MS40-05 **Quantumcrysca: A new approach for the prediction of molecular crystal structures by a crystallographic QM-MM-shell-model** Philipp M. Mörschel[a], Martin U. Schmidt[a] [a]*Institute of Inorganic and Analytical Chemistry, Goethe-University, Max-von-Laue-Straße 7, D-60438 Frankfurt am Main, Germany*
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The *ab initio* treatment of molecular crystals in due consideration of space group symmetry is still an underdeveloped field.

`Quantumcrysca` is an innovative attempt to calculate the energy in periodical systems by quantum-mechanical means including full treatment of space group symmetry using a QM-MM-approach. Dividing the crystal in disjunct spherical regions gives rise to a shell-model. All interactions between atoms in the inner sphere are treated on a quantum mechanical level, whereas the interactions in the outer sphere and between the inner and the outer sphere are calculated by classical force-fields.

A reliable quantum-mechanical calculation of weak long-range interactions (London dispersion, van der Waals-interaction) in periodical systems turns out to be especially challenging. Correlation methods include this kind of interaction but are computationally demanding. Pure density-functional theory neglects long-range interactions. A good compromise can be found in dispersion-corrected density-functional theory (DFT-D).[1,2]

First efforts have been made by Neumann et. al. using plane wave DFT-D in periodical systems.[3] In `Quantumcrysca` the quantum-mechanical sphere is efficiently described using localised orbitals (Gaussian type orbital, GTO), leading to a massive saving of computing time and a more intuitive view of the electronic state using molecular orbitals.

In `Quantumcrysca` various local optimization algorithms using analytical derivatives are implemented, including steepest-descent, conjugate-gradient and quasi-Newton- methods. Faster convergence is achieved by additional linesearch in each optimization step.

The combination of these local optimization techniques with a structure-generation algorithm can be used to perform a complete crystal structure prediction in the absence of experimental data.

`Quantumcrysca` is designed for the validation of crystal structures as well as for the performance of a full crystal structure prediction. First results will be presented.

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[2] S. Grimme, J. Anthony, S. Ehrlich, H. Krieg, *J. Chem. Phys.* **2010**, *132*, 154104.
[3] M.A. Neumann, *J. Phys. Chem. B* **2008**, *112*, 9810.

Keywords: molecular crystals, lattice energy calculations, DFT-D, QM-MM-methods

MS41-01 **Implications of conformational heterogeneity in protein crystals: from interatomic distance measurements to entropy estimation.** Antonija Kuzmanic,[a] Anton A. Polyansky, [a] Ruben Zubac, [a] Mario Hlevnjak, [a] Daniela Kruschel,[b] Wilfred F. van Gunsteren,[c] Navraj S. Pannu,[d] Bojan Zagrovic,[a] [a]*Max F. Perutz Laboratories, University of Vienna, Austria,* [b]*Mediterranean Institute for Life Sciences, Croatia,* [c]*ETH Hönggerberg, Switzerland,* [d]*Leiden University, The Netherlands*
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Biomacromolecular models, which are obtained in traditional X-ray crystallography, are static, time and ensemble averages over many molecules in the crystal and, as such, provide little information about protein dynamics. However, I will show by using molecular dynamics simulations that: 1. dynamics directly affects some of the basic structural parameters measured by X-ray crystallography, and 2. relevant information about dynamics can be derived from crystal structures. In particular, interatomic distances, calculated between average positions in the model and frequently used in structural and mechanistic analyses, can be substantially different from the more appropriate time-average and ensemble-average interatomic distances. Using B-factors, one can deduce corrections to obtain correct average distances as a function of the type of atomic motion. I will show that corrections greater than 0.5 Å should be applied to some X-ray-derived interatomic distances shorter than 5 Å and discuss the implications of this for both structure refinement and structure-based analysis of biological mechanisms. Concerning the dynamical information which can be deduced from X-ray structures, one of the most relevant thermodynamic quantities related to dynamics is conformational entropy. I will demonstrate that relative conformational entropy as calculated by quasi-harmonic analysis of molecular dynamics trajectories represents a remarkably constant fraction of a quasi-harmonic entropy change obtained if one ignores the contribution of covariance terms and uses mass-weighted atom-positional variances only. In other words, the relative contribution of linear correlations to conformational entropy change for different proteins and in different biomolecular processes appears to be largely constant. Based on this, I will show an empirical relationship between relative quasi-harmonic conformational entropy and changes in B-factors induced by different processes, and use it to estimate conformational-entropic contribution to the free energy of binding for a large set of protein complexes based on their X-ray structures.

Keywords: molecular dynamics; refinement; conformational entropy