

Automating Electron Density Map Interpretation by Matching Conformations

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Building a protein model from the initial three dimensional electron density distribution (density map) is an important task in X-ray crystallography. This problem is computationally challenging because proteins are extremely flexible. Our algorithm, *ConfMatch*, is a global real-space-fitting procedure in torsion-angle space. It solves this “map interpretation” problem by matching a detailed conformation of the molecule to the density map (conformational matching). This “best match” structure is defined as one which maximizes the sum of the density at atom positions. *ConfMatch* is a practical, systematic algorithm based on branch-and-bound search. The most important idea of *ConfMatch* is an efficient method for computing accurate bounds. *ConfMatch* relaxes the conformational matching problem, a problem which can only be solved in exponential time, into one which can be solved in polynomial time. The solution to the relaxed problem is a guaranteed upper bound for the conformational matching problem. In most empirical cases, these bounds are accurate enough to prune the search space dramatically, enabling *ConfMatch* to solve structures with more than 100 free dihedral angles. Our experiments have shown that *ConfMatch* may be able to automate the interpretation of density maps of small proteins.

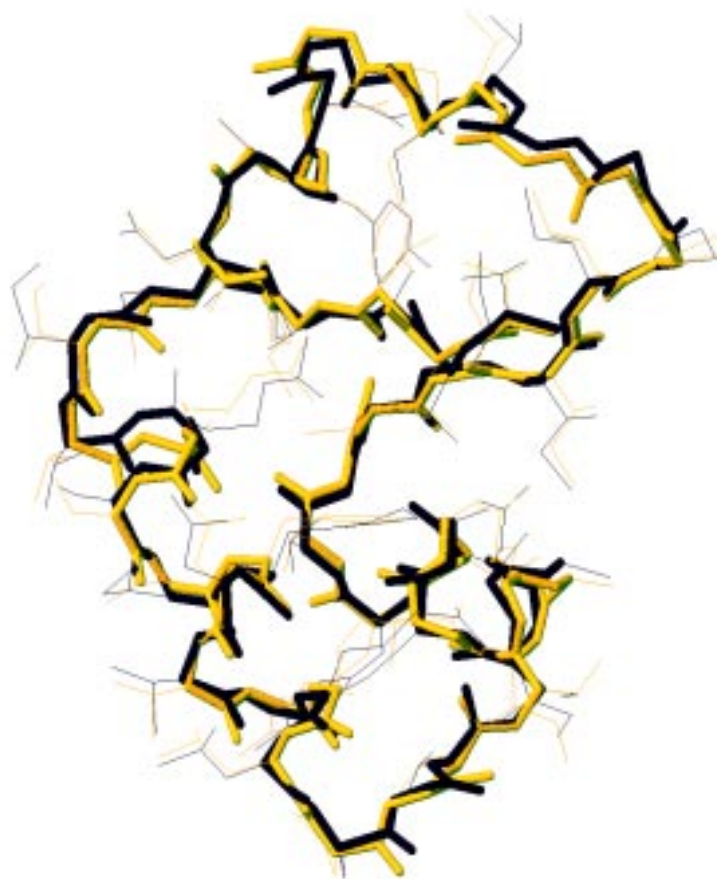


Figure: Confmach's solution structure (darker) of crambin from 2.0Å resolution data and the published 0.89Å structure (lighter). The thicker portions are the backbones of the structures.

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