

# Structure - Fate - Relationships of Organic Chemicals

**R. Brüggemann<sup>a</sup>, G. Restrepo<sup>b,c</sup>, K. Voigt<sup>d</sup>**

<sup>a</sup> *Leibniz-Institute of Freshwater Ecology and Inland Fisheries, Berlin, Germany, brg@igb-berlin.de*

<sup>b</sup> *Laboratorio de Química Teórica, Universidad de Pamplona, Colombia*

<sup>c</sup> *University of Bayreuth, Chair Environmental Chemistry and Ecotoxicology, Germany*

<sup>d</sup> *GSF-National Research Centre for Environment and Health, Neuherberg, Germany*

**Abstract:** The evaluation of the potential risk of chemicals receives again a lot of interest due to the renewed chemicals' policy in the EU. The model package E4CHEM (Exposure Estimation for Potentially Ecotoxic Environmental Chemicals), already developed 1984-1992, is presented in this paper. This is a model which on the one side needs less information or input parameters as the often applied EUSES (European Union System for the Evaluation of Substances) and on the other side provides modules, like EXWAT (Model for the behaviour of the chemical in rivers) and DTEST (Automatic Data Estimation), which as such are not contained in EUSES. The software package E4CHEM does not comprise the modern software techniques as the more recently developed model EUSES, however it follows the general ideas of model supported evaluation. In contrast to the well-known software-program GREAT-ER which allows a geo-referenced risk assessment of chemicals, the simpler module EXWAT is used to obtain fate descriptors, based on the behaviour of chemicals in one river segment. By the fate descriptors a partial order is defined and evaluated by the DELPHI-program WHASSE. In the resulting digraph the chemicals are considered as vertices and the order relation as arcs, connecting (after a transitive reduction) the vertices. It is shown that the resulting directed graph can be separated into subsets which are associated with a specific behaviour of the chemicals.

**Keywords:** Risk assessment; Simulation models; Discrete Mathematics; Hassediagram Technique; posets; WHASSE Software

## 1. INTRODUCTION

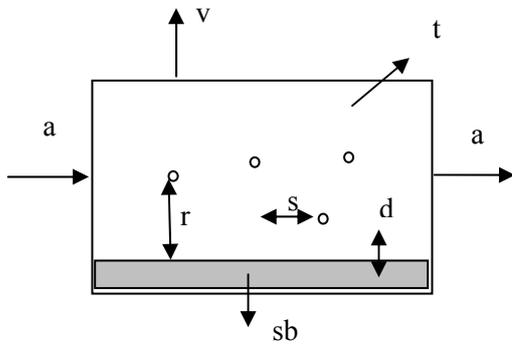
Due to the EU's chemicals policy, exposure models have been developed, like EUSES [Attias et al., 2005] and GREAT-ER [Feijtel et al., 1997], which might be seen as actual and comfortable simulation models for risk assessment in general and risk assessment of chemicals in rivers in particular. These two models have many predecessors with different foci and different user comfort. Here the model E4CHEM [Brüggemann & Drescher-Kaden, 2003] is presented, which was developed in the eighties of the last century and which comprises many modules like estimation of the releases into the environment, data estimation and fate/exposure analysis. In this paper we apply

E4CHEM to several homologous series of chemicals. As usual by simulation models an extensive output can be obtained, and most often statistical software is applied to condense the data. Generally cluster or principal component analysis are applied to extract important information. Here the idea is, to apply order theoretical tools and to check, how far structural characteristics are related to descriptors of the fate of chemicals. As scenario we select a segment of a river. Hence the specific module EXWAT [e.g. Brüggemann & Trapp, 1991] of E4CHEM is applied.

## 2. METHODS

## 2.1 Exwat Software

The model EXWAT is extensively described in the literature. However for the sake of convenience some explanation should be given. EXWAT is a steady state model, which takes into account the processes of advection (a), volatilization (v), sorption (s), deposition of suspended matter (r), resuspension of particles of the sediment (r), degradation (t), diffusive distribution between water and sediment (d) and sediment burial(sb) (Note the abbreviations refer to Fig. 1). Each box, describing a small reach of a river consists of two compartments: One for the water and one for the active sediment zone. This zone interacts with the advective energy of the flowing water. In Figure 1 the scheme of a box describing a river reach is shown:



**Figure 1.** Scheme of a EXWAT box. The grey zone is the active sediment layer.

Simplifying one can calculate the advective transport downstreams ( $n=1,2,3,\dots$ ) as follows:

$$c_{adv}(n) = [1/(E*V + Q)]*(I(n) + Q*c_{adv}(n-1)) \quad (1)$$

where E is a lumped quantity which describes all losses of a chemical within one river box. V is the volume of the water body, Q the water discharge (volume flow), and I a potential input. If there are no other inputs than  $I_0$  then an exponential decay of the chemical's concentration may be observed. Obviously the chemical's structure is embodied in the quantity E. Therefore we concentrate the analysis of the simulation results on just those quantities which appear as sinks. We define the following three descriptors:

$$D1 = D_{Volatilization} = k_v \quad (2a)$$

$$D2 = D_{fate\ general} = c_{aq} \quad (2b)$$

$$D3 = D_{sedimentation} = c_{Sediment} \quad (2c)$$

Since  $c_{aq}$ , the concentration of the dissolved chemical in the water body is the crucial quantity for many other (elimination) processes, we

selected this quantity to describe other fate processes than volatilization and sedimentation. It is sufficient to compare different chemicals by just the fate descriptors derived from one river box, as the profile of the chemical is obtained principally by application of eq. (1).

**Table 1.** Parameters of the river scenario.

OrgC <sup>1</sup>	OrgCs <sup>2</sup>	Porosity of sediment	Deposition rate mm/a	Concentration of suspended matter g/m <sup>3</sup>
0.04	0.04	0.6	10	100
sb m/d	depth of sediment m	Density of sediment g/cm <sup>3</sup>	pH....	Permeability m/d
0.0001	0.05	1.3	6	0.00025

<sup>1</sup> OrgC: organic carbon content (g/g) in suspended material, <sup>2</sup> OrgCs: organic carbon content (g/g) in sediments.

In this paper the river box was taken to be 10 km long, 100 m wide and 3 m deep. The wind velocity 10 cm over the water surface was taken to be 4 m/s. Two different water discharges were assumed: an extreme slow flow of only 10 m<sup>3</sup>/s and a rather high flow of 500 m<sup>3</sup>/s. For other parameters, like concentration of suspended matter, pH-value, organic carbon content etc. the default values were taken as we show in Table 1.

## 2.2 Chemicals and chemical's properties

Twelve compounds were selected (Table 2).

**Table 2** Chemicals used in this study and their acronyms.

Benzene	B	1,2-Dichlorobenzene	12B
Phenol	BO	1,3-Dichlorobenzene	13B
Nitrobenzene	BN	1,4-Dichlorobenzene	14B
para-Nitrophenol	p	1,2,3-Trichlorobenzene	123B
ortho-Nitrophenol	o	1,3,5-Trichlorobenzene	135B
Chlorobenzene	ClB	1,2,4-Trichlorobenzene	124B

The chemical data like sorption coefficient, based on organic carbon, Henry law coefficient etc. were estimated by property-property-relationships, which are included in the E4CHEM - module DTEST explained elsewhere (Brüggemann et al., 2005). The following properties of chemicals appear either as an input, or as an output quantity or as both:

SUM: Stoichiometric formula of the compound; MOLW: Relative mol mass; VOL: Molar volume NRINGS: Number of aromatic rings; DG: Dispersion coefficient Air; DW: Dispersion coefficient Water; WS: Aqueous solubility; KAW: Air/Water partition coefficient; KOW: Partition coefficient Water/ n-octanol; KOC: Sorption coefficient related to organic carbon content; BCF: Bioconcentration factor, fish; MP: Melting point VP: Vapour pressure; BP: Boiling point; EntropV: Entropy of vaporization

### 2.3 Background of the Hassediagram Technique

The background of the Hassediagram Technique (HDT) is explained in a variety of different environmental and chemical as well as statistical journals. A rather comprehensive description can be found in [Brüggemann et al., 2001]. Therefore here only a very brief description is given.

The HDT is based on partial order theory, i.e. on binary relations of the following type:

- asymmetry: if  $x > y$  then  $y > x$  is wrong
- reflexivity:  $x$  can be compared with itself
- transitivity:  $x > y$  and  $y > z$  implies  $x > z$

Let  $q_1(x), q_2(x), \dots, q_m(x)$  be a set of descriptors of object / chemical  $x$  then:  $x > y$  if  $q_i(x) > q_i(y)$  for all  $i$  (generality principle). If for some indices  $q_i(x) > q_i(y)$  and for some others  $q_i(x) < q_i(y)$ , then  $x$  and  $y$  are incomparable (notation:  $x \parallel y$ ). This multivariate variant of order relations is useful, if objects are characterized by more than one attribute/ descriptor. For a more detailed description and the four point program we refer to the paper of Voigt et al, this issue.

The idea which we are following here is that a parsimonious representation of chemicals considering the order relationships among their descriptors is a Hassediagram. As the evaluation is not on the focus of this paper, the orientation of the descriptors can be selected in such a way that the most informative graph (Hassediagram) is obtained. As a qualitative measure for the term "most informative" we selected the clearest directed graphs which show the best groupings of homologous chemicals.

## 3 RESULTS

### 3.1 General Dependences of the descriptors

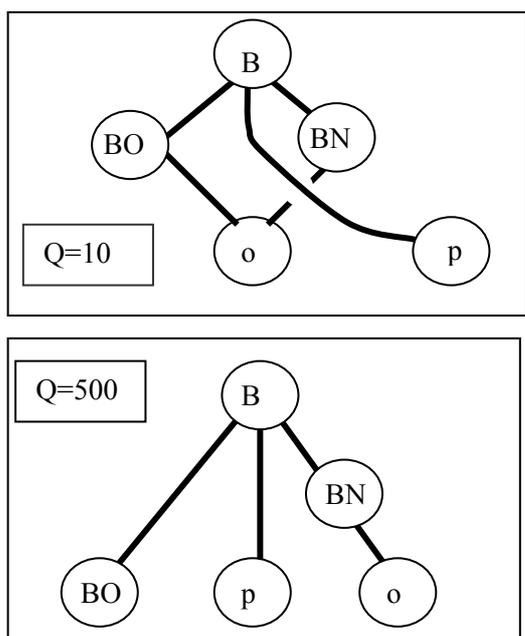
In all cases the enhancement of the water discharge,  $Q$  leads to an enhancement of the volatilization rate, as the transfer coefficients (two-film-theory of Whitman, see e.g. [Levenspiel, 1972]) increase with the linear flow velocity of the water body. Correspondingly  $D_2$  is decreased as  $Q$  increases. As can be expected  $D_3$  decreases with  $Q$ . It is commonly known that chlorination enhances the sorption coefficient. Hence the general trend is that  $D_1$  decreases slightly, whereas  $D_3$  increases with the degree of chlorination (see in this respect also [Ivanciuc, et al., 2005]).  $D_2$  has not a clear tendency compared to the other two descriptors: There is a trade off between volatilization (governed by the Henry law coefficient) and sedimentation governed by the sorption coefficient  $KOC$ .  $D_2$  can be considered as just the result of these two main processes.

It is interesting to observe the role of substitution of a hydrogen in benzene by  $OH$  or  $NO_2$ : Looking at  $D_1$ , the descriptor for volatilization, we find:  $B > BN > o >> p$ . The substitutional pattern leading to an ortho- or a para-position affects the role of intramolecular H-bonding. In ortho-Nitrophenol (o) there is an intramolecular H-bond, hence the polarity is diminished and the tendency to leave the water body is increased. In [Brüggemann et al., 2005] the role of substitution pattern is also explained using a thermodynamical approach.

### 3.2 Digraphs representing structure - fate relationships

Often it is not of interest to quantify the trends numerically but to find their qualitative structure. In chemistry the use of sequences like that in the last section has a long tradition (reactivity series, periodic law, etc.). Here we want to discuss how far the component - wise order, as applied in HDT

can be used to display structure-fate-relations.

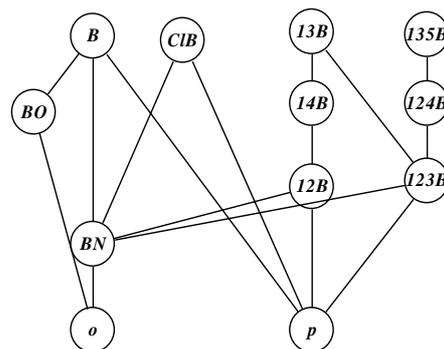


**Figure 2.** Q-poset visualized by two Hasse diagrams of Benzene (B), Nitrobenzene (BN), Phenol (BO), para- and ortho-Nitrophenol. Triple (D1,-D2,D3).

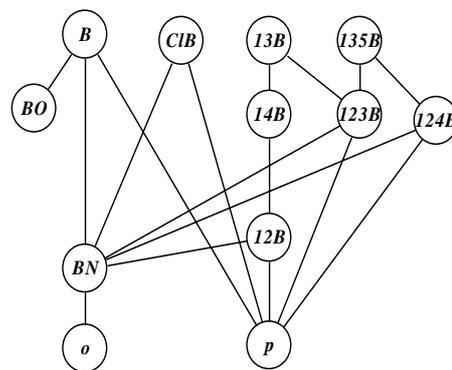
In the present paper we do not only discuss the order relations by the triple (D1,D2,D3) for the 12 chemicals, but by a triple of descriptors depending on a parameter, namely the water discharge. Therefore we would like to introduce the concept of g-posets, which means that posets are considered as depending on additional quantities, which may be a tuple of numbers or – like here – simply a scalar.

Different posets due to different values of g may be related by embeddings, i.e. one poset can be considered as an enriched one in comparison to the other. Here obviously we discuss Q-posets, because the varying parameter is the water discharge Q. As a first example, we want to consider the role of OH, NO<sub>2</sub>-substitution on benzene and the fate, here described by (D1,-D2, D3) (Fig.2)

As the relation  $BO \succ_{Q=10} o$  is not maintained in the Q-500-poset, there is no enrichment, i.e. we cannot consider the Q-500-posets as obtained by an order preserving map. On the other hand there is an order preserving map  $Q=500 \rightarrow Q=10$ : all  $<$ -relations in Q=500 are retained in Q-10-poset, and additionally the relation  $BO \succ_{Q=10} o$  appears. Hence two questions are to be answered: 1) Can the slow Q-poset generally be seen as an embedding of the Q-500-poset? and 2) how far these Hasse diagrams are appropriate structure-fate representations?



**Figure 3.** Q-10-poset visualized by a Hasse diagram. Triple (D1,-D2, D3).



**Figure 4.** Q-500-poset visualized by a Hasse diagram. Triple (D1, D2, D3).

Before discussing these two points in the next section the Q-posets of all 12 chemicals should be presented (Figure 3 (Q=10) and Figure 4 (Q=500)).

Once again, there is an order preserving map, relating Q-500-poset with the Q-10-poset. There are two changes from Figure 4 to Figure 3:  $o \parallel BO$  becomes  $o < BO$  and  $123B \parallel 124B$  becomes  $123B < 124B$ . Symbolically we can write:

$$Q\text{-500-poset} \subset Q\text{-10-poset} \quad (3)$$

If g-posets are discussed then equations like (3) may appear, i.e. we get an overstructure of a poset of posets with the inclusion as order relation.

#### 4. DISCUSSION

We will discuss the second question first:

How far can a Hasse diagram be regarded as an appropriate graphical scheme to represent structure-fate relationships? In [Brüggemann et al., 2006] this question was discussed with help of new indices. The main assumption however was

that the Hassediagram separates chemical-structural different groups. Here the Dichlorobenzenes, the Trichlorobenzenes are quite well separated. The group B, BO, BN, o is related to the Dichloro-group by a fence relation [Schröder, 2002] and hence well separated, whereas o, BN and the group of Trichlorobenzenes are related by a < - relation. Monochlorobenzene is in relation to only a few other chemicals: CIB > BN, CIB > o, CIB > p in the Q-10-and the Q-500-poset. In this case, thinking those posets as topological objects CIB could be considered as a boundary point of the set of chlorobenzenes and non-chlorinated benzenes. It is striking that the two Nitrophenols are not comparable hence we definitely know that there fate must be different. Indeed p-Nitrophenol has a tendency to stay in the water body, whereas the o-Nitrophenol has a volatilization rate which is three orders of magnitudes greater than that of p-Nitrophenol.

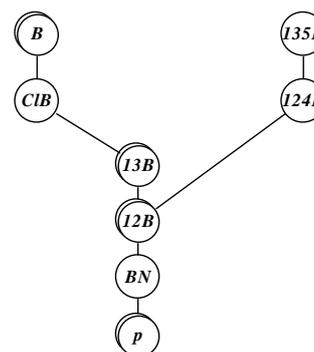
In order to simplify the question 2) the posets are analyzed, which are based on (D1, D3) (the Hassediagrams are not shown here). Since they show a similar tendency than those of Figures 3 and 4 we could avoid the "difficult" descriptor D2. Hence we concentrate ourselves on the posets based on the descriptors D1 and D3.

In Table 3 we summarize those groups of chemicals which are (as a whole group) incomparable with another one and may candidates for exhibiting structure - fate relations. Single chemicals are considered as special groups and are listed too:

**Table 3. Incomparable groups.**

group A	vs	group B
B, BO		CIB
B, BO		13B, 14B, 12B
13B, 14B, 12B		135B, 124B
B, BO, CIB		13B, 14B, 12B, 135B, 124B, 123B
o		p
BO		BN

Before the groups of Table 3 are analyzed we neglect minor numerical differences. If for example an equidistant classification into 10 classes (Interval Max - Min divided into 10 smaller intervals of equal length; see Brüggemann & Bartel, 1999) is performed we arrive at the following diagram (Figure 5):



**Figure 5:** Hassediagram of the Q-500-poset after eliminating minor numerical differences. The diagram is based on D1, D3.

In Figure 5 appear several equivalence classes (Table 4).

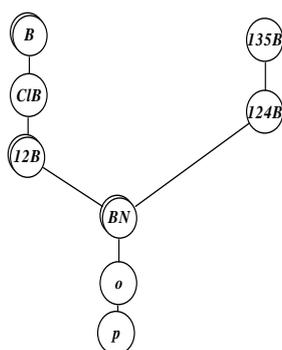
**Table 4. Equivalence classes of Figure 5.**

Class	elements
K1	B, BO
K2	p, o
K3	12B, 123B
K4	13 B, 14 B

Apart from that, some of the original mutual incomparable groups shown in Table 3 are now comparable. For example the equivalence class {B, BO} is now dominating CIB. Due to the original data CIB has a clear dominance for the sediments over B and BO and a slightly less dominance for volatilization. However, by the classification CIB is put into the fate class: no sedimentation as B and BO, hence the clear tendency of B and BO to volatilize leads to B, BO > CIB, as can be seen in Figure 5. Additionally, we see that there are no fate differences, if we compare p-Nitrophenol (p) with ortho-Nitrophenol. The high water discharge quenches differences which are striking, if the pure thermodynamic point of view is taken. According to Figure 5 we discuss the group {B, BO, CIB} vs {135B, 124B}. The left branch (Figure 5) shows those chemicals which have a definite tendency to volatile (which may be enhanced due to the high linear velocity of the river) whereas the right branch (Figure 5) shows those chemicals which accumulate in sediments, although competing processes like outflow and volatilization are important. The third branch, directing toward the bottom of the diagram (Figure 5) are those chemicals which have still a

tendency to volatilize but do not accumulate in the sediments. Hence these chemicals may exert a problem downstreams.

So far we discussed the structure-fate relations which can be detected from the 500-poset (classified). It remains to explain the first question: Can the Q-10-poset be considered as an embedding of the Q-500-poset? In order to try to find an answer we select the same classification described above and arrive at Figure 6.



**Figure 6.** Hasse diagram of the Q-10-poset after eliminating minor numerical differences. The diagram is based on D1, D3.

In contrast to Figure 5 there are now only three equivalence classes. See Table 5.

**Table 5.** Equivalence classes of Figure 6.

Class	elements
K1	B, BO
K5	BN, 123B
K4'	12B, 13B, 14B

It is interesting to note that now, with a very slow linear velocity we find a differentiation among para- and ortho-Nitrophenol ((p) and (o) in the Figure 6). Both are in the same fate class concerning the accumulation in the sediment, but now the intramolecular H-bond enhances the tendency for volatilization. Hence para-Nitrophenol is dominated by ortho-Nitrophenol. Beside this the main two structure fate relations are as well recognized in Figure 6. We return to the first question. Can the Q-10-poset be considered as an embedding of the Q-500 poset? In general this question must be answered with 'no'. An example is 12B. In Q-500-poset  $12B \leq 124B$ , whereas in Q-10-poset:  $12B \parallel 124B$ . However, it might be possible to identify subsets of chemicals for which such order-embeddings occur.

## 5. REFERENCES

- Attias, L., P.Boccardi, G.Boeije, D.Brooke, J.de Bruijn, M.Comber, B.Dolan, S.Fischer, G.Heinemeyer, V.Koch, J.Lijzen, B.Müller, R.Murray-Smith, M.Rikken, J.Tadeo, and T.Vermeire, European union system for the evaluation of substances: the second version, *Chemosphere* 59, 473-485, 2005.
- Brüggemann, R., S. Trapp, and M. Matthies, Behavior Assessment for a Volatile Chemical in the Middle and Lower German Part of the Rhine River, *Envir. Tox. Chem.*, 10, 1097-1103, 1991.
- Brüggemann, R. and H.-G.Bartel, A Theoretical Concept to Rank Environmentally Significant Chemicals, *J. Chem. Inf. Comp. Sci.*, 39, 211-217, 1999.
- Brüggemann, R., E. Halfon, G. Welzl, K. Voigt, C. Steinberg, Applying the Concept of Partially Ordered Sets on the Ranking of Near-Shore Sediments by a Battery of Tests, *J. Chem. Inf. Comp. Sci.*, 41, 918-925, 2001.
- Brüggemann, R. and U. Drescher-Kaden., Einführung in die modellgestützte Bewertung von Umweltchemikalien - Datenabschätzung, Ausbreitung, Verhalten, Wirkung und Bewertung, Springer-Verlag, 1-519 pp., Berlin, 2003.
- Brüggemann, R., G. Restrepo, and K. Voigt, Towards an Evaluation of Chemicals, *WSEAS Transactions on Information Science and Applications*, 2, 1023-1033, 2005.
- Brüggemann, R., G. Restrepo and K. Voigt, Structure - Fate Relationships of Organic Chemicals derived from the Software Packages E4CHEM and WHASSE, *J. Chem. Inf. and Modelling*, in press, 2006.
- Feijtel, T., G. Boeije, M. Matthies, A. Young, G. Morris, C. Gandolfi, B. Hansen, K. Fox, M. Holt, V. Koch, R. Schroder, G. Cassani, D. Schowaneck, J. Rosenblom, and H. Niessen, 1, Development of a Geography - Referenced Regional Exposure Assessment Tool for European Rivers - GREAT-ER. Contribution to GREAT-ER #1, *Chemosphere*, 34, 2351-2373, 1997.
- Ivanciuc, T., O. Ivanciuc, and D. J. Klein, Posetic Quantitative Superstructure/Activity Relationships (QSSARs) for Chlorobenzenes, *J. Chem. Inf. Model.*, 45, 870-879, 2005.
- Levenspiel, O., 1972. Chemical Reaction Engineering, John Wiley & Sons, New York, 1-578 pp.
- Schröder, B.S.W., Ordered sets - An Introduction, Birkhäuser, Boston, 1-391 pp., 2002.