## FA4-MS43-T01

**Iterative algorithms in electron crystallography a brief history.** Andrew Stewart, Enrico Mugnaioli, Tatiana Gorelik, Ute Kolb, *Institute of Physical Chemistry, University of Mainz, Mainz, Germany.*
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Recently there has been a growing interest in iterative algorithms with regards to structure determination of small molecule X-ray crystallographic data. The roots of iterative algorithms originate in electron microscopy community with the Gerchberg-Saxton algorithm[1], which was later refined by Fienup into the Hybrid input-output (Hio) algorithm[2], and Elser produced the difference map algorithm[3]. The reason for particular interest in iterative algorithms is their distinct advantages over the classical direct methods, namely not requiring any knowledge of the crystal symmetry, or composition in order to solve a structure. In classical direct methods the measured intensities are used directly to estimate the phases, this is not the case for the iterative algorithms making them more robust to experimental errors in the measured intensities, which is a distinct advantage for powder and electron crystallography datasets. Electron crystallography data is particularly problematic for direct methods because the underlying assumption of kinematic data does not always hold, due to the much stronger interaction of electrons with matter when compared to x-rays.

An introduction to iterative algorithms with a historical perspective will be presented, with a particular emphasis being placed on the application of charge flipping algorithm[4] to the structure solution of electron crystallographic data sets.

[1] Gerchberg, R. W.; Saxton, W. O.; Optik 35, (1972) 237-246. [2] Fienup, J. R.; Applied Optics 21 (1982) 2758-2769 [3] Elser, V.; Acta Cryst. A59 201-209. [4] G. Oszlanyi, A. Suto, Acta Crystallogr. A 60 (2004) 134-141.

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## FA5-MS43-T02

**Superflip: unpublished features.** Lukas Palatinus *Institute of Physics ASCR, v.v.i., Czech Republic.*
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The structure-solution method called charge flipping [1] attracted a widespread attention of the crystallographic community also thanks to the quick availability of programs implementing the algorithm. Superflip [2] is one of these programs, and provides many unique features, including, for example, applications to aperiodic crystal structures.

The development of Superflip led to several improvements of the charge flipping method and of its practical applicability. Although many of these improvements have been described in scientific literature, many still remain only in the state of computer code, sometimes used by the users without really knowing about it. The purpose of this contribution is to present three such unpublished features of Superflip:

*Generalization of the algorithm:* Charge flipping can be thought as one of a family of related algorithms, with LDE or Elser's Difference Map representing other variants. Superflip includes a generalized algorithm, and all three above-mentioned algorithms are internally implemented just as special cases of the general algorithm. Interested users can specify a generalized scheme allowing them to design new algorithms and their variants.

*Handling of missing reflections:* It has been known since the beginning that missing reflections in the data set can pose problems for the charge-flipping method. Superflip offers three modes of handling missing reflections. Choosing the mode and setting the parameters of these modes properly can be crucial for solving structures with datasets with many missing reflections.

*Definition of initial density:* In the original formulation charge flipping iteration starts from a random initial density. Sometimes, a partial structure model is known, and in that case it is possible to start the iteration from this point, and use charge flipping as a structure-completion method. A particularly attractive starting point is a Patterson superposition map, which can be obtained from the experimental data without any prior information about the structure. Such option is available in Superflip, and tests [3] show that it significantly speeds up the convergence of the charge flipping algorithm,

[1] Oszlányi, G.; Sütö, A. *Acta Cryst.*, 2004, A60, 134. [2] Palatinus, L.; Chapuis, G. *J. Appl. Cryst.* 2007, 40, 786. [3] van der Lee, A., *BCA spring meeting*, Warwick, UK, 2010.

**Keywords: Ab-initio structure determination, Charge flipping, Crystallographic software**

## FA5-MS43-T03

**From a random model to the correct structure : the VLD algorithm.** Carmelo Giacovazzo[b,c], Maria Cristina Burla[a], Giampiero Polidori[a]. *[a]Department of Earth Sciences, University of Perugia, 06100, Perugia Italy. [b]Institute of Crystallography - CNR. Via G. Amendola, 122/O 70126 Bari, Italy. [c]Dipartimento Geomineralogico, Università di Bari , Italy.*
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Most of the crystal structure refinement techniques are based on the use of the joint probability distribution function $P(E, E_p)$, where $E$ and $E_p$ are the normalized structure factors of the target and of a model structure respectively. More recently new contributions shifted the attention to the difference electron density $\rho_q = \rho - \rho_p$ : methods based on its modifications (*DEDM*) started to play an important role, in combination with *EDM* (electron density modification) approaches [1], [2]. The study of the joint probability distribution function $P(E, E_p, E_q)$ suggested a new difference Fourier synthesis [3] particularly useful when the model is a rough approximation of the target structure. Its Fourier coefficients are the sum of the classical difference term (*mF-DF$_p$*) with a flipping term, depending on the model and on its quality. The flipping term is dominant when the model is poor, is negligible when the model is a good representation of the target structure. In case of random model the Fourier coefficient does not vanish and therefore could allow the recovery of the target structure from a random model.

The new phasing algorithm does not require any use of the concept of structure invariant or seminvariant: it is only based on the properties of the new difference electron density and of the observed Fourier synthesis. The algorithm designed for recovering the correct structure from random phases or from a random model is cyclic and very easy to be implemented. It

has been applied to a large set of small and medium size crystal structures, included small proteins.

[1] Caliandro, R., Carrozzini, B., Cascarano, G.L., De Caro, L., Giacovazzo, C. & Siliqi, D. *Acta Cryst.* (2008) A64*,* 519-528. [2] Caliandro, R., Carrozzini, B., Cascarano, G.L., Giacovazzo, C., Mazzone, A., Siliqi, D. *Acta Cryst.* (2009) D65 477-484. [3] Burla M.C., Caliandro R., Giacovazzo C., Polidori G. *Acta Cryst.* (2010) A66, 000-000.

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## FA5-MS43-T04

**Missing data in a modified charge flipping algorithm.** Gábor Oszlányi, András Sütő. *Research Institute for Solid State Physics and Optics, Hungarian Academy of Sciences, Budapest, Hungary.*
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Missing data is a general hindrance for all *ab initio* structure determination methods. Charge flipping [1,2] is no exception, and the problem is more exposed, due to the dual-space nature of the iterative algorithm.

Two publications have already appeared addressing this issue. These either fill the missing data by making the Patterson function positive and smooth with the maximum entropy method and then run the original iteration process [3], or correct phases by the tangent formula and use charge flipping with drastically increased perturbations [4].

Here we offer a third approach that is easier to implement and still works well for structures of usual complexity. Our solution is constructed from the following elements:

i. Normalized data, where normalization means division by the scattering factor of the heaviest atom in the structure.
ii. Freely floating moduli of unobserved structure factors within the observed resolution sphere.
iii. A set of utilized structure factors extended to higher than observed resolution.
iv. Special treatment of extinctions everywhere.
v. A modified iteration scheme that simultaneously increases perturbation in reciprocal space and includes full negative feedback. No extra parameters beyond the dynamical density threshold are introduced. Extended resolution acts as a damping factor.
vi. Figure-of-merits checked in an auxiliary step of the iteration process.

To show the efficiency of the method, a broad selection of successful structure solution examples will be presented, often working with 5-10 times less data than the standard requirement of *Acta Cryst. C*.

[1] Oszlányi G., Sütő A., *Acta Cryst. A*, 2004, 60, 134. [2] Oszlányi G., Sütő A., *Acta Cryst. A*, 2008, 64, 123. [3] Palatinus L. et al., *J. Appl. Cryst.*, 2007, 40, 456. [4] Coelho A.A., *Acta Cryst. A*, 2007, 63, 400.

**Keywords: ab-initio structure determination, direct methods, algorithms**