FlexFilters: A scalable and flexible QSAR platform for addressing complex and diverse types of *in silico* safety assessment of chemicals

Suman Chakravarti *chakravarti@multicase.com*
MultiCASE Inc., Beachwood, OH, USA - *www.multicase.com*

MultiCASE

SOT 2020
Anaheim, CA

Background

- A software platform for diverse types of computational toxicity workflows.
- Editable models contain the bulk of instructions for operations, not the software.
- Modular: A variety of predictive algorithms, descriptors and models can be combined in a hierarchical fashion.
- Able to perform exploratory operations, e.g. database search, alert identification, similarity search etc.
- Allows scalability when new data or new mechanistic knowledge becomes available.

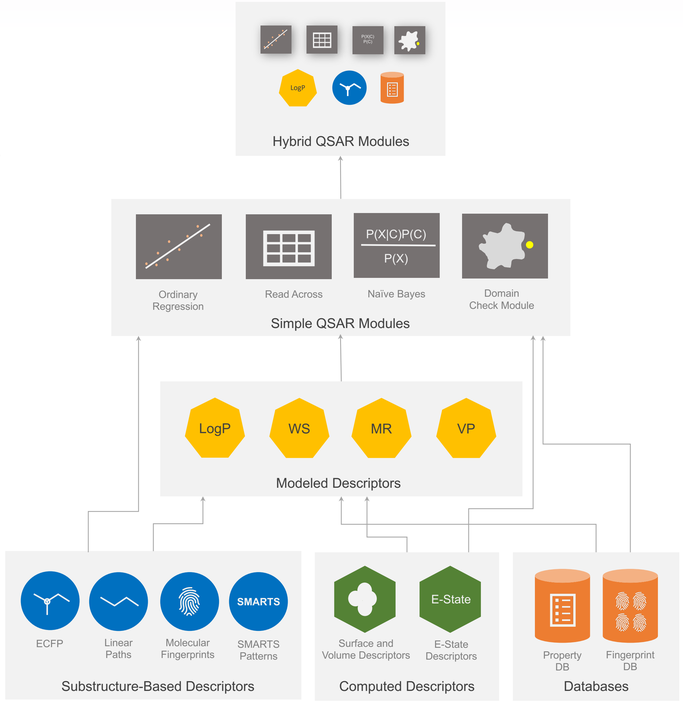
Objectives

- To address the challenges from rapidly evolving field of computational toxicology.
- Scalability, flexibility, upgradability and modularity.
- Combine knowledge from *in vivo*, *in vitro* assays and *in silico* models.

Case Study Data

- LD_{50} rat acute oral toxicity data from NICEATM workgroup.[1]
- LogP and atmospheric hydroxylation data from Mansouri *et al*.[2]

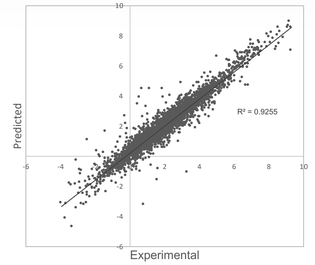
Hierarchical and Modular Workflows



ECFP: Extended connectivity fragments

QSAR Case Studies

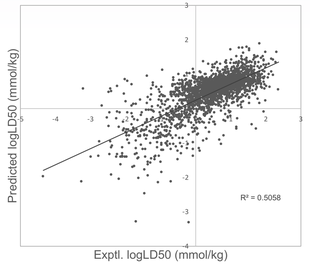
LogP



Training: 9533
Test: 3513
r^2 = 0.926

Descriptors: ECFP
Method: Ordinary regression

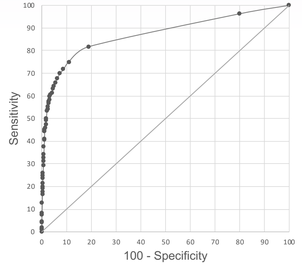
LD_{50} Point Estimates



Training: 5279
Test: 2134
r^2 = 0.506

Descriptors: ECFP
Method: Ordinary regression

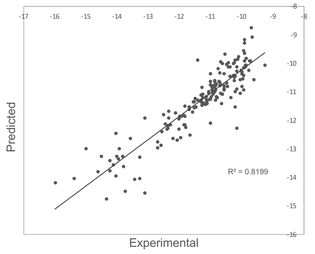
LD_{50} 'Very Toxic' class



Training: 8456
Test: 2841
AUC = 0.869

Descriptors: ECFP
Method: Logistic regression

Atmospheric Hydroxylation Rate



Training: 515
Test: 176
r^2 = 0.820

Descriptors: Phys-Chem, Estate and ECFP
Method: Ordinary regression

LD_{50} EPA Hazard Class

Actual Class	Predicted Class 1	2	3	4
1	62%	19%	14%	6%
2	14%	47%	36%	3%
3	2%	16%	68%	14%
4	1%	6%	45%	48%

Training: 8253
Test: 2813

Descriptors: ECFP
Method: Multi category Naïve Bayes

Conclusions

- A software platform to handle a variety of QSAR tasks.
- For handling statistical, expert rule-based and read across assessments.
- Modular and hierarchical in nature for building simple to complex workflows.
- Workflows can logically combine multiple models.

References

1. Gadaleta et al. J Cheminform (2019) 11:58.
2. Mansouri et al. J Cheminform (2018) 10:10.