Theoretical Environmental Disciplines in Support of Sustainable Chemistry

Kristina Voigt

Hagen Scherb

Rainer Brüggemann

International Environmental Modelling and Software Society (iEMSs)
2010 International Congress on Environmental Modelling and Software
Modelling for Environment's Sake, Fifth Biennial Meeting, Ottawa, Canada
David A. Swayne, Wanhong Yang, A. A. Voinov, A. Rizzoli, T. Filatova (Eds.)
http://www.iemss.org/iemss2010/index.php?n=Main.Proceedings

Theoretical Environmental Disciplines in Support of Sustainable Chemistry

Kristina Voigt[1], Hagen Scherb[1], Rainer Brüggemann[2]
[1]*Helmholtz Zentrum Muenchen, German Research Center for Environmental Health (GmbH), Ingolstaedter Landstr. 1, 85764 Neuherberg,Germany, e-mail:* *kvoigt@helmholtz-muenchen.de, scherb@helmholtz-muenchen.de*
[2]*Leibniz-Institute of Fresh Water Ecology and Inland Fisheries, Berlin, Germany*
brg_home@web.de

Abstract: It has been evident for decades that environmental chemicals pose an enormous risk to the environment as well as to humans. However, this important topic is still underestimated in every part of society. The effects of environmental contaminants on health are a major concern because exposure is associated with a number of diseases, including cancer, diabetes, congenital malformations and infertility. Sustainable Chemistry is a chemical philosophy encouraging the design of products and processes that reduce or eliminate the use and generation of hazardous substances. Sustainability and sustainable development are effectively ethical concepts, expressing desirable outcomes from economic and social decisions. The important matter of principle, therefore, becomes a victim of the desire to set targets and measure progress. In this respect, metrical scientific disciplines like Chemometrics, Environmetrics, Biometrics, Chemoinformatics, Environmental Informatics, etc. are of great importance. The environmetrical data-analysis method applied in this paper is the method of partially ordered sets. Partial order is a discipline of Discrete Mathematics and one may consider partial order as an example of mathematics without numerical arithmetic. The graphical representation of partial orders is laid down in so-called Hasse diagrams. We present the occurrence of Persistent Organic Pollutants (POPs) in breast milk samples. It can be concluded that bioaccumulative chemicals pose a danger to both humans and the environment and that hence much effort should be laid on the development of safer, that is to say biodegradable, chemicals in the future.

***Keywords**:* Sustainable Chemistry; Persistent Organic Pollutants; Hasse diagram technique; Environmetrics; Chemometrics

1. INTRODUCTION

At the start of the twenty-first century, the problem of global sustainability is widely recognised by world leaders, and a common topic of discussion by journalists, scientists, teachers, students and citizens in many parts of the world. Humanity has exceeded the carrying capacity of the global environment. The only real choices for the future are to bring the throughputs that support human activities down to sustainable levels through human choice, human technology, and human organization, or to let nature force the decision through lack of food, energy, or materials, or through an increasingly unhealthy environment [Meadows et al., 2004]. Measures and metrics are therefore of utmost importance in the pursuit of sustainability concepts.

This implies also to the important fields in the context of sustainability, e.g. sustainable chemistry [Anastas and Williamsen, 1998], sustainable pharmacy [Sheldon, 2007], sustainable engineering [Anastas and Zimmermann, 2003], sustainable information, and communication technologies [Hilty, 2008]. A comparison of the concepts of sustainable chemistry, sustainable engineering, and sustainable information technology is given at the EnviroInfo 2009 Conference [Voigt, 2009a]. In addition, more thoughts about sustainable chemistry and sustainable pharmacy in the whole sustainability debate are given by Voigt et al. [2009b].

2. SUSTAINABLE CHEMISTRY

2.1 Definitions and Concepts

With respect to chemicals, we speak of sustainable chemistry (SC) and/or green chemistry (GC). One important element of sustainable chemistry is commonly defined as chemical research aiming at the optimization of chemical processes and products with respect to energy and material consumption, inherent safety, toxicity, environmental degradability, and so on. An increasing number of assessment systems containing quantitative indicators for these aspects are currently being developed. In addition, however, SC should also address the societal aspect of sustainability. One prerequisite for this is the inclusion of SC into chemical education from the very beginning [Boeschen et al., 2003]. The concept of green chemistry was being formulated, by Anastas and Williamsen [1998] at the US Environmental Protection Agency (EPA), to address the environmental issues of both chemical products and the processes by which they are produced. The guiding principle is the design of environmentally benign products and processes (benign by design), which is embodied in the 12 Principles of Green Chemistry, the essence of which can be reduced to the following working definition. Green chemistry efficiently utilises (preferably renewable) raw materials, eliminates waste and avoids the use of toxic and/or hazardous reagents and solvents in the manufacture and application of chemical products. The 12 Principles of Green Chemistry are: 1. Prevention of waste, 2. Atom Economy, 3. Less Hazardous Chemical Synthesis, 4. Designing Safer Chemicals, 5. Safer Solvents and Auxiliaries, 6. Design for Energy Efficiency, 7. Use of Renewable Feedstocks, 8. Reduce Derivatives, 9. Catalysis, 10. Design for Degradation, 11. Real-time Analysis for Pollution Prevention, 12. Inherently Safer Chemistry for Accident Prevention.
We want to focus on the important aspect of degradation of chemical substances.

2.2 Degradation a Major Principle in Sustainable Chemistry

The design for degradation is an extremely important concept of Green Chemistry. Chemical products should be designed so that at the end of their function they break down into innocuous degradation products and do not persist in the environment [Anastas and Williamsen, 1998]. According to Kuemmerer [2007], sustainability should be considered from the very beginning of the design of chemicals. Chemicals are a part of modern life. Products are the main emissions of the chemical and pharmaceutical industries. This makes it difficult to hold them back efficiently. Very often they do not become degraded or fully broken down to water, carbon dioxide and inorganic salts. Often, unknown transformation products are formed in the environment. Therefore, according to the principles of green chemistry, the functionality of a chemical should not only include the properties of a chemical necessary for its application, but also easy and fast degradability after its use. Taking into account the full life cycle of chemicals will lead to a different understanding of the functionality necessary for a chemical. In the present discussion, improvement of synthesis and renewable feedstock are very prominent, whereas the environmental properties of the molecules are somewhat underestimated. The consequence of non-biodegradable, i.e. persistent chemicals is shown in our paper (see Figure 3 top range).

2.3 Measures and Metrics

Theoretical approaches describing, modelling, and predicting the environmental conditions play an important role in the pursuit of sustainability.

It is now generally accepted that two useful measures of the (potential) environmental acceptability of chemical processes are the E factor, defined as the mass ratio of waste to desired product, and the atom efficiency, calculated by dividing the molecular weight of the desired product by the sum of the molecular weights of all substances produced in the stoichiometric equation. The enormity of the waste problem in chemicals' manufacture is readily apparent from a consideration of typical E factors in various segments of the chemical industry. Whereas bulk chemicals have an E factor < 1-5, fine chemicals have a factor 5-10 and pharmaceuticals have E factors between 25 and 100 [Sheldon, 2007].

A different environmetrical approach is the modelling procedure in a recently published paper by Schenker et al. [2007]. In general, global multi-media box models are used to calculate the fate of persistent organic chemicals in a global environment and to assess long-range transport or arctic contamination. Currently, such models assume substances to degrade in one single step. In reality, however, intermediate degradation products are formed. If those degradation products have a high persistence, bioaccumulation potential and/or toxicity, they should be included in environmental fate models. The environmental fate model CliMoChem was modified to simultaneously calculate a parent compound and several degradation products. This is an excellent example to demonstrate three sides' aspects of environmental chemicals: first the modelling approach, second the treatment of one principle of green chemistry, namely degradation, and third the group of chemicals, which are found unbiquitaneously not only in the environment but also in human beings.

The authors performed further chemometrical and environmetrical studies with respect to the detection of Persistent Organic Pollutants in the environment [Voigt et al, 2010a] and human breast milk samples [Voigt et al., 2010b].

3. HASSE DIAGRAM TECHNIQUE USED FOR THE EVALUATION OF ENVIRONMENTAL AND HEALTH DATA SETS

3.1 Environmental and Health Data sets Used

One method for the evaluation of complex environmental and health data sets is the discrete mathematical method Hasse diagram technique based on partial orders. The basic concept of this method can be found in a book edited by the last author [Brüggemann and Carlsen, 2006] and a further publication by the first author [Voigt and Brüggemann 2008].
In this paper we evaluate a possible association between maternal exposure to organochlorine compounds used as pesticides and cryptorchidism among male children in Finland and Denmark [Voigt, 2010b].
We investigated a data set with 20 chemicals. These are all pesticides which are listed with their trivial names, their used acronyms in the data-analysis, as their well as CAS-numbers in Table 1.

Table 1: Chemicals Investigated (Name, Acronym, CAS-Number).

Nr.	Trivial Name	Acronym	Name	CAS-Number
01	**PeCB**	**PECB**	Pentachlorobenzene	608-93-5
02	**alpha-HCH**	**AHCH**	alpha-Hexachlorcyclohexane	319-84-6
03	**beta-HCH**	**BHCH**	beta-Hexachlorcyclohexane	319-85-7
04	**Gamma-HCH**	**GHCH**	gamma-Hexachlorcyclohexane	58-89-9
05	**PCA**	**PCAN**	Pentachloroanisole	1825-21-4
06	**HCB**	**HCBE**	Hexachlorobenzene	118-74-1
07	**OCS**	**OCST**	Octachlorostyrene	29082-74-4
08	**Oxychlordane**	**OXYC**	Oxychlordane	27304-13-8
09	**c-HE**	**CHCE**	cis-Heptachloroepoxide	28044-83-9
10	**(+)-HE**	**PHCE**	+ Enantiomer cis- Heptachloroepoxide	
11	**(-)-HE**	**MHCE**	- Enantiomer cis- Heptachloroepoxide	
12	**t-HE**	**THCE**	trans-Heptachloroepoxide	1024-57-3
13	**o,p'-DDE**	**OPDE**	o, p'-Dichlordiphenyldichlorethene	3424-82-6
14	**p,p'-DDE**	**PPDE**	p, p'-Dichlordiphenyldichlorethene	72-55-9

15	**Endosulfan-1**	**END1**	Endosulfan-1	959-98-8
16	**Endosulfan-2**	**END2**	Endosulfan-2	115-29-7
17	**p,p'-DDD**	**PPDD**	p, p'-Dichlordiphenyldichlorethane	72-54-8
18	**Dieldrin**	**DIEL**	Dieldrin	60-57-1
19	**p,p'-DDT**	**PPDT**	p, p'-Dichlordiphenyltrichlorethane	50-29-3
20	**Mirex**	**MIRE**	Mirex	2385-85-5

In each country (Denmark and Finland), the breast milk of 65 women was analysed. The aim of the study is to find out what kind of differences exists concerning the contamination with chemicals in each country and in the healthy and cryptorchidism data sets [Damgaard et al., 2006]. Further results of this research emphasizing on the Hasse diagram technique are submitted to the scientific journal Environmental Modelling & Software [Voigt et al, 2010b].

3.2 Basic Idea of Partial Order / Hasse Diagram Technique

The data-analysis method is the method of partially ordered sets. Partial order is a discipline of Discrete Mathematics and one may consider partial order as an example of mathematics without arithmetic.

Partial order as a discipline of Discrete Mathematics will only briefly be explained in this paper in order to follow the data-analysis steps.

- First step: We need a set of objects. We call this set of objects the ground set, and denote it as G. Objects can be chemicals [Brüggemann et al., 2001], [Lerche et al. 2002], strategies (for example: water management), geographical units, environmental and chemical databases [Voigt et al., 2004, 2006], [Voigt and Brüggemann, 2008] etc.
- Second step: We need an operation between any two objects. As an evaluation is our aim, we must compare the objects. Is object "a" better than object "b"? If objects a and b are comparable we write $a \perp b$.
- Third step: We do not only want that two objects are comparable, but we also would like to know the orientation: Is "a" better or worse than "b"? Therefore the signs ≤ and ≥ are introduced: $a \le b$ "may" denote that a is better than b, $a \ge b$ "may" indicate that a is worse b.
- Fourth step: Why "may"? The essential point is that we have to define, when we will consider object a as better than b. I.e. the signs "≤" and "≥" alone do not help in an evaluation procedure, we must give them an appropriate sense, i.e. an appropriate orientation..
- Fifth step: Independently of how we define ≤ and ≥, the ground set equipped with e.g. "≤" must obey three axioms, if we want to speak from a partially ordered set (poset):
    - Reflexivity: An object a can be compared with itself: $a \le a$
    - Antisymmetry: If a is better b, and at the same time b is better than a, then a = b. We write:
    - $a \le b$ and $b \le a \Rightarrow a = b$. Later we will relax this axiom.
    - Transitivity: If a is better than b and at the same time b is better than c, then a is better than c.
    - $a \le b, b \le c \Rightarrow a \le c$.

If the ≤-relation is defined properly, the ground set G equipped with ≤ is a partially ordered set. A widespread notation is: $(G, \le)$.

The transitivity axiom is a very important one and filters out many situations, which could also be considered as a matter of evaluation: For example: competitions in sports: Crack "a" wins about crack "b", in turn crack "b" wins about "c", but unexpectedly crack "a" does not win about "c"! The mathematical analysis of this kind of generalized comparisons is done in tournament theory [Simon and Brüggemann, 2000].

- Sixth step: Why can a partially ordered set be represented by a directed graph? Consider the objects of a ground set as vertices. Then in any case, where for $(a,b) \in G^2$ is valid $a \le b$, we draw an arrow starting from b and ending in a. For the visualisation of the concept of a "cover relation" $\prec$ is most important: Two objects a,b for which is valid that $a \le b$ are in a cover relation, if there is no third element in between. Then a Hasse diagram is a graph of cover relations with additional conventions how to locate the objects in the drawing plane.

Example: G:= {a, b, c, d, e} and a ≤ b , b ≤ c , a ≤ c (necessarily) a ≤ d, d ≤ e, a ≤ e (necessarily). Then the directed graph is shown in Figure 1:

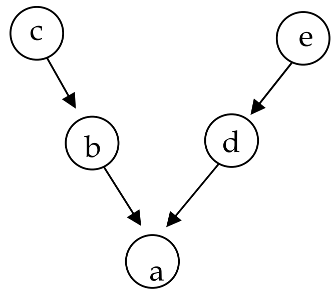

Figure 1. Directed graph of ({a, b, c, d, e}, ≤). The relation a ≤ c and a ≤ e can be derived from the sequences a ≤ b, b ≤ c and a ≤ d, d ≤ e.

3.3 Comparing Danish and Finish Data as an Example

First we analyzed the Finnish data set 20 Chemicals x 65 cases which means all attributes healthy and cryptorchidism. The Hasse diagram is given in Figure 2A. The analysis of the complete Danish data set 20 Chemicals x 65 cases is shown in Figure 2B.

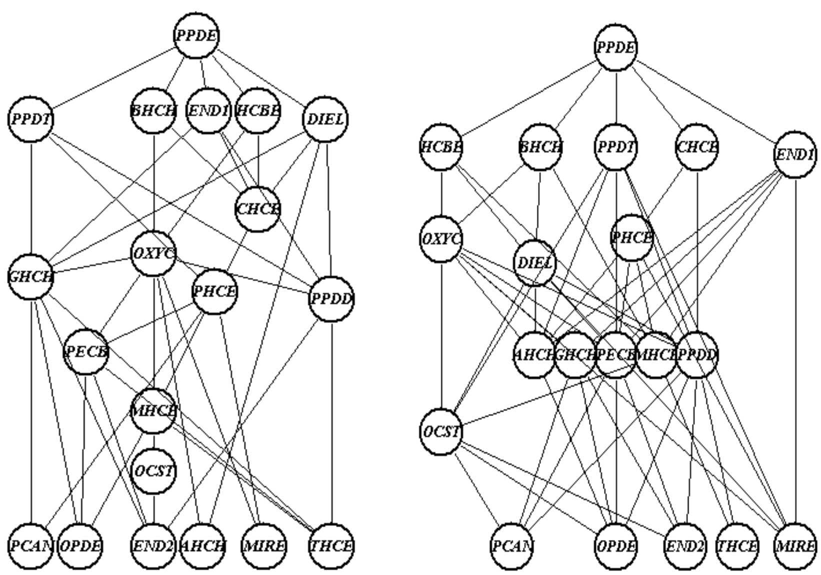

Figure 2. A. 20 Chemicals x 65 Cases, Denmark, B. 20 Chemicals x 65 Cases Finland.

Some differences in the two Hasse diagrams (Figure 2A and B) are evident.

Taking a closer look at the chemicals in the data-analysis, the following statements can be made. Whereas the chemical PPDE is a maximal (greatest) object in both data sets, the situation for the minimal objects is different. AHCH is found in different levels in Denmark and Finland. In the Danish data set AHCH is found as a minimal object whereas it is situated one level higher in Finland. The chemical DIEL is also found in different levels in the two countries, in Denmark one level above Finland. CHCE is found in Denmark one level below the position in the Finish data set.

We can state that there are differences concerning the pollution of breast milk with chemicals in Finland and Denmark. These differences are quantified by the so-called similarity analysis, a method provided in the Hasse diagram technique software PyHasse [Voigt et al, 2010b].

4. CONCLUSIONS AND OUTLOOK

Over the past decades a growing number of animal experiments and epidemiological studies have shown the vulnerability of living beings exposed to adverse chemical or physical environmental conditions. The effect of environmental contaminants on health is a major concern because exposure is associated with a number of diseases, including cancer, diabetes, and infertility [Edwards et al., 2007]. It is a fact that Persistent Organic Pollutants (e.g. organochlorine pesticides, polychlorinated biphenyls (PCBs), dioxins, like polychlorinated dibenzo-pdioxins and dibenzofurans (PCDDs/Fs), some polybrominated flame retardants (BFRs), and other unclassified pollutants, including e.g. phthalate esters are stored in white adidose tussue (WAT). Even in a lean person, white adipose tissue (WAT) represents about 15 to 25 % of body weight, and this percentage can increase by more than 50 % in cases of morbidly obese patients. Since about 70 % of the mass of WAT is formed by lipids, this tissue represents a major reservoir for many different lipophilic contaminants [Muellerova and Kopecky, 2007]. WAT metabolism is regulated by sympathetic innervation and by many hormones, like insulin, catecholamines, thyroid and steroid hormones. It is becoming increasingly apparent that WAT is a major endocrine organ in the body.
In a recently published review article Ropero et al. [2008] came to the conclusion that Bisphenol-A along with other endocrine disruptors such as persistent organic pollutants and phthalates may contribute to exacerbate the development of type II diabetes.
A lot of evidence is given that there is a strong relationship between the exposure of women with chemicals and the development of cryptorchidism. The association between congenital cryptorchidism and some persistent pesticides in breast milk as a proxy for maternal exposure suggests that testicular descent in the fetus may be adversely affected [Damgaard et al., 2006].

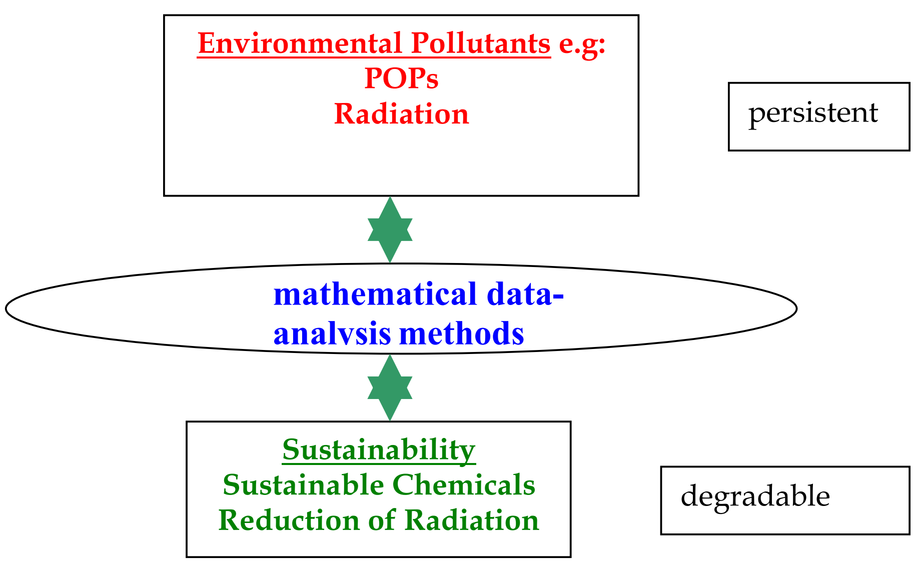

Figure 3. Environmetrical/Chemical Methods in Support of the Transition from Environmental Pollutants to Sustainable Chemicals

Many adverse effects of environmental ionizing radiation have been reported. Children's development is known to be especially radio-sensitive from conception through the

embryonic and fetal periods to infancy. Recently, it has been shown that childhood cancers are significantly elevated in the vicinity of German nuclear reactors [Spix et al. 2008], [Nussbaum, 2009]. Scherb and Voigt [2007] investigated for example trends in the sex odds before and after the Chernobyl accident in several European countries and found and a significant jump in the sex odds after Chernobyl.
In Figure 3 we want to emphasize that is not sufficient to continue to perform research studies on the state of the pollution of the environment. Lessons have to be learnt concerning the production and use of persistent chemicals as well as the radioactive materials. It is extremely urgent that consequences have to be drawn and followed in the very near future. More sustainable methods must urgently be applied. With respect to chemicals, the topic of biodegrading is to be focussed as a major subject according to these authors. The support of environmental research by statistical and mathematical data-analysis methods in order to demonstrate effects of adverse environmental conditions as well as to assess possible remediation measures is essential.

REFERENCES

Anastas, P. T., and T.C. Williamson (Eds), *Green Chemistry: Frontiers in Chemical Synthesis and Processes*, Oxford University Press, Oxford, 1998.

Anastas, P. T., and J.B. Zimmermann, Through the 12 Principles Green Engineering, *Environmental Science & Technology*, 1, 95-101, 2003.

Boeschen, S., D. Lenoir, and M. Scheringer, Sustainable chemistry: starting points and prospects, *Naturwissenschaften*, 90, 93-102, 2003.

Brüggemann, R., S. Pudenz, L. Carlsen, P.B. Sørensen, M. Thomsen, and R.K. Mishra, The Use of Hasse Diagrams as a Potential Approach for Inverse QSAR, *SAR and QSAR. Environ. Res.*, 11, 473-487, 2001.

Brüggemann R, and L. Carlsen (eds), *Partial Orders in Environmental Sciences and Chemistry*, Springer-Verlag, Berlin, 2006.

Damgaard, I. N., N. E. Skakkebaek,. J. Toppari, H.E. Virtanen, H. Shen, K.-W. Schramm, J. H. Petersen, T.K. Jensen, and K. M. Main, Nordic Cryptorchidism Study Group, Persistent Pesticides in Human Breast Milk and Cryptorchidism, *Environmental Health Perspectives*, 114 (7), 1133-1138, 2006.

Edwards T.M., and J. Peterson Myers, Environmental Exposures and Gene Regulation in Disease Etiology, *Environmental Health Perspectives*, 115(9), 1264-70, 2007.

Hilty, L.M., *Information Technology and Sustainability*, Books on Demand GmbH, Norderstedt, 1-180, 2008.

Kuemmerer, K., Sustainable from the very beginning: rational design of molecules by life cycle engineering as an important approach for green pharmacy and green chemistry, *Green Chemistry*, 9, 899-907, 2007.

Lerche, D., R. Brüggemann, P.B. Sørensen, L. Carlsen, and O.J. Nielsen,A Comparison of Partial Order Technique with three Methods of Multicriteria Analysis for Ranking of Chemical Substances, *J. Chem. Inf. Comp. Sci.*, 42, 1086-1098, 2002.

Meadows, D., J. Randers, and D. Meadows, *Limits to Growth, the 30-year update*, Chelsea Green Publishing Company, White River Junction, Vermont, 2004.

Muellerova D, and J. Kopecky, White Adipose Tissue: Storage and Effector Site for Environmental Pollutants, *Physiol. Res*., 56, 375-81, 2007.

Nussbaum R.H., Childhood leukemia and cancers near German nuclear reactors: significance, context, and ramifications of recent studies, *Int J Occup Environ Health*, 15 (3), 318-323, 2009.

Ropero A.B., P. Alonso-Magdalena, E. Garcia-Garia, C. Ripoll, E. Fuentes, and A. Nadal, Bisphenol-A disruption of the endocrine pancreas and blood glucose homeostasis, *International Journal of Andrology*, 31, 194-200, 2008.

Schenker, U., M. Scheringer, and K. Hungerbuehler, Including Degradation Products of Persistent Organic Pollutants in a Global Multi-Media Box Model, *Env Sci Pollut Res*, 14, 145 – 152, 2007.

Scherb H, and K., Trends in the human sex odds at birth in Europe and the Chernobyl Nuclear Power Plant accident, *Reprod Toxicol*, 23 (4), 593-599, 2007.

Sheldon, R. A, The E Factor: fifteen years on, *Green Chemistry*, 9, 1273-1283, 2007.

Simon, U. and R. Brüggemann, Assessment of Water Management Strategies by Hasse diagram technique, In: Sørensen, P.B., L. Carlsen, B.B. Mogensen, and R. Brüggemann (eds), *Order Theoretical Tools in Environmental Sciences*, National Environmental Research Institute, Roskilde (DK), 117-134, 2000.

Spix C, S. Schmiedel, P. Kaatsch, R. Schulze-Rath, and M. Blettner, Case-control study on childhood cancer in the vicinity of nuclear power plants in Germany 1980-2003, *Eur J Cancer*, 44 (2), 275-284, 2008.

Voigt, K., R. Brüggemann, and S. Pudenz, Chemical Databases Evaluated by Order Theoretical Tools, *Analytical and Bioanalytical Chemistry*, 380, 467-474, 2004.

Voigt, K., R. Brüggemann, and S. Pudenz, A multi-criteria evaluation of environmental databases using the Hasse Diagram Technique (ProRank) software, *Environmental Modelling & Software*, 21, 1587-1597, 2006.

Voigt K, and R. Brüggemann, Ranking of Pharmaceuticals Detected in the Environment: Aggregation and Weighting Procedures, *Combinatorial Chemistry & High Throughput Screening*, 11, 770-782, 2008.

Voigt K., Green Chemistry / Green Engineering / Sustainable Information Technology: Common Concepts and Differences, in: Wohlgemuth, V., B. Bernd, and K. Voigt, *EnviroInfo 2009, Environmental Informatics and Industrial Environmental Protection: Concepts, Methods and Tools*, 435-442, Shaker Verlag, Aachen, 2009a.

Voigt K., and H. Scherb, Sustainable Chemistry, Sustainable Pharmacy: Vital Topics in the Sustainability Debate, in: Hilty, L.M., H. Itoh, K. Hayashi, and X. Edelmann (Eds.), *R'09 Twin World Congress and World Resources Forum September 2009, Davos, Switzerland*, pp. 1-6, Empa Materials Science and Technology, St. Gallen, 2009b.

Voigt K., R. Brüggemann, M. Kirchner, and K.-W. Schramm, Influence of Altitude concerning the Contamination of Humus Soils in the German Alps: A Data-Evaluation Approach Using PyHasse, *Environmental Science and Pollution Research*, 17, (2), 429- 440, 2010a.

Voigt K., R. Brüggemann, H. Scherb, H. Shen, and K.-W. Schramm, Evaluating the Relationship between Chemical Exposure and Cryptorchidism by Discrete Mathematical Method using PyHasse Software, submitted to *Environmental Modelling Software*, 2010b.