18.7. The\textit{TNT\textsuperscript{\textregistered}} refinement package

Since it is clear from examinations of higher-resolution models that the $B$ factors generally increase from one side of a bond to the other (e.g. moving from the main chain to the end of a side chain), the traditional restraint is flawed. A restraint library was generated (Tronrud, 1996) where each bond in a residue is assigned a preferred increment in $B$ factor and a confidence (standard deviation) in that increment.

18.7.5.8. Block-diagonal preconditioned conjugate-gradient minimization with pseudo-inverses (1998)

With this enhancement, \textit{TNT\textsuperscript{\textregistered}}’s minimizer treats the second-derivative matrix as a collection of $5 \times 5$ element blocks along its diagonal, one block for each atom. While this method improves the rate of convergence for noncrystallographic symmetry restraints, its most significant feature is that it allows the refinement of atoms located on special positions without special handling by the user.

18.7.5.9. Generalization of noncrystallographic symmetry operators to include shifts in the average $B$ factor (1998)

It is rather common in crystals containing multiple copies of a molecule in the asymmetric unit for one or more molecules to have a higher $B$ factor than the others. If the transformation that generates each copy of the molecule consists only of a rotation and translation of the positions of the atoms, the difference in $B$ factors cannot be modelled. The transformations used in \textit{TNT\textsuperscript{\textregistered}} now consist of a rotation, translation, a $B$-factor shift and an occupancy shift.

18.7.6. \textit{TNT\textsuperscript{\textregistered}} as a research tool

\textit{TNT\textsuperscript{\textregistered}} was intended not only as a tool for performing refinement, but as a tool for developing new ideas in refinement. While most of the latter has been done by \textit{TNT\textsuperscript{\textregistered}}’s authors, several others have made good use of \textit{TNT\textsuperscript{\textregistered}} in this fashion. If one has an idea to test, the overhead of writing an entire refinement package to perform that test is overwhelming. \textit{TNT\textsuperscript{\textregistered}} allows modification at a number of levels, so one can choose to work at the level that allows the easiest implementation of the idea. Several examples follow.

18.7.6.1. Michael Chapman’s real-space refinement package

At Florida State University, Chapman has implemented a real-space refinement package, principally intended for the refinement of virus models, using \textit{TNT\textsuperscript{\textregistered}}. He was able to use \textit{TNT\textsuperscript{\textregistered}}’s minimizer and stereochemical restraints unchanged along with programs he developed to implement his method. More information about this package can be found at http://www.sb.fsu.edu/~rsref.

18.7.6.2. Randy Read’s maximum-likelihood function

When Navraj Pannu wanted to implement Read’s maximum-likelihood refinement functions (Pannu & Read, 1996) in \textit{TNT\textsuperscript{\textregistered}}, he chose not to implement it as a separate program, but modified \textit{TNT\textsuperscript{\textregistered}}’s source code to create a new version of the program \textit{Rfactor}, named \textit{Maxfactor}.

18.7.6.3. J. P. Abrahams’ likelihood-weighted noncrystallographic symmetry restraints

Abrahams (1996) conceived the idea that because some amino-acid side chains can be expected to violate the noncrystallographic symmetry (NCS) of the crystal more than others, one could develop a library of the relative strength with which each atom of each residue type would be held by the NCS restraint. He chose to determine these strengths from the average of the current agreement to the NCS of all residues of the same type. For example, if the lysine side chains do not agree well with their NCS mates, the NCS will be loosely enforced for those side chains. On the other hand, if almost all the valine side chains agree well with their mates, then the NCS will be strongly enforced for the few that do not agree well.

He chose to implement this idea by modifying the source code for the \textit{TNT\textsuperscript{\textregistered}} program NCS. Since the calculations involved in implementing this idea are simple, the extent of the modification was not large.

18.7.6.4. The \textit{Buster\textsuperscript{\textregistered}} refinement package

Bricogne & Irwin (1996) have developed a maximum-likelihood refinement package using \textit{TNT\textsuperscript{\textregistered}}. Not only are \textit{TNT\textsuperscript{\textregistered}}’s minimizer and stereochemical restraints used, but many of the calculations of the maximum-likelihood residual’s derivatives are performed using \textit{TNT\textsuperscript{\textregistered}} programs. While Bricogne and co-workers have not needed to modify \textit{TNT\textsuperscript{\textregistered}} programs to implement their ideas, there is ongoing collaboration between them and \textit{TNT\textsuperscript{\textregistered}}’s authors on the development of commands that allow access to some previously internal calculations. More information about \textit{Buster\textsuperscript{\textregistered}} can be found at http://www.globalphasing.com/buster/.

18.7.7. Current status of \textit{TNT\textsuperscript{\textregistered}}

\textit{TNT\textsuperscript{\textregistered}} is no longer being actively developed at the University of Oregon. The principal use of \textit{TNT\textsuperscript{\textregistered}} today is from within the \textit{Buster\textsuperscript{\textregistered}} package of Global Phasing Ltd. Over the last ten years, they have made considerable modifications to their branch of the source code which have greatly increased the radius and rate of convergence of the optimizer and expanded the scope of the distributed library of standard groups in the ideal stereochemistry library. These enhancements are only available via their distribution of \textit{Buster\textsuperscript{\textregistered}}.

References


