Evaluation of software packages for degradation kinetics

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Fließ- und Stillgewässer-Simulationsanlage

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Data from degradation experiments in various environmental media are routinely evaluated using different software packages to derive parameters that can be used for the purpose of fate modelling or for comparison with regulatory trigger values (FOCUS 2014). Especially parameter estimation for degradation models including formation and decline of transformation products or phase transfer processes, while possible in almost any programming language or mathematical software toolkit, is greatly simplified by software tools that have been tailored to this task.

While the software packages ModelMaker and KinGUI v.1 that were frequently used for this purpose have not received any updates since many years, some new, actively maintained tools have recently been published that specialise in fitting solutions of systems of differential equations to experimental data.

This contribution reports the results of a multicriteria evaluation (Ranke 2014) of these new software tools on behalf of the German Federal Environment Agency (UBA) for three different user groups, including a search for candidate tools, establishment of a system of weighted criteria and a validity check using a number of example datasets.

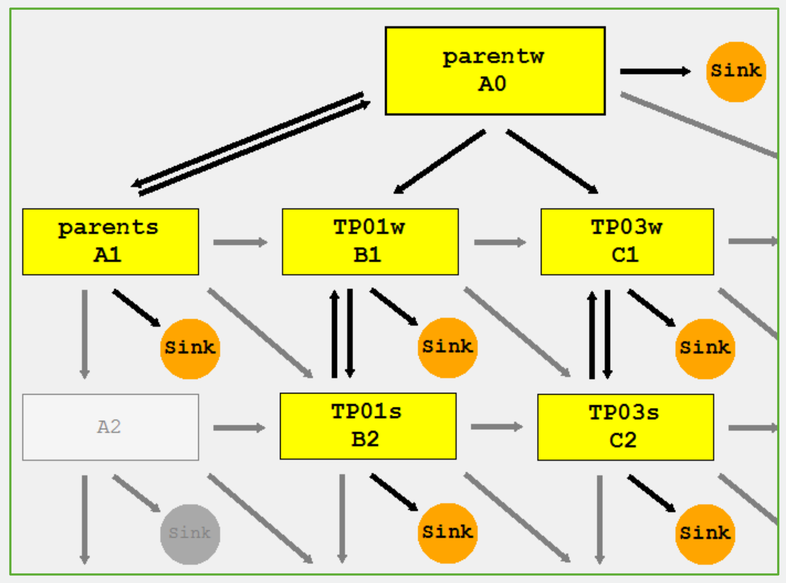

Fig. 1: Kinetic model for a water-sediment-study (KinGUI II)

Definition of user groups

Tab. 1: User group classification

User/Requirements	A	B	C
Regulatory user	X		
Advanced regulatory user		X	
Simulation for planning experimental tests			X
Using basic models, up to 3 metabolites	X	X	
Ready to use model templates preferred	X		
Creating complex models (unlimited number of metabolites & several compartments)		X	X
Using component librarys (e.g. Fluids)	-	-	X
Parameter optimiziation	X	X	-
Graphical user interface required (desirable: *)	X	*	*
Approximate proportion of total users [%]	80	15	5

Search for candidate tools

A broad search for suitable software tools lead to four software categories with increasing specialisation:

- General purpose software with advanced mathematical functions (*Mathematica, Matlab, Maple, SciPy, R, SciLab*)
- Software for analysis and display of scientific data (*Origin/OriginPro, Graphpad PRISM)*
- Software for the simulation of dynamic systems (*SystemModeller, Matlab/Optimization/Statistics Toolboxes, MapleSim, Simile, Stella, ModelMaker, OpenModel, OpenModelica, R + FME package, "EAWAG tool"*)
- Software specialised in degradation kinetics (*R + mkin package, R + gmkin package, R + KineticEval package, KinGUII, CAKE*)

Exclusion criteria

Tab. 2: Exclusion criteria and excluded software

Exclusion criteria	Excluded software	Remarks
Availability	Simusolv, TopFit, KIM	No source for obtaining these tools was identified
Maintenance and active development	ModelMaker 4 incl. DegKin Manager, KinGUI 1	These tools do not appear to be actively developed
Number of metabolites ≥ 3	Origin, Graphpad PRISM	Lacking support for systems of differential equations
Optimizer	Stella, Simile, OpenModelica	External optimizer (e.g. PEST) necessary.
Click system or reusable model templates	KineticEval	Data and models not separated in KineticEval
Free definition of more complex models	CAKE 2.0 (user group B)	CAKE 2.0 excluded for user group B
Graphical user interface (for user group A)	All except for KinGUII, CAKE, gmkin, OpenModel (A)	Only three tools remaining for user group A

Multicriteria evaluation

The system of evaluation criteria established for this purpose includes the areas of functionality, performance, user interface and user-friendliness, extensibility and documentation (Tab. 3). The weighting of the criteria, which was agreed with UBA, is different for two user groups A and B. For user group A, which should represent 80% of the use cases, the focus is on usability. For user group B, the flexibility in the model definition is most important.

Tab. 3: Groups of criteria and maximum attainable score

Categorie	Criteria (i. a.)	Points	
		A	B
Procurement	• Cost and availabilty	45	45
System requirements	• Operating Systems	5	5
Functions	• Number of metabolites • Weighting • Kinetic models and endpoints • Further optimization algorithms (e. g. MCMC) • Complex models	120	139
Performance	• Response time and stability	20	26
User interface	• Graphical user interface and/or model templates • Data import	45	65
Extensibility	• Programmability	5	7
Reporting	• Detailed statistics • Export of graphics	20	15
Help	• Documentation • Tutorials • Support	26	39

Results of multicriteria evalulation

Based on a screening of candidate tools using this evaluation system, the software tools KinGUII (A and B), gmkin (A and B), CAKE (A) and OpenModel (B) were selected for validation and final evaluation (see Tab. 4). For user group C, no multicriteria evaluation was performed.

Tab. 4: Ranking after multicriteria evaluation

Software tool	User group A		User group B	
	Rank	Score	Rank	Score
gmkin (0.5.4)	1	85%	1	74%
KinGUII (2.1)	2	82%	2	73%
CAKE (2.0)	3	72%	-	-
OpenModel (2.2.1)	4	37%	3	56%

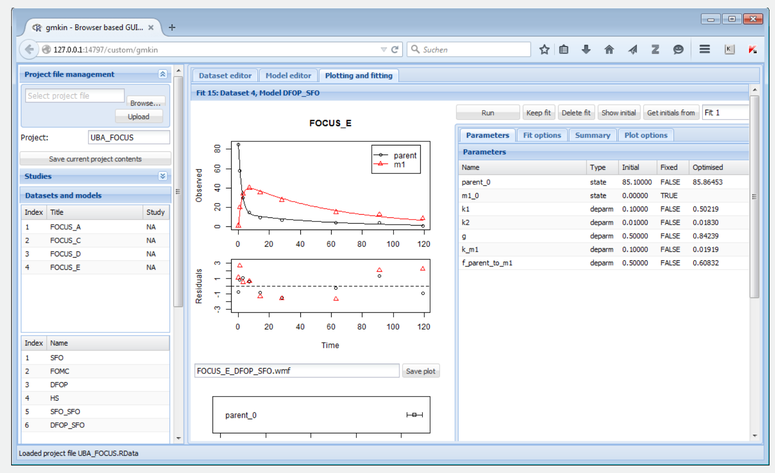

Fig. 2 : Screenshot of gmkin

Cross-checking validity

Validation was performed by comparing the results for a suite of data sets from the FOCUS Kinetic Guidance (2014), experimental data sets from regulatory practice and newly generated test datasets. Generally, a good agreement between the results of the tools was observed for datasets with up to three metabolites. For the different tools, user options were identified that should be taken care of in order to obtain results that are as reliable as possible.
Example results for a synthetic dataset generated using the error model proposed by Rocke and Lorenzato (1995) are shown in Tab. 5.

Tab. 5: Example results for a synthetic dataset (parent p DFOP, metabolites m1, m2 SFO)

Parameter	Input	MM/ DegKin*	KinGUII	Gmkn	Open Model
M0 p	100	103.7	103.7	103.7	103.7
k1 p	0.2	0.2881	0.2890	0.2890	0.2893
k2 p	0.02	0.0222	0.0223	0.0223	0.0223
g	0.5	0.4735	0.4734	0.4734	0.4732
k m1	0.3	0.2323	0.2327	0.2327	0.2326
k m2	0.02	0.0206	0.02066	0.02066	0.02067
f_p_m1	0.5	0.3662	0.3666	0.3666	0.3665
f_m1_m2	0.7	0.9355	0.9345	0.9345	0.9352
chi^2-err p	-	2.97%	2.97%	2.97%	-
chi^2-err m1	-	15.2%	10.80%	10.80%	-
chi^2-err m2	-	4.92%	3.30%	3.30%	-
chi^2-err all	-	-	4.48%	4.48%	-

*Model Maker 4.0 with DegKinManager (a software developted for the UBA) was used as a reference

Conclusion

While KinGUII and gmkin obtained the highest scores in the final evaluation for user groups A and B, CAKE was found to be a valid alternative for user group A, provided, that the degradation scheme is sufficient for the dataset at hand (see also new version CAKE 3.1). Subject to some caveats, the flexible OpenModel software package that is built using a different technical basis was found to be a possible independent alternative for user groups B and C.

The newly generated datasets are well suited for verification of new or updated software tools.

Literature:

FOCUS (2014): Generic guidance for estimating persistence and degradation kinetics from environmental fate studies on pesticides in EU registration (Version 1.1, 18 December 2014).
Ranke, J. (2014): Prüfung und Validierung von Modellierungssoftware als Alternative zu ModelMaker 4.0. Umweltbundesamt Projektnummer 27452. Final report October 2014.
Rocke, David M. und Lorenzato, Stefan (1995): A two-component model for measurement error in analytical chemistry. Technometrics 37(2), 176-184.