**pl2** **Ab Initio Prediction of Crystal Structures.**
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Modeling of crystal structures has traditionally been an important source for force field parameters. It is important that a force field should reproduce observed crystal geometries well. The next question is whether a more ambitious goal can be reached: the model should also be able to predict the observed crystal structure(s) without any experimental information. This problem has attracted some attention during the last decade; a few review papers are available[1, 2].

The problem can be separated in two stages. The first one is to make a preliminary list of candidate structures. This is a search problem in many dimensions, for which various approaches have been developed that will be briefly discussed. Problems to be solved include the choice of space group and the number of independent molecules in the unit cell. For flexible molecules additional difficulties arise.

Most search methods use the energy as a criterion. It turns out, perhaps surprisingly, that the resulting lists may contain hundreds of possible structures within an energy window of about 30 kJ/mol [3]. Of course, it is essential that the experimentally observable polymorph(s) are present. This is usually the case for crystals with one molecule in the asymmetric unit of one of the common space groups. If the molecule has many degrees of conformational freedom, success is less assured.

In the second phase of the structure prediction the most favorable polymorph (at a given temperature and pressure) must be selected. In principle this should be done by looking for the structure with the lowest free energy. It is not obvious that this is a sufficient criterion: in some cases kinetic effects may be the deciding factor. Furthermore, it is common practice to neglect the difference between energy and free energy. So, in fact, the calculated structures refer to an unspecified temperature and no phase transitions between polymorphs can be predicted.

Some results that have been obtained with this approach will be reviewed. This includes a blind test of crystal structure prediction that was organized by the Cambridge Crystallographic Data Centre in 1999. The conclusion was that the best that can be expected at present is a list of structures with comparable low energy, which are all possible candidates to be experimentally observable polymorphs. On the other hand, this observation provides the possibility to calculate an approximate lattice energy without knowing the actual crystal structure.

Accurate energy calculations appear to be a first condition for succesful crystal structure prediction - in fact, this technique is a very severe test for the quality of a force field. Most work relies on (semi)-empirical force fields, but quite successful potentials have been developed on the basis of quantumchemical parameterization [4]. Thus truly ab-initio crystal structure prediction is becoming feasable, even for flexible molecules. One advantage is that the temperature is clearly defined (0 K) which opens the road to the incorporation of thermal effects.

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