Density modification is a method of direct determination of macromolecular structures. By D.S. Moser, M.J. Stanford, and G.J. Mlotow, Department of Crystallography, Sixbeck College, Malet Street, London WC1E 7EX, UK.

The optimum strategy for the initial stages of least-squares refinement of a protein was investigated.

A model of the eye lens protein γ-crystallin II was built into a 2.6A resolution electron density map using an interactive computer graphics system. Least-squares refinement of this model was undertaken using structure amplitudes and isomorphous phases to a resolution of 2.6A. The effect of errors in the observed data was examined by comparing the results of refinements using structure factors derived either from experimental observations or calculated from a high resolution model. Various schemes were employed for weighting the structure amplitudes in several independent schemes of refinement. Each scheme was pursued until the rms atomic shift was less than 0.02Å, at which point intervention on the graphics system would be required.

Progress was monitored by vector mapping the atomic shifts, and comparing refined coordinates with the high resolution model. The CPU time and real time required for each strategy was less than 3%.

2.6A resolution electron density maps of ketosteroid isomerase were improved by substantially increasing the tracing of the backbone. The effect of errors in the observed density was also considered.

Results were monitored by vector mapping the atomic shifts, and comparing refined coordinates with the high resolution model. The CPU time and real time required for each strategy was less than 3%.

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