polarisation transfer between ¹H Zeeman and methyl tunnelling systems. Here, level-crossings between CH₃ tunnelling and ¹H Zeeman energy levels are utilised in the experimental scheme. Depending on the irradiated sideband, both positive and negative polarisations of the CH₃ tunnelling system are achieved, the latter corresponding to population inversion and negative tunnelling temperatures. The transition mechanics will be investigated through a series of experiments and a theoretical model presented that provides good quantitative agreement with experiment.

Empirical Valence Bond studies of decomposition of neurotransmitters catalyzed by monoamine oxidases

Jernej Stare and Janez Mavri

National Institute of Chemistry, Ljubljana, Slovenia, e-mail: jernej.stare@ki.si

Monoamine oxidase enzymes (MAO) catalyze oxidative decomposition of primary amines in the central nervous system, thereby regulating the levels of monoaminergic neurotransmitters. Deficient or elevated activity of MAO enzymes is a source of various neurological and psychiatric disorders and diseases. Due to their high clinical relevance, MAO enzymes have been subject of extensive experimental and theoretical studies. Our earlier quantum studies of MAO give strong support for the hydride transfer mechanism of the rate limiting step (Fig. 1).

![Figure 1. Left: scheme of the reaction mechanism; right: active site of MAO with the residue 335 subject to mutation.](image)

Our recent work on MAO enzymes is mainly based on the Empirical Valence Bond (EVB) methodology, a cost-effective multiscale technique based on the quantum treatment of empirical valence states embedded in a classical environment. We elucidated various aspects of MAO action, among the rest the role of nuclear quantum effects [1] and point mutation effects [2]. The H/D isotope effect computed by the Path Integral quantization method is about 13, which is in fine agreement with the available experimental data, hence confirming the proposed hydride transfer mechanism. Mutation of the residue 335 from Ile to Tyr (Fig. 1) gives rise to an increased free energy barrier, resulting in about an order of magnitude decrease in the reaction rate, again reasonably reproducing experimental observations. The decrease in catalytic activity of MAO on mutation can be readily explained by the change in polar and Van der Waals interactions. Finally, we addressed the issue of the reaction phase space sampling [3], because it critically governs the accuracy and reliability of simulation of enzymatic reactions. For the better understanding of the sampling impact we used a gas phase reaction model treated by EVB.

Proton tunneling reactions in proteins have been probed experimentally and analyzed theoretically and, in the case of $OH--O$ hydrogen bonds, they are found to take place on surprisingly rapid timescales (~400ps) at room temperature [1-3]. It is demonstrated how conformational fluctuations and vibrational excitations associated with “soft” low-frequency protein modes can control the tunneling reaction rates by many orders of magnitude. An example involving a specific biomolecule (Green Fluorescent Protein, GFP) is presented that demonstrates how such motions are utilized to facilitate tunneling reactions along “proton wires” within proteins. This example suggests how high pK amino acid residues, such as serine and threonine, can participate in these “wires” and act to help control the direction of proton flow. Another example involves the enzymatic catalysis of the hydrogen atom abstraction from an aliphatic carbon substrate in soybean lipoxygenase (SLO). In analyzing such a reaction, the anharmonic electronic repulsion between the donor and acceptor atoms can be an important factor. This, along with a quantum chemical calculation of the charge on the active site oxygen acceptor atom, allows an estimate of the mechanical and electric field forces (that are extrinsic to the local $CH--O^{\delta-}$ interaction), which are necessary to establish a donor-acceptor distance distribution that is consistent with the measured tunnelling kinetics.

References

DOI:10.1021/acs.jpca.7b00539.
Heavy-atom tunneling calculations in thirteen organic reactions: Bell’s formula matches multidimensional tunneling at ≥ 250 K.

Edyta M. Greer, Randy Armas, Dana Walker, Christopher V. Cosgriff, Charles Doubleday

\textit{a} Department of Natural Sciences, Baruch College of the City University of New York, 17 Lexington Avenue, New York, New York 10010, United States, e-mail: edyta.greer@baruch.cuny.edu, \textit{b} Department of Chemistry, Columbia University, 3000 Broadway, MC 3142, New York, New York 10027, United States, e-mail: ced3@columbia.edu

Multidimensional tunneling calculations were carried out for thirteen reactions, including pericyclic, cycloaromatization, radical rearrangements and SN2 reactions. Transmission coefficients, $\kappa$, were computed in the small curvature tunneling SCT approximation, $\kappa_{\text{SCT}}$, and compared with the simple Bell formula, $\kappa_{\text{Bell}}$. The two methods agreed remarkably well – mean unsigned errors (MUEs) are 0.09, 0.05, 0.02 at 250, 300 and 400 K. MUEs drop to 0.06, 0.03, and 0.02 if one reaction with a valley-ridge inflection close to the TS was excluded. In 8 of the 13 reactions, tunneling accounts for 20 - 95% of the rate when the reactions are compared at the temperatures that give the same effective rate constant of 3 x 10^{-5} \text{ s}^{-1}, which is commonly encountered experimentally. We will discuss how $\kappa_{\text{Bell}}$ could assist with preliminary scanning for the contributions of heavy-atom tunneling in organic reactions.
Tunnelling and Parity Violation in Chiral Molecules: From Theory towards Spectroscopic Experiment and the Evolution of Biomolecular Homochirality

Martin Quack

*Physical Chemistry, ETH Zurich, CH-8093 Zurich, Switzerland, e-mail: Martin@Quack.CH, www.ir.ETHz.CH*

We shall start with an introductory discussion of three fundamental questions relating physics to molecular quantum dynamics and stereochemistry.
(i) To what extent are the fundamental symmetries and conservation laws of physics and their violations reflected in molecular quantum dynamics and spectroscopy, in general? (ii) How important is parity violation for the quantum dynamics and spectroscopy of chiral molecules, in particular? (iii) How important is parity violation for biomolecular homochirality, i.e. the quasi exclusive preference of L-amino acids and D-sugars in the biopolymers of life (proteins and DNA)? The observation of biomolecular homochirality can be considered as a quasi-fossil of the evolution of life [1], the interpretation of which has been an open question for more than a century. We shall briefly discuss the current status and the relation to the other two questions. The discovery of parity violation leads to the surprising prediction of a small energy difference $D$ of the ground state energies of the enantiomers of chiral molecules, corresponding to a small reaction enthalpy for the stereomutation between the $R$ and $S$ enantiomers [2]. This reaction enthalpy would be exactly zero by symmetry with exact parity conservation. Theory predicts to be $D$ in the sub-femto eV range, typically, depending on the molecule (about 100\,aeV for ClSSCl or CHFClBr, corresponding to an enthalpy of reaction of about 10\,pJ/mol). We have outlined three decades ago, how this small energy $D$ might be measured by spectroscopic experiment [3], and recent progress indicates that experiment might be successful in the near future [4-7]. We shall report about the current status of our experiments and theories including tunneling switching in slightly asymmetric potentials. For background reading see [1-7].

On the use of quantum dynamics to unveil the complex photochemistry of green fluorescent protein.

Miquel Moreno\textsuperscript{a}, Marc Nadal-Ferret\textsuperscript{b}, Ricard Gelabert\textsuperscript{c} and José M. Lluch\textsuperscript{d}

\textsuperscript{a} Departament de Química, Universitat Autònoma de Barcelona, 08193 Bellaterra, Barcelona, Spain. E-mail: miquel.moreno@uab.cat, \textsuperscript{b} Departament de Química. E-mail: marcnadalferret@gmail.com, \textsuperscript{c} Departament de Química. E-mail: ricard.gelabert@uab.cat, \textsuperscript{d} Departament de Química and Institut de Biotecnologia i de Biomedicina, Universitat Autònoma de Barcelona. E-

In this work we show that the use of quantum dynamics is mandatory in order to explain the complex photochemical processes that take place in green fluorescent protein (GFP), a target of enduring scientific interest due to their wide applications as fluorescent marker in biomedicine.

The photochemistry of GFP involves a wire of three hydrogen atoms. In the ground electronic state ($S_0$) the form with the chromophore protonated is dominant whereas in the first singlet excited electronic state ($S_1$) the structure involving an anionic chromophore is predominantly obtained. We have devised a simple model of the proton wire in order to perform quantum dynamical calculations of the GFP system. Our results indicate that the proton transfer is not possible if structural relaxation of the surroundings of the chromophore is prevented and that two of the three hydrogen atoms involved in the wire are found very close to the point halfway between the donor and acceptor atoms, especially after photoexcitation, giving support to the claim that the first transient intermediate detected after photoexcitation has characteristics similar to those of a low-barrier hydrogen bond (LBHB)\textsuperscript{[1]}. The existence of an oscillating stationary state between the reactants and products of the triple proton transfer reaction can explain the dual emission reported for the intermediate of GFP.

As a complement to this work, a method to compute probability current and its surface integral, the total flux, for systems of many particles of different masses is presented. An adaptive Monte Carlo method is proposed with favorable scaling properties to solve the flux integral. Using this new method the flux can quantitatively be divided into tunneling and classical parts. Application of this method to the GFP model reveals that, surprisingly enough, the system, despite having enough energy to afford the classical reaction pathway, in a substantial portion of the wave packet proceeds through classically forbidden areas.

Neutron spectroscopy of water under ultra-confinement

Alexander I. Kolesnikov

Chemical and Engineering Materials Division, Oak Ridge National Laboratory, Oak Ridge, Tennessee 37831, USA, kolesnikovai@ornl.gov

Water confined within microporous materials, inside of nanometer size carbon nanotubes or sub-nanometer channels of silicate minerals, presents an extreme case of confinement, where the restricted molecules are situated in channels whose diameter is not much larger than the water molecule itself. In this talk I will present study dynamics of ultra-confined water by using inelastic and deep inelastic neutron scattering (INS and DINS, respectively). INS is a unique method to study the vibrational and quantum tunneling dynamics of hydrogen-containing materials because of the anomalously large neutron scattering cross section of hydrogen, and DINS provides a means of directly and accurately measuring the momentum distribution of protons, which is determined primarily by the proton ground-state wave function.

Using neutron scattering and ab initio simulations, we recently discovered a new “quantum tunneling state” of the water molecule confined in 5 Å channels in the mineral beryl, characterized by extended proton and electron delocalization [1]. A number of peaks were observed in the INS spectra which were uniquely assigned to water quantum tunnelling. In addition, the water proton momentum distribution measured with DINS directly showed coherent delocalization of the water protons in the ground state. The average kinetic energy of the water protons, directly obtained from the DINS experiment, is a measure of their quantum-mechanical zero point motion, and is found to be ~30% less than it is in bulk liquid or solid water, in complete disagreement with accepted models based on the energies of its vibrational modes. Due to the observation of multiple tunneling peaks in the INS spectra and the coherent delocalization of protons identified from the DINS data, we consider that tunneling water can be described as water with delocalized protons over all possible positions across the beryl channel, and therefore can be called “a new state of the water molecule”.

The dynamics of water in beryl will be compared to the behavior water in carbon nanotubes of 1.4 nm diameter, where a similar large delocalization of water protons and strong reduction of their kinetic energy were observed [2,3]. Molecular dynamics simulations consistently describe the observed phenomena and propose the structure of nanotube water, which comprises a square-ice sheet wrapped into a cylinder inside the carbon nanotube and interior molecules in a chainlike configuration. The anomalously soft dynamics of water was explained by the drastic change in hydrogen-bond connectivity of the central water chain.

The classical dynamics of nuclei is adequate in many situations (high-temperature, high-energy processes), providing insight into chemical processes. Yet it is well-known that quantum features of nuclear behavior -- the zero-point energy, tunneling and nonadiabatic dynamics -- are sometimes important in low-energy reactions and in photochemistry. We are interested in the intermediate regime when quantum-mechanical (QM) behavior of a few selected nuclei influences the properties of a large system. To make qualitative predictions and cheap estimates of the nuclear QM effects we are developing approximate dynamics based on the quantum trajectory (QT) formulation of the Schrödinger equation. The QM effects are incorporated through the quantum potential, computed in the “mean-field” approximation, acting on the trajectory ensemble in addition to the classical potential. Large molecular systems are described in a mixed quantum/classical QT framework with the QM correction incorporated into selected degrees of freedom [1]. The approximate QT dynamics is combined with the Density Functional Tight Binding to compute the electronic structure on-the-fly for systems of up to 200 atoms. Interaction of the quantum hydrogen colliding with the graphene model, C_{37}H_{15} [2], and the proton/deuteron transfer through atomically thin layers of hexagonal boron nitride will be discussed.

The challenging quantum dynamical description of the CH$_4$·H$_2$O complex has been solved variationally [1,2] to provide theoretical explanation and assignment [1] to the high-resolution spectroscopic measurements of the methane-water dimer carried out some twenty years ago [3]. The computational results are in excellent agreement with the reported experimental transitions and the experimentally observed reversed rovibrational sequences, i.e., formally negative rotational excitation energies, are also obtained in the computations. In order to better understand the origin of these peculiar features in the energy-level spectrum, we studied [2] all four possible combinations of the light and heavy isotopologues of methane and water and analyzed their rovibrational states using two limiting model systems: the rigidly rotating (RR) molecule and the coupled rotor (CR) system corresponding to the coupling of the two rotating monomers. Symmetry properties of the coupled-rotor functions also open a route to an automated symmetry assignment of the computed rovibrational states.

All rovibrational quantum dynamical computations were carried out with rigid monomers and J = 0,1,2 total angular momentum quantum numbers using the fourth-age quantum chemical code GENIUSH [3,4] and two different methane-water potential energy surfaces (PES) [5,6]. The numerical and formal analysis of the wave functions give insight into a fascinating complex world worth for further theoretical and experimental inquiries.

Isotopically Different Tunneling-Ready-State Structures in Hydride Transfer Reactions in Solution

Yun Lu

Department of Chemistry, Southern Illinois University at Edwardsville, Edwardsville, Illinois 62026

Contemporary H-tunneling models, including the activated H-tunneling model and multi-dimension H-tunneling model within the variational transition state theory, contain a common concept that the tunneling of a heavier isotope (for example, deuterium (D)) requires a shorter donor-acceptor distance (DAD) than does a lighter isotope (for example, protium (H)). This is due to the fact that the quantum mechanical de Broglie wavelength of the donor(acceptor)-D bond vibration is shorter than that of the H one. The purpose of this research is to examine the “DAD concept” by studying the H-transfer reactions in solution. The hypothesis is that the H/D tunneling takes place by different tunneling-ready states (TRSs), which would have different conformations and different electronic structures. The approach that we use to distinguish the isotopically different TRSs involve the study of the effect of the transferring (“in-flight”) primary (1°) isotope (H vs. D) on the vibrations of the “in-place” secondary (2°) H vs. D bonds, and the effect on the Hammett correlations at the donors or acceptors. Experimentally, we determine the 1° isotope effect on the 2° kinetic isotope effects (KIEs) at various H/D positions and the substituent effect on the 1° KIEs. The systems that we studied include several hydride transfer reactions in solution. The method to determine the 1° and 2° KIEs will be reported. The isotopically different TRS structures for several hydride-tunneling reactions will be discussed. Computational replication of the observed 2° KIEs will help resolve the detailed TRS structures.
We report a method to compute the quantum transition-state structure for H-transfer reactions. A reactive complex structure, in which the H-donor (D) and -acceptor (A) reacting atoms are bonded, is first optimized to obtain the correlation between the two structures. Then a H is placed in between the separated D and A while keeping both geometries intact. The resulting hessian matrix is then subjected to restrictions that place D/H/A in a straight line and keep the H in the middle. Since the restricted hessian matrix confines the middle H from approaching closely to either D or A atom, the method does not allow optimization to reach a reactive complex in which H is actually bonded. The structure is then optimized to reach a minimum energy (allowing any change including the change in donor-acceptor distance (DAD) and hybridization, and structural rotation along the D/H/A axis). The resulting optimized structure has a DAD suitable for H-tunneling and the middle H has an imaginary frequency that reflects the transient nature of the “in-flight” H. This structure is a H-tunneling-ready-state (TRS). We have applied the method to study several self-exchange hydride transfer reactions (D and A are the same) and the TRS structures were found. The corresponding DADs were from 3.0 to 3.4 Å and the imaginary frequencies from 1100 to 2400 cm⁻¹. These imaginary frequencies and DADs reflect the quasi particle nature of the transferring H within appropriate DADs for H-tunneling. The TRSs found were further subjected to energy profile analysis to give the tunneling probability and tunneling rates. We are in a process to find a way to calculate the kinetic isotope effects on the basis of the TRS found.
The mechanism of double proton transfer at very low temperatures.

A. Fernández-Ramos

Center for Research in Biological Chemistry and Molecular Materials (CIQUS), Universidade de Santiago de Compostela, Spain. E-mail: qf.ramos@usc.es

This theoretical study reports a Hamiltonian which has been designed to study systems of two identical symmetric hydrogen bonds, weakly coupled such that the two mobile protons can move either separately (stepwise) or together (concerted). The model consists of two equivalent quartic potentials interacting through (repulsive) dipolar and quadrupolar coupling terms. The resulting two dimensional tunneling Hamiltonian has two imaginary modes, a maximum which turns into a saddle-point of second order in the multidimensional case, and two sets of (inequivalent) minima.

At low energy the resulting eigenvalues tend to be arranged as closely spaced pairs, while at higher energies, they converge to regular vibrational progressions. On the basis of their nodal properties, the eigenfunctions are classified as either symmetric or antisymmetric, and the antisymmetric eigenfunctions as either trans or cis, depending on their orientation with respect to the two sets of minima; for repulsive interaction, the trans axis connects the two equilibrium configurations and the cis axis the two secondary minima. From these data the mechanism of proton transfer is derived. At low energy, the protons move by tunneling and the separation of the closely spaced levels can be interpreted as tunneling splitting. To find out whether the two protons move stepwise or concerted, we introduce a new tool, based on the distribution of the probability flux in the dividing plane of the transfer mode. This distribution varies between a single Gaussian for concerted transfer and two overlapping Gaussians for stepwise transfer, which makes it possible to identify the conditions for concerted, stepwise and mixed transfer, at least for the lowest levels, and relate these to the tunneling splitting. While stepwise transfer dominates for very weak coupling, it is found that concerted tunneling (co-tunneling) always occurs, even when the coupling vanishes. This is a quantum-mechanical effect, due to the symmetry of the Hamiltonian, which imposes permanent entanglement on the motions of the two protons.

For a given set of model parameters the contributions of the two tunneling pathways to the double-proton transfer can be evaluated quantitatively. The model results can be generalized to results for real systems by including coupling of the tunneling modes to the skeletal modes into the parameters defining the Hamiltonian. This is demonstrated for the molecule porphycene for which the observed tunneling splitting is calculated by this method, yielding a value in satisfactory agreement with experiment and the conclusion that the double-proton tunneling is predominantly concerted.
Quantum transition-state theory

Timothy J. H. Hele\textsuperscript{a,*} and Stuart C. Althorpe\textsuperscript{b}

\textsuperscript{a} Department of Chemistry and Chemical Biology, Cornell University, Ithaca, NY 14850, USA; t.hele@cornell.edu \textsuperscript{b} Department of Chemistry, University of Cambridge, CB2 1EW, UK; sca10@cam.ac.uk. *On intermission from Jesus College, Cambridge University, UK.

The accurate and inexpensive calculation of reaction rates in quantized systems is pivotal to understanding tunneling and zero-point energy effects. Here we show how classical transition-state theory [1,2] can be rigorously extended to the quantum regime [3-7], giving a rate theory whose only approximation is the absence of recrossing. The key ingredient is placing the flux and side diving surfaces in the same place in path-integral space in order to give the instantaneous thermal quantum flux through a position-space dividing surface [3]. We also touch upon the origins [1,2] and applications of the theory and areas for future progress [7].

How Important is Nuclear Quantum Tunneling in Enzyme Reactions?

Dan T. Major\textsuperscript{a}, Anil Mhashal\textsuperscript{b}, and Amnon Kohen\textsuperscript{c}

\textsuperscript{a} Department of Chemistry, Bar-Ilan University, Ramat-Gan 52900, Israel, majort@biu.ac.il, \textsuperscript{b} Department of Chemistry, Bar-Ilan University, Ramat-Gan 52900, Israel, anil2000.2008@gmail.com, \textsuperscript{c} Department of Chemistry, University of Iowa, Iowa City, Iowa 52242 USA

How important is nuclear quantum tunneling in enzyme reactions? This question is of great current interest and has created much debate. In this presentation, we will address this question by looking at work in this area through a wide lens, with particular focus on several theoretical studies conducted in our and other group in recent years. Initially, we will present multiscale simulation approaches that allow treatment of quantum tunnelling by combining classical and quantum methods, with emphasis on path-integral methods developed in our group. We will bring benchmark results for our methods on simple organic systems, before turning our attention to enzymatic systems. Specifically, in the current presentation we describe the quantum effects in three oxidoreductase enzymes studied in our group: (1) Nitroalkane Oxidase (NAO),\textsuperscript{1} Formate Dehydrogenase (FDH),\textsuperscript{2} and Dihydrofolate Reductase (DHFR).\textsuperscript{3} In NAO the overall rate limiting step is a proton transfer, while in DHFR and FDH the chemical step entails a stereospecific hydride transfer. In these enzymes, we compute rate constants and kinetic isotope effects using path-integral simulation methods developed in our group. For the NAO reaction, we study the enzymatic reaction as well as an analogous proton abstraction in aqueous solution. Interestingly, we show that in NAO there is a small catalyzing tunneling contribution. This conclusion is based on computationally predicted and experimental primary and secondary kinetic isotope effects, as well as direct tunneling calculations. In the case of FDH and DHFR we present compelling evidence from work in our and other groups for moderate quantum tunneling effects, suggesting that the transition states may be described as diffuse quantum states dominated by zero point vibrational effects.\textsuperscript{4}

References:
Primary Isotope Dependence of the Secondary Kinetic Isotope Effects and Hammett Correlations in Hydride Transfer Reactions in Solution

Paniz Rahmani, Shabnam Jafari, Christopher Hall, Yun Lu

Department of Chemistry, Southern Illinois University at Edwardsville, Edwardsville, Illinois 62026

Recent explanation of the primary (1°) isotope effect on the α- and β-secondary (2°) kinetic isotope effects (KIEs) in H-transfer reactions uses the concept for a H-tunneling mechanism that the donor-acceptance distance (DAD) is shorter in a heavier isotope tunneling process. Results suggest isotopically different tunneling-ready-state (TRS) conformations. In order to further support the “DAD concept”, we determined the 1° isotope dependence of 2° KIEs for hydride transfer reactions from 10-methylacidan (MAH) and 9,10-dimethylacridan (DMAH) to sterically hindered 9-(4-substituted-phenyl)xanthylum ions (ArXn+) in acetonitrile. The 2° KIEs include those on the α-, β- and ε-H/D positions of the MAH and DMAH. Furthermore, in order to study the electronic structures of the TRSs for the H- and D-tunneling processes, the substituent effects on the 1° KIEs were determined and the 1° isotope dependence of Hammett correlations was studied. Differences and similarities in geometrical and electronic TRS structures for H- and D-tunneling processes will be discussed.
Study of the Primary Isotope Dependence of Secondary Kinetic Isotope Effects in a Hydride Transfer Reaction in Solution

Micheal Ontl, Yun Lu

Department of Chemistry, Southern Illinois University at Edwardsville, Edwardsville, Illinois 62026

We recently reported the primary (1°) isotope dependence of the α- and β-secondary (2°) kinetic isotope effects (KIEs) in a few hydride-transfer reactions in solution. Results were explained using the concept for a H-tunneling mechanism that the donor-acceptance distance (DAD) is shorter in a heavier isotope tunneling process. This suggests isotopically different structures of the tunneling-ready-states (TRSs). In order to further support the isotopically different TRS conformations and study the detailed H-tunneling mechanism, herein we report the 1° isotope effect on the 2° KIEs for the hydride transfer reaction from 5-methyl-5,6-dihydrophenathrine (MPH) to N-methylacridinium ion (MA+) in acetonitrile. The 2° KIEs include those at the γ-CH3/CD3 position of the MPH as well as the α-H/D and ε-CH3/CD3 positions of the MA+. The TRS structures of the reaction on both H- and D-transfers will be discussed.
List of Participants

Champion, Paul, Northeastern University, Boston, Massachusetts, p.champion@neu.edu

Eckert, Juergen, Texas Tech University, Lubbock, TX, juergen.eckert@ttu.edu

Felker, Peter, University of California Los Angeles, Los Angeles, California, pmf@chem.ucla.edu

Fernandez-Ramos, Antonio, Universidade de Santiago de Compostela, La Coruña, Spain, qf.ramos@usc.es

Ferro-Costas, David, Universidade de Santiago de Compostela, La Coruña, Spain, gonzalo.ferro@usc.es

Garashchuk, Sophya, University of South Carolina, Columbia, SC, garashch@mailbox.sc.edu

Greer, Edyta, Baruch College, New York, NY, Edyta.Greer@baruch.cuny.edu

Halverson, Tom, University of Waterloo, Waterloo, ON, thalverson@uwaterloo.ca

Hele, Timothy, Cornell University, Ithaca, NY, t.hele@cornell.edu

Horsewill, Anthony, University of Nottingham, Nottingha, UK, a.horsewill@nottingham.ac.uk

Klinman, Judith, University of California Berkeley, Berkeley, CA, klinman@berkeley.edu

Kohen, Amnon, University of Iowa, Iowa City, IA, amnon-kohen@uiowa.edu

Kolesnikov, Alexander, Oak Ridge National Laboratory, Oak Ridge, TN, kolesnikovai@ornl.gov

Limbach, Hans-Heinrich, Freie Universitát Berlin, Kaiserswerther, Berlin, limbachchemie.fu-berlin.de

Lu, Yun, SIUE, Edwardsville, Illinois, yulu@siue.edu

Major, Dan, Bar-Ilan University, Ramat-Gan, Israel, majort@biu.ac.il

McMahon, Robert, University of Wisconsin-Madison Madison, WI, robert.mcmahon@wisc.edu

Mean-Paneda, Ruben, NIH, Rockville, MD, ruben.meana-paneda@nih.gov
Miller, William, University of California Berkeley, 
Berkeley, CA, millerwh@berkeley.edu

Moreno, Miquel, Universitat Autònoma Barcelona, 
Bellaterra, Catalonia, Spain, mmf@klingon.uab.es

Ontl, Michael, SIUE, 
Edwardsville, Illinois

Quack, Martin, ETH Zurich, 
Zürich, Switzerland, Quack@ir.phys.chem.ethz.ch

Rahmani, Paniz, SIUE, 
Edwardsville, Illinois, prahman@siue.edu

Sakhaee, Nader, SIUE, 
Edwardsville, Illinois

Sander, Wolfram, University of Bochum, 
Bochum, Germany, oc2@ruhr-uni-bochum.de

Sarka, János, Eötvös Loránd University, 
Budapest, Hungary, sarkajanos@gmail.com

Saykally, Richard, University of California Berkeley, 
Berkeley, CA, saykally@berkeley.edu

Stare, Jernej, National Institute of Chemistry, 
Ljubljana, Slovenia Jernej.Stare@ki.si