s9'.m2.o1 Forces, Frustration and Fun - A View on the Dimensions of the Packing Problem. P. Erk. *Colorants Laboratory, BASF AG, D-67056 Ludwigshafen Peter.Erk@basf-ag.de*
Keywords: molecular interactions, *ab-initio* structure prediction, crystal packing.

The properties of many crystalline industrial products (e.g. drugs, agrochemicals, neutraceuticals, explosives, pigments and polymers) are related to the solid state structures of these materials. During the development of these products much effort is devoted to tailor crystal properties, e.g. polymorphism, particle size, and morphology. Hence, the possibility of predicting crystal structures ab initio (i.e. without the input of experimental data) would have a major impact on the discovery and development of new products.

To the date there is no analytical solution for the calculation of all possible low energy closed packed structures a given compound may form. Linear optimization procedures are used to compute low energy packings by force field methods. But these algorithms only have the ability to detect the local energy minimum closest to the initial packing. This dilemma has been addressed as the *packing problem.*

Throughout the last decade various strategies have been developed to extensively search the phase space of a crystalline material for low energy packings [1,2]. In general, most methods follow the same conception: In a first step trial packings are generated by means of e.g. Monte Carlo methods, discrete, random or systematic searches. Subsequently, the trial packings are subject to energy minimization, yielding close packed, low energy structures.

In order to use these computational tools for an unquestionable prediction of crystal structures, the calculations must produce accurate and physically reliable structural models. Furthermore the thermodynamic data derived from these models must allow for a prediction of the stability order of different polymorphs.

The present status of force field based calculation methods does not completely meet these requirements, but there is a notable success rate for reasonably rigid molecules without d-elements. Further factors that facilitate or hinder the success of structure predictions will be discussed

The correctness of any crystal structure calculation may be judged by comparison with powder patterns or knowledge based rules from the vast amount of structural data available from CCDC. As general guidelines for crystal engineering purposes, 3d packing architectures can be deduced from the analysis of the low energy close packed structures.

A significant application for structure calculations is the generation of structural input for the refinement of low resolution (non indexable) powder patterns, e.g. of labile metastable forms for which the preparation of highly crystalline powders seems practically impossible. Examples of such low crystalline materials are widely known from the patent literature of pharmaceuticals and pigments.

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s9'.m2.o2 Achievements and challenges in molecular crystal structure prediction. F.J.J. Leusen and M.A. Neumann, *Molecular Simulations Ltd., 230/250 The Quorum, Barnwell Road, Cambridge CB5 8RE, U.K.*
Keywords: polymorph prediction, molecular modeling.

Many industrially relevant compounds are crystallized for purification, separation or formulation. The specific packing of the molecules in the solid state influences a range of physico-chemical properties, and different polymorphs of a compound may exhibit significant differences in these properties. Rational control of polymorphism and thus solid state properties requires detailed knowledge of the crystal structure of each polymorph at the atomic level.

In many cases the material cannot be crystallized in particles of sufficient size and purity for single crystal X-ray diffraction techniques. In those cases it is usually possible to obtain a crystalline powder, for which an X-ray powder diffraction pattern can be recorded.

If the powder diffraction data is of high quality, the underlying crystal structure can be found by optimizing the agreement between the experimental pattern and patterns simulated for a vast number of structures generated in a search procedure. This approach, which can be highly automated, has been successfully applied to relatively complex systems, such as ionic and highly flexible compounds[1].

In cases where high-quality powder diffraction data is not available, the search can be guided by lattice energy calculations instead of powder pattern comparison[2, 3]. The assumptions are that observed crystal structures have low lattice energies, and that these energies can be reliably approximated by force field calculations. A search method constructs all possible crystal structures with low lattice energies. If low-quality powder data is available, it can be used to select the real structure(s) from the list of suggested candidates. Otherwise, only the calculated lattice energy and density are used as selection criteria. Due to inaccuracies in the force field approach and due to the large number of degrees of freedom involved in these simulations, crystal structure prediction with low-quality or no experimental data is currently only feasible for non-ionic and fairly rigid compounds.

In this contribution, we will review recent progress made in the area of crystal structure prediction, and discuss some of the many challenges that remain to be addressed in future research.

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