

Conference Report

47th Symposium on Theoretical Chemistry 2011 (STC 2011)

Designing Molecular Functionality: Challenges for Theoretical Approaches

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Introduction

The 47th Symposium for Theoretical Chemistry (STC 2011) took place at Campus Sursee near Lake Sempach in Switzerland in August 2011. The modern conference center offered comfortable accommodation for the 211 participants. The conference was devoted to theoretical and computational methods for the design of molecules and materials with specific properties and functionality at a molecular level. It brought together experts with a background in quantum chemistry and molecular dynamics. Relevant areas of method development and applications were discussed in 39 lectures distributed over 13 sessions.

Topics covered molecular properties, catalysis, molecular electronics and materials design. The Hellmann Award 2011, whose winner is traditionally announced at the STC, was given to Daniel Sebastiani. He was honored for his contribution to the theoretical characterization of structure and dynamics in disordered supramolecular systems. In addition to the scientific program there was an excursion to mount Pilatus on the third conference day from where one had a marvelous view over the Alps and Lucerne. Also the conference dinner on a boat in Lucerne Harbor was a good occasion for stimulating discussions. The conference was sponsored by IBM, the Swiss National Science Foundation, the Swiss Chemical Society, Novartis, Syngenta, Merck Serono, Roche, BASF and the Swiss Academy of Sciences. Support came also from Campus Sursee, Wiley-VCH and Eichhof. In the following sections a detailed overview on all sessions and talks will be given.

The meeting opened with an experimental keynote lecture by **François Diederich** (ETH Zurich). He reported on novel optoelectronic organic materials derived from acetylene chemistry. Diverse compounds which were recently synthesized in his laboratory were presented. Starting with all-carbon macrocycles which show strong circular dichroism (CD) absorption spectra and a pronounced Cotton effect, he continued with allenacetylenic oligomers which exhibit an ‘amplification of chirality’ in electronic CD spectra which he explained with a helical superstructure. Finally he introduced electronic ‘super acceptors’, obtained by successive pericyclic reactions of donor-substituted alkynes and electron-accepting olefins. Reproduction of properties of these novel compounds is a challenge for theory and the inspiring talk ended with a lively discussion. The first lecture on theory was held by **David N. Beratan** (Duke University, Durham, USA). Addressing the general topic of theoretical guidance for synthesis, he emphasized that this topic is closely related to the exploration of chemical space. Beratan outlined several methods to discover new structures with desired properties. Also the sampling of chemical space with evolutionary algorithms and other methods was described.

The second session was on methodological developments in density functional theory (DFT). **Alán Aspuru-Guzik** (Harvard University, Cambridge, USA) addressed the problem of open quantum systems which interact with their environment. He introduced a framework which was recently developed in his group to calculate such systems with linear response time dependent DFT (TDDFT). He also discussed how TDDFT is related to quantum computing. The next talk was on subsystem approaches to describe large molecules with DFT and was given by **Lucas Visscher** (VU University Amsterdam, NL). Here large molecules (e.g. biomolecules) are partitioned into smaller subsystems which are calculated individually and coupled afterwards. He focussed in particular on frozen-density embedding as coupling scheme and how it performs. Moreover, he discussed a partitioning scheme for biomolecules. The last presentation with a related topic was delivered by **Christoph R. Jacob** (Karlsruhe Institute of Technology, D). He presented a numerical approach to construct a local potential which yields a given target density as its ground state density. Jacob claimed that his approach, which is based on the optimized potential method, is unambiguous and systematically approaches the exact numerical solution.

Session three was devoted to biomolecular simulations. **Wilfred van Gunsteren** (ETH Zurich) reported on methodological advances in the computation of relative free energies. He stressed the importance of calculating the free energy difference for biomolecular simulations and discussed thermodynamic integration (TI) as a benchmark and his recently developed enveloping distribution sampling (EDS) method as an improved alternative. Since EDS is faster than TI and the accuracy is comparable, he noted that it can become a standard method for the computation of free energies. **Brian Kuhlman** (University of North Carolina at Chapel Hill, USA) lectured on the computational design of proteins. Therein the identification of low energy conformations and sequences is the main challenge. He reported on his approach of iterating between sequence design and structure refinement using the Rosetta program. With several examples he showed that the design and refinement of hydrophobic interactions is often successful while the design of novel hydrogen bond networks is still challenging and often fails. **Milan Ončák** (Institute of Chemical Technology, Prague,



The scene at a busy Wednesday poster session.

CZ) lectured on how UV absorption spectra can be calculated using path integral molecular dynamics. After explaining how the spectra are modeled with the reflection principle approximation and path integral molecular dynamic sampling of the ground state, he demonstrated the capabilities of the method at the example of two case studies.

The following fourth session continued the topic of biomolecular simulations starting with a lecture by **Michele Parrinello** (ETH Zurich and USI Lugano) about sampling of complex systems using the metadynamics approach. Similar to the EDS by van Gunsteren it is also employed to enhance sampling in large systems. To represent the desired motion collective variables are chosen and in combination with a recently developed reweighting scheme canonical ensemble averages can be recovered. **Philippe H. Hünenberger** (ETH Zurich) focussed in his talk on how ions are represented in classical simulations. The representation of the electrostatic interactions between charged species and their solvation properties is a true challenge. He pointed out that the Born model is inaccurate and molecular dynamics simulations fail because of the small system size. He discussed P-sum and M-sum methods and concluded that the M-sum method is the method of choice. **O. Anatole von Lilienfeld** (Argonne National Laboratory, Illinois, USA) closed the session with a lecture in which he explained the connection between electronic structure theory and rational compound design. He discussed DFT-based property derivatives in chemical compound space, which are necessary to describe properties that can only be calculated from first principles. He also described the use of alchemical potentials to calculate the response of the system to changes in atom type. In the end he showed how machine learning can be used to rapidly predict molecular potential energies.

The fifth session was devoted to methodological developments in DFT and TDDFT for excited states. **Paul W. Ayers** (McMaster University, Hamilton, CA) presented a generalized and extended version of the weighted density approximation, which solves problems in DFT through a careful design of the exchange-correlation hole. In his approach it is constructed from the uniform electron gas where also correlation is introduced. Ayers showed that it works well for the kinetic energy, exchange energy and exchange-correlation energy. It allows to deal with fractionally occupied sites and is variationally stable. **Andreas Dreuw** (Ruprecht-Karls University, Heidelberg, D) drew attention to electronically excited states of large molecules. He discussed linear response TDDFT and its problems with charge transfer states. To overcome the problems he introduced a long-range exact exchange corrected potential and an orbital overlap dependent empirical energy shift. He also reported on the algebraic diagrammatic construction scheme of second order which is a wavefunction-based method that handles double excitations and charge transfer correctly. **Mathias Nest** (Technical University Munich, D) lectured on the combination of TDDFT with quantum control theory. He compared TDDFT and time-dependent configuration interaction (CI) approaches to achieve various control tasks like switching the dipole moment of a molecule by state-to-state transitions and others. Interestingly, the TDDFT results turned out to be quite independent of the functional chosen. **Tobias Schwabe** (Aarhus University, DK) reported on how the environment affects electronic excitation properties in large systems. He presented a hybrid quantum mechanics/molecular mechanics (QM/MM) approach, where he introduced polarizable embedding as an accurate method to describe the interface between the two regions. The performance was demonstrated at the example of acrolein in water.

The study of chemical problems and bonding situations was the topic of the sixth session. **Paul Geerlings** (Free University of Brussels, B) started with a lecture on conceptual density functional theory. He discussed the role of the energy functional derivatives

which can be identified as classical chemical properties like chemical hardness. Besides these mixed second order partial derivatives, he also mentioned higher derivatives and their application in the interpretation of the Woodward-Hoffmann rules. **Gernot Frenking** (Philipps-University Marburg, D) reported on unusual bonds of main-group elements. He discussed enhanced donor-acceptor interactions, where unusual short bonds between noble gas atoms and carbon can be observed. Also carbones, as an example for divalent compounds of group-14 elements with donor properties and their homologues, were discussed. **Stefan Knecht** (University of Southern Denmark, Odense, DK) focussed on the bond in the di-uranium molecule U_2 , in which the bond order was earlier calculated to be five. In his fully relativistic four-component treatment he revealed a bond order of four. He emphasized the importance of the variational treatment of spin-orbit coupling and that also a large active space is needed to obtain the correct picture.

In the seventh session **Sason Shaik** (The Hebrew University of Jerusalem, IL) started with a lecture on valence bond (VB) theory applied to problems in bio-inorganic reactivity. At the example of the oxy complexes of myoglobin and hemoglobin he illustrated how VB theory resolves the dispute about the bonding situation in these complexes by transforming the CASSCF wave function to a VB wave function. **Franziska Schoenebeck** (ETH Zurich) continued with a lecture on how catalysis in organic chemistry can be seen from a computational perspective. Employing computational chemistry tools she could gain insight into reaction mechanisms of palladium-catalyzed cross-coupling reactions. She illustrated how computational results and experimental studies can be combined to develop improved applications in catalysis. **Hélène Bolvin** (University Paul Sabatier, Toulouse, F) reported on magnetic properties of sandwich complexes of lanthanides and actinides. At the examples of a neptunium and a terbium sandwich complex she showed how the physical mechanisms that determine the crystal field parameters can be understood by performing calculations and changing both the nature of the central ion and of the ligands.

Session eight started with the announcement of the winner of the Hellmann Award 2011. After the laudatory speech by Jurgen Gauß (chairman of the AGTC) **Daniel Sebastiani** (Free University Berlin, D) presented his lecture on 'Theoretische Chemie ungeordneter Systeme: Die Herausforderungen der strukturellen Komplexität', which was delivered in German. In his talk he discussed the theory and applications of computational approaches to disordered systems. **Trond Saue** (University Paul Sabatier, Toulouse, F) reported on the calculation of current densities. He discussed the implementation of the calculation of the magnetically induced ring current density, which is closely related to the aromaticity of molecular systems, in a 4-component relativistic framework. **Dage Sundholm** (University of Helsinki, FI) continued with a talk on how the calculation of magnetically induced ring current density can be used for the design of molecular functionality. He discussed applications like Huckel and Mobius aromatic compounds. He closed with a perspective on molecular conductivity and spintronics as applications.

Jochen Autschbach (State University of New York at Buffalo, USA) started the ninth session with his talk on the calculation and analysis of electric and magnetic response properties in DFT which he illustrated at the example of androstadienone and a cobalt complex. Among the response properties discussed were magnetic resonance parameters, optical activity, magnetizability, dynamic polarizability and some higher order properties. The analysis of such properties in terms of local or orbital contributions can be useful for the design of new molecules. **Kenneth Ruud** (University of Troms, NO) continued with the topic of molecular properties. In his lecture he focussed on the relativistic calculation of molecular properties. He discussed a quasi-energy derivative



The Hellmann Award winner 2011, Daniel Sebastiani (right) and chairman Jürgen Gauß (left).

formalism for self-consistent field approaches. As applications he mentioned the calculation of NMR and EPR parameters, nonlinear birefringence and the relativistic calculation of Raman optical activity. **Christoph van Wüllen** (Technical University of Kaiserslautern, D) closed the session with his talk on the calculation of zero field splittings. He showed how discrepancies existing in the recent literature concerning the calculation of one of the Spin-Hamiltonian parameters can be resolved.

With a talk about coupled-cluster theory **Hans-Joachim Werner** (University of Stuttgart, D) opened the tenth session. He presented recent advances in explicitly correlated local coupled-cluster methods. To span the virtual space he presented two methods: the orbital specific virtuals or the projected atomic orbitals. He discussed the impact of these local approximations in detail. To reach the intrinsic accuracy of the method, the classes of strong and close pairs must be larger than it was previously assumed. **Antonio Rizzo** (CNR - Institute for chemical and physical processes, Pisa, I) continued with a lecture on nonlinear spectroscopies and chirality. Focussing on two photon CD spectroscopy he explained how the spectra can be calculated based on modern analytical response theory. In the end, he discussed excited electronic CD and pump-probe chiral spectroscopies. The session ended with a lecture given by **T. Daniel Crawford** (Virginia Tech, USA) on chiral spectroscopy. He focussed on the calculation of the necessary property tensors for optical activity employing coupled-cluster theory. At some examples he showed the effect of vibrations, solvent and liquid phase on the calculated spectra. His talk comprised the calculation of optical rotation, electronic CD and vibrational Raman optical activity.

In the eleventh session **Haibin Su** (Nanyang Technological University, SG) started with a lecture on the versatile character of carbon. He introduced the audience to carbon nanotubes and fullerenes and showed how the reaction dynamics of C_{60} dimerization and the more challenging complex tubular fullerene formation process can be described. For this he applied DFT and the recently developed Reactive Force Field (ReaxFF). In the end, he presented a study of electron transport in nanotubes. **Gemma C. Solomon** (University of Copenhagen, DK) lectured on local currents in molecular electronic transport. She presented her research on electron transport through single molecules bound between two metallic electrodes. With the help of a Green's function description for local currents she discussed σ - and π -transport. The investigation of π -stacking systems yielded an unexpected result. Here, reduced orbital overlap leads to an increasing transmission. **Carmen Herrmann** (University of Hamburg, D) presented her research on spin transport through single molecules to understand and design spintronic devices.

Also Herrmann used DFT and the Green's function technique to describe transport. She illustrated her methodology with the example of *ortho*- or *para*-substituted benzenes as organic spin filters. As another example, she was able to determine how the electron can tunnel through a heme junction.

Session twelve was devoted to new methodological developments in DFT and wave function methods. It was opened by **Stefan Grimme** (University of Münster, D) who reported on the importance of London dispersion interactions. He presented his semi-empirical DFT-D approach to standard DFT, which corrects the medium- to long-range behavior of most modern density functionals. The improvement on thermochemical data was demonstrated with a test molecule set. As examples he presented a binuclear rhodium complex and discussed the famous hexaphenylethane riddle and finally explained the activation of small molecules by so-called frustrated Lewis pairs. **Roland Lindh** (University of Uppsala, SE) addressed analytic Cholesky Decomposition gradients for HF, DFT, MP2 and CASSCF methods. He showed that the separate treatment of the effective two-particle density matrices in connection with the Coulomb, exchange and active space terms of the 2-center and 3-center two-electron integral derivatives is the key to an efficient implementation. He concluded that this technique is fast, robust and automatically applicable for many methods. The session ended with **Martin Korth's** (MPI for Coal Research, Mülheim an der Ruhr, D) talk on hydrogen-bonding corrections for semiempirical QM (SQM) methods and force fields. His scheme corrects for the poor performance of non-covalent interactions in SQM methods. He emphasized that SQM methods will be improved for many applications like docking and scoring and can reach the accuracy of DFT-D in certain cases.

The thirteenth and last session of the conference covered theoretical inorganic biochemistry. **Walter Thiel** (MPI for Coal Research, Mülheim an der Ruhr, D) lectured on theoretical studies of enzymes, in particular with QM/MM methodology. After reviewing the theory of the QM/MM approach and how it is applied to studies on biomolecules, he presented a three-layer (QM/MM / continuum solvent) approach as a possible improvement. Then he discussed selected QM/MM studies on enzymes and finally reported on a study where it was possible to identify key mutations in an enzyme which was mutated by directed evolution. **Claudio Greco** (Humboldt University of Berlin, D) presented theoretical investigations on [FeFe] hydrogenases, a class of enzymes which catalyzes the formation of molecular hydrogen. He showed a study where IR spectra of different active site models were calculated with DFT and compared to experimental results to obtain structural information on key intermediates of the catalytic cycle. Furthermore, a QM/MM calculation was presented which included the active site and three additional Fe_4S_4 cubane clusters which provided information on oxidation states and the cubanes' interplay. **Matthias Stein's** (MPI for Dynamics of Complex Technical Systems, Magdeburg, D) talk was related to Claudio Greco's presentation. First, he reported on the calculation of EPR spectra of [NiFe] hydrogenases where comparison with experiment could give hints for the assignment of ligands. Then, he showed DFT calculations on structural and on functional active site model complexes.

A more detailed presentation of the contents of the lectures can be found under <http://www.stc2011.ethz.ch>.

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