NoMiracle

Novel Methods for Assessing Chemical Exposure for the 21st Century, Leipzig, 1-2 April, 2008

Report from the 3rd NoMiracle Open Workshop

Scientists and regulators met in Leipzig to present and discuss the novel methods to characterize chemical exposure that have been developed in the EU project NoMiracle

By Ian Cousins and Philipp Mayer

Reliable risk assessment of contaminants is critically dependent on assessment of the effect-relevant exposure. The 3rd NoMiracle Open Workshop organized by NoMiracle partner UFZ in the early spring in Leipzig was a forum for presenting and discussing the novel and often "paradigm-shifting" methods for estimating exposure developed in the project. These novel methods could become commonplace in exposure assessment later in the 21st century. The workshop invited a broad audience of stakeholders from companies, NGOs, regulators, EU representatives, academia (especially young researchers and Ph.D. students) and project partners from related EU projects.

NOvel Methods for Integrated Risk Assessment of CumuLative stressors in Europe

Ian Cousins

Philipp Mayer

A total of 42 participants from 9 EU countries Germany, France, Sweden, Bulgaria, Spain, Denmark, the Netherlands, UK, and the Czech Republic) accepted the invitation and a wide interdisciplinary audience listened to a range of excellent presentations from NoMiracle partners over the two days of the workshop. Following presentations, and at the end of each session, time was dedicated to discussion and these discussion sessions provoked a lively and useful debate.

After an informative introduction to the workshop by Gerrit Schüürmann, the workshop coordinator from UFZ, the first session commenced, which focused on novel methods for predicting partitioning of both non-polar and polar organic contaminants to biotic and environmental media. The current paradigm for estimating partitioning is to use a single parameter linear free energy relationship (LFER) e.g. based on parameters such as the octanol-water partition coefficient (K_{OW}), but such methods cannot account for the specific interactions between contaminant molecules and the sorbent medium. An alternative approach that can account for a range of specific molecular interactions uses so-called Abraham-type LFERs. Gerrit Schüürmann and Kai-Uwe Goss (Swiss Federal Institute of Technology, Zürich, Switzerland) are leading proponents of Abraham-type LFERs and presented novel methods for using them to estimate sorption of non-polar and polar contaminants to biological membranes and soils, respectively. Both presentations included several examples of Abraham-type LFERs that outperformed single parameter LFERs and they highlighted the need for accurate input parameters.

The second session of the workshop focused on the actual measurement of exposure. Philipp Mayer (University of Aarhus, Denmark) and Hao Zhang (University of Lancaster, UK) presented new analytical concepts for the exposure characterization in complex matrices such as soil and sediment. Equilibrium sampling devices that measure chemical activity and freely dissolved concentration of organic contaminants were shown to facilitate the prediction of equilibrium partitioning concentrations in target organisms. Mild extraction and depletive sampling to determine the accessible pool of contaminants were shown to yield information of how much of the total concentration can be released and taken up. Finally, diffusive gradients in thin films (DGT) were presented as a technique that determines the diffusive flux of metals into a diffusive sink. Such DGT measurements were shown to relate well with metal uptake into plants. During the discussion, both researchers emphasized that the association of contaminants to humic acids and other types of dissolved organic matter (DOM) actually can lead to an enhanced diffusive uptake into e.g. plant roots and soil organisms, which is in contrast to the aquatic exposure scenario, where such binding usually would lead to reduced exposure and toxicity. Tibor Kohajda (UFZ) presented the results of several European measurement campaigns of the human exposure to volatile organic chemicals (VOCs). Many VOCs are emitted from both outdoor sources (e.g. industrial facilities, mobile sources) and indoor sources (tobacco smoke, paints, and furniture). The exposure to VOCs inside of residences was typically much higher than outdoors, which can be explained by lower outdoor concentrations and less time spent outdoors. The examined time weighted model for the calculation of the personal VOC exposure was shown to provide valuable information for the personal risk assessment.

Workshop organizer Gerrit Schüürmann and audience

Key information needed for accurately estimating exposure is the degradation rate of contaminants in environmental media. Environmentally realistic degradation rates for contaminants are notoriously difficult to obtain. The 2nd day of the workshop opened with a session in which novel experimental and computational methods were presented for obtaining environmental realistic degradation rates for biotic and abiotic (e.g. photolysis) degradation processes. Thomas Junker (ECT Flörsheim, Germany) began the session by presenting a novel water-sediment experimental system for generating environmentally realistic biodegradation rates of contaminants in the laboratory. Available data sets are typically related to water-only systems, which are not considered to be realistic. The new apparatus is being used to generate a database of degradation rates for contaminants (including the NoMiracle list of target compounds) for water and sediment and results are compared to degradation rates from water-only systems and from computational methods developed in NoMiracle. The remainder of the session included talks by Robert Rallo (University Rovira i Virgili (URV), Tarragona, Spain), Saby Dimitrov (Laboratory of Mathematical Chemistry, Bourgas, Bulgaria), Philip Judson (LHASA Ltd., UK) and Anna Böhnhardt (UFZ) on computational methods for estimating biodegradation and photolysis. Saby Dimitrov and Philip Judson gave a joint presentation and suggested that a weight of evidence approach is needed to estimate biodegradation accurately; in other words, rather than relying on one estimation tool, combine the results from different tools and experimental observations to get a good estimate of the biodegradation pathway (mother compound to terminal metabolites) and rates. Towards this goal, Philip Judson's company (LHASA Ltd.) are developing an expert system (NoMBP- NoMiracle Biodegradation Predictor) that combines CATABOL, which uses a probabil-

istic approach to assess biodegradation pathways, and MEPPS, which uses a qualitative, reasoning-based approach.

The final session of the workshop focused on multimedia modeling methods. Gerrit Schüürmann in the introduction to the session explained that the aim of the modeling workpackage was to integrate the new knowledge developed from the rest of the exposure pillar in NoMiracle into novel modeling tools that can estimate spatially explicit concentrations in environmental media in Europe. Anne Hollander (Radboud University, Nijmegen, The Netherlands) presented a study which considered whether variability in chemical properties or variability in environmental input parameters had the biggest effect on output variance in predicted concentrations. This is a critical question because if chemical variability controls the output variance then there is little point in trying to calculate spatial differences in concentrations. Her findings were that in many cases the chemical variability dominates, which would suggest that the assumption may be valid that the variation in the fate of chemicals in the environment mainly depends on substance-specific partition coefficients and degradation rates. For the estimation of soil and water concentrations with direct emissions to these compartments, however, the influence of spatial variation in environmental characteristics should not be neglected in multimedia mass balance models. Francesc Geralt (URV Taragona) showed how a neural network system could be trained to give the same results as SimpleBox for a large list of contaminants. He suggested that a neural network system offers computational advantages over multimedia models when screening large lists of contaminants. Ian Cousins (Stockholm University, Sweden) presented a study in which the predictions of three multimedia environmental fate models (spatially- and non-spatially-explicit) were evaluated against mentoring data for various contaminants. Model performance for the air and water compartments was good for all models included in the evaluation and the spatially explicit models were able to predict spatial differences in concentrations. On the other hand, all three models consistently underestimated median observed

concentrations in sediment and soil by 1–3 orders of magnitude. The results were discussed in terms of factors influencing model performance and Ian Cousins identified overestimation of degradation rates in soils and sediments as the most likely explanation for the model underestimations. Ian Cousins briefly presented, on behalf of absent Alberto Pistocchi (Joint Research Centre of the EU, Ispra, Italy), the new spatially-explicit modeling tool developed in NoMiracle. This tool, which is called MAPPE, is integrated into GIS-based software, which facilitates input of spatially explicit environmental data and also presentation of outputs as e.g. predicted environmental concentration maps for Europe. New modeling algorithms, e.g. the new Abraham-type LFERs developed to estimate partitioning in NoMiracle, can be readily integrated into this modeling tool.

The workshop concluded with an active discussion session in which many of the key messages from the two-day workshop were discussed. Ian Cousins suggested that proponents of Abraham-type LFERs are faced with a communication challenge in "shifting the paradigm" away from the conceptually simpler models based on single parameters, such as the widely available K_{OW}. Gerrit Schüürmann affirmed that the advantages of Abraham-type LFERs are so many that it is only a matter of time before they become much more widely accepted by scientists and adopted in exposure modeling tools. Philipp Mayer suggested that the likely overestimation of the degradation rates for soils and sediments used as inputs to the models may be because of a lack of consideration of the reduced chemical activity and accessibility for degradation by microorganisms. This once again highlighted the importance of improving our understanding of both chemical availability and degradation in order to get better predictions of exposure. The workshop proved to be stimulating and successful and the beautiful city of Leipzig and Leipziger-KUBUS provided an excellent venue.

EU projects present at the woorkshop:

NOMIRACLE -
Novel Methods for Integrated Risk Assessment of Cumulative Stressors in Europe

MODELKEY -
Models for assessing and forecasting the impact of environmental key pollutants on freshwater and marine ecosystems and biodiversity

ALARM -
Assessing large scale risks for biodiversity with tested methods

CAESAR -
Computer Assisted Evaluation of Industrial Chemical Substances According to Regulations

OSIRIS -
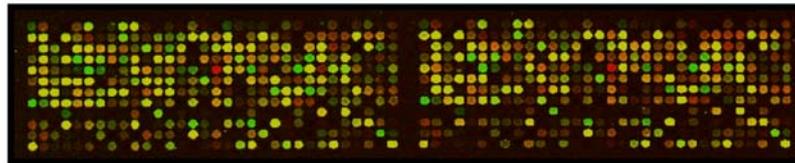**Optimized Strategies for Risk Assessment of Industrial Chemicals through Integration of Non-Test and Test Information".**

NOvel Methods for Integrated Risk Assessment of CumuLative stressors in Europe

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For detailed information on these courses

http://www.bio.ua.pt
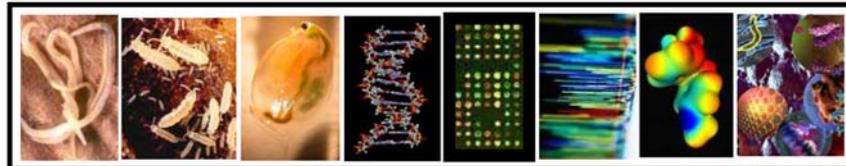http://www.cesam-ua.pt

or contact Mónica Amorim; email:

mjamorim@ua.pt

Summer Courses

PRACTICAL APPROACH TO ECOTOXICOGENOMICS

Advanced Workshop Studies in Biology and Applied Biosciences

**Department of Biology
University of Aveiro, 16-21 June 2008**

This one-week post-graduate workshop aims to provide knowledge on the development of molecular markers of stress using molecular biology techniques. This includes among others the following: RNA extraction, cDNA synthesis, basic cloning techniques, PCR reaction development and optimisation, real time PCR, DNA sequencing, and development of microarrays (cDNA arrays), their hybridization and analysis.
The course is addressed to scientists and PhD and M.Sc. students with a background in Biology, Natural and Environmental Sciences, Chemistry, Environmental engineering or related fields, members of consulting companies and of private and public institutions responsible for environmental management.

FCT Fundação para a Ciência e a Tecnologia
MINISTÉRIO DA CIÊNCIA, TECNOLOGIA E ENSINO SUPERIOR

This course is being held within the NoMiracle project consortium (http://nomiracle.jrc.it/default.aspx) and within the FCT project PTDC/MAT/72974/2006: New statistical methodologies for analysis DNA microarrays data.

CESAM Centre for Environmental and Marine Studies
www.cesam.ua.pt

NOvel Methods for Integrated Risk Assessment of
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NoMiracle presentations at

SETAC Warsaw, 25-29 May, 2008

Author	Title	Time & Place
Monday, 26 May 2008		
ET13A TOXICITY OF CHEMICAL MIXTURES		
Svendsen, C.; Cedergreen, N.; Kamper, A.; Sørensen, H.	Can the effect of ternary mixtures be predicted from binary mixture toxicity results?	10:05 – 10:25 Koncertowa Hall
ET13P TOXICITY OF CHEMICAL MIXTURES, SEQUENTIAL AND TIME-VAR		
Baas, J.; Broerse, M.; Song, Y.; Jager, T; van Gestel, K.; Kooijman, B.	Predicting effects of narcotic mixtures on survival in time	11:40 – 12:00 Koncertowa Hall
Peréz, J.; Loureiro, S.; Soares, A.M.V.M.	Binary mixture toxicity to *Chironomus riparius* and *Pseudokirchneriella subcapitata*: transposing to the lab: the case study of the Alqueva reservoir	
Jager, T.; Baas, J.; Kooijman, B.	Reference model for sub lethal effects of mixtures	051
Broerse, M.; Mense, M.; van Gestel, K.	Development of mixture effects of phenanthrene and nickel on the springtail *Folsomia candida* in time	
Liedtjens, K.; Ratte, H.-T.	Effects of chemical mixtures on *Lemna minor* and *Desmodesmus subspicatus*	015
PG02P USING 'OMICS TO ELUCIDATE MECHANISMS OF TOXICITY		
Vandenbrouck, T.; Soetaert, A.; van der Ven, K; van Remortel, P.; Blust, R.; De Coen, W.	Nickel and binary metal mixture responses in *Daphnia magna*: molecular fingerprints and (sub)organismal responses	09:25 – 09:45 Cinema Hall
Dondero, F.	Molecular analysis of mixture toxicity in the marine mussel Mytilus galloprovincialis: a systems biology approach	12:00 Cinema Hall
Dom, N.; Scheil, V.; Vandenbrouck, T.; Koehler, H.; De Coen, W.	Binary mixtures of two dissimilarly acting compounds: a molecular impression in zebrafish larvae	089
NA01P INTERACTIONS BETWEEN NATURAL AND CHEMICAL STRESSORS		
Kramarz, P.; Urbańska, A.; Laskowski, R.	Response of *Pterostichus oblongopunctatus* (Coleoptera: Carabidae) to multiple stressors: joint effects of nickel, chloropyrifos and Bt (*Bacillus thuringiensis*) toxin	15:25 – 15:45 Koncertowa Hall
Bergmann Filho, T.U.; Loureiro, S.; Soares, A.M.V.M.	Assessment of energy budget in Daphnia magna exposed to natural and chemical stressors	
Scheil, V.; Osterauer, R.; Köhler, H.-R.	3,4-dichloroaniline, diazinon and temperature: Influence on early development and stress protein levels of *Danio rerio* embryos and larvae	206
Świergosz-Kowalewska, R.; Molenda, P.; Halota, A.	Effects of chemical and thermal stress on acetylcholinesterase activity in the brain of bank vole, *Myodes glareolus*	270
MOPC4 MULTIPLE STRESSORS FOR TERRESTRIAL SPECIES AND ECOSYSTEMS		
Bindesbøl, A.-M.; Bayley, M.; Damgaard, C.; Hedlund, K.; Holmstrup, M.	Changes in membrane phospholipids may provide a mechanistic explanation for the synergistic interactions between copper and freezing induced mortality in earthworms	PC4-7

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Author	Title	Time & Place
Tuesday, 27 May 2008		
EC04P MATHEMATICAL MODELS IN FATE AND EXPOSURE ASSESSMENT		
Martinez, I.; Espinosa, G.; Rallo, R.; Giralt, F.; Grifoll, J.	Clustering the chemical space to estimate environmental multimedia partitioning of pollutants with kernel methods and molecular descriptors	
Pistocchi, A.; Bidoglio, G.; Pennington, D.W.; Vizcaino, P.	Fate and transport of pollutants at the continental scale – insights from the MAPPE model for POPs	007
Schwöbel, J.; Kühne, R.(*); Ebert, R.-U.; Schüürmann, G.	Prediction of hydrogen bond donor and acceptor strength through quantum chemical models employing local reactivity parameters	014
Schwöbel, J.; Kühne, R.(*); Ebert, R.-U.; Schüürmann, G.	Supermolecule approach to predict hydrogen bond donor and acceptor strength from molecular structure	015
Böhnhardt, A.; Kühne, R.; Ebert, R.-U.; Schüürmann, G.	Prediction of rate constants for the indirect photolysis of organic compounds – the MOIP method	Poster/Exhibition Hall
RA05P RISK ASSESSMENT OF PESTICIDES AND GMOS		
Chmolowska, D.	Effect of chlorpyrifos and captan on respiration rate in a fallow soil	071
RA07P SEDIMENT ECOTOXICOLOGY AND RISK ASSESSMENT		
Langer, M.; Köhler, H.-R.; Gerhardt, A.	Effects of thiacloprid on the life cycle of the midge, *Chironomus riparius*	TU190
EC04A MATHMETICAL MODELS IN FATE AND EXPOSURE ASSESSMENT		
Strebel, K.; Espinosa, G.; Rallo, R.; Giralt, F.; Richter, M.; Schlink, U.; Herbarth, O.; Kindler, A.	Spatial and Seasonal Prediction of Outdoor Volatile Organic Compound (VOC) – Identifying Optimal Model and Data Set	09:05 – 09:25 Mikolajska Hall
Wednesday, 28 May 2008		
RA09P SPATIAL APPROACHES IN ENVIRONMENTAL RISK ASSESSMENT		
Strebel, K.; Espinosa, G.; Rallo, R.; Giralt[2], F.; Schlink, U.	Outdoor exposure modeling with car and self organizing maps	
PC1 LOCOMOTION AS BEHAVIOURAL TOXICITY PARAMETER		
Kienle, C.; Gerhardt, A.; Köhler, H.-R.	Does exposure to chlorpyrifos, diazinon and 3,4-dichloro-aniline lead to developmental and behavioural effects in zebrafish embryos and larvae?	PC1-3
Bednarska, A.J.; Gerhardt, A.; Laskowski, R.	Nickel affects locomotor activity and respiration rate of the ground beetles *Pterostichus oblongopunctatus*	PC1-5
PS02A SCIENTIFIC APPROACHES IN SUPPORT OF WATER FRAMEWORK DIRECTIVE (WFD)		
Henning-de Jong, I.; Ragas, A.M.J.; Hendriks, H.W.M.; Posthuma, L.; Wintersen, A.; Hendriks, A.J.	The value of an extra ecotoxicity test when deriving ecological quality standards (EQSs)	14:45 – 15:05 Galczynski Hall
RA03P GROUPING, READ-ACROSS, QSAR AND SIMILARITY – USE IN ENVIRONMENTAL RISK ASSESSMENT		
Ost, N.; Ebert, R.-U.; Kühne, R.; Schüürmann, G.	Structural alerts to predict excess toxicity in the Tetrahymena pyriformis assay	
Ost, N.; Böhme, A.; Ebert, R.-U.; Kühne, R.; Schüürmann, G.	Electrophilic reactivity of Michael-type acceptors	
RA09B SPATIAL APPROACHES IN ENVIRONMENTAL RISK ASSESSMENT		
Vizcaino, P.; Pistocchi, A.; Pennington, D.W.; Bidoglio, G.	MAPPE model: a multimedia fate and transport model for persistent organic pollutants. Case study for lindane	11:40 – 12:00 Galczynski Hall

Second Announcement

4th NoMiracle Open Workshop

Integrated Assessment of Environmental and Human Health

8-9 September, 2008

First Day	8 September 2008
9:00 – 10:00	Registration and coffee
10:00 – 10:15	Welcome address/ *Hans Løkke, University of Aarhus, Denmark*

1ST SESSION
INTRODUCTION: THE SCOPE OF INTEGRATED ASSESSMENT OF ENVIRONMENTAL AND HUMAN HEALTH

10:15 – 10:45	EU research on environment and health *Tuomo Karjalainen, DG Research*
10:45 – 11:15	Integration of human and ecological effect assessment *Glenn Suter, US EPA*
11:15 – 11:45	INTARESE tools under development
11:45 – 12:30	Discussion
12:30 – 13:30	Lunch

2ND SESSION
INTEGRATION OF HUMAN AND ECOLOGICAL EXPOSURE ASSESSMENT

13:30 – 13:50	Modelling of exposure and risk in space and time *Uwe Schlink, UFZ, Leipzig, Germany*
13:50 – 14:10	Spatially explicit cumulative exposure modelling for terrestrial vertebrates using an ecological and energetical approach *Mark Loos, Radboud University, The Netherlands*
14:10 – 14:30	Environmental exposure assessment: factors determining external and internal exposure *Kees van Gestel, Free University, Amsterdam, The Netherlands*
14:30 – 14:50	Modeling environmental fate accounting for metabolism *Sabcho Dimitrov, University "Prof. As. Zlatarov", Bulgaria*
14:50 – 15:10	Discussion
15:10 – 15:40	Coffee break

3RD SESSION
MECHANISTIC APPROACHES

15:40 – 16:10	Pollutant molecular mechanisms: a system toxicology approach *Aldo Viarengo, University Piemonte Orientale, Italy*
16:10 – 16:30	Do uncertainty factors take into account toxicokinetic interactions? Conclusions and recommendations *Jean Lou Dorne, University of Southampton, UK*
16:30 – 16:50	Mixture toxicity assays with stable human cell lines *Albert Duschl, University of Salzburg, Austria*
16:50 – 17:10	Mixture toxicity assays on human hepatocyte cell line *Mario Bauer, UFZ, Leipzig, Germany*
17:10 – 17:30	Molecular mechanisms of mixture toxicity *Jan Kammenga, University of Wageningen, The Netherlands*
17:30 – 18:00	Discussion
19:00 –	Conference dinner

NOvel Methods for Integrated Risk Assessment of
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For participation in the workshop

Venue: **Frankfurt, Germany**
Information: **http://nomiracle.jrc.it**
Pre-registration: **nomiracle@dmu.dk**

Second day	9 September 2008
4TH SESSION **EXTRAPOLATION**	
9:00 – 9:20	A comprehensive approach to mixture toxicity. From patterns to mechanisms *Dave Spurgeon, NERC, UK*
9:20 – 9:40	Extrapolation of acute to chronic toxicity *To be announced*
9:40 – 10:00	Extrapolation from single to multiple substances by DEBtox modelling *Jan Baas, Free University, Amsterdam, The Netherlands*
10:00 – 10:20	Quantifying uncertainty and variability in extrapolation from laboratory animals to man *Irmgard Henning - De Jong, Radboud University, The Netherlands*
10:20 – 10:30	Discussion
10:30 – 11:00	Coffee break
5TH SESSION **COMBINED EFFECTS OF NATURAL STRESSORS AND CHEMICALS**	
11:00 – 11:20	Including natural stressors in risk assessment of chemicals: from test designs to integrative risk assesment *Martin Holmstrup, University of Aarhus, Denmark*
11:20 – 11:40	Reduced tolerance of environmental stressors caused by chemicals, exemplified by temperature and oxygen depletion *Amadeu Soares, University of Aveiro, Portugal*
11:40 – 12:00	Using human blood cells to test for interactions between pathogens and chemicals *Irina Lehmann, UFZ, Leipzig, Germany*
12:00 – 12:20	*To be announced*
12:20 – 12:45	Discussion
12:45 – 13:45	Lunch
6TH SESSION **INTEGRATION OF ENVIRONMENT AND HEALTH**	
13:45 – 14:15	Different levels of integration in assessment of environmental and human health: from the policy level to the molecular level *Ad Ragas, Radboud University, The Netherlands*
14:15 – 14:45	New strategies for testing and risk assessment based on the findings of NoMiracle *Hans Løkke, University of Aarhus, Denmark*
14:45 – 15:15	Coffee
15:15 – 16:00	General discussion
16:00	Closure of the workshop

NOvel Methods for Integrated Risk Assessment of CumuLative stressors in Europe

FINAL ANNOUNCEMENT

TOPICS ON ENVIRONMENTAL MIXTURE TOXICITY

Advanced Workshop Studies in Biology and Applied Biosciences

Department of Biology
University of Aveiro, 30th of June – 4th July 2008

This one-week post-graduate workshop aims to provide knowledge on chemical interactions and mixture toxicity in the environment. The course is addressed to scientists and PhD and M.Sc. students with a background in Biology, Natural and Environmental Sciences, Chemistry, Environmental engineering or related fields, members of consulting companies and of private and public institutions responsible for environmental management.

NMiracle
This course is being held within the NoMiracle project consortium (http://nomiracle.jrc.it/default.aspx).

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NoMiracle co-ordination