1970s. In recent years significant results have been achieved with their use. However iterative algorithms to date can only retrieve the complex transmission function of a thin sample. Thicker samples, where dynamical diffraction and propagation are important, can not be examined with these techniques. A recent innovation combines the ptychographical iterative engine technique of phase retrieval, with the multislice method. The result is an iterative approach that uses measured intensities of the exit wave to find the transmission functions of the slices that represent the sample structure. This generalisation of the iterative technique allows the retrieval of depth information in the sample. Much thicker structures can be analysed than was previously possible with such approaches. It is potentially possible to use the technique to solve a structure that is periodic or aperiodic in any direction. The technique is experimentally simple, requiring only a series of intensities recorded at different positions of the incident beam plus known information about that beam. The applications of this approach include any experimental situation where intensities can be measured and a thick, periodic or aperiodic sample is analysed. This includes a huge number of possibilities in crystallography and many other fields.

Keywords: inverse problem, computational methods, structure determination

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Rapid and routine determination of hydrogen positions in inorganic and organometallic compounds

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Hydrogen is a fundamentally important element in many key areas of inorganic materials design, including development of technological materials (e.g. hydrogen storage media and proton-conductor fuel cell components), functional framework materials (e.g. zeolites), catalysts, organometallic co-ordination complexes and inorganic hydrates. Due to weak X-ray scattering by light elements, and hydrogen's large incoherent neutron background, determination of hydrogen positions in inorganic materials traditionally necessitates costly sample deuteration or painstaking synthesis of large single crystals for neutron diffraction. This limitation is now being addressed via development of experimental and data refinement methodologies utilising high flux neutron powder diffractometers such as D20 at ILL. We present a selection of results demonstrating application of this new methodology to technologically important inorganic material systems with significant hydrogen content. These include in-situ studies of functional zeolites (e.g. industrial catalysts ZSM-5 and mordenite, having adsorbed hydrogenous molecules) and metal ammoniates such as $Ni(NH_3)_6Cl_2$ (candidate hydrogen storage materials). Further examples include organometallic compounds such as Zeise's salt and complexes requiring exact determination of hydrogen position (e.g. those with potential agostic hydrogens). The full structures of some heavy metal salt hydrates are also presented, confirming that hydrogen positions can be accurately determined alongside metals as heavy as uranium and bismuth. As well as highlighting the applicability and potential impact of these new methods, this work is aimed at establishing these methodologies as a valuable tool for routine study of hydrogenous materials across all inorganic fields.

Keywords: characterization methods, hydrogen, neutron and X-ray diffractometry

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Development of polarizable force field for the prediction of molecular crystal structures

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Prediction of crystal structures for organic molecules has great importance in many industries like pharmaceuticals, pigments, dyes, and so forth, because many of the macroscopic properties of their products are highly dependent on their crystal structures. The accuracies of predictions for lattice constants and molecular geometries in crystal depend on the performance of intermolecular potential which is normally described as the electrostatic and van der Waals terms in empirical force fields. Although electrostatic parameters of partial atomic charges are generally unchanged in a potential energy calculation during geometry optimization and dynamics simulation, the charge distribution of a molecule should vary depending on conformational transformations and induced interactions with other molecules. To estimate the charge distribution according to their changes, the charge equilibration (QEq) approach [1] is proposed and can provide appropriate partial atomic charges for sufficient representation of the electrostatic interactions. Recently, we proposed new framework of QEq, named NQEq [2], that the empirical formula of Coulomb interaction is employed and that the parameter set is divided into each atom types based on Merck Molecular Force Field (MMFF) [3]. In this presentation, we introduce our extension of NQEq to molecular crystal calculations. This attempt can be obtained the appropriate charge distributions polarized by periodic environment. We will also show the results of lattice constants optimization for some organic molecular crystals using its NQEq and MMFF.

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Keywords: force field development, application development, intermolecular interactions

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Drug virtual screen by GA/GP: Docking studies with tubulin inhibitors as anticancer agents

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It is expected to shorten the required research time spent in the early stage of development of drug design through computer calculation. Computer Aided Drug Design is one of the most powerful concepts applied to satisfy such demand. Upon docking simulations, it is allowed to find out the binding sites and orientations between target

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.

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Durbeej, B. & Eriksson, L. A. (2006). PCCP, 8, 4053－4071.

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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