in maximum-likelihood refinement of partial structures in conjunction with the *TNT* program (Section 25.1.5.8), maximum-entropy structure completion for missing or ambiguous parts of a structure, and accurate electron-density reconstruction based on high-resolution X-ray diffraction data. *BUSTER* is related to *SHARP* (Section 25.1.4.7). See Chapter 16.2 for more details.

Location: http://lagrange.mrc-lmb.cam.ac.uk/buster/Buster Home.phtml. Operating systems: IRIX and OSF1. Type: binary. Distribution: free academic.

#### 25.1.6.2. *DM/DMMULTI*

*DM* (Cowtan, 1994) is a density-modification program package. *DM* applies real-space constraints based on known features of a protein electron-density map in order to improve the approximate phasing obtained from experimental sources. Various information can be applied, including the following diverse elements: solvent flattening, histogram mapping, multi-resolution modification, NCS averaging, skeletonization and Sayre's equation. *DM* is part of the *CCP*4 suite (Section 25.1.2.4). See Chapter 15.1 and Section 25.2.2 for more details.

Operating systems: UNIX, VAX/VMS and LINUX. Type: source code and binary. Distribution: free academic.

#### 25.1.6.3. *FINDNCS*

*FINDNCS* (Lu, 1999) is a program that automatically determines NCS operations from heavy-atom sites to aid in applying averaging techniques in the MIR procedure. The program outputs the NCS operations (a rotation matrix and translation vector), r.m.s. deviations, polar angles and screw distance, matching sites and other useful information for users. The program can also generate files that can be used to display NCS operations using the program *O* (Section 25.1.7.7).

Location: http://gamma.mbb.ki.se/~guoguang/findncs.html. Operating systems: UNIX, IRIX and OSF1. Type: binary. Language: Fortran77. Distribution: free academic.

#### 25.1.6.4. *RAVE*

*RAVE* (Jones, 1992; Kleywegt & Jones, 1994) is a suite of programs for real-space electron-density averaging of crystallographic electron density between single and multiple domains, and between single and multiple crystal forms. It also contains tools for the detection of secondary-structure elements in macromolecular electron-density maps. See Chapter 17.1 for a detailed description.

Location: http://xray.bmc.uu.se/usf/menu.html#sof; ftp://xray.bmc.uu.se/. Operating systems: UNIX, SGI and DEC Alpha/OSF1. Type: binary. Distribution: free.

#### 25.1.6.5. *SOLOMON*

*SOLOMON* (Abrahams & Leslie, 1996) is a program that modifies electron-density maps by averaging, solvent flattening and protein truncation. It can also remove overlapped parts of a mask between itself and its symmetry equivalents. *SOLOMON* is part of the *CCP*4 suite (Section 25.1.2.4).

Location: http://www.dl.ac.uk/CCP/CCP4/dist/html/solomon.html. Operating systems: UNIX, VAX/VMS and LINUX. Type: source code and binary. Distribution: free academic.

#### 25.1.6.6. *SQUASH*

The *SQUASH* program (Zhang & Main, 1990*a*,*b*) provides a tool for phase refinement and extension of macromolecular structures. The starting point is a set of native structure factors to some resolution, and estimated phases and figures of merit for some subset of the phases. The result is a set of improved phases and figures of merit for the whole data set. The program combines Sayre's equation with density modification by histogram matching, solvent flattening and noncrystallographic symmetry averaging. The real-space formulation enables any electron-density constraint to be applied easily, *e.g.* solvent flattening with (eventually) known regions of density. The least-squares solution of a large system of nonlinear equations is achieved by Newton–Raphson iteration that converts the system of nonlinear equations into linear ones. The system of linear equations is solved by the conjugate-gradient method using FFTs.

Location: http://www.msc.com/brochures/software/squash.html. Operating system: UNIX. Type: binary. Distribution: commercial.

### 25.1.7. Graphics and model building

#### 25.1.7.1. *AMBER*

*AMBER* (Assisted Model Building with Energy Refinement; Cornell *et al.*, 1995) is a molecular-dynamics and energy-minimization program. *AMBER* refers to two things: a molecular-mechanical force field for the simulation of biomolecules (which is in general use in a variety of simulation programs) and a package of molecular-simulation programs which includes source code and demonstrations.

Location: http://www.amber.ucsf.edu/amber/amber.html. Operating systems: UNIX, SGI, SUN *etc*. Type: source code and binary. Languages: Fortran and C. Distribution: commercial.

#### 25.1.7.2. *CHARMM*

*CHARMM* (Chemistry at HARvard Molecular Mechanics; Brooks *et al.*, 1983; MacKerell *et al.*, 1998) is a program for macromolecular simulations, including energy minimization, molecular dynamics and Monte Carlo simulations.

Location: http://yuri.harvard.edu/. Operating systems: UNIX, SGI, SUN *etc*. Type: source code. Language: C. Distribution: minor licence fee for academic users.

#### 25.1.7.3. *Insight II*

*Insight* II is a 3D graphical environment for molecular modelling. *Insight* II creates, modifies, manipulates, displays and analyses molecular systems and related data, and provides the core requirements for all *Insight* II software modules. Its powerful user interface enables the seamless flow of data between a wide range of scientific applications. The *Insight* II environment integrates builder modules, development tools, force fields, simulation and visualization tools with tools specifically developed for applications in the life and materials sciences.

Location: http://www.msi.com/life/products/insight/index.html. Operating systems: SGI and IBM UNIX systems. Type: binary. Distribution: commercial.

#### 25.1.7.4. *MidasPlus*

*MidasPlus* (formerly *Midas*) (Ferrin *et al.*, 1988) is an advanced molecular-modelling system developed by the Computer Graphics Laboratory (CGL) at the University of California, San Francisco. The system can be used for display and manipulation of macromolecules such as proteins and nucleic acids. Ancillary programs allow for such features as computation of molecular surfaces and electrostatic potentials and generation of publication-quality space-filling images with multiple light sources and shadows. To address the needs of the structure-based drug-design community, *MidasPlus* has been developed with an emphasis on the interactive





references