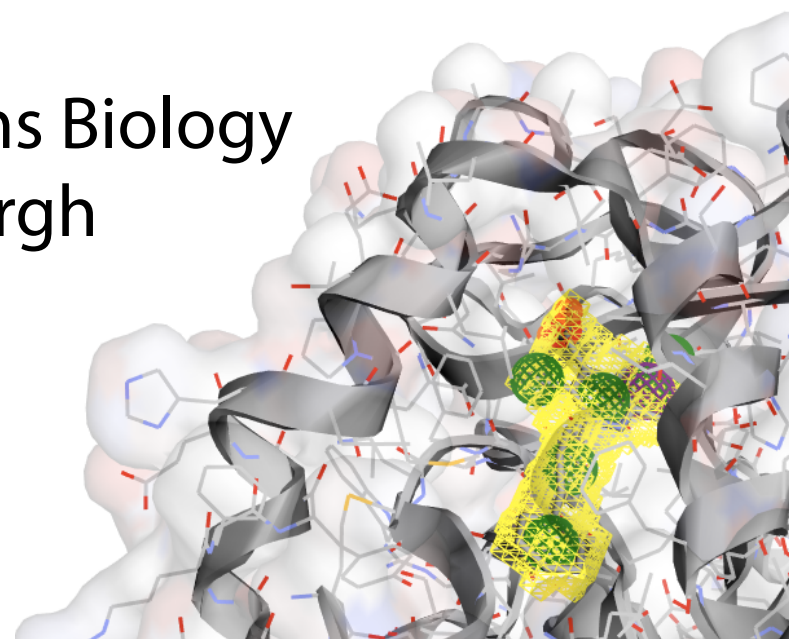


pharmit

interactive exploration of chemical space

David Ryan Koes

Computational and Systems Biology
University of Pittsburgh



pharmit.csb.pitt.edu/search.html

Search PubChem

Pharmacophore Search -> Shape Filter

Load Receptor... Load Features...

Pharmacophore

- ☒ **Aromatic**
(48.19,39.88,-1.88) Radius 1.1
- ☒ **HydrogenAcceptor**
(47.17,41.23,-5.87) Radius 0.5
- ☒ **HydrogenAcceptor**
(49.17,40.46,-6.38) Radius 0.5
- ☒ **NegativeIon**
(48.21,40.91,-5.92) Radius 0.75
- ☒ **Hydrophobic**
(49.4,41.67,-2.93) Radius 1.0
- ☒ **Hydrophobic**
(52.08,44.85,-2.15) Radius 1.0
- ☒ **Hydrophobic**
(48.19,39.88,-1.88) Radius 1.0
- ☒ **Hydrophobic**
(55.14,47.7,-1.04) Radius 1.0
- ☒ **Hydrophobic**
(50.03,43.31,-5.25) Radius 1.0
- ☒ **Hydrophobic**
(46.4,37.97,-1.96) Radius 1.0
- ☐ **Aromatic**
(49.4,41.67,-2.93) Radius 1.1
- ☐ **Aromatic**
(52.08,44.85,-2.15) Radius 1.1

Load Session... Save Session...

Display a menu

Pharmacophore Results

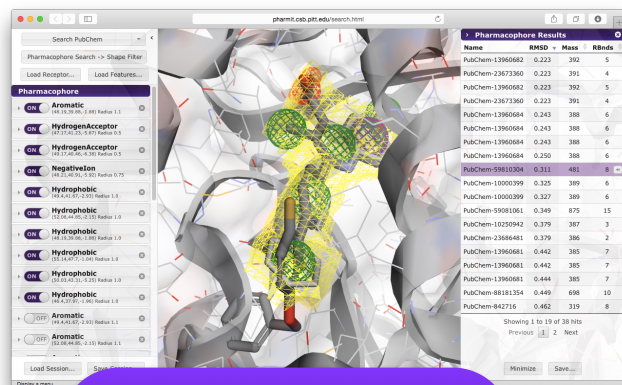
Name	RMSD	Mass	RBnds
PubChem-13960682	0.223	392	5
PubChem-23673360	0.223	391	4
PubChem-13960682	0.223	392	5
PubChem-23673360	0.223	391	4
PubChem-13960684	0.243	388	6
PubChem-13960684	0.243	388	6
PubChem-13960684	0.243	388	6
PubChem-13960684	0.250	388	6
PubChem-59810304	0.311	481	8
PubChem-10000399	0.325	389	6
PubChem-10000399	0.327	389	6
PubChem-59081061	0.349	875	15
PubChem-10250942	0.379	387	3
PubChem-23686481	0.379	386	2
PubChem-13960681	0.442	385	7
PubChem-13960681	0.442	385	7
PubChem-13960681	0.444	385	7
PubChem-88181354	0.449	698	10
PubChem-842716	0.462	319	8

Showing 1 to 19 of 38 hits

Previous 1 2 Next

Minimize Save...

<http://pharmit.sf.net>



pharmit.js

jQuery

3Dmol.js

Client

Search

User Libraries

CHEMBL

PubChem

ChemDiv

NCI

MolPort

Prebuilt
Libraries

pharmitserver

OpenBabel

ShapeDB

Pharmer

Minimization

smina

OpenBabel

Server

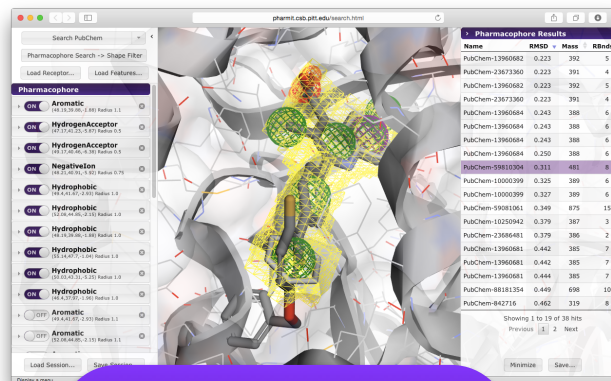
buildlibs.py

RDKit

OpenBabel

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pharmit.js

jQuery

3Dmol.js

Client

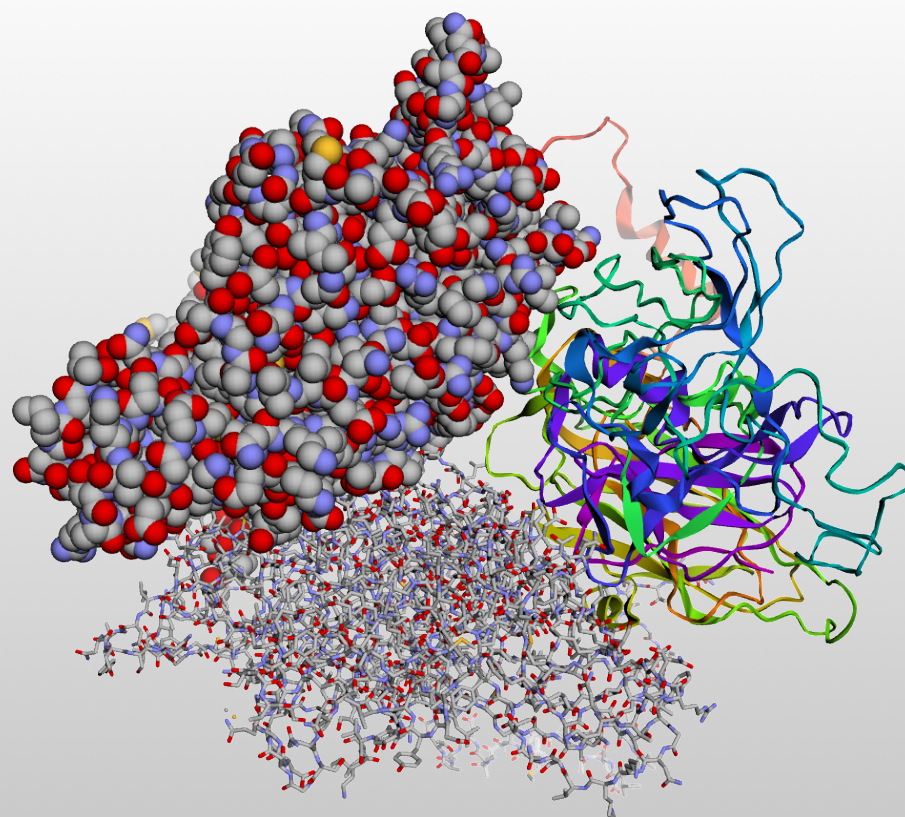
Why web application?

3Dmol.js

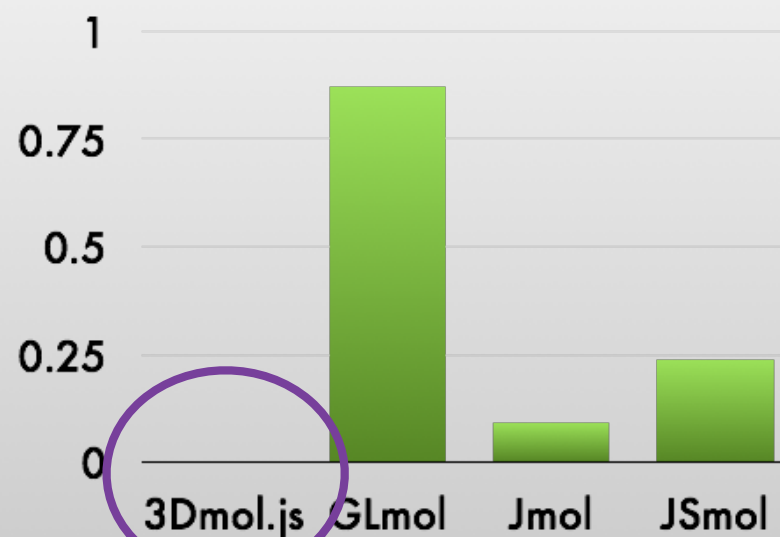
View Embed Develop

Download

A modern, object-oriented JavaScript library for visualizing molecular data

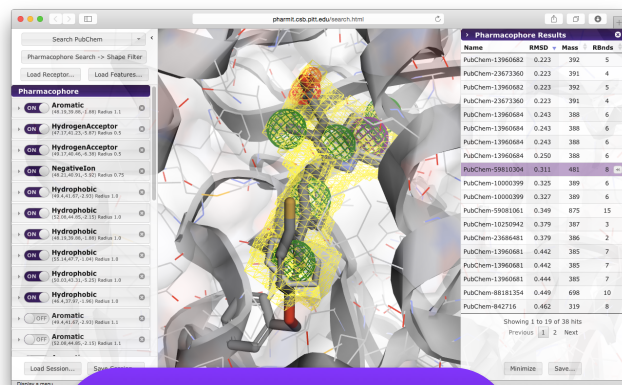


Scene Rotation Time (s)



<http://3dmol.csb.pitt.edu>

Rego, N., & Koes, D. (2014). 3Dmol.js: molecular visualization with WebGL. *Bioinformatics*. doi:10.1093/bioinformatics/btu829



pharmit.js

jQuery

3Dmol.js

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RDKit

OpenBabel

<http://pharmit.sf.net>

CHEMBL

ChemDiv

MolPort

NCI

PubChem

CHEMBL20 ⓘ

17,915,767 conformers of 1,373,120 molecules
Updated: 2015-Aug-13 01:22:24

ChemDiv ⓘ

21,609,241 conformers of 1,456,338 molecules
Updated: 2015-Jul-31 03:13:35

MolPort ⓘ

86,897,080 conformers of 6,098,523 molecules
Updated: 2015-Jul-30 15:04:58

NCI Open Chemical Repository ⓘ

1,311,388 conformers of 125,565 molecules
Updated: 2015-Aug-12 12:04:27

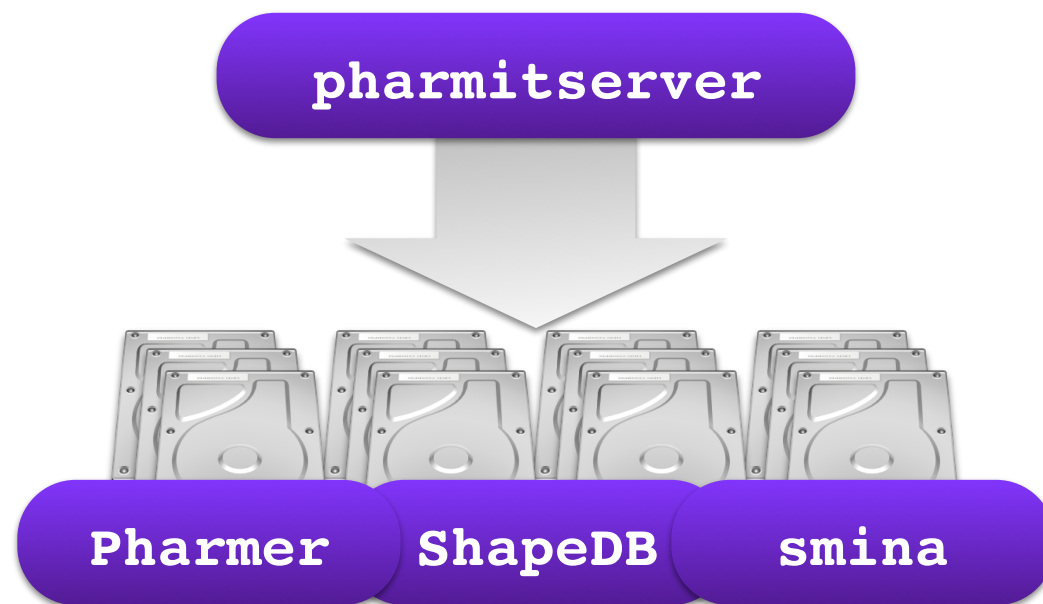
PubChem ⓘ

911,972,985 conformers of 66,023,229 molecules
Updated: 2015-Jul-08 22:48:24

Contributed Libraries



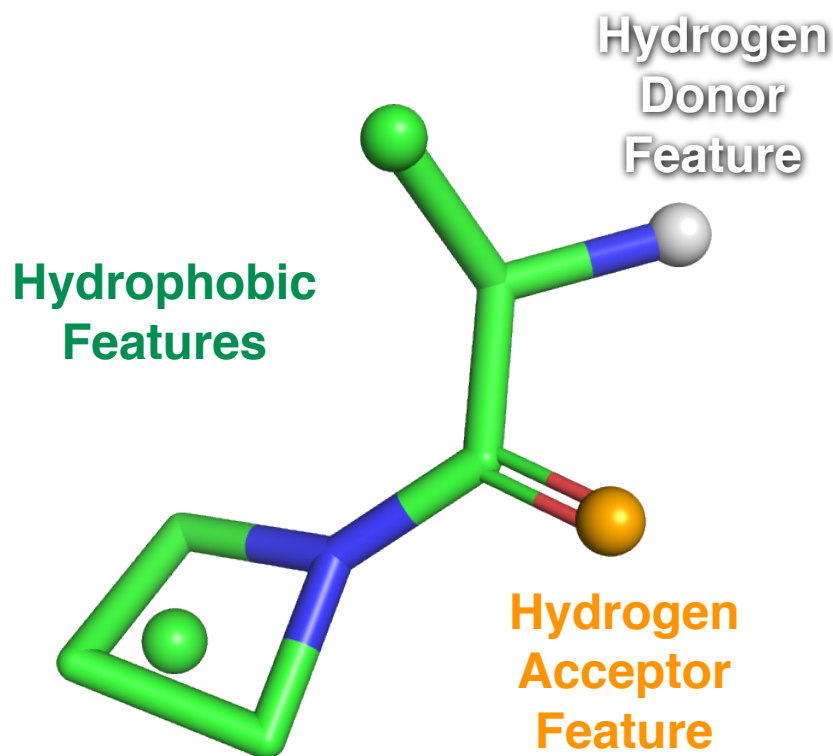
Access Private Library



<http://pharmit.sf.net>

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Efficient and Exact Pharmacophore Search



Pharmacophore

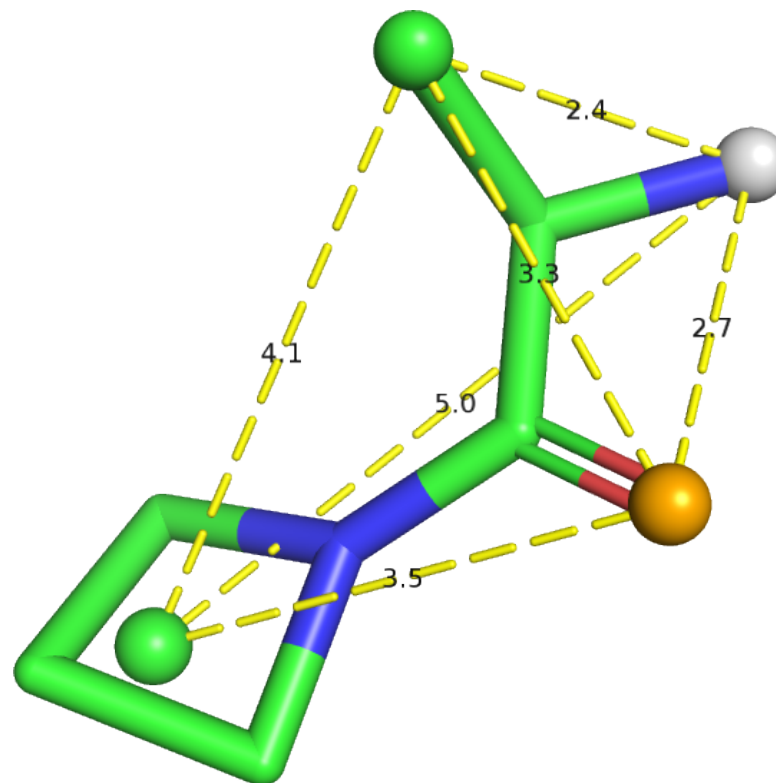
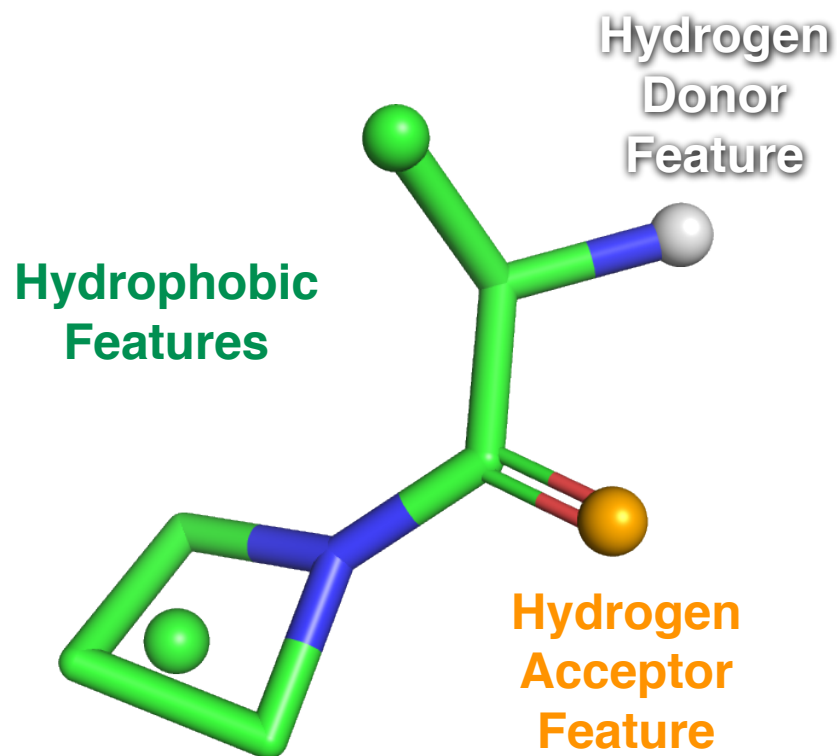
A spatial arrangement of molecular features essential for biological activity

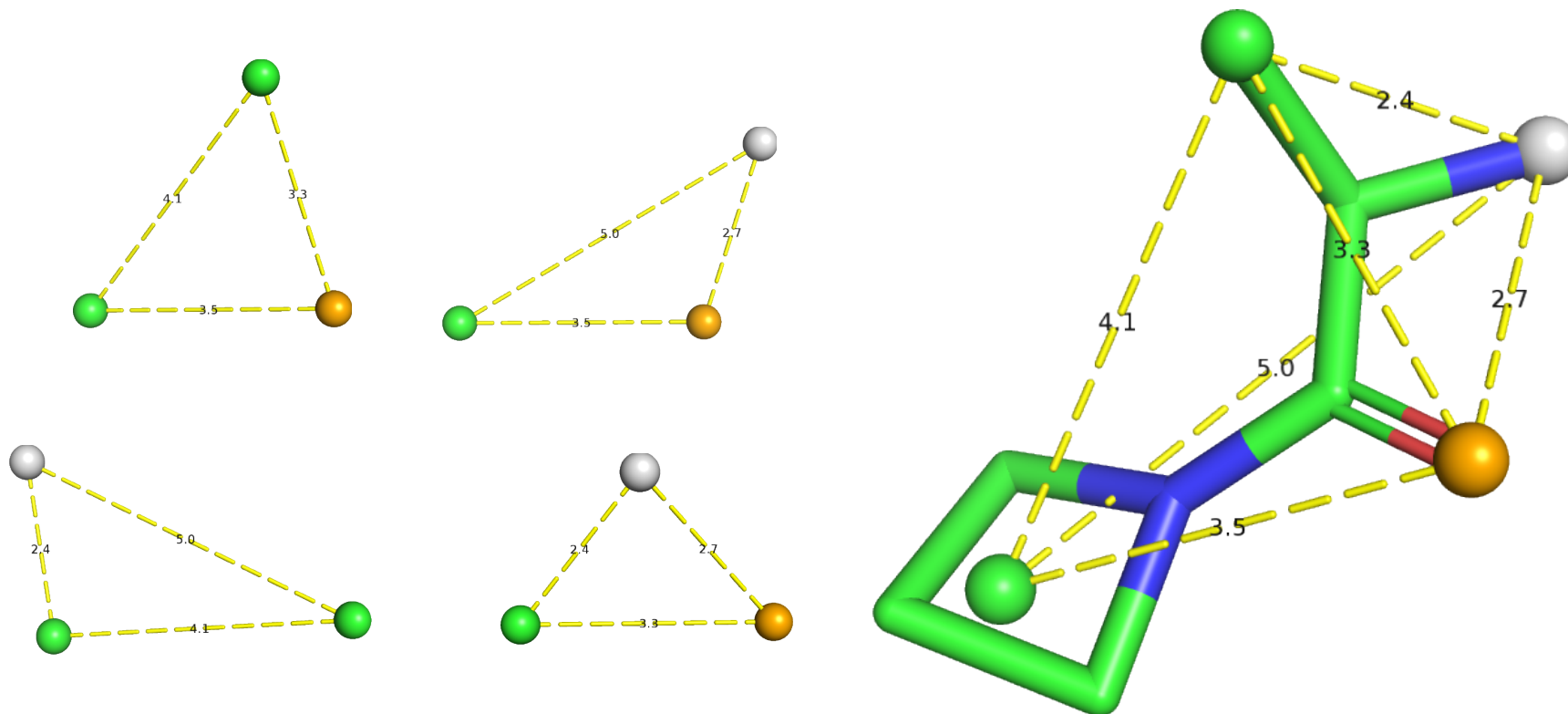
Koes, D. R., & Camacho, C. J. (2011). Pharmer: efficient and exact pharmacophore search.

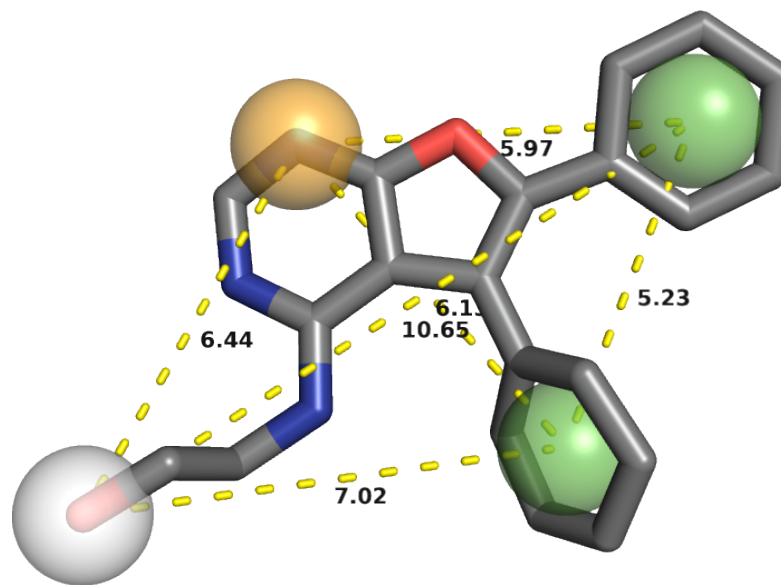
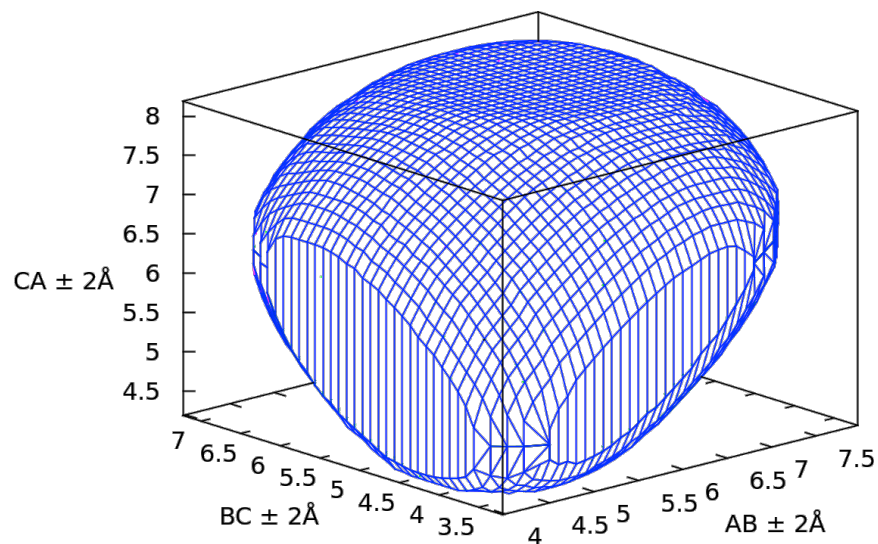
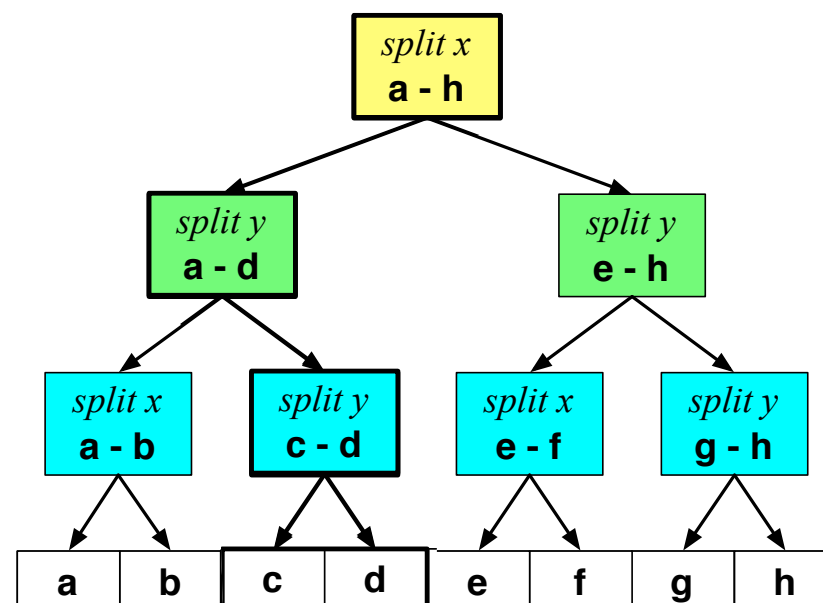
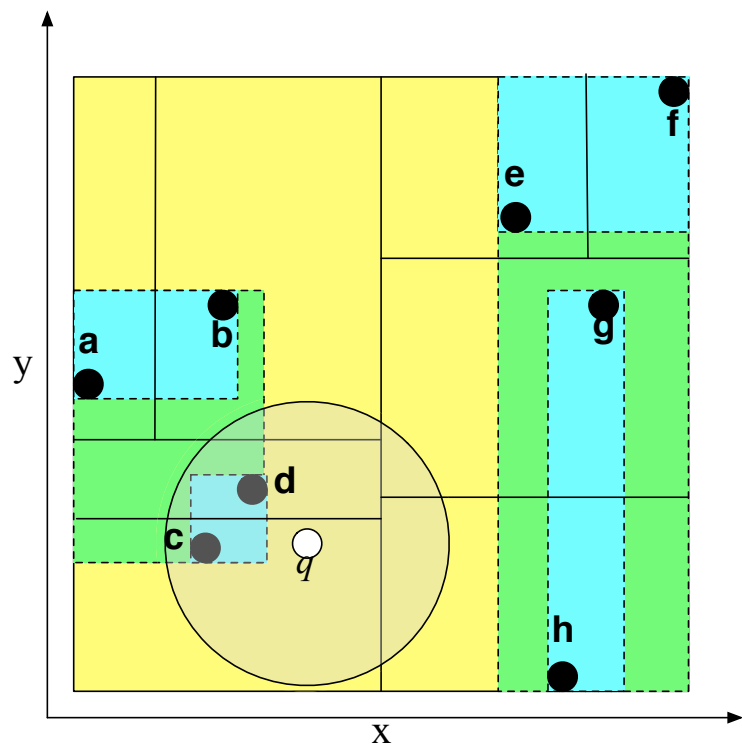
Journal of Chemical Information and Modeling, 51(6), 1307-1314. doi:10.1021/ci200097m

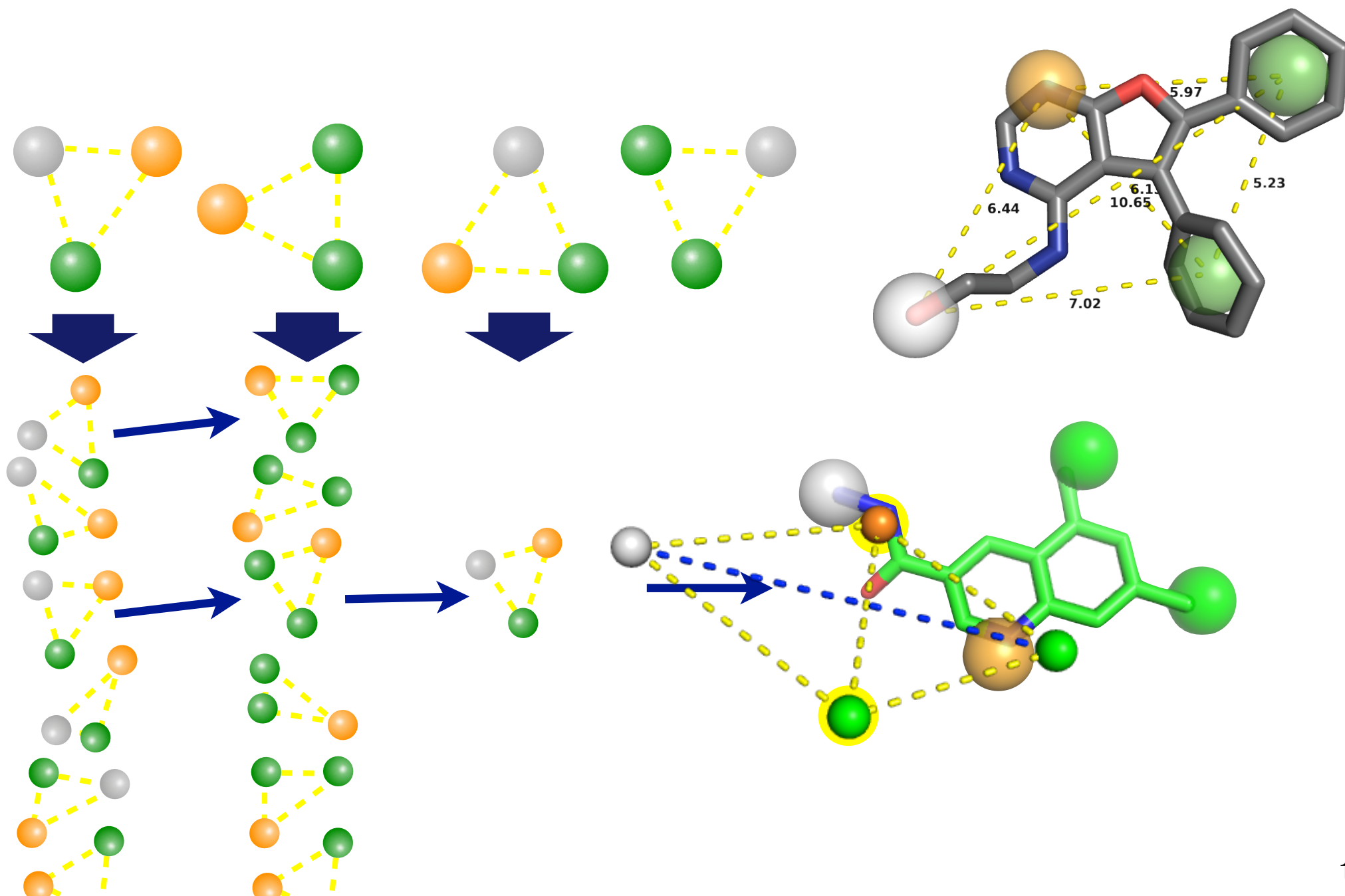
Koes, D. R., & Camacho, C. J. (2012). ZINCPharmer: pharmacophore search of the ZINC database.

Nucleic acids research, 40(Web Server issue), W409-414. doi:10.1093/nar/gks378

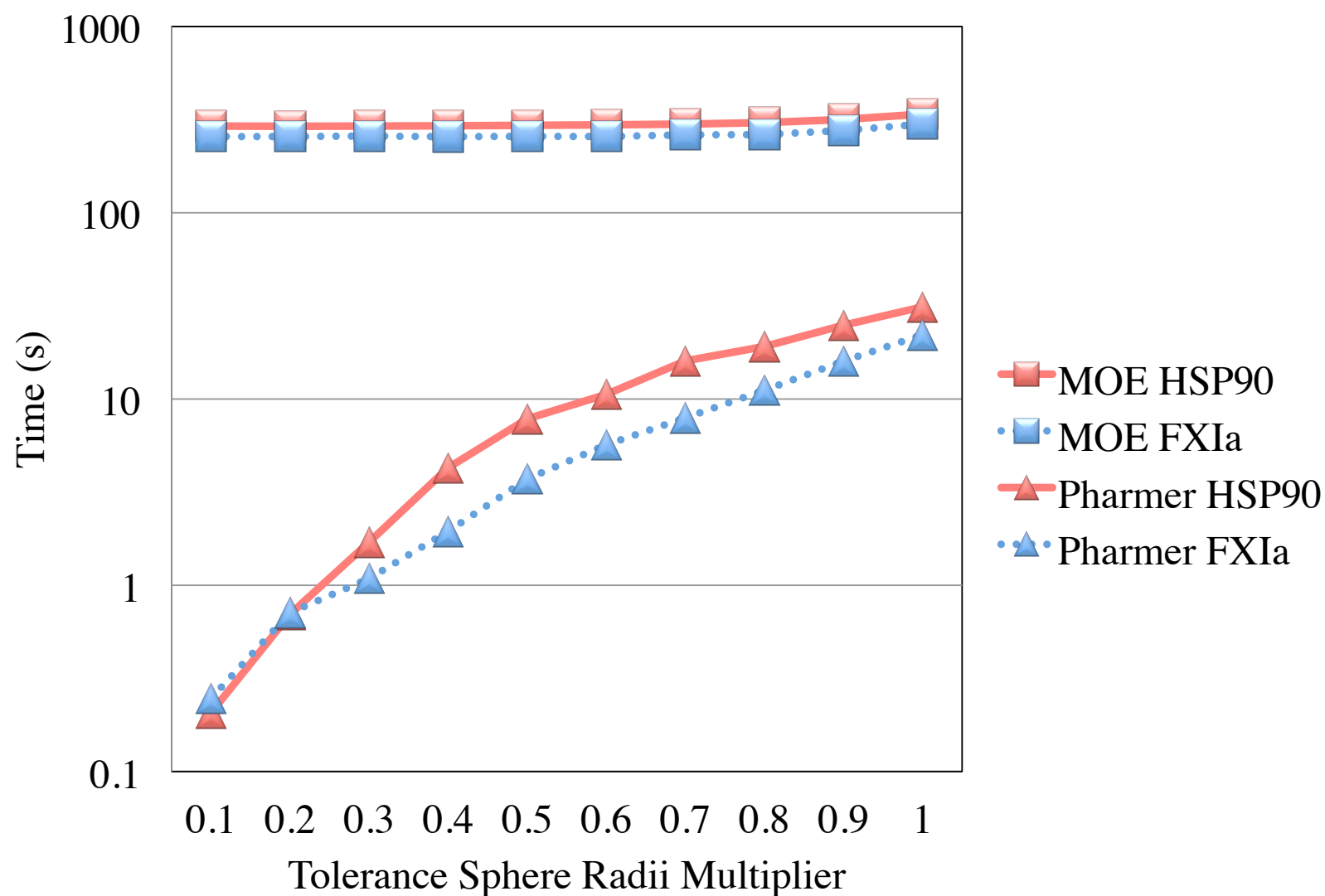


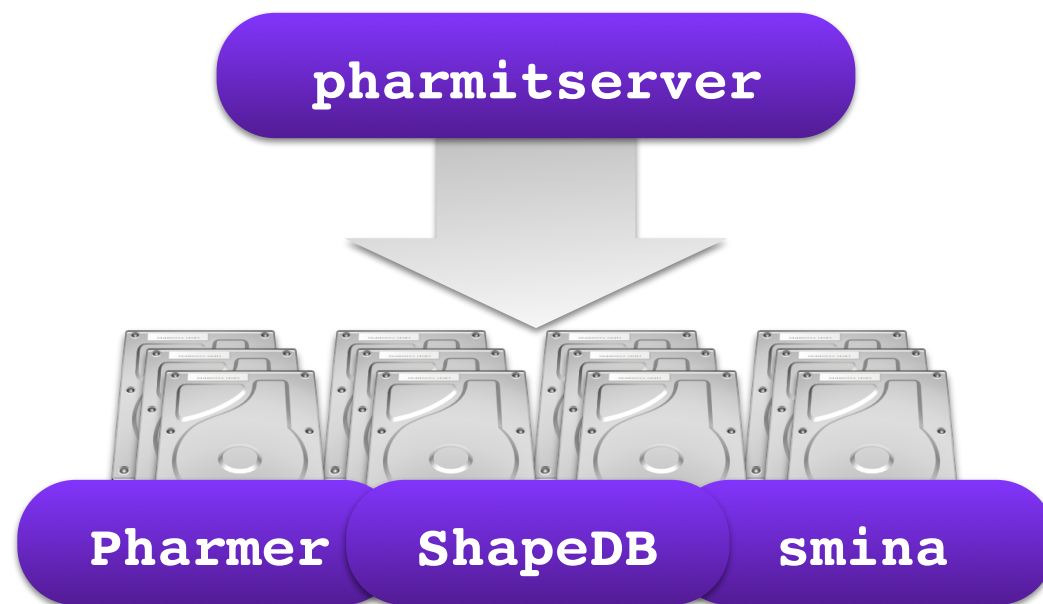






Efficient and Exact Pharmacophore Search

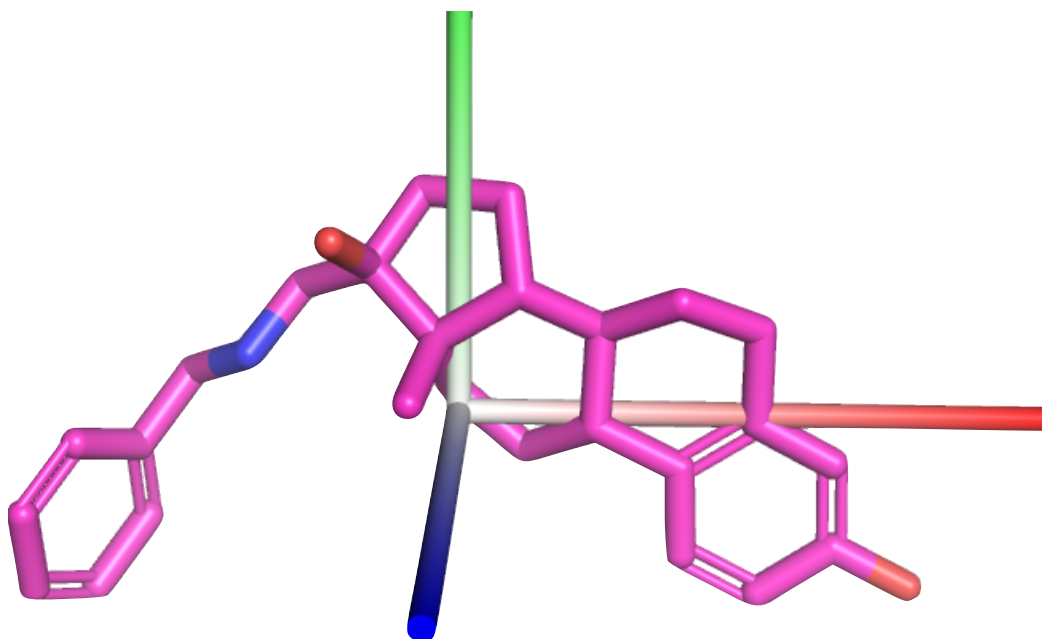




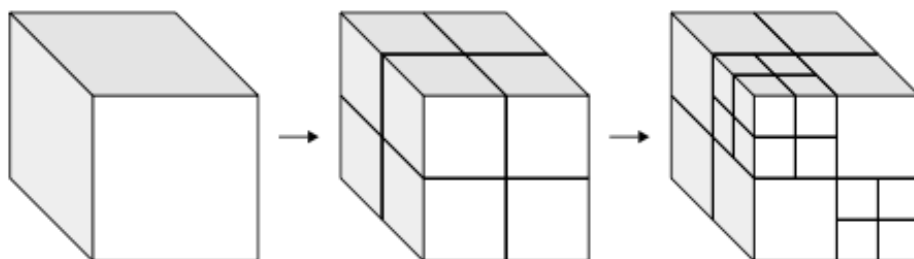
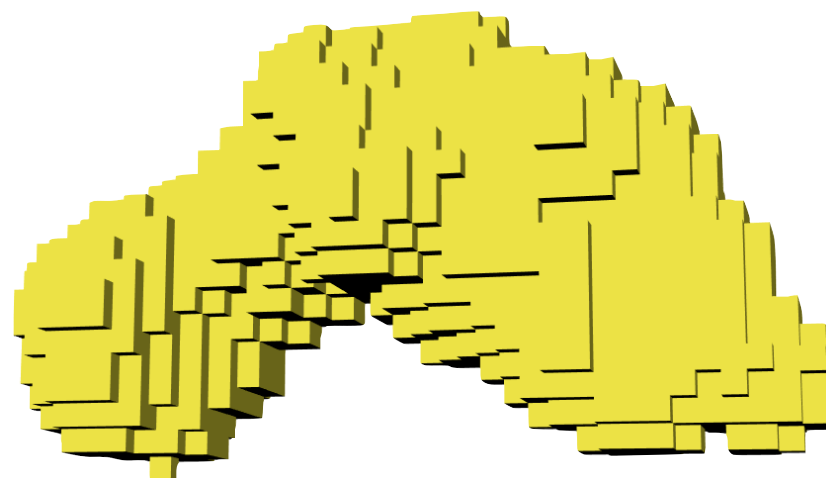
<http://pharmit.sf.net>
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Indexed Search of Molecular Shapes

Align to Moments of Inertia



Voxelize

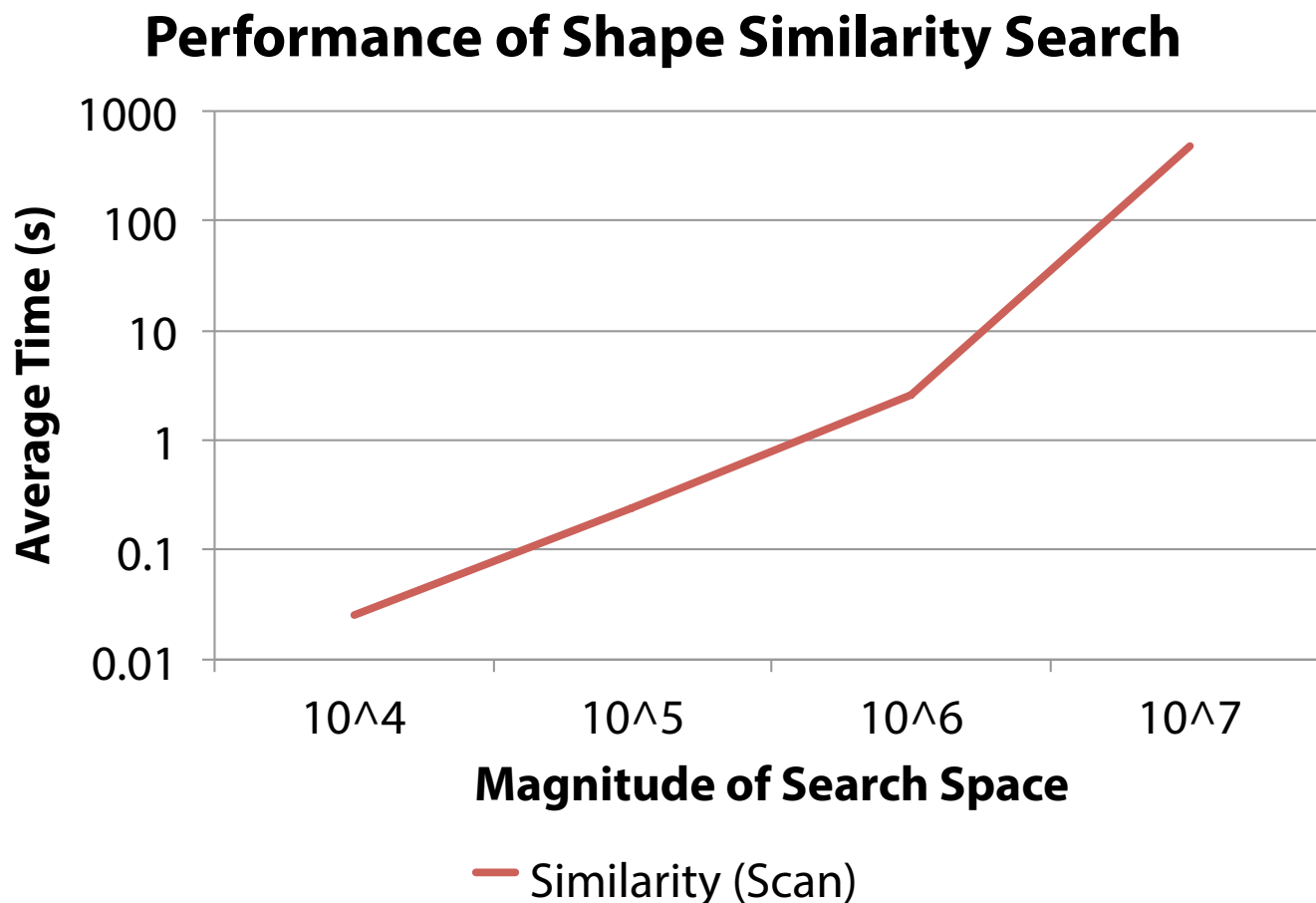


Oct-tree

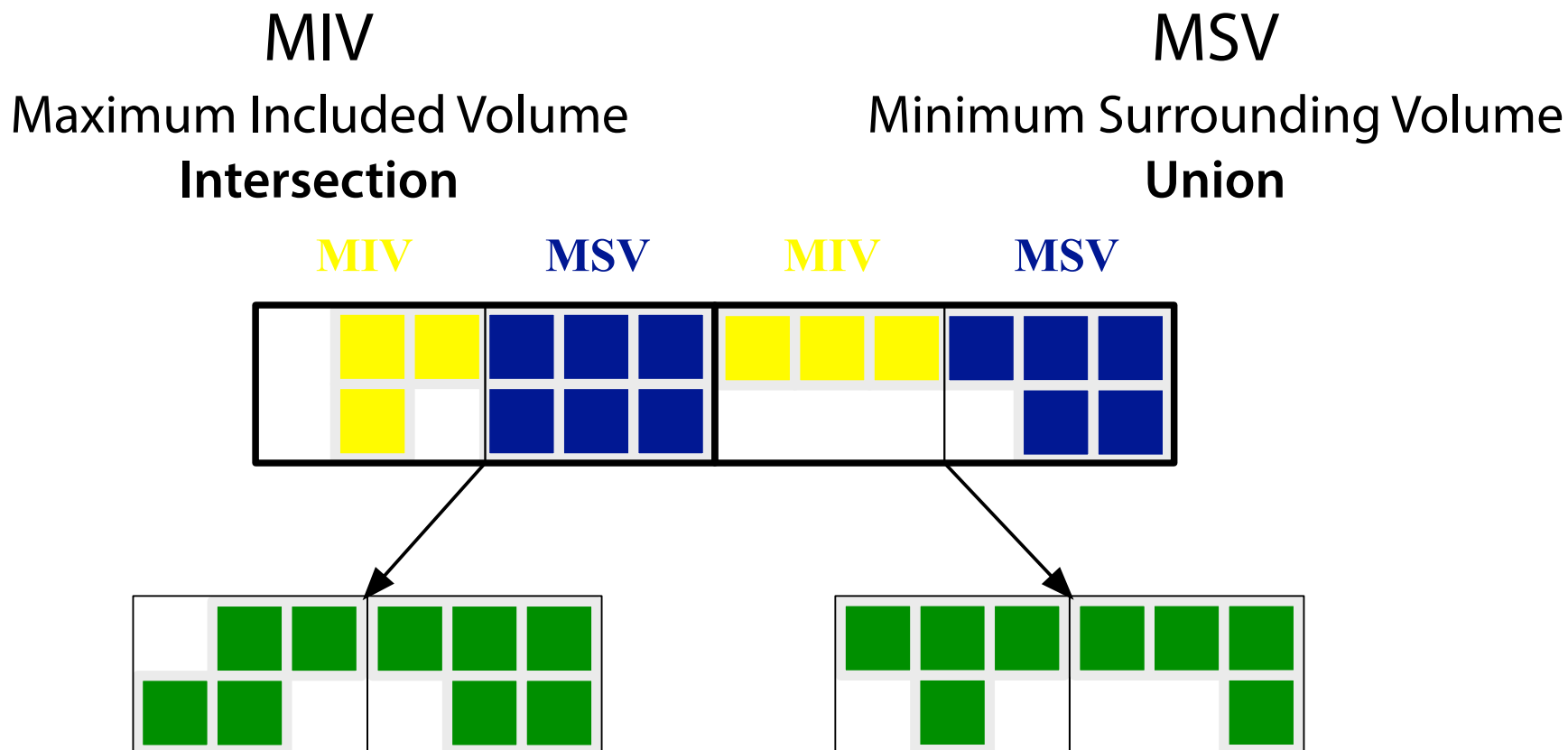
- Scales with Surface Area, not Volume
- Fast Intersection/Union Operations

Indexed Search of Molecular Shapes

$$\delta(A, B) = \frac{A \cap B}{A \cup B}$$



Indexed Search of Molecular Shapes

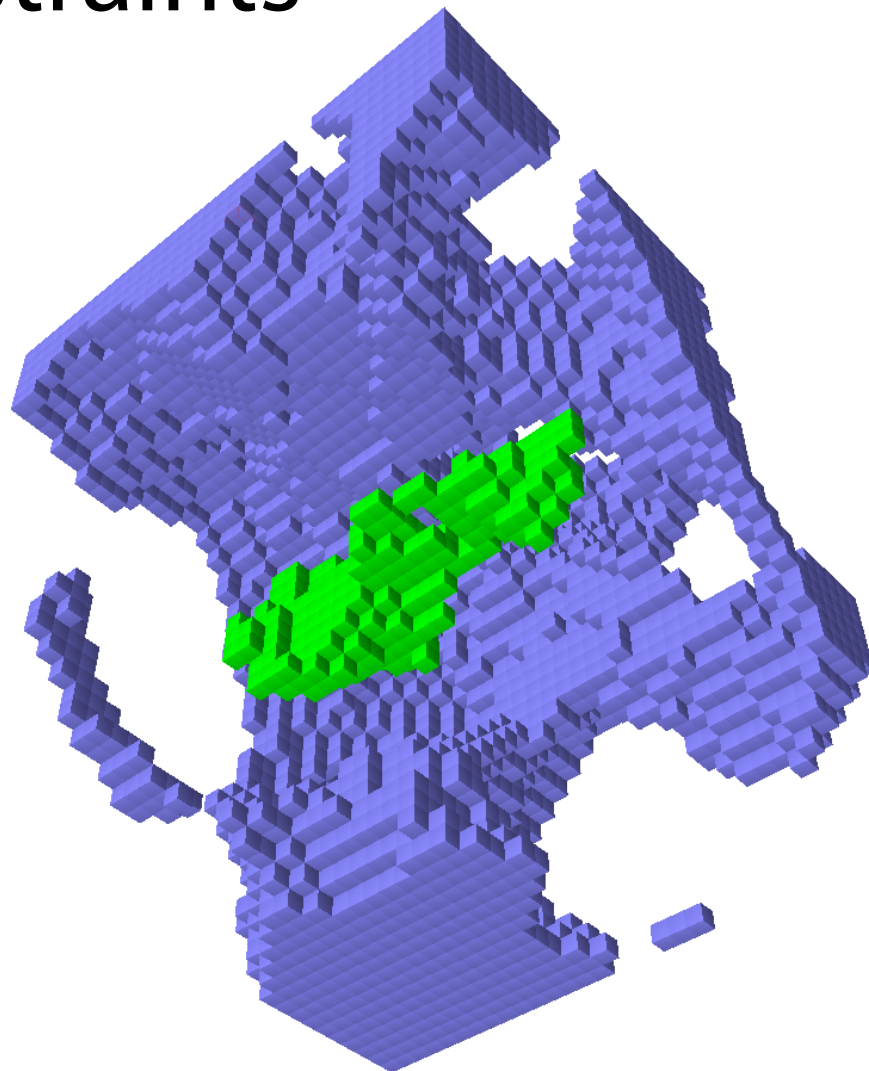
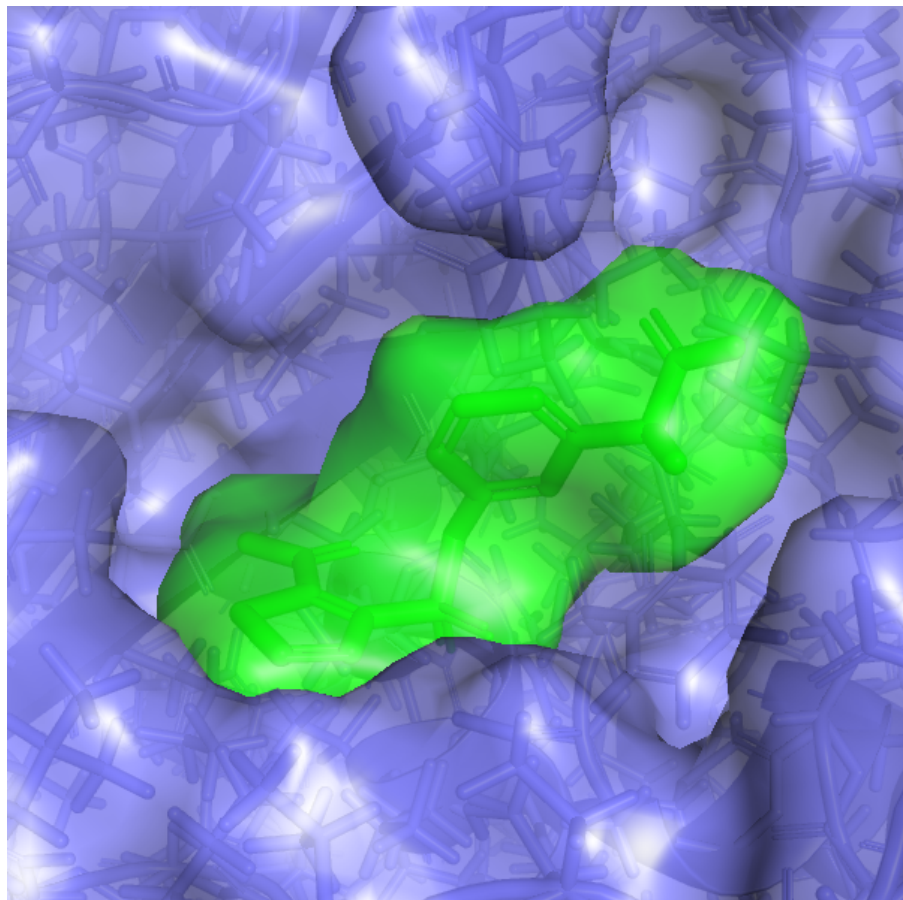


Matching and packing algorithm for
efficient and effective initialization

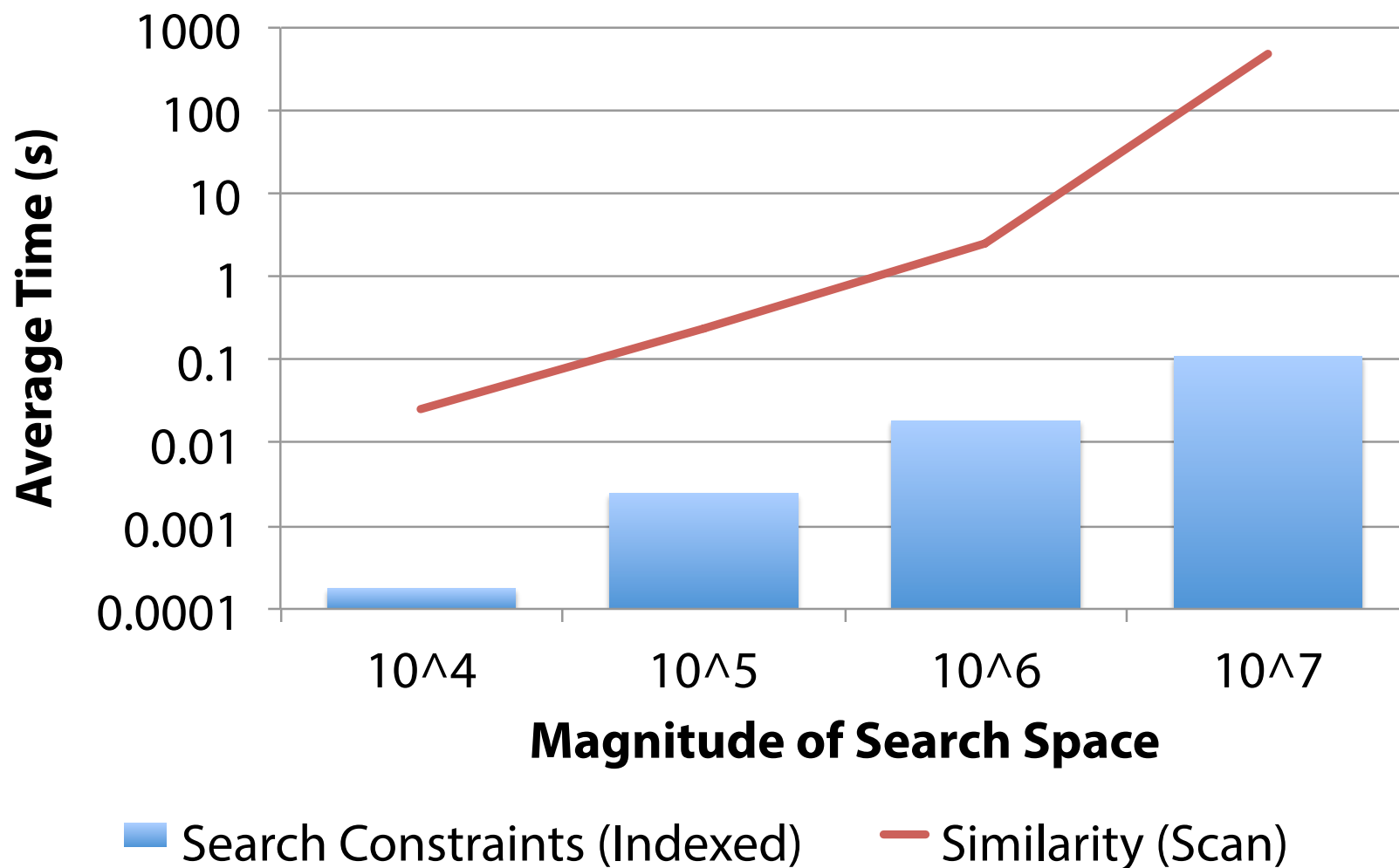
Koes, D. R., & Camacho, C. J. (2014). Shape-based virtual screening with volumetric aligned molecular shapes. *J Comput Chem*, 35(25), 1824-1834. doi:10.1002/jcc.23690

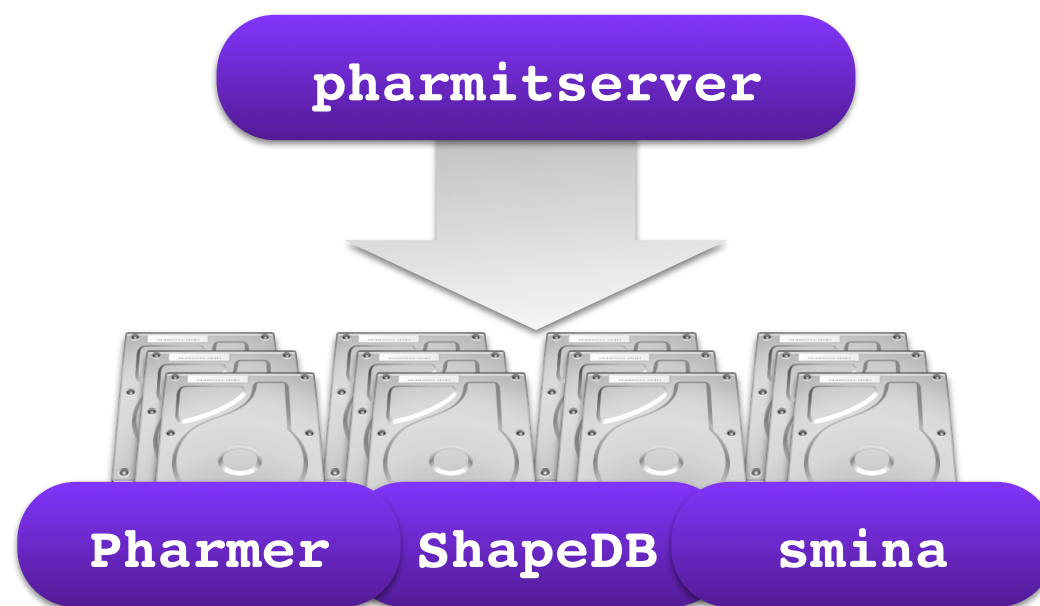
Koes, D., & Camacho, C. (2014). Indexing volumetric shapes with matching and packing. *Knowledge and Information Systems*, 1-24. doi:10.1007/s10115-014-0729-z

Shape Constraints



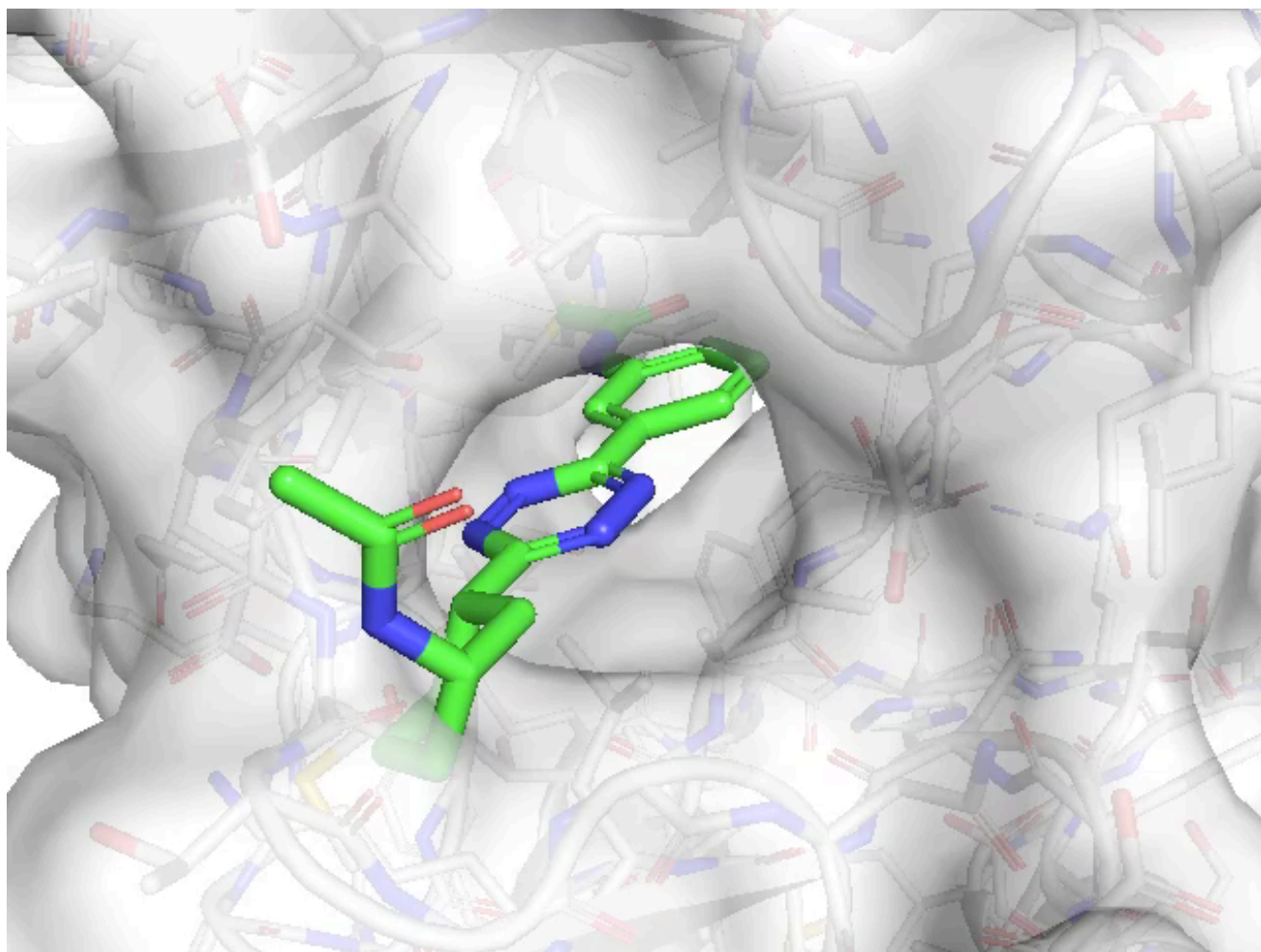
Performance of Shape Constraint Search





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Improved energy minimization

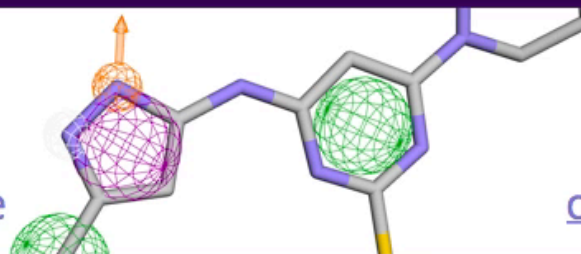
Facilities for scoring function development

Custom format with precomputed torsion tree

Implementation of server protocol

pharmit^{beta}

interactive exploration of chemical space

[code](#)[help](#)[contact](#)

search

virtual screening in your browser

[enter pharmit search](#)

start from PDB:

binding site waters:

[submit](#)

[examples](#)

create

submit your own chemical libraries

[log in to manage libraries](#)

email:

password:

[log in](#)

[register new account](#)

[log in as guest](#)

pharmit currently has

5 built-in libraries containing 1,039,706,461 conformations of 75,076,775 compounds and

7 publicly accessible user-contributed libraries containing

Acknowledgements

Group Members

Jocelyn Sunseri

Jasmine Collins

Matthew Ragoza

Justin Jensen

Collaborators

Lee McDermott

Carlos Camacho

Funding

R01GM108340

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Presentation COMP-Divisio.	COMP 271: Convolutional neural networks for protein-ligand scoring 6:00pm-8:00pm Tue, Mar 15	23 ★ >	Matthew Ragoza
Presentation COMP-Divisio.	COMP 374: Benchmarking computational methods for binding free-energy estimation 6:00pm-8:00pm Tue, Mar 15	23 ★ >	Jocelyn Sunseri
Presentation COMP-Divisio.	COMP 377: Fragment oriented molecular shape (FOMS) search: A novel shape-based virtual screening method 6:00pm-8:00pm Tue, Mar 15	23 ★ >	Ethan Hain
Presentation COMP-Divisio.	COMP 232: GPU implementation of energy minimization for virtual screening 6:00pm-8:00pm Tue, Mar 15	23 ★ >	Jocelyn Sunseri

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