12th PhD seminar, Garching, October 31st 2008

Introduction to Computational Chemistry for Experimental Chemists… (Part 2/2)

Dr. Markus Drees, TU München
A) What is computational chemistry?
   Definitions - Methods - Types of calculations

B) From a Formula to calculated Properties
   Graphical interfaces - input files - basis sets - calculation - output analysis

C) How to evaluate Mechanisms with Computational Chemistry
   Mechanism theorems - energetic evaluation - transition states and kinetics

D) A Word on Costs and Accuracy
   Phrases of prejudice - computational costs - accuracy
Announced last time

- **Population analysis**
  Determines the distribution of the electrons into the molecular orbitals
  Delivers dipole moments
  Creates graphical expressions of orbitals

- **NMR calculation**
  Simulates the external field of the NMR source as perturbation for the electron density
  Delivers chemical shifts (in combination with a standard) and - very time consuming - even coupling constants

- **UV/VIS calculation**
  Calculates the most feasible electron excitations
  Methods: time-dependent DFT or CIS (configuration interaction - singlets)

- **Solvation energies**
  Implicit methods (SCRF) via correlation of an external reaction field in relation to the polarity of the solvent, solvent models: PCM, Dipole, ...
  
  Explicit calculations (addition of the solvent molecules to molecular systems) are more time consuming than implicit methods
Outline of today

E) Population analysis - Where are those little electrons?
Definitions - Mulliken - Natural Bond Orbitals - Atoms in Molecules

F) IR: simulation of vibrations

G) NMR calculations - The influence of the electronic shielding

H) UV/VIS - How to calculate excited states

I) Solvation problems - yet not really solved
E) Population analysis - Definitions

What does a population analysis deliver?
1) Determination of the distribution of electrons in a molecule
2) Creating orbital shapes
3) Derivation of atomic charges and dipole (multipole) moments

Methods of calculation:
- Based on the wave function (Examples: Mulliken, Natural Bond Orbitals)
- Based on the electron density (Atoms In Molecules)
- Fitted to the electrostatic potential (CHELPG, MK)

What is (atomic charge)? Formal versus atomic charge at the ammonium cation:

![Image of ammonium cation]

<table>
<thead>
<tr>
<th>Method</th>
<th>q(N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mulliken</td>
<td>-0.844</td>
</tr>
<tr>
<td>NPA</td>
<td>-0.977</td>
</tr>
<tr>
<td>CHELPG</td>
<td>-0.737</td>
</tr>
<tr>
<td>MK</td>
<td>-0.790</td>
</tr>
</tbody>
</table>

Calculating atomic charges

Negative nitrogen!
(The charge +1 comes from the four positive hydrogens.)
E) Population analysis - Mulliken

- Most popular method
- Standard in program packages like Gaussian
- discussed very controversial

Some formula stuff:

\[ \phi_r = \sum_{\mu} c_{r\mu} \chi_\mu = c_{r1} \chi_1 + \ldots \quad \text{One molecular orbital} \]

\[ |\phi_r|^2 = c_{r1}^2 \chi_1^2 + c_{r2}^2 \chi_2^2 + \ldots + 2 c_{r1} c_{r2} \chi_1 \chi_2 \ldots \]

Density of probability

Integration over the whole space:

\[ \int |\phi_r|^2 d\tau = 1 = c_{r1}^2 + c_{r2}^2 + \ldots + 2 c_{r1} c_{r2} S_{12} \ldots \]

Separation in local and overlapped electrons

\[ = \sum_{\mu} c_{r\mu}^2 + 2 \sum_{\rho} \sum_{\nu} c_{r\mu} c_{r\nu} S_{\mu\nu} \]

Population of the AOs \( \mu \) in the MO \( r \)

\( (n_r = \text{Number of occupancy}) \):

\[ P_{r,\mu} = n_r c_{r\mu}^2 \quad \text{Local (net) contribution} \]

\[ P_{r,\mu\nu} = n_r \left( 2 c_{r\mu} c_{r\nu} S_{\mu\nu} \right) \quad \text{Contribution from the overlap} \]

Sum of all occupied MOs: The fraction of the population is distributed over the two atoms of a bond:

\[ P_A = \sum_{\mu} \sum_{\rho} n_r \left( c_{r\mu}^2 + c_{r\mu} c_{r\nu} S_{\mu\nu} \right) \]

Atomic Charge:

\[ Q_A = Z_A - P_A \]

\[ Z_A = \]

Atomic number (core charge)
Advantages of the method:
Fast and simple method for determinations of electron distribution and atomic charges

Disadvantages of the method:
Strong dependence of the results from the level of theory (basis sets or kind of calculation)

Example: Li-charge in LiF

<table>
<thead>
<tr>
<th>population</th>
<th>basis set</th>
<th>q(Li, RHF)</th>
<th>q(Li, B3LYP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mulliken</td>
<td>STO-3G</td>
<td>+0.227</td>
<td>+0.078</td>
</tr>
<tr>
<td>3-21G</td>
<td>+0.596</td>
<td>+0.421</td>
<td></td>
</tr>
<tr>
<td>6-31G</td>
<td>+0.743</td>
<td>+0.593</td>
<td></td>
</tr>
<tr>
<td>6-31G(d)</td>
<td>+0.660</td>
<td>+0.526</td>
<td></td>
</tr>
<tr>
<td>6-311G(d)</td>
<td>+0.691</td>
<td>+0.558</td>
<td></td>
</tr>
<tr>
<td>6-311+G(d)</td>
<td>+0.687</td>
<td>+0.616</td>
<td></td>
</tr>
<tr>
<td>6-311+G(3df)</td>
<td>+0.750</td>
<td>+0.675</td>
<td></td>
</tr>
<tr>
<td>NPA</td>
<td>6-311+G(3df)</td>
<td>+0.977</td>
<td>+0.963</td>
</tr>
</tbody>
</table>
E) Population analysis - Natural Bond Orbitals

Originally an independent program

Is more and more incorporated into the quantum chemical packages

More info in the WWW:
http://www.chem.wisc.edu/~nbo5/

Based in the theory of “Natural Orbitals” by Löwdin

Two parts of the method:
NPA ➔ Natural population analysis to identify the population numbers
NBO ➔ Analysis of the bond order based on the electron population obtained by NPA

Gains more and more importance in computational publications in the community
E) Population analysis - Natural Bond Orbitals (II)

Simple derivation of the NBO methodology

AOs (atomic orbitals) → Eigenvectors of the density operator

NAOs (Natural Atomic Orbitals)

Distribution → Largest overlap

Core Valence Rydberg

Analysis

NPA (population analysis) → Difference of atomic number and investigated population

Atomic charge

Advantages:

Smaller dependence on the basis set in comparison to Mulliken analysis

Better reproducibility for different molecules

Orientates itself at the formalism for Lewis formulas

NBOs (Natural Bond Orbitals)

Lewis → Analysis for bond orders and hybridizations

Non-Lewis

Core Valence Rydberg

Analysis for bond orders and hybridizations
E) Population analysis - Bader’s “Atoms in Molecules”

Info in the internet:
http://www.chemistry.mcmaster.ca/faculty/bader/aim/

Approach now via electron density, not basis functions:

Based on this theory, new cognitions for the behavior of atoms in molecular structures were developed.

Integration over the whole space leads to calculations of charge distributions and bond orders.
E) Population analysis - “Atoms in Molecules” (II)

Example: Distribution of electron densities at B-F bonds:

- Segmentation of the molecule into a set of volume elements (border: Gradient of the electron density equals 0)

- Two atoms bind, if they have joint sets of volume with an included bond critical point (Gradient of the electron density equals 0).

Advantage: Almost no dependence on the level of basis sets

Disadvantage:
- For a low level of theory mostly inappropriate
- Unstability during calculation runs
Molecular vibrations have fundamental tasks in quantum chemical calculations:

- Derivation of statistical thermodynamics and their units via frequency calculations
- Classification of ground states and transition states (and saddle points of higher order)
- Simulations for assignments of vibrational modes
3N-6 vibrational modes per molecule (linear molecules: 3N-5)

Quantum-chemical derivation procedure:
1) Geometry optimization

2) Calculation of the second derivative of the energy with respect to mass-weighted coordinates (Hessian matrix)

3) Solving of 3N linear equations, while six (or five) of them should deliver a frequency of vibration of zero (rotations and translations)

A complete derivation of the formalism run by Gaussian can be found in the internet via: http://www.gaussian.com/g_whitepap/vib.htm
How is it enabled in theory programs?

Two possibilities of calculations: Analytical frequencies via SCF wave functions, or numerical frequencies via displacements in all three cartesian coordinates (in both directions, positive and negative).

Frequency calculations have to be executed at the same level of theory as the associated geometry optimization. Otherwise the results are worthless, because of the high geometry dependence of the vibrational modes. In some theory packages, a thermodynamical analysis is included in frequency calculations, in other packages a thermodynamical analysis is an additional part.

Also changes in an isotope pattern can be utilized in frequency calculations.
F) IR: simulation of vibrations (III)

Assignment of the calculated vibrational modes:

1) Graphical analysis via animation in programs like Molden and GaussView (incl. plot of the IR spectra)
2) Inspection of the displacement parameters in the output file of the calculation

With respect to scaling factors, even unknown spectra are reliably assigned

Scaling factors for adjustments of the calculation to the experiment:

<table>
<thead>
<tr>
<th>method</th>
<th>scale factor</th>
<th>rms deviation (cm⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AM1</td>
<td>0.9532</td>
<td>126</td>
</tr>
<tr>
<td>PM3</td>
<td>0.9761</td>
<td>159</td>
</tr>
<tr>
<td>HF/6-31G(d)</td>
<td>0.8953</td>
<td>50</td>
</tr>
<tr>
<td>MP2(FC)/6-31G(d)</td>
<td>0.9427</td>
<td>61</td>
</tr>
<tr>
<td>QCISD(FC)/6-31G(d)</td>
<td>0.9537</td>
<td>37</td>
</tr>
<tr>
<td>BLYP/6-31G(d)</td>
<td>0.9945</td>
<td>45</td>
</tr>
<tr>
<td>B3LYP/6-31G(d)</td>
<td>0.9614</td>
<td>34</td>
</tr>
</tbody>
</table>
G) NMR calculations - shielding of electrons

Introduction

Basic question: NMR is a property of the nuclei, why can you simulate a NMR spectra via electron-based quantum chemistry?

Answer: The magnetic field in an NMR spectrometer can be considered as perturbation of the electron density. With a suitable approach (perturbation-theory), the chemical shift can be calculated with respect to the electronic structure.

With a Hessian-like formalism, even the J-coupling can be calculated.

Algorithms: GIAO (Gauge-Independent Atomic Orbital, developed by McWeeny, Ditchfield, Pulay), CSGT (Continuous Set of Gauge Transformations written by R. Bader)
G) NMR calculations - How to do

Quantum chemical procedure:
1) Geometry optimization with a common level of theory

2) NMR simulation (as single point) with a high level of theory, methods like HF/6-311++G** or B3LYP/6-311++G** have been proven as useful

NMR parameters are very tolerable to smaller deviations of the molecular structure. Therefore the level of theories of the optimization and the GIAO/CSGT calculations may differ.

NMR shifts of all (!) atoms are calculated, regardless if there are active NMR isotopes or not.
To draw comparisons to experimental data, the calculated chemical shifts ave to be scaled like in a real NMR measurement (e.g. calculated chemical shifts of TMS (Tetramethylsilane) for $^{13}$C und $^1$H).
G) NMR calculations - comparison with increments

Example adenine: Comparison of increment schemes and quantum chemical calculations

<table>
<thead>
<tr>
<th>Atom</th>
<th>CS ChemNMR Pro</th>
<th>ΔExperiment</th>
<th>Gaussian 03</th>
<th>ΔExperiment</th>
<th>Experiment</th>
</tr>
</thead>
<tbody>
<tr>
<td>C1</td>
<td>150.2</td>
<td>-2.2</td>
<td>161.2</td>
<td>+9.2</td>
<td>152.4</td>
</tr>
<tr>
<td>C2</td>
<td>154.9</td>
<td>+3.6</td>
<td>156.8</td>
<td>+5.5</td>
<td>151.3</td>
</tr>
<tr>
<td>C3</td>
<td>147.9</td>
<td>+8.6</td>
<td>139.5</td>
<td>+0.2</td>
<td>139.3</td>
</tr>
<tr>
<td>C4</td>
<td>128.4</td>
<td>+10.8</td>
<td>124.8</td>
<td>+7.2</td>
<td>117.6</td>
</tr>
<tr>
<td>C5</td>
<td>144.8</td>
<td>-10.5</td>
<td>160.7</td>
<td>+5.4</td>
<td>155.3</td>
</tr>
</tbody>
</table>

Link to similar comparisons: http://www.gaussian.com/g_whitepap/nmrcomp.htm
Determinations of Coupling Constants is also possible

Problems:
- Computational costs as high as twice what is needed for a analysis of vibrational frequencies
- Usage of ECPs for transition metals arise methodical errors => only all-electron treatments are reliable => more computational costs
- Deviations up to 10-20% is normal

What about EPR (also derived from the magnetic property)?
- Hyperfine Coupling is easily calculated via standard packages like Gaussian and Turbomole
- Calculation of g-tensors requires Molecular Dynamics software
### Introduction

Absorptions in the UV/VIS region correlates with excited electronic states.

In the UV/VIS spectroscopy, it is granted, that the geometry of the ground-state is still valid also for the excited state because of the short time-scale.

» no special geometry optimization for the excited state necessary
Quantum chemical procedure:
1) Geometry optimization of the ground state with the desired level of theory

2) Single point calculation for the optimized geometry depending on the level of theory:
   a) DFT methods require a time-dependent DFT approach (TD-DFT)
   b) Hartree-Fock and post-Hartree-Fock methods require a Configuration interaction approach (CIS)
   c) Semiempiric calculations can cover Excited States by the ZINDO method

The standard mode in Gaussian is to calculate the three most probable singlet excitations (and triplet, if desired), including wavelength, amount of energy, and probability factor.

In the newest GaussView version, also the UV/VIS absorption spectra is now plotted from these obtained numbers.
Example: Excitation of a $\pi$-electron in ethylene

<table>
<thead>
<tr>
<th>Transition</th>
<th>SVWN $^a$</th>
<th>BLYP $^a$</th>
<th>B3LYP $^a$</th>
<th>HCTH(AC) $^a$</th>
<th>PBE $^b$</th>
<th>PBE1PBE $^c$</th>
<th>PBE1PBE $^{bc}$</th>
<th>CASPT2 $^d$</th>
<th>Exp $^d$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\pi \rightarrow \pi^*$ ($B_{\alpha}$)</td>
<td>4.70</td>
<td>4.32</td>
<td>4.07</td>
<td>4.33</td>
<td>4.34</td>
<td>3.92</td>
<td>3.94</td>
<td>4.39</td>
<td>4.36</td>
</tr>
<tr>
<td>$\pi \rightarrow 3s$ ($B_{\alpha}$)</td>
<td>6.51</td>
<td>6.13</td>
<td>6.50</td>
<td>7.10</td>
<td>6.48</td>
<td>6.79</td>
<td>6.85</td>
<td>7.05</td>
<td>6.98</td>
</tr>
<tr>
<td>$\pi \rightarrow 3p\sigma$ ($B_{\alpha}$)</td>
<td>6.55</td>
<td>6.18</td>
<td>6.57</td>
<td>7.16</td>
<td>6.52</td>
<td>6.93</td>
<td>6.99</td>
<td>7.17</td>
<td>7.11</td>
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<tr>
<td>$\pi \rightarrow 3p\pi$ ($B_{\alpha}$)</td>
<td>7.03</td>
<td>6.63</td>
<td>7.05</td>
<td>7.76</td>
<td>7.06</td>
<td>7.36</td>
<td>7.42</td>
<td>7.80</td>
<td>7.79</td>
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<tr>
<td>$\pi \rightarrow 3p\pi$ ($B_{\alpha}$)</td>
<td>7.05</td>
<td>6.65</td>
<td>7.08</td>
<td>7.78</td>
<td>7.08</td>
<td>7.51</td>
<td>7.59</td>
<td>7.85</td>
<td>7.80</td>
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<tr>
<td>$\pi \rightarrow 3\pi^*$ ($B_{\alpha}$)</td>
<td>7.04</td>
<td>6.63</td>
<td>7.09</td>
<td>7.77</td>
<td>7.03</td>
<td>7.52</td>
<td>7.62</td>
<td>7.95</td>
<td>7.90</td>
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<td>7.39</td>
<td>7.12</td>
<td>7.36</td>
<td>7.61</td>
<td>7.46</td>
<td>7.58</td>
<td>7.60</td>
<td>8.40</td>
<td>8.00</td>
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<tr>
<td>$\pi \rightarrow 3\pi^*$ ($B_{\alpha}$)</td>
<td>7.27</td>
<td>6.90</td>
<td>7.33</td>
<td>8.15</td>
<td>8.04</td>
<td>8.08</td>
<td>8.34</td>
<td>8.26</td>
<td>8.15</td>
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<td>7.31</td>
<td>6.96</td>
<td>7.41</td>
<td>8.33</td>
<td>8.11</td>
<td>8.04</td>
<td>8.08</td>
<td>8.40</td>
<td>8.28</td>
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<tr>
<td>$\pi \rightarrow 3\pi^*$ ($B_{\alpha}$)</td>
<td>7.10</td>
<td>6.66</td>
<td>7.34</td>
<td>8.64</td>
<td>8.65</td>
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<td>$\pi \rightarrow 3\pi^*$ ($B_{\alpha}$)</td>
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<td>6.68</td>
<td>7.36</td>
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<td>8.65</td>
<td>8.69</td>
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<tr>
<td>$\pi \rightarrow 3\pi^*$ ($B_{\alpha}$)</td>
<td>7.63</td>
<td>7.21</td>
<td>7.75</td>
<td>8.95</td>
<td>8.26</td>
<td>8.76</td>
<td>8.82</td>
<td>9.03</td>
<td>8.90</td>
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<td>$\pi \rightarrow 3\pi^*$ ($B_{\alpha}$)</td>
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<td>7.35</td>
<td>7.87</td>
<td>9.04</td>
<td>8.78</td>
<td>9.02</td>
<td>9.09</td>
<td>9.18</td>
<td>9.05</td>
</tr>
<tr>
<td>$\pi \rightarrow 3\pi^*$ ($B_{\alpha}$)</td>
<td>7.80</td>
<td>7.75</td>
<td>8.14</td>
<td>9.32</td>
<td>8.85</td>
<td>9.33</td>
<td>9.30</td>
<td>9.31</td>
<td>9.33</td>
</tr>
<tr>
<td>mean abs. error</td>
<td>0.94</td>
<td>1.26</td>
<td>0.85</td>
<td>0.67</td>
<td>0.43</td>
<td>0.21</td>
<td>0.19</td>
<td>0.09</td>
<td></td>
</tr>
</tbody>
</table>

$^a$ Taken from Tozer and Handy, 1998; $^b$ taken from Adamo, Scuseria and Barone, 1999; $^c$ with the 6-311++G(d,p) basis set; $^d$ taken from Serrano-Andrés, et al., 1993.
I) Solvation problems - yet not really solved

Why solvent calculations?

Unpolar solvents have only smaller influence on reaction energies => Gas-phase calculations can be considered as suitable model

Polar solvents and ionic systems show relatively high barriers and errors for reaction energies in the gas-phase => Considerations of solvent effects are essential!

Application in computational approaches:
In a lot of cases it is enough to carry out a single-point calculation with implicit considerations of solvents after the geometry optimization in gas-phase in order to estimate the influence of the solvent.

At systems with highly polar solvents, a full geometry optimization in the solvent field (or with explicit solvent molecules) is recommended.
I) Solvation problems - explicit methods

**Explicit solvent effects ➔ Supermolecular approach**

Calculations with a number of solvent molecules that are explicitly considered.

**Advantages:**
- Descriptions of van-der-Waals interactions and hydrogen bridges between solvent and molecule.
- Large scope of application for molecular dynamics and in the biochemistry.

**Disadvantages:**
- Large calculation effort ➔ only molecular mechanics can describe a lot of solvent molecules.
- A lot of empiricism needed (guessing of the solvent distribution).
- Only a small number of solvent molecules can be treated with a full quantum chemical approach.

**Possible simplifications**
- QM/MM-approach (solvent is treated via force field, the rest via quantum chemistry).
- Mixed approach between implicit (siehe dort) and explicit models.
I) Solvation problems - implicit methods

Implicit solvent effects ➔ Solvent continuum

The influence of the solvent is simulated via a continuum. The charges of the solvent is placed on small tiles (tesserae) of the surface of the continuum.

Advantages:
- Lower calculation effort, because the solvent is laid around the molecule as continuous field ➔ The solvent is defined via the corresponding dielectric constant $\varepsilon$ and other properties like solvent radius, or solvent density)
- Diverse possibilities for generating the field, depending on the problem

Disadvantages:
- No simulation of interactions between the molecule and the solvent
- Only the electronic energy gets corrected by implicit methods ➔ Changes for enthalpy, entropy, or free energy are only rough estimations

Combined approach implicit/explicit:
For H-bridges and similar systems both approaches can be combined. Here a number of solvents are considered explicitly (including interactions) and the rest is simulated by the continuous field around that conglomerate.
I) Solvation problems - implicit models

Onsager (or Dipole) model ➔ Spherical solvent “pocket”
Central matter: Influence from the dipole moment of the solvated molecule on the solvent’s dipole moment, estimation of the solvation energy via the induced field

PCM (polarizable continuum model) ➔ solvent pocket is now dependent from the molecular structure and the atomic radius. In contrast to Onsager, a reaction field not a dipolar momentum is simulated numerically from which the resulting solvation energies are calculated.

IPCM, SCIPCM (isodensity polarizable continuum model, or self consistent IPCM) ➔ similar to PCM, the solvent pockets are developed via a separate SCF cycle to obtain the minimum pocket shape (for IPCM), or incorporated in the standard self-consistent field technique (for SCIPCM)
I) Solvation problems - Onsager

Quantum chemical procedure for Onsager:
1) Gas-phase geometry optimization with a common level of theory
2) Volume calculation of the solvated molecule
3) Onsager calculation as single-point or optimization

Downfalls: Molecules without dipole moment cannot be treated via the Onsager model (to be correct: the energy values from the gas-phase is not different from the solvent calculation).
Transition state searches not always possible.

Example: Conversion from trans to gauche conformation for 1,2-dichloro-ethane

<table>
<thead>
<tr>
<th>medium</th>
<th>dielectric constant</th>
<th>E(gauche)-E(trans) [kJ/mol]</th>
</tr>
</thead>
<tbody>
<tr>
<td>vapor</td>
<td>1.00</td>
<td>+7.10</td>
</tr>
<tr>
<td>cyclohexane</td>
<td>2.023</td>
<td>+4.77</td>
</tr>
<tr>
<td>diethylether</td>
<td>4.335</td>
<td>+2.93</td>
</tr>
<tr>
<td>acetone</td>
<td>20.7</td>
<td>+1.25</td>
</tr>
<tr>
<td>acetonitrile</td>
<td>36.64</td>
<td>+0.98</td>
</tr>
</tbody>
</table>
I) Solvation problems - PCM model

PCM model ➔ The mostly used method
Developed by Tomasi and coworkers in Italy

PCM principle:
Separation approach for the solvation energies

\[ G_{\text{sol}} = G_{\text{es}} + G_{\text{dr}} + G_{\text{cav}} \]

Distributions:
Electrostatic part (es), dispersive-repulsive fraction (dr) from the free energy, and finally the cavitation energy (cav/ binding in the solvent pocket/hole).

Calculation via van der Waals surfaces and the corresponding atomic radius
I) Solvation problems - PCM model (II)

Example: $S_N^2$ reaction - gas-phase vs. Water (PCM)

![Chemical structure diagram]

<table>
<thead>
<tr>
<th></th>
<th>Gas-phase</th>
<th>PCM (water)</th>
<th>Solvent influence</th>
</tr>
</thead>
<tbody>
<tr>
<td>F^-</td>
<td>-99.8597</td>
<td>-100.0045</td>
<td>-0.1448</td>
</tr>
<tr>
<td>H3C-F</td>
<td>-139.7511</td>
<td>-139.7552</td>
<td>-0.004</td>
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<td>F^---CH3F</td>
<td>-239.6326</td>
<td>-239.7558</td>
<td>-0.1232</td>
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<tr>
<td>TS</td>
<td>-239.6176</td>
<td>-239.7254</td>
<td>-0.1078</td>
</tr>
</tbody>
</table>

B3LYP/6-31+G* (absolute energies in hartree)
1 hartree = 627.50956 kcal/mol

$\Delta G(solv) = \Delta E(gp) - \Delta E(\text{water})$
I) Solvation problems - PCM model (II)

Example: $S_N^2$ reaction - gas-phase vs. Water (PCM)

B3LYP/6-31+G* (relative energies in kcal/mol)
I) Solvation problems - yet not really solved

Comment on the title “yet not really solved”:

It is still to consider by the computational chemist, what restrictions I can take on:

- Implicit models may give a good result on systems with non-coordinating solvents with an average computational effort (suitable for DFT, post-HF and HF methods), but cannot take care about coordinations or H-bonds

- Explicit models describe solvent-solute interaction more accurate
- But: Explicit models may have huge computational efforts, when QM is used, but may loose computational accuracy when they can “only” be treated by MM or QM/MM methods

==> A combination of both approaches would make sense, but there is still a lot of work to be done.
End of the series!

Thank you very much for your kindest attention!