MAIN in 2004: model building at 100 residues per minute

Automation of interactive macromolecular crystal structure determination process needs to fulfill two requirements: The tools applied should be automated to the extent that a user does not have to provide additional manual input but their triggering and the results should appear on the screen under interactive time restraints (a user's mind did not get enough time to wonder away). In order to achieve these two goals the MAIN routines for automated model building were rewritten more or less from scratch. The new map skeletonization algorithm follows the ridges of electron density maps. The resulting skeleton is not converted into sp3 or sp2 fragments immediately as in the previous releases, but serves as the searching path for recognition of secondary structure and main chain trace. Recognition of secondary structure is not based on a fragment search. Detection of two screw turns in the skeleton are recognized as a helical structure, whereas recognition of beta structures is based on straight stretches of skeleton corresponding to at least five amino acids and their arrangements in pairs or sheets. (Helical structure search is computationally the most time consuming part and may take a few tens of seconds for a 500 residue structure at a moderate resolution.) The found secondary structure elements are used to improve the skeleton by removal of false cross connectivities. The extension of secondary structure elements can continue through breaks in the electron density map and its skeleton presentation. During the next step connections between the secondary structure elements are establisehd on a combinatorial search basis. They are used to reduce further main chain - side chain ambiguities. The resulting labeled and edited skeleton then serves for building of the first main chain trace based on sp3 fragments positioned at potential CA positions. This model is then extended by side chains and main chain carbonyls. If the model looks satisfactory, it is converted to amino acid residues, from where it enters sequence assignment step and refinement. If the model is not satisfactory, then it is used as a starting point for a density modification procedure, which includes refinement and phase combination. Alternatively, a user can manually edit the skeleton (breaking false connections and building new ones) and restart the main chain tracing procedure. The resulting models can continue along the classical path of automated and manual model rebuilding still using the same program with the same interactive 3D graphical user interface.

See “http://www-bmb.ijs.si/”.