Field-Based QSAR

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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].

Field-Based QSAR

If you have a set of aligned ligands, you can build field-based 3D QSAR models for these ligands.

These field-based QSAR models are based on CoMFA [1] and CoMSIA [2, 3]. CoMFA field-based models are constructed by calculating the value of fields, such as the electrostatic field, on a rectangular grid that encompasses the molecules in the training set. The grid locations are the independent variables that are used in a partial-least-squares (PLS) fitting procedure to produce a relationship between the values of the fields and the activity of the training set molecules.

CoMSIA fields are also evaluated at points on a rectangular grid. The fields are calculated by summing the values of properties of a given atom, weighted by a Gaussian function of the distance between the grid point and the atom. The steric contribution is derived from the third power of the atomic radius; the electrostatic field from the partial atomic charges, and the hydrophobic field from estimated ALOGP values. Hydrogen-bond receptor and donor fields have a value of 1 at the projected point locations.

The field-based QSAR models are an implementation of the CoMFA and CoMSIA methods with a specific set of parameters. The Lennard-Jones steric potentials are taken from the OPLS_2005 force field, as are the atomic charges for the electrostatic fields (by default). Hydrophobic fields are based on the atom types and hydrophobic parameters from Ghose et al. [4]. Hydrogen-bond acceptor and donor fields are based on Phase pharmacophore feature definitions, with projected points. As the models are not exactly the same as the standard CoMFA and CoMSIA models, different names have been used in Phase: Force Field for CoMFA-like models, and Gaussian for CoMSIA-like models.

These models are built in the Field-Based QSAR panel. To open this panel:

- **Maestro:** choose Tasks → QSAR → Field-Based or Applications → Field-Based QSAR.
- **BioLuminate:** choose Tasks → Ligand Tasks → Pharmacophore Modeling → Field-Based QSAR.

The workflow is described below, with subsections where it differs between the model types.

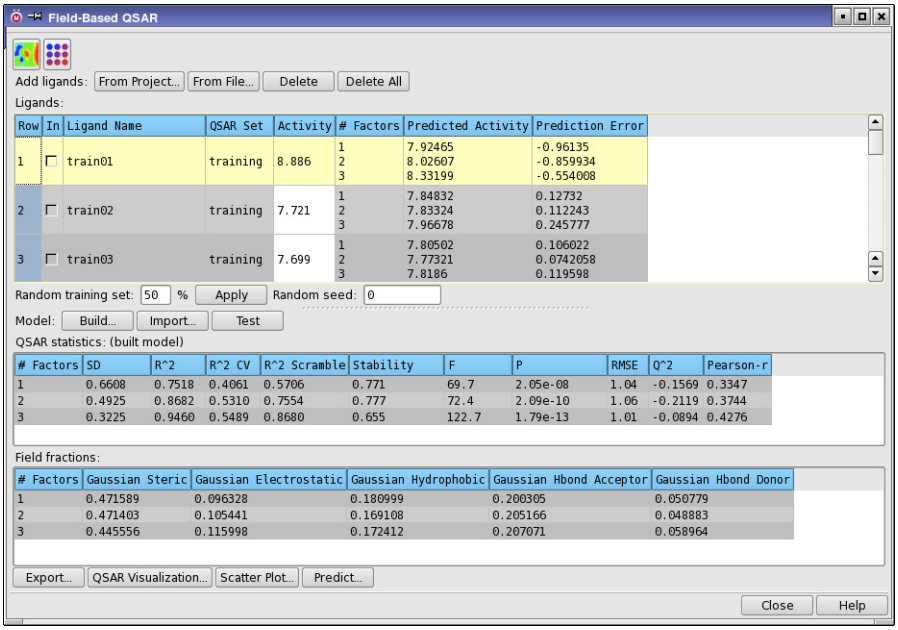

Figure 1. The Field-Based QSAR panel.

1 Selecting Ligands

The first step is to select the ligands to use. The ligands you add must be fully prepared 3D structures that are properly aligned. No facility is provided in these panels for preparing the structures or aligning the ligands. Structure preparation can be done with LigPrep (see the *LigPrep User Manual*), and generation of conformers can be done with ConfGen (see the *ConfGen User Manual*) or MacroModel (see Chapter 9 of the *MacroModel User Manual*). Alignment can be done as follows:

- If the ligands were exported from the Develop Common Pharmacophore Hypotheses panel, they should already be prealigned to the pharmacophore model.
- If you want to align the ligands to a pharmacophore hypothesis, you can use one of the (Phase) Pharmacophore Screening panels to run a screening job. The hit file from this job contains the aligned ligands.
- You can use the Superposition panel (Tools → Superposition) to align the ligands. The best choice is probably to align by a SMARTS pattern for the ligand core. You will also have to select the conformers that have the best alignment.

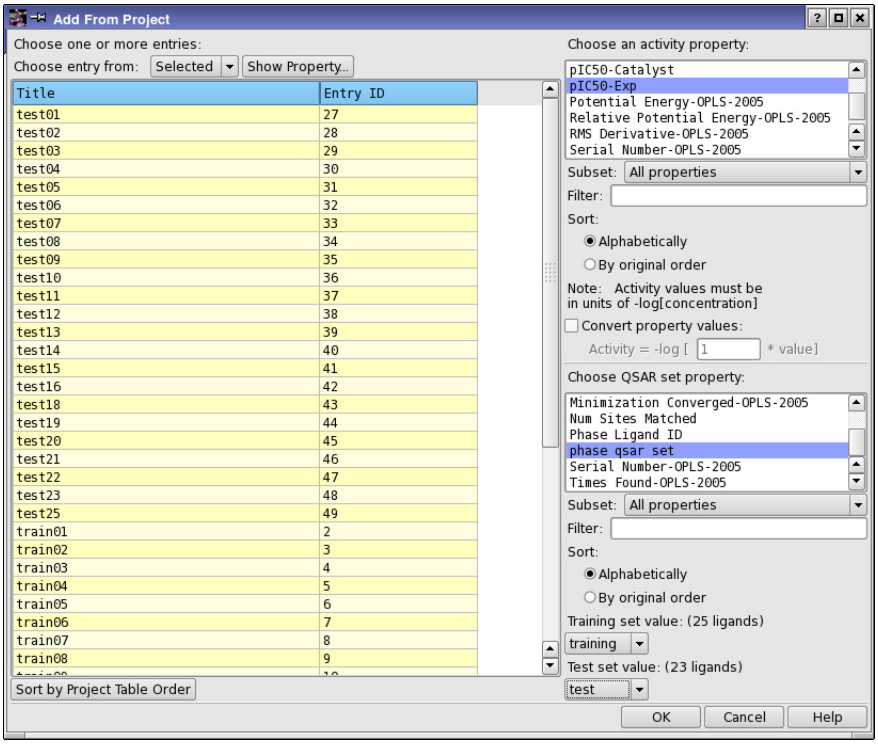

Figure 2. The Add from Project dialog box for QSAR models.

- Another option is the Flexible Ligand Alignment panel (Tools menu, Tasks → Ligand Tasks). This panel does a quick conformational search and aligns the best conformer of the second and subsequent ligands to the first, replacing the structure with this conformer.

You can add ligands to the set to be used for the QSAR model from two sources, by clicking one of the Add ligands buttons:

- From Project—Opens the Add From Project dialog box, in which you can choose a set of entries; select an activity property, converting it into the appropriate units if need be; and select a property to define the training and test sets.
- From File—Opens a file selector, in which you can navigate to and select the file. When you click OK, the Choose Activity Property dialog box opens, in which you can select an activity property, converting it into the appropriate units if need be, and select a property to define the training and test sets.

You can use these buttons more than once to add multiple sets of ligands. The ligands you add are always appended to the Ligands table: there is no replacement of ligands, and no checking

for duplicates is done. If you want to delete ligands, select them in the table and click Delete. This allows you to remove duplicates, or to remove ligands that you don't want in your model. To start again with a new set of ligands, click Delete All, then start adding the new ligands.

When you add ligands, you can assign them to the training and test sets on the basis of the values of a property. The choice is made in the same panel as the choice of the activity property. The assignment is made by choosing a single value of the property for the training set and a single value for the test set. If you want to use this feature, you will have to create an appropriate property beforehand. If you exported ligands from the Build QSAR Model step of the Develop Common Pharmacophore Hypotheses panel, you can use the phase qsar set property.

The ligands are displayed in the Ligands table when they are added. When the ligands are first read, the # Factors, Predicted Activity, and Prediction Error columns are empty. The values in these columns are added after the QSAR model is built. The table columns are described in Table 1.

Table 1. Description of the Ligands table columns.

Column	Description
In	Inclusion status of the ligand. The button is colored black if the ligand is included in the Workspace, and is empty if the ligand is excluded. You can include and exclude ligands with click, shift-click, and control-click.
Ligand Name	The name of the ligand.
QSAR Set	Indicates whether a ligand is in the training set, the test set, or neither (the ligand is ignored). The column is blank if the ligand is ignored. Click the column repeatedly to cycle through the three possible states.
Activity	The ligand's activity. You can alter the activity values by directly editing the table cells.
# Factors	Number of PLS factors used for the QSAR model.
Predicted Activity	Activity predicted by the QSAR model. The number of rows in this column for each ligand is equal to the number of PLS factors specified in the Build QSAR Model - Options dialog box. Each row contains the prediction from a model containing the number of PLS factors indicated in the # Factors column.
Prediction Error	Error in the predicted activity.

2 Choosing a Training Set and a Test Set

The next task is to choose a training set and a test set, and exclude ligands that you do not want in either set. If you did not do this on the basis of a property when exporting the ligands, all of the ligands are initially included in the training set, and you must partition them.

To change the set membership of an individual ligand, click in the QSAR Set column for the ligand. The membership cycles between training, test, and blank, the last of which means that the ligand is excluded from both sets—that is, it is not used. To change the set membership for a group of ligands, select the ligands in the table using shift-click or control-click, then control-click in the QSAR Set column for any of the ligands.

You can select a random fraction of the ligands for the training set by entering a percentage in the Random training set text box and clicking Apply. The specified percentage of ligands is selected at random from the existing training and test sets and assigned to the training set. The rest are assigned to the test set. Ligands that are in neither set are not used in the selection.

If you select the training set randomly, you may want to do this in a reproducible way. By default, the random seed changes each time a random training set is selected, so you get a different training set each time you click Apply. If you change the value in the Random seed text box to any positive integer, the same random training set is created each time you click Apply. The default value of zero ensures that the assignment is always random.

The following subsections describe how to build, test, and use the models.

3 Building and Testing the Model

Once you have chosen the training and test sets, click Build to build the QSAR models. The Build Field-Based Model dialog box opens. This dialog box has a range of settings for the fields and the data that are used to fit the fields.

The first choice is to select the fields that you want to include in the model. The Field style options are:

- Force field—Use the force-field electrostatic and steric fields for the model (CoMFA).
- Gaussian—Use the five Gaussian fields for the model (CoMSIA).
- Custom—Select a combination of force-field and Gaussian fields to use for the model. To make the selection, click Edit, and select the fields from the list in the Custom Field Style dialog box. In this dialog box you can also import feature definitions for the fields.

For the electrostatic fields, you can choose to use input partial charges rather than those from the OPLS_2005 force field, by selecting Use input partial charges.

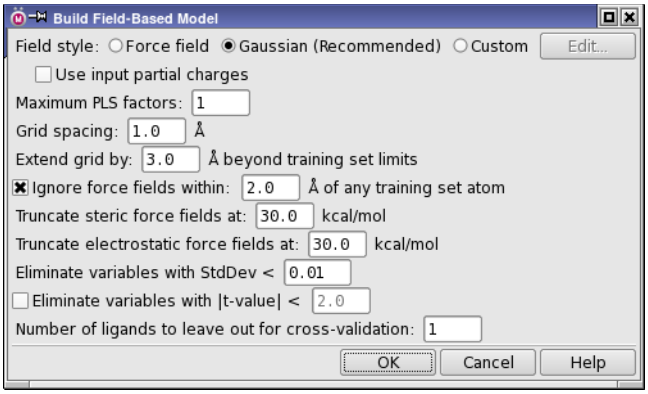

Figure 3. The Build Field-Based Model dialog box.

You can specify the number of PLS factors to use in the Maximum PLS factors text box. A model is built for each number of PLS factors up to the specified maximum. There is no limit on the maximum number of PLS factors, but as a general rule, you should stop adding factors when the standard deviation of regression is approximately equal to the experimental error.

To set the spacing of the grid points on which the fields are evaluated, in angstroms, enter a value in the Grid spacing text box. You can extend the grid beyond the limits of the training set by entering a value in the Extend grid by N Å beyond training set limits text box. This allows you to make predictions for ligands that are larger than the training set ligands.

Once the grid is defined, you can make settings that determine how the fields are evaluated on the grid.

- Ignore force fields within N Å of any training set atom—Set the distance from the training set atoms inside which grid points are discarded when evaluating the fields. A grid point is discarded if it is within the specified distance of any of the atoms of any of the training set molecules. This option essentially prevents the model from being dominated by the strong fields close to the nuclei.
- Truncate steric force fields at *value*—Specify the cutoff value for truncating steric force fields, in kcal/mol. Any field that is greater than this value is set to this value.
- Truncate electrostatic force fields at *value*—Specify the cutoff value for truncating electrostatic force fields, in kcal/mol. Any field that is greater than this value is set to this value.

The values at each included grid point can be further processed to eliminate variations that are not significant.

- Eliminate variables with StdDev < *value*—Eliminate variables whose standard deviation is less than the value given in the text box. The smallest value you can set is 0.01.
- Eliminate variables with |t-value| < *value*—Select this option to use a t-value filter to eliminate independent variables whose regression coefficients are overly sensitive to small changes in the training set composition, and enter the threshold for eliminating variables in the text box. The resulting models have fewer uninformative variables and tend to give better predictions on test set compounds.

You can set the number of ligands to be used in the leave-N-out cross-validation statistics, in the Number of ligands to leave out for cross-validation text box. The default is 1.

When you have finished making settings, click OK to build the model.

When the results are returned, the # Factors, Predicted Activity, and Prediction Error columns are filled in for both the training set and the test set, and the QSAR statistics table is filled in.

If you have ligands that you did not include in the test set, you can include them and click Test to calculate the predicted activity and update the QSAR statistics for the test set.

You can also import an existing model, instead of building it. To import the model, click Import and navigate to the desired `.qsar` file.

4 Examining the Model

There are several ways in which you can assess the accuracy of the model.

- Examine the QSAR statistics, which are described in Table 2. Definitions of the statistics can be found in Appendix A.3 of the *Phase User Manual*. You can add more ligands to the test set, and update the statistics by clicking Test.
- Create a scatter plot of the experimental data against the predicted data. To do this, click Scatter Plot, which opens the Scatter Plot dialog box, in which you can select the number of PLS factors and the ligands to include in the plot, then opens the Manage Plots panel and the Scatter Plot panel to display the plot.
- Visualize the QSAR model in the Workspace, as described in the remainder of this section.

Table 2. Description of the QSAR statistics table columns.

Column	Description
# Factors	Number of factors in the partial least squares regression model.
SD	Standard deviation of the regression.This is the RMS error in the fitted activity values, distributed over *n*–*m*–1 degrees of freedom (*n* ligands, *m* PLS factors).
R^2	Value of R^2 for the regression (the coefficient of determination). A value of 0.80, for example, means that the model accounts for 80% of the variance in the observed activity data. R^2 is always between 0 and 1.
R^2 CV	Cross-validated R^2 value, computed from predictions obtained by a leave-N-out approach.
R^2 Scramble	Average value of R^2 from a series of models built using scrambled activities. Measures the degree to which the molecular fields can fit meaningless data, and should be low.
Stability	Stability of the model predictions to changes in the training set composition. Maximum value is 1. This statistic can be used to compare models.
F	The ratio of the model variance to the observed activity variance. The model variance is distributed over *m* degrees of freedom and the activity variance is distributed over *n*–*m*–1 degrees of freedom (*n* ligands, *m* PLS factors). Large values of F indicate a more statistically significant regression
P	The significance level of F when treated as a ratio of Chi-squared distributions. Smaller values indicate a greater degree of confidence. A P value of 0.05 means F is significant at the 95% level.
RMSE	Root-mean-square error in the test set predictions.
Q^2	Value of Q^2 for the predicted activities. Directly analogous to R-squared, but based on the test set predictions. Q^2 can take on negative values if the variance in the errors is larger than the variance in the observed activity values.
Pearson-r	Pearson r value for the correlation between the predicted and observed activity for the test set.

You can view a representation of the fields as contours (surfaces), or as color intensities of the fields on the grid. To do so, click the View Contours button or the View Intensities button at the top of the panel.


You can control what is displayed in the Workspace by using the Field-Based QSAR Visualization Settings panel. To open this panel, click QSAR Visualization.

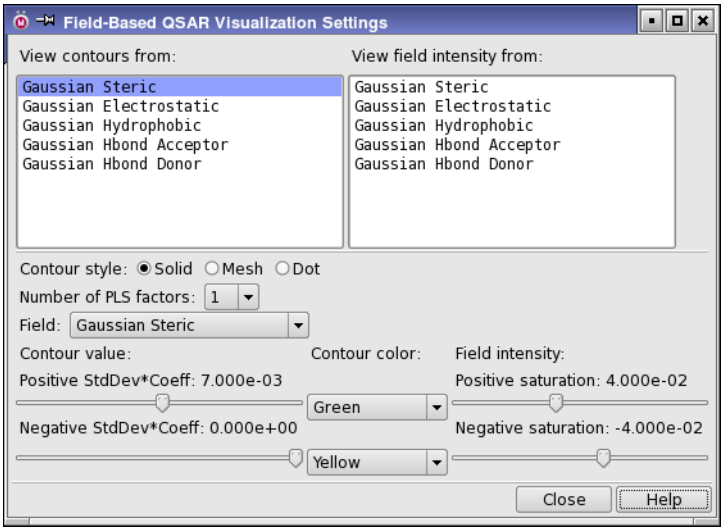

Figure 4. The Field-Based QSAR Visualization Settings panel.

Contours can be displayed in different styles. The default is Solid, but you can choose Mesh or Dot for the Contour style, and this will become the new default.

Multiple contours can be displayed at the same time. The contours that are displayed can be selected from the View contours from list. By default, the first contour is selected. To change the value of the field at which the contouring is done or the colors used, first select the field from the Field option menu, then use the Contour value sliders and Contour color option menus to make the changes. The default colors are given in Table 3.

Table 3. Colors for field contours.

Field Type	Positive	Negative
Force Field Steric	Green	Yellow
Force Field Electrostatic	Blue	Red
Gaussian Steric	Green	Yellow
Gaussian Electrostatic	Blue	Red
Gaussian Hydrophobic	Yellow	White
Gaussian Hbond Acceptor	Red	Magenta
Gaussian Hbond Donor	Purple	Cyan

Field intensities can only be displayed for one field at a time. The field that is displayed can be selected from the View field intensity from list. By default, the first in the list is displayed. You can change the field cutoffs for the color saturation with the sliders under Field intensity. Fields with greater absolute values than the cutoff are displayed at the maximum brightness.

5 Using the Model

Once you are satisfied with the model, you can make use of it in the following ways:

- Export it to an external file. The model can then be used in other projects or applications. To do so, click Export, and use the file selector that is displayed to name the file. The model is exported with a `.qsar` extension. Along with it, the ligands are exported to a file with the same base and a `_qsar_pred.mae` extension. The QSAR Set property is included in the ligand file, so you have a record of which ligands were used for training.
- Add it to an existing hypothesis in the Project Table. To do so, click Add to Hypothesis and select the hypothesis in the entry chooser that is displayed. You can then export the hypothesis from the Project Table for external use.
- Make predictions for other molecules, which must exist as entries in the Project Table. To do so, click Predict, and choose the entries in the entry chooser that is displayed. The predicted property for each number of PLS factors is then added to the entries in the Project Table.
- Use the Field fractions or Atom type fractions to assess the molecular features that are primarily responsible for the activity of the molecule. For example, if steric and hydrophobic Gaussian field fractions are much larger than the other types (as is often the case), that suggests that most of the binding energy is coming from hydrophobic interactions.

6 Running from the Command Line

The field-based QSAR models can be built and tested from the command line with the utility `phase_fqsar`. The command syntax is

`phase_fqsar` *inFile outFile actProp* `-build|-test` [*options*]

The input file, *inFile* is a structure file in Maestro or SD format, compressed or uncompressed, that contains the training set structures, test set structures, or both. The output file *outFile* contains the same structures with predicted activities added, and is in the same format as the input file.

actProp is the name of the experimental activity property in the input file. This is normally a quantity that is linearly related to free energy, such as pKi or pIC50.

The utility has two modes, `-build`, to build a new model, and `-test`, to test an existing model. Build options are given in Table 4, and test options are given in Table 5.

Table 4. Build options for the phase_fqsar command

Option	Description
`-buff` *dbuff*	Ignore force fields at grid points within a distance *dbuff* of any training set atom. Subsequent filters consider only fields not eliminated by previous filters. Default: 2.0.
`-charges` *prop*	Get partial atomic charges from a real-valued atom-level property. Valid only when *inFile* is a Maestro file. Subsequent application of the model to new structures requires the presence of the same atom-level property.
`-coeff`	Write PLS coefficients to *sumFile*. Only valid with `-osum`.
`-ecut` *emax*	Truncate electrostatic force fields at the supplied value in kcal/mol. Default: 30.0.
`-extend` *dext*	Distance in angstroms to extend grid beyond the training set limits. Default: 3.0.
`-factors` *npls*	Maximum number of PLS factors. The default is the larger of 1 and 1/5 the number of training set compounds.
`-grid` *spacing*	Grid spacing in angstroms. Must be in the range 0.5 to 4.0. Default: 1.0.
`-hb` *hbFile*	Phase-style pharmacophore feature definition file for mapping Gaussian hydrogen bond acceptors/donors. If omitted, and these fields are used, default Phase hydrogen bond definitions are applied. Because Gaussian fields use projected acceptors and donors, this convention is always followed when mapping Phase feature definitions.
`-LNO` *n*	Number of training set observations to exclude for cross-validation. Use `-LNO 1` to get leave-1-out, use `-LNO 5` to get leave-5-out. The default value of *n* is equal to 10% of the training set.
`-lt` *list*	Index of training set compounds in the input file, as a comma-separated list of indexes or index ranges given as *n*:*m*. Examples: 1:10,14,15 — 1 through 10, 14, and 15. 1,3,10: — 1, 3, and 10 through last. :5,20:30 — 1 through 5, and 20 through 30. Compounds not in *list* are assigned to the test set. By default, all compounds are in the training set. Not valid with `-pt`.
`-ofield` *fieldFile*	Write field values to the specified CSV file. The output columns are Index, Title, QSAR_Set, Activity, f1, f2, etc.
`-oLNO` *LNOFile*	Write observed and LNO-predicted activities to the specified CSV file. The output columns are the same as in *predFile*.

Table 4. Build options for the phase_fqsar command

Option	Description
`-omod` *modelFile*	Save model to the specified file.
`-opred` *predFile*	Write observed and predicted activities to the specified CSV file. The output columns are Index, Title, QSAR_Set, Activity, Pred(1),...,Pred(npls), Error(1),...,Error(npls), where Index is the position in *inFile*, QSAR_Set is `train` or `test`, and training set rows are written before test set rows.
`-osum` *sumFile*	Write a summary of the results to *sumFile*. The default is standard output.
`-pt` *fraction*	Randomly assign the specified fraction (e.g., 0.5) of compounds to the training set, with the remainder assigned to the test set. Sampling is done to ensure that both sets contain the appropriate numbers of compounds from each activity interval. Not valid with `-lt`.
`-rand` *seed*	Random seed integer in the range 1 to 2147483646, for random assignment of the training set. If omitted, a seed will be assigned from the current local time. Only valid with `-pt`.
`-scut` *smax*	Truncate steric force fields at the supplied value in kcal/mol. Default: 30.0.
`-sd` *sdMin*	Ignore the field at a given grid point if its standard deviation over the training set is less than *sdMin*. If 0, fields will be autoscaled. Default: 0.01.
`-style` *fields*	A comma-separated list of the fields to incorporate into the model. Recognized fields are: `ff_s` Force field steric (Lennard-Jones) `ff_e` Force field electrostatic (q/r) `ff` All force fields (default) `gauss_s` Gaussian steric `gauss_e` Gaussian electrostatic `gauss_h` Gaussian hydrophobic `gauss_a` Gaussian hydrogen bond acceptor `gauss_d` Gaussian hydrogen bond donor `gauss` All Gaussian fields
`-tvalue` *tmin*	Eliminate the field at a given grid point if its t-value is less than *tmin*. The following are suggested *tmin* values for different training set sizes: Size *tmin* 5 2.57 10 2.45 15 2.13 20 2.09 30 2.04 40 2.02 50 2.01 By default, no t-value filter is applied.

Table 5. Test options for the phase_fqsar command.

Option	Description
`-imod` *modelFile*	File containing the model. Required.
`-osum` *sumFile*	Write a summary of the results to *sumFile*. The default is standard output.
`-opred` *predFile*	Write observed and predicted activities to the specified CSV file. The columns are the same as for build mode.
`-ofield` *fieldFile*	Write field values to the specified CSV file. The columns are the same as for build mode.

References

1. Cramer, R. D. III; Patterson, D. E.; Bunce, J. D. Comparative Molecular Field Analysis (CoMFA). 1. Effect of Shape on Binding of Steroids to Carrier Proteins. *J. Am. Chem. Soc.* **1988**, *110*, 5959–5967.

2. Klebe, G.; Abraham, U.; Mietzner, T. Molecular Similarity Indices Analysis in a Comparative Analysis (CoMSIA) of Drug Molecules To Correlate and Predict Their Biological Activity. *J. Med. Chem.* **1994**, *37*, 4130–4146.

3. Klebe, G.; Abraham, U. Comparative Molecular Similarity Index Analysis (CoMSIA) to study hydrogen-bonding properties and to score combinatorial libraries. *J. Comput.-Aided Mol. Des.* **1999**, *13*, 1–10.

4. Ghose, A. K.; Viswanadhan, V. N.; Wendoloski, J. J. Prediction of Hydrophobic (Lipophilic) Properties of Small Organic Molecules Using Fragmental Methods: An Analysis of ALOGP and CLOGP Methods. *J. Phys. Chem A* **1998**, *102*, 3762–3772.

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
- **Product** purchaser (company, research institution, or individual)
- Primary **Product** 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`.

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