

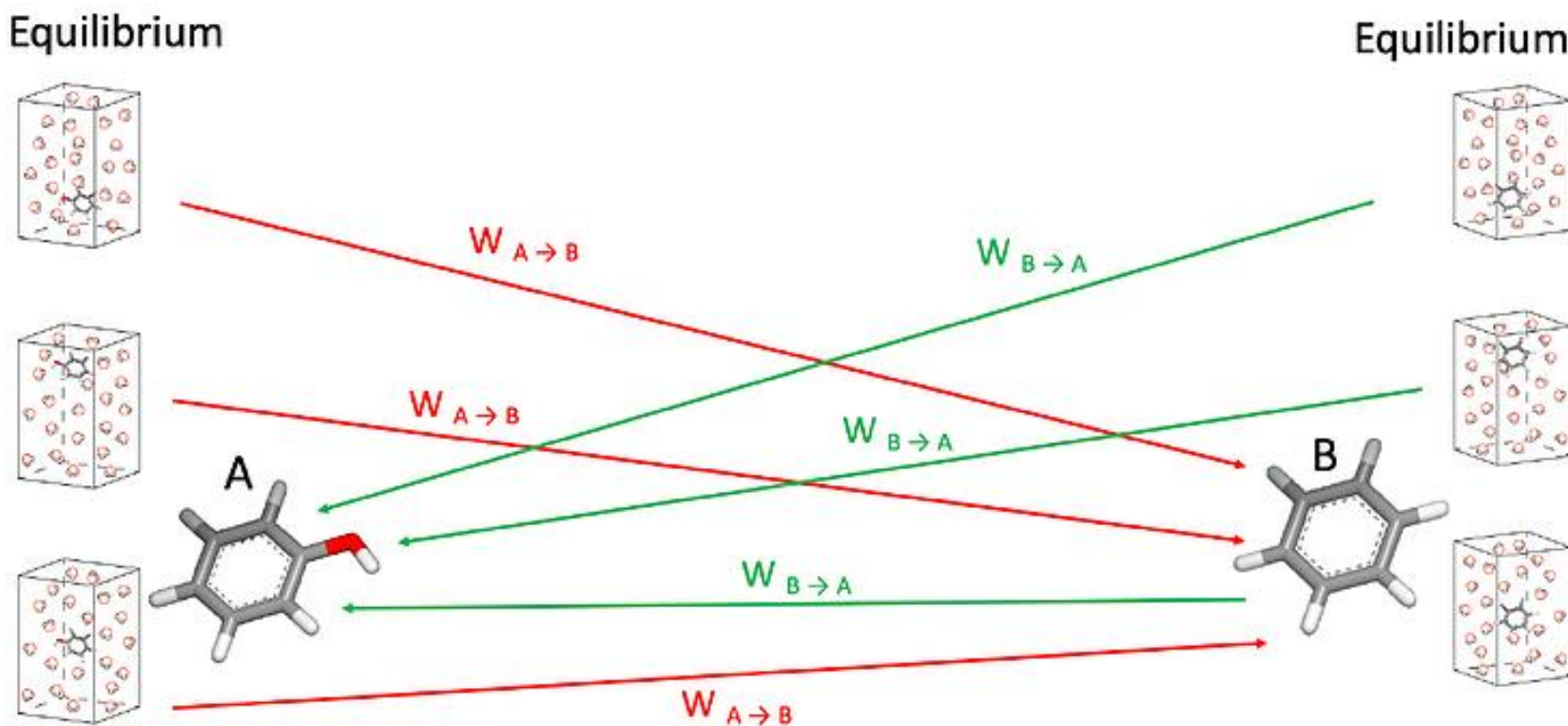
Orion v2021.1 User Update

Matt Geballe
VP of Product
August 18, 2021

Orion v2021.1

- Largest update in several years
- **Science**
 - Free Energy Calculation
 - Reaction-based Library Generation
 - LSVS: New FastROCS and Enamine
- Data Organization and Management
 - Project Data
 - 3D Modeling & Protein Editing
- Cost Alert Thresholds
- Parameter Grouping and Organization
- Collaborative Discussion Boards

Relative BFE via Non-Equilibrium Switching



Non-Equilibrium Switching

Extremely Fast and Ultra Parallelizable

Generative Design – What's new?

- Existing Floes:
 - Generative Structure Floe
 - Generative Structure Floe Site Selection
- NEW Floes in Orion 2021.1. Users now have a choice of specifying Reagents and Reactions
 - Focused Library Core Input Floe
 - Focused Library Molecule Input Floe
 - Focused Library Reagent Join Floe

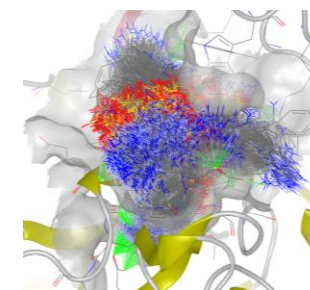
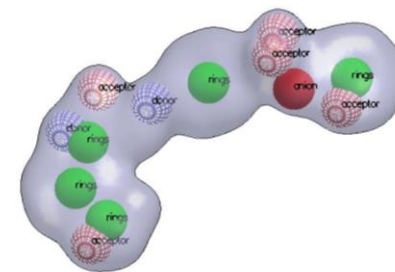
Useful for Hit to Lead

Useful for Lead Optimization

New – “FastROCS Plus”

- FastROCS Plus

- Combine the best of OE methods in one step
- Re-score of top hits with ROCS (Shape) and/or Docking



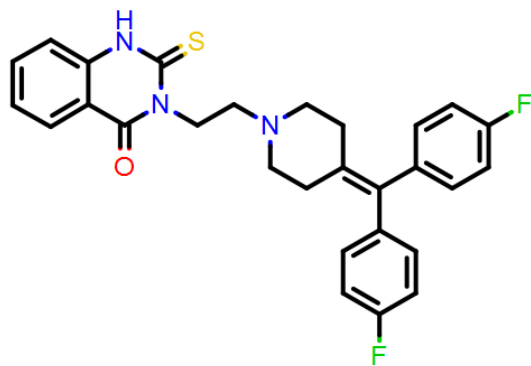
- Analysis made easy - Users can easily analyze and select top hits
 - Create a consensus output chart by Pareto Dominance Ranking
- NOTE: The 2020.3 version of FastROCS floe remains available, renamed “Batch FastROCS”

Vendor Database Update – Enamine 2020q3-4



2D Search

~~1.3~~ 1.95 Billion
Molecules



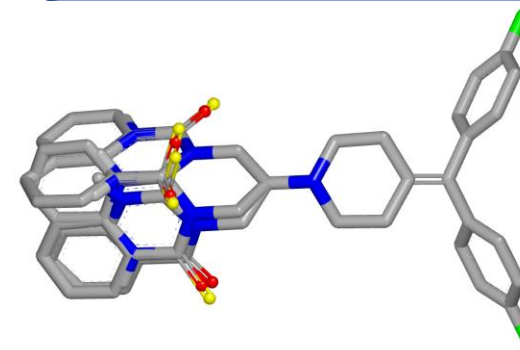
<500 MW
Protonated pH 7.4
Enumerate <4 stereocenters

SMILES to Conformers



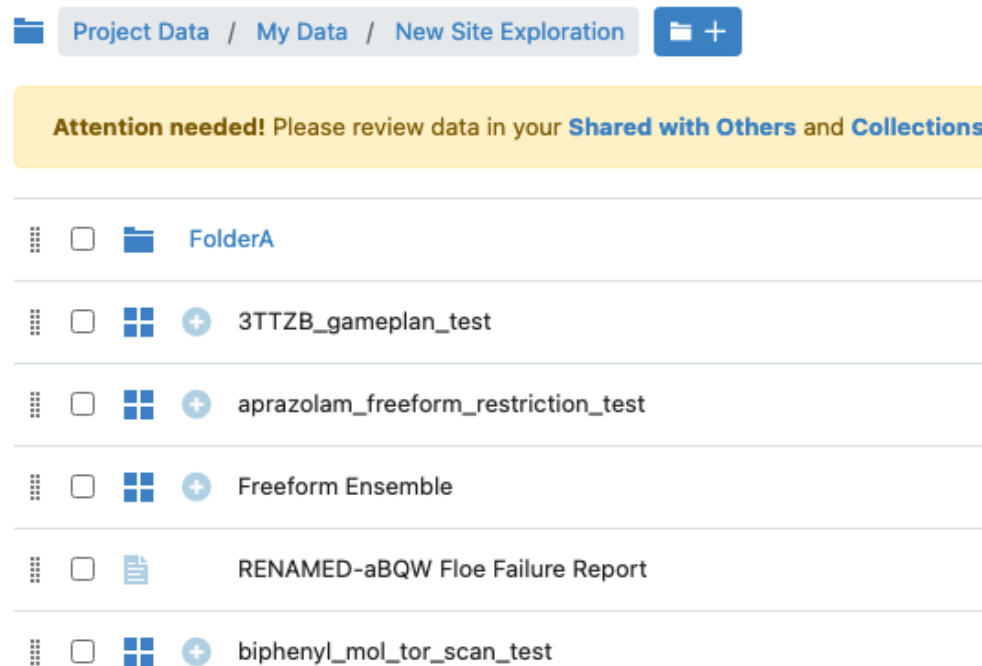
3D Search

~~2.7~~ 3.6 Billion Molecules
~~27~~ 36 Billion Conformers



New Orion Data Organization:

- **Better** organization for **more** data via **familiar** filesystem concepts



Flat structure

All new data into same place

Separate View of Datasets/Files/Collections

Shared access via individual sharing



Multi-level organization with drag & drop, paths, etc.

Control location of upload and floe output

Combined View of resources

Location dictates shared access

Location Controls Data Access



The screenshot shows the Orion Scientific interface. On the left is a dark blue sidebar with navigation icons and labels: OpenEye, Tom's Project, Data, 3D, Analyze, Floe, Sources, System, a notification bell, a graph icon, a user profile icon labeled 'trdiaz', and a question mark. The main content area has a light blue header with 'Active Datasets 1', 'Filters 0', 'Records: All 981', 'Passing Filters 981', 'Selected 0', a search bar, and a 'Data Handling' button. Below the header is a search bar with the placeholder 'enter a tag or resource name...', a 'Show:' dropdown set to 'Datasets, Fi...', and a 'Sort by:' dropdown set to 'Created: Newest First'. There are radio buttons for 'Current folder' (selected) and 'All project folders'. Below this is a folder tree with 'My Data' selected. The main content area displays a dataset named 'pyrrolamides_3D' with 981 records, a date of 06/26/2021, and a value of 1058356. A diagram with arrows points from the text on the right to the 'My Data' folder and the dataset entry.

Data private to you
Data available to all project members
Create a shared workspace with configurable access

Migrations with minimal pain

- No loss of data access
- No change in underlying data resource IDs
- No required work in cubes or floes to support

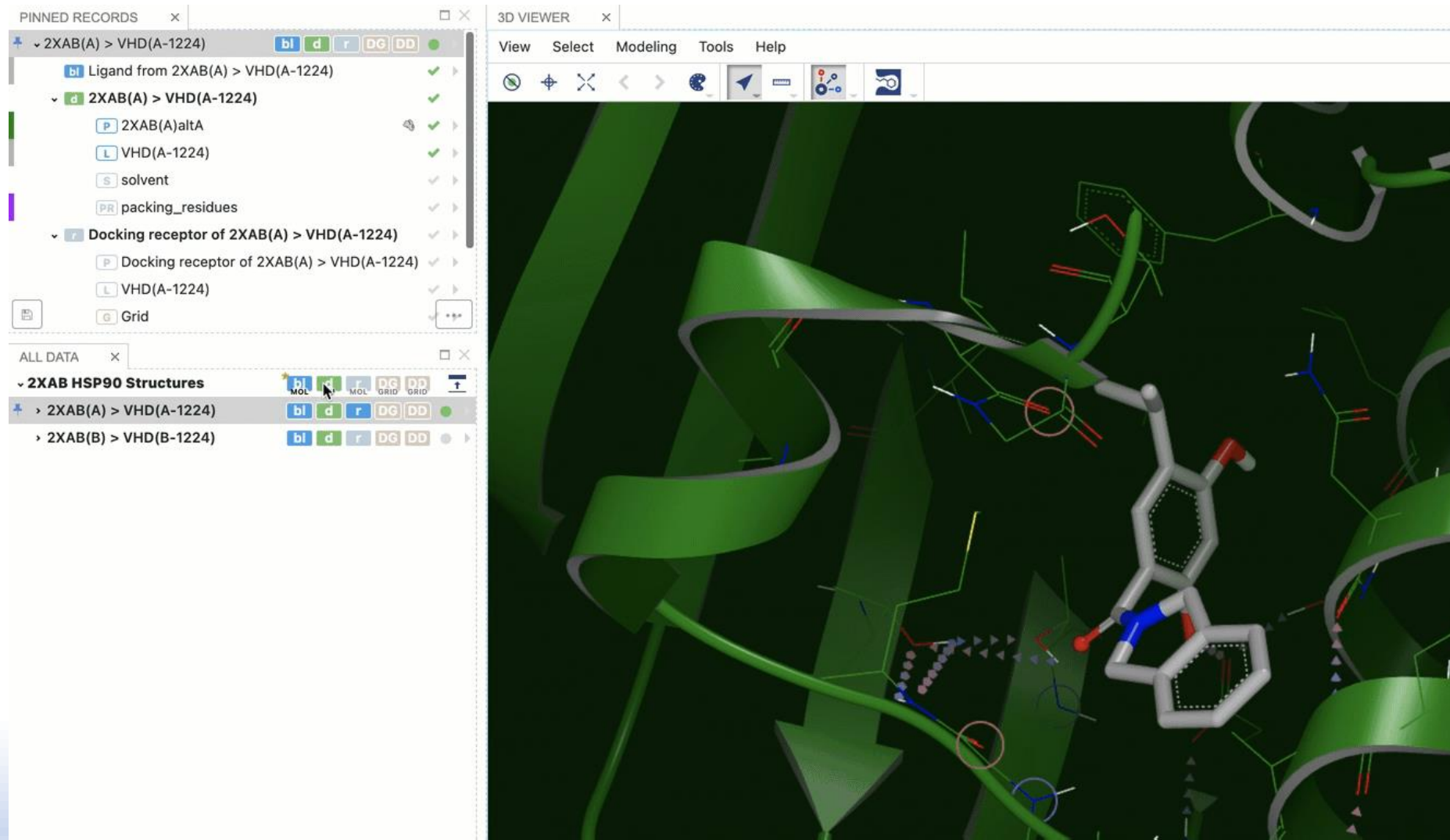
- Additional features

- Handling name collisions
- Orion Client support
- Favorite Folders
- Location-based Search

The screenshot displays the OpenEye Scientific data management interface. On the left, a sidebar contains a green '+ Add Data' button and a list of folders: Active Datasets, Project Data (selected), Organization Data, Trash, Shared with Others, Shared with Me, Collections, Favorite Folders, jobs, Current Best, and Protein Structures. The main area features a search bar with 'Conf' entered, a 'Project Data' filter, and a yellow warning banner: 'Attention needed! Please review data in your Shared with Others and Collections folder'. Below, search results for datasets containing 'Conf' are shown: 'BFS analogs Enamine BestConf' (Folder: My Data/MaaS Results) and 'EMol 5k Omega Conformers' (Folder: Team Data/Current Best).

Managing Data in 3D Modeling






- Badging for visual information and control



Managing Data in 3D Modeling

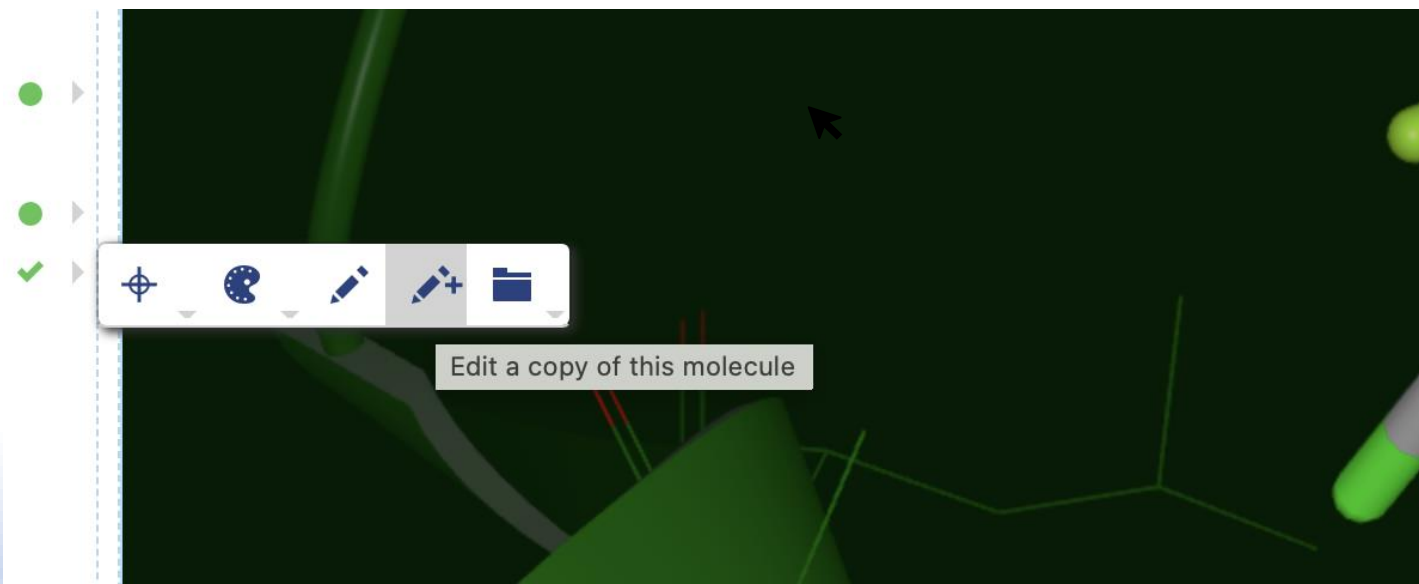
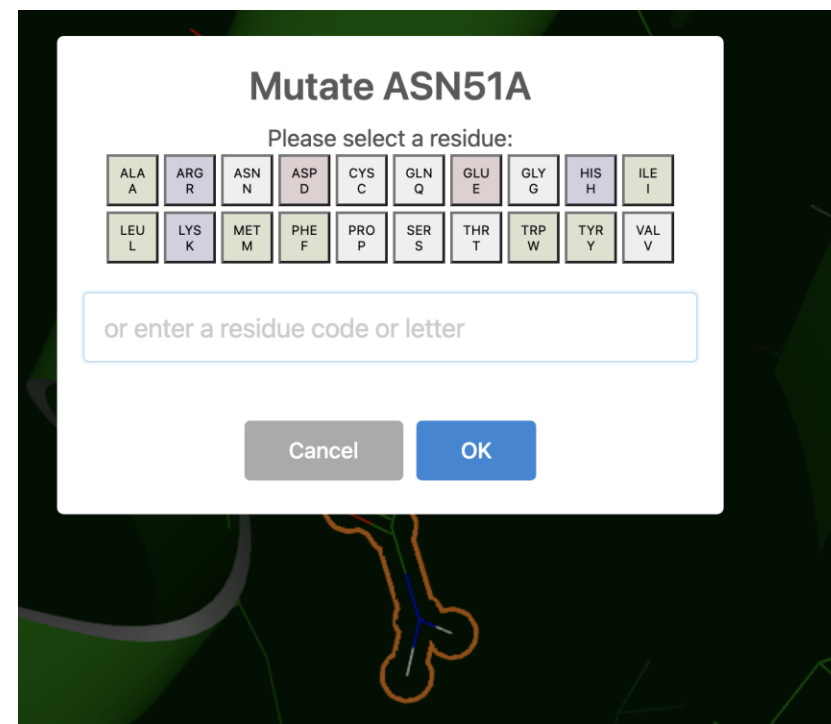
- Badging for visual information and control
- Controls over visibility

Data Handling

Column	Dataset	Type	All	3D	Spreadsheet	Plot	Tile View	Data Completeness
 bound ligand	2XAB HSP90 Structures	Molecule	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<div style="width: 100%; height: 10px; background-color: green;"></div>
Active Site Depiction	2XAB HSP90 Structures	String	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<div style="width: 100%; height: 10px; background-color: green;"></div>
B-Factor Depiction	2XAB HSP90 Structures	String	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<div style="width: 100%; height: 10px; background-color: green;"></div>
 Density Grid	2XAB HSP90 Structures	Grid	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<div style="width: 100%; height: 10px; background-color: green;"></div> 
 designunit	2XAB HSP90 Structures	Design Unit	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<div style="width: 100%; height: 10px; background-color: green;"></div>
 Diff Density Grid	2XAB HSP90 Structures	Grid	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<div style="width: 100%; height: 10px; background-color: green;"></div>
<i>du_single</i>	2XAB HSP90 Structures	Blob	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<div style="width: 100%; height: 10px; background-color: lightgreen;"></div>

Managing Data in 3D Modeling

- Badging for visual information and control
- Controls over visibility
- Easier editing and saving (including DUs)



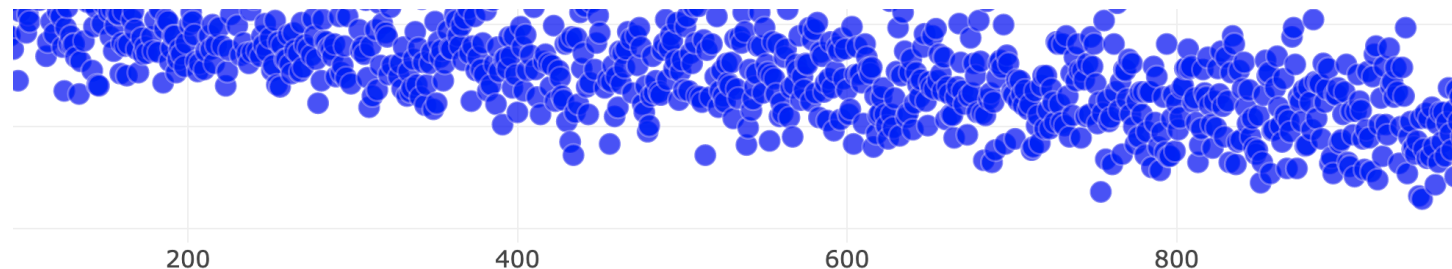
Managing Data in 3D Modeling

- Badging for visual information and control

- Controls over visibility

- Easier editing and saving

- Use Fields as Record Titles



are not plotted due to missing values. This may include conformers.

Column Options ▾ Views:

e URL ▾	Heavy Atom Co... ▾	idnumber ▾	Molecule Weight ▾	Shape Tanimoto ▾	Tanimoto Combo ▾	TPSA ▾	TPSA (Calculat... ▾
www.e...			442.41	0.83	1.38	76.15	
www.e...			401.52	0.81	1.38	66.84	
www.e...			386.44	0.689	1.35	84.94	
www.e...			409.52	0.799	1.35	83.91	

Sort Ascending
Sort Descending
Hide Column
Delete Column
Rename Column
Click to set as record title
Pin Left
Pin Right

Cost Alerts

- Unexpected Job costs are a common concern

✔ Job Cost Limits

Set cost alert and termination thresholds for this Job. To disable a threshold, clear the input or set the amount to zero. The value of these thresholds can be adjusted after job launch from the Job Status page

Email me if this job cost exceeds: \$

Terminate this job if the cost exceeds: \$

Status	Running
Created	Jul 20, 2021 10:48:10 AM
Source Floe	OMEGA - 3D Conformer Ensemble Generation
Source Floe Version	0.8.1
Tags	+ Add a tag
Job ID	414831
Cost	Not available
Email me if this job cost exceeds:	\$10.00 (USD)
Terminate this job if the cost exceeds:	Not set

The job [FastROCS Plus \(Keywords: Shape, Docking, Consensus, Collection, Virtual Screening\)](#) launched by **Mark McGann [mark]** in **HSP90** at **Mon, 19 Jul 2021 17:42:45 +0000** has reached the **All Admin Job Cost Alert** threshold of **\$100.00**.

The current state of the job is:

running

The current cost of the job is:

\$103.26

This job **has a Job Cancellation Cost Threshold of \$250.0** set at the time of this email.

Click [FastROCS Plus \(Keywords: Shape, Docking, Consensus, Collection, Virtual Screening\)](#) to see the latest job cost, cancel the job, reset the cost alert to a higher value, or edit the job cancellation threshold.

- Users can set Job Cost Alert and Job Cancellation thresholds on their jobs
- Admins can set Individual and All Admin Cost Alerts for all jobs

Promoted Parameter Groups

- Users get better organized floes with parameters grouped logically
- Floe Authors can plan and group parameters to make a better floe launching experience

Inputs

Outputs

Intermediate Optimization Output:

Dataset to store QM optimized conformers before deduplication. If a job is cancelled early (either by the user or hitting a cost threshold is reached), these intermediate optimized conformers, will still be saved.

Outputs

Options

Hit List Size:

Size of all output hit lists. (Max value 100,000, Min Value 1000).

FastROCS Similarity Type:

Type of FastROCS Similarity to use to rank molecules sent to the FastROCS, ROCS and consensus ROCS hit lists. This method will also be used by ROCS re-scoring if it is enable (ROCS re-scoring is enabled by default).

Options: Advanced

Conformer Parameters

Specify RMSD, energy cutoffs, and constraint options for this conformer ensemble.

RMSD Threshold For Conformer Generation:

RMSD threshold for conformer duplicate removal

Maximum Conformers For Geometry Optimization:

This parameter limits the number of conformers optimized, to prevent accidentally spending more than expected on a single Floe. If more than this number of conformers are generated, then only one conformer will be optimized to learn about the cost of this floe/conformer. If the max number of conformers is set to 0, then ALL generated conformers are optimized.

Psi4 Energy Window (Kcal/Mol):

Psi4 energy window for filtering high strain conformers. When the filter is set to -1 all conformers are included in output.

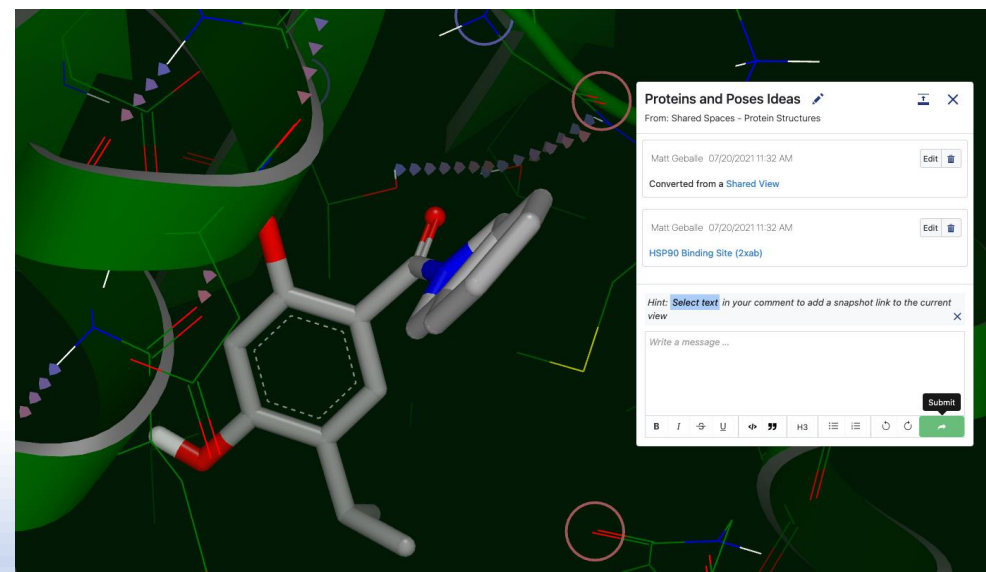
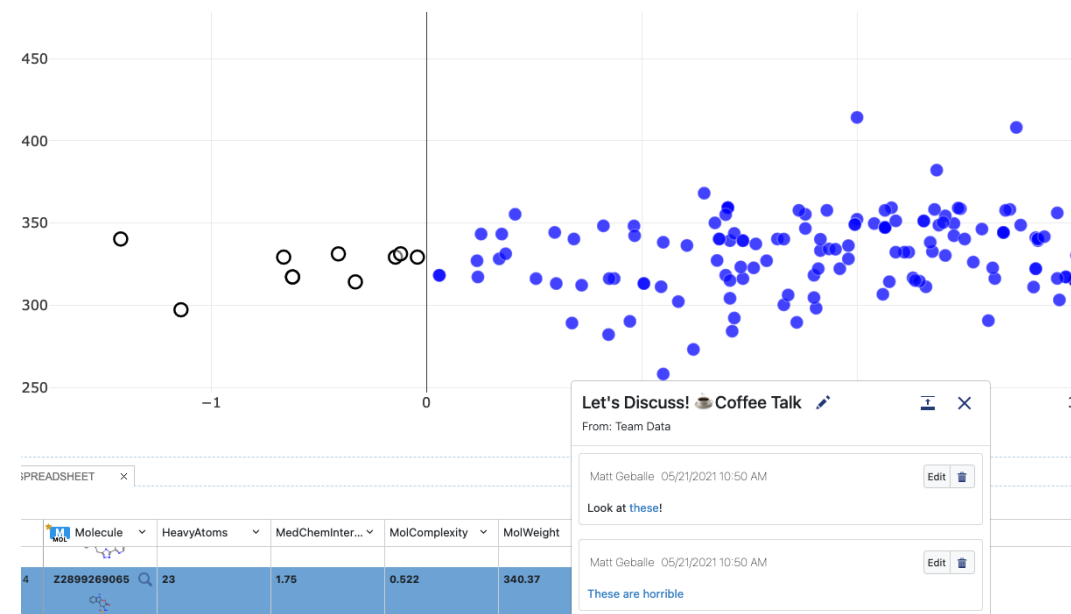
Constrain Torsions With Polar Hydrogens:

Torsions terminating in a polar hydrogen (i.e. hydroxyl groups) will be constrained along with all other rotatable bonds (On). Otherwise (Off), only rotatable bonds with heavy atoms will be constrained.

Psi4 Calculation Parameters

Discussion Boards (Beta)

- Next Evolution of Saved Views
 - Multiple views
 - Discussion & Collaboration
 - Attached to a workspace
- Soliciting Feedback in Beta
 - Impacted by data transition
 - Request feedback on your experience
 - Improve creating new and finding existing boards



Documentation, Tutorials, and Videos

- Training and demonstration videos, FAQs
 - Focus on major UI changes in this release

Data organization video

The features for organizing data have been revamped significantly. For an introduction, try this video: [Data Organization in Orion](#).

Discussion board videos

Discussion boards are a new user interface feature introduced in this version, accessed via an icon on the [Project Data](#) page: [Introducing Discussion Boards](#)

We welcome your feedback on discussion boards after you have used them: [Using Discussion Boards](#).

For more about discussion boards, see [Discussion boards](#).

3D modeling videos

There are new badge and list features on the [3D Modeling](#) page. Here is an introduction: [Badges and Lists in Orion](#).

There are several more new videos about 3D modeling at [Orion Video Tutorials](#).

docs.eyesopen.com

Thank You

Questions?

Next Webinar: August 25, 2021

Please provide feedback to support@eyesopen.com