proteins and drug molecules in several days. This is not only to save the time and the cost used in drug development, but also for us able to understand the structural implications used for further design. However, it is still currently difficult to formularize efficient software to carry out the docking simulations as a standard procedure leading to definite results with high accuracy. Therefore, we are in attempt to propose a new category of programming, for which the standard effectiveness for docking procedure can be anticipated in the near future. To initiate such computer simulations, many factors have to be taken into consideration. The first is to decide which algorithms should be applied to perform the job. The next concern is the determination of scoring function. As being the best commercially available scoring function with high accuracy and flexibility, X-score is used to satisfy this purpose. Target protein is at first regarded as a rigid body, whereas the drug molecule is allowed to be entirely flexible. According to our results, GA and GP indeed improve the search of docking sites between the target protein and the drug molecules in both accuracy and efficiency. Partially flexible protein regions were then added into the docking system. Three complex systems of tubulin and tubulin inhibitors (taxol, colchicine and vinblastine) were used to demonstrate our software in application.

Keywords: docking,, genetic programming, genetic algorithm

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An investigation into protonation prediction implications for protein crystallography

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Biology rests on chemical reactions, many of which involve hydrogens or protons. The determination of hydrogens, as is well known, is particularly challenging for protein crystallography. These limitations are being steadily improved upon via complementary neutron and X-ray developments [eg see Blakeley et al 2004] including perdeuteration biological expression for the neutron approach. In parallel we have investigated the effectiveness of the protein protonation prediction computational tools H++, pKa and MCCE by comparing their agreement against a database of neutron and ultra-high resolution X-ray protein crystal structures, and that are growing in number. These test results indicate that predictions of the protonation states of Asp, Glu and His can be correct but not confidently so. This work may help fine-tune their predictive capabilities and thus benefit cases which are out of range of neutron or X-ray protein crystallography. One such is that of beta-crustacyanin, whose bathochromic shift colouration properties include, as one theory, two critical His residues in the structure [Cianci et al 2002] proposed to be protonated by Durbeej and Eriksson [2006] thereby causing an electronic polarisation of the carotenoid astaxanthin.

M P Blakeley, M Cianci, J R Helliwell and P J Rizkallah Chem Soc Reviews (2004) 548-557.
M Cianci, P J Rizkallah, A Olczak, J Raftery, N E Chayen, P F Zagalsky and J R Helliwell (2002) PNAS USA 99, 9795-9800.
Durbeej, B. & Eriksson, L. A. (2006). PCCP, 8, 4053－4071.

Keywords: protonation states in proteins prediction, complementarity of X-rays and neutrons, beta-crustacyanin

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Advanced strategy for *ab initio* structure determination of pharmaceutical compounds by powder data

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The pharmaceutical compounds are still difficult targets for ab initio structure determination by X-ray powder experiments. For such molecules to be determined by X-ray powder experiments there would be no argument to admit synchrotron radiation (SR) source is necessity. Even SR source is used, ab initio structure determination of pharmaceutical compounds is challenging theme. It is, therefore, useful to find out what would be better strategy for that purpose. In this study, an advanced strategy which utilizes the variations of Maximum Entropy Method (MEM) will be described. The important points of the strategy are mainly comprised by the following three points. First point is that it is extremely important to collect very high counting statistics data not only low angle region (say, d > 2.0 Å) but also high angle region (typically d > 1.0 Å.). Because information concerning atomic coordinates is included intensity data in high angle region, there is no way to determine the accurate crystal structure of the specimen. The most difficult and important part of ab initio structure determination is refinement process. The main concern must be how to eliminate model bias. For this purpose, it is very powerful to obtain omit MEM charge density distribution, which are successfully employed in the analysis of a protein crystal. At the final stage of the refinement, small adjustments of the atomic coordinate are very often required without deforming molecular shape. This could not be done by simply employing restrain refinements. It is helpful to obtain difference MEM density distribution, which often gives clue how to make the small adjustment of the atomic coordinates. A few examples based on the present strategy will be shown.

Keywords: structure determination from powder diffraction, maximum entropy method, pharmaceutical compounds

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Validation of molecular crystal structures using dispersion-corrected DFT

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The information content of an XRPD pattern is too low to determine all atomic coordinates of a molecular crystal structure independently: on top of the lack of phase information, powder patterns suffer from peak overlap and preferred orientation (PO), introducing uncertainties in the intensity data. This is generally solved by relying on the user to supply the correct chemical contents of the asymmetric unit, including most of the molecular geometry. That, however, is a source of errors and bias in itself. It is therefore justified to ask how we can be certain whether a structure determined from XRPD data is correct. Rietveld refinement and its figures of merit can only provide partial reassurance (see e.g. [1]), especially if a PO correction was necessary or if the data is of limited quality. If the powder pattern can be indexed, the unit cell can usually be determined very reliably from powder data, and a good validation method should therefore be aimed

at the atomic coordinates. In this contribution, we will demonstrate the use of dispersion-corrected DFT to reproduce molecular crystal structures in silico with unparalleled accuracy [2]. When the unit cell can be assumed to be reliable enough to be kept fixed, the computer resources required to perform an energy minimisation of all atomic coordinates are small enough for routine application, namely in the order of a couple of days on a single CPU. Because all atoms are treated independently and without reference to any user-supplied parameters or experimental data, the outcome of the dispersion-corrected DFT optimisation provides us an unbiased and independent validation criterion for the correctness of the crystal structure Several examples will be shown.

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[2] J. Phys. Chem. B 109, 15531.

Keywords: *ab-initio* powder structure determination, Rietveld refinement, density functional theory

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A comparison of co-crystal structure solutions through powder and single crystal techniques

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In powder diffraction, much information is lost by the collapse of the 3D space onto a 1D axis. This loss of information makes determination of the structure much more difficult. There is also some worry that this loss of information will lead to incorrect structure determination. However with single crystal techniques, the difficulty is in the preparation and growth of the single crystal. In some cases even, it is not possible to grow a single crystal. We have independently determined structures from powder and single crystal diffraction data of seven organic co crystals. The powder solutions were determined and refined with no knowledge of the single crystal solutions. We will compare the solutions given by these two techniques. This work was partially supported by Transform Pharma. Powder diffraction was performed at the National Synchrotron Light Source. The National Synchrotron Light Source at Brookhaven National Laboratory in New York, is a national user research facility funded by the U.S. Department of Energy's Office of Basic Energy Science

Keywords: powder structure determination, single-crystal structure determination, cocrystals

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The co-crystallisation and thermal behaviour of oxamic acid, nicotinamide and isonicotinamide

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In this poster, we will present our studies on a small group of molecular materials, while addressing three areas of small molecular crystallography that are of significant academic and industrial interest: i) The systems under consideration contain both strong hydrogen bond acceptor and donor groups, making them potentially useful building units for co-crystal design and the study of supramolecular aggregation. The formation of molecular adducts of oxamic acid with both nicotinamide (vitamin B3) and isonicotinamide will be presented and the relative crystallisation and structural properties of these adducts discussed and compared to other results obtained for these isomeric amides1. ii) In order to facilitate the full structural characterisation of these adducts, structure determination from X-Ray powder diffraction was required. By application of our direct space differential evolution algorithm we were able to solve the structures of these relatively complex structures from conventional laboratory data. Few molecular materials of this type have been determined from XRPD to date, but the ability to solve such structures has clear application to the emerging field of pharmaceutical co-crystals. iii) The thermal behaviour from 10 to 295K of both individual components and molecular adducts will also be presented. Such a study can be used as a valuable source of information in which to study the strength and directionality of intermolecular forces. We aim to invoke the reverse process, in which the directionality and strength of the intermolecular forces can be used to predict the thermal behaviour of a crystalline system.

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Keywords: direct space structure determination, molecular co-crystals, powder diffraction

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The third structure determination by powder diffractometry round robin (SDPDRR-3)

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The maturity of a scientific technique is considered established when the method is performed successfully "on demand". While small molecule single crystal structure solution is often described as routine (most structures solve easily and quickly "on demand"), structure solution from powder diffraction (SDPD) is generally not. In consequence of some literature reporting SDPD as "routine" (e.g., [1]), a first structure solution from powder diffractometry round robin was organized in 1998 [2], and a second in 2002 [3]. Both these round robins indicated that SDPD was still difficult, the ratio (submitted correct result)/(data download) being close to 2%. With the chairman of the IUCr Commission on Powder Diffraction (http://www.iucr-cpd.org/) indicating it is time for a new SDPD round robin [4], the competition was announced on the 1st of February this year with a deadline at the end of April 2008, providing three months to perform two SDPDs. Powder Diffraction datasets for an organic phase, and an inorganic phases were downloadable from a webpage (http://sdpd.univ-lemans.fr/SDPDRR3/) with cell parameters and probable chemical formula provided. At the time of writing this abstract (half round), there were 123 data downloads and 3 successful returns. Routine appears unattained yet in spite of 200 or so SDPDs currently published per year vs ~40,000 total structures published each year solved by non-powder methods.

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