02-Methods for Structure Determination and Analysis, Computing and Graphics

**MS-02.03**

PROGRESS TOWARDS APPLICATION OF THE MINMIL FUNCTION TO MACROMOLECULES.


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In the case of gramicidin A, a 0.12Å grid placed in the asymmetric part of the unit cell was used to obtain initial coordinates for 249,956 1-atom trial structures. The 346 trials having an initial mean phase error of 80Å were subjected to the Shake-and-Bake procedure, and three solutions were obtained following 450 cycles of refinement and filtering. Thus, in the worst case scenario, there is one solution per 80,000 trials for gramicidin A. In the case of crambin, initial phases were obtained by performing structure factor calculations based on randomly positioned 2-atom trial structures. The success rate was 1.8% following 200 Shake-and-Bake cycles. Both the gramicidin A and crambin maps can be easily interpreted either by examination of interpeak distances and angles or by graphical electron density listing using RIGDO. The best maps for manual examination are obtained by terminating the procedure with one cycle of Fourier refinement using all statistically reliable measured data.

At present, these experiments leave several questions unanswered. For example: What is the random start success rate for gramicidin A? How important was the presence of the six sulphurs in the crambin application? How long will the procedure, which presently relies on peak picking at the Fourier stage, be applicable as the resolution of the data is decreased? These problems are presently under investigation.

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**MS-02.04**

MAXIMUM ENTROPY, LIKELIHOOD AND THE CRYSTALLOGRAPHY OF BIOLOGICAL MACROMOLECULES

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3. Two structures of biological macromolecules studied using electron diffraction, and phased image data from high resolution electron microscopy.

(a) Purple membrane (*Halobium Halobacterium*) data (Baldwin, J.M., Henderson, R., Beckman, P., & Zahnin, F. J. Mol. Biol. (1988) 202, 585-591). This was as a test of the method, and has produced some controversial results concerning resolution enhancement.

(b) Cholera toxin. Here we are phasing data to 4Å from 56 unique phased reflections at 8.8Å resolution using the M3 method incorporating the application of five-fold non-crystallographic symmetry, and solvent flattening.

In both (a) and (b) a low resolution basis set of phased reflections had been derived from the Fourier transform of optical image data suitably averaged, and used to phase the high resolution diffraction data via a process of entropy maximisation and likelihood evaluation coupled with the building of phasing trees.

The maximum entropy method is ideal in these circumstances because:

1. It will work with projection data.
2. It is stable regardless of data resolution.
3. It can utilize non-crystallographic symmetry, and solvent flattening in a wholly natural and relatively simple way.
4. It uses non-uniform atomic distributions which are constantly updated.
5. Likelihood can be used to determine an effective unit cell contents that reflects the data resolution.

**MS-02.05**

ELECTRON-DENSITY HISTOGRAMS AND THE PHASE PROBLEM.

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The spectra of frequencies (histograms) of different values in Fourier syntheses provide the most adequate representation of information or 'what values may be found in a good Fourier synthesis and how frequent they are'. These Electron-Density Histograms (EDH)