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Towards First Principles Calculation of Electron Impact Mass Spectra of Molecules**

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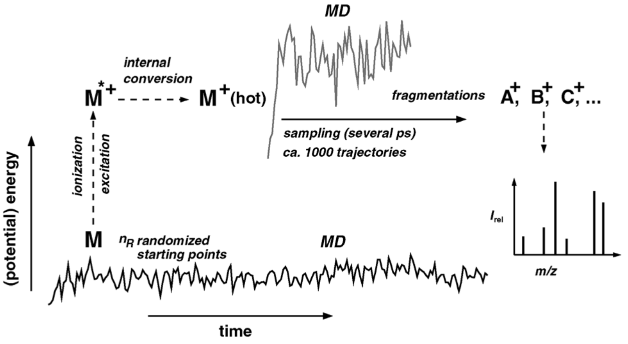
The ability of modern quantum chemistry (QC) to compute or even predict molecular properties and in particular the spectroscopic signatures of molecules has advanced extraordinarily in the past decade.[1] Kohn–Sham density functional theory (DFT) is used routinely to aid interpretation of NMR, IR, UV, and chirality-based spectroscopic data. However, a blank spot on this map of success is represented by electron impact mass spectrometry (EI-MS). This important experimental method is used routinely in chemistry and related fields for various analytical purposes.[2,3] In a typical EI-MS experiment, molecules are bombarded with high-kinetic-energy electrons (typically 70 eV) leading to decomposition as well as more complex chemical rearrangements (often induced by hydrogen-atom transfer). The basic difficulty in the QC treatment of EI-MS is that the recorded intensity for the fragment mass-to-charge (m/z) ratio used for interpretation results from complex chemical kinetics and not from quantized energy levels. According to Ref. [4], the theoretical simulation of EI mass spectra is extremely challenging. While the QC calculation of energy levels is straightforward, the computation of reaction rates of ionized, highly excited (hot) molecules seems to be very complicated even when one disregards the complexities in describing the primary ionization process. Hence, only qualitative and empirical estimates for simple bond-breaking events in organic radical cations have been proposed to date based on computed static properties of the molecules like bond orders, bond energies, and fragment energies to aid in the interpretation of EI-MS data.[5] (For ab initio (mostly DFT) computed energies of stationary points on potential energy surfaces (PESs) in special EI-MS-related reactions see Ref. [6].) The most sophisticated theoretical approach to date is based on RRKM theory and "master equations"[4] which, however, require computed data (e.g. transition states) for a priori defined decomposition channels (which are often not known) and some further approximations (e.g. harmonic vibrations). To the best of our knowledge, no attempt to provide a more general, dynamic, quantitative, and widely applicable theory of EI-MS was published so far.

The present work aims to close this gap. It presents the conceptual and technical ideas accompanied by a few representative spectra showing that the theoretical approach indeed works in practice. All important technical details and further in-depth explanations of various theoretical aspects can be found in the Supporting Information.

A "black-box" type, more or less ab initio based brute force approach is used to compute the decomposition and reaction probabilities of singly ionized molecules with large amounts of internal energy. Only valence ionization and organic molecules are considered here although these restrictions are not due to the theory but just imposed by the majority of applications. The conceptual framework is the combination of standard QC methods, molecular dynamics (MD), and stochastic methods as exemplified in Scheme 1. It includes all basic physical effects except the quantum dynamics of the nuclei and non-Born–Oppenheimer (BO) effects.



Scheme 1. Conceptual framework for QC computations of EI-MS. For details on the combined electronic structure/molecular dynamics/stochastic approach see the text and the Supporting Information.

The computation of EI-MS requires knowledge of relative, energy-dependent chemical reaction rates if collisions, field effects, and photon exchange are neglected which is a safe assumption under normal conditions. Molecular dynamics (MD) is the method of choice for computing such rates by classical propagation of the nuclear degrees of freedom (DOF) based on QC-computed forces (ab initio BOMD[7]). The experimental conditions (isolated molecules and high energy) are very well suited, as short trajectories (frequent events) can be expected. All simulations (except for a heating phase, see below) are conducted at constant total energy (NVE ensemble).

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From an equilibrated trajectory of the neutral molecule (M), a randomized ensemble of instantaneously ionized species (M^+) with different conformations and energies are generated. These are independently propagated in time on the M^+ PES. Excited neutral species that can form ions by auto-ionization are not considered. To facilitate the convergence of the electronic wave function, which was a key problem, the ion is electronically excited (Fermi "smearing"[8]) to temperatures of several thousands of K depending on the QC method because of varying orbital energy gaps. The thereby occurring fractional orbital occupations in unrestricted SCF calculations (see below) account to some extent for the partial multireference electronic structure of the ions and physically correspond to an ensemble of excited states generated by the ionization. The finding that such a relatively simple electronic structure theory can be used for rather complex electronic situations is the first important result of this work.

It is generally assumed that after the primary electron impact an initial (e,2e) process leads to an excited ion state (M^{*+}) which relaxes by internal conversion (IC) to a vibrationally hot ion ground state. The corresponding excitation energy is initially of electronic type but in our model it effectively dissipates into the nuclear degrees of freedom (DOF) in a short time. We take a typical duration of 0.5–3 ps for this IC process as simulated by scaling of the atomic velocities (for details see the Supporting Information). This model is supported by the experimental finding that classes of similar molecules show similar fragmentation patterns in a technically reproducible way. The observed processes must therefore reflect the PES and internal energy of rather well-defined states. These general assumptions are similar to the older statistical quasi-equilibrium theory (QET) of EI-MS.[3,9]

The amount and distribution of an impact excess energy (IEE, typically 5–50 eV) is estimated from the molecular orbital (MO) levels of M which reflect the possible ionization channels and assuming a Poisson-type distribution. (For experimental determinations of IEE values in (e,2e) processes by momentum spectroscopy see Ref. [10].) The vibrational energy is partitioned in the n_R starting molecular structures not uniformly among the nuclear DOF but locally concentrated according to the localized nature of the ionized MO. One finally arrives at a randomized "hot" ion ensemble. Its members are independently propagated in time on the PES until decomposition occurs. Secondary fragmentations of formed ions are found to be very important in large molecules and considered by an ion tracking algorithm. The charged fragments are counted (see the Supporting Information for the computation of the charge and intensity) and for each an isotope pattern is computed leading to a simulated spectrum which is directly comparable to experiment. In order to obtain reliable statistics for the more intense signals several hundred runs have to be performed. The maximum simulation time is normally about 10 ps. The IEE can be adjusted in test calculations such that a small but significant M^+ signal occurs but the default value is often sufficient. An adjusted IEE accounts for imperfections of the simple model for the ionization process and also reflects systematic errors of computed dissociation energies for a particular QC method. The average IEE is noted in the examples and it roughly agrees with estimated experimental values for small organic molecules.[10] No further empirical adjustments are made.

For a typical integration time step in BO-AIMD (0.5 fs) this requires a total of roughly 10^6–10^8 energy and force evaluations for one spectrum. Although this puts stringent limits on the theoretical level that can be employed for the QC part (see below), it is clear that the calculations can be conducted massively parallel as the hundreds of fragmentation trajectories are completely independent.

One basic idea in the first stages of the project was that the decomposition should be significantly affected by the IEE distribution. However, according to the present results this is not the case and different models yield similar spectra. This suggests that many reactions under the typical conditions in larger molecules occur from hot but quasi-equilibrated ions which is in agreement with the assumptions of QET. However, it is found that the results for more complicated reactions critically depend on the quality of the QC method used to compute the PES. Ideally, the QC method should be able to correctly dissociate arbitrary types of chemical bonds in a black-box manner with an accuracy of better than about 1 $\text{kcal}\,\text{mol}^{-1}$ in a very short computation time of about a few CPU seconds for one energy/force evaluation. None of the presently available methods fulfill these requirements. Several semiempirical MO methods (e.g. OM2,[11] DFTB3,[12,13] various NDDO versions) as well as DFT approaches were tested. Most semiempirical methods can safely be used to generate the long trajectory for M (about 20–30 ps) but are in some cases not sufficiently accurate for highly reactive species. While signals resulting from simple bond-breaking processes are often obtained properly from these "low-cost" methods (which is already a very positive result), more complicated rearrangement reactions can be missing. In the Supporting Information dramatic failures of simpler semiempirical methods are documented. Of the tested methods, the D3-dispersion-[14] corrected methods DFTB3[13] and in particular OM2[11] are recommended. Because the OM2-generated spectra are very reasonable and of similar quality as those from DFT, this method was used extensively for exploratorial investigations and testing of model parameters.

A very important finding is that the quality of the simulated spectra often substantially improves if better PES are used; in other words, the accuracy of the QC is directly reflected in the computed spectra (see the Supporting Information for examples). This supports the validity of the general model. Because of the above computational considerations, only small double-zeta-type AO basis sets can be employed at present in the ab initio calculations. This causes additional errors in the computed PES which should be kept in mind in evaluations of the DFT results. Global D3-corrected hybrids based on the PBE functional are used in DFT (PBE0 or PBE38[14,15]) which provide reasonably accurate results for structures and typical thermochemical properties (see Ref. [16] and the Supporting Informaiton). A relatively large amount of Fock exchange is necessary in order to avoid self-interaction error which is problematic for reaction barriers as well as the dissociation of one-electron bonds in radical cations. Using a spin-unrestricted SCF formalism for finite electronic temperatures ($T_{el} \approx 5000$–25 000 K), this theoretical level can break bonds and produce localized spin centers. Typically more than 99 % of all started trajectories finish without errors which is important for obtaining unbiased statistics. The price to pay for such a robust single-reference method is that there is no well-defined spin state which, however, is not of concern here. A new computer program called QCEIMS[17] has been coded which performs all necessary computations except the QC part for which the efficient programs ORCA, DFTB+, and MNDO are used.[18]

A few typical EI-MS of organic molecules are shown in Figures 1–4; in each, both experimental and theoretical intensities are plotted for convenient comparison. All experimental data refer to 70 eV impact energy and are taken from the NIST database.[19] The influence of all technical parameters (e.g. IEE distribution, simulation and relaxation times, temperatures) on the shape of the spectra was investigated very carefully and is discussed in the Supporting Information. A common default technical setup was used and only the QC method and the IEE are given. Generally, the number of counts in the theoretical 100 % (base) signal is about 100–200 which is sufficient for most purposes. Examples for all three recommended methods (DFT/PBE0, OM2, DFTB3) are given.

Before continuing the discussion, a note on the reproducibility of experimental EI-MS seems to be appropriate here: for larger molecules (e.g. *n*-alkanes) the intensity ratio of the M^+ and low-mass ($m/z < 50$) signals depends to a significant degree (changes of 20–30 %; 5–10 % for smaller molecules) on the measurement conditions, in particular the heating of the probe in the ionization chamber.[20] This causes varying (uncertain) IEE in the experiment and should be kept in mind in the comparisons to calculated spectra.

Figure 1 shows spectra for the saturated hydrocarbons octane (linear and branched), *n*-dodecane, and the polycyclic pregnane molecule. This important first test demonstrates that the approach works consistently for small and large molecules. As can be seen, the agreement between the experimental and theoretical data is surprisingly good. This holds true for the main peaks in the *n*-alkanes (series with a difference of $m/z = 14$ mainly due to repeated loss of C_2H_4)

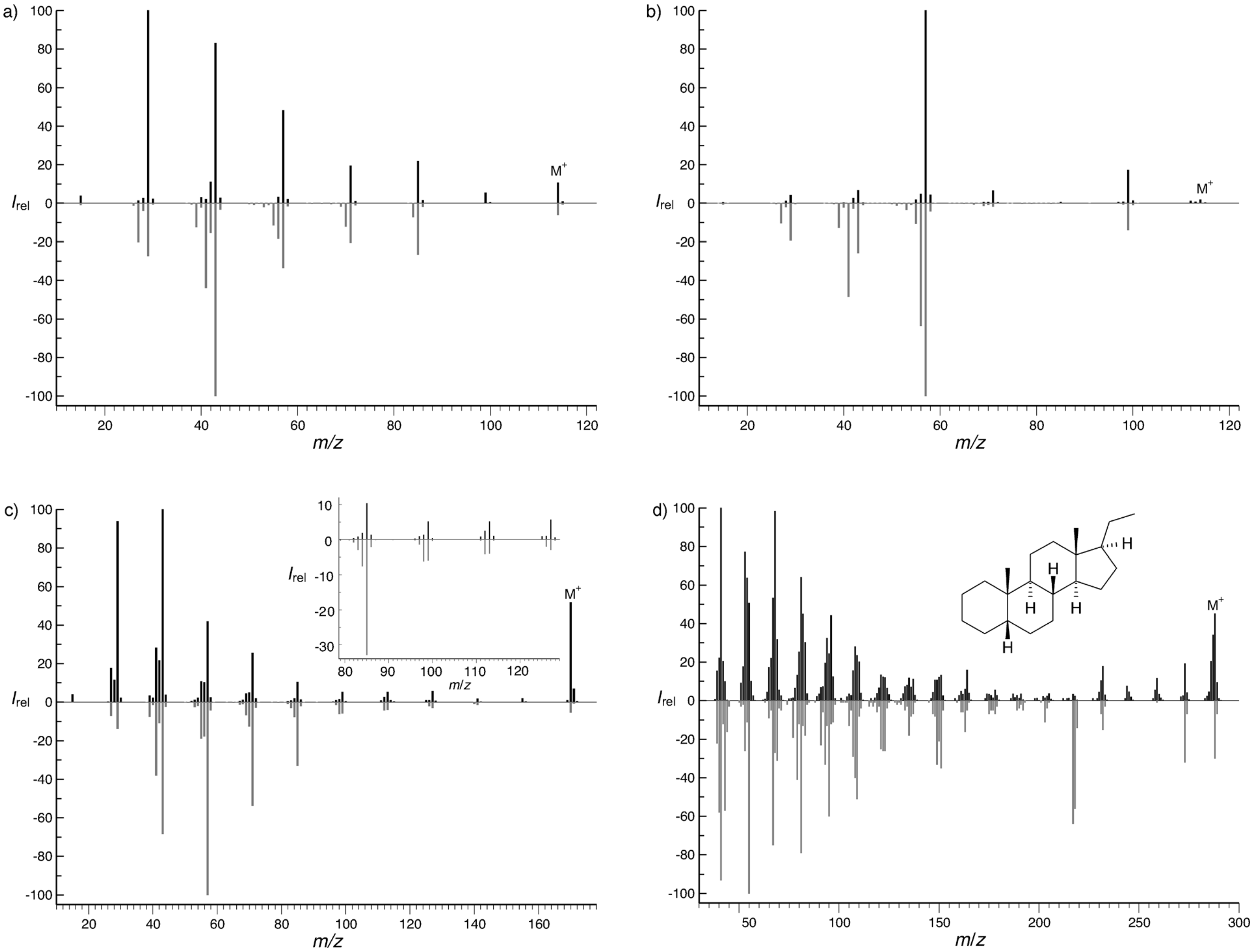

Figure 1. Comparison of experimental and simulated EI-MS of a) *n*-octane (DFT, IEE = 15.2 eV), b) 2,2-dimethylhexane (DFT, IEE = 13.7 eV), c) *n*-dodecane (DFTB3, IEE = 27.4 eV), and d) pregnane (DFTB3, IEE = 45.5 eV). Black spectra with positive intensities are calculated spectra, gray spectra with negative intensities are inverted experimental spectra.

but also for “rare” fragments with small intensity. The characteristic fragment mass distribution is correctly reproduced only for larger masses but the observed maximum is missing for *n*-octane and not very pronounced for *n*-dodecane because the reaction rate yielding small fragments like $C_2H_5^+$ is calculated to be too large.[21] Nevertheless, the theoretical data, in particular regarding the relatively simple QC level employed and the complexity of the problem, are considered to be accurate. Note that weaker signals one and two mass units with less than the $M-n\times 14(CH_2)$ series and formed by loss of H and H_2, respectively, are well reproduced as shown by the expanded inset in Figure 1c. The usually assumed fragmentation mechanisms[3] are corroborated by the calculations except that only 1,2-H shifts (yielding secondary cations with subsequent olefin loss) but no alkyl migration was observed. The computed spectrum of the branched alkane correctly shows not only the strong signal for the *tert*-butyl cation (reflecting its high relative stability), but also the few weaker signals. This demonstrates that the theory is able to distinguish between isomers and is applicable for analytical purposes. The example of the steroid shows that also the spectra of complicated polycyclic ring systems are surprisingly well reproduced.

The majority of primary fragmentations in the simulations occur within 2–3 ps after ionization while secondary reactions in already formed ions (closed-shell as well as radical) can take somewhat longer due to reduced internal energy. Secondary reactions in fragmentation cascades are of particular importance in larger systems (see below).

Figure 2 shows spectra for unsaturated and aromatic molecules (phenol, butylbenzene, 4-methylcyclohexene, naphthalene; the spectrum for indole is given in the Supporting Information) which exhibit signals resulting from more complex but nevertheless typical reactions.

Aromatic compounds normally show inefficient decomposition (strong M^+ signals) which is nicely reproduced for phenol and naphthalene in particular. The EI-MS of phenol features an unusual signal at *m*/*z* 60 due to loss of HCO and ring reclosure to $C_5H_5^+$ which is again found in the calculation. Both spectra for butylbenzene show a characteristic peak at *m*/*z* 92 for $C_7H_8^+$ resulting from a McLafferty-type rearrangement, in which a hydrogen atom is transferred from

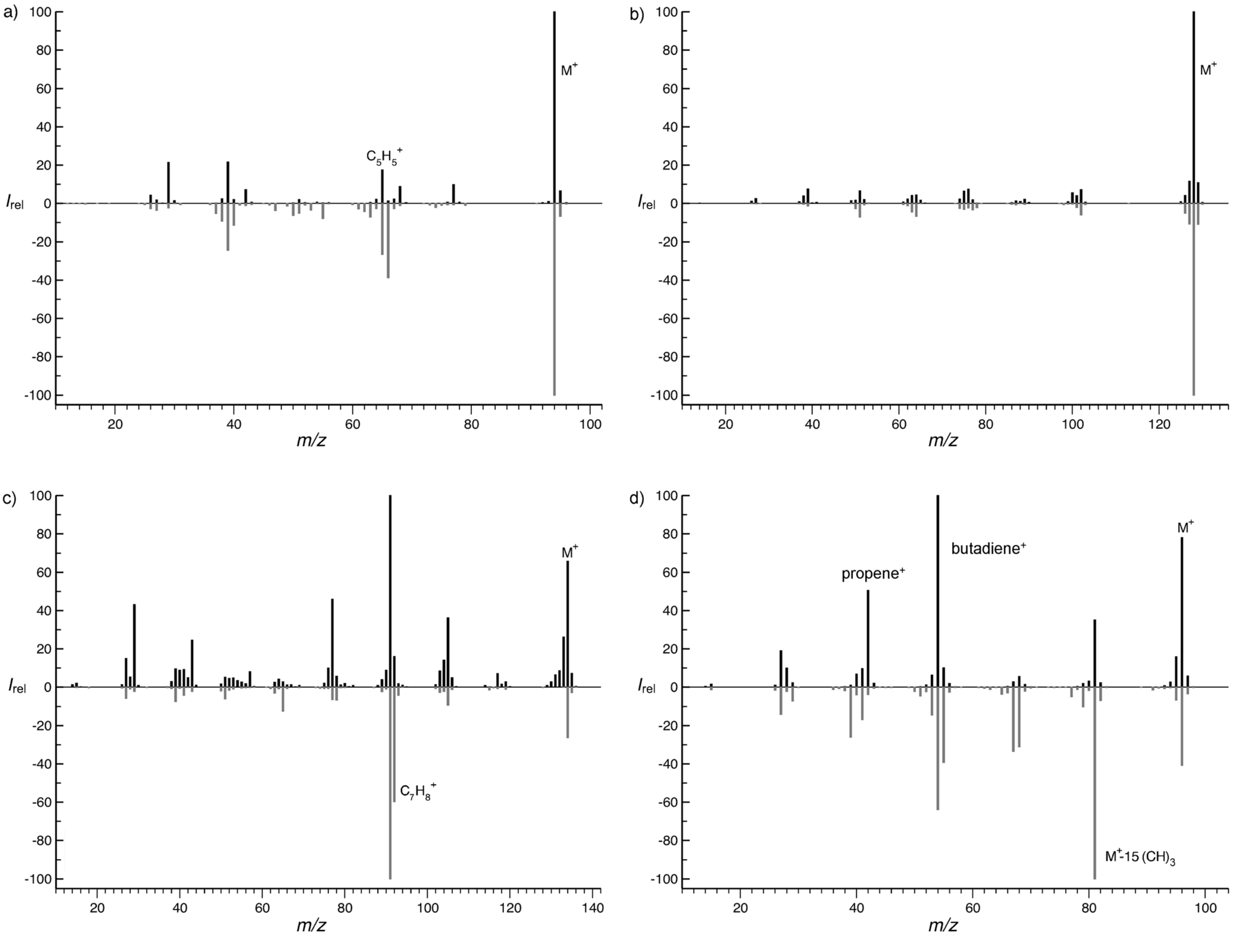

Figure 2. Comparison of experimental and simulated (OM2) EI-MS of a) phenol (IEE = 13.0 eV), b) naphthalene (IEE = 7.8 eV), c) *n*-butylbenzene (IEE = 16.8 eV), and d) 4-methylcyclohexene (IEE = 15.5 eV). Black spectra with positive intensities are calculated spectra, gray spectra with negative intensities are inverted experimental spectra. Labeled signals are discussed in the text.

the alkyl chain to the ring, followed by cleavage of the benzyl group. All these EI-MS obtained at the OM2 level demonstrate the reliability of this efficient QC method which has a systematic bias only towards some excessive hydrogen loss from the parent ion.

The simulated EI-MS of 4-methylcyclohexene (Figure 2d) is dominated by the retro-Diels–Alder (RDA) reaction (signals at *m*/*z* 42, 54) which occurs mostly in a nonconcerted way. For this example, the errors for the theoretical intensities are briefly discussed. In general, QCEIMS reproduces most of the experimentally recorded fragments of M^+ but sometimes with incorrect intensities which is attributed to two different kinds of errors. First, the reaction can be calculated to be too inefficient (or too fast) compared to other processes as, for example, the methyl dissociation leading to the signal at *m*/*z* 82. This can be corrected by better a PES (i.e., better QC methods). The other problem is related to the fragment-charging probability. In the spectra of 4-methylcyclohexene (Figure 2d), the RDA reaction produces 1,3-butadiene (*m*/*z* 54) and propene (*m*/*z* 42) in equal amounts. Hence, the experimental signal ratio of 100:4 should reflect the Boltzmann populations of the corresponding ions at their dissociation temperature in our equilibrium model. The difference of DFT-computed ionization potentials (IPs) for the two fragments is accurate to within 0.1 eV compared to a benchmark CCSD(T)/TZVP result. Thus, the reason for the overestimation of the propene intensity can only be really caused by a too high temperature (which is reasonably about 6000 K in this case) or a breakdown of the BO picture of dissociation (i.e., the charge does not "follow" the fragment with smaller IP).

Figure 3a–c shows spectra for 2-pentanone as a textbook example for reactions induced by hydrogen transfer. In the famous McLafferty rearrangement[3] an H atom is first transferred from the γ-carbon to the carbonyl group followed by loss of ethene giving a characteristic signal at *m*/*z* 58. This reaction represents a challenging test because the observed rate relative to the competing α-cleavage results from a detailed balance between entropic and energetic effects. Obviously, the McLafferty signal is not found with DFTB3 while the better methods OM2 and DFT are able to reproduce it although the intensity is somewhat too low. This is

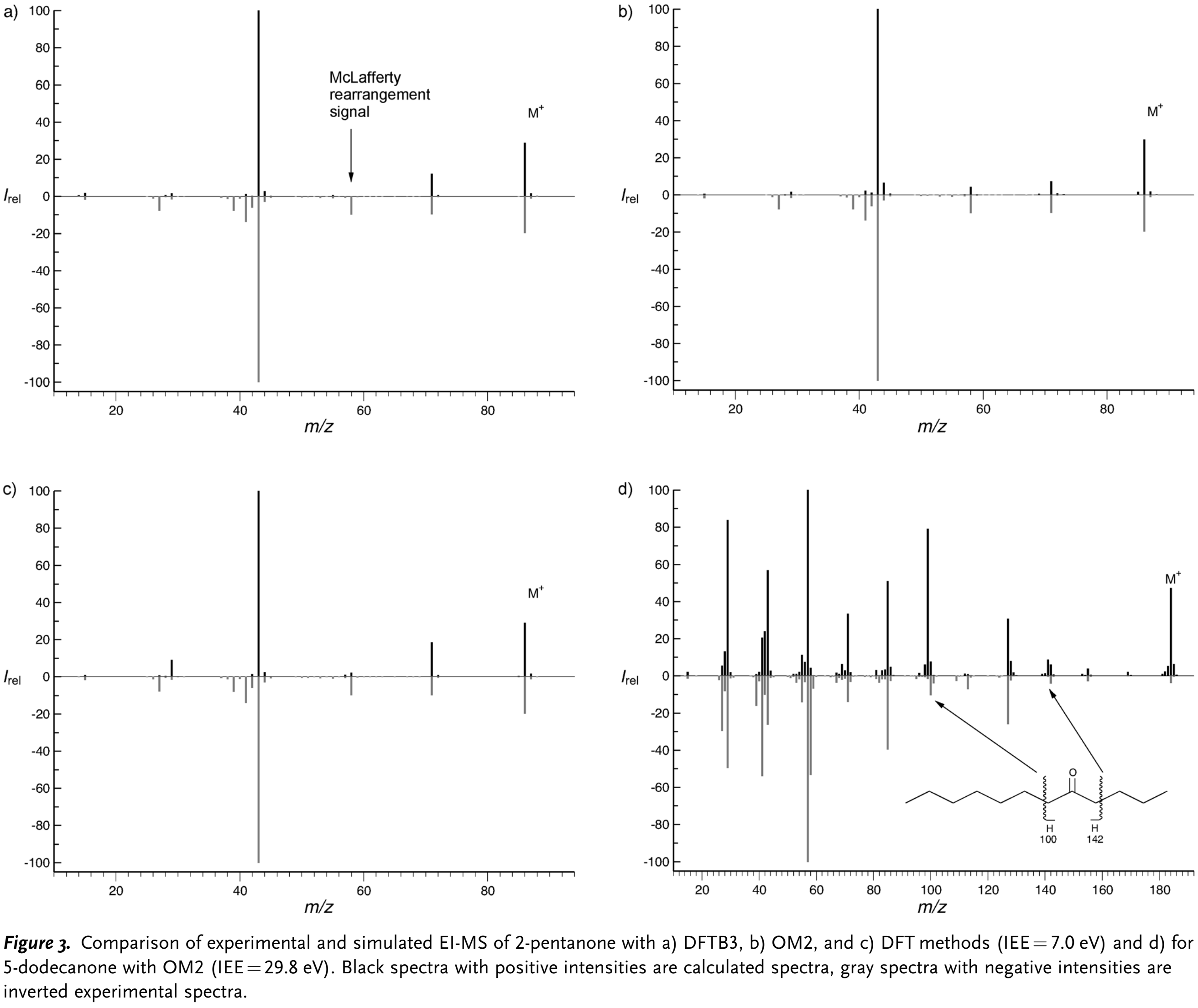

Figure 3. Comparison of experimental and simulated EI-MS of 2-pentanone with a) DFTB3, b) OM2, and c) DFT methods (IEE = 7.0 eV) and d) for 5-dodecanone with OM2 (IEE = 29.8 eV). Black spectra with positive intensities are calculated spectra, gray spectra with negative intensities are inverted experimental spectra.

tentatively explained by the α-cleavage being too fast, in other words, the C−C bonds being too weak.

The spectrum for 5-dodecanone (Figure 3d) shows that ineffective McLafferty rearrangements in larger molecules are computed correctly with low probability compared to various simple dissociation processes. In general we find non-hydrogen-rearrangement reactions to be disfavored in larger systems since their high entropy penalty is very significant at the typical vibrational temperatures of several thousands of K.

The final example in Figure 4 is strychnine, a medium-sized but rather complex molecule with a polycyclic structure, various functional groups, and a huge number of different possible decomposition pathways. This example demonstrates that the proposed approach can be used as a tool in natural product chemistry. As can be seen in Figure 4, the EI-MS shows signals for almost all possible masses and characteristic "bands" with increased intensity at *m*/*z* 100–150. This "real-life" example is considered to be a very difficult and decisive test especially since decomposition cascades are important in such molecules. Because of its size and the numerous possible reactions, only semiempirical methods can be used at present. The calculation required about 2000 runs, corresponding to roughly 2×10^7 single QC computations, and yielded a M(fragments)/M^+ ratio similar to the experiment. In this example (and similar to the case of pregnane, Figure 1d), only 30–40% of the signals result from primary reactions but still about 10% in the third or fourth step of the ion fragmentation cascade.

Considering the overall complexity of the problem and the molecule, the agreement between theory and experiment is very good although one notes excessive intensity for large fragments due to the overly efficient loss of CO and C_2H_3O. This example strongly underlines the general validity of the theory. Note again that the computed intensities directly result from a stochastically sampled PES without molecule-specific empirical adjustments except for the choice of the IEE which is also experimentally not well-defined. For molecules of this complexity with hundreds of important decomposition channels, "hand-made" transition-state-based computations and application of QET seem to be hopeless.

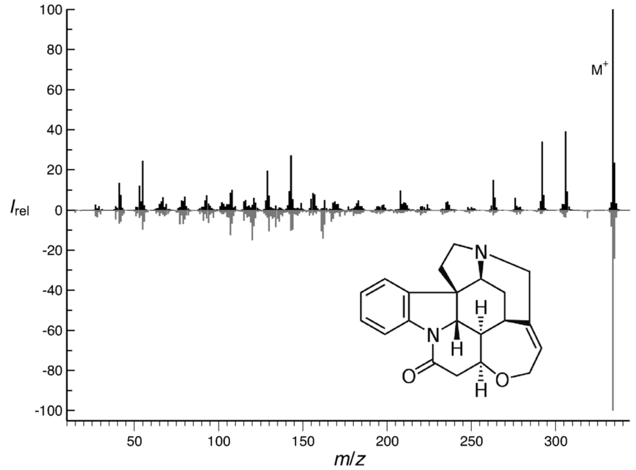

Figure 4. Comparison of experimental and simulated (DFTB3) EI-MS of strychnine for an IEE of 24.2 eV. The black spectrum with positive intensities is the calculated spectrum, the gray spectrum with negative intensities is the inverted experimental spectrum.

In conclusion, a general method to compute EI-MS based on a combination of fast quantum chemical methods, molecular dynamics, and stochastic preparation of "hot" ionized species for subsequent propagation on a ps time-scale was presented. It considers all elementary processes more or less non-empirically, constitutes a "black-box" approach, and provides spectra that compare well with their experimental counterparts, even in subtle details. Thereby, for the first time this chemically very important spectrometry could be put on firm (predictive) theoretical ground. For the 18 organic molecules considered in this study, on average 3/4 of all the stronger signals in the experimental spectrum are obtained with reasonable intensity in the calculation and the overall mean absolute intensity deviation is only about 20%. The neglected quantum effects of the nuclei, the simple internal energy distribution and dissipation model, and the restricted ps MD time-scale seem to introduce fewer errors than the imperfections in the QC-computed PES. The unprecedented success is obtained without molecule-specific fitting and is based on robust quantum chemistry and a physically reasonable model. Its widespread applicability is only somewhat limited by the tremendous amount of required computation time (at least if DFT is used[22]) although this will likely change in the future with the development of improved hard- and software. At present, routine calculations of EI-MS with OM2 or DFTB3 and the QCEIMS program are possible for many molecules and the accuracy seems to be sufficient for practical purposes. Note that calculations for isotopomers are straightforward without any further approximations or changes in the theory.

An important "by-product" of the simulated spectra is the detailed information about corresponding decomposition mechanisms. This is conveniently accessible from the MD trajectory that directly corresponds to a particular mass signal. Some "movies" of interesting decomposition and rearrangement reactions can be found on our homepage.[23] Moreover, it is noted that the calculated EI-MS are sensitive to the quality of the underlying PES and hence, they can be used to test the performance of approximate QC methods in particular in electronically complicated (open-shell) situations. Besides many possible applications in the future, this work might also stimulate further research for robustly dissociating QC methods (which is necessary for planned applications in the area of organometallic compounds) as well as into the question how to compute the amount and dissipation of the impact energy in the ion based on first principles. Detailed studies of reactions occuring on the 10 ps to 1 ns time range will be conducted in the future in our laboratory.[24]

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[21] The error (too intense $C_2H_5^+$ and $C_3H_7^+$ signals) appears for most tested QC methods and it hence seems unlikely that it is caused by wrong PES. At present we have no further explanation for the observation but cannot exclude errors from the IEE distribution model for this sensitive property.
[22] On a parallel computer with 400 common CPUs, the semi-empirical calculation of an EI-MS for a medium-sized molecule takes a few hours of real-time (a few hundred hours of CPU time). DFT calculations at the PBE0/SVx level take about 100 times longer, corresponding to several days of real-time.
[23] See http://www.thch.uni-bonn.de/tc/downloads/movies/.
[24] The relevant maximum reaction time in the spectrometer is on the order of several ns to ms so that very slow reactions can contribute in principle. It is currently not clear how important this contribution is for a larger molecule. While the ms scale cannot be reached by the proposed theory, three very long simulations with a maximum MD time of 1 ns were conducted at the semiempirical level (see the Supporting Information) and some changes compared to the standard cut-off (5–10 ps) were observed. There seems to be, however, some redundancy with the IEE used; in other words, the results of longer simulations with smaller IEE are similar to those from shorter run times with higher IEE. In any case according to these preliminary tests it seems that reactions occurring in the 10–100 ps range are of small to medium importance in some systems but that the ms regime likely is unimportant. Investigations in the 0.1–1 ns range require huge amounts of computer resources but can be conducted for medium-sized molecules with OM2 or DFTB3. Note that absolute rate constants in an EI-MS experiment have apparently never been measured directly. Often cited slow rates (ns to ms range) were deduced from experimental relative ion yields and theory (QET) under the assumption of relatively small IEE (e.g. for propane see Ref. [9c]). Because according to newer (e,2e)-spectroscopy data (see for example, Ref. [10b] for the case of butane) the actual IEE is higher than originally assumed, a ps time-scale as considered here seems to be realistic.