Notes

pl9 The phase problem at medium resolution. P. Main, J. Wilson*, G. Reynolds, *Department of Physics, University of York, York YO10 5DD, U.K., *Department of Chemistry, University of York, York YO10 5DD, U.K.*
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Methods are now available for the improvement of electron density maps at about 5Å or higher resolution, for example as implemented in the program DM which is part of the CCP4 program library[1]. Methods are also being developed for the ab initio determination of molecular envelopes which are capable of yielding low resolution images[2].

However, there is a gap at medium resolution (12 - 5Å) where almost no methods are available for the improvement of maps or for phase refinement and extension. We have recently started to make progress with two different ways of dealing with this problem and the latest results will be presented in the lecture.

The first method makes use of wavelet analysis to increase the resolution of a 10Å resolution starting map[3,4]. The problem of increasing the resolution is one of adding the right amount of detail to the right places in the map. Wavelet analysis helps with this by decomposing an image into different levels of detail, described by the wavelet coefficients. An inverse wavelet transform reverses the process and reconstructs the image from the coefficients. Control over the detail in the image is exercised through the statistics (histograms) of the wavelet coefficients, which can be predicted for any protein map asa function of resolution and solvent content. New features in the map are positioned by the X-ray data. At present, 10Å starting phases can be extended to about 7Å with acceptable phase errors. This resolution limit is extended if some secondary structure is recognised in the 7Å map and used in a repeat of the phase extension. The goal is to increase the resolution to at least 5Å where existing map improvement techniques can take over.

Our second approach is to use newly derived phase probability formulae that make use of known features of the structure. The most useful formulae give the probability distributions of either single phases or of three-phase structure invariants. The single-phase formula is used to measure the reliability of individual phases to provide a weighting scheme for the calculations. The three-phase formula forms the basis of a tangent formula summation for phase refinement and extension. The features of the structure that can easily be incorporated into the formulae are the probability distribution of the atoms (usually given by the molecular envelope) and any known atomic positions (usually from a partially interpreted map). The formulae give their best results at high resolution, but useful phase refinement can be achieved at about 6Å resolution. After further development, it is anticipated that this will be combined with the wavelet analysis to form a more robust calculation.

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