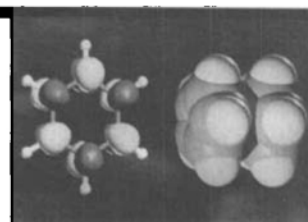


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Column Editors:
Prof. Dr. J. Weber, University of Geneva
Prof. Dr. H. Huber, University of Basel
Dr. H. P. Weber, Sandoz AG, Basel



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Bulk Properties of Liquids and Molecular Properties in Liquids from a Combination of Quantum Chemical Calculations and Classical Simulations

Hanspeter Huber*, Elena Ermakova, Jan Solca, and Gerold Steinebrunner

After an introduction to the title subject and some educational aspects in the first [1], and an overview over the calculation of bulk properties in the second Column [2], we close this series with a presentation of the calculation of solvent effects on nuclear and molecular properties.

Part III. Solvent Effects

How to calculate them

In recent years several schemes to include solvent effects in quantum chemical calculations have been published and they are now implemented in popular programs like GAUSSIAN or SPARTAN (see, e.g. [3] and [4]). They usually treat the solvent as a continuum and take only electrostatic effects into account. Here we will discuss a more general scheme, which can be used in principle for any molecular or nuclear property either *ab initio* or including empirical steps.

Fig. 1 shows a graphical representation of the method to be discussed here. It starts either by calculating quantum chemically a pair potential or by taking a potential surface (empirical or quantum chemical) from the literature. Its analytical form is built into a Monte Carlo or molecular dynamics program which is then applied to run a simulation. After equilibration, snapshots are taken periodically, *i.e.*, the coordinates of all atoms are saved on disk. Typically ten to several hundred such configurations of the liquid are stored. In the centre of *Fig. 1* such a configuration obtained from a simulation of water is shown. From each configuration one atom or molecule is randomly selected (other procedures are possible). Let us assume we would like to calculate the chemical shielding in proton nuclear magnetic resonance of liquid water. Then we would randomly select one proton in each configuration and calculate the distances to all other molecules to select its nearest neighbours. In such a way we could select a cluster of

water molecules as shown on the right-hand side in *Fig. 1*, typically made of 5–15 molecules, depending on the property we want to calculate and on the desired accuracy. Each cluster corresponds to a typical liquid surrounding. In a subsequent quantum chemical calculation of the proton chemical shielding, we treat the cluster as a molecule (usually called a 'supermolecule'). This yields the proton chemical shielding in a typical liquid surrounding. Repeating the quantum chemical calculation for clusters from all configurations and averaging, leads to the proton shielding of liquid water at the proper temperature and pressure used in the simulation.

This method is quite expensive in computer time and it has been applied only in a few cases. Hence, the experience of its applicability and of the problems involved is very limited. In the following section some of the problems will be discussed.

Problems

First, the question arises to what extent the results depend on the quality of the potential. The limited experience available shows quite different results for different properties (see below). If the potential has much influence on the calculated property, then the problem arises how to select a potential, *i.e.*, how do we know in advance, which of the available analytical potentials is the best.

As in the calculation of bulk properties, there are approximations in the simulation, which partially can be made negligible, but might partially influence the result. At low temperatures quantum effects and at higher temperatures many-body effects might be important. Although, the cluster approach takes care of many-body effects in the quantum chemical calculation of the desired property of the supermolecule, the geometry of the cluster was obtained from simulations which used a pair potential. The results for the radial pair distribution function of rare gases [5], discussed in the last Column [2], makes us confident that many-body effects have little influence on the structure,

*Correspondence: Prof. Dr. H. Huber
Institut für Physikalische Chemie
der Universität Basel
Klingelbergstrasse 80
CH-4056 Basel

and that, therefore, the above procedure is reasonable. Further work is necessary to show to what extent this is true for polar or even hydrogen bonded molecules. Additional problems can arise for molecular systems in the simulations. If the property of interest is strongly dependent on ro-vibration, this effect will be in general different in the liquid and in the gaseous state. In the simulation one takes either not care of this at all (rigid molecule approximation) or only classically (flexible molecule approximation). It is not possible at the moment to treat these effects in the liquid quantum chemically, *i.e.*, in an adequate way.

The third part, the quantum chemical treatment of the supermolecule, does not lead to basic problems beyond the ones found in single molecule calculations corresponding to the gas phase. However, it is required a significant amount of computer time, as one has a system roughly ten times larger than the single molecule and the calculation has to be repeated typically 10–100 times.

A Few Examples

We are aware of only three cases of solvent effects which have been treated as discussed above, all of them in pure liquids: vibrational spectra, nuclear quadrupole coupling constants and chemical shieldings in nuclear magnetic resonance (NMR).

Vibrational Spectra

Before discussing the pioneering work of *Hermansson et al.* [6] let us notice that vibrational frequency shifts in liquids have been calculated from simulations in a different scheme from the above, namely in molecular dynamics simulations *via* a *Fourier* transform of velocity autocorrelation functions. In this way the vibrations are treated classically and the approximation of pair additivity of the potentials is also used for the vibration itself. *Clementi et al.* [7] obtained, for example, for the bending and the two stretching modes in water solvent frequency shifts of 71 cm^{-1} , -220 cm^{-1} and -261 cm^{-1} , respectively,

whereas the experimental values are 50 cm^{-1} , -167 cm^{-1} , and -266 cm^{-1} . But let us turn now to the method discussed in the first two sections.

This method was first suggested in a slightly different form by *Hermansson, Knuts, and Lindgren* four years ago [6]. These authors studied the solvent shift of the O–H frequency in liquid water. To simplify, they investigated a system where experimental results were obtained by the isotope-isolation technique. HDO was studied in D_2O as a solvent, hence decoupling the O–H vibration nearly completely from other vibrations. Clusters of size 5 were obtained from a Monte Carlo simulation performed with an *ab initio* potential for rigid molecules from the literature. Modifying the above method, they embedded the pentamer in a sea of point charges out to 1500 pm from the vibrating molecule. The point charges were situated at the Monte Carlo generated atomic positions and selected to give the right dipole moment of the monomer. The O–H bond lengths of the central water in the penta-

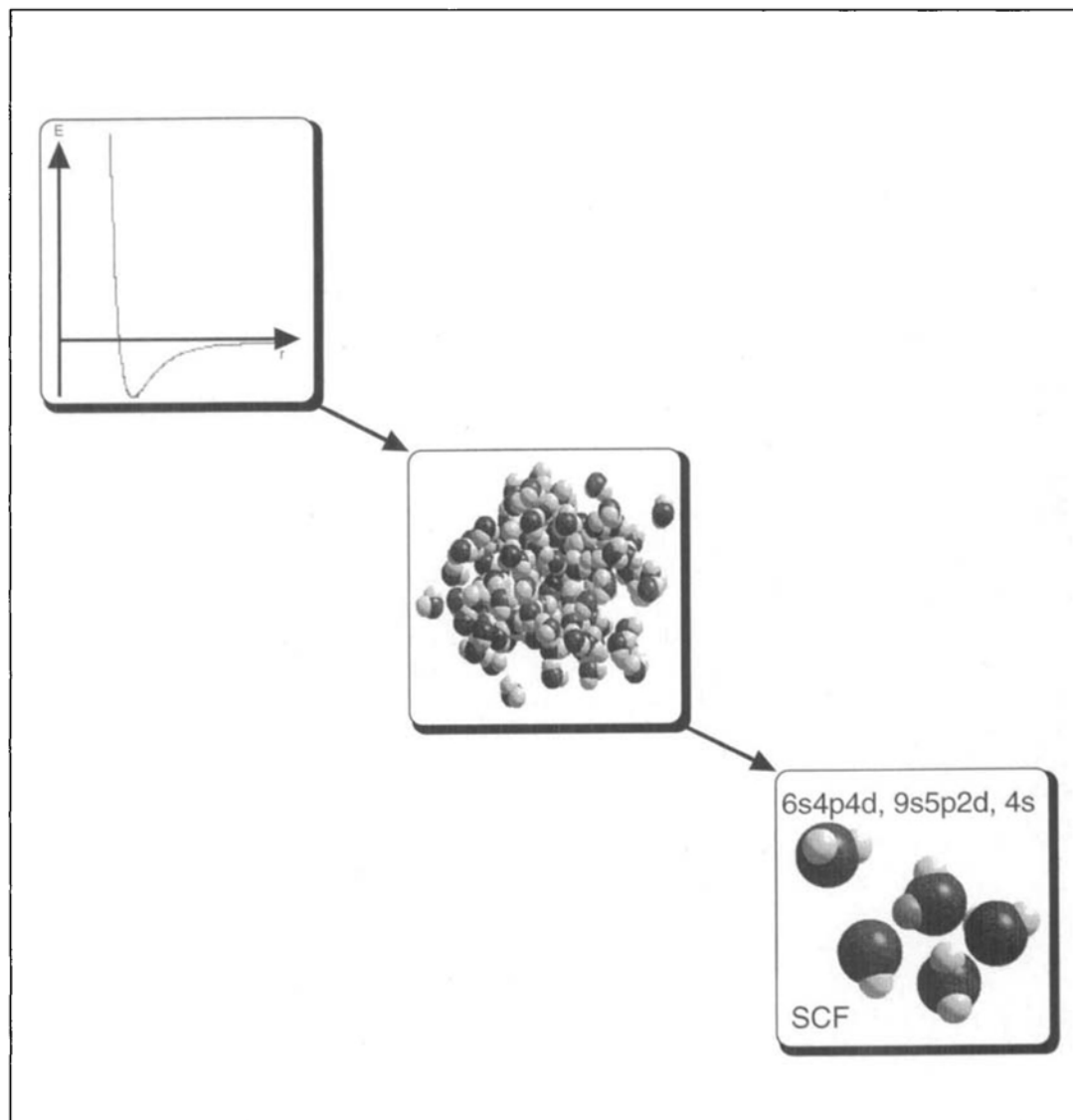


Fig. 1. Graphic representation of the discussed method. Simulations are performed with calculated or empirical potentials (left) to obtain snapshots of the liquid (centre). Clusters are selected from these snapshots and used as supermolecules in quantum chemical calculations of a property. Averaging the results of many calculations yields the desired property in the liquid phase.

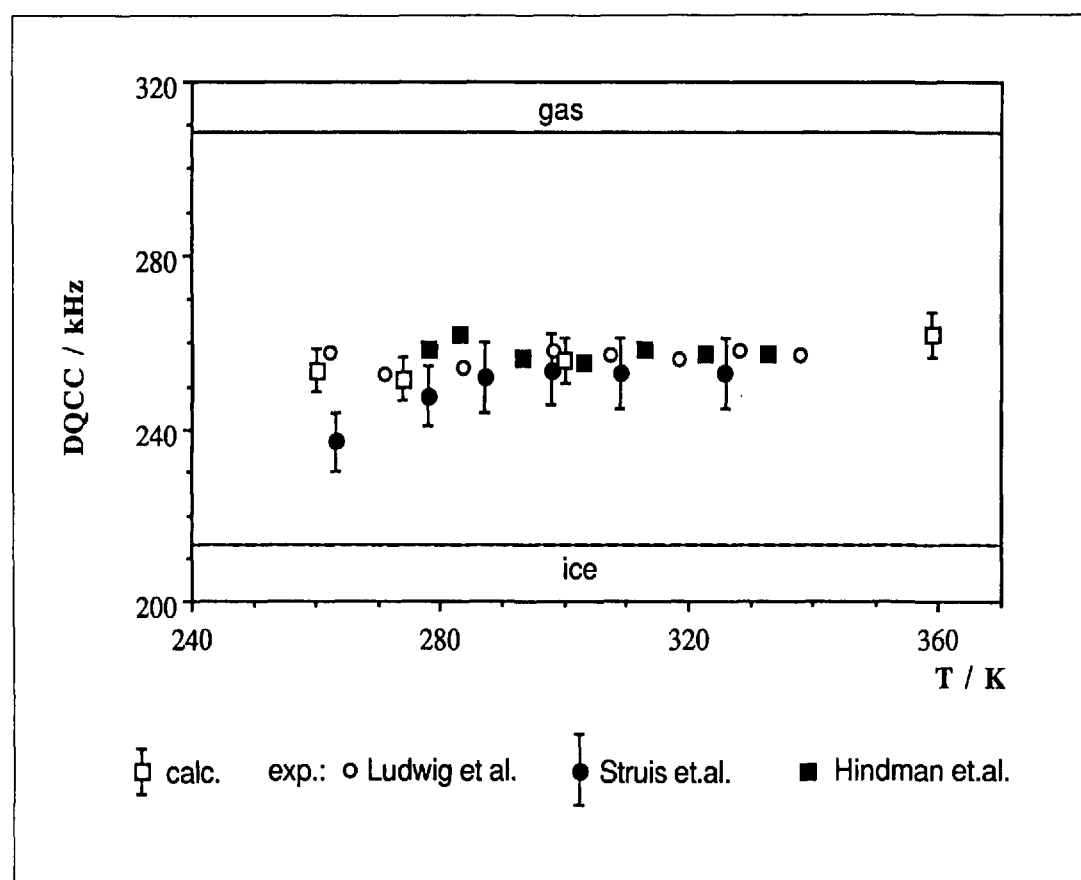


Fig. 2. Calculated and experimental deuterium quadrupole coupling constant (DQCC) in liquid water as a function of temperature

mer were varied, one at a time, in 12 steps and the energy was calculated quantum chemically using an *ab initio* method including correlation. The potential energies were fitted to a fifth order polynomial and the one-dimensional *Schrödinger* equation solved numerically. This procedure was repeated for 22 clusters to obtain an average surrounding typical of the liquid. A histogram of the frequencies together with the *ab initio* obtained intensities yields an intensity band for a comparison with the experimental liquid spectrum. The spectrum is downshifted by 260 cm^{-1} compared to an experimental shift of 307 cm^{-1} . The half-width of 236 cm^{-1} also compares favourably with the experimental value of 255 cm^{-1} . Further calculations on a few heptamers gave hints that the results had not yet converged and could be improved when going to larger clusters. The dependence on the potential function applied in the simulation was not investigated.

In a somewhat related paper from *Hermansson's* group ([8], see also for a review of related work) a modification of the method was applied. The clusters obtained from simulations using an *ab initio* potential were not treated quantum chemically to obtain the potential function of the vibration, but the latter was built from different classical intra- and intermolecular potentials from literature, hence using

the pair additivity approximation for the potential. The one-dimensional vibrational problem was then solved quantum chemically as above. In this way several potentials from the literature were found to give quite different results. A further related study [9] showed that a classical treatment of the one-dimensional vibrational problem does not describe correctly the anharmonicity of the potential and results in similar shifts as a harmonic treatment. What has not been tested yet is the dependence of the shift on the potentials applied to obtain the clusters in the original approach.

Nuclear Quadrupole Coupling Constants

Chemists are usually not very familiar with nuclear quadrupole couplings. In gas phase, the couplings lead to an additional splitting of lines in microwave spectra and can be measured relatively easily, but they are mainly a subject for specialists. It is in the liquid phase that we usually meet them, although in a very superficial contact. In NMR spectra of compounds containing nitrogen, one often finds very broad peaks, which are the result of quadrupole couplings. Only nuclei with a spin ≥ 1 show a nuclear quadrupole moment and, hence, are responsible for this phenomenon. However, if a nuclear quadrupole coupling is present, it is usually the dominant mecha-

nism in the relaxation of nuclei. Its measurement in liquids is, therefore, performed by relaxation time measurements. The relaxation time is roughly the product of the square of the quadrupole coupling constant times the rotational correlation time. However, it is not easy to separate these two properties in an accurate way. Therefore, there are not yet many accurate measurements available and it would be helpful to have the possibility to calculate couplings to improve the evaluation of experiments [10]. Calculations with the above method have been performed until now for deuterium and ^{17}O couplings in liquid water [11–13], and for deuterium and ^{14}N in liquid ammonia [14]. A slightly different method was recently applied to liquid water by *Ludwig et al.* [15].

For deuterium in liquid water at 300 K a solvent shift of -55 kHz (-17.4%) was calculated [11][13], in excellent agreement with an experimental value of $-54 \pm 8\text{ kHz}$ (-17.6%) [16]. For ^{17}O the calculated shift was -1.2 MHz (-11.9%) [12], much less than the -2.0 MHz (-19.6%) deduced experimentally [16]. It is not yet clear to what extent the discrepancy is due to inaccuracies in the calculations or in the experiments. *Ludwig et al.* [15] calculated results closer to the experiment and claim that the deviation is due to the pair approximation. An interesting result of the investigations of *Eggenberger et al.* [11–13] is

that the calculated values are independent from the potentials applied (3 and 2 different potentials for D and ^{17}O , respectively; one of them an *ab initio* potential) within statistical errors. Another conclusion from these calculations was that cluster sizes of 5 were large enough for water to obtain accurate couplings. The largest contribution to the solvent effect stems from the hydrogen bonds. The solvent shift of 55 kHz for D consists of *ca.* 20 kHz (40%) due to a direct (electronic) influence of the neighbours and *ca.* 35 kHz (60%) due to an indirect influence (through a change of the monomer structure). The temperature dependence of the deuterium quadrupole coupling constant is shown in Fig. 2. The calculated values [11] are compared with experimental values from Ludwig *et al.* [15], Struis *et al.* [16], and Hindman *et al.* [17].

No experimental ^{14}N quadrupole coupling constant is available for liquid ammonia. It is usually assumed to be equal to an estimated value for the solid phase at 0 K. Under this assumption the experimental solvent effect is -0.62 MHz (-15.2%), whereas calculated values of -0.42 MHz (-10.3%), -0.53 MHz (-13.0%) and -0.66 MHz (-16.1%) were obtained at 271 K, 232 K, and 197 K, respectively. The liquid value at the lowest temperature is in excellent agreement with the coupling deduced from experiment. For the deuterium coupling the comparison is even more difficult, as the experimental gas phase value is very uncertain and only a rough value has been found for the liquid. The calculated solvent effects are -17% at 271 K and -20% at 197 K, in agreement with the experimental estimates. These data were obtained using one empirical potential only, which is justified from the results for water. However, the cluster size was studied independently, as it is known from literature that ammonia has a larger number of neighbours in the first solvation shell. Convergence was obtained for a cluster size of *ca.* 10.

Chemical Shieldings in Nuclear Magnetic Resonance

Gas-liquid shifts of the chemical shielding obtained by the above method have been reported only for proton and ^{17}O NMR of water. Chesnut and Rusiloski [18] performed simulations with the CFF-91 (class II) force field built in the program DISCOVER and quantum chemical shielding calculations with the *ab initio* coupled Hartree-Fock gauge including atomic orbitals (GIAO) method. A cluster size of 10 was found to be appropriate. For ^{17}O these authors calculated a gas-liquid shift of

-20.3 ppm which has to be compared with an experimental value of -36.1 ppm, whereas for protons the corresponding numbers are -2.28 ppm and -4.26 ppm. The discrepancy between experiment and calculation could not be resolved. As a possible source of error, the fact that the mechanical force field was not dedicated to water was suggested. These authors separated also their calculated shifts into a direct (electronic) and an indirect (through a change in the structure) influence. The direct influence turned out to be the larger part, -12.1 ppm for ^{17}O and -1.93 ppm for H. The indirect part was -8.2 ppm for ^{17}O and -0.34 ppm for H, respectively.

Malkin *et al.* [19] extended the studies of Chesnut and Rusiloski to three dedicated force fields and to two different quantum chemical methods for the calculation of chemical shieldings to resolve the discrepancies. With the sum-over-states density-functional perturbation theory (SOS-DFPT) approach they found for the gas-liquid shifts of ^{17}O values between -37 ppm and -45 ppm and for the protons between -2.8 ppm and -3.4 ppm, depending on the force fields, in better agreement with experiment. Clearly, there is a strong dependence on the force field. A resolution into direct and indirect effects gives a more detailed insight. The indirect effects turned out to be within a small range, namely between -6 ppm and -7.5 ppm for ^{17}O and between -0.25 ppm and -0.33 ppm for H. This compares favourably with the above values of Chesnut and Rusiloski (-8.2 and -0.34 ppm, respectively). The direct effects are much larger and their range depending on the force field is between -30.4 ppm and -37.3 ppm for ^{17}O and between -2.51 ppm and -2.70 ppm for H. Clearly the intermolecular force field has a significant influence on the shifts, in contrast to the results obtained in the calculations of quadrupole couplings in liquids. However, additional calculations using different basis sets comparing the GIAO method with the SOS-DFPT method showed that the crucial part of these calculations is the choice of the quantum chemical method combined with an appropriate basis set.

It was shown in a few cases that calculations of solvent effects are now feasible and that a wide field is open to validate such calculations and to improve the methods.

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