

Orion[®]: State of the U(I)nion

Ash Jogalekar

CUP XXII

March 14, 2023

Dead guy quote

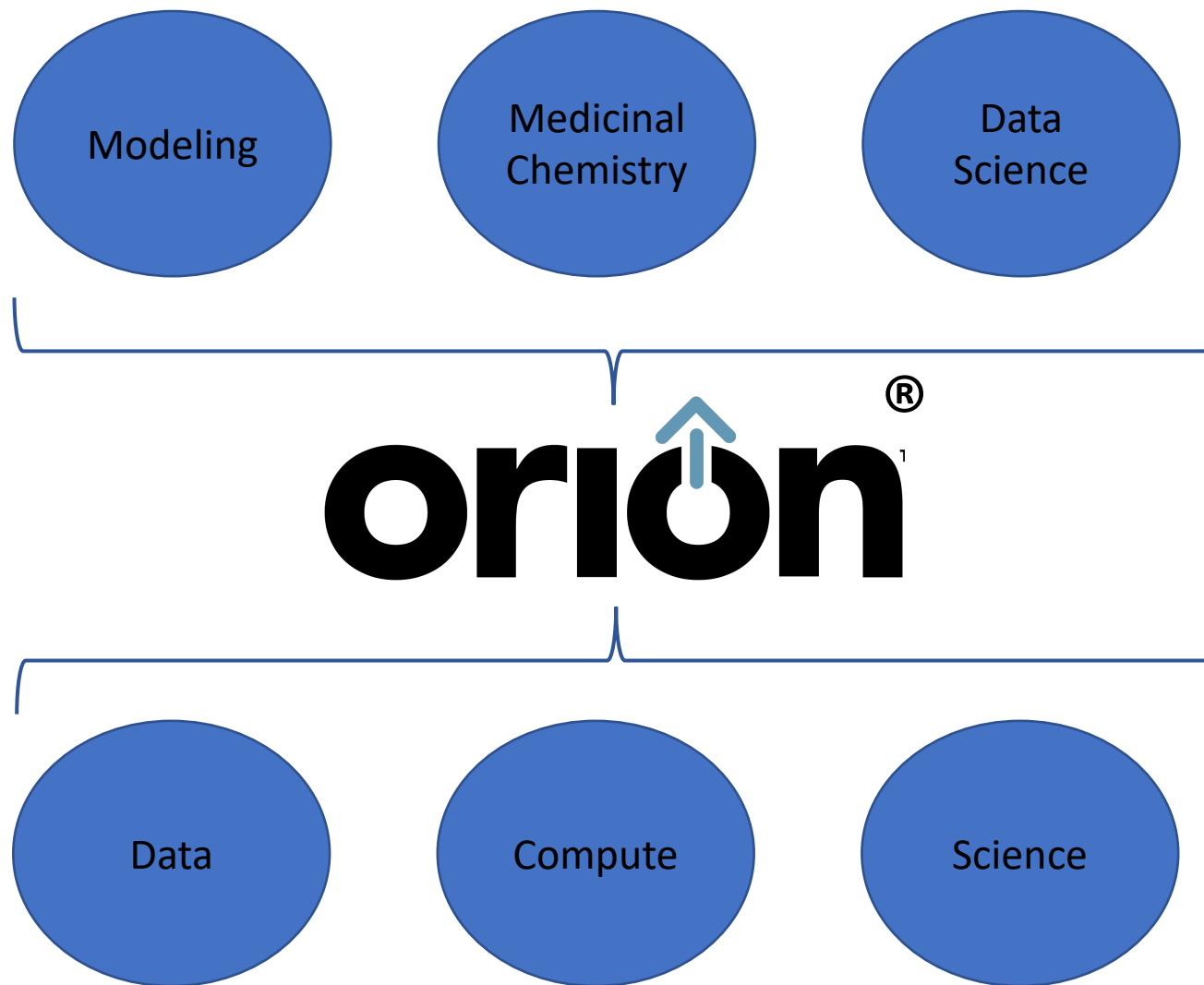
“The career of a young theoretical physicist consists of treating the harmonic oscillator in ever-increasing levels of abstraction.” – Sidney Coleman



Orion[®] as destination



The universe as a (alien) simulation

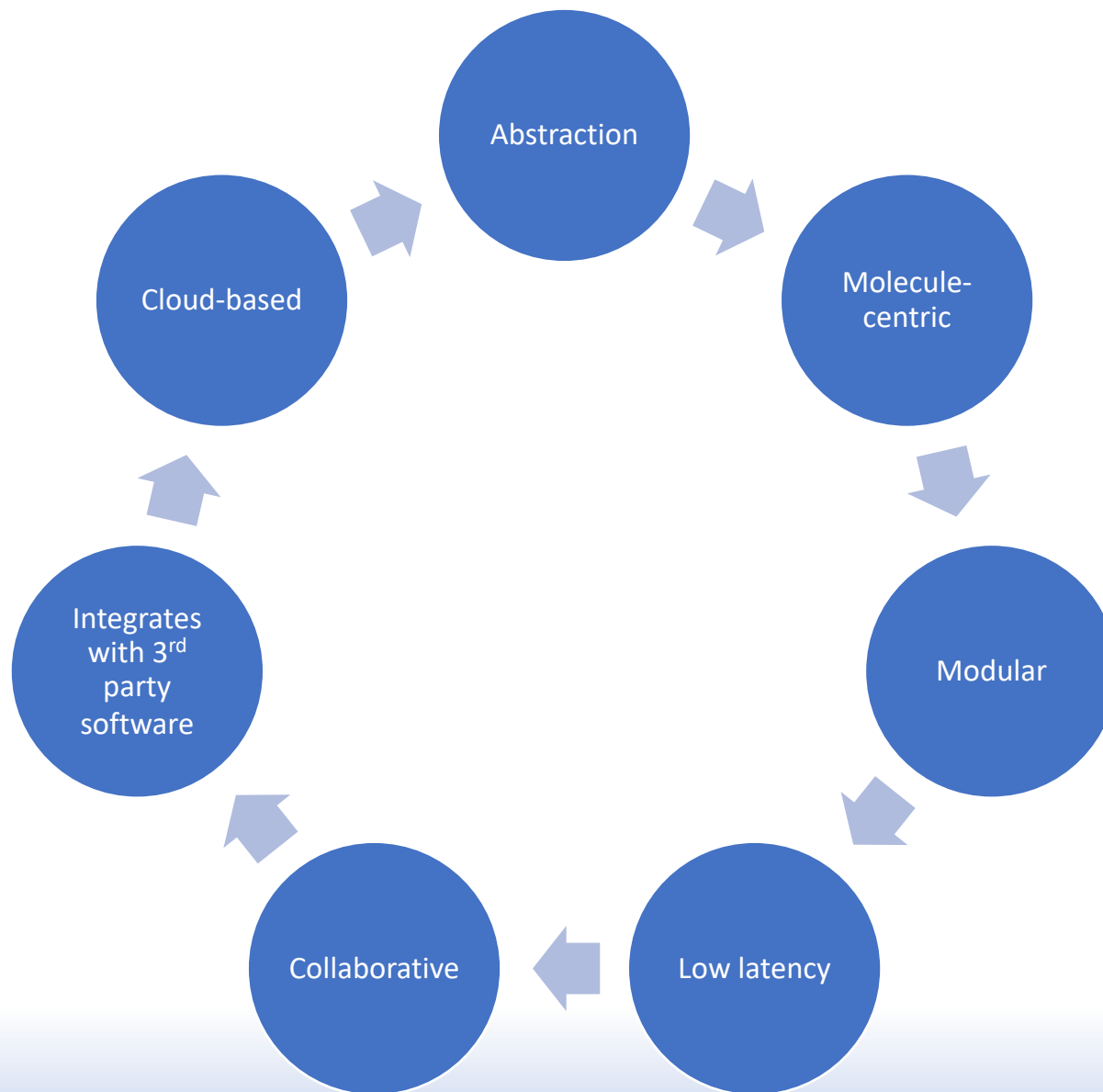


Orion: From then to now and beyond

- Orion: State-of-the-art HPC platform with UI bolted on top
- Bottom-up vs top-down approach
- *“Big jobs (eg. Gigadock™) sped up, small jobs (eg. interactive modeling, I/O) slowed down.”* – Jonas Boström (Treeline)



Building an industry-leading CADD interface



Current Orion UI highlights

Annotate Docking Hits with Interaction Hints
Owner: OpenEye Org Administrator
Package: OpenEye Classic Floes
Version: 0.11.0b5
Description: Annotates docking results with interaction hints and fingerprints.

Filter Docking Hits by Interactions
0.11.2
Description: Annotates docking results with interactions to enable filtering by interactions in Orion and calculates an interaction fingerprint with respect to the cognate ligand in the receptor

OEDocking - Dock into an Active Site for Virtual Screening
0.11.2
Description: Docks and scores a database of molecules to a protein receptor site using OEDocking.

OEDocking - Dock into an Active Site for Virtual Screening
0.11.0b5
Description: Docks and scores a database of molecules to a protein receptor site using OEDocking.

Floes

Active Datasets: 20 | Filters: 0/0 | Records: All 523 | Passing Filters: 523 | Selected: 1

Search: enter a tag or resource name. Show: [Icons] Sort by: Created, Newest First

Folder/Resource	Records	Last Modified	Size
ash-test	3 records	last Wednesday at 4:00 PM	1628696
ash_test_mar6_3	4 records	last Wednesday at 8:26 AM	1628256
ash_test_mar6_2	3 records	last Wednesday at 8:22 AM	1628250
ash_test_mar6	5 records	last Wednesday at 8:18 AM	1628241
Preparation Success Report 1	2 KB	last Tuesday at 10:52 AM	679488
Spruce Prep for 1UA2	4 records	last Tuesday at 10:51 AM	1628163
ash_new_test1	2 records	last Tuesday at 10:37 AM	1626141
ash_test6	1 record	03/01/2023	1619773
ash_ant_demo	2 records	03/01/2023	1619766
ash_test5	3 records	03/01/2023	1619764
ash_test4.1	4 records	03/01/2023	1619752
subsearch query vs. Enamine Complex (QED Agt; 0.85 and No PAINS) - Graphsim Results 1	200 records	02/27/2023	1619054
ash_test4	2 records	02/27/2023	1619052
ash_test3	4 records	02/27/2023	1619018

Data and Folders

Boxplot: Molecular Weight (Calculated) vs. Bin 1 to Bin 10. 23 (out of 523 loaded) points are not plotted due to missing values.

Molecule	Abbvie Bioavail...	Chemgauss4 S...	Chiral Centers ...	Complexity (Ca...	designunit	Heavy Atom Co...	Hydrogen-bon...	Lipinski
TRZ_4B2L_A	0.55	-9.59	1	0.325	6SCM(A) > L7...	16	1	4
GVO_ZUW8_A	0.55	-9.13	1	0.293		16	0	3

Analyze spreadsheet

Properties: XLogP, Complexity, MMFF Internal Energy, TPSA, Lipinski Violations, Abbvie Bioavailability Score, Heavy Atom Count, Chiral Centers, Hydrogen-bond Acceptors, Hydrogen-bond Donors, Lipinski H-bond Acceptors, Lipinski H-bond Donors, Molecular Weight, MoWT Halide Fraction.

Output for OEDocking - Dock into an Active Site for Virtual Screening:

Molecule	Abbvie Bioavail...	Chemgauss4 S...	Chiral Centers ...	Complexity (Ca...	designunit	Heavy Atom Co...	Hydrogen-bon...	Lipinski
TRZ_4B2L_A	0.55	-9.59	1	0.325	6SCM(A) > L7...	16	1	4
GVO_ZUW8_A	0.55	-9.13	1	0.293		16	0	3

3D viewer

Present and future Orion UI: A blueprint

Molecule-centricity (vis-à-vis floe-centricity): Elevate 3D viewer

Fewer clicks, minimal to no context-switching

Format-agnostic file uploads (files...datasets...collections, oh my!)

More exposed functionality: editing, styling, duplication etc.

3rd-party integrations

Enhanced spreadsheet capabilities: annotation, multi-conformer handling etc.

UI performance and latency improvements

What's shipped and shipping soon

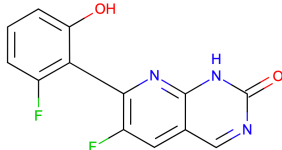
- 2022.3 – 2023.1
 - Shareable links
 - 2D search, potential replacement for MaaS
 - Make Receptor in Orion
 - Collections v2: Better I/O stability for large collections
- 2023.2 – beyond
 - Support for ARM instances
 - Lower latency for interactive calculations
 - Ability for users to upload their own databases
 - Improved I/O for database collections
 - Spruce and protein preparation
 - ELN and compound registry integration
 - Generative chemistry
 - Medicinal chemistry roles in Orion

2D search page (beta)

OpenEye
Ashutosh's Project
Data
3D
Analyze
Search
File
Sources
System

Search

Similarity Exact Match By Title



Sketch query or paste SMILES/MOL/SDF with **Ctrl-V**

HISTORY

Search Database

- FDA Approved Drugs - ChEMBL
molecules: 7,885
- SureChEMBL 20210101
molecules: 20,136,458 version: 2021-06-02
- Molecule ULTIMATE
molecules: 126,471,523 version: 200407
- Zinc2015 DrugLike/Available
molecules: 10,516,591 version: Zinc2015
- MolPort SSC
molecules: 4,629,850 version: Jan 2022
- Enamine Complex (QED > 0.85 and No PAINS)
molecules: 583,415,144 version: 2021q3-4
- WuXi GalaXi (MW<450)
molecules: 290,346,437 version: 201910
- Enamine Simple
molecules: 804,407,565 version: 2021q3-4

Search Parameters

Fingerprint Type
circulars

Similarity Measure
Tanimoto

Output
Max Hits
100

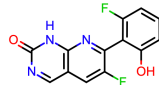
START SEARCH

OpenEye
Ashutosh's Project
Data
3D
Analyze
Search
File
Sources
System

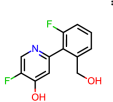
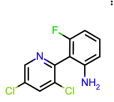
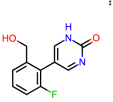
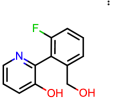
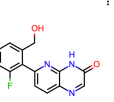
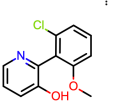
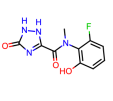
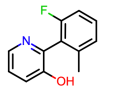
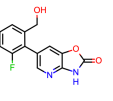
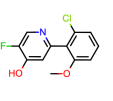
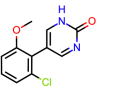
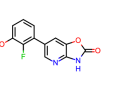
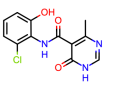
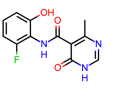
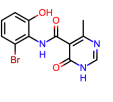
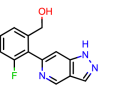
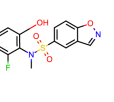

Search Result

READY

select all



Database: Enamine Simple
Query Type: graphsim
Fingerprint Type: circulars
Similarity Measure: tanimoto
Max Hits: 100
Found Count: 100
Search Time: 2.9679 secs

 PV-002798205228 Score: 0.247	 PV-004448339507 Score: 0.244	 PV-002993740697 Score: 0.242	 PV-002913510416 Score: 0.239	 PV-006792442957 Score: 0.238	 PV-002901135968 Score: 0.238
 PV-002919360318 Score: 0.234	 PV-002841442780 Score: 0.233	 PV-002886020291 Score: 0.231	 PV-002825463039 Score: 0.231	 PV-002969153373 Score: 0.228	 PV-002820698225 Score: 0.228
 PV-002485206413 Score: 0.228	 PV-002362552453 Score: 0.228	 PV-006638071493 Score: 0.228	 PV-002731101678 Score: 0.227	 PV-002930902155 Score: 0.226	 PV-002874958340 Score: 0.226

HISTORY

NEW SEARCH REFINER SEARCH

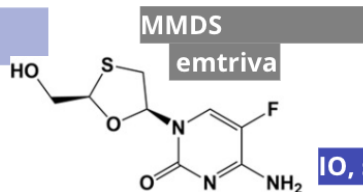
SAVE RESULTS

UI-based workflows: universal OE tool coverage

CADD Modeler 1

scaffold 1 - structure

finding analogs



IO, sharing handoff

3D Similar

using VROCS
(shape) and EON
(electrostatic)

IO, sharing handoff

Docking - Fred

IO, sharing handoff

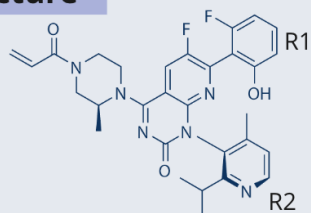
SZMAP

IO, sharing handoff

Property Calc

CADD Modeler 2

scaffold 2 - structure



Pull in from PDB -
Protein Prep

IO, sharing handoff

SiteHopper

explore cryptic
pocket further

IO, sharing handoff

Docking - Posit
to dock, also to
KRAS

IO, sharing handoff

Freeform

look at exact conformation of compound -
make probabilistic guess about
favorability of conformation in terms of
energy

IO, sharing handoff

Gameplan

SZMAP

IO, sharing handoff

library

STMD

IO, sharing handoff

NES

IO, sharing handoff

Property Calc

Acknowledgements

- Product team



Brent Jenkins
Technical
Product
Manager



Linda Smyth
Project Manager



Caitlin Everett
UX/UI Strategist

Acknowledgements

- Product
- Development and Infrastructure
- Application Science
- Sales and Marketing
- Customer Success
- Senior Leadership
- Our Customers, Users and Programmers (“CUP”)

Thank you

“Every great and deep difficulty bears in itself its own solution.” – Niels Bohr