s1.m3.p6 **A Global/Local Optimisation Technique with Application to Structural analysis of macromolecules.** F. Long and G.N. Murshudov, *Structural Biology Laboratory, University of York Heslington, York YO10 5YW, UK. E-mail: fei@ysbl.york.ac.uk*

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Many problems in macromolecular X-ray structure analysis are attributed to locating the desired minimizers in an objective function. However, the objective functions are usually highly non-linear and non-convex. This implies the existence of many local minima and therefore local minimization techniques widely used to those problems are not appropriate especially when "good" initial values of parameters are not available. Traditional global optimisation technique of the simulated annealing, which is based on either Monte Carlo (MC) or molecule dynamics (MD), is computationally expensive because of too much sampling in the "state" space. Moreover for many objective functions it is not guaranteed that they will give the minimum even the initial values are not far from it. To avoid these problems we have developed a global/local optimisation technique. Molecular dynamics simulations are carried out and controlled. If algorithm oscillates around the minima then local optimisation is switched on. Once local minimum is reached then a penalty function is used for further MD simulation to scan remaining state space. For MD simulation Numerov's integration technique is used to increase time steps thus to speed up calculations. Several local optimisation techniques including Newton-Raphson, conjugate-gradient methods have currently been implemented. Algorithms have been implemented in both Cartesian and torsion angles spaces. The program developed using this technique has been applied to the dictionary of monomers used by the refinement program REFMAC. Performance of the program and contents of the dictionary have been mutually tested. Updating torsion angles corresponding to global energetic minimum of the monomers in the dictionary is currently under way. The results of these calculations will be fed to quantum chemical geometry optimisers. We are also planning to apply this technique to Macromolecular crystal structure refinement.

s1.m3.p7 **Ab initio structure solution by charge flipping.** Gabor Oszlanyi and Andras Suto, *Research Institute for Solid State Physics and Optics, H-1525 Budapest, POB 49, Hungary. E-mail: go@szfki.hu*

We present an amazingly simple ab initio structure solution method termed charge flipping. It works ab initio on high resolution x-ray diffraction data in the manner of Fourier recycling. The real space modification simply changes the sign of charge density below a threshold, while in reciprocal space the modification is the Fobs map without any weighting. All structures are handled in spacegroup P1 neglecting any symmetry constraints. We tested the algorithm using synthetic data for a wide range of structures, analysed the solution statistics and checked the quality of reconstruction. We also considered mathematical aspects of the algorithm in detail, showing that in this chaotic iteration process the solution is a limit cycle and not a fixed point.

Ref: G. Oszlanyi, A. Suto, *Acta Cryst* A**60**, 134-141 (2004)