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The 'Buccaneer' software for automated protein chain tracing

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Keywords: automated structure solution, model building, electron density

'Buccaneer' is a new software package for automated tracing of protein chains in electron density maps obtained after experimental phasing and density modification. It employs a 6-dimensional search using a likelihood-based target function for location of probable alpha-carbon positions, followed by real space application of the same target function along with Ramachandran constraints to grow the initial candidates into chains. Multiple models of the same chain segment are merged, and a threading algorithm based on dynamic programming is used to resolve chain branches. Finally, clashing chain segments are pruned.
The likelihood function is prepared by use of a simulated electron density map for a known, reference structure, which is processed to match the features and noise in the map for the unknown, target structure. The likelihood function is prepared by comparison of the simulated noisy map for the reference structure around the known alpha-carbon positions. The resulting likelihood function is thus optimised for the current problem.
The software is reasonably fast, taking between a few minuted and an hour, and initial tests against a database of real data from the JCSG data archive suggest that it is less dependent on data resolution but more dependent on phasing quality than the current ARP/wARP software. Further developments are in hand to broaden the range of applicability of the software, and also to implement the missing steps of sequence assignment and the correction of chain direction and register errors. The same approach should also be applicable to the building of DNA and RNA.
The current version of the software is available from *http://www.ysbl.york.ac.uk/~cowtan/*.

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The Bayesian approach to absolute structure determination

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Keywords: absolute structure, resonant scattering, anomalous dispersion

The refinement of the Flack *x* parameter [1] is the standard method to determine the composition of potential racemic twin crystals. The same method is also used to determine the absolute configuration of enantiopure compounds such as pharmaceuticals. However, the Flack *x* parameter does not provide a direct way to quantify the reliability of the absolute structure assignment. Statistical methods have therefore been designed to judge this reliability [2]. We introduce an alternative method that uses Bayesian statistics over intensity differences between Bijvoet pairs [3] to make an absolute structure assignment. Our method includes a rigorous estimate of the reliability of the assignment. It is shown that using this method, a trustworthy absolute structure determination can sometimes even be performed using molybdenum Kα radiation on structures containing only atoms not heavier than oxygen. A very reliable assignment could be obtained from all tested data sets for equally light atom structures that were measured using copper Kα radiation.

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