Impact 5.8

User Manual

Schrödinger Press

Revision A, September 2012

Contents

Document Conventions v

Chapter 1: Introduction to Basic Impact 1

1.1 **Running Schrödinger Software** 1

1.2 **Citing Impact in Publications** 3

Chapter 2: Energy Minimization 5

2.1 **Introduction to Basic Impact Applications** 5

2.2 **Common Features of Basic Impact Panels** 5

2.2.1 Source of Structure Input 5

2.2.2 Common Buttons 6

2.2.3 Starting Jobs 7

2.3 **The Energy Minimization Panel** 8

2.4 **The Potential Tab** 8

2.4.1 Potential Tab Methods 10

2.4.2 The Truncation Panel 11

2.4.3 The Fast Multipole Method Panel 12

2.4.4 The Periodic Boundary Conditions Panel 13

2.4.5 The Continuum Solvation Panel 14

2.5 **The Constraints Tab** 15

2.5.1 The Frozen Atoms Panel 16

2.5.2 The Constrained Atoms Panel 17

2.6 **The Minimization Tab** 19

Chapter 3: Molecular Dynamics Simulations 23

3.1 **The Constraints Tab** 24

3.2 **The MD Parameters Tab** 25

3.3 **The Dynamics Tab** 27

3.4 **The Replica Exchange Tab** 30

3.5 **Viewing Trajectories** 32

Chapter 4: Hybrid Monte Carlo Simulations 37

Chapter 5: Soak—Add Explicit Water Solvent 39

Chapter 6: Running Impact from the Command Line 41

6.1 Running Impact From the Command Line 41

6.2 File Name Conventions 43

Getting Help 45

Index 49

Document Conventions

In addition to the use of italics for names of documents, the font conventions that are used in this document are summarized in the table below.

Font	Example	Use
Sans serif	Project Table	Names of GUI features, such as panels, menus, menu items, buttons, and labels
Monospace	`$SCHRODINGER/maestro`	File names, directory names, commands, environment variables, command input and output
Italic	*filename*	Text that the user must replace with a value
Sans serif uppercase	CTRL+H	Keyboard keys

Links to other locations in the current document or to other PDF documents are colored like this: Document Conventions.

In descriptions of command syntax, the following UNIX conventions are used: braces { } enclose a choice of required items, square brackets [ ] enclose optional items, and the bar symbol | separates items in a list from which one item must be chosen. Lines of command syntax that wrap should be interpreted as a single command.

File name, path, and environment variable syntax is generally given with the UNIX conventions. To obtain the Windows conventions, replace the forward slash / with the backslash \ in path or directory names, and replace the $ at the beginning of an environment variable with a % at each end. For example, `$SCHRODINGER/maestro` becomes `%SCHRODINGER%\maestro`.

Keyboard references are given in the Windows convention by default, with Mac equivalents in parentheses, for example CTRL+H (⌘H). Where Mac equivalents are not given, COMMAND should be read in place of CTRL. The convention CTRL-H is not used.

In this document, to *type* text means to type the required text in the specified location, and to *enter* text means to type the required text, then press the ENTER key.

References to literature sources are given in square brackets, like this: [10].

Introduction to Basic Impact

Impact is a molecular mechanics and dynamics program that provides the molecular mechanics component of Glide, Liaison, and QSite calculations. Some of the basic capabilities of Impact are also available from Maestro. These capabilities include molecular mechanics (MM) energy minimization, molecular dynamics (MD) simulations, including temperature replica exchange, hybrid Monte Carlo (HMC) simulations, and addition of explicit water solvent to a structure.

For information related to the installation and use of Impact, see the following documentation:

- The *Installation Guide*, which includes installation instructions for all Schrödinger products and documentation.
- The *Impact Command Reference Manual,* which contains syntax and keywords for Impact command input files.
- The *Maestro User Manual*, which describes how to use the features of Maestro, including the Atom Selection dialog box. An appendix describes command-line utilities, some of which may be used with Liaison.
- The *Maestro Command Reference Manual*, which contains commands, options, and arguments for running Maestro from the command line, including the Atom Specification Language (ASL) and the Entry Specification Language (ESL).

1.1 Running Schrödinger Software

Schrödinger applications can be started from a graphical interface or from the command line. The software writes input and output files to a directory (folder) which is termed the *working directory*. If you run applications from the command line, the directory from which you run the application is the working directory for the job.

Linux:

To run any Schrödinger program on a Linux platform, or start a Schrödinger job on a remote host from a Linux platform, you must first set the `SCHRODINGER` environment variable to the

installation directory for your Schrödinger software. To set this variable, enter the following command at a shell prompt:

csh/tcsh: `setenv SCHRODINGER` *installation-directory*

bash/ksh: `export SCHRODINGER=`*installation-directory*

Once you have set the `SCHRODINGER` environment variable, you can run programs and utilities with the following commands:

```
$SCHRODINGER/program &
$SCHRODINGER/utilities/utility &
```

You can start the Maestro interface with the following command:

```
$SCHRODINGER/maestro &
```

It is usually a good idea to change to the desired working directory before starting Maestro. This directory then becomes Maestro's working directory.

Windows:

The primary way of running Schrödinger applications on a Windows platform is from a graphical interface. To start the Maestro interface, double-click on the Maestro icon, on a Maestro project, or on a structure file; or choose Start → All Programs → Schrodinger-2012 > Maestro. You do not need to make any settings before starting Maestro or running programs. The default working directory is the Schrodinger folder in your documents folder (Documents on Windows 7/Vista, My Documents on XP).

If you want to run applications from the command line, you can do so in one of the shells that are provided with the installation and that have the Schrödinger environment set up:

- Schrödinger Command Prompt—DOS shell.
- Schrödinger Power Shell—Windows Power Shell (if available).

You can open these shells from Start → All Programs → Schrodinger-2012. You do not need to include the path to a program or utility when you type the command to run it. If you want access to Unix-style utilities (such as `awk`, `grep`, and `sed`), preface the commands with `sh`, or type `sh` in either of these shells to start a Unix-style shell.

Mac:

The primary way of running Schrödinger software on a Mac is from a graphical interface. To start the Maestro interface, click its icon on the dock. If there is no Maestro icon on the dock, you can put one there by dragging it from the SchrodingerSuite2012 folder in your Applications folder. This folder contains icons for all the available interfaces. The default working directory

is the Schrodinger folder in your Documents folder (`$HOME/Documents/Schrodinger`).

Running software from the command line is similar to Linux—open a terminal window and run the program. You can also start Maestro from the command line in the same way as on Linux. The default working directory is then the directory from which you start Maestro. You do not need to set the `SCHRODINGER` environment variable, as this is set in your default environment on installation. If you need to set any other variables, use the command

`defaults write ~/.MacOSX/environment` *variable* `"`*value*`"`

1.2 Citing Impact in Publications

The use of this product and its components should be acknowledged in publications as:

Impact, version 5.8, Schrödinger, LLC, New York, NY, 2005.

Energy Minimization

2.1 Introduction to Basic Impact Applications

You can launch general-purpose Impact molecular mechanics calculations, called Basic Impact applications, from Maestro or from the command line, as described in Chapter 6. There are four Basic Impact applications:

- Energy Minimization
- Molecular Dynamics
- Hybrid Monte Carlo
- Soak

The common features of Impact panels and Impact Energy Minimization are described in this chapter; the other three applications are described in the chapters that follow.

For an extensive set of examples of input files for Basic Impact applications, see Appendix C of the *Impact Command Reference Manual*.

2.2 Common Features of Basic Impact Panels

Maestro panels for Basic Impact applications can be opened from the Impact submenu of the Applications menu. These panels have many common features. Some features described here appear in all panels; others are common to a subset of panels.

Controls that are specific to a panel appear in the middle section of the panel. Usually the controls will be contained in a series of tabs. Each tab contains settings relevant to the task that the panel performs.

2.2.1 Source of Structure Input

Use structures from

This option menu appears in all four Basic Impact panels. The options are:

Workspace (included entry)

This is the default option. The structure that is currently included in the Workspace is used as input to the job. This includes whatever atoms, molecules, or entries are part of the structure, even atoms that have been undisplayed. Calculations with Frozen or Constrained Atoms (see

the Constraints tab, Section 2.5 on page 15) requires that you use the Workspace structure to which the constraints have been applied.

Project Table (selected entry)

Select this option to use the entry that is currently selected in the Project Table. This may be different from the structure in the Workspace. Because atom constraints are applied to the Workspace structure, they are ignored if this option is chosen.

Input for Impact jobs from Maestro must be a single entry in the Project Table. To use a system consisting of two or more entries as the input, choose Merge from the Entry menu, create a combined entry, and run the job on that entry. If you want to run jobs with more than one structure, you can run them from the command line.

2.2.2 Common Buttons

In the lower part of most panels, the following buttons appear:

Start

Click the Start button to open the Start dialog box. Section 2.2.3 summarizes starting jobs using the Start dialog box.

Write

The Write button writes out all the files required for the job but does not actually start the job. Once the run files (an input file, *jobname*`.inp`, and one or more input structure files, *jobname_structure*`.maegz`) are written by Maestro, the job can be run from the command line in a terminal window using the syntax:

```
$SCHRODINGER/impact -i jobname.inp
```

where *jobname*`.inp` is the input file for the job in question. The log output will be written to *jobname*`.log` by default; a different filename can be specified via `-o` *othername*`.log`.

Type `$SCHRODINGER/impact -h` for a usage summary of the `impact` command, or see Chapter 6 for a discussion of running Basic Impact applications from the command line.

Close

The Close button, which is located on all Maestro panels, dismisses the current panel without starting the job or writing any files.

Help

The Help button opens your browser with an appropriate help topic displayed.

2.2.3 Starting Jobs

The features of the Start dialog box depend on the type of job which is being launched. The basic options include the following:

Output

The Start dialog box for Impact tasks includes an Output section containing one feature, the Incorporate option menu:

- Incorporate—Choose whether the new entries are appended to the Project Table, replace the existing entries, or are not incorporated into the Project Table at all.

Job

- Name—Type the name of the job in this text box, or accept the default name. When the job is started, the job name is used as the base name for files associated with the job. The Start dialog box for Impact jobs supplies an appropriate default name for each type of job (for example, `impact_soak`). However, a new default name is not automatically supplied each time you run a job of the same type. To avoid overwriting the job files from a job named `impact_soak`, use new names for the second and subsequent Soak jobs. You can also click Compose to compose a job name from an existing file name or a job name from the current project.

  Note: Impact does *not* automatically assign new names to jobs or files. If files of the same name exist, a warning is displayed before any files are overwritten.

- Host—Choose a host, if you want to run the job on a remote machine. This option menu displays all the hosts defined in the `$SCHRODINGER/schrodinger.hosts` file, with the number of processors on the host in parentheses. The default is `localhost`.
- Entry title—Enter the title that you want to use for the output structure in this text box.
- CPUs—Specify the number of CPUs to use to run the job.

Once you have finished setting these options, you can click Start to start the job.

2.3 The Energy Minimization Panel

The Impact Energy Minimization panel is used to set up and run an Impact energy minimization calculation on the structure in the Workspace or on an entry selected in the Project Table.

Note: *Only one entry from the Maestro Project Table can be displayed and used for each minimization job.* If you need to minimize a system that spans two entries, use the Project Table's Merge option to create a combined entry, and use that as the basis for your simulation.

To open the Impact Energy Minimization panel, choose Minimization from the Impact submenu of the Applications menu in the main window.

The Energy Minimization panel has three tabs:

- Potential
- Constraints
- Minimization

All three tabs are described in detail in this chapter. The first two tabs also appear in the Maestro panels of two other Basic Impact applications: Molecular Dynamics Simulations and Hybrid MC Simulations.

2.4 The Potential Tab

The Potential tab sets parameters that control how Impact calculates the molecular-mechanics energy in a minimization calculation or dynamics simulation. This tab is included in the Impact Minimization, Impact Molecular Dynamics, and Impact Hybrid Monte Carlo panels. The options in the Potential tab are described below.

Force field option menu

The molecular-mechanics force field to use for the calculation is chosen from this menu. Only OPLS-AA force fields are available: the options are

- OPLS_2001
- OPLS_2005 (the default)

For calculations that use Surface Generalized Born (SGB) continuum solvation, you may want to select the OPLS_2005 force field. With this force field, the improved parameterized nonpolar model (input file keyword `npsolv`) is used instead of the default SGB terms.

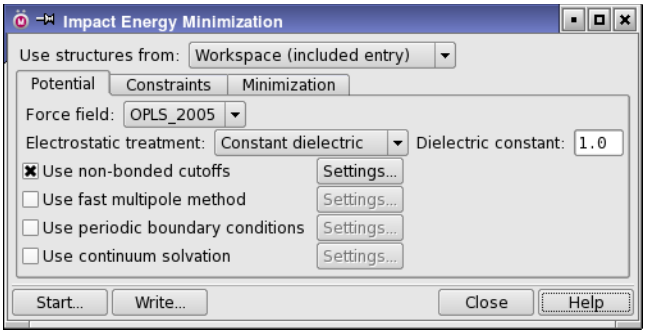

Figure 2.1. The Potential tab of the Impact Energy Minimization panel.

Electrostatic treatment

This option menu offers two methods for calculating the electrostatic component of the energy:

- Constant dielectric

  This option calculates the electrostatic interaction between atoms *i* and *j* as:

  $$E_{ele} = 332.063762\ q_i q_j/(\varepsilon\ r_{ij})$$

  A constant dielectric is appropriate for a vacuum (gas-phase) calculation or when an explicit or implicit solvent model is used.

- Distance dependent dielectric

  This option calculates the electrostatic interaction between atoms *i* and *j* as:

  $$E_{ele} = 332.063762\ q_i q_j/\varepsilon\ r_{ij}^2$$

  A distance-dependent dielectric is sometimes used as a primitive model for the effect of solvent. In this model, the electrostatic interaction between a pair of atoms falls off rapidly as the distance between the atoms increases. However, continuum and explicit solvent models are much better at accounting for solvent effects than a distance-dependent dielectric.

The variables in the above formulae are defined as follows:

- E_{ele} is the electrostatic interaction in kcal/mol
- q_i and q_j are the partial atomic charges on atom *i* and *j*
- r_{ij} is the distance in Å between atoms *i* and *j*
- ε is the Dielectric constant (see below)

Dielectric constant

This text box specifies the value of the dielectric constant ε used in the electrostatic treatment.

2.4.1 Potential Tab Methods

The lower part of the Potential tab allows you to choose among molecular mechanics treatments. When the check box for a method is selected, clicking the associated Settings button opens a panel of relevant options. The methods are listed briefly in this section, and then each Settings panel is described in more detail.

Use non-bonded cutoffs

In molecular-mechanics calculations it is often impractical to include the nonbonded (electrostatic and van der Waals) interactions between every pair of atoms. For large systems, many such pairs are separated by a great distance and contribute little to the interaction energy. Judicious truncation of the non-bonded interactions between widely separated pairs of atoms is an important strategy for reducing the resources needed for calculations on large systems.

The default is to use non-bonded cutoffs. The Settings button for this option opens the Truncation panel, in which settings for non-bonded cutoffs can be specified.

Use fast multipole method

The Fast Multipole Method (FMM) is an algorithm for speeding up the electrostatic part of the molecular mechanics calculation for large systems. It is generally used for systems without periodic boundary conditions, where Ewald summation cannot be used, and for periodic boundary explicit solvent simulations with more than 20,000 atoms.

The Settings button for this option opens the Fast Multipole Method panel (see below).

Note: The Truncated Newton (TN) minimization method and the SGB and AGB continuum solvation methods are not available for use with the Fast Multipole Method.

Use periodic boundary conditions

Periodic boundary conditions are commonly used for calculations with explicit solvent, but can be employed for any periodic system.

The Settings button for this option opens the Periodic Boundary Conditions panel (see below).

Use continuum solvation

Three implicit solvent models, Surface Generalized Born (SGB), Analytic Generalized Born (AGB), and Poisson-Boltzmann (PBF) are available in Impact. (SGB is not available if FMM has been selected.) These methods account for the effects of solvent without the use of explicit water molecules. For details on these models, see the *Impact Command Reference Manual*.

The Settings button for this option opens the Continuum Solvation panel, in which the choice of implicit solvation method and other settings relevant to continuum solvation can be specified.

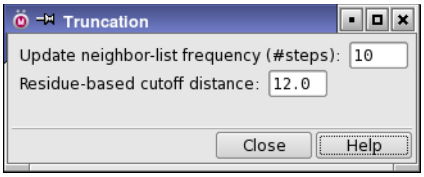

Figure 2.2. The Truncation panel.

2.4.2 The Truncation Panel

The Truncation panel defines the non-bonded cutoffs settings for an Impact calculation.

When sufficient care is taken, the use of non-bonded cutoffs to remove interactions between widely separated pairs of atoms is an important strategy for reducing the resources required to perform calculations on large systems. At present only residue-based cutoffs are supported for calculations set up in Maestro. This means that all atoms within complete residues that have any pair of atoms within the cutoff distance will be included in the non-bonded interaction list.

To open the Truncation panel, select Use non-bonded cutoffs and click the adjacent Settings button. The selection options in the Truncation panel are:

Update neighbor-list frequency (# steps) text box

When truncation is active, all the pairs that fall within the cutoff radius are stored in a "neighbor list". During a minimization calculation or dynamics simulation, the geometry of the structure may change so as to bring some pairs of atoms that were originally outside the cutoff distance to within the cutoff. Conversely, some pairs of atoms may move outside the cutoff distance. For these reasons, the neighbor list needs to be updated from time to time. The frequency of this update is controlled by this integer field. By default the neighbor list is updated every 10 minimization or dynamics steps. Increasing this value (updating the neighbor list *less* often) will speed up the calculation but may affect the accuracy of the results. Decreasing this value (updating the neighbor list *more* often) will slow down the calculation but may improve the accuracy.

Residue-based cutoff distance

This text box specifies the value for the cutoff distance. Increasing the cutoff distance will slow the calculation and require more memory, but may yield more accurate results. Decreasing the cutoff will speed up the calculation, but may reduce the accuracy of the results if significant non-bonded interactions are omitted. This is especially true for systems that include formally charged atoms, as such systems can have large long-range electrostatic interactions.

2.4.3 The Fast Multipole Method Panel

For large systems, the Fast Multipole Method (FMM) speeds the evaluation of the electrostatic and van der Waals parts of the molecular-mechanics energy by using interacting hierarchical multipoles to approximate the true electrostatic potential.

In systems where long-range electrostatic effects are important, the Fast Multipole Method or Ewald summation can be used to approximate these forces. For systems of fewer than 20,000 atoms, with explicit solvent and periodic boundary conditions, Ewald summation is typically used. At about 20,000 atoms, the Fast Multipole Method becomes faster than Ewald summation: FMM calculations scale linearly with the number of atoms N, while Ewald summation scales as N^2. FMM is also used for systems to which periodic boundary conditions cannot be applied, where Ewald summation cannot be used.

If the Fast Multipole Method is to be used with periodic boundary conditions:

- The simulation box must be a cube. Ensure that the Box [X,Y,Z] length values in the Periodic Boundary Conditions panel are equal.
- The system must be electrically neutral (the sum of all point charges must be zero).

The Fast Multipole Method cannot be used with the Truncated Newton minimization algorithm or with SGB continuum solvation.

To open the Fast Multipole Method panel, select Use fast multipole method and click the adjacent Settings button. The following options can be set:

Level

This text box sets the number of levels in the hierarchical tree used in the FMM calculation. This setting is relevant only when the reversible RESPA integrator is used with more than two inner stages. (See Section 3.2 on page 25.)

The Level parameter specifies the number of times the simulation box is divided into halves along each direction, a procedure known as octree decomposition. If a Level of 1 is set, one division is made along X, one along Y, and one along Z, so that the box is divided into 8 subcubes (octants). If Level=2 (the default), each sub-cube is further divided into 8 smaller cubes,

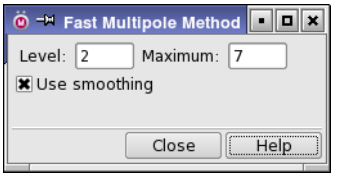

Figure 2.3. The Fast Multipole Method panel.

for a total of 64, and so on. The value of Level should be at least 2: larger values yield increased accuracy at the cost of longer execution time, but may be useful in very large systems.

Maximum

This text box sets the maximum number of multipole moments to be used to approximate the potential and field produced by "far" clusters. Currently a minimum of 4 multipoles and a maximum of 20 multipoles are permitted; the default is 7.

Use smoothing

This option, selected by default, specifies the use of a smooth cutoff to separate into "near" and "far" components the forces that are computed explicitly from Coulomb's Law, rather than from the multipole expansions. This setting is relevant only when the reversible RESPA integrator is used with more than two inner stages. (See Section 3.2 on page 25.)

2.4.4 The Periodic Boundary Conditions Panel

Impact calculations can be performed with periodic boundary conditions. This technique is usually applied with explicit solvent in order to avoid nonphysical "edge effects." The system of interest is defined to be in a box of a given size, images of which are replicated throughout space to form an infinite 3D lattice.

The options in this panel allow you to set the size of the simulation box and to select and specify parameters for the Ewald summation method, which is used to efficiently sum long-distance electrostatic interactions in periodic systems. (This option cannot be used if you have selected Use fast multipole method.)

To open the Periodic Boundary Conditions panel, select Use periodic boundary conditions, then click the adjacent Settings button. The options of this panel are described below.

Box [X,Y,Z] lengths

Use these three text boxes to set the size of the simulation box. The minimum size for any dimension that Maestro will use is 18.65 Å, which is also the default in each dimension.

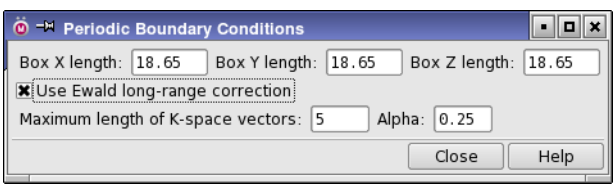

Figure 2.4. The Periodic Boundary Conditions panel.

Use Ewald long-range correction

Click to select the Ewald summation method for efficiently summing long-distance electrostatic interactions in periodic systems. Unlike the Fast Multipole Method, Ewald summation does not require the net charge of the system to be zero. This setting is ignored when the Fast Multipole Method is used.

- Maximum length of K-space vectors

  If Use Ewald long-range correction is selected, you can use this text box to specify the number of component terms to retain in the reciprocal-space part of the summation. The default value is 5. Larger values yield increased accuracy but result in slower execution.

- Alpha

  If Use Ewald long-range correction is selected, you can use this text box to set the value of the a parameter. A reasonable value is 5.5/*L*, where *L* is the length of the cubic simulation box. The default value is 0.25.

2.4.5 The Continuum Solvation Panel

Impact supports three implicit solvent models, the Surface Generalized Born (SGB) model, the finite-element Poisson-Boltzmann Solver (PBF), and the Analytic Generalized Born (AGB) model. These methods simulate the effects of solvent without using explicit solvent molecules.

To open the Continuum Solvation panel, select Use continuum solvation and click the adjacent Settings button. The options of this panel are described below.

Solvation Method

From this option menu you can choose from the three continuum solvation models: Surface Generalized Born Model, Poisson Boltzmann Solver, and Analytic Generalized Born. If you use SGB solvation, you might want to select the OPLS_2005 or OPLS_2008 force field in the Potential tab; the improved parameterized nonpolar model (input file keyword `npsolv`) will then be used instead of the default SGB terms.

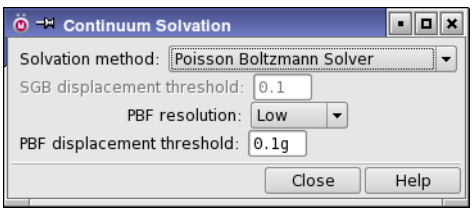

Figure 2.5. The Continuum Solvation panel.

SGB Displacement Threshold

When the Solvation method chosen is Surface Generalized Born Model, this text box specifies how far (in Å) any atom may move from the coordinates used in the previous SGB calculation before a new SGB calculation must be performed. If no atom has moved this distance, the previously calculated SGB energy and forces are used.

PBF Resolution

The Poisson-Boltzmann solver involves a finite-element calculation on a grid. The grid spacing controls both the accuracy of and time required for the PBF calculation. The default is to use a Low resolution grid, which should suffice for most protein work. If needed, greater accuracy can be achieved by setting this option menu to Medium or High.

PBF Displacement Threshold

This text box specifies how far (in Å) any atom may move from the coordinates used in the previous PBF calculation before a new PBF calculation must be performed. If no atom has moved this distance, the previously calculated PBF energy and forces are used.

2.5 The Constraints Tab

The Constraints tab of the Impact Energy Minimization panel is used to set up Impact *atom constraints.* These include constraints that freeze selected atoms at their input coordinates (frozen atoms) or keep them near their initial coordinates by applying a harmonic force (constrained atoms). Frozen atoms and constrained atoms can also be specified for Impact Molecular Dynamics (MD) and Impact Hybrid Monte Carlo (HMC) simulations, Liaison simulations, and QSite calculations, using the Constraints tabs in those panels.

The Constraints tabs in the Impact Dynamics and Impact Hybrid Monte Carlo panels can also be used to set up *bond constraints.* The MD and HMC simulations set up using these panels can use the SHAKE/RATTLE algorithm to constrain all bond lengths to ideal or reference values. Bond constraints are not available for Impact energy minimization calculations, and the Constraints tab of the Impact Energy Minimization panel does not include bond constraint options; these options are described in Chapter 3.

In the Impact and Impact Energy Minimization panels, the Constraints tab contains only two buttons: the Frozen Atoms button and the Constrained Atoms button.

Frozen Atoms

Impact calculations can be performed with some atoms completely “frozen” so that they never move from their initial position during minimization or dynamics. Click this button to open the Frozen Atoms panel, in which you can select the atoms to be treated as frozen.

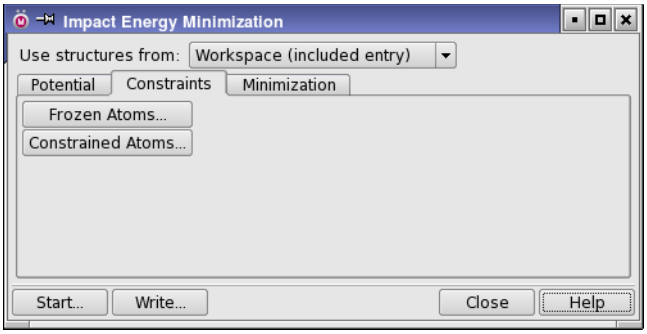

Figure 2.6. The Constraints tab of the Impact Energy Minimization panel.

Constrained Atoms

Click this button to open the Constrained Atoms panel, in which you can select the atoms to be treated as "constrained". Constrained atoms are allowed to move, subject to harmonic penalty-function restraints that tether them elastically to their initial positions.

Note: The selection of atoms to be frozen or constrained applies only to the structure included in the Workspace when you make your selection. To apply the constraints, you must choose Workspace (included entry) as the source of structures (Use structures from option.)

2.5.1 The Frozen Atoms Panel

Use the Frozen Atoms panel to specify a set of atoms to be frozen during an Impact minimization calculation or dynamics simulation. Open the Frozen Atoms panel by clicking the Frozen Atoms button in the Impact Constraints tab.

The features of this panel are described below.

Frozen atoms list

The upper portion of the Frozen Atoms panel is a text area that lists the atom number of each atom that has been selected to be frozen.

Define frozen atoms

In this section you can specify atoms to be frozen using the standard picking controls: the Pick check box and menu, which is set to Atoms by default; the All button; and the Atom Selections button menu, which has predefined atom selections, and also opens the Atom Selection dialog box.

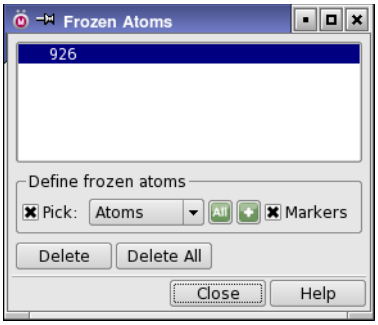

Figure 2.7. The Frozen Atoms panel.

Markers option

This option is selected by default. The atoms to be frozen are marked with a red cross and a "padlock" icon in the Workspace display. To distinguish the currently selected frozen atom, Maestro colors the marker turquoise. Markers may be inconvenient if you are selecting large numbers of atoms. To hide or remove the markers, deselect the option.

Delete

Click this button to remove the currently selected frozen atom from the frozen atoms list.

Delete All

Click this button to remove all currently defined frozen atoms from the frozen atoms list.

2.5.2 The Constrained Atoms Panel

You can use the Constrained Atoms panel to specify a set of atoms to be harmonically restrained during a molecular mechanics calculation. Such atoms are referred to as "constrained" atoms to distinguish them from "frozen" (completely fixed) atoms. To open the Constrained Atoms panel, click the Constrained Atoms button in the Constraints tab.

Constrained atoms list

The upper part of the Constrained Atoms list displays the list of atom numbers that have been selected to be constrained (restrained with a harmonic potential).

Constraining force

This text box sets the value of the harmonic force constant applied to the selected constrained atoms. The same force constant is used for all atoms. The default is 25.00 kcal/(Å^2 mol).

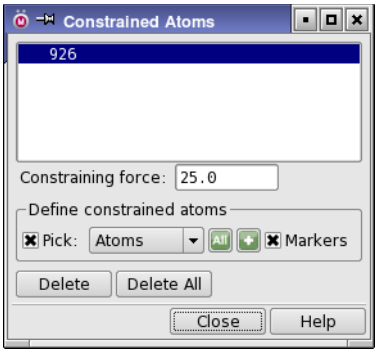

Figure 2.8. The Constrained Atoms panel.

Define constrained atoms

In this section you can specify atoms to be constrained using the standard picking controls: the Pick check box and menu, which is set to Atoms by default; the All button; and the Atom Selections button, which has predefined atom selections, and also opens the Atom Selection dialog box.

Markers

This option is selected by default. The atoms to be constrained are marked with a brown cross and a "spring" icon in the Workspace display. To distinguish the currently selected constrained atom, Maestro colors the marker turquoise. Markers may be inconvenient if you are selecting large numbers of atoms. To prevent markers being added, or to remove the markers, deselect the option.

Delete

Click this button to remove the selected constrained atom from the constrained atoms list.

Delete All

Click this button to remove all defined constrained atoms from the constrained atoms list.

2.6 The Minimization Tab

The basic settings of the Impact energy minimization task are defined in the Minimization tab. You can use this tab to set options for an Impact energy minimization calculation on the structure specified in the Use structures from option menu in the Impact Energy Minimization panel. The Impact Minimization tab is available in the Impact Energy Minimization panel.

Note: In Liaison, minimization options for simulations are available in the Parameters tab.

The options available in this tab are described below.

Maximum minimization cycles

This text box sets the maximum number of cycles for the minimization calculation. The minimization terminates if it has not converged by this point. The default value of this setting is 100 iterations, but you can specify any value greater than or equal to zero. "Zero cycles" is a special case; it instructs Impact just to evaluate the energy for the current coordinates.

Algorithm

This option menu selects the minimization algorithm. The choices are:

- Truncated Newton (TN). This is a very efficient method for producing optimized structures and is the current default selection. A short conjugate gradient pre-minimization stage is performed first to help improve the convergence of the Truncated Newton algorithm. There are some restrictions on the use of this algorithm:
  - It is not available with the fast multipole method (FMM) or with periodic boundary conditions (PBC).
  - It is only available with the generalized Born (SGB and AGB) continuum solvation methods. It is not available with explicit solvent models, such as set up in the Soak panel.
- Conjugate gradient. This is a good general optimization method.
- Steepest descent. This can be a good method for initiating a minimization on a starting geometry that contains large steric clashes. Convergence is very poor towards the end of minimization, where the conjugate gradient algorithm should be used.

Initial step size

This text box specifies the initial step size of the minimization cycle for conjugate gradient and steepest descent minimizations. The default value is 0.05 Å, but any positive value is allowed.

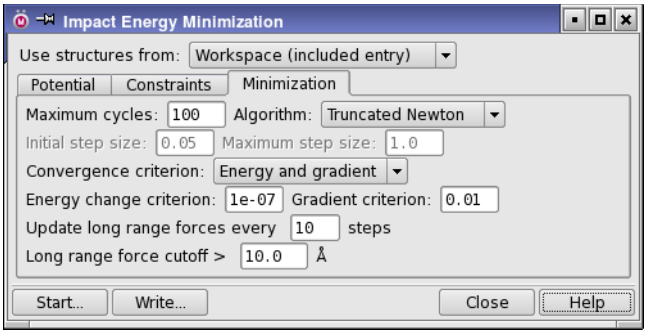

Figure 2.9. The Minimization tab of the Impact Energy Minimization panel.

Maximum step size

This text box specifies the maximum step size of the minimization cycle for conjugate gradient and steepest descent minimizations. If the step size exceeds this value, the minimization will halt. The default value is 1.00 Å, but any positive value is allowed. The maximum step size is the maximum displacement allowed for an atom in any step of a minimization calculation.

Convergence criteria

This option menu sets the convergence criteria for the minimization. Either or both of two criteria—energy change and gradient—can be specified. Thus, the options are:

- Energy and Gradient. Choosing this option allows access to both the Energy change criteria and Gradient criteria text boxes.
- Energy change criteria. Use this text box to specify the value of the energy change criterion. The default value is 10^{-7} kcal/mol, but any positive value is allowed. The criterion is applied to the average energy per atom, and is satisfied if two successive average energies differ by less than the specified value.
- Gradient criteria. Use this text box to specify the value of the gradient criterion. The default value is 0.01 kcal/(mol∗Å), but any positive value is allowed. The criterion is satisfied if the norms of two successive gradients differ by less than the specified value.

Long-range forces options (for Truncated Newton minimizations):

- Update long range forces every *n* steps. Use this text box, when Truncated Newton minimization is selected, to specify the frequency with which long range forces are updated. Between these intervals, estimates of these forces are used. Every 10 steps is the default; smaller numbers (more frequent updates) can be used to improve convergence, but will make the optimization slower. Larger numbers for n may speed the calculation, but the maximum recommended value is 20.

- Long range force cutoff > *d* Angstroms. Use this text box, when Truncated Newton minimization is selected, to specify the distance beyond which forces are considered long range and are therefore updated every n steps. The default value is 10.000 Å.

Molecular Dynamics Simulations

You can use the Dynamics panel to set up and run a Molecular Dynamics (MD) simulation on the Workspace structure. Molecular Dynamics simulations examine stable, ground state molecules by applying Newton's equations of motion. The constant volume and temperature (NVT) ensemble is the default ensemble for MD simulations. The constant volume and energy (NVE) and constant pressure and temperature (NPT) ensembles are also supported, as is temperature replica exchange.

NPT simulations require the use of periodic boundary conditions (see Section 2.4.4 on page 13). Such calculations often, but not always, use explicit solvent (see Chapter 5).

To open the Dynamics panel, choose Dynamics from the Impact submenu of the Maestro Applications menu. The Dynamics panel has the following tabs:

- Potential
- Constraints
- MD Parameters
- Dynamics
- Replica Exchange

The Potential and Constraints tabs are described in Chapter 2. The Constraints tab in the Dynamics panel includes features not available for energy minimization or Impact. These features are described here, along with the MD Parameters tab, and the Dynamics tab, and the Replica Exchange tab.

When you have set the options in the Dynamics panel tabs to the desired value, click the Start button to open the Impact Dynamics - Start dialog box. The standard job start options are displayed, including the Incorporate option menu and the Job options: Name, Host machine. For a description of these options, see Section 2.2.3 on page 7. The default job name for Impact Molecular Dynamics jobs is `impact_dyn`.

The input for an Impact Molecular Dynamics job can be either the contents of the Workspace or a single entry in the Project Table.

Note: *Only one entry from the Maestro Project Table can be displayed and used for each dynamics job.* If you need to merge two entries, use the Project Table's Merge option to create a combination entry, and use that as the basis for your simulation.

3.1 The Constraints Tab

In addition to the features described in Section 2.5 on page 15, the following features appear in the Constraints tab in the Impact Dynamics and HMC calculations:

Constrain all bonds

When this option is selected, all bond distances are constrained to their "ideal" values as defined by the molecular force field, using SHAKE to constrain the bond length and RATTLE to remove the relative motion (velocity) of the bonded atoms along the interatomic axis.

By default, Constrain all bonds is selected in the Impact Dynamics panel, but not selected in the Impact Hybrid Monte Carlo panel.

Make water molecules rigid

When this option is selected, the internal coordinates of water molecules are constrained to their "ideal" values as defined by the molecular force field. If you select Constrain all bonds, the HO distances are fixed but the HOH angles are not. This option adds the HH distances and the HO distances to the SHAKE distance constraints list, so that the water molecules become rigid. (The HO distances are not added if they are already in the list).

By default, Make water molecules rigid is selected in the Impact Dynamics panel, but not selected in the Impact Hybrid Monte Carlo panel.

SHAKE tolerance

This text box sets the tolerance for the SHAKE/RATTLE algorithm. The default value is 10^{-7} Å for SHAKE and 10^{-7} Å/ps for RATTLE. Increasing the tolerance will speed the calculation at the cost of allowing greater variation from the ideal values. Any value greater than zero is

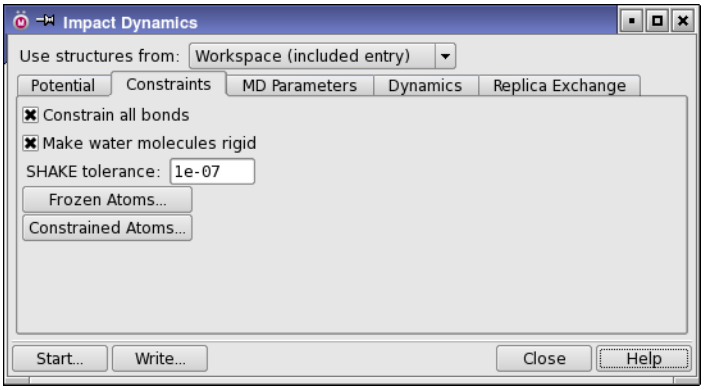

Figure 3.1. The Constraints tab of the Impact Dynamics panel.

allowed. Note that the same numeric value is used for both tolerances, even though the units are different.

3.2 The MD Parameters Tab

In the MD Parameters tab you can specify molecular dynamics settings that affect both Molecular Dynamics (MD) and Hybrid Monte Carlo (HMC) calculations (see Chapter 4). The options are described below.

Integration algorithm

This option menu specifies the integration algorithm employed to integrate the Equations of Motion (EOM). The options are Verlet and RRESPA. There are no other settings to specify for the Verlet option. When RRESPA is selected, three other text boxes become active, as noted below.

- Verlet. The widely used velocity Verlet integration algorithm is the default for integrating the equations of motion in standard Cartesian-space molecular dynamics.
- RRESPA. The Reversible REference System Propagator Algorithm), the other choice offered by Impact for integrating the EOM, can be much more efficient. By breaking up the integration into large, medium, and small time steps (see the RRESPA update frequencies text boxes), this integrator devotes appropriate computational power to specific classes of forces—and thus keeps the calculation from being dominated by the small time steps needed to accurately integrate the fast motions (such as bond stretches). In particular, RRESPA integrates the fast motions with small time steps and the slow motions (far more numerous) with larger time steps.

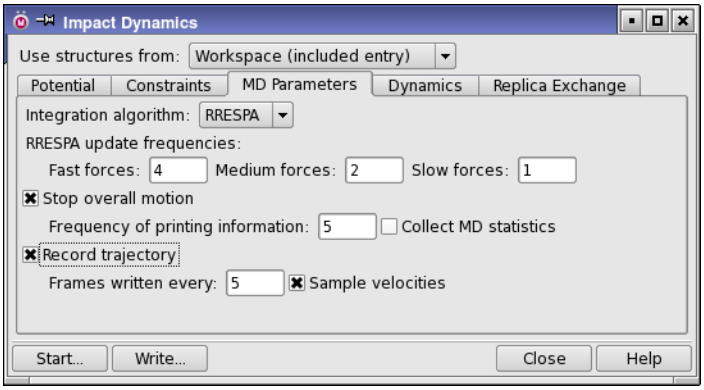

Figure 3.2. The MD Parameters tab of the Impact Dynamics panel.

- RRESPA update frequencies. If you select RRESPA, text boxes for Fast forces, Medium forces, and Slow forces are enabled.

  When the Fast Multipole Method (FMM) is also used, the forces are separated into three groups: those arising from well-separated bodies, those arising from first and second neighbors that are not very close, and those coming from the local expansions, which include bonded terms.

  Table 3.1. RRESPA text boxes

Force	Interacting Species	Default Setting
Fast	Bonded and short-distance electrostatics	4
Medium	1^{st} and 2^{nd} neighbors that are not close	2
Slow	Long-distance non-bonded	1

  All text boxes have acceptable ranges of any integer value greater than one. These entries modify the time step for the underlying MD or HMC simulation in the following way. Suppose that the global Time step specified in the Dynamics tab of the Impact Dynamics panel or the Hybrid MC tab of the Impact Hybrid Monte Carlo panel is δ. Then the time step used to integrate the slow forces is $\delta/1$, while the time step for medium forces is $\delta/(1 \times 2)$, and that for fast forces is $\delta/(1 \times 2 \times 4)$. Thus, the integration time step decreases as the product of the cumulative RRESPA update frequencies in going from slow to fast forces.

  When FMM is not used (this is the more common case), only the Fast forces update frequency affects the calculation. In this case, the Medium and Slow forces are combined and use the global Time step set in the Dynamics tab of the Impact Dynamics panel or in the Hybrid MC tab of the Impact Hybrid Monte Carlo panel. Fast forces use the shorter time step computed by dividing the global Time step by the Fast forces update frequency.

Stop overall motion

When this option is selected (the default), overall rotational and translational motion (drift) of the system is subtracted from the calculation.

Frequency of printing information

This text box selects the frequency with which MD information is written during the simulation. The default is to print information every 5 MD steps. Any integer value greater than zero is allowed.

Collect MD statistics

This option is deselected by default. When it is selected, the MD statistics are collected and are written to the end of the Impact output file. These statistics measure fluctuations of the different energy terms.

Record trajectory

This option is deselected by default. When it is selected, trajectory information is written to the file *jobname*`.trj` in the Maestro working directory. This information is written in binary format, but can be analyzed using the `ANALYSIS` task of Impact (which is not, however, supported by Maestro). A trajectory file contains a sequence of snapshots of the coordinates of the system and, if requested, of the velocities as well.

Note: The Impact analysis task must be run using Impact from the command line. See Chapter 6 for a brief overview of command-line Impact. See the *Impact Command Reference Manual* for additional information.

You can view trajectories in Maestro using the Trajectory panel. When the results are incorporated into the project, click the T button in the Title column of the Project Table for the incorporated entry to open the panel. See Section 3.5 on page 32 for more information.

The following two options are applicable when Record trajectory has been selected:

Frames written every

This text box specifies how often trajectory information is written to the trajectory file. The default is every 5 MD steps. Any integer value greater than zero is allowed.

Sample velocities

This option is on by default. When it is selected, velocity information is written to the trajectory file.

3.3 The Dynamics Tab

Use the Dynamics tab to choose the ensemble type, number of steps, time step, and other settings for a molecular dynamics calculation. The major options are described below. The other options in this tab are described under the major option to which they apply.

Number of MD steps

This text box sets the number of MD steps to be used for the simulation. The default setting is 100 steps, but any number greater than zero is allowed.

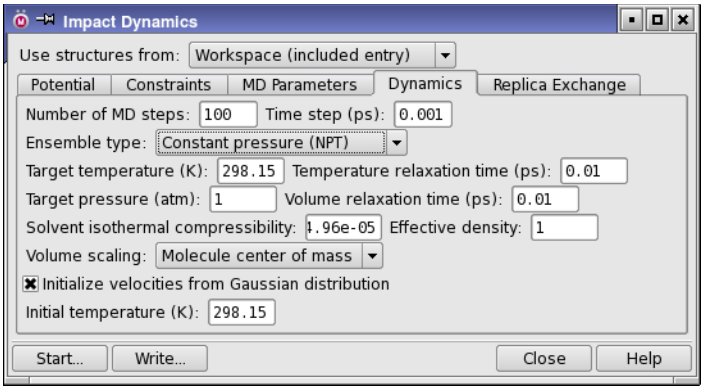

Figure 3.3. The Dynamics tab of the Impact Dynamics panel.

Time step

This text box sets the time step for the MD simulation. The default value is 0.001 ps, but any value greater than zero is allowed. A somewhat larger value (0.0015 or 0.002) may be suitable if bond lengths are constrained (see Section 3.1 on page 24) or if the RRESPA integrator is employed (see the MD Parameters tab in Section 3.2 on page 25).

Ensemble type

Impact offers three choices:

- Constant temperature (NVT)
- Constant energy (NVE)
- Constant pressure (NPT)

Depending on the ensemble chosen, various subsidiary settings become active.

Constant temperature (NVT) (the default)

With this ensemble type, volume and temperature are held constant during the simulation. This selection simulates coupling the system to an external heat bath (with a target temperature that is the same for all molecular species). Two settings become available when this ensemble type is chosen:

- Target temperature (K)—This text box sets the target temperature for an NVT or NPT simulation. The actual temperature will fluctuate about the specified value. At each MD step the velocities will be scaled so that the temperature will approach the desired value on a time scale determined by the Temperature relaxation time parameter. The default temperature is 298.15 K; the acceptable range is any value greater than or equal to 0 K.

- Temperature relaxation time (ps)—This text box sets the temperature relaxation time in picoseconds for velocity scaling. The default value is 0.01 ps; the acceptable range is any value greater than zero.

Constant energy (NVE)

With this ensemble, no temperature, volume, or pressure scaling is done. However, the total energy may not be conserved if nonbonded interaction cutoffs or too long an MD time step is used. In most cases, failure of energy conservation will lead to an unstable MD simulation. It is recommended that for this ensemble you deselect the nonbonded cutoffs option in the Potential tab, which is selected by default.

Constant pressure (NPT)

For this ensemble, both temperature and pressure are held constant during the simulation. This is accomplished by also coupling the system to a pressure bath using the algorithm of Berendsen et al. (*J. Chem. Phys*. **1984**, *81*, **3684**). Seven settings become available when this ensemble type is chosen. Along with Target temperature and Temperature relaxation time, described above, these are:

- Target pressure (atm)—This text box specifies the desired pressure in atmospheres. The actual pressure will fluctuate about the desired value. At each MD step the system will be scaled such that the pressure will approach the desired value on a time scale determined by the Volume relaxation time parameter. The default pressure value is 1 atm; the acceptable range is any positive or negative real value.
- Volume relaxation time (ps)—This text box sets the volume relaxation time in picoseconds for volume scaling in a constant pressure MD simulation. The default value is 0.01 ps; the acceptable range is any value greater than zero.
- Solvent isothermal compressibility—Isothermal compressibility or *k* (*1/V(dV/dP)*, in units of atm^{-1}) is the pressure analogue of the heat capacity and relates to the tendency of the solvent's volume to increase or decrease during pressure fluctuations in the system. The default is the value for water: $4.96x10^{-5}$ atm^{-1}; the acceptable range is any value greater than zero.
- Effective density—This text box specifies the effective density (g/cm^3) of solute molecules. This quantity is used to compute long-range corrections to the pressure during NPT molecular dynamics simulations. The default value is 1.0 g/cm^3; the acceptable range is any value greater than zero.

- Volume scaling

  Select one of two options for volume scaling in a MD simulation:

  - Molecule center of mass—This method of volume scaling, the default, is best for small molecules and is implemented by scaling the coordinates of the center of mass for each molecular species, relative to the center of the simulation box.
  - Atom based—This method of volume scaling is best for large molecules and is implemented by uniformly scaling all atomic coordinates relative to the center of the simulation box.

Initialize velocities from Gaussian distribution

When this option, available for all three ensembles, is selected, molecular velocities will be initialized as described, and the Initial temperature text box becomes available.

Initial temperature

When Initialize velocities from Gaussian distribution is selected, this text box specifies the initial temperature for the MD simulation. The default value is 298.15 K; the acceptable range is any value greater than or equal to 0 K.

3.4 The Replica Exchange Tab

Impact supports state-of-the-art temperature replica exchange simulations. These simulations can be run in parallel, using the MPI message passing interface. Use the Replica Exchange tab to set up the number of replicas, the number of steps between exchanges and the temperature settings.

Note: Replica exchange calculations are only supported on Linux-x86 platforms.

The options are described below.

Replica exchange MD

Select this option to enable the use of replica exchange. When you do so, the remaining controls in the tab become available.

Number of replicas

Enter the desired number of replicas in this text box. The maximum allowed is 100.

Number of MD steps between exchanges

Enter the number of MD steps to take between exchanges of replicas.

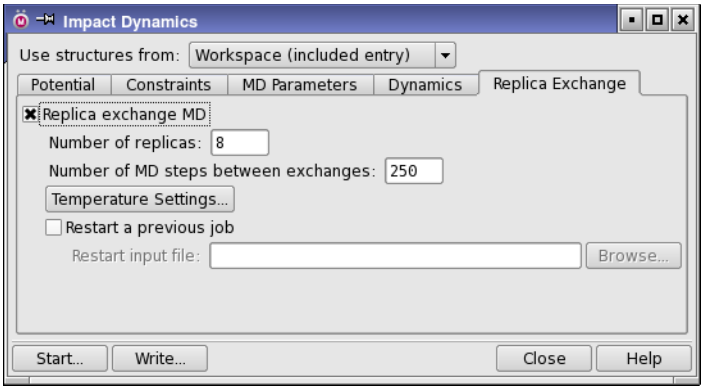

Figure 3.4. The Replica Exchange tab of the Impact Dynamics panel.

Temperature Settings

This button opens the Temperature Settings dialog box, in which you can set the target temperature for each replica and select the temperature of interest. The dialog box has the following options:

- Temperature—Enter the temperature for each replica in these text boxes. The temperatures must be entered in increasing order. The default value for the first temperature is 300 K.
- Temperature of interest—Use one of these buttons to select the temperature of interest. Only one temperature can be selected. This is the temperature of the replica whose trajectory will be incorporated into Maestro at the end of the job.

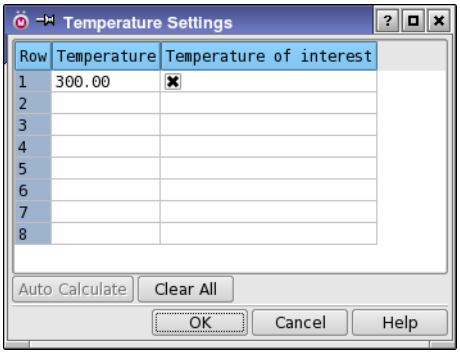

Figure 3.5. The Temperature Settings dialog box.

- Auto Calculate—Calculate the temperatures as a geometric series. This button becomes available when the first two temperatures have been entered. These temperatures define the ratio that is used to generate all the other temperatures.
- Clear All—Clear all the temperature text boxes.

Restart a previous job

Select this option to restart a calculation using the reference structure output from a previous replica exchange job. You can change parameters except for the temperature settings and the number of replicas.

Restart input file

Enter the name of the reference structure output file you want to use to restart the job, or click Browse and navigate to the output file. The file should normally end in `-out.maegz`.

3.5 Viewing Trajectories

You can play through trajectories, examine individual frames, and export trajectory data in a variety of forms, in the Trajectory panel. To open the Trajectory panel, click the T button in the Title column of the Project Table for the entry whose trajectory you want to view.

If you have entries in the Workspace, a panel opens asking if you want to keep them in the Workspace while the trajectory is played, or to remove them. Keeping the entres in the Workspace allows you to view the trajectory against a fixed background. You can superimpose the trajectory atoms on the background, and you can set up measurements, such as H-bonds, between the background atoms and the trajectory atoms, which are updated during play.

The toolbar in the Trajectory panel contains a standard set of controls for playing through the trajectory frames, which are listed below. The menu bar has one menu, Play, which contains items that correspond to the toolbar buttons.

Go to start
Display the first frame.

Previous
Display the previous frame.

Play backward
Display the frames in sequence, moving toward the first.

Stop
Stop playing through the frames.

Play forward
Display the frames in sequence, moving toward the last.

Next
Display the next frame.

Go to end
Display the last frame.

Loop
Choose an option for repeating the display of the frames. Single direction displays frames in a single direction, then repeats. Oscillate reverses direction each time the beginning or end of the frame set is reached.

You can control the selection of frames and the speed of play in the Frame control section of the panel.

- The Start and End text boxes define the frames at which play starts and ends. Frames are numbered from 0.
- The Frame slider and frame text box can be used to select the frame to view. The current frame number is displayed in the text box below the slider. The total number of frames is also displayed in a noneditable text box.
- The Step text box sets the number of frames to step when playing through frames. This value does not affect the Frame slider. The frames that are selected for play can be exported as a selection of frames, using the output buttons.
- The Time text boxes display the time for the current frame and the total time for the trajectory. You can enter a time in the text box to select a frame.
- The Speed slider sets the speed at which the frames are played.

By default, the clipping planes window is automatically hidden when you play through a trajectory, as this speeds up play by about 50%. It is displayed again (if it was originally displayed) when play stops. If you want to see the clipping planes window during play, deselect Hide clipping planes during continuous play.

In the Display section you can control how frames are displayed in the Workspace and what features are displayed:

- Use lower quality drawing to speed up play—Use a lower quality representation of objects (tubes, spheres) in the Workspace to speed up play. This option has no effect on wire frame representation.
- Update secondary structure—Update the secondary structure assignment for each frame.

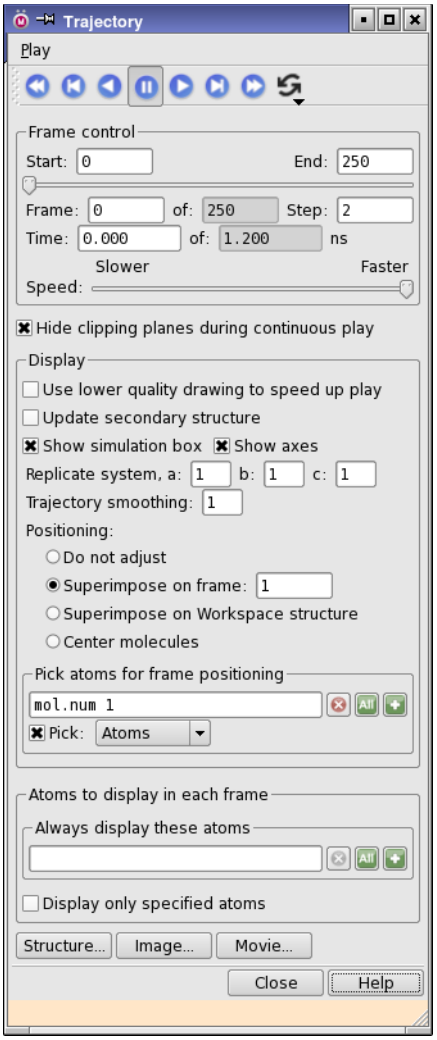

Figure 3.6. The Trajectory panel.

- Show simulation box—Show the edges of the simulation box (in purple).
- Show axes—Show the coordinate axes in green.
- Replicate system—Enter the number of replicas of the system to display in each of the three directions. This enables you to visualize the movement across the simulation box boundaries. These text boxes are unavailable if there are no periodic boundary conditions.
- Trajectory smoothing—Smooth the trajectory by averaging the coordinates over the specified number of frames.

- Positioning—Select on of these options to control the positioning of each frame relative to the Workspace during play.
  - Do not adjust—Do not adjust the positioning of each frame.
  - Superimpose on frame—Align the structure in each frame by superimposing a selection of atoms on the corresponding atoms in the frame number given in the text box. Use the Pick atoms for positioning picking controls to make the atom selection.
  - Superimpose on Workspace structure—Align the structure in each frame by superimposing a selection of atoms on the corresponding atoms in the Workspace (that are not part of the trajectory). Use the Pick atoms for positioning picking controls to make the atom selection, which must match both the Workspace structures and the trajectory structure.
  - Center molecules—Center the selected molecules in the Workspace. Use the Pick atoms for positioning picking controls to make the atom selection.
- Pick atoms for positioning—Use these picking controls to select the atoms to superimpose or to center. You should consider picking atoms that do not change their position much during the simulation.

If you want to superimpose the trajectory on the Workspace structure, you must take care when you select the atoms to superimpose. The ASL expression for the selection in the Workspace structure is applied to each trajectory frame. If the ASL expression depends on the numbering (atom number, molecule number, etc.) and the order of the objects in the trajectory frames is not the same as in the Workspace structure, you may get unexpected results. You should use ASL expressions that are not order-dependent. You can use the atom selection button to choose from a variety of structural features whose ASL expressions are not order-dependent, like Backbone or Ligands. If the ordering is a problem, you could instead align the Workspace structure to a particular frame, and then play the trajectory by superimposing on that frame.

The atoms that are visible in each frame can be set either with the Workspace toolbar buttons, or with the tools in the Atoms to display in each frame section.

To select the atoms that are visible when frames are displayed, use the toolbar buttons that control the atom display:

The choice that you make with the toolbar buttons is recorded as an atom set, and is applied to each frame. The same atoms are always displayed in each frame, no matter where they move in the trajectory.

To display the atoms that come within a given distance of a particular set of atoms (such as a ligand or a binding site), use the Atoms to display in each frame section. You can select the atoms that are always visible with the Always display these atoms selection tools. You can then choose to display entire residues that have any atoms within a specified distance of these atoms. This expression is evaluated for each frame, which allows residues (such as water) to move in and out of this distance. The particular set of atoms that is visible can therefore change from frame to frame.

The output buttons allow you to export the trajectory data in various forms. You can export individual frames, all frames, or the selection of frames defined by using the Start, End, and Step text boxes. The buttons have the following actions:

- Structure—Save structures from the trajectory to a file or create project entries from the structures. Opens the Export Structure dialog box, in which you can specify where the structures will go, which structures to export, and which atoms to export.
- Image—Create an image of the Workspace with the current frame displayed. Opens the Save Image panel.
- Movie—Save a movie of the trajectory in MPEG format. Opens the Export Movie panel, in which you can select the frames to be exported, the speed and the resolution.

Trajectories that are larger than 4GB cannot be viewed in Maestro.

Hybrid Monte Carlo Simulations

You can use the Hybrid Monte Carlo panel to set up and run a Hybrid Monte Carlo (HMC) simulation on the Workspace structure or on a selected entry in the Project Table. HMC simulations achieve relatively efficient sampling by interleaving Monte Carlo moves with a short sequence of molecular-dynamics steps. Because HMC is used mainly as a sampling method, for example, in Liaison binding affinity calculations, the MD steps can use a somewhat larger time step than would normally be advisable. The Metropolis algorithm determines which MD moves should be accepted or rejected. This ensures that the simulation will not go far astray, even if the MD time step would normally lead to a failure of energy conservation. This is why HMC is sometimes called “bad MD but good MC”.

To open the Impact Hybrid Monte Carlo panel, choose Hybrid MC from the Impact submenu of the Maestro Applications menu.

The Impact Hybrid Monte Carlo panel has four tabs:

- Potential
- Constraints
- MD Parameters
- HybridMC

The Potential and Constraints tabs are described in Chapter 2. Additional features of the Constraints tab appear in Section 3.1 on page 24. Features of the MD Parameters tab relevant to both Impact Dynamics and Impact HMC are discussed in Section 3.2 on page 25. The HybridMC tab is discussed below.

When you have set the options in the Impact Hybrid Monte Carlo panel tabs to the desired value, click the Start button to open the Impact Hybrid Monte Carlo - Start dialog box. The standard job start options are displayed, including the Incorporate option menu and the Job options: Name, Host machine. For a description of these options, see Section 2.2.3 on page 7. The default job name for Impact Hybrid MC jobs is `impact_hmc`.

The input for an Impact Hybrid MC job can be either the contents of the Workspace or a single entry in the Project Table.

Note: *Only one entry from the Maestro Project Table can be displayed and used for each HMC job.* If you need to merge two entries, use the Project Table’s Merge option to create a combination entry, and use that as the basis for your simulation.

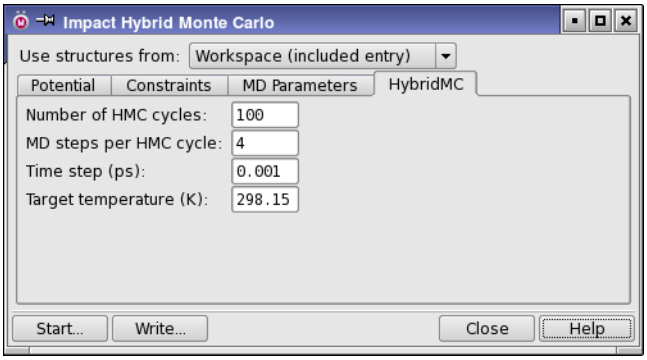

Figure 4.1. The HybridMC tab of the Impact Hybrid Monte Carlo panel.

The HybridMC tab defines the basic settings of the HMC task for an Impact Hybrid Monte Carlo simulation. The selection options are:

Number of HMC cycles

The default number of HMC cycles is 100. The acceptable range is any number greater than zero.

MD steps per HMC cycle

The default number of MD steps per HMC cycle is 4. The acceptable range is any value greater than zero. Liaison simulations use 5 MD steps per HMC cycle.

Time step

This text box sets the MD global time step (in picoseconds) for the simulation. The default value is 0.001 ps. The acceptable range is any value greater than 0 ps. Because energy conservation is less important in HMC simulations, a time step of 0.002 ps or greater may be suitable.

Target temperature

This text box sets the target temperature (in Kelvin) for the HMC simulation. The default initial temperature is 298.15 K. The default target temperature is also 298.15 K. The acceptable range is any value greater than 0 K.

Soak—Add Explicit Water Solvent

Soak surrounds a structure with a box of solvent molecules. You can specify the box size and the solvent type and density. Then Impact adds the solvent molecules, removes any that are too close to the solute, and writes a Maestro-format file for the soaked system.

By default, Soak places 216 water molecules in the smallest permitted solvent box (at least 18.65 Å in each dimension.) The resulting box is not equilibrated due to edge effects. A short minimization is usually sufficient to obtain a fully equilibrated solvated system. It is recommended that constant temperature molecular dynamics, described in Chapter 3, be used for this and any other explicit solvent systems.

To model active sites or water shells around proteins with explicit solvent:

1. Run Soak.
2. Run a short minimization and constant temperature MD equilibration at room temperature.

You can set up a Soak job in the Soak panel. To open the Soak panel, choose Soak from the Impact submenu of the Maestro Applications menu.

When you have set the options in the Soak panel to the desired values, click Start, to open the Start dialog box. In this dialog box you can make job settings and start the job. The Incorporate option menu allows you to append the results to the Project Table or to leave them as a file, which is named *jobname*`_out.mae`. There is no option to replace existing entries. The default job name for Soak jobs is `impact_soak`. For a description of the Start dialog box options, see Section 2.2 of the *Job Control Guide*.

The input structure for a Soak job can be either the contents of the Workspace or a single entry in the Project Table.

The Soak panel has features common to Impact application panels, such as the Use structures from option menu and the Start, Write, Close, and Help buttons at the foot of the panel. For information on these common features, see Section 2.2 on page 5. The Soak panel also includes a single tab, labeled Soak, with the following options:

Solvent type

The solvent types available are SPC water (Simple Point Charge), TIP4P water, and TIP3P water.

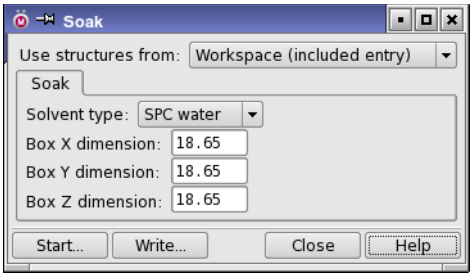

Figure 5.1. The Soak panel.

Box [X,Y,Z] dimensions

Use these three text boxes to specify the required size of the solvent box in angstroms. The minimum (and default) size for any dimension that Maestro will use is 18.65 Å. These values also update the size of the simulation box when periodic boundary conditions are applied. (See the discussion of periodic boundary conditions in Section 2.4.4 on page 13.)

Running Impact from the Command Line

Although you will normally set up jobs using the controls and settings in the Maestro GUI, you can submit Impact jobs either from within Maestro or from the command line. Advantages of running from the command line include:

- The command-line scripts can run all full-featured jobs written using the Impact panels in Maestro, and also allow you to override specific run-time values that are not accessible through the Maestro interface.
- Command-line scripts allow you to run jobs when you want.
- Command-line scripts can be modified and jobs can be re-run without reconfiguring and reloading job settings in Maestro.
- Some job options, such as trajectory file analysis, are available only when you run Impact from the command line.

The `SCHRODINGER` environment variable must be set to run jobs. You can define `SCHRODINGER` as follows:

csh/tcsh: `setenv SCHRODINGER` *installation-directory*

bash/ksh: `export SCHRODINGER=`*installation-directory*

Unless otherwise specified, Schrödinger applications and utilities run under a job control system and are automatically run in the background. You need not add an `&` at the end of the commands to have them run and immediately return your command prompt. The `-WAIT` option of the `impact` command forces the shell to wait until the job is finished, so you can embed such commands in other scripts.

6.1 Running Impact From the Command Line

Basic Impact calculations can be run from the command line using the syntax shown below.

```
$SCHRODINGER/impact [options] [-i] input-file
```

To run `impact`, you must specify the input file, *input-file*. If *input-file* does not end in `.inp`, Impact looks first for *input-file* as specified. If that file doesn't exist, it then looks for *input-file*`.inp`. If `-i` is omitted, then *input-file* **must** end in `.inp` and must be the last argument in

the command line. If -i is included, the input file specification can be placed anywhere on the command line.

The options that you can specify when initiating jobs from the command line are described in Table 6.1. The standard Job Control options and the options -WAIT and -LOCAL, described in Table 2.1 and Table 2.2 of the *Job Control Guide*, are also supported. To view the usage summary information, define the SCHRODINGER environment variable and enter $SCHRODINGER/impact -h in a terminal window.

The impact driver script automatically selects the appropriate executable for the size of the system. The options -e and -s for selecting the size of the executable are therefore obsolete, but can still be used.

Table 6.1. Impact *command options*

Option	Description
-h	Print usage summary and exit
-v	Print version number of startup script and exit
-e *executable*	Specify the executable to use. Allowed values are main1m, main1h, and main1x, with size limits (atoms or bonds) of 8000, 40000, and 90000 respectively. Overrides -s.
-o *output-file*	File for writing output and log messages. If this option is omitted, Impact names the log file *jobname*.log, where *jobname* is taken from the Impact input file name.
-s *size*	Use specific "size" version of the Impact executable. Allowed values for *size* are medium, huge, and extrahuge. If omitted, medium is assumed in most cases; it is valid for up to 8000 atoms or 8000 bonds. The huge option allows up to 40000 atoms or bonds, and extrahuge up to 90000 atoms or bonds.

Note: The default molecular mechanics force field for Basic Impact applications is the OPLS_2005 version of OPLS-AA. OPLS_2001 is also available. OPLS_2001 and OPLS_2005 are designed to work with automatic atom-typing, and are incompatible with template mode. If you attempt to write a template file (Impact command WRITE TEMPLATE) while using OPLS_2001, an error message is displayed to remind you that this command can only be used with OPLS1999 or OPLS2000 force fields. To use one of these older force fields, add a line to the input file before the CREATE task, such as:

```
SET FFIELD OPLS1999
```

For distributed processing, the run_jobs.pl script can be used. (Distributed processing for Basic Impact calculations is not available from Maestro.)

Impact jobs run under the Job Control facility. You can use the `$SCHRODINGER/jobcontrol` command to monitor and manage jobs. For more information on this command and the Job Control facility, see the *Job Control Guide*.

6.2 File Name Conventions

A typical Impact job has one command-script file (*jobname*`.inp`), one or more structure files (*jobname*`.mae`, *jobname*`.pdb`, or *jobname*`.sdf`), and after execution, several output files (e.g., *jobname*`_out.mae` for structure files and *jobname*`.out` for textual data).

If a file already has the name of an output file, in many cases Impact renames the old file with a numerical extension (*filename*`.out.01`, *filename*`.out.02`, and so on) for archival purposes. The new job's output is then written to the base name (*filename*`.out`). If you do not need the old files, you can remove them.

Some files, such as *jobname*`.log` files, are newly written each time Impact runs a calculation. Likewise, old *jobname*`_pv.mae` files are overwritten. For Impact minimization jobs, the *jobname*`_out.mae` structure file is *not* incremented.

Table 6.2 contains descriptions of the various file types. For more information, see the Maestro online help or the *Impact Command Reference Manual*.

Table 6.2. Liaison file extensions

Extension	Description
`.inp`	Impact input file or script. Impact input files are formatted plain-text files written in the Impact input file language, DICE. Maestro creates Impact input files before job submission, or you can create or edit them manually with a text editor.
`.mae`	A Maestro format structure file, a plain-text file written by Maestro containing atom, bond, and other information for one or more molecules.
`.log`	An Impact log file. If specified, a `.log` file captures standard output and standard error messages in text form. This file is overwritten during subsequent runs.
`.out`	An Impact output file containing information similar to that found in log files (no standard error). Output files are appended with numerical extensions when the input file is run again. Up to 99 output files are retained.
`.01`, `.02`, etc.	A file containing results from previous Impact calculations run from the corresponding *jobname*`.inp` file.
`_out.mae`	An Impact output structure file written in the Maestro file format. Liaison and some Impact jobs do not write *`_out.mae` output structure files.

Getting Help

Information about Schrödinger software is available in two main places:

- The `docs` folder (directory) of your software installation, which contains HTML and PDF documentation. Index pages are available in this folder.
- The Schrödinger web site, http://www.schrodinger.com/, particularly the Support Center, http://www.schrodinger.com/supportcenter, and the Knowledge Base, http://www.schrodinger.com/kb.

Finding Information in Maestro

Maestro provides access to nearly all the information available on Schrödinger software.

To get information:

- Pause the pointer over a GUI feature (button, menu item, menu, ...). In the main window, information is displayed in the Auto-Help text box, which is located at the foot of the main window, or in a tooltip. In other panels, information is displayed in a tooltip.

  If the tooltip does not appear within a second, check that Show tooltips is selected under General → Appearance in the Preferences panel, which you can open with CTRL+, (⌘,). Not all features have tooltips.
- Click the Help button in a panel or press F1 for information about a panel or the tab that is displayed in a panel. The help topic is displayed in your browser.
- Choose Help → Online Help or press CTRL+H (⌘H) to open the default help topic in your browser.
- When help is displayed in your browser, use the navigation links or search the help in the side bar.
- Choose Help → Manuals Index, to open a PDF file that has links to all the PDF documents. Click a link to open the document.
- Choose Help → Search Manuals to search the manuals. The search tab in Adobe Reader opens, and you can search across all the PDF documents. You must have Adobe Reader installed to use this feature.

For information on:

- Problems and solutions: choose Help → Knowledge Base or Help → Known Issues → *product*.
- Software updates: choose Maestro → Check for Updates.
- New software features: choose Help → New Features.
- Scripts available for download: choose Scripts → Update.
- Python scripting: choose Help → Python Module Overview.
- Utility programs: choose Help → About Utilities.
- Keyboard shortcuts: choose Help → Keyboard Shortcuts.
- Installation and licensing: see the *Installation Guide*.
- Running and managing jobs: see the *Job Control Guide*.
- Using Maestro: see the *Maestro User Manual*.
- Maestro commands: see the *Maestro Command Reference Manual*.

Contacting Technical Support

If you have questions that are not answered from any of the above sources, contact Schrödinger using the information below.

E-mail:	help@schrodinger.com
USPS:	Schrödinger, 101 SW Main Street, Suite 1300, Portland, OR 97204
Phone:	(503) 299-1150
Fax:	(503) 299-4532
WWW:	http://www.schrodinger.com
FTP:	ftp://ftp.schrodinger.com

Generally, e-mail correspondence is best because you can send machine output, if necessary. When sending e-mail messages, please include the following information:

- All relevant user input and machine output
- Impact purchaser (company, research institution, or individual)
- Primary Impact user
- Installation, licensing, and machine information as described below.

Gathering Information for Technical Support

This section describes how to gather the required machine, licensing, and installation information, and any other job-related or failure-related information, to send to technical support.

For general enquiries or problems:

1. Open the Diagnostics panel.
   - **Maestro:** Help → Diagnostics
   - **Windows:** Start → All Programs → Schrodinger-2012 → Diagnostics
   - **Mac:** Applications → Schrodinger2012 → Diagnostics
   - **Command line:** `$SCHRODINGER/diagnostics`
2. When the diagnostics have run, click Technical Support.

   A dialog box opens, with instructions. You can highlight and copy the name of the file.
3. Attach the file specified in the dialog box to your e-mail message.

If your job failed:

1. Open the Monitor panel in Maestro.

   Use Applications → Monitor Jobs or Tasks → Monitor Jobs.
2. Select the failed job in the table, and click Postmortem.

   The Postmortem panel opens.
3. If your data is not sensitive and you can send it, select Include structures and deselect Automatically obfuscate path names.
4. Click Create.

   An archive file is created in your working directory, and an information dialog box with the name of the file opens. You can highlight and copy the name of the file.
5. Attach the file specified in the dialog box to your e-mail message.
6. Copy and paste any log messages from the window used to start Maestro (or the job) into the email message,or attach them as a file.
   - **Windows:** Right-click in the window and choose Select All, then press ENTER to copy the text.
   - **Mac:** Start the Console application (Applications → Utilities), filter on the application that you used to start the job (Maestro, BioLuminate, Elements), copy the text.

If Maestro failed:

1. Open the Diagnostics panel.

   - **Windows:** Start → All Programs → Schrodinger-2012 → Diagnostics
   - **Mac:** Applications → Schrodinger2012 → Diagnostics
   - **Linux/command line:** `$SCHRODINGER/diagnostics`

2. When the diagnostics have run, click Technical Support.

   A dialog box opens, with instructions. You can highlight and copy the name of the file.

3. Attach the file specified in the dialog box to your e-mail message.

4. Attach the file `maestro_error.txt` to your e-mail message.

   This file should be in the following location:

   - **Windows:** `%LOCALAPPDATA%\Schrodinger\appcrash`
     (Choose Start → Run and paste this location into the Open text box.)
   - **Mac:** `Documents/Schrodinger`
   - **Linux:** Maestro's working directory specified in the dialog box (the location is given in the terminal window).

5. On Windows, also attach the file `maestro.EXE.dmp`, which is in the same location as `maestro_error.txt`.

Index

A

alpha parameter, in Ewald method 14
atom constraints 15
atoms
  constrained 5, 17
  frozen 16
  harmonically restrained 17

B

bond constraints 15, 24
boundary conditions, periodic 13

C

conjugate gradient algorithm 19
constant dielectric 9
constrained atoms 5, 17
constraints
  constrained atoms 17
  frozen-atom 16
  Impact energy minimization 15
  Impact MD, HMC 24
Constraints tab, Energy Minimization panel 16
continuum solvation 10
  methods 14
conventions, document v
convergence criteria, energy minimization 20
cutoff distance, residue-based 11

D

dielectric constant 9
directory
  installation 1
  Maestro working 2
distance-dependent dielectric 9
drift, stopping in MD simulation 26
Dynamics panel 23
dynamics simulations 23
Dynamics tab, Dynamics panel 27

E

electrostatic treatment 9
energy minimization 19
  algorithms 19
  convergence criteria 20
  cycles, maximum 19
  input restrictions 8
  steric clashes in 19
environment variable
  SCHRODINGER 1
Equations of Motion (EOM) 25
Ewald long-range correction 14
explicit solvent 23

F

Fast Multipole Method (FMM) 10, 12
  hierarchy level setting 12
  limitations on use 19
  and RRESPA 26
force constant, default for constraints 17
force field 8
  default 42
frozen atoms, selecting 16

H

HybridMC tab, Hybrid Monte Carlo panel 38

I

images
  saving trajectory frame 36
Impact constraints 15
Impact Dynamics panel
  Constraints tab 24
  Dynamics tab 28
  MD Parameters tab 25
  Replica Exchange tab 31
implicit solvent models 10, 14
initial step size, of minimization cycle 19
input restrictions 8, 16
integration algorithms in MD 25

J

jobs
  restarting replica exchange 32
  running from Maestro 6
  running from the command line 41

K

K-space vectors, maximum length 14

L

levels, number of in FMM 12
list, neighbor 11
long range forces, in TN optimizations 20

M

maximum step size of minimization cycle..... 20
MD Parameters tab 25
MD simulations, frequency of printing information 26
MD statistics, collection of 27
Minimization tab, Energy Minimization panel. 20
minimization—*see* energy minimization
molecular dynamics (MD) 23

N

neighbor-list frequency, updating 11
nonbonded interactions, truncation of 10

O

OPLS-AA force fields..... 42
overall motion, stopping in MD simulation..... 26

P

periodic boundary conditions..... 10, 13, 23
Potential tab, Energy Minimization panel 9
product installation 46

R

RATTLE algorithm 24
relative motion, removal of 24
residue-based cutoff distance 11
RRESPA integration algorithm..... 25

S

Schrödinger contact information 46
SHAKE algorithm 24
smoothing, of force components..... 13
solvation method..... 14
solvation, continuum..... 10
solvent, implicit 10
steepest descent algorithm 19
steric clashes, in energy minimization..... 19
summation method, Ewald 14

T

Temperature Settings dialog box 31
templates, compatibility with force fields..... 42
templates, writing 42
tolerance, SHAKE/RATTLE 24
trajectory
  analysis 27
  availability of analysis..... 41
  frame image..... 36
  frame positioning..... 35
  recording..... 27
  saving as movie 36
  saving structures from 36
  smoothing during play..... 34
  superimposing on Workspace structure..... 35
  viewing in Maestro 27, 32
  visible atoms..... 35
Trajectory panel 34
Truncated Newton (TN) algorithm 19, 20
truncation of nonbonded interactions 10

V

Verlet integration algorithm..... 25

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