Annual Report 2014

Environmental Engineering Laboratory

ENVELab

Edited by:

Assoc. Professor

Dimosthenis Sarigiannis, Director

Welcome message

2014 – A year of challenges and success

The Environmental Engineering Laboratory (ENVE Lab) was established at the Chemical Engineering department of Aristotle University of Thessaloniki (AUTH) in the second half of 2011. Its objective is to become an international center of reference for environmental engineering addressing the interactions between environment and human health and exploiting this knowledge to the design of novel chemical processes and products servicing the sustainability objectives.

The main thematic areas of ENVE Lab are:

- Environment and health – development of integrated methodologies to assess the impact environmental pollution may have on human health
- Advanced technologies for monitoring environmental pollution and waste management
- Industrial ecology approaches to the design of industrial systems with reduced ecological footprint

Our work paradigm is based on extensive collaboration and scientific networking. Within AUTH, ENVE Lab collaborates with the Analytical Chemistry Laboratory of the Chemical Engineering department and the Environment and Analytical Chemistry Laboratories of the Chemistry department, the Laboratory of Applied Thermodynamics and the Laboratory of Heat Transfer and Environmental Engineering of the Mechanical Engineering department, as well as with the Biochemistry laboratory of the Medical School. Particularly close collaboration has been established with the Natural Resources and Renewable Energy laboratory of the Chemical Process and Energy Research Institute of the Centre for Research and Technology Hellas. This collaboration encompasses four international projects running over the last four years.

In Greece ENVE Lab has been providing scientific support to the Ministry of Development, the Ministry of Environment, Energy and Climate, and the Ministry of Health. It has forged working links with the environmental consultancy ENVIROPLAN S.A. and chairs the scientific committee of the Citizens' Inspectorate for Sustainable Development (CISD). ENVE Lab supports the long-range research initiative of CEFIC (the European Federation of Chemical Industry) by leading 3 projects on integrated exposure and risk assessment. The Lab is an active member and since 2013 it has assumed the Presidency of the Mediterranean Scientific Association for Environmental Protection (MESAEP), forging thus close links with environmental scientists across the Mediterranean.

On a more global scale, good collaborative links have been established with the World Health Organization European Center for Environment and Health, the US Environmental Protection Agency (US EPA), the National Institutes for Environmental Health Science (NIEHS) and the School of Public Health of the University of California at Berkeley and Emory University focusing on the development of operational methodologies and novel tools towards unraveling the exposome, i.e. the totality of exposures from conception onwards, simultaneously identifying, characterizing and quantifying the exogenous and endogenous exposures and modifiable risk factors that predispose to and predict diseases throughout a person's life span. We collaborate with Beijing University, Nanjing University and the Beijing Academy of Sciences to assess the health effects of climate change mitigation and adaptation policies in large cities, as well as with.

During 2014 the main challenges included

(a) leading the Europe-wide effort on the human exposome and contributing to the international debate on rendering the exposome operation for precision prevention in environmental health;
(b) monitoring, assessing and proposing solutions to the problem of increased air pollution from biomass combustion for space heating in large urban centres (induced by the energy poverty of the Greek population in conjunction to the financial crisis); and
(c) contributing to the launching of a new COST network on risk management and rehabilitation of contaminated industrial sites in the European Union Member States.

In Greece ENVE Lab contributed to the expert Working Group on biomass boiler certification on behalf of the Ministry of the Environment, Energy and Climate. In the Balkans, ENVE lab led scientifically the transboundary collaboration between Greece and Bulgaria on chemical and radiological risk in indoor environments. On the international level, ENVE Lab became a member of the Global Chemical Risk network of the WHO and acted as temporary advisor to the WHO on the state of human biomonitoring in the European region of WHO placing particular emphasis on integrated exposure and risk assessment of endocrine disrupters and continued its work on environmental health economics aiming at rendering it a tangible and practical tool for assessing environmental and fiscal policy options.

I hope you will enjoy reading our 3rd annual report. We would be happy to work with you to roll further back the boundaries of error in our understanding of the world..

Assoc. Prof. Dimosthenis Sarigiannis
Laboratory director

Scientific Signature:

2014 – A Year of integration

EnvE-Lab aims at developing integrated methodologies and knowledge management systems that can effectively shed light on the interactions between human health and the environment. Our concept brings together state-of-the-art advances in **environmental monitoring**, **human biomonitoring** and **systems biology**, **exposure monitoring** technologies and advanced tools for **computational analyses** of the **exposure-to-health effect continuum**. The above are put together in a novel exposure biology-based methodology translated into an integrated computational platform and knowledge management system, which is at the core of the "**EnvE-Lab Assessment Platform - ELAP**". Expanding the applicability domain of ELAP to a wide variety of environmental stressors is a key issue for its scientific soundness and policy impact. Several sub-compartments of ELAP are put to test through their application in a number of population studies across different exposure settings in Europe and worldwide tackling relevant health endpoints. In addition to the technical research and the continuous development work, horizontal activities provide the infrastructure necessary for putting ELAP in its policy context.

Better understanding of environmental fate, exposure and toxicity mechanisms is required to ensure refined exposure and risk characterization, e.g. the precise quantification of exposure scenarios and circumstances that might set the basis for inducing potential adverse effects on humans. However, social cost increases exponentially as we approach the maximum benefit in terms of exposure reduction; it seems that there is a threshold beyond which social cost increases disproportionally to social benefit. The aim of refining the overall assessment is to identify this optimal point, so as to design cost-effective public health protection policies.

The assessment process focuses on several instances as follows: hazard potency of a substance, its uses and mobility in the environment (affecting the amount that the population groups will come into contact), the biologically effective dose of the compound reaching the target tissue and finally the response of the human body to this dose. These processes are influenced strongly by the interaction of the physicochemical properties of the substance with physiological attributes (e.g. susceptibility to xenobiotics or variability of exposure strongly depend to inter-individual differences). Thus, well targeted interventions at different stages of the source-to-outcome continuum ensure the optimal management of chemicals in the environments in terms of quantities released and intended (or not) uses. Our final objective is to redner this analysis a *sine qua non* tool for guiding new chemical synthesis in industry (Figure 1), in accordance with the "safe by design" principle.

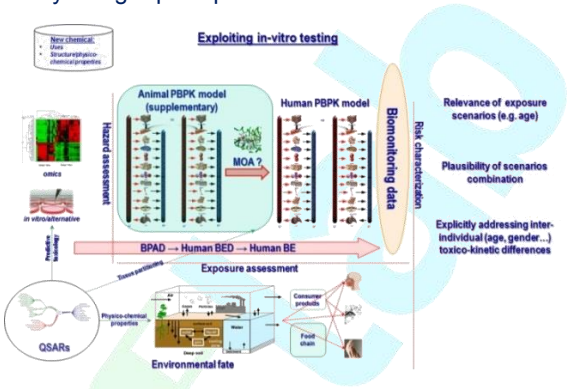

Figure 1. Integrating environmental contamination, human exposure and toxicology for refined risk characterization

The necessity of using ELAP as a novel tool for interpretation of environment and health data in order to better understand the mechanistic relationship between lifelong exposure to environmental stressors and health response has been widely recognized by the scientific, regulatory and chemical industry community; EnvE-Lab's resilience in supporting this scientific signature, as well as dedication to a solid work ethics model, was rewarded by the number of different projects granted the last 2 years, namely:

INTEGRA - European Chemical Industry Council (CEFIC)

HEALS - FP7 project

CROME – LIFE project

CheRRIE – INTERREG project

(ICSHNet) - Industrially Contaminated Sites and Health Network

These projects follow the scientific principles described above, yet they focus on different aspects of the "source-to-outcome" continuum. These projects (together with the now closed projects URGENCHE and TRANSPHORM) act in a synergistic manner so as to further develop the holistic approach of EnvE-Lab.

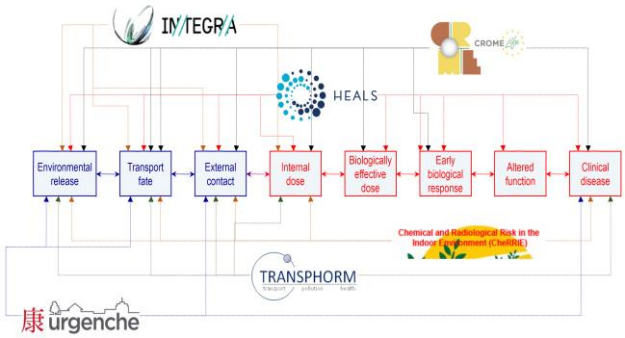

Figure 2. Involvement of EnvE-Lab projects across "source to effect" continuum

Highlights of the year 2014

Socioeconomic components of exposure

Financial crisis, austerity measures and biomass use

Over the last couple of years, the use of biomass as heating source was allowed in Greece as a CO_2-neutral means of space heating in the large metropolitan areas of Athens and Thessaloniki affecting more than half of the country's population. At the same time the use of light heating diesel was heavily taxed. In the same period Greece faces a financial crisis with significant repercussions on the average household income. This combination resulted in an increased use of biomass for residential heating in year 2012, followed by a significant increase of ambient air, indoor air and exposure to PM10 and PM2.5. EnvE-Lab aimed to quantify the health and socioeconomic effects related to that shift from light heating diesel to biomass burning, as well as to evaluate alternative scenarios of residential heating energy share. The extensive study of the biomass burning attributed PM problem to Thessaloniki air quality raised public awareness (TV interviews, newspaper articles), which in turn resulted to policy interventions (two Joint Ministerial Decrees).

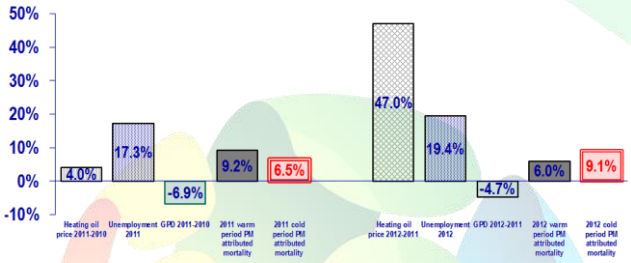

Figure 3. Socioeconomic dimension of financial crisis and the relevance to mortality associated socioeconomic costs between the cold periods of 2011-2012 and 2012-2013 seasons

Based on the results of the study and taking into account the importance of public health and the related socioeconomic cost, specific interventions are recommended, such as:

- Reduction of the price of light heating diesel
- Financial motivations for the light heating diesel to be replaced by natural gas

If biomass continues to be used, then we need to take into consideration the followings:

- Closed fireplaces are more efficient in terms of performance/PM emissions and indoor PM emissions are almost negligible.
- Emission factors for fine particles are highly dependent on the fuel characteristics and burn conditions (smoldering vs. flaming), as well as fuel moisture content and burning conditions.

Socioeconomic components of exposure from global scale biomonitoring

Analysis of the socioeconomic aspects of exposure can provides useful insights on the effect that socioeconomic disparities have on exposure to chemicals and finally on health risk. Analysis of the levels of phthalate exposure as evidenced by levels of urinary DEHP metabolites at country level shows a strong inverse association with the national GDP per capita (Figure 4). Indeed, exposure to phthalates has declined in high income countries following the adoption of national and international regulations. However, this effect might be partly obscured in countries with lower GDP due to a consumer preference towards cheaper imported plastic materials. As a consequence, policies for consumer protection might not be adequate for public health protection if related only to products manufactured in the EU.

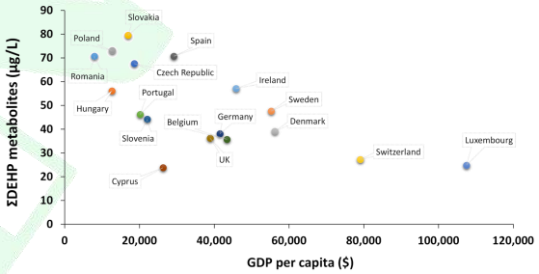

Figure 4. Socioeconomic dimension of exposure to phthalates: exposure to DEHP (in terms of total DEHP metabolites in urine)

On the contrary, blood levels of PCDDs/PCDFs are positively correlated to GDP per capita (Figure 5). Considering that more than ninety percent of typical human uptake of PCDDs/PCDFs comes from diet and especially from food of animal origin, the observed higher exposure levels in countries with higher GDP might be attributed to higher consumption of beef meat, dairy products and fish, where these compounds tend to accumulate more.

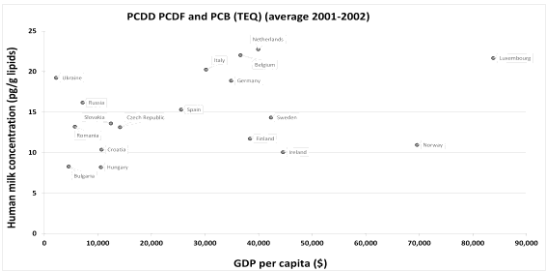

Figure 5. Socioeconomic dimension of exposure to PCDDs/PCDFs.

Exposome

The exposome represents the totality of exposures from conception onwards, simultaneously identifying, characterizing and quantifying the exogenous and endogenous exposures and modifiable risk factors that predispose to and predict diseases throughout a person's life span. The methodology for assessing individual exposome proposed by EnvE-Lab brings together a comprehensive array of novel technologies, data analysis and modeling tools that support efficient design and execution of exposome studies.

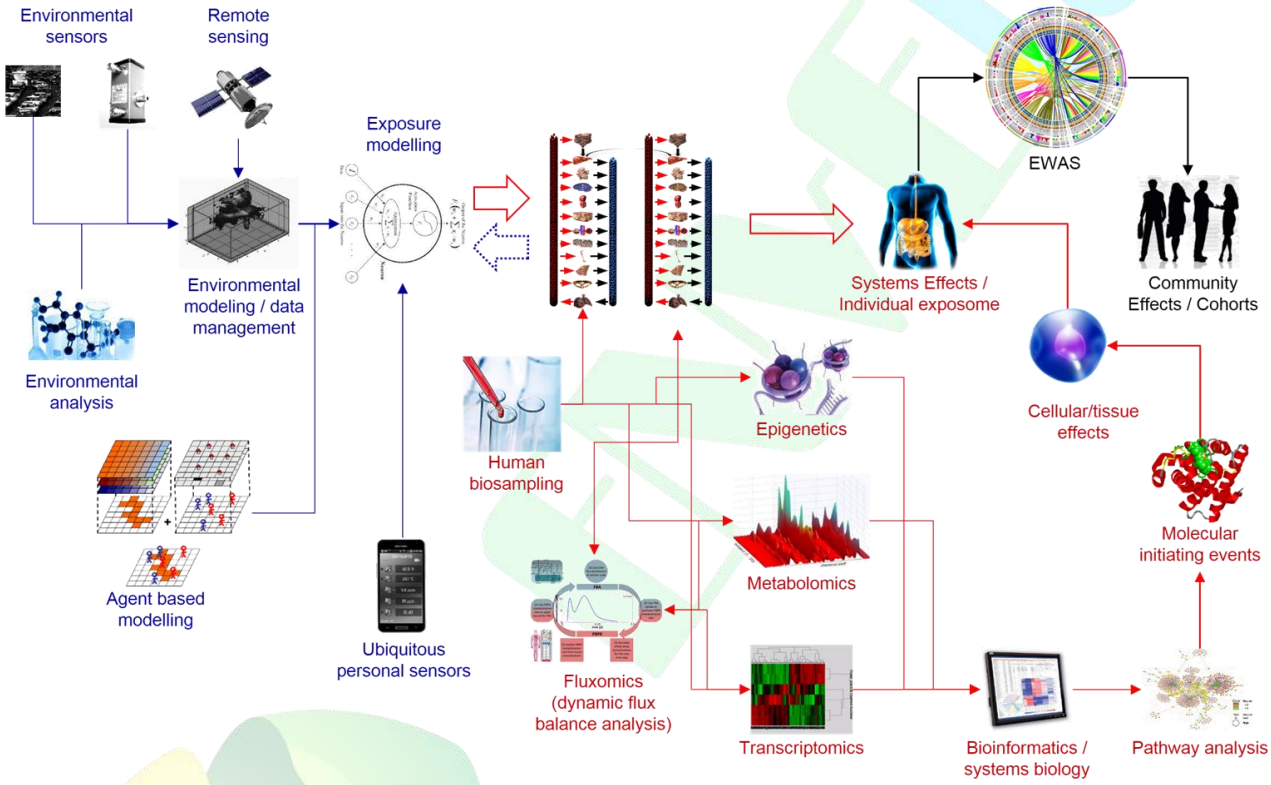

Figure 6. Conceptual representation of the technological arrays involved in the exposome assessment

This approach brings together and organizes environmental, socio-economic, exposure, biomarker and health effect data; in addition, it includes all the procedures and computational sequences necessary for applying advanced bioinformatics coupling advanced data mining, biological and exposure modeling so as to ensure that environmental exposure-health associations are studied comprehensively. The following key issues will be addressed to characterize the individual exposome:

- Human biomonitoring (HBM) and biobanking are seen as a central theme.
- Understanding of the interaction between HBM and exposure modeling (EM) or estimation is another key factor for elucidating the exposome.
- Lifestyle/behaviour patterns (such as time-activity-location, food consumption, use of consumer products, etc.) are needed to understand individual and population-based geospatial lifelines.
- Innovations in sensor technology allows to collect environmental data at unprecedented depth and breadth.
- We propose simulating movement and interaction behaviour using agent-based models (ABM) informed by sensor technologies. ABM aim to simulate and organise social behaviours in order to understand the dynamics of real-world systems.
- Current toxicological state of the art couples estimations of biologically effective dose (BED) with early biological events to derive dose-effect models, which can be used in combination with the probabilistic exposure estimates to derive biomarkers of exposure and/or effect. Combined use of epidemiological, clinical and genetic/epigenetic analysis data will shed light on the effect of risk modifying factors such as lifestyle choices and DNA polymorphisms and methylation. Exposure assessed prospectively and tightly linked to proposed periods of vulnerability of the epigenome (e.g., periods of placental invasion or sex specification in utero) would be ideal. Observation of real clinical data and/or results of biomonitoring, coupled with exposure/effect biomarker discovery systems, will produce predictive biomarkers allowing estimations of individual response to toxic insults. Metabolomics and adductomics are key to this analytical and data interpretation process. They will be functionally integrated with transcriptomics and proteomics to provide the mechanistic underpinning for establishing causality in the association between health status and exposure to environmental stressors.

HEALS

Health and Environment-wide Associations based on Large population Surveys

Health and Environment-wide Associations based on Large population Surveys (HEALS - www.heals-eu.eu) is the most important FP7 project funded by the European Union on environment and health topic. EnvE-Lab co-coordinates the project providing scientific leadership and coordinating the scientific strategy and ethical aspects of the project.

Assessing the exposome at its most complete degree in order to encompass life-course internal and external environmental exposures, from the preconception period onwards in order to explain the development of asthma and allergies, overweight, obesity and diabetes, as well as neurodevelopmental and neurodegenerative disorders is the first challenge taken up by HEALS. HEALS will disentangle the ”internal exposome” by developing and validating biological markers using data from European pre-existing and new population-based studies and their bio-banks. This will allow detecting signals in body fluids through proteomics, metabolomics and transcriptomics permitting to characterize exposures to environmental contaminants and identify intermediate markers that lead to chronic diseases. To be exhaustive other ”omics” technologies and measures in relation to external exposures (namely heavy metals, POPs, etc.) as well as the assessment of DNA adducts in relation to a number of exposures are being conducted.

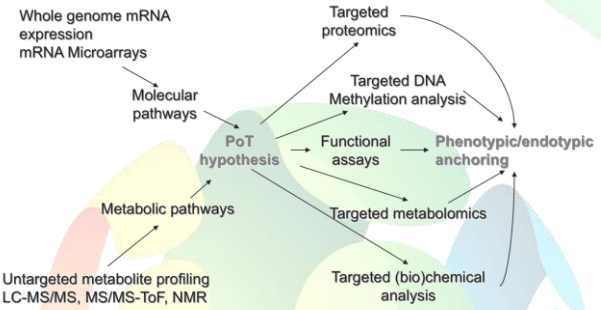

Figure 7. Analytical exposure biology workflow according to the HEALS paradigm

Research on ”external exposome” includes analysis of data from lifetime exposures to environmental pollutants in air, food, water, physical activity, medications, homes and daily stressors.

To this aim HEALS completed a pre-pilot study in seven cities in Europe where four participants per city were asked to carry for one week several personal sensors to track position, movement and activity. The successive step is to extend the variables measured by using other personal sensors in a second pilot study aiming at defining an exposure assessment protocol to be implemented in the Exposure and Health Examination Survey (EXHES) study. This is the prospective cohort study through new cohorts of singletons and twins that are being to be recruited in 10 EU Member States since in utero life and followed-up for 3 years and of their parents that best suits the “exposomics” approach. This study design gives us the opportunity to perform repeated sampling of questionnaires, clinical data and biological specimens in a longitudinal mode. Because monozygotic twins develop from a single fertilized egg, they have the same genome any differences between twins are due to their environments. Recent studies have shown that many environmentally induced differences are reflected in the epigenome. The available large-scale epigenetic studies of monozygotic and dizygotic twins in HEALS will provide data useful to the understanding of how genetic and environmental factors impact through an individual’s lifespan upon epigenetics, and how epigenetics impacts on complex traits underlying disease onset and/or exacerbation.

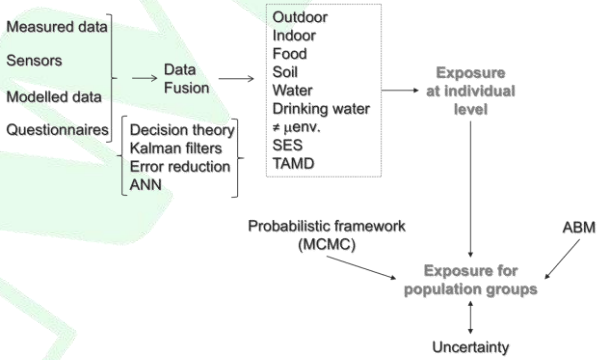

Figure 8. Workflow of external exposome assessment according to the HEALS paradigm

Developing reliable tools for assessing a complete exposure history is the second challenge taken up by HEALS. Such tools have to achieve very high precision and reliability in order to be applied in other investigations. Data mining will be used to extract information from the large data set obtained, transform it into an understandable structure for further analyses and discover patterns in the environment-wide associations (EWAS) underlying diseases. The HEALS approach will be a mechanistic one, based not only on data associations but coupling bionformatics analysis with mechanistic modeling to ensure that causal associations between exposures and health outcomes are elucidated.

Dissemination, communication and training activities were key foci last year. International scientific workshops were organized to disseminate the project outcomes to the scientific community and EnvE lab scientists took part in major international Conferences (ISEE, SETAC, ICCA-LRI), participation and oral lecture at the US-NIEHS webinar series on the exposome, publication of scientific papers in peer-reviewed journals.

CROME

Cross-Mediterranean Environment and Health Network

The Cross-Mediterranean Environment and Health Network project - CROME (www.crome-life.eu) is a 42 months demonstration project coordinated by EnvE-Lab started in July 2013 and funded under the EU LIFE+ Programme 2007-2013.

The main objective of CROME-LIFE is to demonstrate a technically feasible integrated methodology for interpretation of human biomonitoring (HBM) data to quantitatively assess the impact on human health due to acute/chronic exposure to chemicals acting as neurodevelopmental and neurological toxicants and/or human carcinogens such as toxic and organic substances.

The CROME-LIFE method and tool is being applied in the four demonstration sites (Greece, Slovenia, Italy and Spain) tackling different levels of environmental exposure, age windows, and socio-economic and genetic variability.

First results include the definition of the methodological framework which starts by estimating exposure using human biological monitoring data and work both forward to disease linking internal doses in target tissues with health impacts through advanced statistical methods and backwards (using reverse dosimetry) to environmental exposures.

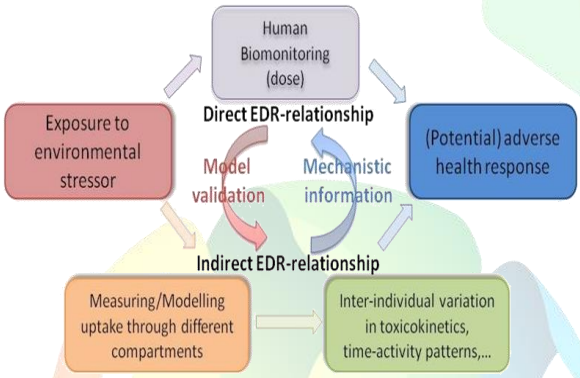

Figure 9. CROME methodological framework "middle out approach"

Already existing data from past population studies (PHIME, PROBE, INMA) were collected and stored into the CROME geo-database after Quality Assessment / Quality Control. Statistical analysis of Latium (Italy) population data (450 human blood samples collected among adolescents) has been carried out through the application of GLM models in order to identify the associations between metals concentration levels in blood and several exposure determinants including the residence and the land use of the participants locations addresses, the frequency of fish and milk consumption and the exposure to PM10 data. Results showed that Cr has a statistically significant association with diet (i.e. fish and milk consumption) and with land use both alone and in combination. Hg has a more complex interaction between diet and human activities (i.e. proximity to industrial activities). No pathway alone is dominant but the combined effect results in statistically significant associations with blood concentration levels. Pt and W show an interaction effect between diet and land use. Internal exposure to Ni is mainly driven by diet (co-exposure to milk and fish).

Figure 10. Manhattan plot of associations of the environmental factors with HBM levels of metals ($p < 0.05$). The red line represents a $p < 0.02$, which means a more robust association.

Next step is the execution of the fields campaigns both environmental and human biomonitoring which will start in the first months of 2015. These include four National case studies (one for each participating Country) and one common case study in all the participating countries focusing on exposure to Hg and neurodevelopmental disorders Applications for Ethical Review have been prepared and submitted to the National Ethical Committees. Applications consist of detailed explanation of the studies from background to design. They include also the questionnaires and inform consent to be distributed to the study participants. Environmental campaigns already started in the demonstration sites through the sampling of several food items, with a special emphasis on fish species, and drinking water.

Dissemination activities have been continued throughout this year with the aim of disseminating the project outcomes to the scientific community, informing citizens and involving stakeholders about the associations between exposure to chemical and the impact on human health. They involved a wide range of dissemination channels including the participation to major International and National conferences, publication of scientific papers in peer-reviewed journals, written and electronic press releases and TV interviews, technical newsletters and project leaflets to be distributed during the main project events.

Genotoxic effects of inhaled particulate matter (PM) are mainly attributed to absorbed polycyclic aromatic

hydrocarbons (PAHs). Human respiratory tract (HRT) deposition of a specific particle depends on its aerodynamic diameter. Thus, xenobiotics contained in finer particles can easily be transferred in human body via systemic circulation. Benzo[a]pyrene (B[a]P) is the only PAH classified as known carcinogen to humans by IARC.

An extensive campaign was carried out from January to April 2013 at two locations in the urban area of Thessaloniki to determine the chemical composition of urban aerosols and to correlate their toxicity with biomass combustion as a way of residential heating. PM1, PM2.5 and PM10 particles were collected in Teflon filters using low flow air samplers in two air pollution monitoring stations, representative of urban/residential and traffic influenced pollution respectively.

Nineteen individual PAHs were analyzed by GC/MS and concentrations in air were calculated for both monitoring stations. Potential cancer risk due to exposure to the mixture of urban ambient air PAHs was calculated using the toxicity equivalent factor (TEF) approach based on Benzo(a)pyrene (B[a]P) (Figure 11).

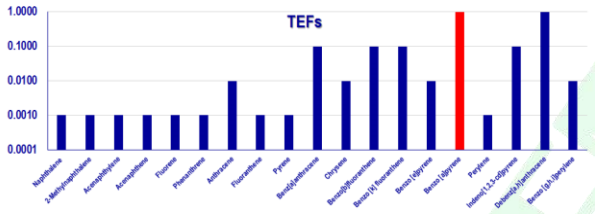

Figure 11. Toxic Equivalent Factors (TEFs) for the different PAHs, on the assumption that the TEF for B[a]P is equal to 1

The TEQ (Toxicity Equivalent Quotient) (carcinogenicity equivalent, in ng/m^3) was calculated by multiplying the concentrations of each compound in the PAH mix with the respective TEF for cancer potency relative to BaP. Daily inhalation rate (*IR*) and deposition fractions of particulate matter to the main regions of the respiratory system were calculated for eight age groups of human population. The ultimate cancer risk was estimated for each age group using the CEPA Inhalation Unit Risk (*IUR*) for B[a]P.

The results showed that PM (PM1, PM2.5, PM10) and PAHs concentrations, during the cold period, were higher in the urban background monitoring station than in the traffic station. This pattern was attributed to biomass combustion, which can be considered as the primary source of PAHs in the populated areas of Thessaloniki during the last two years winters. PAH and levoglucosan levels were highly correlated, indicating that particles emitted from biomass combustion are more toxic than PM emitted from other sources. The median ΣPAHs levels at the urban background site are 8.31, 9.82 and 9.91 ng/m^3 for the PM1.0, PM2.5 and PM10 fraction respectively. At the traffic station, the corresponding levels are 2.82, 3.52 and 3.92 ng/m^3 (Figure 12). Therefore, practically, most of the PAHs are adsorbed in fine particles (PM2.5 and finer).

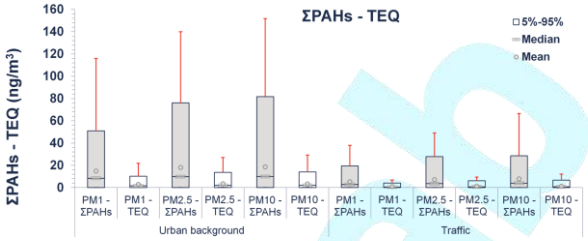

Figure 12. Total PAHs concentrations for the two monitoring stations

At the urban background site median TEQs are 1.61, 1.93 and 1.96 ng/m^3 for PM1.0, PM2.5 and PM10; the corresponding values at the traffic site are 0.43, 0.63 and 0.69 respectively (Figure 12). The TEQ at the urban background monitoring station is 3 times greater than the equivalent value found at the traffic station. TEQ/PM ratios at the urban background site are 0.091, 0.083 and 0.066 ng/μg PM for PM1, PM2.5 and PM10 respectively. At the traffic site, the respective ratios are 0.045, 0.44 and 0.032 ng/μg PM.

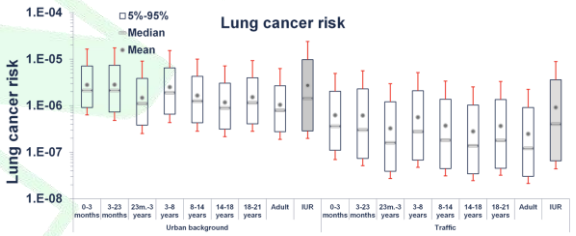

Figure 13. ICR calculated for each age group

The estimated lung cancer risk was non-negligible for residents close to the urban background monitoring site. Higher risk was estimated for infants and children, due to the higher bodyweight normalized dose and the human respiratory tract (HRT) physiology. HRT structure and physiology in youngsters favor deposition of particles that are smaller and more toxic per unit mass. In all cases, the estimated risk (5.7E-07 and 1.4E-06 for the urban background site and 1.4E-07 to 5.0E-07 for the traffic site) was lower to the one estimated by the conventional methodology (2.8E-06 and 9.7E-07 for the urban background and the traffic site respectively) that is based on Inhalation Unit Risk; the latter assumes that all PAHs adsorbed on particles are taken up by humans. With the methodology proposed herein, the estimated risk presents a 5 to 7 times difference between the two sampling sites (depending on the age group). These differences could not have been identified had we relied only on conventional risk assessment method. Consequently, the actual cancer risk attributable to PAHs on PM emitted from biomass burning would have been significantly underestimated.

CheRRIE

Chemical and Radiological Risk in the Indoor Environment

The Chemical and Radiological Risk in the Indoor Environment (CHERRIE) is an 18-month project funded under the European Territorial Cooperation Programme Greece- Bulgaria 2007-2013 INTERREG IV programme. The project overall budget is 1,226 K€ and will be funded by ERDF with a total contribution of 1,042 K€. Cherrie started officially on February 28, 2014. Four Greek and two Bulgarian partners will participate; the lead beneficiary is the Bulgarian Academy of Sciences and EnvE-Lab assumes the scientific coordination of the project.

This project will perform a thorough assessment of the current chemical and radiological risks of building materials and will set up a comprehensive database of building material properties that would affect the respective attributable risk.

The main expected results will be the improvement in the quality of the materials used in building construction and/or refurbishing in the trans-boundary regions resulting from a more systematic and thorough information available to the building constructors who will be able to base their purchasing decisions for raw materials on the findings of this study and avoid those that are found to have increased levels of radioactivity and chemicals emissions.

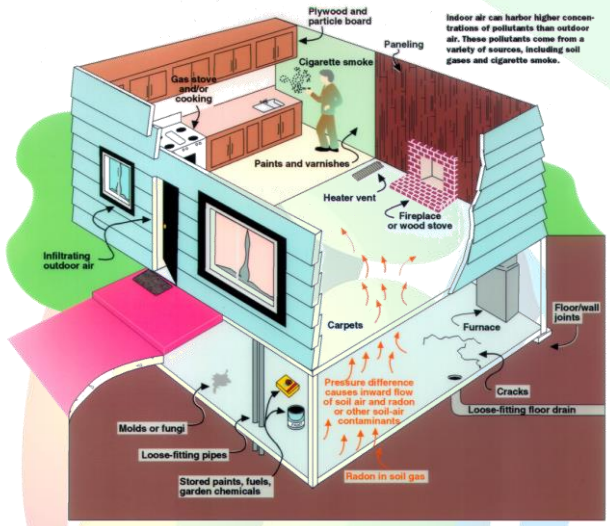

Figure 14. Typical sources of air pollution within a residential building

Quantitative health impact related to the use of building materials will be quantitatively assessed calculating the final radiological and toxic burden of the population from exposure to ionizing radiation of radionuclides and toxicants in different places both in Greece and Bulgaria. The final results expressed as an annual dose rate (external gamma-radiation, radon, VOCs, formaldehyde and other carcinogens and allergens indoors), illustrating the final whole body burden of the population compared to the international standard of radiological protection (in the case of radiological hazards) and reference doses or their biomonitoring equivalents (in the case of chemical hazards). The system for human exposure to indoor physical and chemical stressors/ health impact assessment and management will be largely based on already existing computational and data reception/management platform (INTERA) developed by EnvE-Lab in the frame of the CEFIC-LRI funded project INTERA.

The first set of measurements campaign in Thessaloniki included emissivity analysis of a long list of basic and artificial, as well as other type of other materials such as floorings, gypsum products and plaster boards, paints and varnishes and wood based panels, as well as in situ measurements 50 residential locations of non-smokers (aiming at capturing only the contribution of building materials) were sampled, including different type of residential buildings.

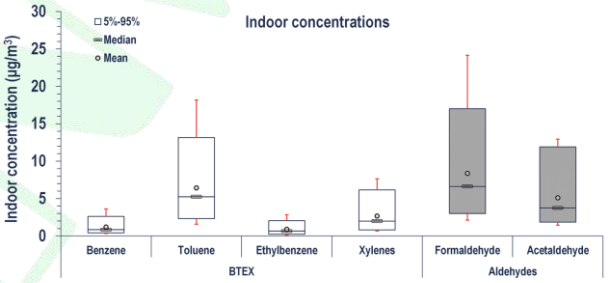

Figure 15. Indoor air levels of BTEX, formaldehyde and acetaldehyde attributed to building materials

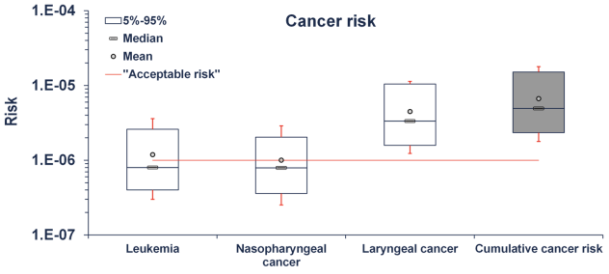

Figure 16. Estimated cancer risk in the residential area of Thessaloniki

Calculated risks are on the order of 10-6 related to benzene and formaldehyde exposure, and around 10-5 regarding exposure to acetaldehyde. However, we need to mention that the existing methodology for acetaldehyde is quite conservative, overestimating actual risks compared to the ones related to benzene and formaldehyde. In any case, it is advisable to avoid combination of materials that result in high levels of indoor air VOCs concentration, aiming to minimize the cumulative cancer risk.

INTEGRA

Integrated External and Internal Exposure Modelling Platform

The INTEGRA project -

The *Integrated External and Internal Exposure Modelling Platform* (INTEGRA) is a project funded by the CEFIC-LRI programme, aimed to bring together all available information within a coherent methodological framework for assessing the source-to-dose continuum for the entire life cycle of substances covering an extensive chemical space (www.integra-lri.eu). The major component of INTEGRA will be a flexible and user-friendly web-based computational platform that integrates environmental fate, exposure and internal dose dynamically in time allowing to differentiate between biomonitoring data corresponding to steady exposure patterns as opposed to acute, one-off exposures (Figure 17). The platform will be largely validated using human biomonitoring data from Europe and the USA.

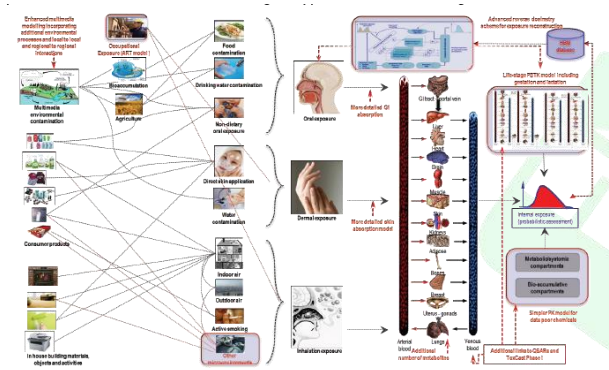

Figure 17. INTEGRA conceptual representation

The project started on January 1, 2013 and has a total budget of 299 K€ entirely funded by CEFIC for a duration of 27 months with the participation of four leading Institutions in Europe coordinated by EnvE-Lab.

The INTEGRA methodology (and the relevant computational platform) is a clear advance in terms of indoor micro-environmental interactions (contamination exchange between gaseous, particles and dust phases, chemical reactivity), towards an integrative exposure assessment framework which allows to capture the dynamics of biological processes involved and to reduce unnecessary conservatism contributing to a more comprehensive cost/benefit analysis and efficient risk management.

INTEGRA allows the multimedia interaction between different spatial environmental scales, taking into account environmental releases and related processes at global, regional and local scale, up to the level of personal microenvironment. In addition, the implementation of equally refined tools for internal dosimetry, allows Risk Characterization based on internal dosimetry metrics; these provide the capability to exploit the Tox21 *in vitro* testing results, providing a new Tier of analysis that incorporates refined exposure (tissue dosimetry) and toxicity testing (Biological Pathway Altering Dose – BPAD), starting from multiple scales environmental contamination.

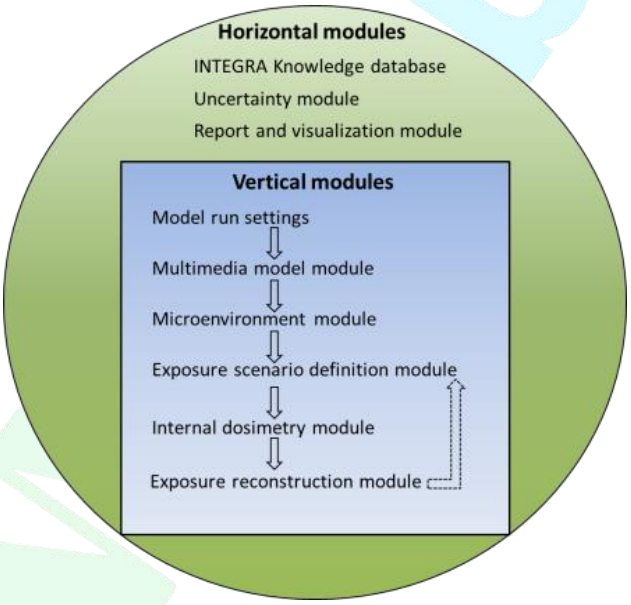

Figure 18. Modules of INTEGRA computational platform

The functional specifications of the INTEGRA computational platform has been defined after extensive consultation with identified stakeholders. To this aim a series of international scientific events were followed and co-organised by the INTEGRA team during the year to better embed the work of the project within international efforts towards improved risk assessment of chemicals. The INTEGRA platform will be a multimodular software following the open architecture paradigm especially designed to execute aggregate exposure assessment. The platform will enable the integration and assimilation of model and data needed to execute a "full-chain" aggregate exposure assessment focusing on both environmental and occupational exposure to a single chemical. It will encompass three horizontal modules and six vertical modules, each addressing a step along the source-to-dose (external and internal) continuum (Figure 18).

QSARs

A major area of work within the INTEGRA project is the development of Quantitative structure–activity relationship models (QSARs). QSAR models are regression or classification models used in the chemical and biological sciences and engineering. QSARs form a relationship between biological effects and chemistry of each chemical and comprise three parts:

- The activity data to be modeled,

- The data with which to model and
- A method to formulate the model.

The biological effects are normally the property to be modeled, which are linked with the physical or structural chemistry of the molecules. QSAR methods are used particularly for the estimation of physicochemical properties, biological effects as well as understanding the physicochemical features governing a biological response.

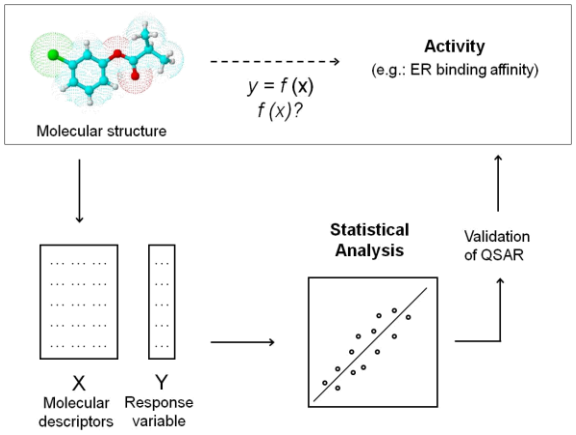

Figure 19. Basic methodological scheme for deriving a QSAR

The input parameters required for solving the set of Physiologically Based Pharmacokinetic (PBPK) model equations are either species- specific or chemical-specific and should reflect biological or mechanistic determinants of absorption, distribution, metabolism and elimination (ADME) of the chemical being modeled. The species-specific parameters, for example, relate to alveolar ventilation rate (Q_p), cardiac output (Q_c), tissue blood flow rates (Q_t) and tissue volumes (V_t) should be within the documented range for the particular species and life stage. The chemical-specific input include partition coefficients (blood:air (P_{ba}), tissue:air (P_{ta}) or tissue:blood (P_{tb})) as well as metabolic parameters such as the maximal velocity (V_{max}) and Michaelis affinity constant (K_m) or the intrinsic clearance (V_{max}/K_m). These physicochemical parameters should have been obtained on the basis of independent measurements (in vitro, in vivo) or using algorithms in the valid domain of application, like QSARs. In particular, in the case of a chemical for which pharmacokinetic parameter database is either incomplete or lacking, the internal dose cannot be reliably estimated. The internal dose measure associated with a particular exposure scenario could vary from anywhere between zero (theoretical minimum) and the potential dose (theoretical maximum). This large uncertainty is due to the fact that there is a lack of precise knowledge regarding the key chemical-specific determinants of ADME. Since these parameters, together with the physiology of the animal species, determine the pharmacokinetics of chemicals in biota, integrated QSAR-PBPK models can effectively predict or identify the possible range of internal dose.

EnvE-Lab research focuses on the estimation of an expanded QSAR model in order to predict physicochemical parameters of a large group of chemicals. Up until now, a unified algorithm by Peyret, Poulin and Krishnan has been examined, which is applied both for environmental chemicals and drugs and predict the rat tissue:blood, tissue:plasma water and tissue:plasma partition coefficients for liver, muscle and adipose tissue. The predicted values are very close to the experimental ones, obtained from literature. Generally, the algorithm applies quite well to acidic compounds and neutrals. It should be mentioned that there have to be improvements regarding the prediction of strong bases' parameters.

Furthermore, attention is given at Abraham's solvation equation:

$$\log SP = c + r \cdot R_2 + s \cdot \pi_2^H + a \cdot \Sigma\alpha_2^H + b \cdot \Sigma\beta_2^H + v \cdot \log V_x$$

where SP: a biological property for a series of solutes.

The equation above can be solved by multiple linear regression (MLRA), to yield the constants c, r, s, a, b and v, which are used to characterize the receptor area involved. Not every term in the equation may be significant, and each term is analyzed using students t-test. The properties of the solvent phase are constant and the various interactions are described by particular solute parameters, namely:

R_2 is an excess molar refraction that can be determined simply from a knowledge of the compound refractive index, π_2^H is the compound dipolarity/polarizability, $\Sigma\alpha_2^H$ is the solute effective or summation hydrogen-bond acidity, $\Sigma\beta_2^H$ is the solute effective or summation hydrogen-bond basicity, V_x is the McGowan characteristic volume that can trivially be calculated for any solute simply from a knowledge of its molecular structure.

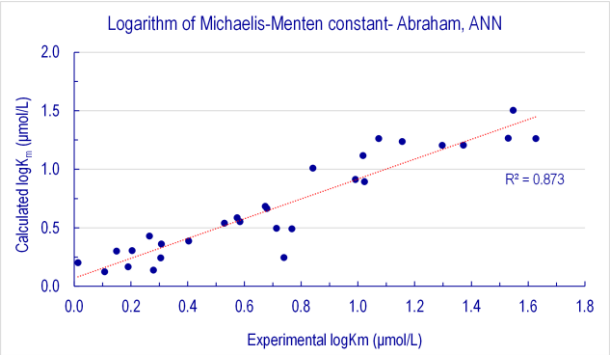

Figure 20. Observed vs predicted Michaelis - Menten constant values for selected low volatile compounds

Up to now, these QSARs seem to perform well for a number of chemical families, relevant to the aims of INTEGRA.

A major breakthrough came from the use of Artificial Neural Networks coupled to Abraham's solvation equation for predicting biological/biochemical properties such as blood-tissue partition coefficients, Maximal Velocity (V_{max}) and Michaelis - Menten constant.

This was a remarkable advance, since till now, prediction capability of the Michaelis - Menten constant was rather poor (R^2 up to 0.35); with our coupled ANN - Abraham's solvation equation method for the investigated group of chemicals R^2 went up to 0.87 (Figure 20), which is by far higher to any other existing methodology.

The improved performance of ANN-Abraham's equation combination can be ascribed to its capacity to represent mathematically the complex interactions of biochemical micro-processes, which are lumped into the Michaelis-Menten constant.

Exposure reconstruction

The establishment of relationships among events along an exposure chain, health evaluation as well as risk assessment is the key issue to understand how the exposure of environmental chemicals effect on public health. Although daily, Biomonitoring Data (BD) are reported in order to evaluate the internal exposure, the gap between the correlation of external exposure and BD stills remain. That procedure to estimate the relationship between internal and external exposure is termed as "Exposure Reconstruction" (ER) or "reverse dosimetry". Exposure reconstruction is an ongoing scientific research field and various computational techniques have been formulated such Deterministic Inversion, Stochastic Inversion/Bayesian Approach, Exposure Conversion Factor Approach, Discretized Bayesian Approach and Bayesian Markov Chain Monte Carlo in order to give a solution to the problem.

Considering that these techniques are the foundations for developing new and improved approaches ER, a conceptual/computational framework was been developed based on Bayesian Markov Chain Monte Carlo combined with a generic Physiological Based Pharmacokinetic (PBPK) model (Figure 21).

The analysis of the developed ER framework consists of 3 basic steps. At first the prior parameter distribution, the joint probability distribution, the population model and the determination of the measurement model have to be specified.

At the next step exposure is calculated using MCMC simulation considering the observed biomonitoring data. Finally, the evaluation of the results is realized using MC simulation, with emphasis to the comparison of prior and posterior distribution as well as parameter independence.

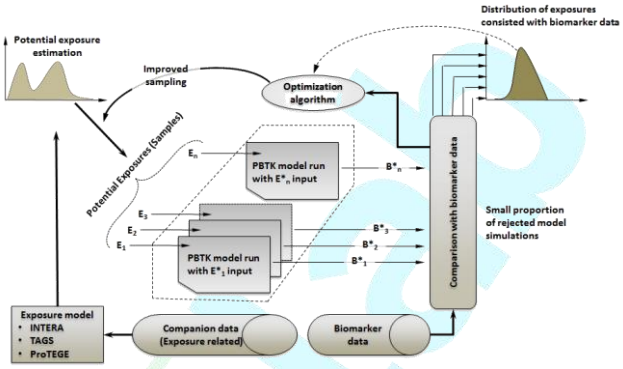

Figure 21. Optimization-aided exposure reconstruction based on HBM data using time-evolving PBPK models

MCMC simulation (Figure 22) refers to a class of iterative simulations in which the random variables of interest are drawn from a sequence, or chain, of distributions that eventually converge to a stable posterior distribution.

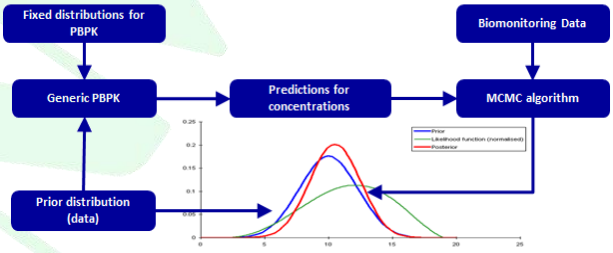

Figure 22. Conceptual/computational framework for the exposure reconstruction

Moreover, Differential Evolution (DE) and MCMC algorithms have been combined to this problem for the first time. Differential Evolution Markov Chain is a population MCMC algorithm, in which multiple chains run in parallel. In fact DE is a simple genetic algorithm for numerical optimization in real parameter spaces. As a result, this combined computational framework speeds up the calculation and convergence, even for nearly collinear parameters and multimodal densities.

The results of the simulation corresponded very well to a dataset of synthetic data, as well as to real biomonitoring data (Figure 23).

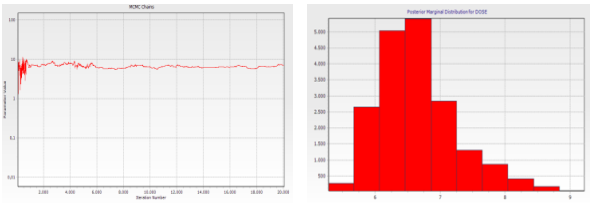

Figure 23. MCMC simulation convergence and Posterior Distribution for dose

URGENCHE

Urban Reduction of GHG Emissions in China and Europe

URGENCHE is a project aiming to develop and apply a methodological framework for the assessment of the overall risks and benefits of alternative greenhouse gas (GHG) emission reduction policies for health and well-being in China and Europe.

Under the perspective of urban transportation, the co-benefits to urban air quality, noise and public health were investigated from the introduction of greenhouse gas (GHG) emission reduction policies to the city of Thessaloniki and the Great Thessaloniki Area (GTA). The traffic related policies implemented, included the introduction of underground rail in the city centre and changes in vehicle composition, i.e. allowing a larger share for the diesel engine passenger cars, the hybrids and the electric cars.

Air and noise pollution were assessed for a baseline scenario in year 2010 and two future scenarios in year 2020, a business-as-usual (BAU) and a GHG emission reduction scenario (CO2 scenario). This assessment was carried under an integrated methodological framework, composed of a series of interconnected models and repeated for the years 2010 and 2020. The models used, included the (a) SIBYL, to project vehicle stock numbers; the (b) VISUM, to simulate traffic flow as a result of changes in travel demand; the (c) COPERT IV, to compute the pollutant emission (PM10, PM2.5, NO_2, NO_X, O_3, CO and benzene) per vehicle engine and type; the (d) OSPM to compute pollutant concentrations in traffic corridors; the (e) CALPUFF, to compute pollutant concentrations on motorways and urban/peri-urban roads; and the (f) NMRB-2008, noise model to evaluate traffic noise generation and its propagation from traffic corridors and motorways under the ISO 9613-1 and the 9613-2 constraints.

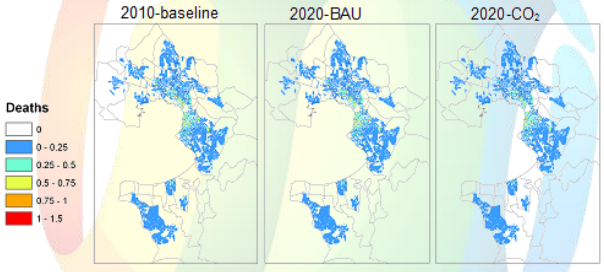

Figure 24. Spatial distribution of annual number of deaths attributed to PM_{10} in 2010, 2020-BAU and 2020-CO_2

Exposure to air population was assessed via the inhalation pathway and its health impact was estimated by concentration response functions on high resolution population data (per building block, differentiated by age and gender). The health end points computed include annual mortality attributable to PM10 and NO_2 exposure and the leukemia lifetime expected cases due to benzene exposure, which were aggregated at the municipality level (Figure 24).

Noise was computed from the shortest distance of Source (e.g. motorway) to the Receptor (e.g. building block of a particular height) and its exposure was weighted by the population and differentiated between each municipality in the Thessaloniki Area. The health end points computed include, sleep disturbance, sleep annoyance due to road transport and myocardial infractions.

The impact of the Greenhouse Gas (GHG) emission reduction scenarios to health was identified to be significant. Simulations show that traffic flow will decrease by 33% on roads in direct proximity to the metro line (e.g. Monastiriou, Egnatia, Nea Egnatia, Delfwn), by 44% on roads within the historic center and by 22% in all adjacent roads to the historic centre. These reductions in flow were further amplified by changes in the traffic mode, where diesel, hybrids and electric cars will constitute 22%, 7.7% and 2% respectively, to the total vehicle fleet.

It was estimated that for the municipality of Thessaloniki, the expected decrease (%) in the annual number of deaths for the GHG scenario were 8% and 11% attributed to the PM10 and NO_2 respectively and 27% to the leukemia lifetime expected cases due to Benzene. In comparison, for the municipality of Panorama, the expected % decrease in the annual number of deaths for the GHG scenario are 1% and 23% from PM10 and NO_2 respectively and 33% to the leukemia lifetime expected cases due to benzene (Figure 25).

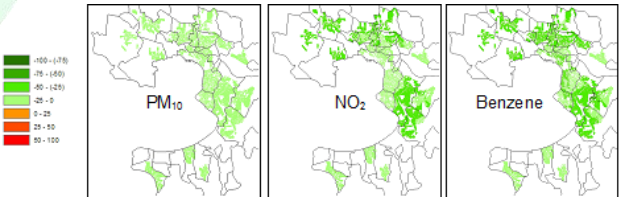

Figure 25. Decrease (%) in the annual number of deaths for the GHG scenario

Similarly the highest reductions in sleep annoyance due to road transport noise and the myocardial infractions were identified in the municipality of Thessaloniki, where the aforementioned policies have the highest impact.

ICSHNet

Industrially Contaminated Sites and Health Network

The Industrially Contaminated Sites and Health Network (ICSHNet) is a four-year-long COST Action due to start in the beginning of 2015. The Network is coordinated by the Istituto Superiore di Sanità (Italy) and aims at establishing and consolidating a European Network of experts and institutions involved in assessing the health impacts and/or managing remediation and response in industrially contaminated sites.

cost
EUROPEAN COOPERATION
IN SCIENCE AND TECHNOLOGY

Figure 26. The cost logo

This will be achieved by developing a common framework for human health exposure and risk assessment through conferences, workshops, training and dissemination activities.

To implement the scientific programme ICSHNet involves 65 members from 15 different COST countries and it is structured in four working groups: WG1 – Environment and health data; WG2 –Methods and tools for exposure assessment; WG3 – Methods and tools for health risk and health impact assessment and WG4 – Risk management and communication.

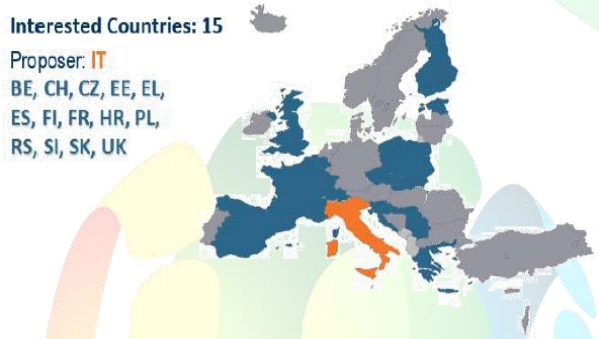

Figure 27. Participant countries of the ICSHNet

Through expert networking, conferences, workshops, training and dissemination activities, ICSHNet aims at clarifying knowledge gaps and research priorities; supporting collection of relevant data and information; stimulating development of harmonised methodology; promoting collaborative research initiatives, developing guidance and resources on risk assessment, management and communication and creating the conditions for the undertaking of comparable health impact assessments of contaminated sites in Europe and beyond.

Figure 28. A typical industrially contaminated site in Italy

Expected outcomes of the networking activities include:

1) guidelines, evidence-based reviews, compilation of case studies on: (a) strategies for studying environment and health in contaminated sites, focusing on methodology; and (b) strategies for risk management and communication;

2) resources, materials and training modules on: (a) approaches and methods to be applied in different sites and contexts; and (b) risk management and communication strategies;

3) expert consensus on methodology for exposure assessment;

4) expert consensus on methodology for health assessments that allows: (a) the separate analysis of population subgroups (in particular, children), and (b) consideration of social gradients, confounding and interactions with socioeconomic factors and social health determinants;

5) plans of a system, criteria and requirements for collecting and compiling data and producing comparative analyses of the health impact that different industrial sources of contamination have within and among different European countries, allowing for the inclusion of socioeconomic factors.

This COST Action intends to provide an appropriate framework to collect the contribution from different countries and disciplines, aiming to overcome fragmentation in the existing research approaches, and integrating approaches for a better exploitation of existing datasets (air, soil, water and food chain) in characterizing human health exposure assessment in response to the priorities of EU legislation and EU Programmes.

Advanced satellite data fusion

PM estimation and related health impact assessment

The method developed in the frame of the EU-funded projects ICAROS, ICAROSNET, SMAQ and HEREPLUS dealt with the development of a novel methodology which integrates ground-based measurements, atmospheric transport modeling results and satellite-derived information through a range of data fusion techniques to provide a comprehensive estimate of tropospheric pollution from particulate matter at different spatial and temporal resolutions at the urban to regional scales. Linking the latter with epidemiological data and activity modeling, allows reckoning the geo-referenced health risk to population form fine and ultra-fine PM.

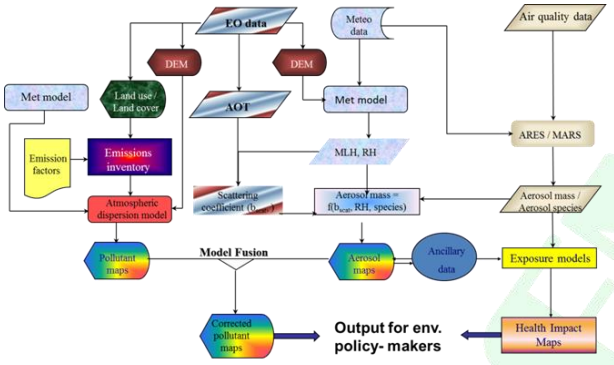

Figure 29. Conceptual representation of the advanced satellite data fusion system

High resolution sensors can provide high spatially resolved data but generally lack of high temporal resolution making them inappropriate for routinely operational use in air quality management; on the contrary moderate spatial resolution sensors have the capacity to provide images with high temporal frequency having a coarser spatial resolution as a major drawback. The developed methodology combines the use of both the above types of sensors providing a powerful tool for assessing and managing air quality at different spatial and temporal resolution. The methodology we developed was applied in Athens (Greece), Munich (Germany), Rome (Italy), Budapest (Hungary), the region of Western Macedonia (Greece) and Lombardy (Italy) covering a broad spectrum of climatic conditions, pollution patterns and land use types. The results converge towards a theoretical model that explains the link between the optical signal retrieved by satellites sensors and the mass concentration of tropospheric aerosol.

The key to the success of the data fusion approach developed is the combination of physical and chemical process modeling that allows linking physical (e.g. optical) properties of tropospheric aerosol with the atmospheric physical-chemical processes that determine total mass concentration, size distribution and chemical composition of particulate matter. The method permits the estimation of PM concentration from high to moderate spatial resolution ranging from 10 m to 4 km covering a domain as large as 80-100 x 80-100 km^2.

Results showed that the conceptual model for tropospheric aerosol formation and fate in the atmosphere that has been developed allows highly accurate estimates of particulate pollution and their health effects at high to moderate spatial resolution providing a valid approach for overcoming the pitfalls of current atmospheric observation systems and allowing to reduce the overall error to levels lower than the current atmospheric models as well as the pollutant concentration maps produced by spatial interpolation of measurements from the ground.

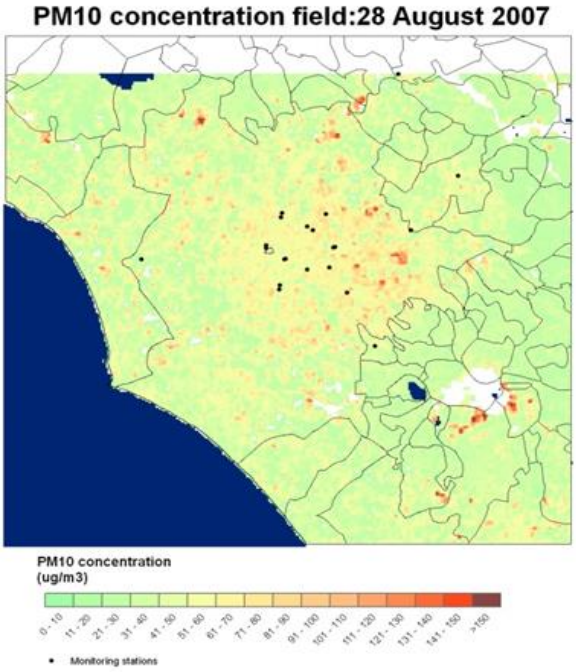

Figure 30. Application of the fusion system in Rome

Its translation into a prototype computational platform is being used in W. Macedonia, Greece, where it has proven its efficacy in accurate estimation of tropospheric aerosol. Its use represents a valid alternative to conventional air quality monitoring, which necessitates the employment of dense and, thus, costly analytical measurement networks reducing significantly the operational cost of air quality management. Moreover, the derivation of high precision and high resolution estimates of PM mass concentration can support the optimization of air quality monitoring networks using Earth observation data as input relieves the monitoring from its most significant bias: the location of the monitoring stations, which are used to give the basic information on the spatial distribution of particulate pollution.

Indoor environment multiple risks

Combined or multiple exposure to health stressors in indoor built environments

The objective of this study (a task assigned by WHO to EnvE-Lab) was to undertake, summarize and present a systematic review of literature and project reports presenting evidence on multiple or combined risk exposure in indoor built environments. The review covered safety threats and injuries, indoor air pollution, use of household chemicals, noise, damp and mould, thermal conditions, crowding, inadequate hygiene standards, and harmful building and equipment/furnishing materials.

There is a lot of evidence and studies on non-occupational indoor risks. Often, however, the focus is on health outcomes of exposure to single stressors and multiple risks are often related to confounding in epidemiological studies. As a consequence, these studies, do not necessarily provide a good overview of multiple exposure to these health stressors and their association to adverse health outcomes per se. In fact aside of simple additivity of effects and some specific cases of exposure to at most two simultaneous stressors, which may enhance or counteract each other, the actual evidence on health effects of co-exposure to multiple stressors is limited.

Among the several health threats, exposure to multiple chemical agents still remains the silent threat: poor indoor environment quality (in terms of exposure to chemicals) is not always perceived by the occupants. As a result, occupants are continuously exposed to a cocktail of carcinogens (benzene, formaldehyde, PM-PAHs) and endocrine disruptors (phthalates, PCBs). The combined effects of these chemicals are still not sufficiently elucidated, since their physic-chemical and biochemical properties would favor multiple ways of interaction upon human uptake (Figure 31); there might be synergies in effect (e.g. PAHs and nitrosamines of ETS, both causing lung cancer), or they might inhibit each other's metabolism – this is the case for the almost ubiquitous indoors BTEX mixture. In any case, although further investigation on the mechanisms elucidating mixture toxicity is needed, no significant departure from additivity in the health effect assessment was observed for the concentrations encountered usually in non-occupational settings.

Combined exposure to chemical and biological agents in the indoor environment may result in increasing risk of adverse health effects. A case that stands out in this context, is the study of co-exposure to chemicals from carpeting and mould, which was conclusively shown to produce adverse health effects beyond additivity; indeed the observational data hint to synergistic mechanisms coming into play or to enhanced physiological susceptibility of adults to biological agents when co-exposed to phthalates and other organic chemicals emitted from building materials and consumer goods frequently used in residential settings indoors.

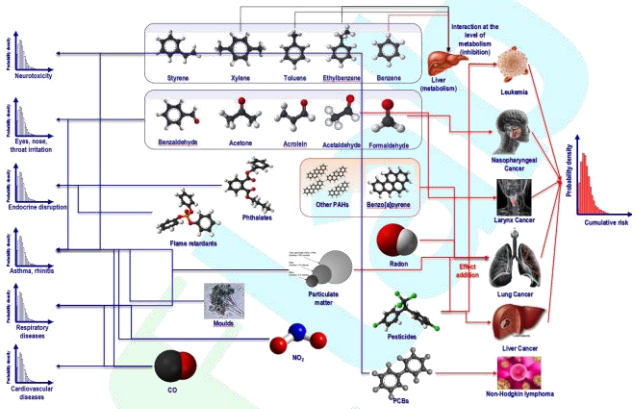

Figure 31. Multiple ways of interaction for chemicals

Children living in houses regularly cleaned with bleach and consequently exposed to volatile chlorination products were found to be less likely to have asthma and of being sensitized to indoor aeroallergens, especially house dust mite. These protective effects were independent of gender, ethnicity, previous respiratory infections, total serum immunoglobulin E (IgE) level and of family history of allergic diseases. Of great interest is the finding that the above protective effects were nullified by parental smoking, which also interacted with the use of bleach to increase the risk of recurrent bronchitis. Thus, cleaning with chlorine bleach appears to protect children from the risks of asthma and of sensitization to indoor allergens but when co-exposure to environmental tobacco smoke (ETS) occurs the risk of recurrent bronchitis increases.

Considering the complexity of the multiple stressors encountered in indoor environments, the proper identification of the effects of combined/cumulative exposure among them requires:

- integrated analysis of indoor environment quality assessment and other housing-related hazards clustered by type of indoor setting.
- identification of potential synergies of stressors on a mechanistic basis, using the latest advances in in vitro testing and computational toxicology.
- confirmation of these hypotheses by comprehensive environment-wide association studies (such as HEALS).

Human biomonitoring

Integrating exposure, biomonitoring and biokinetic modelling

Human biomonitoring to EDCs in Europe

A major contribution of EnvE-Lab in the human biomonitoring domain was the preparation of the report entitled "***Human biological monitoring of exposure to EDCs: current practices***", which was a review prepared for the WHO workshop "***Identification of risks of endocrine disrupting chemicals: overview of existing practices and steps ahead***", held in Bonn on July 7-8, 2014. The report presented a review of national and regional biomonitoring programs in several European countries, including the collation of the relevant data. The results showed that human exposure to endocrine disrupting compounds (EDCs) has significantly declined in the recent years, especially with regard to persistent and bioaccumulative compounds such as PCBs and perfluorinated compounds. This trend reflects the regulatory restrictions on the production and use of these chemicals.

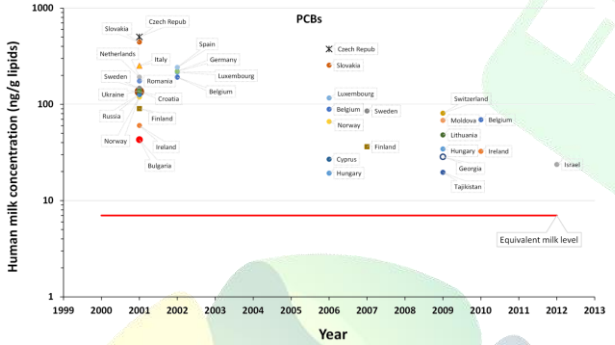

Figure 32. Time trend of PCBs in human milk for several countries of the European region

Regulatory interventions have resulted in similar trends in the case of non-persistent compounds such as phthalates (mainly DEHP) or bisphenol-A. However, restriction in the use of one chemical might lead to increased levels of a similar compound found in human biological matrices. For instance, phasing out of DEHP resulted in increased levels of DiNP, its substitute in many applications. A closer look at the HBM data across Europe shows that the effects of chemical usage restrictions are reflected later in the population exposure of countries with lower GDP per capita. This reveals a socio-economic dimension to chemical exposure that is worth further investigation for designing effective public health protection policies. Based on the lessons drawn from the detailed analysis of the current programs a step-by-step procedure for setting up a biological monitoring program for EDCs at the national or international (European) scale. A key conclusion from the overall study was that exploitation of biomonitoring data could be significantly enhanced using physiology based biokinetic models and advanced bioinformatics algorithms for efficient data mining. Using these computational tools, allows the better interpretation of the results, as well as the quantification of the factors modifying biomarker levels, comprising both time profiles of exposure and gene polymorphisms. The coupled use of well-designed biological monitoring with advanced bioinformatics and biokinetic modeling tools is expected to advance significantly our understanding of the interactions between environment and health.

Human biomonitoring practices in Europe

In an additional collaboration with the WHO, EnvE-Lab contributed to the report entitled "***Human biomonitoring: facts and figures***", providing insights related to the HBM concepts and methodology such as sample matrices in HBM, types of biomarkers and objectives and design of HBM surveys. Moreover, EnvE-Lab provided the overview and interpretation of available HBM data in the WHO European Region for organic compounds. Finally, the opportunities and challenges related to the application of HBM data for evaluating the associations between human exposure and human health were also presented. From the data it was identified that although the levels of persistent organic compounds tend to decrease, exposure levels associated to emerging compound tend to increase.

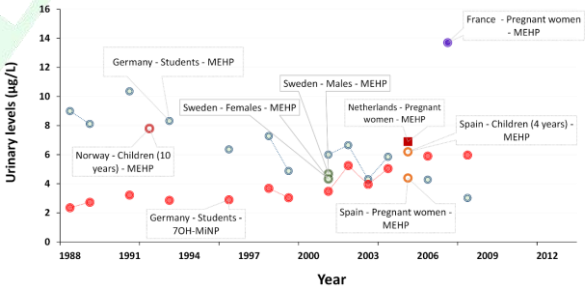

Figure 33. Time trend for the urinary concentrations of MEHP (DEHP metabolite) and MiNP (DiNP metabolite). The German ESB data indicate that MEHP (blue dots) is decreasing due to the continuous restrictions in DEHP use. On the contrary, MiNP levels tend to increase, reflecting the progressive replacement of DEHP by other phthalates such as DiNP

As a result, monitoring efforts should be continued under a more harmonized way. It is also of equal importance to use the necessary tools for data assimilation and association of these with health effects; it is noticeable that some epidemiological studies have demonstrated associations between (low-level) exposure and adverse health outcomes that were not expected under the current risk assessment evaluation schemes. This reflects the need for additional mechanistic interpretation of the data obtained from the current HBM schemes.

Exposure reconstruction of chloroform based on HBM data

Aiming at investigating the effect of domestic cleaning activities on children passive exposures to trichloromethane from their mere physical presence at home, we evaluated urinary TCM data from children and matched-mothers. In practice, using the children urinary chloroform levels, indoor air background chloroform concentrations were reconstructed. These concentrations were used for estimating mother exposure. Re-running forward the model using these concentrations levels as exposure for the mothers, their urinary chloroform was predicted, as well as the respective chloroform blood levels (internal exposure). Regarding our study on the effect of domestic cleaning activities, our analysis showed the valid use of urinary chloroform levels as a proxy to internal exposure to chloroform, but only if background exposure concentrations were considered. Given that chloroform are metabolized and excreted rather rapidly, their levels in morning urine reflect primarily indoor air concentration and, to a smaller extent, drinking water levels. Activities that lead to significant increase in chloroform release into the indoor air such as dishwashing, bleaching, showering, bathing etc. affect the observed biomarker levels, by raising the uptake rate of chloroform from the indoor air. Based on the urinary levels and by reconstructing exposure so as to fit the measured biomonitoring data, blood and exhaled breath chloroform levels were also calculated for the matched-mothers' and children.

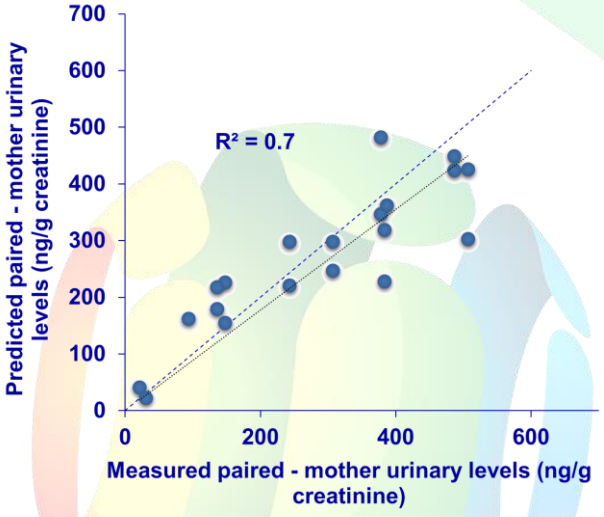

Figure 34. Measured vs. predicted urinary chloroform levels for the paired mothers, based on indoor concentrations derived from exposure reconstruction of paired-children data

In order to identify the contribution of In the current study highly dynamic exposure phenomena had to be investigated. Thus differences in: (a) intensity of activity (which is affecting inhalation rate, thus actual uptake, as well as elimination through exhalation) and (b) urinary excretion rate were incorporated as physiologic parameters in the model. This allowed us to better account for the effect of human physiology differences on the observed differences in TCM urinary levels. Thus we managed to attribute the exposure levels resulting in the observed urinary TCM levels more accurately. The effect of gender, age and activity intensity on inhalation rates was also taken into account. Excretion rates were estimated based on the measured urine volumes collected. When this data was not available, age and gender specific urinary excretion rates were used; this is because blood flow to the kidneys and the subsequent excretion rate are not altered by intensity of activity. By reconstructing exposure, it was found that the related cleaning activities contribute to different levels of chloroform exposure. Among these activities, mopping was found to result in exposure up to 15 μg/m^3, followed by showering. However, different cleaning activities affected differently the exposure of study participants; this reflects differences in the use of domestic products such as varying chloroform concentrations in the product used, the amount of products used, housing and ventilation conditions as well as physiological differences among the exposed subjects.

Translating urinary concentration into exposure levels, allowed us to estimate internal exposure as well. Cleaning activities resulted in chloroform blood concentrations close to 100 ng/L, while mopping seems to be associated to higher internal exposure levels; this is the result of the higher intensity of activity during mopping, when intake rate is increased due to increased inhalation rate.

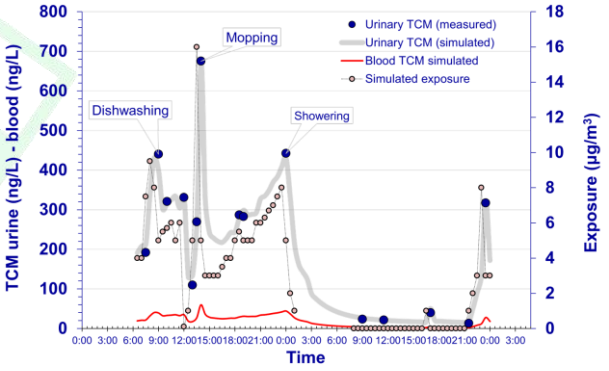

Figure 35. Measured urinary TCM (blue dots) and modelled chloroform levels in urine (grey line), blood (red line) and ambient air (dashed line)

However, potential differences in consumer product-related exposure (amount of product use, chlorine concentration of the product) and housing conditions (air exchange rate) act as confounders prohibiting the derivation of robust conclusions about the relative significance of the respective activities. In any case, we need to highlight that the use of a validated PBBK model allows us to use a biomarker acquired by a non-invasive technique (urinary chloroform), which is also one magnitude of order higher than the respective blood biomarker. This allows us to better differentiate exposure conditions and thus identify the contribution of cleaning activities in the overall exposure to chloroform.

Connectivity

Toxicology of chemical mixtures in the environment and consumer products

The advent of new technologies in biological science and in the improved understanding of the mechanisms of response to toxicological insults at different biological levels provides novel possibilities to improve the current state of the art in health risk assessment. In particular, the combined use of -omics methodologies including genomics, proteomics and metabolomics may help to approach the source-to-outcome continuum more effectively In addition advances in computational toxicology methods and biological modeling help put together a systems approach for the derivation of dose-response functions and their effective application in risk assessment. The translation of this integrated thinking into a new paradigm for modern toxicology is known as connectivity approach. The connectivity approach to mechanistically-based risk assessment of environmental chemicals both as individual and as mixtures can be tackled with an integrated, multi-layer computational methodology, ideally comprising the following steps (Figure 36):

- Characterization of exposure factors quantifying the parameters that affect human exposure to environmental chemicals, such as time-activity relationships, seasonal and climatic variation, and consumer choice. These exposure factors can be used to derive aggregate and cumulative exposure models, leading in probabilistic exposure assessments.
- Current toxicological state of the art combines estimations of biologically effective dose (BED) with early biological events to derive dose-effect models, which can be used in combination with the probabilistic exposure estimates to derive biomarkers of exposure and/or effect. Combined use of epidemiological, clinical and genetic analysis data may shed light on the effect of risk-modifying factors such as lifestyle choices and DNA polymorphisms. Observation of real clinical data and/or results of biomonitoring, if coupled with the exposure/effect biomarker discovery systems, can produce biomarkers of individual susceptibility and thus allow estimations of individual response to toxic insults. Toxicogenomics and in particular transcriptomics and metabolomics/adductomics, is key to this kind of analytical and data interpretation process.
- The integrated analysis of the biomarker data (including results on biomarkers of exposure, effects and individual susceptibility) results in the integrated assessment of risk factors. Use of information on risk factors with molecular dosimetry data (i.e., estimation of the actual internal and BED of xenobiotic substance found in the target organ and, indeed, perturbing cellular response) enables population risk studies to be done, by converting generic exposure profiles into population risk metrics having taken into account inter-individual variability of response and exposure uncertainty.

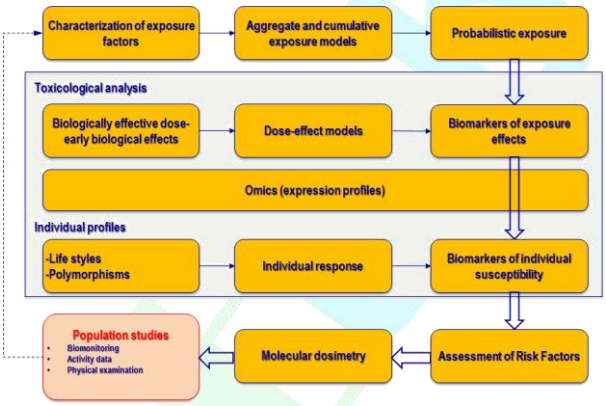

Figure 36. Connectivity – a multi-layered approach

Additional elements towards the implementation of the connectivity approach is the integration of multiple factors that comprise exposome, against genetics (e.g. susceptibility) and epigenetic alterations, in junction to dietary and other behavioral factors that affect overall exposure through metabolic profiling and systems biology integration (Figure 37). By understanding the individual exposome we can have a better understanding of the causal associations of individual disease, thus a more personalized prevention, as well as treatment of the disease. Personalized prevention and treatment are more efficient, thus improving overall health status and well-being, in addition to reduced socioeconomic burden from morbidity and mortality.

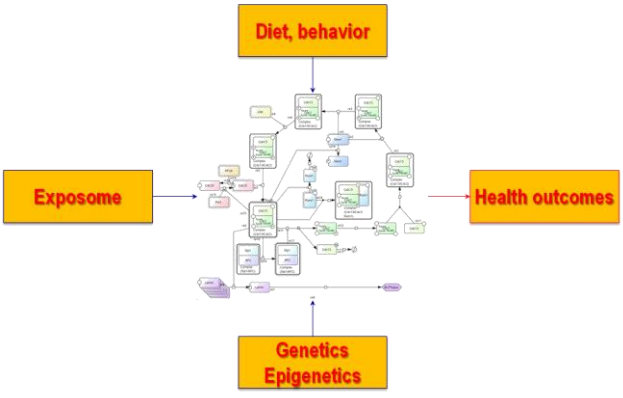

Figure 37. Metabolic profiling and systems biology integration

Sensors

Advancing personal and population exposure assessment

Technological advances in the recent years have produced sophisticated monitoring devices which can be carried or worn by a person during their regular daily routine allowing for personal exposure to be monitored explicitly. Smartphone apps, wireless devices and the downsizing of monitoring technologies and costs make it possible for various environmental stressors and exposure factors to be measured more easily and frequently, thus providing a more reliable "time–geography of exposure" shifting the current paradigm from a population to an individual level.

From an operational point of view personal sensors can be grouped according to the type of data they can provide: passive pollution measuring sensors which can measure the pollution levels encountered in the different locations where users spend their days, tracking location and physical activity sensors which provide information about the spatial patterns of user location and physical activity.

Direct reading monitors will help us to identify whether peak exposures are more important than average exposure values, identify specific exposure pathways that dominate in critical time windows over an individual's lifetime, and finally build individual exposure profiles. Combining information on individual position with spatially resolved pollution levels allows us to assign pollutant concentrations to a person as they move through different microenvironments. Moreover, information on individual physical activity as tracked by personal sensors allows the estimation of the breathing rates during different activities which in turns translated into inhaled dose.

This highly novel and promising approach will give us access to an unprecedented amount of "individualized exposure data," which could greatly improve our understanding of exposure and health associations but which are worthless without interpretation (e.g. human behaviour recognition). This requires statistical advances, sophisticated data mining techniques, computing power as well as a careful sharing of data sources while also maintaining privacy protections for personal data. Big data is difficult to be used with classical relational databases, desktop statistics and traditional visualization packages. What is common for big data treatment is that it is not just about storing huge amounts of data; it is the ability to mine and integrate data, extracting new knowledge from it. Appling this innovative framework to construct the individual exposome in the pilot EU-wide Exposure and Health survey (EXHES) as well as in the existing cohorts, HEALS will bring advances in this area to overcome the current limiting factors related to the analysis and the interpretation of the enormous wealth of data generated necessary to move the current approach from a population to a personalized level.

As part of the HEALS project, a preliminary study took place during the summer of 2014, aiming to examine the feasibility of using a series of sensors for tracking personal location and activities. Four participants in the city of Thessaloniki, Greece, wore a series of devices such as a) a temperature logger to detect changes between indoor and outdoor conditions, b) a commercially available fitness monitor to capture motion and intense of activity, c) a GPS device to track location and speed along with d) Moves, a smartphone application that enables tracking of location and activity. Additionally, a time activity diary was filled out on paper by participants for each day.

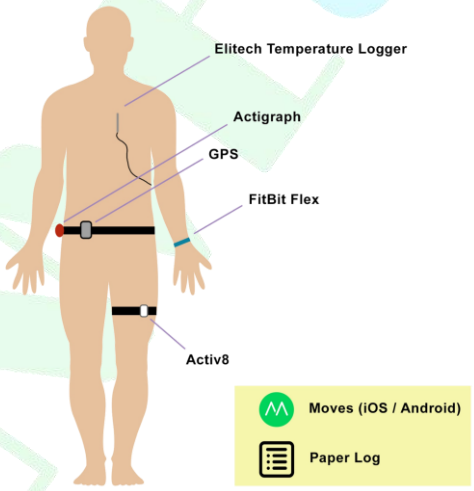

Figure 38. Overview of the personal sensors used during the preliminary trial campaign

Since location data alone does not reliably determine whether a person is indoors, outdoors or in transit, the predictive value of additional sensors data (e.g.: personal speed, personal air temperature and historical weather data) was explored using an Artificial Neural Network (ANN) model, aiming to derive to a time-activity model based *solely* on sensor data.

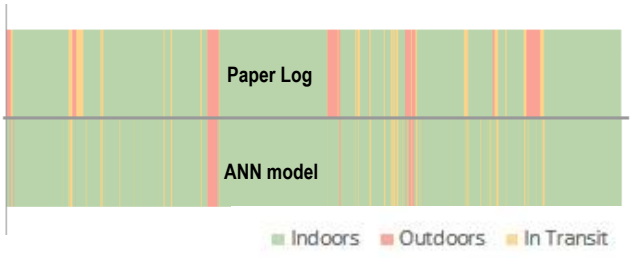

Figure 39. A visual comparison between the real location data and the predicted ones derived by the ANN model.

The independent variables that fed the ANN input layer were consisted of a) personal temperature, Temp, derived from the wearable temperature sensor, b) the change of temperature with time, dTemp/dt, c) personal speed, derived from the GPS devices wore by the participants,

Speed, e) the observed temperature, derived from a meteorological station located in the historical centre of Thessaloniki, $Temp_{out}$, d) and the ratio of the personal temperature to the observed one, $Temp/Temp_{out}$. Moreover, information on day light - whether it is day or night based on time - was transformed into a categorical element (day or night) which was also included as an input variable. The ANN predicted results were then compared to the real data based on time-activity log records that were filled out on paper by participants. The accuracy of the ANN predictions is close to 87%.

Using a Monte Carlo analysis, distributions of participant's movement and activities - derived from the sensors experiments - were extrapolated to a larger population. The final distribution of a representative sample helped us to define the way with which people are moving in space and time (what time they start/finish work/school, their speed) as well as their different types of activity (sleeping, working, resting etc.) within the boundaries of a city. This was valuable information that was then translated into moving agents inside an Agent Based Modelling (ABM) platform.

ABM is a modelling technique that simulates the actions and interactions of autonomous software objects, the "agents", enabling a better understanding of the behaviour of individuals and populations in social and evolutionary settings. The agents (which can be people, vehicles, roads, cities, animals, products, etc.) are programmed to react and act in their environment and to have goals that they aim to satisfy. An agent based model requires many simulations to evaluate any particular situation as it is based upon an underlying stochastic model. In this study we used the GAMA agent-based simulation platform that provides a complete modelling and simulation development environment for building spatially explicit multi-agent simulations.

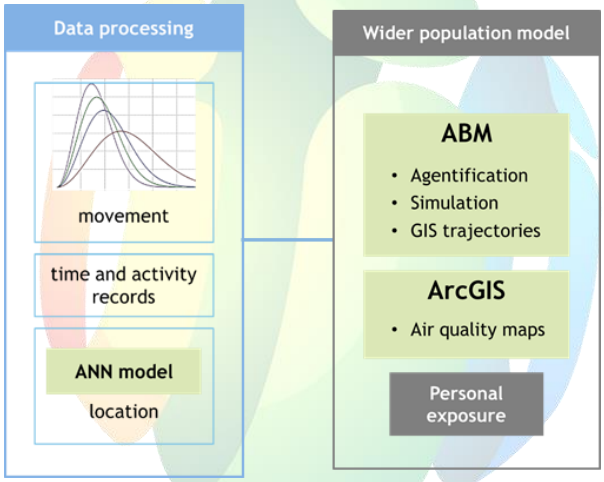

Figure 41. From sensors data to a personal exposure model.

By storing data in a geographic information system (GIS) format and using geographically explicit ABM architecture, the trajectory of an individual participant, "agent", was modelled and projected on a single layer, superposed onto urban air quality modelled maps of particulate matter PM10 concnentration in Thessaloniki. Personal exposure as well as inhale adjusted exposure to air pollutants was then evaluated by assigning pollutant concentrations to a person depending on his/her coordinates as well as their different activities, the level of intensity and the corresponding inhalation rate.

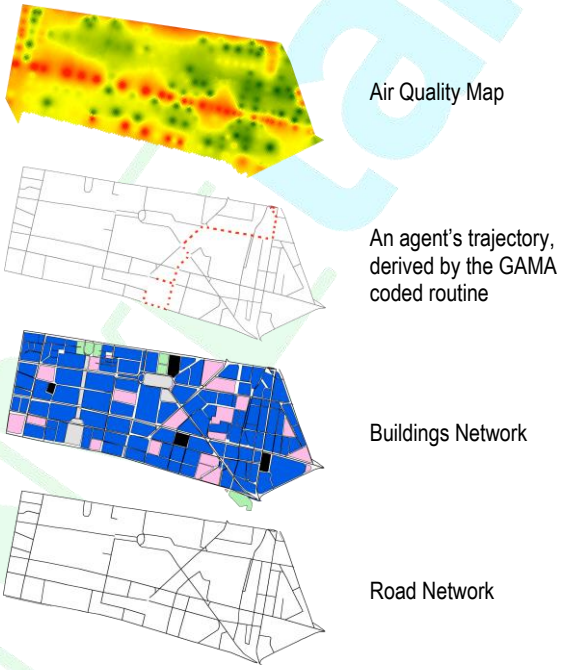

Figure 40. Exposure assessment using Agent Based Modelling (ABM).

This study represents the first step towards improving the calculation process of population exposure to environmental substances so that we would be able to draw better conclusions on the association between environment and health.

- The sensors investigations offer valuable information on the utility of several commercial devices as modular add-ons to exposure studies. It is clear that data collected by "smart" devices can help provide more accurate exposure assessment for exposure simulation modelling and epidemiology studies.
- the ABM approach brings a new way to study the complex systems, allowing to take into account the heterogeneity of the entities composing a system. Such a model would be useful for exposure assessment not only for population as a whole but most importantly, for specific vulnerable subgroups, such as children, the elderly and people with low socioeconomic status, taking into account their different activity patterns, consumer behaviors and other lifestyle factors.

Life cycle analysis of municipal waste management

Industrial symbiosis options for reduced ecological footprint

Municipal solid waste (MSW) management is nowadays one of the biggest problems in both developed and developing countries. Prevention, recycling, treatment and final disposal of MSW are regulated through a number of general policy principles and international directives.

It is imperative therefore to create awareness among local authorities, manufacturers, companies and generally society of the available varied technological solutions.

Integrated waste management solutions using the concept of industrial symbiosis (IS) have been developed and evaluated taking into account the European and national waste management legislation. IS, as part of the emerging field of industrial ecology focuses on the flow of materials and energy through local and regional economies. IS engages traditionally separate industries in a collective approach to drawing competitive advantage involving physical exchange of materials, energy, water, and/or by-products. The keys to IS are collaboration and potential synergies offered by geographical proximity and industrial function.

Life Cycle Assessment (LCA) provides the methodological framework. LCA is conducted according to ISO 14040 Moreover, LCA used to describe the environmental impacts of products and processes while assessing the material and energy flows throughout their lifetime.

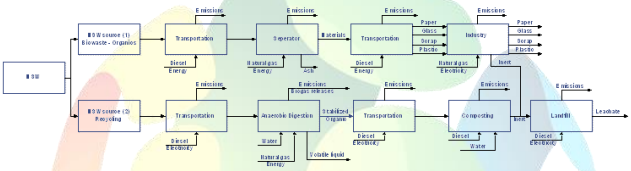

Figure 42. Waste management scenario: Waste is pre-treated and pre-sorted into biodegradable and non-biodegradable material for further anaerobic digestion and composting. Residues end in landfill. Plastic, paper and ferrous material are recycled.

Indicators of efficiency, effectiveness, and environmental and public health impacts are used to facilitate the comparative evaluation of the different MSW management scenario. Hence, material flow accounting, gross energy requirement, exergy and emergy intensity, local, regional and global emission and release intensity and morbidity or mortality indicators are used to support the comparative assessment.

The integrated framework was applied to the case of MSW management in the two larger cities in the country, Athens and Thessaloniki, with a special focus on energy and material balance, including potential global and local scale airborne emissions as well as groundwater and soil releases.

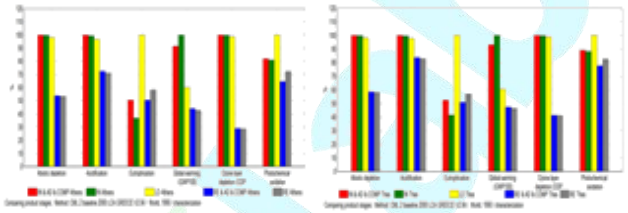

Figure 43. Impact categories of life cycle assessment for Athens and for Thessaloniki

Finally with regard to public health impacts, adverse effects on respiratory health, congenital malformations, low birth weight and cancer incidence were estimated.

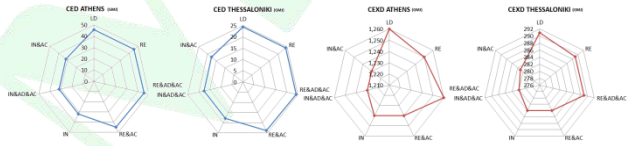

Figure 44 Cumulative Energy and Exergy Demand for Athens and for Thessaloniki

A significant and not intuitive result is the fact that integrated framework analysis produces different conclusions than a simple environmental impact assessment based only on estimated or measured emissions. Taking into account the overall life cycle of both the waste streams and of the technological systems and facilities envisaged under the plausible scenarios analyzed herein, modifies the relative attractiveness of the solutions considered. The results of the assessment based on selected impact indicators lead to the following conclusions: biological methods have the smallest abiotic matter, acidification potential, greenhouse gas effect, ozone depletion and photochemical oxidation among the waste management systems considered. In terms of energy and exergy demand biological methods prove to be more sustainable options. Landfilling was deemed the worst waste management strategy; other options for waste treatment coupled with energy and material recovery would result in very important benefits such as reduction of greenhouse emissions. However, not all options are benign to the local environment and to the health of the local population, since both can be influenced by non-negligible local emissions. As far as public health is concerned, adverse effects on respiratory health, congenital malformations, low birth weight and cancer incidences are still observed especially from incineration and landfilling.

Innovative waste management and energy recovery systems

Anaerobic digestion

Anaerobic digestion (AD) of organic material occurs in the absence of oxygen and the presence of anaerobic microorganisms. It occurs in three stages, Hydrolysis/ Liquefaction, Acidogenesis and Methanogenesis.

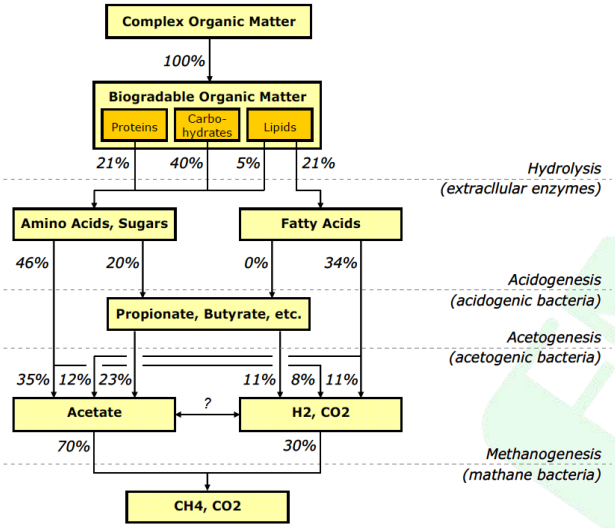

Figure 45. Anaerobic digestion process

The EnvE-Lab apparatus contains a system of coupled four anaerobic bioreactors, of 6.5 L in volume each, equipped with stirrers for waste agitation. The digesters are single- stage units, which can operate both as a CSTR and a Batch work reactors.

EnvE-Lab research deals with anaerobic digestion from biodegradable matter in order to produce biogas (waste to energy). In particular, the organic fraction of Municipal Solid Waste (OfMSW) was used as feedstock trying to optimize the reactor operation considering the percentage of wastes and inoculums.

The four anaerobic digesters give to EnvE-Lab the independence to compare different feedstock and conditions at the same time aiming at optimizing the design of integrated AD systems for different operational conditions, feedstock composition and treatment goals.

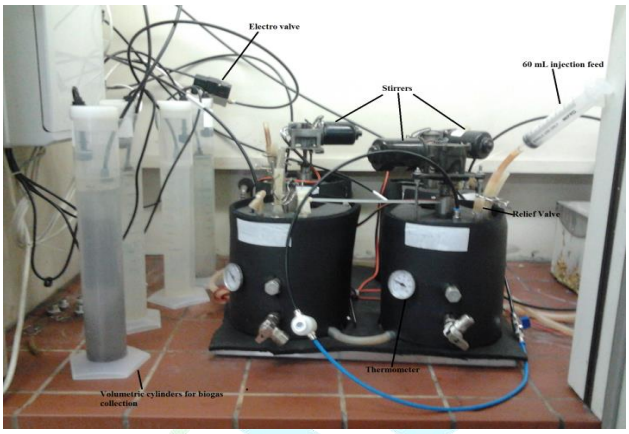

Figure 46. Anaerobic bioreactors

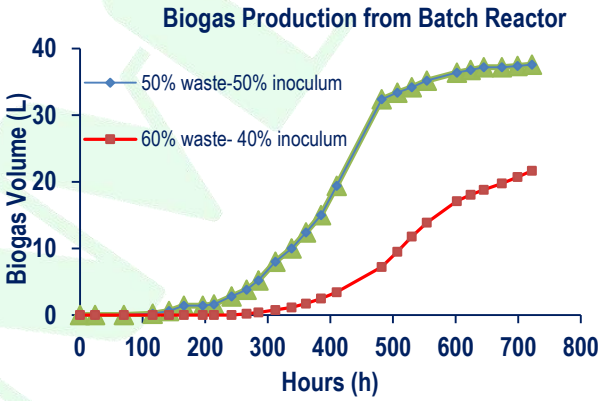

Figure 47. Biogas production from a batch work bioreactor using as feedstock the OfMSW 50% and inoculums 50%

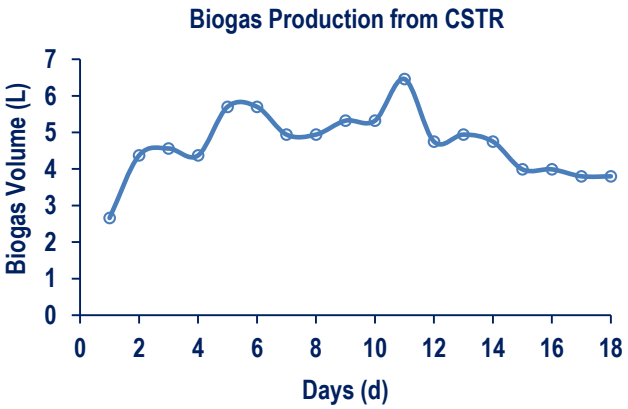

Figure 48. Biogas production from a CSTR bioreactor using as feedstock 0.2L/d of optimal waste

Waste to energy systems and algae photo-bioreactors

Valorization of zero or negative value raw materials has become the hot spot of the 21st century with the biological methods leading the way. From the composting to the fourth generation bio-refinery, microorganisms are utilized thanks to their abilities to bio-convert different organic macromolecules into valuable materials and renewable energy resources. Throughout this quest, for the identification of renewable resources, great attention has been paid into the evolution of the anaerobic digestion into a robust process able to treat a plethora of mixed substrates. While the microorganisms are able to valorize different waste streams, at the same time they are presenting a number of inherent limitations which in a number of cases and through appropriate management can be bypassed or ever used in advantage of another biological process in a win-win operation. One of these limitations is the inefficiency of the anaerobic microorganisms to bio-convert a number of natural macromolecules into biogas mainly due to a slow hydrolysis stage.

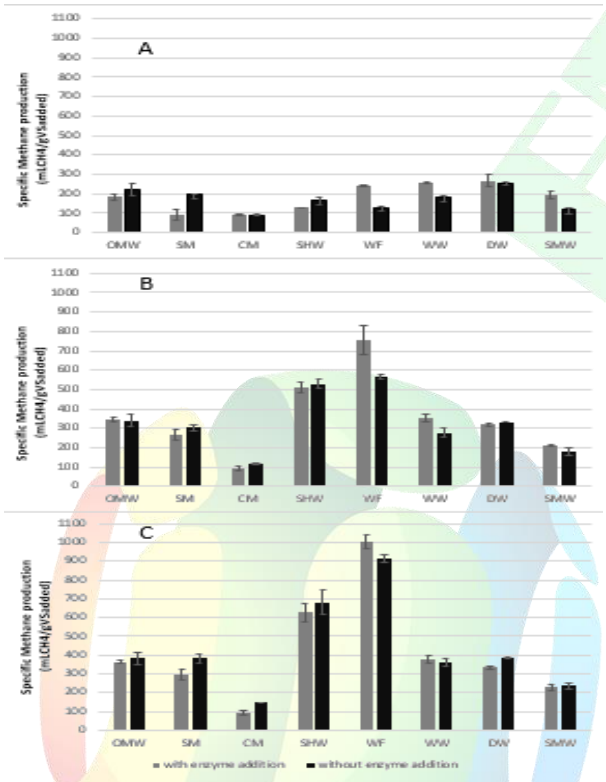

Figure 49. Specific methane production (mL/gVS$_{added}$) on days 5, 12 and 30 for the enzymatically pretreated and not pretreated substrates (Olive Mill Waste, Sterilized Mass, Cattle Manure, Slaughterhouse Wastes, White Fat, Winery Wastes, Distillery Wastes, Slaughterhouse, Solid Mill Wastes)

In order to improve the efficiency of the process toward these macromolecules, during 2014 a number of small scale digestion experiments took place in our laboratory where it was assessed the effectiveness of an initial enzymatic pretreatment stage enhanced by the addition of commercially available enzymes. Based on the generated data, the effect that the examined enzymes have on the anaerobic digestion of the mixed substrates can be divided into three categories. A) No effect or neglectable effect, as is the case of olive mill waste and distillery wastes. B) Positive effect on the process with the methane production taking place faster and the organic matter exhausts more rapidly. This category includes the white fat and the olive mill solid wastes. C) Negative effect with the methane production taking place slower and the cumulative methane production being lower when compared to the methane generated by the batches that no external enzymes added, this category includes the cattle manure and the sterilized mass.

Photo bioreactors

Another inherent limitation of the anaerobic digestion is the generation, during the anaerobic respiration, of carbon dioxide which in some cases can be volumetrically equal to the generated methane. The presence of carbon dioxide into the biogas is undesirable as it is reducing the heating value of the gas while increasing storage and management costs. Toward the reduction of the concentrations of the carbon dioxide from the biogas, during 2014 took place the design and construction of a bench scale anaerobic digestion system coupled to photo-bioreactors where algae will be employed for the valorization of the carbon dioxide, hydrogen sulfide and ammonia available in the biogas.

Figure 50. The photo-bioreactors within the temperature controlled cabinet

After harvesting the algae biomass will be used for the recovery of high value added products, raw material for fuel manufacturing and industrial product development. Algae are a group of photosynthetic microorganisms that can fix carbon dioxide from different sources into biomass. During the last years this ability of the algae has been examined in order to identify pathways through which the application of these species can reduce the environmental burden of human activities. Algae can be considered as an important carbon sink and their cells can contain more than 50% of fats and oils, sometimes rich in omega 3, from where pharmaceuticals or raw material for biodiesel production can be extracted. It is important to be mentioned that for every kg of algal biomass, 1.65-1.83 kg of CO_2 must be consumed. The spent algae cells can be further valorised as activated carbon building blocks or substrate to the anaerobic digesters.

Fur farming by-product bio-methanation

The production of fur based commodities in Greece is driven by a dynamic and well established industry with long tradition in the production of quality products, which moreover presenting significant exporting experience. The Western Macedonia region is the area where nearly all of the fur production in Greece is taking place including the feed manufacturing, the farming and the transformation of the pelts into final commodities. The wastes that are being generated from the mink breading facilities are manures and waste feed both of which are collected underneath the cages in small piles of up to 50cm in height. The waste management options for this waste stream is restricted by the high solids, organics and nitrogen content that are significantly hampering the abilities of aerobic biological processes to effectively treat these waste streams. This work investigated, for the first time, the potential of the mink farming wastes as substrates to AD systems. According to the results, the mink farming wastes can be considered as excellent substrates for AD systems where large volumes of methane gas (up to 670mLCH_4/gVS_{added}) can be recovered. At the same time the generated digestate, which after the anaerobic treatment is presenting improved characteristics compared to the initial substrate, can be used as an organic soil amendment, minimizing in this way the land application of expensive chemical products.

The main limitation identified at the present stage is the seasonal availability of the substrates with most of the manures and waste feed to becoming available between July and October, while between October and November the mink bone and meat meal is becoming available, rendering the mono-digestion of mink farming wastes as challenging. Better utilization of these waste streams can be achieved in centralized digestion plants where their high bio-methane potential could significant improve cash flows during the period where they are becoming available.

The applicability of farm scale biomethanation plants for the valorization of the municipal organic wastes

Redirection of organic municipal wastes away from landfills is one of the challenges that waste managers face every year. Only in Greece more than 2.7 million tons of municipal organic wastes are generated annually. Currently most of these are landfilled, resulting in wastage of a resourceful substrate, over exploitation and pollution of surface and ground waters, as well as in releases of greenhouse gases into the environment.

The anaerobic digestion process provides a waste management option for OFMSW, while offers the opportunity for recovering marketable products both in the forms of biogas and slow release bio-fertilizers. As a result, fewer wastes are dumped into landfill sites, while at the same time the process can be used by local authorities to meet the waste redirection targets set by the European Community Landfill Directive (1999/31/EC). As a way to improve the bio-methane production of AD systems, different wastes-wastewaters can be mixed and treated together in co-digestion schemes. This mixing of different substrates is not only desirable for improving methane recovery rates and reducing life cycle costs, but it also provides better organic load removal efficiencies as an effect of C/N ratio correction, pH balancing and improvement on the buffering capacity of the treatment systems.

The experiments performed under thermophilic conditions in batch and large volume laboratory digesters, with the addition rate of food wastes to manures reaching as high as 70% based on VS loading, the total solids levels at 15.7% and the OLR at 6.85kgVS/m^3/d. In the higher addition rate the digestion process was slightly inhibited, probably due to simple sugar accumulation. In contrast waste mixtures containing up to 65.3% food wastes with the OLRs as high as 6.2 kgVS/m^3/d with the influent TS levels up to 14.3% can be accepted by CSTR systems with no signs of inhibition.

Based on the results the addition of food wastes to anaerobic digesters operating under manure monodigestion conditions can improve specific methane production by 86% and the volatile solids reduction by 19%. In a farm scale digester (3000m3, HRT 21-d) the addition of food wastes can improve cash flow fourfold by only slightly increasing operational costs due to pasteurisation requirements. Additionally, gate fees and carbon credits can further improve the financial situation of the treatment facilities.

EnvE-Lab international profile

World Health Organization (WHO)

EnvE-Lab has established a close collaboration with the WHO European centre for Environment and Health, which includes:

- The development of integrated methodologies for health impact assessment, taking into account multiple air pollutants and noise, related to GHGs emissions policies. EnvE-Lab carries a long inheritance in integrated health impact assessment from previous projects such as HEIMTSA, HEREPLUS, INTARESE, 2FUN. Now, within the frame of the project URGENCHE, EnvE-Lab has developed an integrated framework for assessing the health impact of GHG policies in Thessaloniki, bringing together different tools of environmental modelling and monitoring, composing novel methodologies. The knowledge exchange between EnvE-Lab and WHO were strengthened by the close collaboration on expanding the methodologies to other cities/case studies in China involved in the project; to this aim an EnvE-Lab team member visited the WHO Europe headquarters in Bonn for 3 months in early 2014.
- The assessment of combined or multiple exposure to health stressors in indoor built environments. The objective of this study was to undertake, summarize and present a systematic review of literature and project reports presenting evidence on multiple or combined risk exposure in indoor built environments. The review covered safety threats and injuries, indoor air pollution, use of household chemicals, noise, damp and mould, thermal conditions, crowding, inadequate hygiene standards, and harmful building and equipment/furnishing materials. In terms of indoor settings the review covered residential buildings as well as day care centers and schools. The results of the study were presented and used as the main scientific background at a capacity building workshop geared to public authorities of the WHO Europe member states in October 2013. WHO entrusted EnvE-Lab with this task, because of our extensive experience and pioneering work on multiple stressors and more specifically chemical mixtures[1].
- Analysis of Environmental Health Economics to quantify the socioeconomic dimension of environmental pollution. Greece is an excellent case study considering the recent financial crisis, which has significantly altered the pattern of emissions and air pollution and introduced significant issues of environmental injustice.
- A further collaboration scheme deals with human biomonitoring focusing on optimal design of biomonitoring campaigns, as well as on the exploitation of biomonitoring data through internal dose modelling.

HEALS workshop in Thessaloniki

The “HEALS concepts and methodology” workshop took place at the Aristotle University of Thessaloniki from 17th to 19th March 2014. The workshop was a successful opportunity to create a common understanding of the exposome concepts and to share and discuss the HEALS approach to unravel the exposome.

The workshop was Led by Prof Denis Sarigiannis. Around 70 delegates from the 29 HEALS Partners took part and delivered a number of presentations on the different facets of the exposome concept. The event consisted of one day technical meeting (17 March) on the project workpackages, which was followed by one and a half day scientific workshop (18 and the morning of 19 March). In addition to presentations from the project team, from the afternoon of March 19 until lunch time of March 20, Agilent Technologies co-hosted a dedicated event on the Agilent exposomics workflows with external high-level expert discussion on the use of advanced analytical and -omics technologies for exposome research both in the EU and the USA and demonstration of Agilent technology and data analysis tools. Both the HEALS workshop and the Agilent seminar were held at the Research Dissemination Center of Aristotle University of Thessaloniki (KE.D.E.A).

Figure 51. HEALS workshop participants

After three days of presentations and scientific discussion there was a general agreement that the workshop was a successful step toward the development of a common agreed methodology to unravel the exposome. The final discussion reflected this collective understanding as witnessed by the active participation of all delegates. Several issues were discussed and clarified reinforcing the energy needed to face the great challenges we need to address in the next years.

[1] Sarigiannis DA, Hansen U. Considering the cumulative risk of mixtures of chemicals - A challenge for policy makers. Environmental Health: A Global Access Science Source 2012; 11.

Advancing exposome science

From 2006-2011, the US National Institute of Environmental Health Sciences (NIEHS) and other US National Institutes of Health (NIH) coordinated research on exposure biology and genetics through the Genes, Environment, and Health Initiative. As part of this effort, NIEHS oversaw the establishment of the Exposure Biology Program, which funded the development of wearable and field deployable sensor systems for measuring chemical exposures, dietary intake, physical activity, psychosocial stress, and the use of substances of abuse. In parallel, the Exposure Biology Program supported work to identify biomarkers that show biological response to these stressors.

In 2012, NIEHS implemented a new Strategic Plan, which includes a major goal to promote exposome research and create a blueprint for incorporating exposure science into human health studies. The Institute is working to transform exposure science by improving the characterization of environmental exposures, defining and disseminating the concept of the exposome, and creating the necessary tools, technologies, and research capacity. In 2013, NIEHS funded the HERCULES Center at Emory University, which is conducting exposome-focused research and also developing new tools and technology for assessing the exposome.

In the framework of this NIEHS initiative EnvE-Lab was officially involved in the bioinformatics, biostatistics, and data management of the exposome Working Group focusing on integrative and computational biology with the exposome and on harmonization and data infrastructure for the exposome. The work of this working group produced a working document which reviewed the state-of-science, and identified needs on capacity development and study design principles for exposome implementation. The document will be discussed in January 2015 on a two-day workshop organized by NIEHS to further define the exposome and discuss technical approaches to implement exposome studies.

EnvE-Lab will participate to this important event which will bring together international leading scientists from a range of disciplines in the environmental health community to provide their insights and perspectives on how to approach researching the exposome. Through the many break-out sessions and opportunities for discussion scheduled during the workshop, the goal is to create recommendations to the broader Environmental Health Sciences community about the approaches to the exposome and how they might be best implemented into current and future research settings.

Global Chemical Risk Assessment

In October 2014 EnvE-Lab was invited to become a formal member of the WHO's Global Chemical Risk Assessment Network, which is fostered by the International Program on Chemical Safety.

The WHO Chemical Risk Assessment Network is an initiative whose overall goal is to improve chemical risk assessment globally through fostering and facilitating sustainable interaction between institutions on chemical risk assessment issues and activities. The specific objectives of the Network are to:

a) Provide a forum for scientific and technical exchange;

b) Facilitate and contribute to capacity building;

c) Promote best practices and the harmonization of methodologies;

d) Assist in the identification of research needs and promote the application of new science in risk assessment practice;

e) Assist in the identification of emerging risks to human health from chemicals;

f) Share information about work programmes to avoid duplication of effort;

g) Upon request, assist WHO in the development of training and other materials in support of the above.

The WHO Chemical Risk Assessment Network Meeting was held at ANSES (French Agency for Food, Environmental and Occupational Health and Safety) in Maisons-Alfort, Paris, France from 8 to 10 October 2014. Prof. Sarigiannis, EnvE-Lab Director, chaired the working group on Specific Risks where proposals for collaborative international projects on specific risks related to chemical exposures were discussed and agreed upon. These activities will start in the course of 2015.

The next face to face meeting of the Network would provisionally be planned for mid-2017. Participants were invited to submit their ideas for the format and content of that meeting to WHO.

EnvE-Lab response to societal needs

The extensive activities of EnvE-Lab on the hot environmental issues of biomass combustion and the related PM pollution resulted in increased public awareness.

Health impact and monetary cost of exposure to particulate matter emitted from biomass burning in Thessaloniki

A major issue related to the extensive use of biomass as a space heating means during wintertime in Greece is the high levels of particulate matter. The study deals with the assessment of health impact and the respective economic cost attributed to particulate matter (PM) emitted into the atmosphere from biomass burning for space heating, focusing on the differences between the warm and cold season in 2011-2012 and 2012-2013 in Thessaloniki (Greece). Health impact was assessed based on estimated exposure levels and the use of established WHO concentration-response functions (CRFs) for all-cause mortality, infant mortality, new chronic bronchitis cases, respiratory and cardiac hospital admissions. Monetary cost was based on the valuation of the willingness-to-pay/accept (WTP/WTA), to avoid or compensate for the loss of welfare associated with illness.

The results of the 2012-2013 measurements were compared to the ones made in 2011-2012 to understand better the effect that different policy measures regulating the market price of heating fuel in tandem with the incumbent economic crisis in Greece and other countries in the European South may have on non-occupational exposure of the urban population to particulate matter and the associated health and monetary impact. Own-price elasticity of light heating oil was taken as el_{oil} = -0.39. A field survey encompassing ca. 300 households across the greater area of Thessaloniki implemented using the on-line SurveyMonkey tool provided consumer behavior information that was used to generate the cross-fuel elasticity table below.

The scenarios are based on reasonable assumptions and existing trends related to the energy market; however the interplay of multiple factors such as financial pressures or incentives might result in unexpected figures (as occurred with the increased biomass use), favoring one technological solution for space heating over another. Through analysis of specific scenarios we highlighted the attributable differences in public health burden, should specific space heating practices be adopted.

Table 1. Cross-price elasticities of alternative space heating energy carriers

	Light heating oil	*Natural gas*	*Biomass*	*Electricity*
Light heating oil	----	n/a	-0.97	-0.24
Natural gas	n/a	----	n/a	n/a
Biomass	-1.03	n/a	----	0.25
Electricity	-4.1	n/a	3.98	----

n/a: sufficient data non available to support the estimation of elasticity

The different policy scenarios examined resulted in lower average urban background concentrations are presented in Table 4.

Table 2. Fuel/technology use distribution and corresponding urban background concentrations

	Oil	Natural gas	Biomass burning	Electricity	PM2.5 (μg/m^3)
2011-2012	44.0%	40.0%	5.6%	10.4%	**41.2**
2012-2013	22.3%	40.0%	26.7%	15.7%	**62.6**
Scenario 1	38.5%	41.5%	10.0%	10.0%	**36.3**
Scenario 2	43.5%	41.5%	5.0%	10.0%	**28.4**
Scenario 3	23.5%	62.5%	4.0%	10.0%	**26.5**
Scenario 4	20.0%	70.0%	0.0%	10.0%	**20.0**

Results showed that long term mortality during the 2012-2013 winter increased by 200 excess deaths in a city of almost 900,000 inhabitants or 3540 years of life lost, corresponding to an economic cost of almost 200-250m€. New chronic bronchitis cases dominate morbidity estimates (490 additional new cases corresponding to a monetary cost of 30m€.

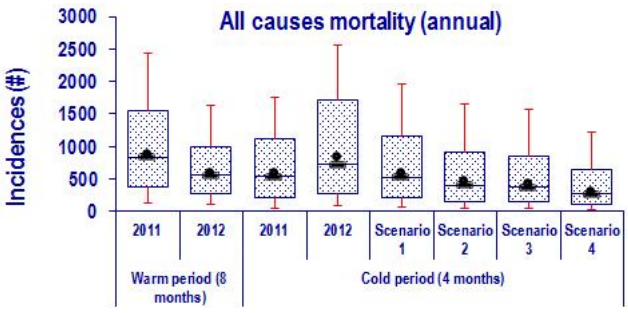

Figure 52. Estimated annual mortality due to PM exposure under current situation and "what if" scenarios.

Estimated health and monetary impacts are more severe during the cold season, despite its smaller duration (4 months).

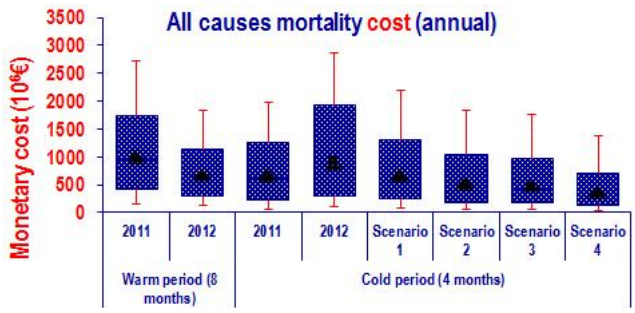

Figure 53. Estimated socioeconomic cost of PM attributed mortality based on total welfare change

Policy scenario analysis revealed that significant public health and monetary benefits (up to 2b€ in avoided mortality and 130m€ in avoided illness) might be obtained by limiting the biomass share in the domestic heat energy mix. Fiscal policy affecting fuels/technologies used for domestic heating needs to be reconsidered urgently, since the net tax loss from avoided oil taxation due to reduced consumption was further compounded by the public health cost of increased mid-term morbidity and mortality.

Recommendations on the technologies of pellet boilers

EnvE-Lab expert opinion was requested by the General Secretarial of Industry for providing recommendations on the PM emission specifications of pellet and wood combustion boilers available in the Greek market. This reflected the concerns about the current emission levels of biomass combustion of modern devices present in the Greek market; the question posed was whether an intermediate level of emissions limit should be implemented before the Eco-Design directive becomes effective in 2018. In order to address this question, a thorough review related to technological aspects of boilers technology as well as a servey of the current situation in the Greek market were carried out.

From the review, it was found that the mass of particulate emissions is 180 times higher for old construction boilers compared to boilers based on newer specifications. Moreover, the number of particles emitted increases with an increase in emissions of unoxidised gaseous components. Since the distributions of the number and mass depends on the particle size, it is concluded that the emission of particles, in particular ultrafine (size <100 microns) is amplified by non-ideal combustion conditions. Pellet burning results in coarser particle emissions compared to liquid fuels. The size distribution of aerosols is influenced by many factors such as the humidity of the fuel, the content of ash and the combustion process.

The European Committee for Standardization (CEN) has adopted standard EN 303-5 on 10-05-2012. This standard classifies the boilers into 3 categories, setting thresholds for their performance and emission limits for boilers that burn solid fuel. The boilers using as fuel solid biomass for non-industrial use in the Greek market intended for use in heating installations must comply the minimum performance and quality limits of exhaust gas set by the standard ELOT EN 303-5 according to Class 3. For this reason, the EN 303-5 is often used by local authorities as part of their regulations, to promote the purchase of high efficiency boilers and to create incentives for the use of efficient boilers with low emissions. This is the only European standard for boilers. Besides this standard apply another 4 standards for small residential applications of biomass:

- *EN 13240: For heaters - Solid Fuel*
- *EN13229 and EN 12815: For cooking Solid-Fuel fireplaces*

According to research conducted in Greece there are about 18 companies which manufacture pellet boilers and solid fuel some of which manufacture and fireplaces and stoves. It is important to stress that many of these companies have EN 303-5 with solid fuel boilers to category 3 but some of them have even certification of class 4-5, while the pellet boilers usually belong in category 4-5. Given the implementation of Directive 2009/125 / EC on Eco-Design requirements for (a) boilers and (b) local space heaters fired by solid fuels in 2018, the projected emission values Class 5 (40 mg/m^3) will be significantly reduced compared to the class 3 emission levels (150 mg/m^3). The technology and emissions of class 3 devices are closer to those of classes 1 (200 mg/m^3) and 2 (180 mg/m^3). Therefore, the reduction of emissions from existing boilers must be combined with changes in the technology, which will include the installation of electrostatic filters, the addition of secondary combustion, the increase of the gas paths inside the boiler and the construction of reverse steering technology boiler flame. Because the modification of existing boilers Class 3 are difficult to be transformed into class 4-5, a measure that would contribute significantly to reducing actual emissions is the use of better quality fuels.

The above analysis of available data shows that around 66% of Greeks biomass boiler manufacturers produce devices Class 4 and 5, i.e. with emissions below 100 mg/m^3. Emissions from the biomass boilers can be further reduced by using good quality biomass in accordance with the technical specifications of boilers. We may conclude that it is legitimate to establish an intermediate emission limit to 100 mg/m^3 for all Greek construction companies in order to push them towards more rapid harmonization with Community policy on eco-design (eco-design) by on the one hand and to protect public health from excessive aerosols emissions as occurred in the winter periods 2012-2013 and 2013-2014.

Publications & Conferences

Journal Publications

Sarigiannis DA, Karakitsios SP, Kermenidou M. Health impact and monetary cost of exposure to particulate matter emitted from biomass burning in large cities. *Science of The Total Environment 2015*; 524-525: 319-330.

Sarigiannis DA, Karakitsios SP, Zikopoulos D, Nikolaki S, Kermenidou M. **Lung cancer risk from PAHs emitted from biomass combustion**. *Environmental Research* 2015; 137: 147-156.

Andra SS, Charisiadis P, Karakitsios S, Sarigiannis DA, Makris KC. **Passive exposures of children to volatile trihalomethanes during domestic cleaning activities of their parents**. *Environmental Research* 2015; 136: 187-195.

Sarigiannis DA, Gotti A. **New methods for personal monitoring of air pollution through the use of passive sensors during childhood**. *Pneumologia Pediatrica* 2014; 54: 37-43

Sarigiannis DA, Karakitsios SP, Kermenidou M, Nikolaki S, Zikopoulos D, Semelidis S, Papagiannakis A, Tzimou R. **Total exposure to airborne particulate matter in cities: The effect of biomass combustion**. *Science of The Total Environment* 2014; 493: 795-805.

Karakitsios S, Asikainen A, Garden C, Semple S, De Brouwere K, Galea KS, Sánchez-Jiménez A, Gotti A, Jantunen M, Sarigiannis D: **Integrated exposure for risk assessment in indoor environments based on a review of concentration data on airborne chemical pollutants in domestic environments in Europe**. *Indoor and Built Environment*, 2014; doi: 10.1177/1420326X14534865.

Sarigiannis D, Karakitsios S, Gotti A, Loizou G, Cherrie J, Smolders R, De Brouwere K, Galea K, Jones K, Handakas E, Papadaki K, Sleeuwenhoek A. **Integra: From global scale contamination to tissue dose**. iEMSs 2014; 2; 1001-1008.

Conference presentations

D.A. Sarigiannis, **Multiscale connectivity for chemical mixture toxicity assessment**, 2014 AIChE Annual Meeting, Atlanta, USA, 16-21/11/2014.

D.A. Sarigiannis, A. Gotti, S. Karakitsios, **Biology based dose response (BBDR) of chemical mixtures using exposomics**, 2014 AIChE Annual Meeting, Atlanta, USA, 16-21/11/2014.

D.A. Sarigiannis, E. Handakas, S.P. Karakitsios, M.P. Antonakopoulou, A. Gotti, **Life cycle analysis for urban waste treatment optimization**, 2014 AIChE Annual Meeting, Atlanta, USA, 16-21/11/2014.

D.A. Sarigiannis, S. Karakitsios, A. Gotti, E. Handakas, K. Papadaki, **Development of a generic physiology based biokinetic model for predicting internal dose and assimilation of biomonitoring data for industrial chemicals**, 2014 AIChE Annual Meeting, Atlanta, USA, 16-21/11/2014.

D.A. Sarigiannis, S. Karakitsios, **Artificial Neural Networks for environmental and biochemical mod**elling, 2014 AIChE Annual Meeting, Atlanta, USA, 16-21/11/2014.

D.A. Sarigiannis, P. Kontoroupis, S. Karakitsios, A. Gotti,S. Nikolaki, D. Chapizanis, **Health co-benefits of traffic related GreenHouse Gas (GHG) mitigation policies in cities**, 24th ISES Annual Meeting, Cincinnati (Ohio), USA, 12-16/10/2014.

D.A. Sarigiannis, S. Karakitsios, A. Gotti, G. Loizou, J. Cherrie, R. Smolders, Katleen De Brouwere, K. Galea, K. Jones, E. Handakas, K. Papadaki, A. Sleeuwenhoek, **INTEGRA: Advancing exposure continuum from global scale contamination to tissue dose**, 24th ISES Annual Meeting, Cincinnati (Ohio), USA, 12-16/10/2014.

D.A. Sarigiannis, D. Zikopoulos, M. Kermenidou, S. Nikolaki, S.P. Karakitsios, **Refining assessment of PAH exposure and potential carcinogenic risk assessment from biomass burning incorporating internal dosimetry metrics**, 24th ISES Annual Meeting, Cincinnati (Ohio), USA, 12-16/10/2014.

D.A. Sarigiannis, S. Karakitsios, M. Kermenidou, **A new metric of fine and ultrafine PM exposure: the region-specific oxidative stress index (SOS)**, 24th ISES Annual Meeting, Cincinnati (Ohio), USA, 12-16/10/2014.

D.A. Sarigiannis, E.J. Handakas, S.P. Karakitsios, **A Detailed Multi-compartmental Skin Penetration Model Coupled to a Physiologically Based Pharmacokinetic Model for Assessing Exposure to Chemical Compounds: the Case of Bisphenol A**, 24th ISES Annual Meeting, Cincinnati (Ohio), USA, 12-16/10/2014.

D.A. Sarigiannis, S.P. Karakitsios, A. Gotti, M. Braubach, **Combined exposure to harmful indoor air pollutants in Europe**, 24th ISES Annual Meeting, Cincinnati (Ohio), USA, 12-16/10/2014.

D.A. Sarigiannis, S.P. Karakitsios, A. Gotti, M. Braubach, **Combined Exposure to Health Stressors in Indoor Built Environments in Europe**, 24th ISES Annual Meeting, Cincinnati (Ohio), USA, 12-16/10/2014.

D.A. Sarigiannis, **Unravelling the Exposome through Health and Environment-wide Associations based on Large population Surveys**, 24th ISES Annual Meeting, Cincinnati (Ohio), USA, 12-16/10/2014.

M. Loh, J. Cherrie, A. Pronk, E. Kuijpers, C. Schieberle; A. Stamatelopoulou, D. Chapizanis, J. Bartzis, Z. Spiric, D. Sarigiannis, **A Comparison Study of Location and Activity Monitoring For Exposure Studies**, 24th ISES Annual Meeting, Cincinnati (Ohio), USA, 12-16/10/2014.

H. Price, K. Douglas, R. Sokhi, M. Keuken, M. Kermenidou, D.A. Sarigiannis, **Source apportionment of PM2.5 and PM10: within-city and between-city variation in Europe**. 2014 International Aerosol Conference, Busan, Korea, 28/8-2/9/2014.

D.A. Sarigiannis, D. Zikopoulos, M. Kermenidou, S. Nikolaki, S.P. Karakitsios, **Refining assessment of PAH exposure and potential carcinogenic risk assessment from biomass burning incorporating internal dosimetry metrics**, 26th Annual ISEE Conference, Seattle (Washington), USA, 24-28/8/2014.

D.A. Sarigiannis, S. Karakitsios, A. Gotti, G. Loizou, J. Cherrie, R. Smolders, Katleen De Brouwere, K. Galea, K. Jones, E. Handakas, K. Papadaki, A. Sleeuwenhoek, **Integrated external and internal exposure to chemicals: the INTEGRA computational platform**, 26th Annual ISEE Conference, Seattle (Washington), USA, 24-28/8/2014.

D.A. Sarigiannis, **Modeling from external exposure dose down to internal doses – bridging the gap**, 2014 ICCA-LRI & JRC Workshop, Lugano, Switzerland, 17-18/6/2014.

D.A. Sarigiannis, S. Karakitsios, A. Gotti, G. Loizou, J. Cherrie, R. Smolders, Katleen De Brouwere, K. Galea, K. Jones, E. Handakas, K. Papadaki, A. Sleeuwenhoek, **INTEGRA: From global scale contamination to tissue dose**, 7th International Congress on Environmental Modelling and Software (iEMSs), San Diego (California), USA, 15-19/6/2014.

D.A. Sarigiannis, **Integrated external and internal exposure to chemicals: the INTEGRA computational platform**, SETAC Europe 24th Annual Meeting, Basel, Switzerland, 11-15/5/2014.

D.A. Sarigiannis, E. Handakas, A. Gotti, S. Karakitsios, **Risk and life cycle impact assessment of municipal waste management**, SETAC Europe 24th Annual Meeting, Basel, Switzerland, 11-15/5/2014.

D.A. Sarigiannis, S.P. Karakitsios, A. Gotti, **Integrated external and internal exposure to chemicals: the INTEGRA computational platform**, SETAC Europe 24th Annual Meeting, Basel, Switzerland, 11-15/5/2014.

D.A. Sarigiannis, E. Handakas, A. Gotti, S.P. Karakitsios, **Risk and life cycle impact assessment of municipal waste management**, SETAC Europe 24th Annual Meeting, Basel, Switzerland, 11-15/5/2014.

D.A. Sarigiannis, I. Annesi-Maesano, J. Cherrie, J. Bartzis, M. Schumacher, **The HEALS approach to health and environment-wide associations**, SETAC Europe 24th Annual Meeting, Basel, Switzerland, 11-15/5/2014.

D.A. Sarigiannis, **Computational toxicology**, 7th conference of Forensic Medicine & Toxicology, Larisa, Greece, 26-27/4/2014.

D.A. Sarigiannis, S.P. Karakitsios, A. Gotti, M. Braubach, **Combined exposure to harmful indoor air pollutants in Europe**, Air Quality 2014, Garmisch-Partenkirchen, Germany, 24-28/3/2014.

D.A. Sarigiannis, S. Karakitsios, M. Kermenidou, **Enhancing PM epidemiological concentration-response functions by incorporating lung deposition and oxidative stress**, Air Quality 2014, Garmisch-Partenkirchen, Germany, 24-28/3/2014.

D.A. Sarigiannis, S. Karakitsios, M. Kermenidou, **PM attributed mortality and morbidity due to biomass use in Thessaloniki – estimation of socioeconomic cost**, Air Quality 2014, Garmisch-Partenkirchen, Germany, 24-28/3/2014.

D.A. Sarigiannis, P. Kontoroupis, D. Chapizanis, S. Karakitsios, **Public health co benefits from traffic related greenhouse gas emission policies**, Air Quality 2014, Garmisch-Partenkirchen, Germany, 24-28/3/2014.

D.A. Sarigiannis, D. Zikopoulos, M. Kermenidou, S. Nikolaki, S. Karakitsios, **Carcinogenic risk of PAHs in particulate matter from biomass combustion**, Air Quality 2014, Garmisch-Partenkirchen, Germany, 24-28/3/2014.

D.A. Sarigiannis, S.P. Karakitsios, A. Gotti, **INTEGRA: advancing exposure and risk characterization**, Phoenix, Arizona, USA SOT's 53rd Annual Meeting, 24–27/3/2014.

D.A. Sarigiannis, D. Zikopoulos, M. Kermenidou, S. Nikolaki, S. Karakitsios, **Carcinogenic risk of PAHs in particulate matter from biomass combustion**, USA SOT's 53rd Annual Meeting, 24–27/3/2014.

Invited talks

HERCULES Exposome Research Center, Emory University, Atlanta, USA, November 20, 2014. Invited lecture titled ***"Multi-scale connectivity An integrated methodology to unravel the exposome"***.

Conference of the Society of Cell Pharmacology and Toxicology, Keynote lecture on ***Systems Biology and its applications on Pharmaco-Toxicology***, University of Rennes, France, October 9-10, 2014.

WHO-International Program for Chemicals Safety (IPCS), Chair of working group on ***Specific Risks*** of the **Chemical Risk Assessment Network**, Paris, France, October 8-10, 2014.

International meeting "***Expanding nuclear medicine frontiers***". September 27, 2014, Thessaloniki, Greece. Invited lecture titled "***Radiological exposome: lifelong ionising and non-ionizing radiation exposure and human health***".

NIEHS Exposure Science and the Exposome Webinar Series, July 14, 2014. Invited lecture titled "***HEALS – Health and Environment-Wide Associations via Large Population Surveys***".

WHO - Global Public Health workshop on the *"**Identification of risks of endocrine-disrupting chemicals: overview of existing practices and steps ahead**"*. Chair of workshop. Bonn, Germany 7-8 July, 2014.

ICCA-LRI and JRC Workshop, "***What Is Safe? Integrating Multi-Disciplinary Approaches for Decision Making about the Human Health and Environmental Impacts of Chemicals"***. Lugano, Switzerland, 17-18 June, 2014. Invited lecture titled "***Modeling from external exposure dose down to internal doses – bridging the gap***".

7th Toxicology and Forensic Medicine conference. April 26-27, 2014 Larissa, Greece. Invited lecture titled "***In silico toxicology; Quantitative structure–activity relationship models (QSAR)***".

Cyprus International Institute for Environmental and Public Health, "***Urban Water Symposium***". January 31, 2014, Nicosia, Cyprus. Invited lecture titled "***From water to human exposome***".

Laboratory Personnel

Dimosthenis A. Sarigiannis, Director

M.Sc., PhD (University of California, Berkeley, USA) is Associate Professor specialising on environment and health issues at the Department of Chemical Engineering of the Aristotle University of Thessaloniki, Visiting Professor at the Master's Program on Toxicology and Environmental Risk at the Medical School of the University of Pavia and senior scientist at the Chemical Assessment and Testing unit of the Institute for Health and Consumer Protection at the European Commission's Joint Research Centre (currently on leave). At the European Commission he has served as Scientific Coordinator of the IHCP, Action Leader for Consumer Product Safety and Quality and Community Reference Laboratory for Food Contact Materials, Action Leader for Human Exposure to Environmental Stressors and Health Effects and for Assessment of Chemicals at the European Chemicals Bureau, Scientific Assistant to the JRC Director General, Strategy Manager of the IHCP and as science advisor to the Greek Minister of the Environment. He was a principal contributor to the REACH Regulation and to the Environment and Health Action Plan and is currently member of the Health and Environment Working Party and of the Health Security Committee. He has been pioneering efforts to coupling biology-based modelling with toxicogenomics discovery systems for developing a mechanistically based understanding of the health risk of environmental chemical mixtures. He is member of the international forum for evidence-based toxicology, of the scientific committee for chronic risks of INERIS, and secretary-general of MESAEP. He has contributed to the IPs HEIMTSA, 2-FUN, NO MIRACLE, HENVINET and, CAIR4HEALTH, HEREPLUS, TRANSPHORM, GENESIS, TAGS and INTERA.

Dr A Gotti is a Physicist of the University of Milan with over 20 years of experience in environment and health impact assessment, data assimilation and exposure modelling including physiology-based biokinetic modelling. In the last ten years he has worked for the European Commission"s Joint Research Centre, for the Intedisciplinary Institute of Environmental Research and for CERTH in the frame of the projects INTARESE, SMAQ, HEIMTSA, 2-FUN, HEREPLUS, TAGS, INTERA.

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