Coordinate Uncertainties in Protein Structure Comparison

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When deriving conclusions from the comparison of crystal structures, one needs to know the error-levels in the structures used in order to discriminate significant differences from random noise.

In small molecule crystallography, the variances obtained from the inversion of the full least-squares matrix at the end of the refinement are accepted (although not completely unchallenged) as measures for the standard deviations of geometric properties in a structure. In protein crystallography, the applicability of a least-squares based target function for refinement is already being questioned. Even if least-squares refinement is performed and the computational means allow the inversion of matrices corresponding to several thousand parameters, it is not clear how to treat the restraints terms used in the refinement during the inversion. For these reasons, we have resorted to using a heuristic estimate for coordinate uncertainties put forward by Durward Cruickshank in 1999 [1] to estimate coordinate uncertainties in crystal structures of proteins. The approximate formula suggested allows to put the mean coordinate errors of structures to be compared onto approximately the same scale; estimates for coordinate uncertainty of individual atoms can then be derived by assuming a simple B-factor dependence of the errors.

Using these error estimates, we have implemented a structure comparison framework ('ESCET', [2]) that is based on the automatic interpretation of difference distance matrices. To make the method robust and to avoid the use of absolute thresholds, the elements of the matrices are scaled to their errors as derived by error propagation from the coordinate uncertainties.

The basic ideas behind the method will be discussed and some representative examples will be shown.

[1] D. Cruickshank, Acta Cryst, D55, 583 (1999).

[2] T.R. Schneider, Acta Cryst. D58, 195 (2002).