

Investigation of the R_{wp} factor and energy of paracetamol crystal structure

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May 2022

Abstract

The combination of energy evaluation of crystal structure and powder diffraction data may successfully be used in structure determination. Using only powder diffraction factors (e.g. R_{wp} factor) cannot guarantee finding reasonable crystal structure. Some structures with acceptable R_{wp} factor are physically unrealistic because their atoms are too close to each other. This problem can be solved by setting restraints to atomic distances or by calculating the energy of the system. We use the energy evaluation because it can tell us not only which structure is unrealistic but also which structure is more preferred in nature. The energy of the crystal structure can be calculated in two ways – by Molecular Mechanics (MM) or by Density Functional Theory (DFT). MM is based on substitution to the preset mathematical relation so it is fast to compute (compared with DFT). The advantage of DFT is its accuracy. MM was used in our work. We expect that MM could be used to speed up the convergence of structure determination and DFT could be used for the final validation of the structures. The crystal structure can be predicted only with energy evaluation.

Another possibility of speeding the structure determination up is to use optimizing algorithms. For example global optimizing algorithm simulated annealing is used in program Dash [1] and parallel tempering and also simulated annealing are used in program FOX [2]. The diffraction pattern data can be combined with the energy value of the structure to new cost function which we minimize. The usage of the combination of powder diffraction data and energy evaluation can accelerate the structure determination, help to avoid wrong solutions of the crystal structure, or tell us more information about the determined structure (e.g. if it could be a metastable structure of the material). We made the examination of

energy and R_{wp} functions on the structure parameter was made. For simplicity, we used only three structure parameters and made cuts through the hypersurface of the functions.

We made the examination of energy and R_{wp} factor of the crystal structure of paracetamol with two or three deviated parameters. To gain pictures of the hypersurface of the R_{wp} and the energy function of paracetamol it must be done cuts through the hypersurface. Our hypersurface has six parameters: Δx , Δy , Δz , $\Delta\alpha$, $\Delta\beta$ and $\Delta\gamma$. These parameters correspond to motion parameters of the molecule of paracetamol – Δx means deviation of the molecule in the direction of lattice vector \vec{a} , similarly Δy is the deviation of the molecule in direction of \vec{b} and Δz is the deviation of the molecule in direction of \vec{c} ; $\Delta\alpha$ means rotational deviation of the molecule about the molecule’s own Axis 1, similarly $\Delta\beta$ is the rotational deviation of the molecule about the molecule’s Axis 2 and $\Delta\gamma$ is the rotational deviation of the molecule about the molecule’s own Axis 3 (in the Figure 1 there are the translational degrees of freedom; in the Figure 2 there are the rotational degrees of freedom). We chose three degrees of freedom i.e. Δx , $\Delta\gamma$, Δy as parameters which we deviated from the crystal structure.

We made three cuts though the R_{wp} function hypersurface. The parameters Δx and $\Delta\gamma$ went through all their possible combinations and parameter Δy was set consecutively to 0.0 Å, 0.5 Å and 2.0 Å.

The diffraction pattern was obtained by simulating the diffraction pattern of paracetamol crystal structure [3] in the program Materials Studio in the module Reflex. The parameters of diffraction were set: the refinement method Rietveld, convergence quality Medium, the range of diffraction pattern from 5 to 45 2θ with step 0.015° 2θ , Bragg-Brentano instrumental geometry, zero-point shift 0.013, Pseudo-Voigt profile function, profile parameters $U = 0.02192$, $V = -0.01152$, $W = 0.00788$, $N_A = 0.1615$, $N_B = -0.00075$. The other diffraction patterns were simulated with the same settings of the module.

The energy was calculated with the program Materials Studio, too. Module Forcite was chosen because it can quickly compute the energy of the structure (it uses Molecular Dynamics). The parameters were set to: compute only the energy of the structure, use forcefield COMPASS [4, 5, 6], quality was set to Ultra-fine, charges were assigned by the forcefield, and summation methods were made atom-based.

We have found some interesting results which the R_{wp} function follows with changes of structure parameters. The first one is that when the molecule rotates there are not many local minima in the R_{wp} function and the second one is that when the molecule is translated there is only one – global minimum in the R_{wp} function. In energy hypersurface, there are significantly more local minima and local maxima. From this view, we can easily recognize the structures with too high energy and discard them instead of optimizing them. The cut through hypersurface of R_{wp} function is plotted in Figure 3a. The cut through hypersurface of the energy function is plotted in Figures 3b. When comparing these two cuts there is a local minimum in R_{wp} function at 180° $\Delta\gamma$ but in the energy function at 180° $\Delta\gamma$ the local minimum is not. So the energy evaluation can help us to avoid searching the structure with this parameter set.

Computational results were obtained by using Dassault Systèmes BIOVIA software programs. BIOVIA Materials Studio was used to perform the calculations and to generate the graphical results. This work was supported by the Grant Agency of the Czech Technical University in Prague, grant No. SGS22/183/OHK4/3T/14.

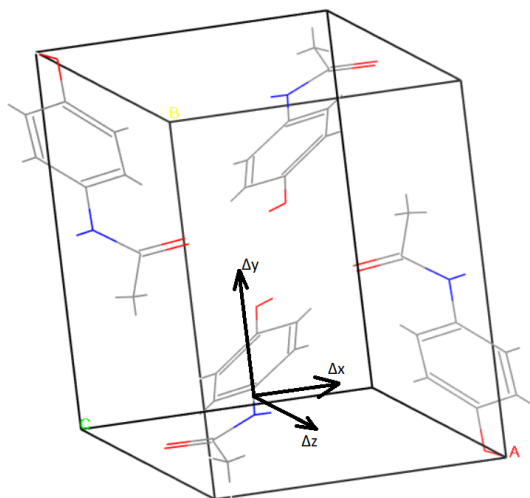


Figure 1: Crystal structure of paracetamol with illustrated translational degrees of freedom.

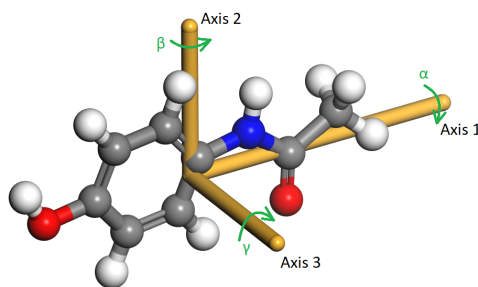


Figure 2: The molecule of paracetamol with illustrated rotational degrees of freedom.

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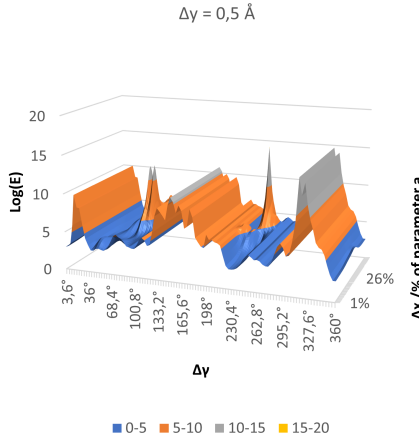
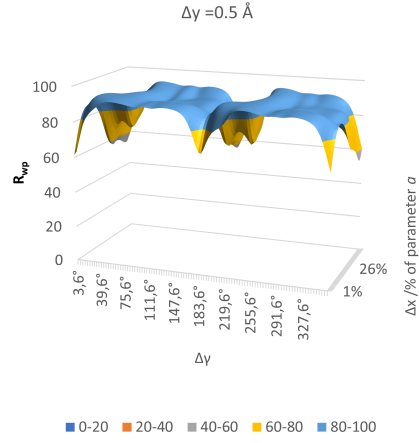


Figure 3: Cut through paracetamol R_{wp} function hypersurface (3a). The hypersurfaces were cut in Δx and $\Delta \gamma$ degrees of freedom and $\Delta y = 0.5 \text{ \AA}$. The local minimum can be observed at $180^\circ \Delta \gamma$ in Figure 3a. In energy cut the local minimum at $180^\circ \Delta \gamma$ is not.

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