

## SOLVING ORGANIC STRUCTURES FROM POWDER DATA AT LOW RESOLUTION USING CHARGE FLIPPING COMBINED WITH MAXIMUM ENTROPY TECHNIQUES

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The solution of crystal structures of pharmaceutical interest has been revolutionized by the use of model building coupled with global optimization methods and simulated annealing in particular [1]. The charge flipping technique for solving crystal structures [2] has also had a considerable impact in areas such as incommensurate structures, and situations where the space group is uncertain or unknown. It is widely presumed that data to atomic resolution are needed for success with this technique, but with the incorporation of the maximum entropy formalism [3], the method can be shown to work with data at *ca.* 2Å resolution. This combined approach works as follows:

1. Reflection intensities are extracted from the powder diffraction data using either the Pawley or the LeBail method.
2. The reflection data are passed to the *Superflip* computer program [4] which carries out charge flipping. A total of 100 phase sets, starting from random phase choices, are generated and passed to the maximum entropy program *MICE* [5].
3. Each phase set is subjected to constrained entropy maximization and an associated log-likelihood (LLG) figure of merit is computed.
4. Electron density maps are computed for the top 24 solutions as ranked by LLG.
5. These maps are filtered by histogram matching, and the top 5-15 retained.
6. The maps are examined using the criteria of density continuity.

The method has been used successfully on a number of laboratory-based powder XRD datasets collected from structures of varying molecular and crystallographic complexity [6]. In favourable cases, maximum entropy alone (without the use of *Superflip*) can be successful. The solutions may well prove useful in defining approximate molecular envelopes that can be used as a starting point for model building methods, and we are investigating this.

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[2] G. Oszlányi and A. Süto. *Acta Cryst.* (2008). **A64**, 123-134.

[3] C. J. Gilmore, W. Dong and D. L. Dorset. *Acta Cryst.* (2008). **A64**, 284-294.

[4] L. Palatinus and G. Chapuis *J. Appl. Cryst.* (2007). **40**, 786-790.

[5] C. J. Gilmore and G. Bricogne, *Methods in Enzymology* (1997). **277**, 65-78.

[6] See: <http://www.powderdata.info/data.htm>