

## QSAR MODELLING OF FATHEAD MINNOW USING OPENTOX FRAMEWORK

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There are more than 100 000 chemicals in use today and many more synthesized. The new EU chemical legislation REACH would require more than 3 million additional test animals, if no alternative methods were accepted. This solution has been supported by the on the EC-funded FP7 project development platform "OpenTox" [1], which provides a unified open source access to *in vitro* and *in vivo* toxicity data, *in silico* models, procedures supporting validation and additional information to help of the predictions interpretation.

As an example of application we chose the EPA Fathead Minnow Acute Toxicity database that includes 580 tested industrial organic chemicals, which was used as the training set for development of predictive quantitative structure-activity models. This dataset is present at Ambit servers [2], which are used as a repository for OpenTox platform. The toxicity endpoints are based on the 96 h LC<sub>50</sub> (mmol/L) values for the fathead minnow. For QSAR modeling we utilized OpenTox applications, which are based on a set of distributed, interoperable OpenTox API-compliant REST web-services. We have developed a service for OpenTox framework, which includes MakeMNA, MakeQNA and MakeSCR algorithms. These algorithms are based on Multilevel (MNA) [3] and Quantitative (QNA) [4] descriptors, and Self-Consistent Regression for QSAR modelling. Initial data was randomly divided on the training and test sets in proportion 90% and 10%, respectively. The statistical parameters of the correlation are the following: training set - 522 compounds, test set - 58 compounds,  $R^2_{\text{test}}$  exceeded 0.7,  $Q^2_{\text{train}}$  exceeded 0.6. These results show robustness and satisfactory predictive ability of our method, hence, it may be used for acute toxicity assessment of chemical compounds under study. These algorithms and data are represented in free access as OpenTox web application service.

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### References:

1. <http://www.opentox.org>
2. <https://ambit.uni-plovdiv.bg:8443/ambit2>
3. <http://www.pharmaexpert.ru/passonline>
4. <http://www.pharmaexpert.ru/gusar>