Forge™ V10.6 Release Notes

About Forge

Forge™ is a tool to understand how and why molecules bind to a protein and design or virtually screen new molecules using this knowledge. It is available with two licensing levels – the full Forge package and 'Forge Design', a version focused at molecule design with simplified functionality. Forge Design replaces Cresset's previous 'Torch' application.

Forge takes molecules as 2D drawings and creates 3D pharmacophore models of binding by cross comparing the shapes and electrostatic surfaces of the ligands. This pharmacophore can be used as the basis for analysis of other molecules within Forge. The molecules for analysis are not limited by 2D similarity to the reference molecule. When used on a congeneric series the tool can be used to decipher complex SAR or calculate a QSAR model that predicts activity for new molecules. With or without a QSAR mode, Forge helps in new molecule design and gives a rationale for the prioritization of compounds for synthesis. Using Forge on a diverse set of active molecules can help define the requirements of the protein of interest, aiding the synthetic chemist in the design of new actives.

Supplied Binaries

Forge functionality is available through a graphical user interface with two interlinked binaries (Forge, FieldEngine) and as command line binaries (falign, fbuild, fscore, aminer, ftemplater, fproject, FieldEngine):

Forge.exe	The main graphical interface for Forge.
FieldEngine.exe	The calculation engine for Forge and command line binaries. FieldEngine is started directly by the primary interface to perform specific calculation tasks. By default, one FieldEngine binary is started for each CPU core on the host machine (but this can be reconfigured in the application preferences or by command line switches). The applications communicate with the FieldEngine using a TCP/IP protocol that can cause network access warnings in some situations.
	The FieldEngine process can be run on a remote machine with communication managed through a variety of methods including Cresset's Engine Broker.
ftemplater.exe	The FieldTemplater command line interface.
falign.exe	The Forge alignment algorithm can be accessed using this command line binary. This binary reads molecules to be aligned and a reference structure or template and outputs the molecules aligned to the reference. Full details for operating the binary are available through "man" pages on Linux systems and html files.
aminer.exe	The Activity Miner™ command line binary takes aligned molecules (such as those from falign) and outputs either a similarity or a disparity matrix. It is used to identify regions of structure activity relationship where small changes in structure result in high changes in activity or to cluster molecules using 3D metrics.
fbuild.exe	The Forge build binary takes aligned structures (such as those from falign) and constructs a 3D(Q)SAR model (either Field QSAR, Activity Atlas™ or Machine Learning regression and classification models) to explain the observed activity using the Forge algorithm. Full details are given in the fbuild man and html pages.
fscore.exe	The Forge score binary uses a designated Forge model to predict activities for molecules that have been previously aligned (e.g., using falign). As with the other

command line utilities, full details on the operation of fscore are available from the appropriate man and html page packaged with the binary.

fproject.exe   The Forge project tool is used for extracting molecules, conformations, alignments, notes and roles out of a Forge project.

fsurface.exe   The Forge surface tool is used for generating and exporting Cresset field surfaces (positive, negative, hydrophobic and vdW) for an input set of molecules.

Supported Platforms

Minimum specifications

Hardware	Specifications
RAM	4GB
Processor	Intel i5 processor or equivalent
Disk space	200MB

Recommended specifications

Hardware	Specifications
RAM	8GB
Processor	Intel i7 processor or equivalent
Disk space	200MB

Supported Operating Systems

Forge is supplied as 64bit binaries for Windows®, macOS® and Linux®.

Windows®	macOS®	Linux®
Windows 7	macOS 10.13	Red Hat Enterprise Linux 6.10+ CentOS 6.10+
Windows 10	macOS 10.14	Red Hat Enterprise Linux 7

Installation

Platform based installation instructions are given below and at http://cresset-group.com/installing-desktop-applications.

Windows

1. Browse to the Windows folder of the Forge distribution media or locate the installer in your Downloads folder.
2. Double click the executable installer file. Installers are named according to the application and version that you are installing.
3. Follow the on-screen instructions. If you have a previous version of Forge installed, then this will be removed before installation of this version.

Linux

1. Browse to the Linux folder of the Forge distribution media or navigate to your Downloads directory.
2. Applications can be installed using a relocatable `rpm` or from a `tgz` file.
3. Install the Forge re-locatable rpm package using the command below (where <vers> is the version number and <arch> is the architecture) and <path> is install location (`/opt` by default).

```
yum install cresset-forge-<vers>-1.<arch>.rpm
```

or

```
rpm -U [--prefix <path>] cresset-forge-<vers>-1.<arch>.rpm
```

4. Alternatively, unpack the supplied tgz file to a suitable location (e.g., `$HOME` or `/usr/local` or `/opt`).

macOS

1. Open the supplied disc image.
2. Read and agree to the license agreement.
3. Drag the Forge icon onto the Applications icon to install the application in the Applications folder.

Start Forge

Windows

The install process places an entry in the 'Start menu' and a shortcut on your desktop. Double click this shortcut or navigate:

Windows 7

```
Start menu→Programs→Cresset→Forge
```

Windows 10

Choose **Start**, and type Forge (the search panel opens automatically as you type). In the search results, click Forge to start the application.

Linux

If installation was from rpm then select the shortcut in the Applications menu.

Alternatively, in a terminal window type

```
/path_to_installation/cresset/Forge/bin/Forge
```

where *path_to_installation* is the directory where the Forge distribution was unpacked. If Forge was installed from an rpm package with the default locations, then the installation will be in `/opt`.

macOS

Navigate to the Applications folder and double click the Forge icon.

Licensing

To run Forge, you will require a valid license file, available from enquires@cresset-group.com. To install a license, start the application and click on the 'Install license' button.

Changes in V10.6

- New Machine Learning methods (Support Vector Machines, Relevance Vector Machines, Random Forests) for building regression and classification models

- New kNN method for building classification models

- New 'Automatic' model building option to automatically run all the Machine Learning regression or classification models and save the model with the best statistics in the Forge project

- New Activity Atlas algorithm for small and medium sized data sets to enhance the information content and reduce the reliance on individual compounds

- New graphics engine generating enhanced 3D objects, thus delivering strong performance, improved pictures and new smooth transitions between storyboard scenes

- New function to automatically assign the selected molecules to roles, based on their Murcko scaffold

- New function to run clustering from the main Forge GUI, specifying the desired similarity metric and threshold

- New advanced Conformation Hunt option to filter out any boats and twist-boats conformations

- New option to use all available local CPUs, relaxing the 16-CPUs limitation in previous Forge releases

- New and improved 3D window functionality, including:

  o New tooltips for all surfaces (Activity Atlas, fields, molecular surfaces)

  o New surface pattern for Activity Cliffs Summary of Hydrophobics, to highlight differences with Shape surfaces

  o Improved display of bonds in 'thin stick' and 'capped stick' display style

  o Improved readability of constraints labels

  o More intuitive display of reference molecules *vs.* protein interactions

- New 'Clip Protein Only' function, toggling whether proteins only, or both proteins and ligands should be affected by clip planes

- New import and export of Forge preferences from the command line

- New export of the 2D and 3D structure of each molecules with a REST service

- New Molecules table right-click menu functions to:

  o Choose any user column as the molecule title

  o Choose the column to use as a label in the 3D window

  o Merge the conformations of different isomers of the same molecule into a single conformation ensemble

  o Set the user column type (text/number)

- New Edit menu function to invert current selection

- New 'Remove all Tags' function to remove all tags from a Forge project

- Improved QSAR Model widget, now including:

  o Plots and relevant statistics for the chosen regression model

  o Information (confusion matrix) and relevant statistics for the chosen classification model

  o New PCA components plot to identify grouping of molecules and outliers in the 3D descriptors space

  o New Notes tab to annotate relevant model information

  o New 'pop-up' button to visually compare different models

  o Improved logging for all models

- Improved Forge processing widget, now including:

  o New settings button to open the Activity & Model Manager

  o New link to the 'Data Set Partition' dialogue

  o New settings button to import/export or delete all customized process settings

  o New summary of the number of processes running on local and remote Field Engines

- More responsive GUI for large projects (more than 1,000 molecules with multiple alignments and QSAR models), with improved performance on common operations such as application of filters, calculation and interaction with custom plots, exporting data

- Faster, more robust and less memory-consuming calculation of Activity Miner and Activity Atlas large similarity matrices

- Improved 2D display of molecules

- Improved interface in the Activity & Model Manager for handling categorical data in support to classification models

- Improved Molecule Editor, now enabling the processing of all the molecules created during the same editing session

- Improved handling of multiple references in complex alignment experiments, now enabling exclusion of one or more references completely from the alignment

- Improved Conformation Explorer, now including:

- o New column listing chiral center configuration for each conformation

- o New right-click menu option to invert the current selection

- o Improved export functionality, enabling the export of all the data calculated within the Conformation Explorer

- o Improved copy behavior, now copying the selected conformations into the clipboard for pasting into other applications

- Improved Radial Plots and Multi-Parameter Scoring, including:

  - o New settings button in the Radial Plots Properties window, enabling import and export of the radial plot properties profile, and to restore the radial plot properties to default values

  - o New option to specify whether invalid values for each property should be shown at the edge or at the center of the radial plot

- Improved CSV import

- Improved Filters window, now including a green/red toggle to control whether each filter is enabled or disabled

- Improved filtering options for text columns, now including 'equal', 'not equal', 'containing' and 'not containing' options

- Improved structural filters now including pre-defined filters for Ring, Aromatic Ring, Non-ring atom, Chiral atom, H-bond donor and H-bond acceptor

- Improved Activity Miner GUI, including:

  - o Disparity matrix can now be filtered by Similarity, Disparity and Δ Activity from a dedicated widget

  - o New 'Find Molecule' function in the Disparity Matrix

  - o New function to tag all the molecules currently visible in the Activity View with a user defined tag in the Forge Molecules table

- Molecule color options are now available also from the Color button in the Style toolbar

- In the Constraints Editor, pharmacophore constraints can now be added to hydrogens atoms

- Improved Blaze™ results window now shows an enrichment plot and statistics for each Blaze refinement level

- Improved 'Send to Flare™' functionality for selected molecules, now giving an option to send also the reference molecules and the protein if present

- Improved plots now showing a regression line for selected molecules

- Improved PDB download widget now supporting multiple PDB download paths

- Improved export of molecules with drag-and-drop, now exporting all Molecules table data as sdf tags.

Changes in V10.5

- New Conformation Explorer to visualize and inspect the conformations created for one or more selected molecules. With the Conformation Explorer you can:
    - Visualize all the conformations created for each molecule in your Forge project
    - Delete unwanted conformations
    - Calculate and plot distances, angles and torsions
    - Calculate CSD torsion frequencies for all rotatable bonds using the Torsion Library method
    - Filter conformations by energy, CSD torsion frequency and calculated distances, angles, torsions
    - Smart coloring of conformations by energy and by CSD torsion frequency
- New Constraint and Field Point Editor window, enabling users to:
    - Define pharmacophore constraints to bias aligned molecules to have a particular feature (for example, a H-bond acceptor) at a specific position, by introducing a penalty which down-scores results that do not satisfy the constraint
    - Define field point constraints to specify that a particular type of field must be present in the aligned molecule, by introducing a penalty which down-scores results that do not satisfy the constraint
    - Add customer-defined field points to be constrained
    - Enable protein display to help you set up pharmacophore and field constraints appropriately
- Significantly improved molecule alignment. New and enhanced functionality includes:
    - Improved substructure alignment algorithm
    - New capability to specify the substructure you wish to match by writing a SMARTS pattern
    - New alternative similarity metrics
    - New individual field similarity weighting
    - Improved quick alignment calculation method
- Additional weighting schemes now available for calculating kNN models
- Enhanced Molecular Editor, including:
    - A more rational layout
    - A Radial Plot window showing critical calculated physico-chemical properties, which are updated as changes are made to a molecule
    - New 'Save a copy' button, to save an annotated copy of the molecule being edited into the Forge molecules table without leaving the Editor
- New functionality to enable removal of duplicate molecules
- New 'Send to Flare' functionality to send either all molecules, favorite molecules or selected molecules to Flare, including as appropriate the reference molecules(s) and the protein

- New functionality to tag project molecules according to cluster membership, as calculated in the Cluster View of Activity Miner

- New functionality to sort disparity matrixes in Activity Miner by Forge project tags, enabling easier identification of molecules of interest

- New functionality to export Activity Atlas models as surfaces from the GUI

- New Forge surface (fsurface) command-line binary to export Cresset field surfaces (positive, negative, hydrophobic and vdW)

- New capability to annotate and re-name Storyboard scenes

- New capability to export molecules by drag-and-drop to the Windows desktop (Windows only)

- Improved accessibility of conformation hunt, alignment and build model advanced options, which can now be accessed directly *via* a 'settings' button in the Forge processing widget

- New button in Forge Appearance preferences to swap color of fields (blue/red)

- New 'Copy column' behavior, duplicating the data for the selected column into a new column, prompting the user to define a new column name

- New functionality to control 3D display font and font size separately from the Forge application font size

- Enhanced stereo view functionality with improved accessibility

- New support for touch screen displays

- Improved File menu functionality, now also showing a list of recently opened molecules files in addition to recently opened project files

- Improved 'Grid' button functionality, replacing the old 'Sep' and 'Grid' buttons

- Improved right-clicking behavior in the 3D window enabling actions to be applied (as appropriate) to multiple molecules

- Improved display of protein ribbons, offering a choice of different ribbon styles and capability to show ribbons for the active site only

- Improved import of CSV files now enabling de-salting of imported molecules

- Improved automatic detection of activity columns. Automatic detection of activity columns can now be disabled in the Forge preferences when importing files with a large number of activity data

- Improved functionality enabling show/hide of the text displayed in the 3D window from the Forge View menu

- Improved tagging of molecules, now enabled also from the 3D window

- Improved handling of numerical filters

- Text data stored in Forge project cells can now be copied into the clipboard

- Improved look and feel of the GUI with re-designed toolbars and icons.

Changes in V10.4.2

- The man and html pages for the command line tools have been improved

- Fixed bugs in SMARTS filtering

- Fixed export of Field QSAR field sample data from fscore

- Fixed crash when attempting to load more than 9 molecules into the reference role

- fbuild and aminer no longer charges the molecules if an activity tag is set. Note the molecules can still be charged by setting the –charge option

- Improved the error handling and error messages for all the command line tools

- fbuild and aminer now always read activity values as log units. Previously there were some rare cases where the activity value units was auto-detected. Note the units can be manually set using the --units option, see fbuild or aminer help documents for more details

- When generating an Activity Atlas with fbuild --molecules-explore-count option, the correct Activity value is now used

- When generating a similarity matrix using aminer the diagonal similarity values are now 1.0 instead of 0.0.

Changes in V10.4.1

- Fixed bug where Forge could become unresponsive when communicating with a license server.

Changes in V10.4

- New Activity Atlas method to summarize activity data into a visual model
  - Calculates and displays as 3D visualizations:
    - Average of actives: what do active molecules have in common?
    - Activity Cliff Summary: what do the activity cliffs tell us about the SAR?
    - Regions explored analysis: where have I been? For a new molecule, would making it increase our understanding?
  - Calculates Novelty score for each molecule
- New k-Nearest Neighbour QSAR method to carry out robust activity predictions
- New option to ignore a protein excluded volume in alignment tasks
- New Storyboard dock, to capture scenes recording all details from the 3D window that can be easily recalled when needed
- New tile view

  - View results in a tiled layout to see multiple results at a glance
  - Customize tiles to include
    - radial plots
    - the new tags

- ▪ project notes
- ▪ selected other data

- New Tags feature enables the tagging of any result with a custom label

- New filtering on structure enables visualization of molecules that include or exclude a specific substructure specified by means of either:

  - o A SMARTS pattern

  - o A fragment drawn using a molecule editor

- New concept of preferred alignments (complementing the use of Favorites)

- New external REST service for properties, enabling the connection to an external web service to import external properties and data as additional project columns in the Molecules table

- New Flexibility molecular property column

- New export of MEP surfaces in the CCP4, Cube, Insight and MOE formats

- New export of 3D window image

- New capability of combining selected molecules into a single disconnected entry

- New Forge-project-tool binary to retrieve information and molecules from a Forge project file

- Rotating a torsion in the Molecule Editor will display a graph of the torsion energy

- Improved Radial Plots to support enhanced Multi-Parameter Optimization

  - o A weight can be associated to each property in the Radial Plot to calculate a single numerical score for each molecule which represents the overall fit of the compound to the ideal profile

  - o The score can be used to rank the molecules and colour molecules, columns, and radial plot by score

- New QSAR Model Dock to save, analyze and visualize multiple (Q)SAR models in the same Forge project

- Improved Forge Processing dialogue:

  - o Completely re-designed to better handle different model building choices and options

  - o More intuitive to use

  - o Provides information and warning notifications to support the correct processing of molecules

- Improved Plotting

  - o Histograms

  - o Second y-series in scatter plots

  - o Statistics reported for single series scatter plots

- Activity Miner improvements:

  - o Activity Miner now supports the use of 2D metrics without the need to pre-align the molecules

  - o User Interface now enables the selection of the desired 3D/2D metric from the toolbar

- New control to optimize the relative orientation of each pair of conformers during Activity Atlas, Activity Miner and kNN analysis by means of a simplex optimizer

- Improved interaction with Blaze™ and simplified Blaze Search Results windows

- Project Notes promoted to separate window for recording experimental details

- Improved visualization of protein active site

    o Protein active site radius control in Protein Display Toolbar

    o Active site radius now saved with the project and the storyboards

    o Separate display of H-bonds and steric clashes

    o Measurements can be individually cleared

- Improved import/export of PDBs (PDB importer now correctly importing DNA/RNA)

- Improved tooltips

- AccelrysDraw and ChemDraw structures can now be pasted directly into the Molecule Editor

- Any applied filters are now saved with the project

- Improved substructure alignment algorithm

- New option to control the behavior of falign when reading project files containing molecules

- Improved interface to CEBroker enables easy disabling

- New option to control the time between autosaves

- New option to clear contents of a column in the Molecules table

- Reduced file size for Forge projects by compression of the 3D coordinates of molecule conformations. Please note that this may result in small changes in the coordinates' values when the projects are re-opened.

Changes in V10.3.1

- Removal of Section 2.4(vii) from EULA:

    o *(vii) use the SOFTWARE for any of the following purposes; the discovery, modification, improvement, alteration, use, application, sale or distribution of compounds intended for the control of weeds, pathogens in plants, parasites, pests and/or compounds intended for affecting the yield or output of any plant;*

- Assorted bug fixes.

Changes in V10.3.0

- New support for multiple activities in activity miner

    o Find and understand selectivity cliffs

    o Visualize SAR across multiple assays

    o Set different error bars on each activity

- o Automatic calculation of selectivity between primary and secondary activities

- New ability to create 3D-QSAR models for multiple activities

- New 'Score only' calculation setting to rescore molecules using different settings

- Improved conformation hunt settings for Accurate mode that creates fewer, lower energy conformations

- New automatic enumeration of flat chiral centers into multiple isomers that are conformation hunted separately but treated as an ensemble in alignments

- Increased all limits

    - o Use more threads in a calculation

    - o Read more molecules into a project in a single read

    - o Removed 100,000 compound limit on GUI

    - o Increased maximum size of protein that can be read to 25,000 atoms including hydrogens

- New interface to Cresset's (new) Engine Broker enables Forge desktop and command line applications to use cloud or local cluster resources to complete calculations

- New activity manager to select and control multiple activities and import 3D QSAR models

- New integrated FieldTemplater module

    - o Multiple FieldTemplater projects for each Forge project

    - o Cloning of FieldTemplater projects

    - o Drag and drop molecules from Forge to FieldTemplater module

    - o Drag and drop templates from FieldTemplater to Forge

- New filters in FieldTemplater enable selection and viewing of templates that contain specific molecules

- New FieldTemplater command line interface ('ftemplater')

- New wizard to guide users through new calculations

    - o Cleaner and easier to use

- Significantly improved integration to Blaze

    - o Start a Blaze search directly from Forge, selecting collections to be searched and heavy atom ranges

    - o Browse completed and running searches

    - o Download search results directly into Forge

    - o Constraint and protein information from Blaze search is automatically loaded and displayed correctly

- New radial plots of values in the molecule table including physical properties. Quickly assess compounds for the fit to standard corporate or project profiles

- New column script editor to interact with all data in the molecule table

- o Automate data processing tasks such as removing ">" symbols from activity values

- o Create new columns based on molecule properties such as atom counts or normalized lipophilic ligand efficiency

- o Create standard scripts that run on every project

- o Deploy scripts to colleagues using Forge or Torch™

- New preference to perform all conformation hunts using a specified external command line tool

- New capability to plot any values in the molecules table as an interactive scatter plot

- o Compare molecules in multiple plots simultaneously

- o Select molecules with interesting properties and examine the SAR around them

- New ability to display field surfaces as a difference in the main application when two molecules are selected. Previously this was only possible in the Activity Miner interface

- Improved protein display handling

- o New button to toggle display of the protein active site

- o New option and button to display protein backbone as a ribbon

- New option to enable conversion of categorical data to numerical data

- New option to automatically color the selected ligands in an individual color, enabling rapid differentiation of multiple ligands in the 3D display

- Improved management of information windows that causes unused windows (such as those associated with 3D QSAR) to be hidden until needed

- New preference settings to control which columns are displayed in the molecules table by default

- Improved 'drag and drop' behavior for files and molecules.

- Improved keyboard shortcuts for 3D window and for Activity Miner

- Added option to command line activity miner to enable writing of Forge project files

- Improved feedback when converting large number of molecules into aligned molecules

- Added measurements to the molecular editor

- Added ability to set the title of molecules in the molecular editor

- Added index of conformation used to alignment information in the molecules table, color coded based on energy

- Added preference options to control colors used for displaying QSAR models

- Added correlation of y scramble sets with original values to the Model log window

- Improved MCS code that runs at approximately ten times the speed of the previous algorithm making application more responsive

- Improved license reporting in the 'About Forge' box

- New option to epimerize a chiral center in the molecular editor

- New option to 'Restore previous version' that enables roll back of experiments

- New option to remove specific clusters from the activity miner analysis by right clicking on the cluster dendrogram

- Improved labeling of atoms, field points, molecules and residues in the 3D window

- Improved display of protein active site to clip molecular surfaces to just the displayed residues

- Numerous minor bug fixes and improvements

Changes in V10.2.0

- New Activity Miner module to enable deciphering and navigating SAR

  - Uses 'disparity' or 'activity cliff' concept to find important changes

  - 4 new views on the disparity data

  - Uses 3D similarity as a measure of distance

  - Optionally uses 2D similarity as measure of distance

- Added capability to read molecules from csv data

- Added ability to update molecule data from csv files.

- Added ability to open files by dragging and dropping onto the main window of the application (Windows)

- Add capability to upload protein/ligand pair to Blaze (requires blazeV10.1)

- Added ability to capture specific interaction by converting a protein atom to a field point for all references

- Added spin and rock functions to 3D window

- Added full screen view by pressing F11

- Added option to prune the view only the protein residues surrounding the reference molecules

- Added option to color molecules by residue information

- Added "No calculation" options to the processing window

- Added preference to disable auto save function

- Added menu entry to remove unused conformations from a project

- Added a "Clear" option to the wizard

- Added ability to create additional molecule roles in the results table

- Added Ligand Efficiency and Lipophilic Ligand Efficiency columns to the Results table

- Added a special per molecule "Notes" column that can edited in the table or the molecule editor

- Improved logging of model building and reporting of statistics

- Improved display of log data for templates in FieldTemplater

- Improved the information present in the log for templates in FieldTemplater

- Improved drag and drop of molecules from one role to another in the results table

- Improved column handling including ability to hide, sort and set as activity value

- Column orders now saved with the project

- SDF export now only includes visible columns

- StarDrop model directory now accessible through the CRESSET_STARDROP_DIR environment variable

- Autosave function now presents a dialogue box to advise of status

- Columns in the results table can now be renamed

- Added ability to test connection to Blaze directly from the configuration page

- Added multiple circular fingerprint methods for 2D similarity calculation

- Added preference setting for control over which 2D similarity method should be used

- Fixed bug where copying more than 7 molecules in 2D omitted remaining molecules

- Fixed bug where activity values for activities specified as Molar were off by one

- Numerous small bug fixes and enhancements

Changes in V10.1

- New capability to load and view molecules without alignment

- New capability to load and view Blaze (FieldScreen) result files

- Added capability to open and view FieldView projects

- New context menu on the 3D display.

- New feature - paste molecule as conformations.

- Now able to apply differing weights to multiple reference molecules.

- Now able to move molecules into protein "set".

- Now able to convert conformations of a molecule into alignments (for viewing).

- Molecules loaded as pre-aligned are now scored against reference molecules on loading.

- Command line falign now able to provide a score without aligning molecules

- Fixed a bug where field sample values were not being calculated correctly in the QSAR model building and playing

- New warnings for loading a reference or a protein from a 2D file.

- No longer able to hide the first column in Forge.

- Improved transfer of molecules from Spark™.

- Fixed a bug in the licensing that caused licensing to fail when third party license files were found.

- New warning on export if the StarDrop thread is still running.

- Selected reference molecules are now displayed even if "Show refs" is turned off.

- Forge - activity graph now updates on initial model creation.

- Fixed a bug in the editor where left clicking on an atom and at the same time right clicking caused a crash.

- Fixed bond lengths for thiazoles.

- Forge CSV export now exports error bars for StarDrop predicted properties.

- Fixed bug where Forge re-adds fields on reading .xed files when it shouldn't.

- Fixed bug where the FieldTemplater manual was not found.

- Fixed bug where Forge produces NaN models where the block standard deviation is zero

- Fixed a bug where sample data from the Test/Prediction Set was not being correctly exported.

Changes in V10.0.1

- Introduced command line interfaces to alignment (falign), model building (fbuild) and model playing (fscore)

- Added pdb file reading support

- Adding "copy and cut selection" to right click menu of molecule editor

- Molecule editor can now select water molecules directly from the right click menu

- Favorite molecules are now labelled with a '*' in the grid view of the 3D window

- Improved tooltips on 3D window to make identification of specific molecules and features easier

- Added a column to the results table to indicate the filename that the molecule was read from

- Improved error messages from licensing code

- Improved the export of model data to csv to include more information

- Improved the "Manage columns" function to allow column ordering

- Fixed an OpenGL related crash on application exit on OS X

- Fixed residue labeling

- Fixed bug in substructure alignment method that could cause some conformations to be created without field points

- Fixed bug in copy 2D to clipboard

- Fixed rare crash of FieldEngine on Windows

Version 10.0

- Initial release of Forge based on FieldAlign 3.0.1 and FieldTemplater 3.0.0

File Format Compatibility

Forge project files saved with a patch version of Forge can be read by any version of Forge with the same minor version number. For example, a Forge project file saved with Forge 10.4.2 can be opened with 10.4.0, likewise a Forge project file saved with Forge 10.4.0 can be read with 10.4.2.

Newer versions of Forge can open any project file saved with an older version of Forge, FieldAlign or FieldTemplater. For example, Forge 10.5.6 can open Forge 10.1.0 project files.

Forge can save project files as an older format by selecting 'File' → 'Save Project As' and setting the 'Save as Type' to an older version. For example, Forge 10.6 can save a Forge 10.5 project file.

Forge can also read Torch and TorchLite projects. The same rules apply to Torch/TorchLite as they apply to Forge projects. For example, Forge 10.4.2 can read Torch 10.4.2 and 10.3.0 projects but not Torch 10.5.0 projects.

Uninstalling Forge

Windows

Forge can be uninstalled using the standard 'Programs' Control Panel shortcut.

Linux

If Forge was installed from a rpm package, it can be uninstalled with one of the following command lines, depending on whether it was installed with the `rpm` or `yum` command:

```
rpm -e cresset-forge-<vers>-1.<arch>
```

or

```
yum erase cresset-forge-<vers>-1.<arch>
```

If Forge was installed by unpacking a tgz file, it will be sufficient to remove the containing folder from the disk.

macOS

In the Finder sidebar, click Applications. Drag the Forge from the Applications folder to the Trash (located at the end of the Dock).

Known Issues and Bugs

Forge may not operate optimally on remote systems like Citrix Virtual Apps. For optimal user experience, it is recommended to run Forge locally.

Forge will crash when the File dialog is opened if "Dell Backup and Recovery Application" between versions 1.7.5.64 and 1.9.2.8 (list not inclusive) is used on your computer. You should update the Dell utility if this issue affects you.

Scaling of GUI elements may be sub-optimal with high resolution monitors connected through legacy VGA cables.

When using multiple monitors with differing text scaling settings the toolbars and other GUI elements can display poorly requiring the layout of the GUI to be reset using Windows menu→Reset Layout.

On some graphics cards transparent surfaces are not displayed properly. Setting the 'Surface transparency' option to zero in the display preferences fixes the problem.

Occasionally the selection engine gets confused over which molecule is selected such that the display does not update when you click on another molecule. The selection can be reset by right clicking on the displayed molecule and choosing 'Select'. New selections should now be displayed correctly.

Occasionally Forge is able to find similarities greater than 1 or less than 0. These occur with small molecules using quick settings or using constraints with a high degree of shape based scoring.

The 'Optimize and score the template' section in 'The Science – Generating templates' chapter is not populated in the built-in Forge manual. Please refer to the online [Forge Manual](#) to read this section.

macOS

In some circumstances, after using the full screen function the application reports a crash instead of exiting cleanly. The report is not harmful as it only happens as the application closes and no data is lost.

In the manage columns in results table widget, selecting and dragging many elements between the displayed and un-displayed sections causes the application to crash.

Found a bug or problem that is not listed? Please contact us to help us improve our software!

Third party software

A range of open source and free software libraries and executables are incorporated in each Forge installation. License agreement information for each third party software can be found in the 'documentation' subdirectory of the Forge installation directory and at https://www.cresset-group.com/products/third-party-licenses/. Contact us at support@cresset-group.com if you wish to obtain the source code for any open source component.

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