Using coordinate uncertainties in structure comparison

Schneider T.R. (1,2)

(1) FIRC Institute of Molecular Oncology, Via Adamello, 16, 20139 Milan, Italy (2) European Institute of Oncology, Via Ripamonti 435, 20141 Milan, Italy

Motivation

Coordinate uncertainties in crystal structures of biological macromolecules can vary from 0.01 Angstroem for a well determined atom in a high-resolution structure to 1 Angstroem for a mobile atom in a structure determined at low resolution. Given this wide range, it is essential to take into account the coordinate uncertainties in the comparison of structural models in order to discriminate significant differences from noise. Furthermore, given the rapid growth of available structure data, new methods for the analysis of large numbers of structural models need to be implemented.

Methods

Heuristic estimates of coordinate uncertainties are obtained by evaluation of a modified form of Cruickshank's DPI formula [1] and are used via error propagation to construct 'error-scaled difference distance matrices' [2]. In a first step, these matrices are used to define a metric that allows to identify clusters of similar conformers which are then collapsed to representative models. In a second step, large sets of error-scaled difference distance matrices ((N x N - N)/2 for N models) are rapdily interpreted by a genetic algorithm[3]. The result of the analysis is the division of a molecule into conformationally invariant regions or domains, in which all interatomic distances are identical within error in the ensemble of models considered.

Results

The method was applied to a number of biological macromolecules and the conformationally invariant regions found were used in functional interpretation. The molecules analysed range from polypeptide antibiotics (mersacidin, 20 residues, 6 models) via single and multi-domain enzymes (Epimerase, 310 residues, 10 models; src-Kinase, 450 residues, 2 models) to ribosomal subunits (30S subunit, 1480 nucleotides, 2 models).

Contact email: thomas.schneider@ifom-ieo-campus.it
URL: http://www.ifom-ieo-campus.it/escet
Supplementary Information: [1] Cruickshank (1999) Acta Cryst. D55:583-601. [2] Schneider (2000) Acta Cryst. D56:714-721. [3] Schneider (2002) Acta Cryst. D58:195-208. [4] Schneider (2004) Acta Cryst. D60:2269-75.