

# QSARINS (QSAR-INSubria)

*Software for QSAR MLR model development and validation*

*From ideas of Prof. Paola Gramatica, applied in “QSAR Research Unit in Environmental Chemistry and Ecotoxicology” at University of Insubria, Italy*

The image is a promotional graphic for the QSARINS software. It features a dark background with a sunset or sunrise scene. In the top left corner is the circular logo of the University of Insubria, which contains a stylized 'U' and 'I' intertwined. To the right of the logo, the word 'QSARINS' is written in large, bold, light blue capital letters. Below the title, the text 'QSAR INSubria, version 2.2.3 - 2018' is displayed in a smaller, light blue font. Further down, the text 'Software for QSAR MLR Model Development and Validation' and 'Includes the QSARINS-Chem module' are written in the same light blue font. Below this, the authors are listed: 'By Gramatica P.', 'Cassani S., Chirico N. (software developer), Kovarich S., Papa E., Sangion A.' in a light blue font. The affiliation 'QSAR Research Unit in Environmental Chemistry and Ecotoxicology', 'Department of Theoretical and Applied Sciences (DiSTA)', and 'University of Insubria, Varese, Italy' is also listed in light blue. At the bottom, the website 'http://www.qsar.it' and contact email 'paola.gramatica@uninsubria.it' are provided in a yellow font.

## How to cite:

Each user of QSARINS (whether for QSAR models' development/validation or for application of QSARINS-Chem models or for use of the stored Insubria datasets or for analysis and validation of personal models) must cite the web: [www.qsar.it](http://www.qsar.it) and the following papers, where the software is presented:

- Gramatica, P., Chirico, N., Papa, E., Kovarich, S., Cassani, S. QSARINS: A New Software for the Development, Analysis, and Validation of QSAR MLR Models. *Journal of Computational Chemistry, Software news and updates*, **2013**, 34, 2121-2132, DOI: 10.1002/jcc.23361.
- Gramatica, P., Cassani, S., Chirico, N. QSARINS-Chem: Insubria Datasets and New QSAR/QSPR Models for Environmental Pollutants in QSARINS. *Journal of Computational Chemistry, Software news and updates*, **2014**, 35, 1036–1044. DOI: 10.1002/jcc.23576

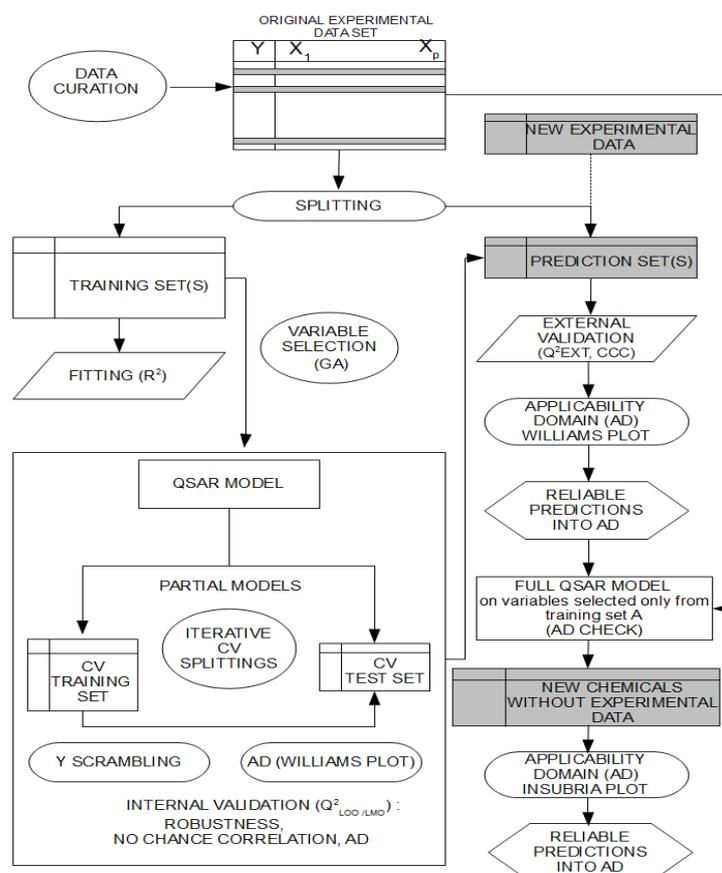
The provider Prof. Paola Gramatica should also be acknowledged for the free license.

## General information about QSARINS

**QSARINS (QSAR-INSubria)** is a software for the development and validation of Multiple Linear Regression (MLR) models by Ordinary Least Squares (OLS) and Genetic Algorithm (GA) for variable selection, based on QSAR experience of Prof. Paola Gramatica since 1995 and developed by Nicola Chirico (2008-2012). It is implemented according to the statistical/chemometric approach for QSAR models' predictivity (Tropsha et al. 2003; Gramatica 2007, 2009, 2012, 2013, 2014, 2016; Chirico and Gramatica 2011, 2012; Gramatica et al. 2012; Gramatica and Sangion 2016), which is applied by the QSAR group of the University of Insubria in all the modeling researches.

In the module **QSARINS-Chem** the 3D- chemical structures of many Insubria datasets are stored, in addition to several QSAR models, based on PaDEL Descriptors (Yap 2011), developed by the Insubria QSAR group and applicable also to new chemicals, directly in QSARINS, where the PaDEL Descriptors can be calculated.

The following scheme (from Gramatica et al. 2012) summarizes the procedure for a validated QSAR modeling, applicable in QSARINS:



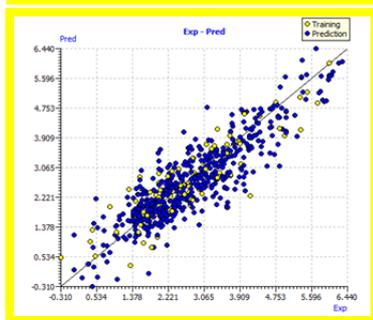
**QSARINS** provides a user-friendly interface that includes tools for:

- Data normalization;
- Dataset analysis (by Principal Component Analysis (PCA), etc.);
- Splitting of the data sets (by Random, Ordered response or Structure by PCA of molecular descriptors);
- OLS Model development by All Subset Selection;
- Genetic Algorithm (GA) for Variable Selection (with tracing of the models while being developed);
- Analysis of all individual variables, as well as those more frequently selected in the models;
- Internal validation, including the following criteria:  $Q^2_{LOO}$ ,  $Q^2_{LMO}$ , Concordance Correlation Coefficient (CCC), RMSE, MAE, Y-Scrambling, etc...;
- External validation, including the following criteria:  $Q^2_{F1}$ ,  $Q^2_{F2}$ ,  $Q^2_{F3}$ , Golbraikh and Tropsha parameters,  $r^2_m$  metrics,  $CCC_{EXT}$ , RMSE, MAE;
- Structural applicability domain by the leverage from the diagonal values of the Hat matrix (including Williams plot for chemicals with experimental data, y axis: standardized residuals and Insubria graph for chemicals without data, y axis: predicted values);
- Principal Components (PCs) Regression;
- Multi-Criteria Decision Making (MCDM) for selection of the best models;
- Consensus modeling (weighted and not, different tools for selection of models to be average);
- Check and validation of imported single models;
- Calculation of molecular descriptors and fingerprints with the open source software PaDEL-Descriptor (Yap 2011) (version currently included: 2.21).
- Application of several QSAR/QSPR models for environmental pollutants, developed by PaDEL-Descriptor software and stored in the QSARINS-Chem module, with the corresponding QMRF (QSAR Model Reporting Format). In particular: the PBT Index model (Papa and Gramatica 2010), re-developed (Gramatica et al. 2013, 2015) using PaDEL-Descriptor (Yap 2011);
- Database of compounds used to develop Insubria QSAR models: chemicals can be explored in different ways (CAS, SMILES, names) and visualized in 3D;
- Ranking of chemicals, based on PCA and MCDM

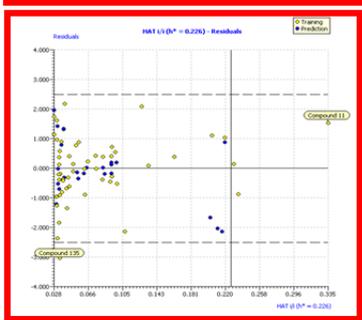
All outcomes of QSARINS are reported in the software with corresponding **plots** for quick graphical interpretation.

Example of some available **plots**:

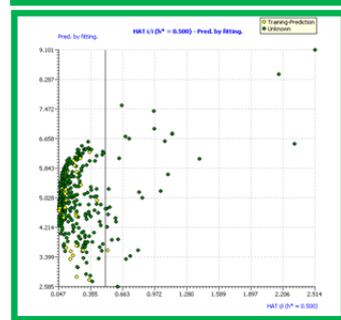
Plot Exp vs Pred



Williams Plot

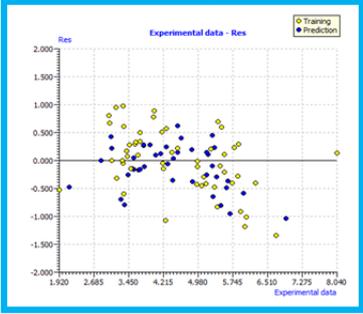


Insubria Graph

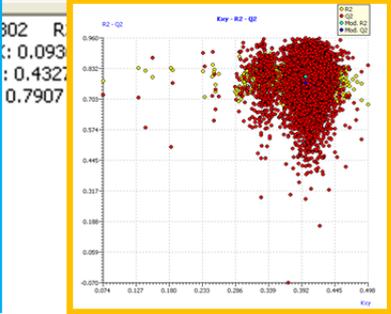


Model: T(N..S) AEigZ Seigv

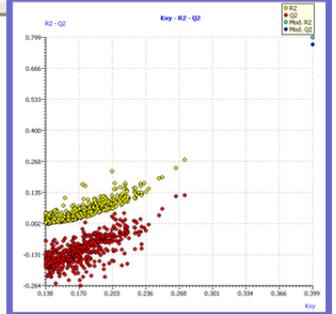
Variable	Coeff.	Std. coeff.	Co. int. 95%
Intercept	3.3922		0.4385
T(N..S)	0.1033	0.5632	0.0425
AEigZ	0.0145	0.8464	0.0033
Seigv	0.1531	0.3758	0.0986



Residuals Plot



LMO plot



Y-scramble plot

## SCREENSHOTS

**DATA SETUP** - Selection of variables and response. Three different splitting (Random, by ordered response, by structure based on PCA of molecular descriptors). PCA of the selected descriptors and generation of PC scores as variables for Principal Components Regression.

**Data Setup**

**Variables setup**

Select var. Select resp. Clear all  
Hold var. Release resp. Set splitting  
Release var. Normalize var. View resp. d.

No.	Variable	Status
1	Log Koc Exp	Response
2	Splitting	Splitting
3	MW	Selected
4	TopoPSA	Selected
5	VAdjMat	Selected
6	nH	Selected
7	nC	Selected
8	nN	Selected
9	nO	Selected
10	nS	Selected
11	nP	Selected
12	nF	Selected
13	nCl	Selected
14	nBr	Selected
15	nI	Selected
16	nX	Selected
17	nAromBond	Selected
18	WPATH	Selected
19	WPOL	Selected
20	XLogP	Selected
21	Zagreb	Selected
22	MAXDN2	Selected

**Objects setup**

Training Prediction Create splitting  
Excluded Reset objects Delete splitting

No.	Name	Status
1	000050-00-0	Prediction
2	000050-29-3	Training
3	000050-32-8	Prediction
4	000051-66-1	Prediction
5	000052-68-6	Prediction
6	000053-70-3	Prediction
7	000054-11-5	Training
8	000055-21-0	Prediction
9	000055-38-9	Training
10	000056-23-5	Prediction
11	000056-38-2	Prediction
12	000056-49-5	Prediction
13	000056-53-1	Prediction
14	000056-55-3	Prediction
15	000057-13-6	Prediction
16	000057-55-6	Prediction
17	000057-97-6	Prediction
18	000058-89-9	Prediction
19	000058-90-2	Prediction
20	000060-09-3	Prediction
21	000060-11-7	Prediction
22	000060-12-8	Prediction

**Splitting setup**

Name: Split - SOM  
Random percentage: [ ]  
Ordered by:  Response  Structure  
Second mol.: Training  
Training comp.: [ ]  
Prediction comp.: [ ]  
Swap  
Var. PCA Des. from PCA  
Correlation Single model  
LOF smooth: 1.0  
Selected variables: MW, TopoPSA, VAdjMat, nH, nC, nN, nO  
Missing values: [ ]  
Cancel OK

Training: 93 Prediction: 550 Variables: 661  
Excluded: 0 Missing: 0 Unknown: 0

**SINGLE MODEL** – Model’s parameters related to internal and external validation, predicted values, HAT values, and standardized residuals are calculated.

In addition, it is possible to view the PCA and the correlation matrix of the modeling descriptors. If available, the QMRF can be exported. It is present for the large majority of the models available in QSARINS-Chem.

**IMPORTANT INFORMATION:** Any user can upload personal MLR models and use QSARINS to manage them for storing, visualization, validation, ranking etc..

Model: VP-0 nAromBond MAXDP nHBacc

Variable	Coeff.	Std. coeff.	Std. err.	(+/-) Co. int. 95%	p-value
Intercept	0.8728		0.0640	0.1256	0.0000
VP-0	0.2596	0.7481	0.0076	0.0150	0.0000
nAromBond	0.0755	0.3344	0.0045	0.0088	0.0000
MAXDP	-0.1854	-0.2777	0.0156	0.0307	0.0000

(Fitting criteria)  
R2: 0.7942      R2adj: 0.7929      R2-R2adj: 0.0013      LOF:  
Kxx: 0.3831      Delta K: 0.1057      RMSE tr: 0.5428      MAE tr: 0.4287  
RSS tr: 189.4573      CCC tr: 0.8853      s: 0.5449      F: 615.5260

(Internal validation criteria)  
Q2loo: 0.7907      R2-Q2loo: 0.0035      RMSE cv: 0.5474      MAE cv: 0.4323

Std. res. thresh. 2.5

ID	Name	Status	Exp. endpoint	Pred. by model eq.	Pred.Mod.Eq.Res.	Pred. LOO	Pred. LOO Res.	HAT i/j (h*=0.0233)	Std.Pred.Mod.Eq. Res.	Std.Pred.LOO Res.
426	002008-41-5	Training	2.9000	2.3284	-0.5716	2.3242	-0.5758	0.0074	-1.0527	-1.0606
427	002008-58-4	Training	0.5300	1.9465	1.4165	1.9513	1.4213	0.0034	2.6037	2.6125
428	002032-65-7	Training	2.3200	2.7576	0.4376	2.7587	0.4387	0.0025	0.8041	0.8061
429	002050-68-2	Training	4.3000	4.1187	-0.1813	4.1174	-0.1826	0.0070	-0.3340	-0.3363
430	002051-60-7	Training	3.5200	3.8475	0.3275	3.8497	0.3297	0.0068	0.6030	0.6072
431	002051-61-8	Training	4.4200	3.8359	-0.5841	3.8320	-0.5880	0.0067	-1.0755	-1.0827
432	002077-99-8	Training	3.6100	2.8200	-0.7900	2.8155	-0.7945	0.0057	-1.4538	-1.4621
433	002104-64-5	Training	3.1200	4.2119	1.0919	4.2187	1.0987	0.0062	2.0099	2.0224
434	002122-70-5	Training	2.4800	2.8219	0.3419	2.8235	0.3435	0.0047	0.6288	0.6318
435	002136-79-0	Training	3.5100	2.2798	-1.2302	2.2754	-1.2346	0.0036	-2.2616	-2.2697
436	002150-93-8	Training	2.3400	2.2223	-0.1177	2.2220	-0.1180	0.0023	-0.2163	-0.2168
437	002163-68-0	Training	2.9500	1.7934	-1.1566	1.7833	-1.1667	0.0086	-2.1317	-2.1502
438	002164-17-2	Training	2.0000	2.1054	0.1054	2.1057	0.1057	0.0028	0.1938	0.1943
439	002212-67-1	Training	1.9400	1.7733	-0.1667	1.7723	-0.1677	0.0058	-0.3068	-0.3086
440	002234-13-1	Training	5.8900	5.3179	-0.5721	5.3092	-0.5808	0.0150	-1.0578	-1.0739
441	002303-16-4	Training	3.2800	2.5263	-0.7537	2.5195	-0.7605	0.0089	-1.3893	-1.4017
442	002303-17-5	Training	3.3500	2.7775	-0.5725	2.7714	-0.5786	0.0106	-1.0562	-1.0675
443	002307-68-8	Training	2.7600	2.7642	0.0042	2.7642	0.0042	0.0041	0.0077	0.0077
444	002310-17-0	Training	2.9800	3.3075	0.3275	3.3098	0.3298	0.0069	0.6031	0.6073
445	002312-35-8	Training	3.6000	3.6252	0.0252	3.6253	0.0253	0.0075	0.0463	0.0467
446	002327-02-8	Training	2.5300	1.9204	-0.6096	1.9186	-0.6114	0.0030	-1.1203	-1.1237
447	002385-85-5	Training	6.0000	5.6873	-0.3127	5.6717	-0.3283	0.0474	-0.5880	-0.6172
448	002425-10-7	Training	1.7100	2.2361	0.5261	2.2374	0.5274	0.0024	0.9666	0.9689

## QSARINS-Chem Module

QSARINS-Chem is the module where 3012 chemicals, collected from the literature, curated and modeled by the Insubria group, are available with their 3D structure and experimental responses. In addition, 45 QSAR models of environmental end-points for organic pollutants, based on free software for molecular descriptors (Yap 2011), are available. These models, supported by their QMRF, can be applied for any new chemical without experimental data or also not yet synthesized, verifying the structural applicability domain by the Insubria graph.

### List of QSAR models in QSARINS-Chem:

1. Brominated Flame Retardants (BFR) Log Koa (Papa et al. 2009; Gramatica et al. 2014)<sup>§</sup>
2. BFR MP (Papa et al. 2009; Gramatica et al. 2014)<sup>§</sup>
3. BFR VP (Papa et al. 2009; Gramatica et al. 2014)<sup>§</sup>
4. Benzo-Triazole (BTAZ) *D. magna* tox (Cassani et al. 2013; Gramatica et al. 2014)<sup>§</sup>
5. BTAZ Log Kow (Bhatarai and Gramatica 2011a; Gramatica et al. 2014)<sup>§</sup>
6. BTAZ MP (Bhatarai and Gramatica 2011a; Gramatica et al. 2014)<sup>§</sup>
7. BTAZ *O. mykiss* tox (Cassani et al. 2013; Gramatica et al. 2014)<sup>§</sup>
8. BTAZ *P. subcapitata* tox (Cassani et al. 2013; Gramatica et al. 2014)<sup>§</sup>
9. BTAZ Sw (Bhatarai and Gramatica 2011a; Gramatica et al. 2014)<sup>§</sup>
10. BTAZ VP (Bhatarai and Gramatica 2011a; Gramatica et al. 2014)<sup>§</sup>
11. Endocrine Disruptor Chemicals (EDC) Estrogen Receptor Binding (Li and Gramatica 2010; Gramatica et al. 2014)<sup>§</sup>
12. Esters *D. magna* tox (Papa et al. 2005a; Gramatica et al. 2014)<sup>§</sup>
13. Esters *P. promelas* tox (Papa et al. 2005a; Gramatica et al. 2014)<sup>§</sup>
14. Fish Biotrans. logHLn M1\_day (Papa et al. 2014)\*
15. Fish Biotrans. logHLn M2\_day (Papa et al. 2014)\*
16. Fish Biotrans. logHLn M3\_day (Papa et al. 2014)\*
17. Global Half-Life Index (GHLI) (Gramatica and Papa 2007; Gramatica et al. 2014)<sup>§\*</sup>
18. Human Biotrans. logHLB1\_h (Papa et al. 2018)\*
19. Human Biotrans. logHLB2\_h (Papa et al. 2018)\*
20. Human Biotrans. logHLB3\_h (Papa et al. 2018)\*
21. Human Biotrans. logHLB4\_h (Papa et al. 2018)\*
22. Human Biotrans. logHLT\_h (Papa et al. 2018)\*
23. Log Koc of Pesticides (Gramatica et al. 2007a, 2014)<sup>§\*</sup>
24. Nitro PAH Mutagenicity (Gramatica et al. 2007b, 2014)<sup>§</sup>
25. *Pimephales promelas* tox (Papa et al. 2005b; Gramatica et al. 2014)<sup>§\*</sup>
26. Persistence Bioaccumulation Toxicity (PBT) Index (Papa and Gramatica 2010; Gramatica et al. 2013)<sup>§\*</sup>
27. Personal Care Products (PCP) Aquatic Toxicity Index-ATI (Gramatica et al. 2016)\*
28. PCP *D.magna* acute tox (Gramatica et al. 2016)\*
29. PCP *P.promelas* acute tox LogP-based (Gramatica et al. 2016)\*
30. PCP *P.promelas* acute tox (Gramatica et al. 2016)\*

31. PCP *P.subcapitata* acute tox (Gramatica et al. 2016)\*
32. PerFluorinated Chemicals (PFC) Mouse Inhalation tox (Bhatarai and Gramatica 2010; Gramatica et al. 2014)<sup>§</sup>
33. PFC Rat Inhalation tox (Bhatarai and Gramatica 2010; Gramatica et al. 2014)<sup>§</sup>
34. PFC Rat Oral tox (Bhatarai and Gramatica 2011b; Gramatica et al. 2014)<sup>§</sup>
35. PFC Sw (Bhatarai and Gramatica 2011c; Gramatica et al. 2014)<sup>§</sup>
36. PFC VP (Bhatarai and Gramatica 2011c; Gramatica et al. 2014)<sup>§</sup>
37. Pharm. Aquatic Toxicity Index-ATI (Sangion and Gramatica 2016a)\*
38. Pharm. *D.magna* acute tox (Sangion and Gramatica 2016a)\*
39. Pharm. *O.mykiss* acute tox (Sangion and Gramatica 2016a)\*
40. Pharm. *P.promelas* acute tox (Sangion and Gramatica 2016a)\*
41. Pharm. *P.subcapitata* acute tox (Sangion and Gramatica 2016a)\*
42. PPCP intertox *D.magna-O.mykiss* (Sangion and Gramatica 2016b)
43. PPCP intertox *D.magna-P.promelas* (Sangion and Gramatica 2016b)
44. PPCP intertox *O.mykiss-P.promelas* (Sangion and Gramatica 2016b)
45. PPCP intertox *P.promelas-O.mykiss* (Sangion and Gramatica 2016b)

<sup>§</sup>Models originally developed using proprietary software (DRAGON v 5.5 or former versions) and updated using PaDEL Descriptor software (models are described in Gramatica et al. 2014).

\*Models reported in QSARINS-Chem Standalone version

### ***Additional information***

QSARINS can be used for every modeling work involving Multiple Linear Regression (MLR) calculations, based on Genetic Algorithm for variable selection and Ordinary Least Squares (OLS) as modeling method. However, any personal MLR model, even if developed by other software, can be analyzed by the plots available in QSARINS as well as validated by several statistical validation parameters (both for internal and external validation: see above list).

Other chemometric tools (Principal Component Analysis (PCA), Multicriteria Decision Making (MCDM)) for explorative analysis and ranking are also implemented, **therefore QSARINS is not limited to QSAR studies.**

It is also important to note that not only chemicals, but any kind of objects can be analyzed or modeled in a multivariate way.

## **Bibliography**

- Bhhatarai B, Gramatica P (2011a) Modelling physico-chemical properties of (benzo)triazoles, and screening for environmental partitioning. *Water Res* 45:1463–1471. doi: 10.1016/j.watres.2010.11.006
- Bhhatarai B, Gramatica P (2010) Per- and Polyfluoro Toxicity (LC50 Inhalation) Study in Rat and Mouse Using QSAR Modeling. *Chem Res Toxicol* 23:528–539. doi: 10.1021/tx900252h
- Bhhatarai B, Gramatica P (2011b) Oral LD50 toxicity modeling and prediction of per- and polyfluorinated chemicals on rat and mouse. *Mol Divers* 15:467–476. doi: 10.1007/s11030-010-9268-z
- Bhhatarai B, Gramatica P (2011c) Prediction of Aqueous Solubility, Vapor Pressure and Critical Micelle Concentration for Aquatic Partitioning of Perfluorinated Chemicals. *Environ Sci Technol* 45:8120–8128. doi: 10.1021/es101181g
- Cassani S, Kovarich S, Papa E, et al (2013) Daphnia and fish toxicity of (benzo)triazoles: Validated QSAR models, and interspecies quantitative activity–activity modelling. *J Hazard Mater* 258–259:50–60. doi: 10.1016/j.jhazmat.2013.04.025
- Chirico N, Gramatica P (2011) Real External Predictivity of QSAR Models: How To Evaluate It? Comparison of Different Validation Criteria and Proposal of Using the Concordance Correlation Coefficient. *J Chem Inf Model* 51:2320–2335. doi: 10.1021/ci200211n
- Chirico N, Gramatica P (2012) Real External Predictivity of QSAR Models. Part 2. New Intercomparable Thresholds for Different Validation Criteria and the Need for Scatter Plot Inspection. *J Chem Inf Model* 52:2044–2058. doi: 10.1021/ci300084j
- Gramatica P (2007) Principles of QSAR models validation: internal and external. *Qsar Comb Sci* 26:694–701. doi: 10.1002/qsar.200610151
- Gramatica P (2009) Chemometric Methods and Theoretical Molecular Descriptors in Predictive QSAR Modeling of the Environmental Behaviour of Organic Pollutants, Chapter 12 in *Recent Advances in QSAR Studies*. In: Puzyn T, Leszczynski J, Cronin MT (eds) *Recent Advances in QSAR Studies*. Springer Netherlands, pp 327–366
- Gramatica P (2012) Modelling Chemicals in the Environment. In: Livingstone D, Davis A (eds) *Drug Design Strategies Quantitative Approaches*. RSC Publishing
- Gramatica P (2013) On the Development and Validation of QSAR Models. In: Reisfeld B, Mayeno AN (eds) *Computational Toxicology*. Humana Press, pp 499–526
- Gramatica P (2014) External Evaluation of QSAR Models, in Addition to Cross-Validation: Verification of Predictive Capability on Totally New Chemicals. *Mol Inform* 33:311–314
- Gramatica P (2016) Prioritization of Chemicals Based on Chemoinformatic Analysis. In: Leszczynski J (ed) *Handbook of Computational Chemistry*. Springer Netherlands, pp 1–33

- Gramatica P, Cassani S, Chirico N (2014) QSARINS-Chem: Insubria Datasets and New QSAR/QSPR Models for Environmental Pollutants in QSARINS. *J Comput Chem* 35:1036–1044. doi: 10.1002/jcc.23576
- Gramatica P, Cassani S, Roy PP, et al (2012) QSAR modeling is not “push a button and find a correlation”: a case study of toxicity of (benzo-)triazoles on algae. *Mol Inf* 31:817–835. doi: 10.1002/minf.201200075
- Gramatica P, Cassani S, Sangion A (2015) PBT assessment and prioritization by PBT Index and consensus modeling: Comparison of screening results from structural models. *Environ Int* 77:25–34. doi: 10.1016/j.envint.2014.12.012
- Gramatica P, Cassani S, Sangion A (2016) Aquatic ecotoxicity of personal care products: QSAR models and ranking for prioritization and safer alternatives’ design. *Green Chem* 18:4393 – 4406. doi: 10.1039/C5GC02818C
- Gramatica P, Chirico N, Papa E, et al (2013) QSARINS: A new software for the development, analysis and validation of QSAR MLR models. *J Comput Chem* 34:2121–2132. doi: 10.1002/jcc.23361
- Gramatica P, Giani E, Papa E (2007a) Statistical external validation and consensus modeling: A QSPR case study for K-oc prediction. *J Mol Graph Model* 25:755–766. doi: 10.1016/j.jmgm.2006.06.005
- Gramatica P, Papa E (2007) Screening and ranking of POPs for global half-life: QSAR approaches for prioritization based on molecular structure. *Environ Sci Technol* 41:2833–2839. doi: 10.1021/es061773b
- Gramatica P, Pilutti P, Papa E (2007b) Approaches for externally validated QSAR modelling of Nitroated Polycyclic Aromatic Hydrocarbon mutagenicity. *SAR QSAR Environ Res* 18:169–178. doi: 10.1080/10629360601054388
- Gramatica P, Sangion A (2016) A Historical Excursus on the Statistical Validation Parameters for QSAR Models: A Clarification Concerning Metrics and Terminology. *J Chem Inf Model* 56:1127–1131. doi: 10.1021/acs.jcim.6b00088
- Li J, Gramatica P (2010) The importance of molecular structures, endpoints’ values, and predictivity parameters in QSAR research: QSAR analysis of a series of estrogen receptor binders. *Mol Divers* 14:687–696. doi: 10.1007/s11030-009-9212-2
- Papa E, Battaini F, Gramatica P (2005a) Ranking of aquatic toxicity of esters modelled by QSAR. *Chemosphere* 58:559–570. doi: 10.1016/j.chemosphere.2004.08.003
- Papa E, Gramatica P (2010) QSPR as a support for the EU REACH regulation and rational design of environmentally safer chemicals: PBT identification from molecular structure. *Green Chem* 12:836–843. doi: 10.1039/B923843C
- Papa E, Kovarich S, Gramatica P (2009) Development, Validation and Inspection of the Applicability Domain of QSPR Models for Physicochemical Properties of Polybrominated Diphenyl Ethers. *QSAR Comb Sci* 28:790–796. doi: 10.1002/qsar.200860183

- Papa E, Sangion A, Arnot JA, Gramatica P (2018) Development of human biotransformation QSARs and application for PBT assessment refinement. *Food Chem Toxicol* 112:535–543. doi: screening level
- Papa E, van der Wal L, Arnot JA, Gramatica P (2014) Metabolic biotransformation half-lives in fish: QSAR modeling and consensus analysis. *Sci Total Env* 470–471:1040–1046
- Papa E, Villa F, Gramatica P (2005b) Statistically validated QSARs, based on theoretical descriptors, for modeling aquatic toxicity of organic chemicals in *Pimephales promelas* (fathead minnow). *J Chem Inf Model* 45:1256–1266. doi: 10.1021/ci050212l
- Sangion A, Gramatica P (2016a) Ecotoxicity interspecies QAAR models from *Daphnia* toxicity of pharmaceuticals and personal care products. *SAR QSAR Environ Res* 0:1–18. doi: 10.1080/1062936X.2016.1233139
- Sangion A, Gramatica P (2016b) Hazard of pharmaceuticals for aquatic environment: Prioritization by structural approaches and prediction of ecotoxicity. *Environ Int* 95:131–143. doi: 10.1016/j.envint.2016.08.008
- Tropsha A, Gramatica P, Gombar VK (2003) The importance of being earnest: Validation is the absolute essential for successful application and interpretation of QSPR models. *Qsar Comb Sci* 22:69–77. doi: 10.1002/qsar.200390007
- Yap CW (2011) PaDEL-Descriptor: An open source software to calculate molecular descriptors and fingerprints. *JComput Chem* 32:1466–1474. doi: 10.1002/jcc.21707

**QSARINS is currently used by the Insubria group and several international QSAR groups: about 500 free licenses active into 2018.**

## **QSARINS citations**

**QSARINS has been cited in the following peer-reviewed publications (December 2018, source ISI Web of Knowledge and Google Scholar):**

- Aalizadeh, R., Pourbasheer, E., Ganjali, M.R., 2015. Analysis of B-Raf inhibitors using 2D and 3D-QSAR, molecular docking and pharmacophore studies. *Mol. Divers.* 19, 915–930. <https://doi.org/10.1007/s11030-015-9626-y>
- Ahmed, L., Rasulev, B., Kar, S., Krupa, P., Mozolewska, M.A., Leszczynski, J., 2017. Inhibitors or toxins? Large library target-specific screening of fullerene-based nanoparticles for drug design purpose. *Nanoscale* 9, 10263–10276. <https://doi.org/10.1039/c7nr00770a>
- Ambure, P., Aher, R.B., Roy, K., 2014. Recent Advances in the Open Access Cheminformatics Toolkits, Software Tools, Workflow Environments, and Databases, in: *Computer-Aided Drug Discovery*. Springer, pp. 257–296.
- Amrani, L.K., Tazir, A., Mazouni, N.S., 2015. Crop protection and preservation of environment: evaluation in vivo of bisacylhydrazine ecdysteroid mimics (RH-5849 and RH-5992) on pupae of *Epehestia kuehniella*, in: *18th International Symposium on Environmental Pollution and Its Impact on Life in the Mediterranean Region*. p. 51.
- Antypenko, L.M., Kovalenko, S.I., Los', T.S., Rebec', O.L., 2017. Synthesis and Characterization of Novel N-(Phenyl, Benzyl, Hetaryl)-2-([1,2,4]Triazol[1,5-c]Quinazolin-2-ylthio)Acetamides by Spectral Data, Antimicrobial Activity, Molecular Docking and QSAR Studies. *J. Heterocycl. Chem.* 54, 1267–1278. <https://doi.org/10.1002/jhet.2702>
- Antypenko, O.M., Kovalenko, S.I., Karpenko, O.V., Nikitin, V.O., Antypenko, L.M., 2016. Synthesis, Anticancer, and QSAR Studies of 2-Alkyl(aryl,hetaryl)quinazolin-4(3H)-thione's and [1,2,4]Triazol[1,5-c]quinazoline-2-thione's Thioderivatives. *Helv. Chim. Acta* 99, 621–631. <https://doi.org/10.1002/hlca.201600062>
- Aswathy, L., Jisha, R.S., Masand, V.H., Gajbhiye, J.M., Shibi, I.G., 2016. Computational strategies to explore antimalarial thiazine alkaloid lead compounds based on an Australian marine sponge *Plakortis Lita*. *Journal of Biomolecular Structure and Dynamics* 1–23. <https://doi.org/10.1080/07391102.2016.1220870>
- Ataide Martins, J.P., Rougeth de Oliveira, M.A., Oliveira de Queiroz, M.S., 2018. Web-4D-QSAR: A web-based application to generate 4D-QSAR descriptors. *Journal of Computational Chemistry* 39, 917–924. <https://doi.org/10.1002/jcc.25166>
- Aytac, P.S., Durmaz, I., Houston, D.R., Cetin-Atalay, R., Tozkoparan, B., 2016. Novel triazolothiadiazines act as potent anticancer agents in liver cancer cells through Akt and ASK-1 proteins. *Bioorg. Med. Chem.* 24, 858–872. <https://doi.org/10.1016/j.bmc.2016.01.013>
- Bahmani, A., Saaidpour, S., Rostami, A., 2017. A Simple, Robust and Efficient Computational Method for n-Octanol/Water Partition Coefficients of Substituted Aromatic Drugs. *Scientific Reports* 7, 5760. <https://doi.org/10.1038/s41598-017-05964-z>
- Barycki, M., Sosnowska, A., Gajewicz, A., Bobrowski, M., Wilenska, D., Skurski, P., Gieldon, A., Czaplowski, C., Uhl, S., Laux, E., Journot, T., Jeandupeux, L., Keppner, H., Puzyn, T., 2016a. Temperature-dependent structure-property modeling of viscosity for ionic liquids. *Fluid*

- Phase Equilib. 427, 9–17. <https://doi.org/10.1016/j.fluid.2016.06.043>
- Barycki, M., Sosnowska, A., Piotrowska, M., Urbaszek, P., Rybinska, A., Grzonkowska, M., Puzyn, T., 2016b. ILPC: simple chemometric tool supporting the design of ionic liquids. *J. Cheminformatics* 8, 40. <https://doi.org/10.1186/s13321-016-0152-4>
- Barycki, M., Sosnowska, A., Puzyn, T., 2018a. AquaBoxIL – a computational tool for determining the environmental distribution profile of ionic liquids. *Green Chemistry* 20, 3359–3370. <https://doi.org/10.1039/C8GC01582A>
- Barycki, M., Sosnowska, A., Puzyn, T., 2018b. AquaBoxIL–computational tool for determining the environmental distribution profile for ionic liquids. *Green Chemistry*.
- Barycki, M., Sosnowska, A., Puzyn, T., 2017. Which structural features stand behind micelization of ionic liquids? Quantitative Structure-Property Relationship studies. *J. Colloid Interface Sci.* 487, 475–483. <https://doi.org/10.1016/j.jcis.2016.10.066>
- Beier, R., Labudde, D., 2016. Numeric promoter description - A comparative view on concepts and general application. *J. Mol. Graph.* 63, 65–77. <https://doi.org/10.1016/j.jmgm.2015.11.011>
- Beiknejad, D., Chaichi, M.J., Fatemi, M.H., 2016. Prediction of photolysis half-lives of dihydroindolizines by genetic algorithm-multiple linear regression (GA-MLR). *J. Phys. Org. Chem.* 29, 312–320. <https://doi.org/10.1002/poc.3540>
- Biswas, S., Kayaleh, R., Pillai, G.G., Seon, C., Roberts, I., Popov, V., Alamry, K.A., Katritzky, A.R., 2014. Long-Range Chemical Ligation from N → N Acyl Migrations in Tryptophan Peptides via Cyclic Transition States of 10-to 18-Members. *Chem.-Eur. J.* 20, 8189–8198. <https://doi.org/10.1002/chem.201400125>
- Bukhari, S.N.A., Jantan, I., Masand, V.H., Mahajan, D.T., Sher, M., Naeem-ul-Hassan, M., Amjad, M.W., 2014. Synthesis of alpha, beta-unsaturated carbonyl based compounds as acetylcholinesterase and butyrylcholinesterase inhibitors: Characterization, molecular modeling, QSAR studies and effect against amyloid beta-induced cytotoxicity. *Eur. J. Med. Chem.* 83, 355–365. <https://doi.org/10.1016/j.ejmech.2014.06.034>
- Cañizares-Carmenate, Y., Hernandez-Morfa, M., Torrens, F., Castellano, G., Castillo-Garit, J.A., 2017. Larvicidal activity prediction against *Aedes aegypti* mosquito using computational tools. *Journal of vector borne diseases* 54, 164.
- Cañizares-Carmenate, Y., Mena-Ulecia, K., Perera-Sardiña, Y., Torrens, F., Castillo-Garit, J.A., 2016. An approach to identify new antihypertensive agents using Thermolysin as model: in silico study based on QSARINS and Docking. *Arabian Journal of Chemistry*. <https://doi.org/doi.org/10.1016/j.arabjc.2016.10.003>
- Caruso, E., Gariboldi, M., Sangion, A., Gramatica, P., Banfi, S., 2017. Synthesis, photodynamic activity, and quantitative structure-activity relationship modelling of a series of BODIPYs. *Journal of Photochemistry and Photobiology B: Biology* 167, 269–281. <https://doi.org/10.1016/j.jphotobiol.2017.01.012>
- Cassani, S., Gramatica, P., 2015. Identification of potential PBT behavior of personal care products by structural approaches. *Sustainable Chemistry and Pharmacy* 1, 19–27. <https://doi.org/10.1016/j.scp.2015.10.002>
- Cassano, A., Marchese Robinson, R.L., Palczewska, A., Puzyn, T., Gajewicz, A., Tran, L., Manganelli, S., Cronin, M.T., 2016. Comparing the CORAL and random forest approaches for modelling the in vitro cytotoxicity of silica nanomaterials. *Altern. Lab. Anim* 44, 533–556.
- Ceriani, L., Papa, E., Kovarich, S., Boethling, R., Gramatica, P., 2015. Modeling ready biodegradability of fragrance materials. *Environ. Toxicol. Chem.* 34, 1224–1231. <https://doi.org/10.1002/etc.2926>
- Chayawan, Vikas, 2016. Quantum-mechanical parameters for the risk assessment of multi-walled carbon-nanotubes: A study using adsorption of probe compounds and its application to

- biomolecules. *Environ. Pollut.* 218, 615–624. <https://doi.org/10.1016/j.envpol.2016.07.045>
- Chayawan, Vikas, 2015. Externally predictive single-descriptor based QSPRs for physico-chemical properties of polychlorinated-naphthalenes: Exploring relationships of log S-W, log K-OA, and log K-OW with electron-correlation. *J. Hazard. Mater.* 296, 68–81. <https://doi.org/10.1016/j.jhazmat.2015.04.028>
- Chen, C., Lee, M.-H., Weng, C.-F., Leong, M., 2018. Theoretical Prediction of the Complex P-Glycoprotein Substrate Efflux Based on the Novel Hierarchical Support Vector Regression Scheme. *Molecules* 23, 1820. <https://doi.org/10.3390/molecules23071820>
- Chen, M., Jabeen, F., Rasulev, B., Ossowski, M., Boudjouk, P., 2018. A computational structure-property relationship study of glass transition temperatures for a diverse set of polymers. *Journal of Polymer Science Part B: Polymer Physics* 56, 877–885. <https://doi.org/10.1002/polb.24602>
- Chitemere, R.P., Stafslie, S.J., Rasulev, B., Webster, D.C., Quadir, M., 2018. Soysome: A surfactant-free, fully biobased, self-assembled platform for nanoscale drug delivery applications. *ACS Applied Bio Materials*.
- Crisan, L., Funar-Timofei, S., Borota, A., 2017. Qsar and ligand-based pharmacophore models of dibenzoylhydrazines with insecticide activity against the silkworm *Bombyx mori* L. *Rev. Roum. Chim* 62, 699–706.
- Crisan, L., Iliescu, S., Funar-Timofei, S., 2016. Structure-flammability relationship study of phosphoester dimers by MLR and PLS. *Polimeros* 26, 129–136. <https://doi.org/10.1590/0104-1428.2306>
- de Campos, L.J., de Melo, E.B., 2014. Modeling structure–activity relationships of prodiginines with antimalarial activity using GA/MLR and OPS/PLS. *Journal of Molecular Graphics and Modelling* 54, 19–31. <https://doi.org/doi.org/10.1016/j.jmgm.2014.08.004>
- Dems, M.A.E., Laib, S., Latelli, N., Ouddai, N., 2017. A DFT-based Quantitative structure activity relationship Study of organometallic estradiol derivatives 10, 483–487.
- Devi, J., Devi, S., Kumar, A., 2016a. Synthesis, antibacterial evaluation and QSAR analysis of Schiff base complexes derived from [2,2'-(ethylenedioxy)bis(ethylamine)] and aromatic aldehydes. *MedChemComm* 7, 932–947. <https://doi.org/10.1039/c5md00554j>
- Devi, J., Devi, S., Kumar, A., 2016b. Synthesis, characterization, and quantitative structure-activity relationship studies of bioactive dehydroacetic acid and amino ether Schiff base complexes. *Heteroatom Chem.* 27, 361–371. <https://doi.org/10.1002/hc.21347>
- Devi, J., Yadav, M., Kumar, Anil, Kumar, Ashwani, 2018. Synthesis, characterization, biological activity, and QSAR studies of transition metal complexes derived from piperonylamine Schiff bases. *Chemical Papers* 72, 2479–2502. <https://doi.org/10.1007/s11696-018-0480-0>
- Ding, Y.-L., Lyu, Y.-C., Leong, M.K., 2016. In silico prediction of the mutagenicity of nitroaromatic compounds using a novel two-QSAR approach. *Toxicology in Vitro* 40, 102–114. <https://doi.org/doi.org/10.1016/j.tiv.2016.12.013>
- Dong, J., Yao, Z.-J., Zhu, M.-F., Wang, N.-N., Lu, B., Chen, A.F., Lu, A.-P., Miao, H., Zeng, W.-B., Cao, D.-S., 2017. ChemSAR: an online pipelining platform for molecular SAR modeling. *Journal of cheminformatics* 9, 27. <https://doi.org/doi.org/10.1186/s13321-017-0215-1>
- Doucet, J.P., Papa, E., Doucet-Panaye, A., Devillers, J., 2017. QSAR models for predicting the toxicity of piperidine derivatives against *Aedes aegypti*. *SAR QSAR Environ. Res.* 28, 451–470. <https://doi.org/10.1080/1062936X.2017.1328855>
- Drgan, V., Zuperl, S., Vracko, M., Como, F., Novic, M., 2016. Robust modelling of acute toxicity towards fathead minnow (*Pimephales promelas*) using counter-propagation artificial neural networks and genetic algorithm. *SAR QSAR Environ. Res.* 27, 501–519. <https://doi.org/10.1080/1062936X.2016.1196388>

- Ermondj, G., Vallaro, M., Caron, G., 2018. Learning how to use IAM chromatography for predicting permeability. *European Journal of Pharmaceutical Sciences* 114, 385–390.  
<https://doi.org/10.1016/j.ejps.2018.01.001>
- Erzincan, P., Saçan, M.T., Yuçe-Dursun, B., Danis, O., Demir, S., Erdem, S.S., Ogan, A., 2015. QSAR models for antioxidant activity of new coumarin derivatives. *SAR QSAR Environ. Res.* 26, 721–737. <https://doi.org/10.1080/1062936X.2015.1088571>
- Fan, T., Sun, G., Zhao, L., Cui, X., Zhong, R., 2018. QSAR and Classification Study on Prediction of Acute Oral Toxicity of N-Nitroso Compounds. *International Journal of Molecular Sciences* 19, 3015. <https://doi.org/10.3390/ijms19103015>
- Ferrari, T., Lombardo, A., Benfenati, E., 2018. QSARpy: A new flexible algorithm to generate QSAR models based on dissimilarities. The log Kow case study. *Science of The Total Environment* 637–638, 1158–1165. <https://doi.org/10.1016/j.scitotenv.2018.05.072>
- Fu, Y., Sun, Y.-N., Cao, H.-F., Yi, K.-H., Zhao, L.-X., Li, J.-Z., Ye, F., 2017. New Research for Quinazoline-2,4-diones as HPPD Inhibitors Based on 2D-MLR and 3D-QSAR Models. *Comb. Chem. High Throughput Screen* 20, 748–759.  
<https://doi.org/10.2174/1386207320666170622073738>
- Funar-Timofei, S., Avram, S., Borota, A., 2016. Structure-toxicity study of some pyrethroidal ester insecticides. <https://doi.org/doi:10.3390/ecsoc-17-e012>
- Funar-Timofei, S., Borota, A., Crisan, L., 2017. Combined molecular docking and QSAR study of fused heterocyclic herbicide inhibitors of D1 protein in photosystem II of plants. *Molecular diversity* 21, 437–454. <https://doi.org/doi.org/10.1007/s11030-017-9735-x>
- Funar-Timofei, S., Iliescu, S., Suzuki, T., 2014. Correlations of limiting oxygen index with structural polyphosphoester features by QSPR approaches. *Struct. Chem.* 25, 1847–1863.  
<https://doi.org/10.1007/s11224-014-0474-7>
- Furuhama, A., Hayashi, T.I., Tatarazako, N., 2016. Acute to chronic estimation of *Daphnia magna* toxicity within the QSAAR framework. *SAR QSAR Environ. Res.* 27, 833–850.  
<https://doi.org/10.1080/1062936X.2016.1243151>
- Gajewicz, A., 2018. How to judge whether QSAR/read-across predictions can be trusted: a novel approach for establishing a model's applicability domain. *Environmental Science: Nano.*  
<https://doi.org/10.1039/C7EN00774D>
- Garg, R., Smith, C.J., 2014. Predicting the bioconcentration factor of highly hydrophobic organic chemicals. *Food Chem. Toxicol.* 69, 252–259. <https://doi.org/10.1016/j.fct.2014.03.035>
- Geethaavacini, G., Poh, G.P., Yan, L.Y., Deepashini, R., Shalini, S., Harish, R., Sureshkumar, K., Ravichandran, V., 2018. QSAR and Pharmacophore Mapping Studies on Benzothiazinimines to Relate their Structural Features with anti-HIV Activity. *Medicinal Chemistry* 14, 733–740.  
<https://doi.org/10.2174/1573406414666180529091618>
- Gooch, Aminah, Sizochenko, N., Rasulev, B., Gorb, L., Leszczynski, J., 2017. In Vivo Toxicity of Nitroaromatics: A Comprehensive Quantitative Structure-Activity Relationship Study. *Environ. Toxicol. Chem.* 36, 2227–2233. <https://doi.org/10.1002/etc.3761>
- Gooch, A., Sizochenko, N., Sviatenko, L., Gorb, L., Leszczynski, J., 2017. A quantum chemical based toxicity study of estimated reduction potential and hydrophobicity in series of nitroaromatic compounds. *SAR and QSAR in Environmental Research* 28, 133–150.  
<https://doi.org/dx.doi.org/10.1080/1062936X.2017.1286687>
- Gramatica, P., 2016. Prioritization of Chemicals Based on Chemoinformatic Analysis. *Handbook of Computational Chemistry* 1–33.
- Gramatica, P., 2014. External Evaluation of QSAR Models, in Addition to CrossValidation: Verification of Predictive Capability on Totally New Chemicals. *Mol. Inf.* 33, 311–314.  
<https://doi.org/10.1002/minf.201400030>

- Gramatica, P., Cassani, S., Chirico, N., 2014. QSARINS-Chem: Insubria Datasets and New QSAR/QSPR Models for Environmental Pollutants in QSARINS. *J. Comput. Chem.* 35, 1036–1044. <https://doi.org/10.1002/jcc.23576>
- Gramatica, P., Cassani, S., Sangion, A., 2016a. Aquatic ecotoxicity of personal care products: QSAR models and ranking for prioritization and safer alternatives' design. *Green Chem.* 18, 4393–4406. <https://doi.org/10.1039/C5GC02818C>
- Gramatica, P., Cassani, S., Sangion, A., 2016b. Are some “safer alternatives” hazardous as PBTs? The case study of new flame retardants. *Journal of Hazardous Materials* 306, 237–246. <https://doi.org/10.1016/j.jhazmat.2015.12.017>
- Gramatica, Paola, Cassani, S., Sangion, A., 2015. PBT assessment and prioritization by PBT Index and consensus modeling: Comparison of screening results from structural models. *Environ. Int.* 77, 25–34. <https://doi.org/10.1016/j.envint.2014.12.012>
- Gramatica, P., Cassani, S., Sangion, A., Papa, E., 2015. Screening and prioritization of chemicals for REACH: The cumulative PBT Index model in QSARINS. *Toxicol. Lett.* 238, S338–S338. <https://doi.org/10.1016/j.toxlet.2015.08.964>
- Gramatica, P., Papa, E., Sangion, A., 2018. QSAR modeling of cumulative environmental end-points for the prioritization of hazardous chemicals. *Environmental Science: Processes & Impacts* 20, 38–47. <https://doi.org/10.1039/c7em00519a>
- Gramatica, P., Sangion, A., 2016. A Historical Excursus on the Statistical Validation Parameters for QSAR Models: A Clarification Concerning Metrics and Terminology. *J. Chem Inf. Model.* 56, 1127–1131. <https://doi.org/10.1021/acs.jcim.6b00088>
- Grzonkowska, M., Sosnowska, A., Barycki, M., Rybinska, A., Puzyn, T., 2016. How the structure of ionic liquid affects its toxicity to *Vibrio fischeri*? *Chemosphere* 159, 199–207. <https://doi.org/10.1016/j.chemosphere.2016.06.004>
- Hamadani, M., Keshavarz, M.H., Nazari, B., Mohebbi, M., 2016. Reliable method for safety assessment of melting points of energetic compounds. *Process Saf. Environ. Protect.* 103, 10–22. <https://doi.org/10.1016/j.psep.2016.06.025>
- Hou, T.-Y., Weng, C.-F., Leong, M.K., 2018. Insight Analysis of Promiscuous Estrogen Receptor  $\alpha$ -Ligand Binding by a Novel Machine Learning Scheme. *Chemical Research in Toxicology* 31, 799–813. <https://doi.org/10.1021/acs.chemrestox.8b00130>
- Huang, L., Fantke, P., Ernstoff, A., Jolliet, O., 2017. A quantitative property-property relationship for the internal diffusion coefficients of organic compounds in solid materials. *Indoor air* 27, 1128–1140. <https://doi.org/DOI:10.1111/ina.12395>
- Jabeen, F., Chen, M., Rasulev, B., Ossowski, M., Boudjouk, P., 2017. Refractive indices of diverse data set of polymers: A computational QSPR based study. *Computational Materials Science* 137, 215–224. <https://doi.org/doi.org/10.1016/j.commsci.2017.05.022>
- Jagiello, K., Grzonkowska, M., Swirog, M., Ahmed, L., Rasulev, B., Avramopoulos, A., Papadopoulos, M.G., Leszczynski, J., Puzyn, T., 2016. Advantages and limitations of classic and 3D QSAR approaches in nano-QSAR studies based on biological activity of fullerene derivatives. *J. Nanopart. Res.* 18, 256. <https://doi.org/10.1007/s11051-016-3564-1>
- Jagiello, K., Makurat, S., Pereć, S., Rak, J., Puzyn, T., 2018. Molecular features of thymidine analogues governing the activity of human thymidine kinase. *Structural Chemistry* 29, 1367–1374. <https://doi.org/10.1007/s11224-018-1124-2>
- Jimena Martinez, M., Ponzoni, I., Diaz, M.F., Vazquez, G.E., Soto, A.J., 2015. Visual analytics in cheminformatics: user-supervised descriptor selection for QSAR methods. *J. Cheminformatics* 7, 39. <https://doi.org/10.1186/s13321-015-0092-4>
- Judycka, U., Jagiello, K., Gromelski, M., Bober, L., Błażejowski, J., Puzyn, T., 2018. Chemometric approach to correlations between retention parameters of non-polar HPLC columns and

physicochemical characteristics for ampholytic substances of biological and pharmaceutical relevance. *Journal of Chromatography B* 1095, 8–14.

<https://doi.org/10.1016/j.jchromb.2018.07.019>

Judycka-Proma, U., Bober, L., Gajewicz, A., Puzyn, T., Blazejowski, J., 2015. Chemometric analysis of correlations between electronic absorption characteristics and structural and/or physicochemical parameters for ampholytic substances of biological and pharmaceutical relevance. *Spectroc. Acta Pt. A-Molec. Biomolec. Spectr.* 138, 700–710.

<https://doi.org/10.1016/j.saa.2014.11.067>

Jukić, M., Rastija, V., Opačak-Bernardi, T., Stolić, I., Krstulović, L., Bajić, M., Glavaš-Obrovac, L., 2017. Antitumor activity of 3, 4-ethylenedioxythiophene derivatives and quantitative structure-activity relationship analysis. *Journal of Molecular Structure* 1133, 66–73.

<https://doi.org/dx.doi.org/10.1016/j.molstruc.2016.11.074>

Kahraman, E.N., Saçan, M.T., 2018. On the prediction of cytotoxicity of diverse chemicals for topminnow (*Poeciliopsis lucida*) hepatoma cell line, PLHC-1<sup>S</sup>. SAR and QSAR in *Environmental Research* 29, 675–691. <https://doi.org/10.1080/1062936X.2018.1509235>

Kapusta, K., Sizochenko, N., Karabulut, S., Okovytyy, S., Voronkov, E., Leszczynski, J., 2018. QSPR modeling of optical rotation of amino acids using specific quantum chemical descriptors. *Journal of Molecular Modeling* 24. <https://doi.org/10.1007/s00894-018-3593-z>

Karabulut, S., Sizochenko, N., Orhan, A., Leszczynski, J., 2016. A DFT-based QSAR study on inhibition of human dihydrofolate reductase. *J. Mol. Graph.* 70, 23–29.

<https://doi.org/10.1016/j.jmgm.2016.09.005>

Kolaric, A., Minovski, N., 2017. Structure-based design of novel combinatorially generated NBTIs as potential DNA gyrase inhibitors against various *Staphylococcus aureus* mutant strains.

*Molecular BioSystems* 13, 1406–1420. <https://doi.org/10.1039/C7MB00168A>

Kulthong, K., Duivenvoorde, L., Mizera, B.Z., Rijkers, D., Dam, G. ten, Oegema, G., Puzyn, T., Bouwmeester, H., van der Zande, M., 2018. Implementation of a dynamic intestinal gut-on-a-chip barrier model for transport studies of lipophilic dioxin congeners. *RSC Advances* 8, 32440–32453. <https://doi.org/10.1039/C8RA05430D>

Lata, S., Vikas, 2018. Concentration dependent adsorption of aromatic organic compounds by SWCNTs: Quantum-mechanical descriptors for nano-toxicological studies of biomolecules and agrochemicals. *Journal of Molecular Graphics and Modelling* 85, 232–241.

<https://doi.org/10.1016/j.jmgm.2018.08.012>

Lata, S., Vikas, 2017. Dispersibility of carbon nanotubes in organic solvents: do we really have predictive models? *Journal of Nanoparticle Research* 19, 211.

<https://doi.org/10.1007/s11051-017-3883-x>

Li, J., Bai, F., Liu, H., Gramatica, P., 2015. Ligand Efficiency Outperforms pIC(50) on Both 2D MLR and 3D CoMFA Models: A Case Study on AR Antagonists. *Chem. Biol. Drug Des.* 86, 1501–1517. <https://doi.org/10.1111/cbdd.12619>

Li, J., Li, S., Bai, C., Liu, H., Gramatica, P., 2013. Structural requirements of 3-carboxyl-4 (1H)-quinolones as potential antimalarials from 2D and 3D QSAR analysis. *Journal of Molecular Graphics and Modelling* 44, 266–277. <https://doi.org/doi.org/10.1016/j.jmgm.2013.07.004>

Li, S., Li, J., Ning, L., Wang, S., Niu, Y., Jin, N., Yao, X., Liu, H., Xi, L., 2015. In Silico Identification of Protein S-Palmitoylation Sites and Their Involvement in Human Inherited Disease. *J. Chem Inf. Model.* 55, 2015–2025. <https://doi.org/10.1021/acs.jcim.5b00276>

Liu, L., Brailsford, J.A., 2015. *Protein Ligation and Total Synthesis*: I. Springer.

Maria Olguin, C.J., Sampaio, S.C., dos Reis, R.R., 2017. Statistical equivalence of prediction models of the soil sorption coefficient obtained using different log P algorithms. *Chemosphere* 184, 498–504. <https://doi.org/10.1016/j.chemosphere.2017.06.027>

- Martincic, R., Kuzmanovski, I., Wagner, A., Novic, M., 2015. Development of models for prediction of the antioxidant activity of derivatives of natural compounds. *Anal. Chim. Acta* 868, 23–35. <https://doi.org/10.1016/j.aca.2015.01.050>
- Martincic, R., Venko, K., Zuperl, S., Novic, M., 2014. Chemometrics approach for the prediction of structure-activity relationship for membrane transporter bilitranslocase. *SAR QSAR Environ. Res.* 25, 853–872. <https://doi.org/10.1080/1062936X.2014.962082>
- Masand, V.H., El-Sayed, N.N., Bambole, M.U., Quazi, S.A., 2018. Multiple QSAR models, pharmacophore pattern and molecular docking analysis for anticancer activity of  $\alpha$ ,  $\beta$ -unsaturated carbonyl-based compounds, oxime and oxime ether analogues. *Journal of Molecular Structure* 1157, 89–96.
- Masand, V.H., El-Sayed, N.N.E., Bambole, M.U., Patil, V.R., Thakur, S.D., 2019. Multiple quantitative structure-activity relationships (QSARs) analysis for orally active trypanocidal N-myristoyltransferase inhibitors. *Journal of Molecular Structure* 1175, 481–487. <https://doi.org/10.1016/j.molstruc.2018.07.080>
- Masand, V. H., El-Sayed, N.N.E., Mahajan, D.T., Rastija, V., 2017. QSAR analysis for 6-arylpyrazine-2-carboxamides as *Trypanosoma brucei* inhibitors. *SAR QSAR Environ. Res.* 28, 165–177. <https://doi.org/10.1080/1062936X.2017.1292407>
- Masand, Vijay H., El-Sayed, N.N.E., Mahajan, F.T., Mercader, A.G., Alafeefy, A.M., Shibi, I.G., 2017. QSAR modeling for anti-human African trypanosomiasis activity of substituted 2-Phenylimidazopyridines. *J. Mol. Struct.* 1130, 711–718. <https://doi.org/10.1016/j.molstruc.2016.11.012>
- Masand, V.H., Mahajan, D.T., Gramatica, P., Barlow, J., 2014. Tautomerism and multiple modelling enhance the efficacy of QSAR: antimalarial activity of phosphoramidate and phosphorothioamidate analogues of amiprofos methyl. *Med. Chem. Res.* 23, 4825–4835. <https://doi.org/10.1007/s00044-014-1043-8>
- Masand, V.H., Mahajan, D.T., Maldhure, A.K., Rastija, V., 2016. Quantitative structure–activity relationships (QSARs) and pharmacophore modeling for human African trypanosomiasis (HAT) activity of pyridyl benzamides and 3-(oxazolo [4, 5-b] pyridin-2-yl) anilides. *Medicinal chemistry research* 25, 2324–2334. <https://doi.org/10.1007/s00044-016-1664-1>
- Masand, V.H., Mahajan, D.T., Nazeruddin, G.M., Hadda, T.B., Rastija, V., Alfeefy, A.M., 2015. Effect of descriptor selection before splitting and method of splitting (rational and random) on external predictive ability and on behaviour of different statistical parameters of QSAR model. *Medicinal Chemistry Research* 24, 1241–1264. <https://doi.org/10.1007/s00044-014-1193-8>
- Masand, V.H., Rastija, V., 2017. PyDescriptor: A new PyMOL plugin for calculating thousands of easily understandable molecular descriptors. *Chemometrics Intell. Lab. Syst.* 169, 12–18. <https://doi.org/10.1016/j.chemolab.2017.08.003>
- Mikolajczyk, A., Gajewicz, A., Rasulev, B., Schaeublin, N., Maurer-Gardner, E., Hussain, S., Leszczynski, J., Puzyn, T., 2015. Zeta Potential for Metal Oxide Nanoparticles: A Predictive Model Developed by a Nano-Quantitative Structure-Property Relationship Approach. *Chem. Mat.* 27, 2400–2407. <https://doi.org/10.1021/cm504406a>
- Mikolajczyk, A., Malankowska, A., Nowaczyk, G., Gajewicz, A., Hirano, S., Jurga, S., Zaleska-Medynska, A., Puzyn, T., 2016. Combined experimental and computational approach to developing efficient photocatalysts based on Au/Pd-TiO<sub>2</sub> nanoparticles. *Environ.-Sci. Nano* 3, 1425–1435. <https://doi.org/10.1039/c6en00232c>
- Mirchi, A., Sizochenko, N., Leszczynski, J., 2018. Fullerene quinazolinone conjugates targeting *Mycobacterium tuberculosis*: a combined molecular docking, QSAR, and ONIOM approach. *Structural Chemistry* 29, 765–775. <https://doi.org/10.1007/s11224-018-1100-x>

- Molnar, M., Brahmhatt, H., Rastija, V., Pavić, V., Komar, M., Karnaš, M., Babić, J., 2018. Environmentally Friendly Approach to Knoevenagel Condensation of Rhodanine in Choline Chloride: Urea Deep Eutectic Solvent and QSAR Studies on Their Antioxidant Activity. *Molecules* 23, 1897. <https://doi.org/10.3390/molecules23081897>
- Molnar, M., Komar, M., Brahmhatt, H., Babić, J., Jokić, S., Rastija, V., 2017. Deep Eutectic Solvents as Convenient Media for Synthesis of Novel Coumarinyl Schiff Bases and Their QSAR Studies. *Molecules* 22, 1482. <https://doi.org/10.3390/molecules22091482>
- Nazari, B., Hamadani, M., Keshavarz, M.H., Rezaei, J., 2016. New method for assessment of melting points of organic azides using their molecular structures. *Fluid Phase Equilib.* 427, 27–34. <https://doi.org/10.1016/j.fluid.2016.06.051>
- Nosulenko, I.S., Voskoboynik, O.Y., Antypenko, O.M., Berest, G.G., Kovalenko, S.I., Носуленко, I.C., Воскобойник, O.Ю., Антипенко, O.M., Берест, Г.Г., Коваленко, С.И., others, 2015. Methodology for prediction of anticancer action of (2-oxo-2H-[1, 2, 4] triazino [2, 3-c]-quinazolin-6-yl) thiones via QSAR and docking studies.
- Önlü, S., Saçan, M.T., 2018. Toxicity of contaminants of emerging concern to *Dugesia japonica*: QSTR modeling and toxicity relationship with *Daphnia magna*. *Journal of Hazardous Materials* 351, 20–28. <https://doi.org/10.1016/j.jhazmat.2018.02.046>
- Önlü, Serli, Saçan, M.T., 2016. An in silico algal toxicity model with a wide applicability potential for industrial chemicals and pharmaceuticals. *Environmental Toxicology and Chemistry*. <https://doi.org/10.1002/etc.3620>
- Önlü, Serli, Saçan, M.T., 2016. An in silico approach to cytotoxicity of pharmaceuticals and personal care products on the rainbow trout liver cell line RTL-W1. *Environmental Toxicology and Chemistry*. <https://doi.org/10.1002/etc.3663>
- Önlü, S., Türker Saçan, M., 2017. Impact of geometry optimization methods on QSAR modelling: A case study for predicting human serum albumin binding affinity. *SAR and QSAR in Environmental Research* 28, 491–509. <https://doi.org/10.1080/1062936X.2017.1343253>
- Orucu, E., Tugcu, G., Saçan, M.T., 2014. Molecular structure-adsorption study on current textile dyes. *SAR QSAR Environ. Res.* 25, 983–998. <https://doi.org/10.1080/1062936X.2014.976266>
- Panda, S.S., Jones, R.A., Hall, C.D., Katritzky, A.R., 2014. Applications of Chemical Ligation in Peptide Synthesis via Acyl Transfer, in: *Protein Ligation and Total Synthesis I*. Springer, pp. 229–265.
- Papa, E., Arnot, J.A., Sangion, A., Gramatica, P., 2017. In Silico Approaches for the Prediction of In Vivo Biotransformation Rates, in: *Advances in QSAR Modeling*. Springer, pp. 425–451.
- Papa, E., Doucet, J.P., Doucet-Panaye, A., 2016a. Computational approaches for the prediction of the selective uptake of magnetofluorescent nanoparticles into human cells. *RSC Adv.* 6, 68806–68818. <https://doi.org/10.1039/c6ra07898b>
- Papa, E., Doucet, J.P., Doucet-Panaye, A., 2015. Linear and non-linear modelling of the cytotoxicity of TiO<sub>2</sub> and ZnO nanoparticles by empirical descriptors. *SAR QSAR Environ. Res.* 26, 647–665. <https://doi.org/10.1080/1062936X.2015.1080186>
- Papa, E., Doucet, J.P., Sangion, A., Doucet-Panaye, A., 2016b. Investigation of the influence of protein corona composition on gold nanoparticle bioactivity using machine learning approaches. *SAR QSAR Environ. Res.* 27, 521–538. <https://doi.org/10.1080/1062936X.2016.1197310>
- Papa, E., Sangion, A., Arnot, J.A., Gramatica, P., 2018. Development of human biotransformation QSARs and application for PBT assessment refinement. *Food and Chemical Toxicology* 112, 535–543. [https://doi.org/screening level](https://doi.org/screening%20level)
- Papa, E., van der Wal, L., Arnot, J.A., Gramatica, P., 2014. Metabolic biotransformation half-lives in

- fish: QSAR modeling and consensus analysis. *Sci. Total Environ.* 470, 1040–1046. <https://doi.org/10.1016/j.scitotenv.2013.10.068>
- Papadaki, K.C., Karakitsios, S.P., Sarigiannis, D.A., 2017. Modeling of adipose/blood partition coefficient for environmental chemicals. *Food Chem. Toxicol.* 110, 274–285. <https://doi.org/10.1016/j.fct.2017.10.044>
- Paterno, A., Goracci, L., Scire, S., Musumarra, G., 2017. Modeling from Theory and Modeling from Data: Complementary or Alternative Approaches? The Case of Ionic Liquids. *ChemistryOpen* 6, 90–101. <https://doi.org/10.1002/open.201600119>
- Patil, R.B., Barbosa, E.G., Sangshetti, J.N., Sawant, S.D., Zambre, V.P., 2018a. LQTA-R: A new 3D-QSAR methodology applied to a set of DGAT1 inhibitors. *Computational Biology and Chemistry* 74, 123–131. <https://doi.org/10.1016/j.compbiolchem.2018.02.021>
- Patil, R.B., Barbosa, E.G., Sangshetti, J.N., Zambre, V.P., Sawant, S.D., 2018b. Structural insights of dipeptidyl peptidase-IV inhibitors through molecular dynamics-guided receptor-dependent 4D-QSAR studies. *Molecular Diversity* 22, 575–583. <https://doi.org/10.1007/s11030-018-9815-6>
- Pillai, G.G., 2015. Computational Modelling of Diverse Chemical, Biochemical and Biomedical Properties (PhD Thesis).
- Pillai, G.G., Mederos, L., Panda, C.S., Gronski, A., Burk, P., Hall, C.D., Katritzky, A.R., Tamm, K., Karelson, M., 2016. Robust Modeling and Scaffold Hopping: Case Study Based on HIV Reverse Transcriptase Inhibitors Type-1 Data. *Med. Chem.* 12, 513–526. <https://doi.org/10.2174/1573406411666151005110141>
- Pourbasheer, E., Aalizadeh, R., Ardabili, J.S., Ganjali, M.R., 2015. QSPR study on solubility of some fullerenes derivatives using the genetic algorithms - Multiple linear regression. *J. Mol. Liq.* 204, 162–169. <https://doi.org/10.1016/j.molliq.2015.01.028>
- Putz, M.V., Dudas, N.A., Isvoran, A., 2015. Double Variational Binding-(SMILES) Conformational Analysis by Docking Mechanisms for Anti-HIV Pyrimidine Ligands. *Int. J. Mol. Sci.* 16, 19553–19601. <https://doi.org/10.3390/ijms160819553>
- Qin, L., Zhang, X., Chen, Y., Mo, L., Zeng, H., Liang, Y., 2017. Predictive QSAR Models for the Toxicity of Disinfection Byproducts. *Molecules* 22, 1671. <https://doi.org/10.3390/molecules22101671>
- Qin, L.-T., Chen, Y.-H., Zhang, X., Mo, L.-Y., Zeng, H.-H., Liang, Y.-P., 2018. QSAR prediction of additive and non-additive mixture toxicities of antibiotics and pesticide. *Chemosphere* 198, 122–129. <https://doi.org/10.1016/j.chemosphere.2018.01.142>
- QSARpy: A new flexible algorithm to generate QSAR models based on dissimilarities. The log Kow case study - ScienceDirect [WWW Document], n.d. URL <https://www.sciencedirect.com/science/article/pii/S0048969718317078> (accessed 12.11.18).
- Rácz, A., Bajusz, D., Héberger, K., 2018. Chemometrics in Analytical Chemistry. *Applied Chemoinformatics: Achievements and Future Opportunities* 471–499.
- Racz, A., Bajusz, D., Heberger, K., 2015. Consistency of QSAR models: Correct split of training and test sets, ranking of models and performance parameters. *SAR QSAR Environ. Res.* 26, 683–700. <https://doi.org/10.1080/1062936X.2015.1084647>
- Rastija, V., Agic, D., Tomic, S., Nikolic, S., Hranjec, M., Karminski-Zamola, G., Abramic, M., 2015. Synthesis, QSAR, and Molecular Dynamics Simulation of Amidino-substituted Benzimidazoles as Dipeptidyl Peptidase III Inhibitors. *Acta Chim. Slov.* 62, 867–878.
- Rastija, V., Masand, V.H., 2014. QSAR of Antitrypanosomal Activities of Polyphenols and their Analogues Using Multiple Linear Regression and Artificial Neural Networks. *Comb. Chem. High Throughput Screen* 17, 709–717.

<https://doi.org/10.2174/1386207317666140804161605>

- Rastija, V., Molnar, M., Siladi, T., Masand, V.H., 2018. QSAR Analysis for Antioxidant Activity of Dipicolinic Acid Derivatives. *Combinatorial Chemistry & High Throughput Screening* 21, 204–214. <https://doi.org/10.2174/1386207321666180213092352>
- Rasulev, B., Jabeen, F., Staflien, S., Chisholm, B.J., Bahr, J., Ossowski, M., Boudjouk, P., 2017. Polymer Coating Materials and Their Fouling Release Activity: A Cheminformatics Approach to Predict Properties. *ACS Appl. Mater. Interfaces* 9, 1781–1792. <https://doi.org/10.1021/acsami.6b12766>
- Rath, E.C., Bai, Y., 2016. Quantitative Structure-Activity Relation Study of Quaternary Ammonium Compounds in Pathogen Control: Computational Methods for the Discovery of Food Antimicrobials. *Chemical Informatics*. <https://doi.org/10.21767/2470-6973.100017>
- Rath, E.C., Gill, H., Bai, Y., 2017. Identification of potential antimicrobials against *Salmonella typhimurium* and *Listeria monocytogenes* using Quantitative Structure-Activity Relation modeling. *PloS one* 12, 1–17. <https://doi.org/doi.org/10.1371/journal.pone.0189580>
- Ravichandran, V., Shalini, S., Venkateskumar, K., Dhanaraj, S.A., 2016a. Exploring the Structural Insights of Indole-7-Carboxamides as Anti-Hiv Agents. *Farmacia* 64, 745–756. <https://doi.org/doi.org/10.1016/j.chemolab.2016.03.017>
- Ravichandran, V., Venkateskumar, K., Shalini, S., Harish, R., 2016b. Exploring the structure-activity relationship of oxazolidinones as HIV-1 protease inhibitors-QSAR and pharmacophore modelling studies. *Chemometrics Intell. Lab. Syst.* 154, 52–61. <https://doi.org/10.1016/j.chemolab.2016.03.017>
- Reenu, Vikas, 2016. Evaluating the role of electron-correlation in the external prediction of the toxicity of nitrobenzenes towards *Tetrahymena pyriformis*. *New J. Chem.* 40, 2343–2353. <https://doi.org/10.1039/c5nj02552d>
- Reenu, Vikas, 2015a. Role of exchange and correlation in the real external prediction of mutagenicity: performance of hybrid and meta-hybrid exchange-correlation functionals. *RSC Adv.* 5, 29238–29251. <https://doi.org/10.1039/c4ra14262d>
- Reenu, Vikas, 2015b. Exploring the role of quantum chemical descriptors in modeling acute toxicity of diverse chemicals to *Daphnia magna*. *J. Mol. Graph.* 61, 89–101. <https://doi.org/10.1016/j.jmgm.2015.06.009>
- Reenu, Vikas, 2014. Electron-correlation based externally predictive QSARs for mutagenicity of nitrated-PAHs in *Salmonella typhimurium* TA100. *Ecotox. Environ. Safe.* 101, 42–50. <https://doi.org/10.1016/j.ecoenv.2013.11.020>
- Rehman, T.U., Khan, I.U., Ashraf, M., Tarazi, H., Riaz, S., Yar, M., 2017. An Efficient Synthesis of bi-Aryl Pyrimidine Heterocycles: Potential New Drug Candidates to Treat Alzheimer's Disease. *Archiv der Pharmazie* 350. <https://doi.org/10.1002/ardp.201600304>
- Ruusmann, V., Sild, S., Maran, U., 2015. QSAR DataBank repository: open and linked qualitative and quantitative structure-activity relationship models. *J. Cheminformatics* 7, 32. <https://doi.org/10.1186/s13321-015-0082-6>
- Rybinska, A., Sosnowska, A., Barycki, M., Puzyn, T., 2016a. Geometry optimization method versus predictive ability in QSPR modeling for ionic liquids. *J. Comput.-Aided Mol. Des.* 30, 165–176. <https://doi.org/10.1007/s10822-016-9894-3>
- Rybinska, A., Sosnowska, A., Grzonkowska, M., Barycki, M., Puzyn, T., 2016b. Filling environmental data gaps with QSPR for ionic liquids: Modeling n-octanol/water coefficient. *J. Hazard. Mater.* 303, 137–144. <https://doi.org/10.1016/j.jhazmat.2015.10.023>
- Rybinska-Fryca, A., Sosnowska, A., Puzyn, T., 2018. Prediction of dielectric constant of ionic liquids. *Journal of Molecular Liquids* 260, 57–64. <https://doi.org/10.1016/j.molliq.2018.03.080>
- Saaidpour, S., 2016. Quantitative Modeling for Prediction of Critical Temperature of Refrigerant

- Compounds. *Phys. Chem. Res.* 4, 61–71. <https://doi.org/10.22036/pcr.2016.11759>
- Şahin, A.D., Saçan, M.T., 2018a. Understanding the toxic potencies of xenobiotics inducing TCDD/TCDF-like effects. *SAR QSAR Environ. Res.* 1–15. <https://doi.org/doi.org/10.1080/1062936X.2017.1414075>
- Şahin, A.D., Saçan, M.T., 2018b. Understanding the toxic potencies of xenobiotics inducing TCDD/TCDF-like effects. *SAR and QSAR in Environmental Research* 29, 117–131. <https://doi.org/10.1080/1062936X.2017.1414075>
- Sangion, A., Gramatica, P., 2016a. PBT assessment and prioritization of contaminants of emerging concern: Pharmaceuticals. *Environ. Res.* 147, 297–306. <https://doi.org/10.1016/j.envres.2016.02.021>
- Sangion, A., Gramatica, P., 2016b. Ecotoxicity interspecies QAAR models from Daphnia toxicity of pharmaceuticals and personal care products. *SAR QSAR Environ. Res.* 27, 781–798. <https://doi.org/10.1080/1062936X.2016.1233139>
- Sangion, A., Gramatica, P., 2016c. Hazard of pharmaceuticals for aquatic environment: Prioritization by structural approaches and prediction of ecotoxicity. *Environ. Int.* 95, 131–143. <https://doi.org/10.1016/j.envint.2016.08.008>
- Shaik, B., Deeb, O., Agrawal, V.K., Gupta, S.P., 2017. QSAR and Molecular Docking Studies on a Series of Cinnamic Acid Analogues as Epidermal Growth Factor Receptor (EGFR) Inhibitors. *Lett. Drug Des. Discov.* 14, 83–95. <https://doi.org/10.2174/1570180813999160721160833>
- Shaik, B., Kaushal, T., Agrawal, V.K., 2016. Quantitative structure activity relationship studies on a series of 4-pyridones as antimalarial agents. *J. Indian Chem. Soc.* 93, 871–876.
- Shao, Y., Liu, J., Wang, M., Shi, L., Yao, X., Gramatica, P., 2014. Integrated QSPR models to predict the soil sorption coefficient for a large diverse set of compounds by using different modeling methods. *Atmos. Environ.* 88, 212–218. <https://doi.org/10.1016/j.atmosenv.2013.12.018>
- Sikorska, C., 2015. Toward predicting vertical detachment energies for superhalogen anions exclusively from 2-D structures. *Chem. Phys. Lett.* 625, 157–163. <https://doi.org/10.1016/j.cplett.2015.03.002>
- Sikorska, C., Gajewicz, A., Urbaszek, P., Lubinski, L., Puzyn, T., 2016. Efficient way of designing fullerene derivatives based on simplified DFT calculations and QSPR modeling. *Chemometrics Intell. Lab. Syst.* 152, 125–133. <https://doi.org/10.1016/j.chemolab.2016.02.003>
- Sosnowska, A., Barycki, M., Gajewicz, A., Bobrowski, M., Freza, S., Skurski, P., Uhl, S., Laux, E., Journot, T., Jeandupeux, L., Keppner, H., Puzyn, T., 2016. Towards the Application of Structure-Property Relationship Modeling in Materials Science: Predicting the Seebeck Coefficient for Ionic Liquid/Redox Couple Systems. *ChemPhysChem* 17, 1591–1600. <https://doi.org/10.1002/cphc.201600080>
- Sosnowska, A., Grzonkowska, M., Puzyn, T., 2017. Global versus local QSAR models for predicting ionic liquids toxicity against IPC-81 leukemia rat cell line: The predictive ability. *J. Mol. Liq.* 231, 333–340. <https://doi.org/10.1016/j.molliq.2017.02.025>
- Su, E., 2015. Parallellization of evoQSAR modeling framework and graphical user interface design using PyQt for drug design (PhD Thesis). San Diego State University.
- Subhranian, S., Sizochenko, N., Melge, A.R., Leszczynski, J., Mohan, C.G., 2018. Multiple e-Pharmacophore modeling to identify a single molecule that could target both streptomycin and paromomycin binding sites for 30S ribosomal subunit inhibition. *Journal of Biomolecular Structure and Dynamics* 1–15.
- Subirats, X., Redón, L., Rosés, M., 2018. Lipophilicity determination of acidic compounds: MEEKC as a reliable high-throughput methodology. *ADMET and DMPK*.

<https://doi.org/10.5599/admet.491>

- Sun, G., Fan, T., Sun, X., Hao, Y., Cui, X., Zhao, L., Ren, T., Zhou, Y., Zhong, R., Peng, Y., 2018. In Silico Prediction of O6-Methylguanine-DNA Methyltransferase Inhibitory Potency of Base Analogs with QSAR and Machine Learning Methods. *Molecules* 23, 2892.
- Tang, H., Cui, F., Liu, L., Li, Y., 2018. Predictive models for tyrosinase inhibitors: Challenges from heterogeneous activity data determined by different experimental protocols. *Computational Biology and Chemistry* 73, 79–84.  
<https://doi.org/10.1016/j.compbiolchem.2018.02.007>
- Tarazi, H., Abu Odeh, R., Al-Qawasmeh, R., Abu Yousef, I., Voelter, W., Al-Tel, T.H., 2017. Design, synthesis and SAR analysis of potent BACE1 inhibitors: Possible lead drug candidates for Alzheimer's disease. *Eur. J. Med. Chem.* 125, 1213–1224.  
<https://doi.org/10.1016/j.ejmech.2016.11.021>
- Tetko, I.V., Maran, U., Tropsha, A., 2017. Public (Q) SAR Services, Integrated Modeling Environments, and Model Repositories on the Web: State of the Art and Perspectives for Future Development. *Mol. Inf.* 36, UNSP 1600082.  
<https://doi.org/10.1002/minf.201600082>
- Tromelin, A., 2016. Prediction of perception using structure–activity models, in: *Flavor: From Food to Behaviors, Wellbeing and Health*. p. 181.
- Tugcu, G., Erturk, M.D., Saçan, M.T., 2017. On the aquatic toxicity of substituted phenols to *Chlorella vulgaris*: QSTR with an extended novel data set and interspecies models. *J. Hazard. Mater.* 339, 122–130. <https://doi.org/10.1016/j.jhazmat.2017.06.027>
- Tugcu, G., Saçan, M.T., 2018. A multipronged QSAR approach to predict algal low-toxic-effect concentrations of substituted phenols and anilines. *J. Hazard. Mater.* 344, 893–901.  
<https://doi.org/10.1016/j.jhazmat.2017.11.033>
- Veerasamy, R., Sivadasan, S., Krishnamoorthi, V., Rajak, H., Krishnan, S., 2016. QSAR study on quinolinecarbaldehyde derivatives as potential anti-tubercular agents. *Thai Journal of Pharmaceutical Sciences (TJPS)* 40.
- Vikas, Chayawan, 2015. Single-descriptor based quantum-chemical QSPRs for physico-chemical properties of polychlorinated-dibenzo-p-dioxins and -dibenzo-furans (PCDD/Fs): Exploring the role of electron-correlation. *Chemosphere* 118, 239–245.  
<https://doi.org/10.1016/j.chemosphere.2014.08.072>
- Vikas, Chayawan, 2014. Externally predictive quantitative modeling of supercooled liquid vapor pressure of polychlorinated-naphthalenes through electron-correlation based quantum-mechanical descriptors. *Chemosphere* 95, 448–454.  
<https://doi.org/10.1016/j.chemosphere.2013.09.093>
- Wang, L., Li, J., 2017. Structure–activity relationship analysis of carbobicyclo and oxabicyclo succinimide analogs as potential androgen receptor antagonists. *Journal of Biomolecular Structure and Dynamics* 1–17.
- Wang, L., Song, T., Wang, X., Li, J., 2018. Discovery and Identification of Pyrazolopyrimidine Analogs as Novel Potent Androgen Receptor Antagonists. *Frontiers in Pharmacology* 9.  
<https://doi.org/10.3389/fphar.2018.00864>
- Wang, T., Tang, L., Luan, F., Cordeiro, M., 2018. Prediction of the Toxicity of Binary Mixtures by QSAR Approach Using the Hypothetical Descriptors. *International journal of molecular sciences* 19, 3423.
- Wang, T., Yuan, X., Wu, M.-B., Lin, J.-P., Yang, L.-R., 2017. The advancement of multidimensional QSAR for novel drug discovery-where are we headed? *Expert opinion on drug discovery* 12, 769–784. <https://doi.org/10.1080/17460441.2017.1336157>
- Wang, Y., Bai, F., Cao, H., Li, J., Liu, H., Gramatica, P., 2015. A Combined Quantitative Structure-

Activity Relationship Research of Quinolinone Derivatives as Androgen Receptor Antagonists. *Comb. Chem. High Throughput Screen* 18, 834–845.  
<https://doi.org/10.2174/1386207318666150831125750>

Wang, Y., Han, R., Zhang, H., Liu, Hongli, Lia, J., Liu, Huanxiang, Gramatica, P., Li, J., 2017. Combined Ligand/Structure-based Virtual Screening and Molecular Dynamics Simulations of Steroidal Androgen Receptor Antagonists.  
<https://doi.org/doi.org/10.1155/2017/3572394>

Wilde, M.L., Menz, J., Leder, C., Kümmerer, K., 2017. Combination of experimental and in silico methods for the assessment of the phototransformation products of the antipsychotic drug/metabolite Mesoridazine. *Science of The Total Environment*. <https://doi.org/doi:10.1016/j.scitotenv.2017.08.040>.

Wyrzykowska, E., Mikolajczyk, A., Sikorska, C., Puzyn, T., 2016. Development of a novel in silico model of zeta potential for metal oxide nanoparticles: a nano-QSPR approach. *Nanotechnology* 27, 445702. <https://doi.org/10.1088/0957-4484/27/44/445702>

Xi, L., Li, S., Yao, X., Wei, Y., Li, J., Liu, H., Wu, X., 2014. In Silico Study Combining Docking and QSAR Methods on a Series of Matrix Metalloproteinase 13 Inhibitors. *Arch. Pharm.* 347, 825–833. <https://doi.org/10.1002/ardp.201400200>

Yousefinejad, S., Hemmateenejad, B., 2015. Chemometrics tools in QSAR/QSPR studies: A historical perspective. *Chemometrics and Intelligent Laboratory Systems* 149, Part B, 177–204. <https://doi.org/10.1016/j.chemolab.2015.06.016>