Final report for the NKFI PD_16 120776 Project

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Methodological developments in molecular dynamics and reaction dynamics simulations

(updated title)

Method of adiabatic switching for the preparation of rovibrationally quantized classical states

Detailed theoretical investigation of the dynamics of reactant rovibrational state-resolved bimolecular reactions beyond four atoms is feasible only with quasiclassical trajectory (QCT) simulations as application of exact quantum scattering methods is limited by the exponential scaling of the computational effort. In the QCT method, the motion of the atoms is simulated classically based on forces determined from electronic structure calculation and the only quantum effect considered is the energy quantization of the reactant molecules.

Semiclassical (SC) theory allows one to approximately determine the quantum energy levels of a system by setting the classical action for a period of a bound motion to discrete values directly determined by the semiclassical quantum number. SC theory provides exact energies for model systems, like the harmonic oscillator and the rigid rotor, however, it is difficult to apply in more dimensions. Thus, the standard method for the preparation of quantized ensembles, called normal mode sampling (NMS), decouples the motion into harmonic oscillators and rigid-rotors, and assigns quantized energies to them. By randomly selecting the phases of the modes, an ensemble of classical states is obtained, which is the quasiclassical representation of the quantum state. However, the total energies of these states evaluated on the true anharmonic potential energy surface (PES), will show a scatter and the ensemble won't be stationary (e.g. mean bond lengths oscillate), despite they supposed to represent a monoenergetic stationary quantum state. Thus, the reactivity calculated by QCT method for some bimolecular reactions may depend on the chosen initial distance of reactions.

Some decades ago, for the semiclassical treatment of vibrational anharmonicity, the method of adiabatic switching (AS) was proposed. According to the adiabatic principle the semiclassical quantum number is an adiabatic invariant as it is conserved upon the slow perturbation of the system, unless the structure of the accessible phase space changes during the process (e.g. bifurcation appears). Thus for a vibrating molecule, which has been semiclassically quantized within the harmonic approximation and prepared using random phases, the semiclassical quantum numbers are conserved if the anharmonicity is switched on sufficient slowly (starting from the harmonic system) and the motion stays integrable. The energy of each state in the ensembles converges to the same semiclassical energy value after very long switching periods and the ensemble represents the corresponding quantum state of the anharmonic system. However, molecules with more than three atoms usually vibrate chaotically, especially at higher excited states, and the energies of the states will show more or less scatter even for infinite switching times. The method was successfully applied to chaotically vibrating 3 and 4 atomic molecules using analytically derived Hamiltonians, but its application to methane in Cartesian coordinates was a failure (large scatter of energy), which ceased the interest in the method for two decades.

I recognized that the application of AS to methane was unsuccessful not because of its vibrations are overly chaotic, but because the initial, harmonic part of the time-dependent Hamilton function was defined in Cartesian coordinates, thus it inherently exerts a torque on the system. To avoid rotations, I proposed the use of internal coordinates and numerically constructed Hamiltonians, which can be generally applied to any molecules without the need of complicated derivations. Previously, AS has been applied to prepare pure vibrational states only. I recognized that rotations can be treated as perturbations, and extended the method to rovibrational states by slowly spinning up the vibrationally quantized molecules to the quantized angular momentum value. I successfully applied the method to methane using spectroscopically accurate analytic PESs for which exact quantum mechanical results were also available. The mean energies of the ensembles agreed very well with the exact values: the zero-point energy and the excitation energies of the 15 lines were within 20cm^{-1}, the rotational levels for J=1-50 agreed within 1% with the exact value, and energy scatter was always below 1%, whereas NMS always generated at least 1-2 order of magnitude larger errors. The ensembles were stationary and insensitive to the choice of internal coordinates (e.g. rectilinear vs curvilinear), which were not true for NMS ensembles. Applying the new AS methods instead of NMS, it become possible to prepare unambiguously defined, largely monoenergetic quantized stationary ensembles of classical states with semiclassically accurate energies (far within chemical accuracy) even for flexible molecules and excited states.

I published the results in the leading journal of Physical Chemistry [1] co-authoring Prof. György Lendvay, and presented at conferences [2-4]. Leading experts of reaction dynamics, Prof. George Schatz (editor in chief of JPC* journals) and Prof. Joel Bowman, praised the new developments, as they extended the range of applicability of quasiclassical trajectory simulations.

A novel form of the vibrational kinetic energy expression

Detailed quantum mechanical investigation of the dynamics of bimolecular reactions in full dimensionality (FD) is not possible yet for more than four atoms, therefore often reduced-dimensional models are applied, in which less important degrees of the freedom are frozen. The goodness of reduced-dimensional (RD) models usually cannot be tested precisely as the solution of the FD problem is not known. On the other hand, classical trajectory simulations can be performed practically for any gas-phase reactions even in full dimensionality if an appropriate analytic PES is provided, thereby the comparison can be done using QCT simulations (idea proposed by Prof. György Lendvay).

As the QCT method of RD systems had not been worked out before, I derived the exact classical pure vibrational internal-coordinate Hamiltonian for full- and reduced-dimensional vibrational motion of polyatomic molecules by removing rotations within the body-fixed frame by projections. The form of the kinetic energy expression turned out to be novel, and its advantage that it directly constructs the vibrational mass matrix without explicitly defining the constrained coordinates (done in s-vector formalism) and rotational coordinates (done in t-vector formalism). The exactness of the new Hamiltonian form was tested numerically by showing that the predicted intramolecular motion matched precisely the constrained Cartesian dynamics obtained using Lagrange's multipliers. The work has been published [5] and presented at both international and domestic meetings [4,6-7].

The new form induced vivid discussions between me and Professors Tucker Carrington and Viktor Szalay, two leading scientist of field, thus I gave analytic proofs for its equivalence for vibrations with the s-vector and t-vector formalisms [8]. Recently, I found a more direct derivation of the form by carrying out projections already in the space-fixed frame and presented the results in front of Hungarian experts [9]. Sadly, Professor Szalay ($1956-2019$ †) could not be present and our debate remained open.

The reduced-dimensional quasiclassical trajectory method

Based on the novel Hamiltonian form, I developed a complete framework for reduced-dimensional QCT calculations by providing procedures for normal mode analysis, reactant state sampling and product state analysis, as well as for following the dynamics. The results have been published and presented in conferences [4-7].

Using the novel AS and RD QCT methods, we investigated the goodness of the Palma-Clary RD model of the $CH_4 + H \rightarrow CH_3 + H_2$ reaction on an accurate analytic PES. The Palma-Clary (PC) model constrains the geometry of the methyl group to C_{3v} symmetry. Using internal coordinate AS, I prepared FD and RD ground state ensembles for four methane isotopologs and calculated unambiguous FD excitation functions, opacity functions and product angular distributions, while dr. Anna Vikár (PhD student of mine and Prof. Gy. Lendvay) calculated the RD ones. The FD and RD results agreed qualitatively well. For CH_4, the agreement was within Monte Carlo error, whereas for other isotopologs the RD model gave lower reactivity parameters, for CD_3H and CD_4 deviations were large (>30%). This indicates that the quantitative goodness of PC model cannot be taken for granted. Such comparison could not be possible by NMS, as the reactivity in the case of the PC model is highly sensitive to the choice of coordinates used for the harmonic expansion. Our results are documented in dr. Vikár's thesis [10] and two publications are in preparation.

A general procedure for the development of torsional force fields and its application to beta-peptidic foldamers

Foldamers are biomimetic chain molecules that can self-assemble into regular structures. Peptidic foldamers built up from β-amino (and α-amino) acids are more flexible than their natural counterparts, thus they can form a wider variety of secondary structures. The in-silico design of novel foldamer constructs demands an accurate computational treatment, however, for which no reliable force field (FF) had existed before. Aiming at a realistic reproduction of backbone torsional motion of acyclic β^2-, β^3- and $\beta^{2,3}$- peptides, in a collaboration with dr. Tamás Beke-Somfai and dr. András Wacha, we extended the CHARMM36m FF by new backbone atom types and proper dihedrals potentials.

For this we established a generally applicable procedure, which identifies the necessary multiplicities of dihedral potential terms and by exploiting various spatial and chemical symmetries it reduces the number of independent parameters and efficiently eliminates parameter correlations. For three simple model β-peptides 3-3 backbone torsional minimum energy paths (MEPs) were determined applying quantum mechanical (QM) relaxed scans at MP2/6-31G(d) level in order to maintain consistency with the CHARMM36m FF. Instead of fitting FF energies along the QM MEP to QM energies, we fitted FF energies along the FF MEPs to them (at same backbone dihedral angle values), therefore the true heights of the torsional barriers could be captured. This modification is vital for success as FFs are not flexible enough to match the QM energies along the same path, and thus the true FF MEPs would have significantly lower barriers, which would lead to enhanced rotations. This issue can be observed for previous literature force fields, which predict overly low stability for experimentally observed secondary structure for three selected acyclic peptides, whereas the new FF could reproduce them in molecular dynamics simulations.

Owing to the CHARMM36m-consistent parametrization, the proposed extension is suitable for exploring new foldamer structures and assemblies, and their interactions with diverse biomolecules. The development of the general FF construction method and the actual FF developments were done with my direction and active participation. The work was published [11] and I presented it at a conference [12].

A thermodynamically defined objective function for the parameterization of molecular mechanics force fields

Conventional force fields (FFs) are sum of potential energy terms that are usually parameterized based on optimized geometries, relative energies, vibrational normal modes and frequencies of conformers determined from electronic structure calculations. However, the harmonic vibrational analysis of a single conformer provides more information than the number of conventional FF parameters, thus either a single, but usually ad hoc, objective function incorporating different types of information is minimized, or a multi-objective optimization procedure is employed.

I proposed a single, physically established objective function that compares the QM and FF Boltzmann vibrational distributions within the harmonic approximation using their Bhattacharyya distance. As a function of the temperature of application it compares geometries, relative energies, normal modes and harmonic frequencies of the conformers in a thermodynamically balanced manner, and it even eliminates the need for normal mode matching, which is an issue in other methods. The method has been extended to the parameterization of transition state force fields: the mass-scaled Hessians are decomposed into parts with positive and negative eigenvalues using spectral decomposition and the distance of the distributions were measured separately for the two parts (after changing the sign of eigenvalues for the transition modes). The overall distance was calculated as the product of the two distances. I wrote a general code that automatically constructs a CHARMM compatible force field and determines its parameters based on the results of electronic structure calculations (reads formatted Gaussian checkpoint files). I presented the method at conferences [13-14], and a paper with the available code and elaborated applications is in preparation [15].

Automatic kinetic model generation and selection based on concentration vs time curves

A fundamental problem of chemical kinetics is the explanation of noisy experimental concentration profiles by finding the underlying kinetic reaction mechanism. In a collaborative work with Professor János Tóth (BME, Budapest) and dr. Tamás Ladics (John von Neumann University, Kecskemét) we proposed a methodology for the construction, parametrization of candidate kinetic models using the framework and theorems of formal reaction kinetics. We showed that requirement of simple chemical considerations, mass conservation, reachability of species from reactants and the detailed balancing property can drastically reduce the number of formal models and independent parameters, thus it becomes possible to investigate all possible formal models having 5-10 species with modern computers in reasonable time.

Surprisingly, these developments recently gained a great relevance to reaction dynamics simulations, as results of novel reactive molecular dynamics simulations (e.g. REAXFF) are actually noisy concentration profiles, to which it is practical to fit a simple kinetic model to extract rate coefficients and utilize the results for long-period predictions. We published the work [16] and I gave oral and poster presentations on it at conferences [17-18].

Other published theoretical-computational studies

As a member of the Green chemistry group at RCNS, Eötvös Loránd Research Network (previously Hungarian Academy of Sciences), I carried out theoretical calculations related to the experimental research on metathesis reactions in our group (lead by dr. Róbert Tuba). Equilibrium constants for ring opening metathesis reactions of cyclopentadiene (CPD) with ethylene, cis-stilbene, cis-butenediol-diacetate leading to 1,3-butadiene and 1,6-hexandiol derivatives were determined using combined DFT and high-level wave function theory and statistical thermodynamic calculation. In another project, I carried out complex stability constant calculations based on results of NMR titrations, and did DFT calculation (conformer search) for crown-ether functionalized norbornene monomers and polymers. Two publications were published related to these projects [19-20]. The support of the grant made possible for me to work on a review paper on kinetic parameter estimation in combustion with Professor Tamás Turányi in a high-profile journal [21].

The support of the NKFIH grant is acknowledged in all publications, talks and poster presentations.

Publications, talks and poster related to the project

[1] Tibor Nagy*, György Lendvay*
Adiabatic switching extended to prepare semiclassically quantized rotational-vibrational initial states for quasiclassical trajectory calculations
Journal of Physical Chemistry Letters, 8 (18), 4621–4626, 2017

[2] Tibor Nagy, György Lendvay
Semiclassical quantization of rovibrational states of methane by adiabatic switching (talk)
Quantum Reactive Scattering Conference, July 3-6, 2017, Trieste, Italy.

[3] Tibor Nagy
"Az adiabatikus bekapcsolási módszer kiterjesztése kváziklasszikus trajektóriaszámítások forgási kezdeti feltételeinek előállítására" (talk)
Meeting of the Reaction Kinetics and Photochemistry Working Committee, November 2-3, 2017, Budapest.

[4] Tibor Nagy, Anna Vikár, György Lendvay
A novel form of the full- and reduced-dimensional vibrational Hamiltonian and its application to the preparation of quantized ensembles of classical states using adiabatic switching (talk)
3rd Meeting on Anharmonicity in Medium-Sized Molecules and Clusters (AMOC), April 16-19, 2018, Budapest

[5] Tibor Nagy*, Anna Vikár, György Lendvay*
A general formulation of the quasiclassical trajectory method for reduced-dimensionality reaction dynamics calculations
Phys. Chem. Chem. Phys., 20, 13224-13240, 2018

[6] Tibor Nagy
A novel form of the vibrational Hamiltonian - the true counterpart of the s-vector formalism? (talk)
Seminars of the laboratory of molecular structure and dynamics, March 1, 2018, Budapest

[7] Tibor Nagy, Anna Vikár, György Lendvay
"Redukált-dimenziós reakciódinamikai modellek klasszikus mechanikai alkalmazásának problémái" (talk)
Meeting of the Reaction Kinetics and Photochemistry Working Committee, the Coordination Chemistry Working Committee, and the Veszprém Regional Committee of HAS, November 8, 2018, Veszprém.

[8] Tibor Nagy
On the exactness of the projected vibrational Hamiltonian
(paper - was rejected from Mol. Phys., now being updated and extended with applications)

[9] Tibor Nagy
Projektált rezgési Hamilton-függvény II. (talk)
Seminar at RCNS, HAS, April 9, 2019, Budapest.

[10] Anna Vikár
"A CZ3Y + X → CZ3 + YX típusú reakciók redukált-dimenziós modelljeinek vizsgálata kváziklasszikus trajektória módszerrel" (PhD thesis)
Chemistry Doctoral School, ELTE, 2018, Budapest

[11] András Wacha, Tamás Beke-Somfai *, Tibor Nagy *
Improved Modelling of Peptidic Foldamers Using a Quantum Chemical Parametrization Based on Torsional Minimum Energy Path Matching
ChemPlusChem 84 (7), 927-941, 2019

[12] A. Wacha, T. Beke-Somfai, Tibor Nagy
"Egy új, ígéretes molekulamechanikai erőtér β-peptid foldamerek szimulációjára" (talk)
KeMoMo–QSAR 2019 szimpózium, June 6-7, 2019, Szeged

[13] Tibor Nagy
"Új Módszerek a Molekularezgések és a Kémia Reakciók Potenciális Energia Felületének Empirikus Erőterekkel Történő Leírására" (talk)
Meeting of the Reaction Kinetics and Photochemistry Working Group of HAS, 29-30 May 2017, Balatonalmádi.

[14] Tibor Nagy, Markus Meuwly

A novel, thermodynamics-based objective function for the parameterization of molecular mechanics force fields (talk)
17th Central European Symposium on Theoretical Chemistry, September 9-12, 2019, Stadtschlaining, Austria.

[15] Tibor Nagy*, Maksim Soloviov, Markus Meuwly
A thermodynamically defined objective function for the parameterization of molecular mechanics force fields
(paper in preparation)

[16] Tibor Nagy*, János Tóth, Tamás Ladics:
Automatic kinetic model generation and selection based on concentration vs. time curves
International Journal of Chemical Kinetics, 52 (2), 109-123, 2020

[17] Tibor Nagy, János Tóth, Tamás Ladics
"A reakciókinetika inverz problémája: a kinetikai modell automatizált meghatározása koncentráció-idő görbék alapján" (talk)
Meeting of the the Reaction Kinetics and Photochemistry Working Committee, HAS, May 20, 2019, Balatonalmádi

[18] Tibor Nagy*, János Tóth, Tamás Ladics
Automatic kinetic model generation and selection based on concentration vs. time curves (poster)
3rd Workshop on Formal Reaction Kinetics and Related Areas, January 9-10, 2020, Budapest

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Further (not related) publications in which the support of the NKFIH grant is acknowledged

[19] Gábor Turczel, Ervin Kovács Eszter Csizmadia, Tibor Nagy, Imre Tóth, Róbert Tuba*
One-pot One-pot Synthesis of 1, 3-Butadiene and 1, 6-Hexandiol Derivatives from Cyclopentadiene (CPD) via Tandem Olefin Metathesis Reactions
ChemCatChem, 10 (21), 4780-4780

[20] Ervin Kovács, János Deme, Gábor Turczel, Tibor Nagy, Vajk Farkas, László Trif, Sándor Kéki, Péter Huszthy, Róbert Tuba*
Synthesis and supramolecular assembly of fluorinated biogenic amine recognition host polymers
Polymer Chemistry 10 (41), 5626-5634

[21] Turány Turányi*, István Gy. Zsély, Tibor Nagy*
Optimization of combustion mechanisms and efficient interpretation of experimental data
Invited paper to Progress in Energy and Combustion Science (IF: 26.467)
(manuscript in preparation)