Introduction

According to the encyclopaedic definition, chemistry is the science that deals with the properties, composition and structure of substances, the transformations they undergo and the energy that is released in these transformations. The modern paradigm of chemistry can be considered to consist of three parts: theory (first principles of physics), model and experiment. Since the advent of quantum mechanics 80 years ago, the theoretical fundamentals are essentially unchanged. On the other hand, the relationship between modelling and experimentation is continually changing. With the steady development of faster and bigger computers, it is possible to stretch the applications of the first principles of theory into more and more complex systems. In all instances, mathematical and numerical approximations are made and the resulting methods are applied to molecular systems of practical interest, often with great accuracy and predictability. At the same time, computers are used for experimental design, instrument steering, data acquisition, data processing and data analysis. In this respect, models and experiments are entangled. Alternatively, it can be described as a complete merger of scientific methodology. The relationship between model and experiment in today’s science is, therefore, rather complicated and the field of mass spectrometry is no exception, since the appearance of a mass spectrum is largely determined by the chemical reaction of ions. Chemical reactions are described by statistical and quantum physics.

The success of this point of view is, of course, governed by how well computed and experimentally obtained observations agree. If the discrepancy is too large, it is interpreted to be either the result of an incomplete model or due to misinterpretation of the experiment. Normally, whether inconsistency could be due to wrong or incomplete first principles is not questioned—a circumstance which, at least in principle, may impede scientific progress. However, this interesting philosophical question will not be the topic of this lecture. In the present context, modelling should be regarded as a purely empirical exercise. The chemist will only need to ask whether a given model is sufficiently accurate.

Scope of quantum chemical model calculations

We will now look further into the relationship between computational modelling and experiment in gas-phase ion chemistry. In judging computational chemistry, we must have three concerns in mind—accuracy, predictability and insight. The question of accuracy is the simplest, since it may be answered by direct comparison with experiment. Predictability is more difficult, since it requires a priori calculation of a quantity for which there is no experimental estimate. We may wonder whether computation, in the end, may make experiment obsolete. For example, in mass spectrometry, it would be of significant importance if an unknown species,
some time in the future, may be identified on the basis of a mass spectrum calculated from first principles alone, i.e. a previous entry in the NIST or Wiley databases would not be necessary. On the other hand, the question of insight is a more humble one. In this situation, computation is done in order to provide qualitative information not easily available through experiment. A minimum of reliability of the model is, of course, also required in this case. This is how computational modelling is practised today, for example in our own laboratory.

Methodology

Apart from quantum mechanics, the theoretical fundamentals of chemistry come from statistical physics and atomic physics. The object of chemical modelling is normally to solve the time-independent Schrödinger equation of a molecular system. The Born–Oppenheimer (BO) approximation is central, since minimum energy structures are a direct consequence of this approximation. Based on this, the computational chemist is faced with the obligation of obtaining electronic structures as functions of fixed nuclei. This is usually a straightforward exercise for stable molecules, but may sometimes possess a considerable challenge for excited electronic states and non-equilibrium geometries (for example, transition structures). In order to obtain the electron structure of a molecule, well-established methods and programs are most often used. Two conceptually different approaches to solving the electronic Schrödinger equation exist; density functional theory (DFT)\(^1\) and wave function theory (WFT)\(^2\)—both being essentially \textit{ab initio}. In applying wave function theory it is necessary to obtain an accurate description of each single electron, as well as the interaction between the electrons. The first can be achieved by using an atomic basis set of sufficient size. The second, the manybody problem, can be solved using different hierarchical approaches; for example, configuration interaction and coupled cluster theory. The advantage of WFT is the well-defined hierarchy of methods, which arrive asymptotically at the exact wave function in the (infinite) limit of full correlation and complete basis sets. The disadvantage of WFT is the poor scaling properties in terms of demand of computer power. Only rather small molecules can be treated with the resulting inherent high confidence. A cheaper alternative is DFT and hybrid DFT approaches. Using this methodology, it is possible to treat very large molecules, often with good result. The disadvantage of DFT is non-transparency in how it behaves when the complexity and sophistication of the function is improved.

Accuracy of structures

By using highly extended wave function theory, it is possible to arrive at molecular geometries of impressive quality. By extending the model beyond the BO approximation, Csaszar \textit{et al.} have recently reported isotope-corrected equilibrium geometries for the water molecule with five significant figures in the bond parameters.\(^3\) In this way, they claim geometries “deemed to be of higher accuracy than can be determined by analysing experimental data”. This author is critical of the use of the term “accuracy” in this brave statement, but not to the reality of the situation described.

Accuracy of thermochemical properties

For medium-sized molecules, it is not possible to achieve this level of accuracy in molecular properties. However, higher-level estimates can be achieved using skilful schemes for extrapolation from lower levels. In these cases, geometry optimisation is obtained at a modest level of approximation. One should notice that the resulting, often small and systematic, errors in geometry turn out to be rather unimportant in this connection. This is particularly so when comparing relative energies. Based upon these geometries, high-level estimates are acquired by combining various contributions from high-level calculations, either with a large basis set and/or with extensive correlation. For example, the G2\(^*\) method developed by Pople and co-workers is aimed at providing energies efficiently at QCISD(T)/6-311+G(3df,2p). G2 includes a few empirical parameters and was specifically designed to provide accurate estimates of heats of formation and ionisation energies. This is demonstrated by the fact that the G2 proton affinities of the hydrides and hydride anions of the elements of Groups 15–17, including the elements of Row 4 of the periodic table are, typically, accurate to within 10\,kJ\,mol\(^{-1}\).\(^5\)

Accuracy of barrier heights

As already stated, computing properties of equilibrium species pose relatively few challenges to the practitioner. The situation can be much more complicated and uncertain when working with molecules severely displaced from their equilibrium geometries. This is particularly pertinent in the case of transition structures (TS), which correspond to saddle points of the potential energy surface—the energetically most favourable “mountain passes”. Due to the more delocalised electronic structure of a TS, it is less likely that errors compensate due to similarities of the two structures that are compared (reactant and TS). On the contrary, a more sophisticated treatment of both the one electron function (basis set) and electron correlation is necessary. This point is exemplified by the results obtained for barrier heights (activation enthalpies) of \(S_n2\) reactions.\(^5\)–\(^8\) It has been demonstrated that the high level approach including G2 provides very accurate estimates of the height of these barriers. On the other hand, the very popular MP2/6-31G(d) and B3LYP/6-31G(d) approximations fail, by providing
severely underestimated values. In this respect, B3LYP is definitely the poorest. On the positive side, we notice that both MP2 and B3LYP give quite reliable trends in reactivity when changing substrate or nucleophile.

**Predictability**

Based upon the considerations given above, we may conclude that the predictive power of highly correlated WFT methods is high, providing the molecular system is sufficiently small and that the molecular structures in question are correctly described using single determinant wave functions. The situation for medium-sized and large molecules is more difficult. We have noted the limitations of the intermediate level approximations such as MP2/6-31G(d) in giving reliable estimates of different properties such as reaction energies and barriers, irrespective of size. During the last decade, the use of DFT-based methods has increased enormously, thanks to the very favourable scaling properties. In addition, many molecular properties are calculated with surprisingly good accuracy, often for unclear reasons. One notices that many users are quite uncritical or optimistic about their results. It should become mandatory practice that any use of intermediate level approximation methods should be validated, in particular DFT methods. Only direct comparison with experiment (best) or with high level WFT calculations (second best) should be done. The predictive power is, therefore, in practice and in principle, limited. Any use of quantum chemical-based methods on new ground, without validation or calibration, should be met with the greatest amount of scepticism.

**Insight: mechanisms of ion–molecule reactions**

Nowadays, mechanistic and kinetic studies of ion–molecule reactions are normally accompanied by quantum chemical calculations. Provided a sufficiently accurate level of approximation is available, the details of the potential energy surface may give rise to a consistent picture of the course of events that lead to the observed reaction. Furthermore, the type of insight available from the model may not be easily available through experiment and it may, therefore, be unique. One such example is the reaction between protonated hydrogen peroxide and propane. From experiments with specific deuterium-labelled propane, we observe three reaction channels, of which the former two stem from a common initial hydride abstraction:

\[
\begin{align*}
C_3H_8 + H_2O\text{OO}^- &\rightarrow C_3H_7^+ + 2 H_2O & (1) \\
C_3H_8 + H_2O\text{OH}^- &\rightarrow C_3H_7 + H_2O + H_2O^- & (2) \\
C_3H_7 + [H\text{OO}OH]^+ &\rightarrow C_3H_6 + [H\text{OO}OH]^+ & (3)
\end{align*}
\]

The third reaction, a hydrogen exchange reaction with 8% overall abundance, is quite different. Moreover, there is a preference for exchange of hydrogen of the central carbon and a normal kinetic isotope effect is observed. The quantum chemical reaction clarified the situation. Transition structures corresponding to synchronous flip-flop mechanisms or each of the central and terminal carbons were observed. The atomic motions of the incoming and outgoing hydrogens resemble an asymmetric stretch combination. By using the G3 reaction barriers and the calculated spectroscopic parameters, it was possible to conduct subsequent Rice–Ramsperger–Kassel–Marcus calculations giving a very satisfactory description of the experimentally-observed branching ratios. Compared to the previously mentioned G2 method, G3 provides comparably accurate barriers at a reduced computational cost.

**Insight: spectroscopy and structure of ions**

Ion spectroscopy is another discipline of ion chemistry that benefits from the development in computational quantum chemistry. One may say there is a symbiosis between the two disciplines. Assignment of spectroscopic features obtained in pioneering experiments would be more difficult, and even impossible or speculative, without the use of accurate models. At the same time, accurate experiments are required for testing and developing accurate computational methods. A recent study on the vibrational pre-dissociation spectrum of H(H_2O)\text{H}^+Ar illustrates these points very well. It would hardly have been possible to provide a detailed and consistent picture of the vibrational motions within individual water clusters of the proton using only the classical Wilson FG matrix method. The success of the study depended very much on the availability of quantum chemical models.

**Insight: dynamics of ion fragmentation**

One last example on the use of computation comes from the simulation of reaction trajectories calculated in situ on BO potential energy surfaces. The unimolecular chemistry of protonated formic acid, [HCOOH]H^+, was studied by using mass-analysed ion kinetic energy (MIKE) spectrometry and Fourier transform ion cyclotron resonance (FT-ICR) mass spectrometry. Two reactions are observed for HCO(OH)\text{H}^+:

\[
\begin{align*}
[H\text{COOH}]H^+ &\rightarrow HC^+O + H_2O & (4) \\
[H\text{COOH}]H^+ &\rightarrow H_2O^+ + CO & (5)
\end{align*}
\]

In addition to high-level WFT calculations of the potential energy surface, a series of direct dynamic calculations were conducted. The only stable isomer in the mass spectrometric experiments is HC(OH)\text{H}^+, which is the precursor to both observed ionic products, HCO^+ and H_2O^+, via the same saddle point of the potential energy surface. The detailed
motion of the dissociating molecule during the passage of the post-transition state region of the potential energy surface therefore determines which product ion is formed. After passing the TS, a transient HCO\textsubscript{2}OH\textsuperscript{+} molecule is formed first. High total energy increases the probability that the nascent water molecule will have sufficient speed to escape the HCO\textsuperscript{+} moiety (Reaction 4). Otherwise, typically at low energies, the two units recombine, at which point intracomplex proton transfer is very likely to occur. Eventually, this will give the more stable H\textsubscript{3}O\textsuperscript{+} (Reaction 5).

**Conclusion**

In this lecture, we have seen that computational quantum chemistry has achieved a central standing in gas-phase ion chemistry. Highly reliable reaction models can now be created for reactions of small- and medium-sized molecules. In the future, we will probably see a continuous change in this direction. This will, to a large degree, depend on the availability of faster and more powerful computers. In parallel with the development in computer technology there has been parallel progress in experimental methodology. For example, detection systems have become smaller and faster, yet more selective and sensitive. While many classical models for experimental interpretation were quite rudimentary, it is likely that the degree of experimental sophistication in the future will require models of higher complexity and detail and the models will be based directly on first principles.

**References**


Received: 28 November 2006
Revised: 20 December 2006
Accepted: 29 December 2006
Publication: 9 January 2007