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The Application of Novel Modelling and Refinement Strategies to Crystallography. Mustapha Sadki[a], David J. Watkin[a]. [a]*Inorganic Chemistry Department, University of Oxford, South Parks Road, OX1 3QR, UK.*
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In current well-established crystallographic software packages, data refinement and other analytic fitting models are often embedded as a process engine. As such, they lack maintainability, extensibility and scalability; hence, the need for a mathematical programming infrastructure which offers a modelling design and is able to support the whole crystallographic modelling *life-cycle*, as well as keep separate model formulations from the optimisation process, bearing in mind that this separation is the key principle of modelling language design. In such a context and more specifically within small molecule crystallography software, this infrastructure will not only address the aforementioned drawbacks, but also allow for the investigation of solver performance of ill-conditioned problems and sensitivity analysis. This is made possible as one model formulation can work with numerous solvers, each of which implements one or more optimisation algorithms.
We have defined a strategy and designed a toolkit for small molecule computational crystallography, which delivers optimisation components in general and refinement-based applications in particular, as applied to crystallographic computing. This design benefits from the major advances made in optimisation methods over recent decades, knowledge which is encoded in widely available software libraries and/or web-servers. We use the concept of a modelling environment, which consists of objective and constraint expressions, a concept that has become an essential tool for a wide range of optimisation and related problems.
The toolkit provides users with an easy and efficient means to test ideas, construct new algorithms and models which can be readily adapted to any new situation, so by enabling users to develop and explore the full capabilities of crystallography, and upon which other researchers can build new applications.
We discuss the concept of the toolkit and describe the adopted strategies, so as to combine the modelling facilities with a powerful object-oriented programming language, support the whole crystallographic modelling *life-cycle* (building model – refining – analysing – revising) and fulfil the common development practice issues, consisting of: (i) supporting model formulations and streamlining the construction of problem descriptions; (ii) handling automatic differentiation, to keep the user free from developing computational procedures for computing derivatives; (iii) handling restraints/constraints which can be provided as a symbolic form and (iv) interfacing the modelling environments with numerous solvers to take advantage of the different minimisation methods for a more accurate sensitivity analysis.

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Keywords: computational modelling methods; computational crystallography; refinement methods

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Mining old Programs to Build Better Ones. Luc J. Bourhis. *Durham University, UK.*
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On the one hand, there is a wealth of crystallographic software written in the FORTRAN black-box paradigm, i.e. a monolithic program that only its few authors can contribute to while the rest of the community is restricted to just use it through the user interface devised by those authors. Some of them are mainstream (e.g. ShelX, Platon, Crystals) whereas others have become nearly extinct. On the other hand, there are a few initiatives to write crystallographic libraries which are modular and reusable in a very fine-grained manner in different programs, the most prominent of which being the Computational Crystallography ToolBox (cctbx). The latter should obviously be built with the knowledge hidden in the former when appropriate and possible. One of the key problem in doing so is that the algorithms implemented in those FORTRAN programs are not always expounded in details in the literature, or too often, published articles describe an early, cruder and now obsolete version of those algorithms. It is therefore of utmost importance to thoroughly study those FORTRAN programs so as to extract the crystallographic knowledge embedded therein and then inject it in a library such as the cctbx. We will illustrate on a few examples some of the recipes to successfully fulfil this goal.

Keywords: cctbx; FORTRAN; algorithms

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Comparison of Different Approaches for Automatic Structure Solution. Arie van der Lee. *Institut Européen des Membranes, Université de Montpellier II, 34095 Montpellier, France.*
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High-throughput crystallography needs robust algorithms capable to deal with a large variety of different cases, should be largely insensitive to experimental and structural criteria, and needs to have a seamless transition between the different steps that can be identified in the complete structure determination process. These steps have remained largely unchanged since decades, i.e. space group determination using the systematic extinction conditions followed by the structure solution step by (usually) direct methods using the symmetry determined in the preceding step, and finalized by structural refinement. The newly developed structure solution method charge flipping has made it very advantageous to postpone the symmetry determination step to after the structure solution step using a robust analysis of the symmetry of the determined phases in P1. This makes it possible to determine in one step structures where the symmetry analysis based on systematic extinctions is doubtful or even incorrect [1]. We present here a comparison between the traditional approach based on symmetry determination by analysis of systematic absences and structure solution by direct methods on the one hand and structure solution by charge