modification based on satisfying the Sayre equation. In the event that the structure contains one type of heavy atom then a modified equation can be used which involves both squaring and cubing the current electron density (Woolfson, M M, 1958, Acta Cryst 11, 287-283).

A process has been devised, the ABC method, which enables density to be modified to satisfy the constraints of solvent flattening, histogram matching, Sayre's equation and the magnitudes of structure factors, all in terms of refining only a few (4-6) parameters. It may also be possible to introduce other constraints, for example a model distribution of atomic environments.

Preliminary results will be described and their potentiality discussed - in particular for *ab initio* phasing.

PS-02.01.11 A DENSITY MODIFICATION PROCEDURE FOR SOLVING SMALL & MIDDLE SIZE STRUCTURES AND PHASE REFINEMENT FOR PROTEINS. By M.Shiono, Y.Yada*, Department of Physics, Kyushu University, Higashi-ku, Fukuoka, Japan. L. S. Refaat and M. M. Woolfson, Department of Physics, University of York, Heslington, York, YO1 5DD.

The Low Density Elimination (LDE) procedure (Shiono, M. and Woolfson, M. M., *Acta Cryst.*(1992),A48,451-456) which was developed for phase extension and refinement in order to solve macromolecules has been investigated regarding its power to solve small and middle size structures starting from random phase sets. In fact, the method is competitive against conventional direct methods. The LDE method, however, is time-consuming compared with conventional direct methods (e.g. MULTAN) since the procedure includes two Fourier transforms in one cycle. We have, therefore, combined MULTAN and LDE procedure. The LDE can be run in three different modes as follows.
Mode 1. Run the LDE with phases estimated by anomalous scatterings or isomorphous replacements. Mode 2. Employing multi-solution strategy, run the LDE individually assigning all reflexions random phases. Mode 3. Run MULTAN and then proceed to the LDE using MULTAN phases as initial phase sets in order of figures of merit.
For small and middle size structures, mode 3 is most effective. We might eventually solve the structures with MULTAN trial. Even if MULTAN fails to find any useful structural configurations, MULTAN phases increase the power of the LDE in solving structures.

PS-02.01.12 DIRECT PHASING OF MACROMOLECULAR STRUCTURES BY MULTIPLE BEAM DIFFRACTION
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The feasibility of experimental phase determination of small protein structures using three-beam diffraction has already been demonstrated (K. Hümmer, W. Schwegle & E. Weckert (1991) Acta Cryst. **A47**. 60-62). It has been shown that triplet-phase invariants $\phi = -\varphi(\mathbf{h}) + \varphi(\mathbf{g}) + \varphi(\mathbf{h}-\mathbf{g})$ can be deduced from three-beam interference profiles (K. Hümmer, E. Weckert & H.Bondza (1989) Acta Cryst. **A45**, 182-187), where the φ's are the phases of individual structure factors of the involved reflections with recipriocal lattice vectors **h**, **g**, and **h-g**.
In experimental phase determination of macromolecular structure significant differences compared to small molecule structures occur. Among others they concern the weaker scattering power of individual reflections, increasing overlap of multiple-beam interference effects due to larger unit cells and in general higher sensitivity to radiation damage.

Because of the large number of overlapping multiple-beam interference patterns in protein crystal structures only three-beam cases of reflections with large structure factors are suitable for phase determination. It was possible to determine about 80 triplet phases of the small protein lysozyme in the low and medium resolution range with a mean phase error of about 17°.
Radiation damage can often be significantly reduced by using higher energy radiation, i.e. $\lambda = 0.7$ Å . Therefore, interference effects of lysozyme were systematically investigated in the range from 0.7 Å to 1.58 Å . As a result also in the short wavelength regime phase determination is possible.
Theoretical calculations by dynamical theory and experimental results confirm the existence of three-beam interference effects even for crystal sizes smaller than the "Pendellösung" lengths. Further investigations show that it is this range where an unique correlation exists between the interference profiles and the triplet phases independent whether the primary reflection is in Bragg- or Laue-diffraction geometry. In general the crystal size of proteins is smaller than the "Pendellösung" length.
Due to the weak reflectivity of protein crystals "Aufhellung" effects are weaker compared to the higher reflectivity of small molecule structures. Therefore, the high number of overlapping three-beam cases does not severely affect the phase exploitation in proteins.
First experiments with catalase crystals (space group $P4_22_12$, a = 106.7Å , c = 106,3 Å) indicate that even for large proteins experimental phase determination may be feasible.
The possibilities to integrate measured triplet-phase invariants into statistical structure solution methods are discussed. First results to extend this phase information by an approach using maximum entropy will be presented.

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PS-02.01.13 **FOURIER SERIES PROBABILITY DISTRIBUTION OF STRUCTURE FACTORS AND ITS RELATION WITH OTHER DISTRIBUTIONS.** By G. B. Mitra*, CSS Department, Indian Association for the Cultivation of Science, Calcutta-700 032, India and Sabita Das, Victoria Institution (College), Calcutta-700 009, India.

In his pioneering work, Wilson (Acta Cryst, 1949, 2, 318), showed that the distribution of structure factor components was Gaussian. Later, introduction of Edgeworth series (Mitra and

