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Discussion after Talk by J. M. Stewart

An interesting discussion on the maximum-entropy approach took place following Stewart's paper. The discussion was not recorded, but at the suggestion of the editors an attempt has been made by the session chairman and the discussants to summarize the main points of the discussion.

The discussion centered on the choice and phasing of basis sets in the early stages of maximum-entropy structure solution. In his talk, Stewart had praised the phase extension provided by entropy maximization, saying that in trials with protein data it has shown considerable ability to lead to maps which, if not actually interpretable in terms of chain tracing, at least have the general look of a protein map. At the same time, he felt that in the early stages of the solution attempt, at the point where the basis set is still small, it is still very possible to miss the correct phasing path and hence the correct structure. With this in mind, he expressed the feeling that the critical need is for some additional criteria to guide a good start. It was this remark which prompted the discussion which followed.

The most extensive remarks were made by Gerard Bricogne. He agreed with Stewart's point, and stated his belief that the best approach to the problem will be through the maximum-likelihood technique. In maximum entropy, path guidance is achieved partly by choosing phase extensions which cause minimum entropy loss, and partly by observing which extensions lead to the best appearing or most promising maps. In maximum likelihood the situation is the same, but in addition one calculates a likelihood measure for a phase set, based on determining how well predictions made from the set agree with other data obtained from the system. Many types of data can be incorporated in the likelihood calculation, including the not-yet-phased X-ray magnitudes, data concerning envelopes, histograms and partial structures, *etc.* [see Bricogne (1988). *Acta Cryst.* A**44**, 517–545 and his paper in this issue for more detail]. Thus likelihood can provide a predictive figure of merit based on what can be extensive structure-specific information, and this may give a means of keeping the basis-set phases close to the true values even in the early stages of the solution process. Bricogne stated that his current work is mainly devoted to adding careful guidance strategies based on likelihood to his phasing program.

Ted Prince said that he doubts that a likelihood measure based on the not-yet-phased X-ray data can have much power in the early stages, because of the weakness of the phase coupling between a small basis set and the other reflections. He also feels that phase sets, even early ones, may be better judged by experienced crystallographers looking at relatively artifact-free maps produced from them than by any other technique. Thus he plans to stay with maximum entropy for the present. The result is that the field will be getting the benefit of the best efforts in both entropy and likelihood maximization.

Finally, it may be of interest to note that the problem of losing the phasing path during the small basis-set stage is one which affects macromolecular direct methods generally, and that there are three main approaches currently being pursued in answer to it (papers were given at the conference on all three), namely:

(1) repeated tries (random starting-phase approach);

(2) not working with small basis sets (phase annealing; minimization approaches);

(3) permitting relatively artifact-free maps to be obtained from small basis sets (maximum entropy); obtaining good figures of merit for small basis sets (maximum likelihood).

It may be noted that there does not seem to be any reason why, if needed, (3) could not be combined with (1) or (2).

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