ChemicalToolBoX and its application to the study of the drug-like and purchasable space

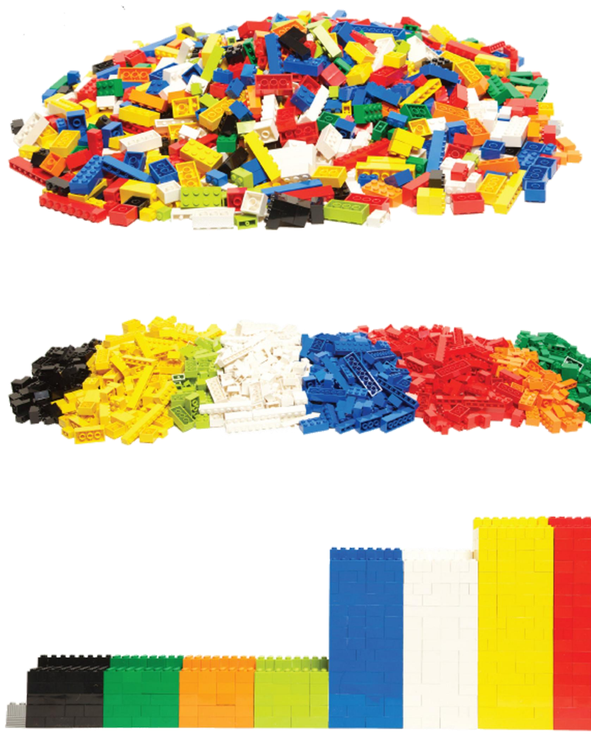
Lucas X, Grüning BA, Bleher S, Günther S

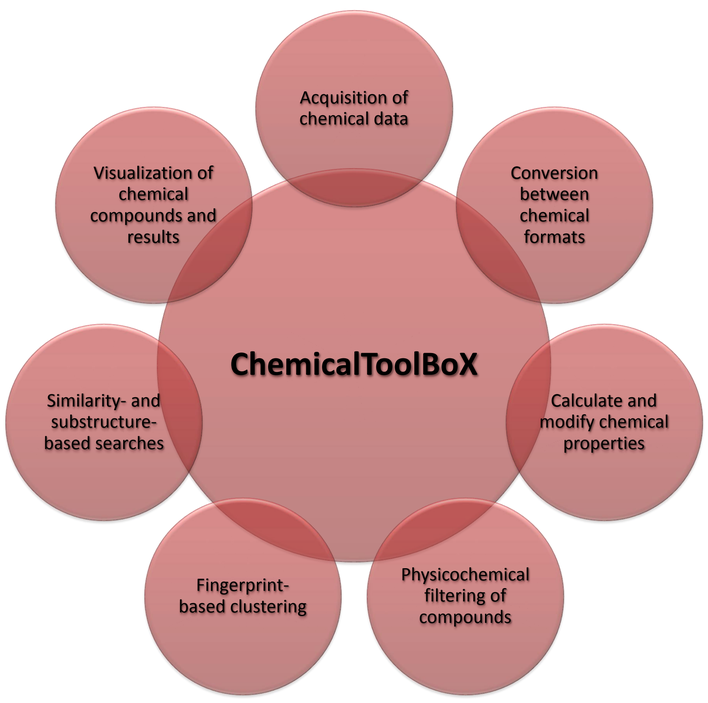
Pharmaceutical Bioinformatics, Institute of Pharmaceutical Sciences, University of Freiburg, Germany

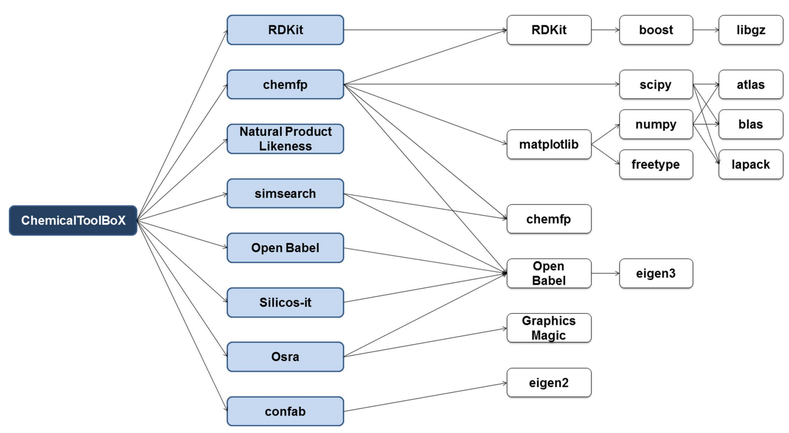
xavier.lucas@pharmazie.uni-freiburg.de

ChemicalToolBoX [1] is a freely-available compilation of more than 30 tools integrated into a single computational chemistry and cheminformatics platform based on the Galaxy workflow management system [2]. We present some case studies to demonstrate the versatility of this suite in the cheminformatics and drug discovery fields.

ChemicalToolBoX





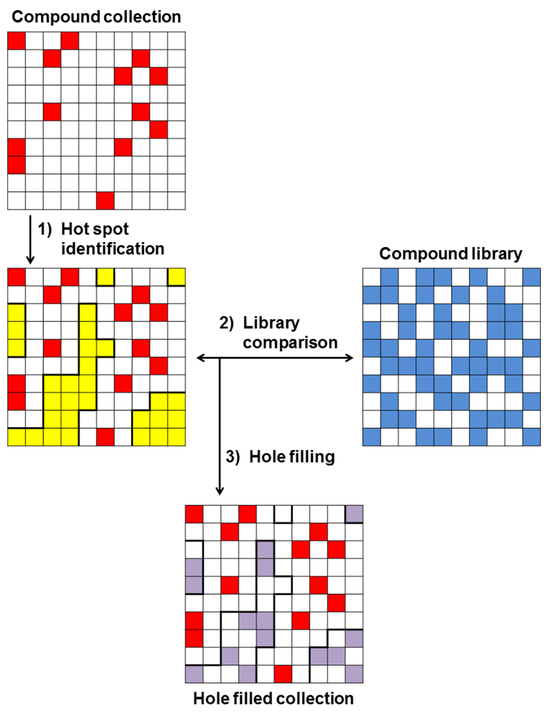


ChemicalToolBoX offers cheminformatics and computational chemistry tools for the collection, physicochemical-based filtering, clustering, manipulation, library screening, and visualization of chemical data. Tools can be assembled into workflows, allowing for the automatized, reproducible treatment of chemical data.

Multiple modules underlie ChemicalToolBoX, yet all of them are automatically handled by means of a comfortable point-to-click installation.

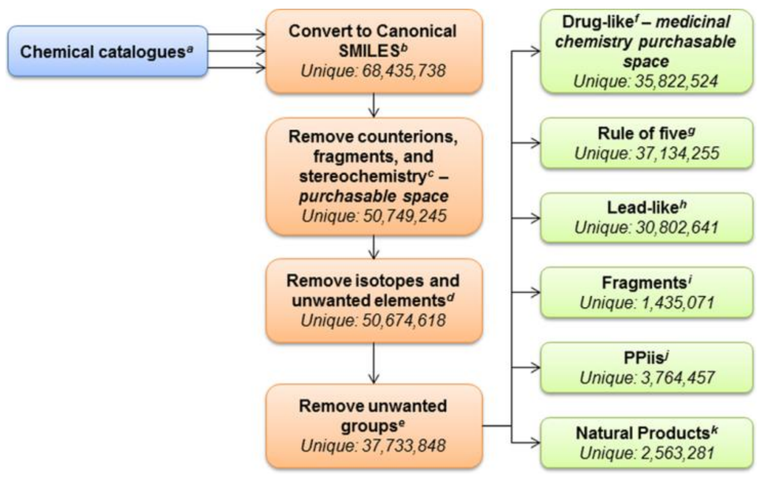
Case I: Hole filling

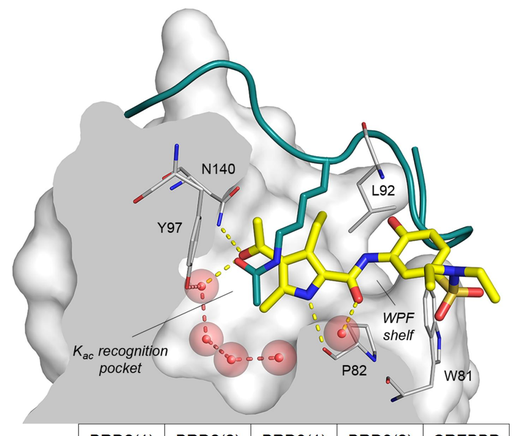
ChemicalToolBoX can be used to fill spots in compound libraries based on fingerprint diversity selections, using the following scheme:



Case II: Chemical libraries

We have collected over 65M unique commercially available chemicals, partitioned them into focused ligand libraries, and studied their physicochemical properties [3]. These data sets are a valuable source of novel bioactive small molecules. For example, we have recently screened several million drug-like molecules and identified XD14, a potent modulator of bromodomains [4].





	BRD2(1)	BRD2(2)	BRD3(1)	BRD3(2)	CREBBP
K_D (nM)	170	830	380	490	1600

	BRD4(1)	BRD4(2)	BRDT(1)	BRDT(2)	EP300
K_D (nM)	160	850	1200	3700	2600

Conclusions

We present the freely-available cheminformatics and computational chemistry platform ChemicalToolBoX, and show its usability in two exemplarily cases in the cheminformatics and drug discovery fields. As an open-source initiative, ChemicalToolBoX is permanently under development and new tools are implemented in a regular basis.

http://pharmaceutical-bioinformatics.org

Baden-Württemberg
MINISTERIUM FÜR WISSENSCHAFT, FORSCHUNG UND KUNST

[1] https://github.com/bgruening/galaxytools/tree/master/chemicaltoolbox
[2] Goecks J, Nekrutenko A, Taylor J, Galaxy T, *Genome Biol.* (2010), *11*, R86.
[3] Lucas X, Grüning BA, Bleher S, Günther S (submitted).
[4] Lucas X, Wohlwend D, Hügle M, Schmidtkunz K, Gerhardt S, Schüle R, Jung M, Einsle O, Günther S, *Angew. Chem. Int. Ed.* (2013), DOI: 10.1002/anie.201307652

UNI FREIBURG