

Statistical Direct Methods of Phase Determination

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In the minimal principle method, one of the most successful direct methods of phase determination, the phase problem is formulated as a problem in constrained global minimization. The cosine minimal function, based on probabilistic estimates of the cosines of the structure invariants, serves as the foundation of an optimization procedure called *Shake-and-Bake* [1] that automatically and repetitively alternates reciprocal-space phase refinement with a complementary real-space density modification to impose the atomicity constraints.

A new statistical minimal function and its minimal principle, based on the statistical properties of the structure invariants themselves, have recently been formulated. Favorable applications of the corresponding statistical *Shake-and-Bake* algorithm have been made to the *ab initio* phase determination of small proteins as well as Se-atom substructures, and the results have shown an overall improvement in success rate relative to traditional *Shake-and-Bake*.

Statistical *Shake-and-Bake* is being incorporated as the default optimization procedure in newly distributed versions of the *SnB* and *BnP* computer programs. This research was supported by NIH grants EB002057 and GM072023.

[1] Weeks C.M., Miller R., *J. Appl. Cryst.*, 1999, **32**, 120.

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