corrected rather easily by changing the residue name, deleting surplus atoms or editing the LINK or CONECT records. Other problems, however, require more sophisticated methods to fix them. To fix e.g. stereochemistry problems, atoms have to be relocated. In some instances, e.g. when wrong stereochemistry is involved in glycosidic linkages, entire residues might have to be rearranged, which involves refinement of the 3d structure. Here, we present an approach to combine a tool for carbohydrate validation (pdb-care [3], www.glycosciences.de/tools/pdb-care/) with the modeling software WHAT IF [4] (swift.cmbi.ru.nl/whatif/) and the refinement tool PDB-redo [5] (www.cmbi.ru.nl/pdb_redo/) to enable a (semi-)automatic correction of erroneous carbohydrate structures in PDB entries.

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Keywords: fefinement, validation, glycoproteins

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A molecular dynamics approach to equilibrium structures in crystals

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The equilibrium structure of a crystal represents the system in a theoretical vibrationless state at the absolute minimum of its potential-energy surface. Such structures can be compared directly between different phases and polymorphs and with theoretical calculations. Structures determined using X-ray and neutron-diffraction experiments are time-averaged over all of the molecular vibrations occurring in the crystal. If these motions are anharmonic or curvilinear then the time-averaged and equilibrium structures will differ. There remains no general and simple method for removing the structural inconsistencies that result. We have recently developed a new method using molecular dynamics (MD) simulations that allows experimental positions to be corrected to equilibrium positions. The corrections are determined by taking the differences between theoretical equilibrium structures and time-averaged structures obtained from MD trajectories. The application of the method to the crystal structure of nitromethane using an empirical force field will be detailed. Comparisons will be made with literature X-ray and neutron data sets. Thermal motion is incorporated into the crystal-structure refinement process using the Debye-Waller factor, which is the Fourier transform of an atom's vibrational probability density function. This probability function is typically assumed to be a trivariate Gaussian and yields the ubiquitous probability ellipsoids. The MD simulations allow us to determine the true function numerically. In the case of nitromethane this leads to highly curved probability functions for the H atoms.

Keywords: thermal motion, molecular dynamics simulations, Debye-Waller factor

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Restrained anisotropic refinement with SHELXL

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The successful refinement of macromolecular crystal structures usually requires the use of restraints based on our knowledge of similar structures. Whereas geometrical restraints are relatively well understood and quantified, there is still much room for improvement of the restraints applied to the atomic displacement parameters (isotropic and anisotropic temperature factors). We are currently investigating a variety of potential restraints and other features with a view to making the SHELXL program for crystal structure refinement more suitable for the refinement of macromolecular structures at modest resolution. The step from isotropic to anisotropic refinement increases the number of parameters refined by more than a factor of two and often results in over-fitting of the data. A good approach to this problem is the use of TLS constraints (Schomaker & Trueblood, 1968; Winn, Isupov & Murshudov, 2001) because, as usually implemented, the number of extra parameters is limited to 20 per 'rigid' domain. However, it is not always easy to subdivide a macromolecular crystal structure into suitable domains and an atom may not be in more than one domain at the same time. A flexible alternative is to extend the rigid bond restraints by Rollett (1970) and known as the DELU restraint in SHELX, to much greater distances (say 6-8 Å) than normally employed. Didisheim and Schwarzenbach (1987) showed that in the limit of very tight restraints this asimptotes to the TLS model. The main technical problem in the implementation of such 'TLS restraints' for large structures is finding the appropriate atom pairs efficiently, since this needs to be performed each refinement cycle and should take symmetry equivalents into account.

Keywords: restrained refinement, anisotropic atomic displacement parameter, macromolecular structure

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Computational chemistry approach to polymorphism of aspirin

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It is strongly expected that practical techniques on computational analysis of molecular crystal structures can provide knowledge for molecular designs of functional materials or drugs, and for crystallographic studies of solid state phenomena, such as nucleation, growth, polymorphism, and phase transition. To cope with the expectations, we have been developing a computational chemistry system (CONFLEX/KESSHOU) to crystallographic analysis and prediction of conformational and packing polymorphism based on rational evaluations for many energy minima of crystal structures and their dynamical behaviors. In this conference, as an extension of CONFLEX/KESSHOU, we propose our computational investigation for the recent topic on the aspirin crystal polymorphism [1-3]. In order to quantitatively elucidate this polymorphic transition between form I and form II without purported ambiguity, we have calculated energy minimum crystal structures by using CONFLEX/KESSHOU crystal calculations. In comparison with their free energies of two polymorphic forms at room temperature and 100 K, the predominant stability of form I has been computationally ascertained as well