Annual Report 2016

Environmental Engineering Laboratory

ENVELab

Edited by:

Assoc. Professor

Dimosthenis Sarigiannis, Director

Table of contents

Welcome message

2016 – A year of challenges and success

The Environmental Engineering Laboratory (ENVE Lab) was established at the Chemical Engineering department of the Aristotle University of Thessaloniki (AUTH) in the second half of 2011. Its objective is to act as 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 processes and products serving sustainability objectives.

The main scientific foci 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 and urban systems with reduced ecological footprint

Our work paradigm is based on international collaboration and scientific networking. Within AUTH, ENVE Lab collaborates with several analytical and biochemistry laboratories in the Schools of Engineering, Natural Sciences and Medicine. Close collaboration has been established with 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 five years.

In Greece ENVE Lab has been providing scientific support to the Ministry of Education, Research and Religious Affairs, the Ministry of Development, the Ministry of Environment, Energy and Climate, and the Ministry of Health. The ENVE Lab Director and staff participate in the permanent Committee on the Environment and several working groups of the Technical Chamber of Greece on air pollution and waste management. We have working links with the environmental consultancy ENVIROPLAN S.A. and chair 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 its Director has assumed the Presidency of the Mediterranean Scientific Association for Environmental Protection (MESAEP).

On a global scale, good collaborative links have been established with the World Health Organization, the European Center for Environment and Health, the US Environmental Protection Agency, the National Institutes for Environmental Health Science and the Schools of Public Health of the University of California at Berkeley and Los Angeles 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. Moreover, 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.

During 2016, 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);
(c) contributing to the launching of a new EU-wide COST network on risk management and rehabilitation of contaminated industrial sites in the European Union and to the organization of a WHO expert meeting exploring the link between waste and health; and
(d) representing Greece at the Program Committee on Climate Action, Environment and Resource Efficiency of Horizon 2020 and contributing to the launching of the European Human Biomonitoring Initiative

In Southeastern Europe, 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 link between waste and public health placing particular emphasis on integrated exposure and risk assessment. ENVE Lab continued its work on environmental health economics rendering it a tangible and practical tool for assessing environmental and fiscal policy options.

I hope you will enjoy reading our 5th 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

EnvE Lab aims at developing integrated methodologies, knowledge management systems and technologies that can effectively shed light on the interactions between human health and the environment. Our ultimate goal is to generate the knowledge necessary to optimize interventions that protect public and consumer health cost-effectively. These include the design of technological systems that serve sustainability and respect human health.

Our concept brings together beyond-the-state-of-the-art advances in **environmental monitoring**, **human biomonitoring** and **systems biology**, **exposure monitoring** technologies and tools for **computational analyses** of the **exposure-to-health effect continuum**. The above are collated in a novel exposure biology-based methodology supported by an integrated knowledge management system 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 prerogative for its scientific soundness and its impact on public policy. Various ELAP modules 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 technical research and continuous development work, horizontal activities provide the infrastructure necessary for setting ELAP in its proper 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 that foster technical and societal innovation in parallel.

The assessment process focuses on the following: (a) hazard potency of a substance; (b) its uses and mobility in the environment (affecting the amount that the population groups will come into contact); (c) the biologically effective dose of the compound reaching the target tissue; and finally (d) the response of the human body to this dose.

These attributes are influenced strongly by the interaction of the physicochemical properties of the substance(s) under study with biological and physiological characteristics. Thus, well targeted interventions at different stages of the source-to-outcome continuum ensure the optimal management of chemicals in the environment and consumer products. Our final objective is to render this analysis a *sine qua non* tool for guiding new chemical synthesis in industry (Figure 1), in accordance with the "safe by design" principle.

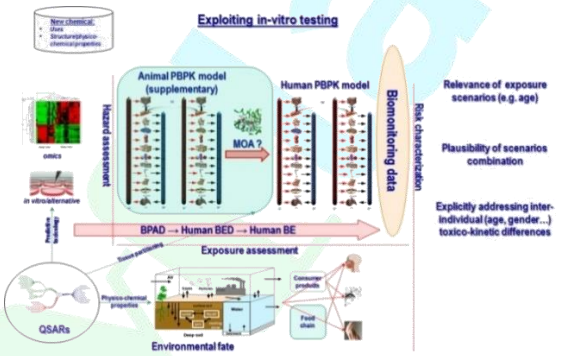


Figure 1. Integrating environmental contamination, human exposure and toxicology for refined risk characterization

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 over the last 5 years, namely:

INTEGRA - European Chemical Industry Council (CEFIC)

HEALS – EU FP7 project

CROME – LIFE+ project

CheRRIE – INTERREG project

ICSHNet – COST Action

BlueHealth – EU Horizon 2020 project

ICARUS – EU Horizon 2020 project

PEC – EU Civil Protection project

HBM4EU – European Human Biomonitoring Initiative

GRIN - GReen INfrastructures for disaster risk reduction protection: evidence, policy instruments and marketability

These projects follow the scientific principles described above, while focusing on different aspects of the "source-to-outcome" continuum. Acting synergistically, they contribute to the further development of the holistic EnvE Lab paradigm to exposure science and environmental health management.

Highlights of the year 2016

Excellence prize awarded to EnvE Lab Director Prof. Sarigiannis

In 2016, EnvE Lab Director, Prof. Sarigiannis was awarded by the Aristotle University of Thessaloniki for his success on bringing in the University finances from competitive EU projects for the years 2014-2015, among all members of the AUTH academic community.


Το Αριστοτέλειο Πανεπιστήμιο Θεσσαλονίκης

απονέμει

Βραβείο Αριστείας

στον Αναπληρωτή Καθηγητή του Τμήματος Χημικών Μηχανικών

Δημοσθένη Σαρηγιάννη

για την Εισροή Ερευνητικών Κονδυλίων στο ΑΠΘ από την Ευρωπαϊκή Ένωση
κατά τη Χρονική Περίοδο 2014-2015

Θεσσαλονίκη, 31 Μαρτίου 2016

Ο Πρύτανης

Καθηγητής Περικλής Α. Μήτκας

Figure 2. 2015 Excellence prize awarded to Prof. Sarigiannis.

WHO - Waste, health, sustainability: what way forward

On October 5-6, 2016 Prof. D. Sarigiannis (AUTH) presented an invited talk at the workshop: "Waste, health, sustainability: what way forward" in Bonn (Germany) organized by WHO European Center for Environment and Health.

Figure 3. WHO, Bonn, October 5-6 2016

Prof. D. Sarigiannis, based on the outcomes of CROME-LIFE, made clear proposals on waste management policy actions in Europe to ensure health and sustainability in his capacity as WHO advisor on integrated health impact assessment. This will be used as input to the forthcoming Ministerial Conference of the WHO (13-15 June 2017 @Ostrava, Czech Republic).

Integrated exposure assessment of bisphenol-A

Exposure to BPA and the potential adverse health effects constitute one of the hottest public health topic. The main controversy regards the toxicokinetic behavior of BPA; although BPA glucuronidation (the dominant detoxification mechanism) is complete and rapid, due to the reduced metabolic capacity of infants-neonates, there is still ample opportunity for internal exposure. EnvE Lab answered many of these questions, through a comprehensive analysis supported by an integrated exposure modelling framework that comprises far field and near field exposure modelling coupled to a dynamic lifetime PBTK model. Exposure analysis was done on European data of BPA food residues and human biomonitoring (HBM). The latter were further assimilated through an advanced exposure reconstruction modelling framework to estimate the corresponding external and internal systemic dose of BPA and its metabolites. Special attention was paid on the assessment of exposure to BPA during critical developmental stages such as gestation by modelling the mother-fetus toxicokinetic interaction. Our findings showed that current exposure levels in Europe are below the temporary Tolerable Daily Intake (t-TDI) of 4 μg/kg_bw/d proposed by the European Food Safety Authority.

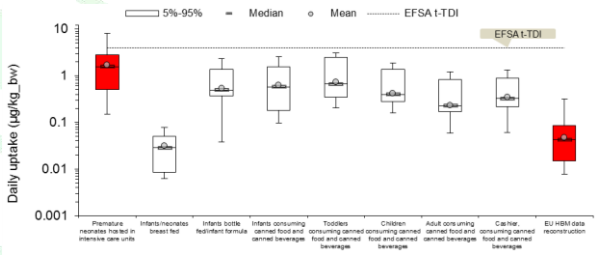


Figure 4. Daily uptake for the most important exposure scenario combinations. The reference dose is 4 μg/kg_bw/d (EFSA t-TDI)

Taking into account age-dependent bioavailability differences, internal exposure of premature neonates hosted in intensive care units was reckoned close to the biologically effective dose (BED) resulting from translating the EFSA temporary total daily intake (t-TDI) into equivalent internal dose. Use of the ToxCast21 Biological Pathway Altering Dose (BPAD) as an alternative internal exposure reference value, resulted in increased margins of safety.

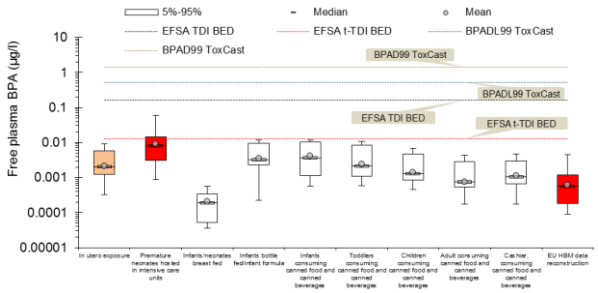


Figure 5. Free plasma BPA under most important plausible exposure scenario combinations (refined internal exposure analysis)

Exposure science

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.

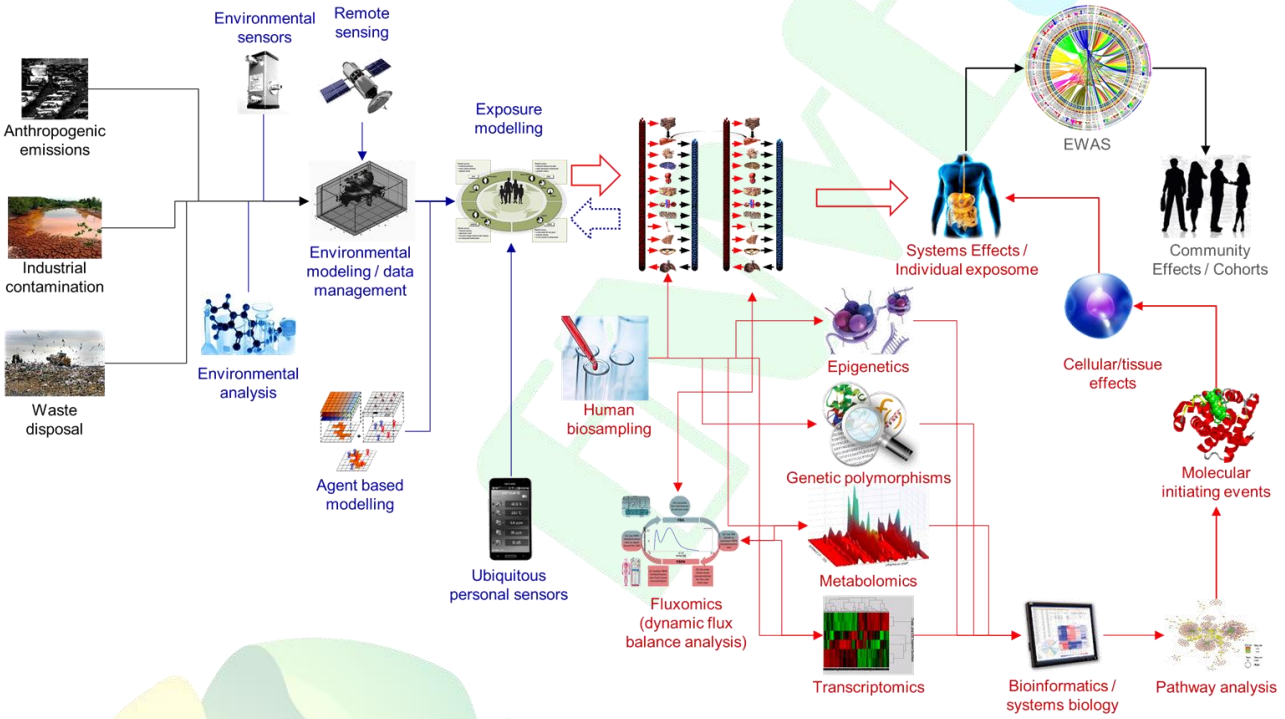


Figure 6. Conceptual representation of the technological arrays involved in the exposome assessment

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 are key components of the EnvE Lab paradigm towards unraveling 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 allow us 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 in order to understand the dynamics of real-world societal and environmental 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 probabilistic exposure estimates to derive biomarkers of exposure and/or effect. Combined epidemiological, clinical and genetic/epigenetic data analysis will shed light on the effect of risk modifiers 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.

Health and Environment-wide Associations based on Large population Surveys (HEALS)

The concept

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. EnvE Lab co-coordinates the project providing scientific leadership and coordinating the scientific strategy and ethical aspects of the project.

Assessing the exposome in order to encompass life-course internal and external environmental exposures, from preconception 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 investigation of DNA adducts in relation to a number of exposure types are being conducted.

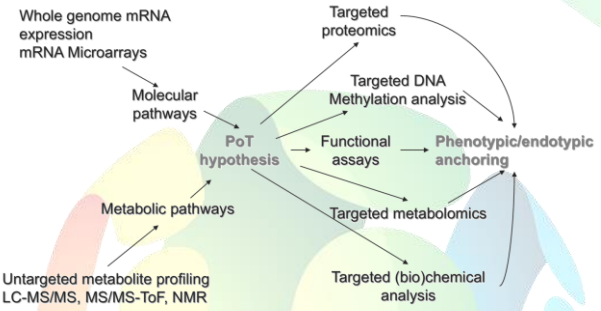


Figure 7. Analytical exposure biology workflow according to the HEALS paradigm

Research on the "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 was to extend the variables measured by using other personal sensors in a second pilot study involving 50 households in four European cities 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 2016 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.

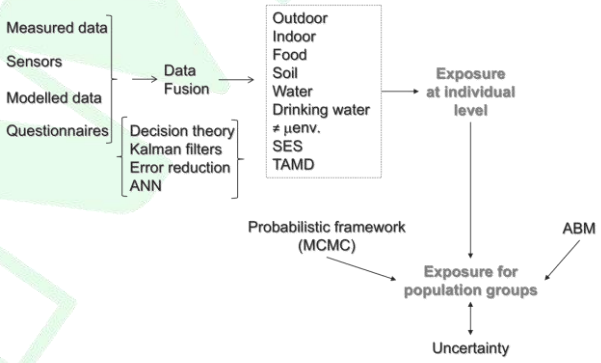


Figure 8. Workflow of external exposome assessment according to the HEALS paradigm

Developing reliable tools for assessing a complete exposure history is the second challenge taken up by HEALS. 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 were key activities 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), gave one of the first lectures at the US-NIEHS webinar series on the exposome, and published in the peer-reviewed literature.

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 are used 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 novel and promising approach gives 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.

As part of the HEALS project, during 2016, larger scale measurements have been initiated that include a series of commercially available location tracking and physical activity sensors together with pollution measuring sensors. Data was captured based on both in-home and personal monitoring. In more than 25 households a series of devices was placed, such as: a) the *Dylos*, a small, noiseless PM sensor that captures particles concentration in 2 size ranges >0.5 um and >2.5 um diameter, b) the *Netatmo*, which measures indoor air temperature, humidity, CO_2 and noise and c) *Radiello*® passive diffusive air samplers that capture aldehydes and benzene, toluene, ethylbenzene, and xylenes (BTEX). Participants' location and activity data was captured with physical activity sensors and smartphone apps. Specifically, the *Fitbit Flex* fitness monitor captured motion and intensity of activity, *Moves* app tracked location and activity, *WideNoise Plus* app tracked noise and *FatSecret* app tracked nutrition patterns. In addition, participants were asked to fill in a time activity diary and to answer to a series of questionnaires with the aim to capture further information regarding their personal exposure to potential sources of pollution, household conditions, SES and preferences/frequency of usage of consumer products. Occasionally in-house exposure assessment experiments took place with additional high accuracy equipment such as a) the AQ Expert Indoor Air Quality Monitor, that tracks CO_2, CO, tVOC, CH_2O, O_2, NO_2, O_3, SO_2, H_2S, NO/NO_x, relative humidity, temperature, barometric pressure and air velocity and b) Aerocet-531S Mass Particle Counter, that tracks six mas ranges and four particle sizes.

Wider scale sensors campaigns (HEALS – EXHES) will soon take place. This approach is a characteristic of *exposome* studies, where data is being gathered with the aim to do exploratory analyses to discover associations that lead to further, more targeted hypothesis driven research.

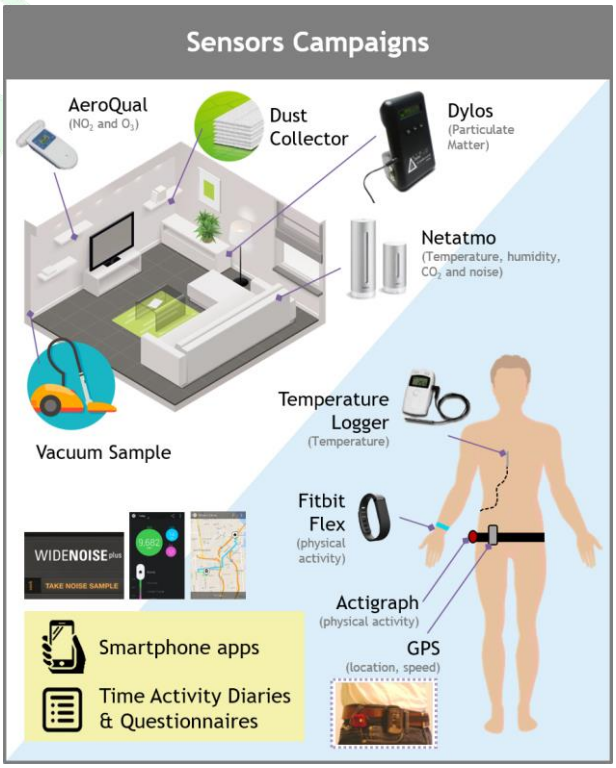


Figure 9. Overview of the personal sensors used during the preliminary trial campaign.

Personal exposure assessment using portable sensors data and Agent Based Modelling (ABM).

As already mentioned, innovations in sensor technology create possibilities to collect environmental data at unprecedented depth and breadth. Measuring, though, personal exposure directly requires a large number of people and therefore is often not feasible due to time and financial constraints. Considering the substantial hurdles involved in collecting personal exposure data for whole populations, a decision has been made to simulate human movement and interaction behaviour using Agent Based Modelling (ABM), a simulation technique that enables a better understanding of the behaviour of individuals and populations in social and evolutionary settings. This approach, allows the extrapolation of data from a local scale sensors campaign to the larger population of a region and can produce data that could fill in gaps that exist in traditional datasets, taking into account different activity patterns and Socioeconomic Status (SES) data.

A spatially explicit ABM platform was established, modelling the city of Thessaloniki. The model can feed into a population-based exposure assessment without imposing prior bias, but rather basing its estimations onto emerging properties of the behaviour of the computerised autonomous decision makers (agents) that compose the modelled system (city). City's population data, vehicles fleet information, road and buildings networks were transformed into human, vehicle, road and building agents respectively. Particular emphasis is being given in the case of in-model incorporation of SES data. Survey outputs with data on lifestyle/behavioural patterns were associated with human agent behavioural rules, aiming to model representative to real world conditions.

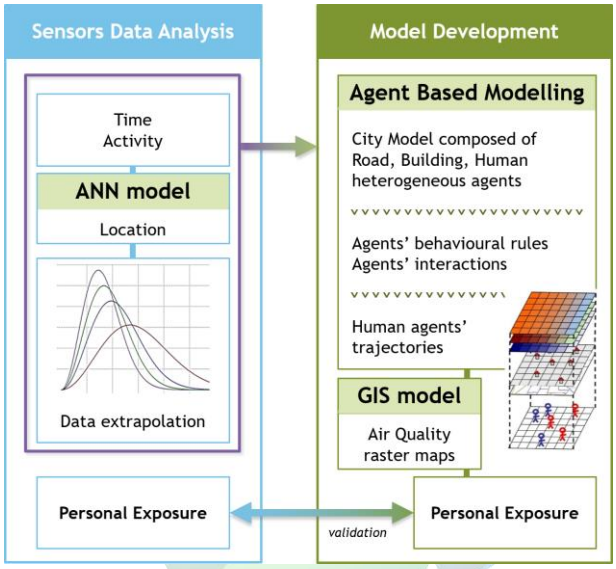


Figure 10. From sensors data to a personal exposure model.

Moreover, observations on spatiotemporal behaviours, derived from the sensors campaign (mentioned in the previous section), were extrapolated to the larger population of the city and translated into human agents' rules, taking into account sociodemographic variations.

At the end of a model run, activity patterns can be determined for every human agent, as an outcome of the prevalence of specific preferences and decision-making throughout the simulated time of experiment. Different human agents based on different characteristics (age, gender, SES indicators) will express different behaviours and this could lead to a different exposure profile. It is then possible to extract human agents' trajectories on a GIS format together with a database that contains their coordinates and activities in time through different locations/microenvironments (Time-Activity-Diaries). The GIS layer can then be superposed onto Air Quality maps. In this model, individual exposure to PM concentration is deduced via superimposing the human agent's trajectory on daily average PM concentration maps, modelled for the same region. These maps are the outcome of data fusion from ground observations, pollutants dispersion modelling and satellite images. GIS zonal statistics are then utilized to compute the average concentration an agent is exposed to per space and time. The high spatial resolution map allows us to calculate exposure at the level of building block. For the cases where human agents are located indoors, indoor concentration is estimated using the INTERA computational platform. Personal exposure, expressed as inhalation-adjusted exposure to air pollutants is then evaluated by assigning pollutant concentrations to an agent based on his/her coordinates, activities and the corresponding inhalation rate.

Figure 11. Personal exposure assessment using Agent Based Modelling (ABM).

Changes in exposure levels can be calculated for individuals and specific subgroups of population based on different spatio - temporal behaviours.

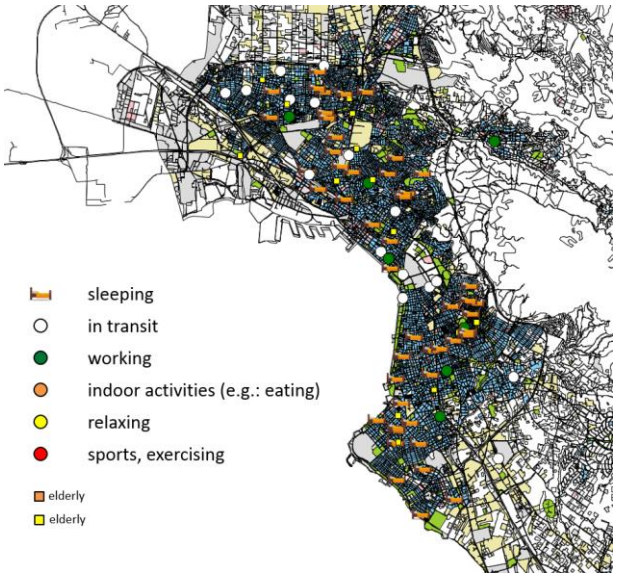


Figure 12. Moving human agents on a representative day in the city of Thessaloniki - running example of the ABM platform.

On average, personal exposure results were between 10 and 20% more accurate than the equivalent estimate using outdoor PM concentration as exposure proxy. The identification of exposure peaks and troughs throughout the day leads to useful conclusions regarding capping exposure to high pollution levels. The following figures showcases the activity profile, exposure to PM10 (*black line)*, inhalation-adjusted exposure (*blue line)* as well as daily intake dose of a randomly picked child agent (male, 12 years old).

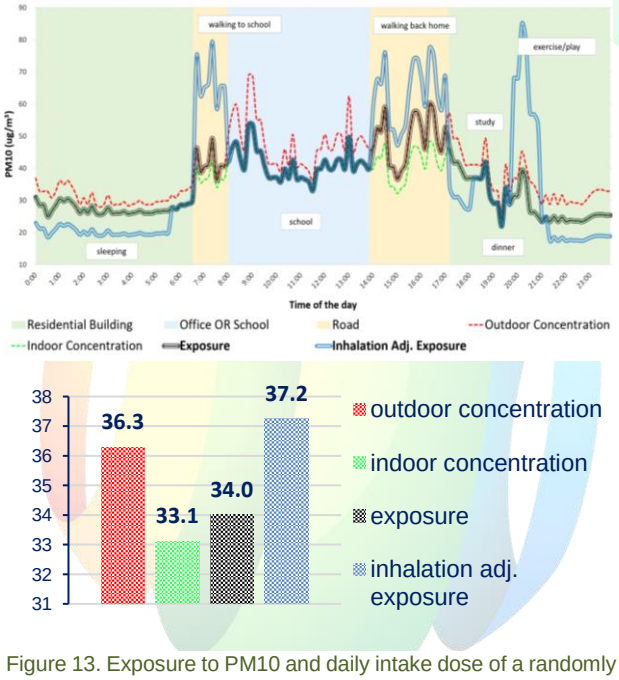


Figure 13. Exposure to PM10 and daily intake dose of a randomly picked child agent. Personal exposure *in black*; inhalation adjusted exposure *in blue.*

Overall:

- It is clear that data collected by "smart" devices can help provide more accurate exposure assessment for exposure simulation modelling and environmental health studies. The sensors investigations offer valuable information on the utility of several commercial devices as modular add-ons to exposure 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.

- More SES variables, associated with behavioural rules, are now incorporated in the personal exposure ABM model. Individual variations in factors such as age, gender, educational level and occupational status are considered and mechanisms for interactions to occur between individuals are being established.

- Utility functions are provided that can shape human agents' preferences based on individual characteristics. **Different SES groups will follow different behaviours and this will be reflected in different decisions regarding mode of transport, consumer products and selection or diet patterns**. Eventually this will result to a more accurate exposure assessment.

- ABM-generated distributions of human agents' behavioural patterns can also work as an input into a probabilistic exposure assessment model.

- 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 establishment of an approach with the capacity for aggregation at various levels of population size, together with the integration of SES indicators, can lead to an exposure assessment model that can be useful especially for vulnerable groups of population, such as children, the elderly and people with low socioeconomic status.

- The model can be further used as a means for estimating and comparing the probable effects of different public health strategies prior to implementation, therefore reducing the time and expense required to identify effective policies.

The dietary exposome

Food as consumed contains many different chemicals which are either desirable (e.g. micronutrients) or undesirable (e.g. pesticide residues or mycotoxins). For all these chemicals, levels in the diet that are either too high (e.g. pesticides residues) or too low (e.g. essential vitamins) maybe detrimental to human health.

Food is the most important exposure pathway for trace metals (e.g. As, Cd, Pb, Hg) and POPs for the general population. Indeed, food is typically responsible for more than 90% of total adult exposure to PCDDs/Fs and co-planar PCBs (WHO 2002; Centre for Food Safety 2012) and to Hg and Cd (for non-smokers). In this light, when considering human exposure through the whole life it is imperative to properly take into account exposure to chemicals through diet. In the course of the risk assessment process, exposure estimates are required based on the consumption of the foods containing these substances and the level of the substances present in those foods. In both cases dietary intakes were calculated using the following formula:

$$I_j = \sum_{k=1}^{n} C_k \cdot L_{k,j}$$

where I_j is the dietary intake of chemical j; C_k is the consumption of food k and $L_{k,j}$ is the concentration level of chemical j in food k.

Dietary exposure to each contaminant of interest was calculated individually using the following formula:

$$E_j = \frac{\sum_{k=1}^{n} C_k \cdot L_{k,j}}{BW}$$

Where E_j is dietary exposure to the chemical j and BW is the human body weight

The above methodology was applied to a population study as well as to an individual level.

For the first application we have used data collected in the frame of the French Total Diet Study undertaken between 2006 and 2009 by the French National Institute for Agricultural Research (INRA), in collaboration with the French Food Safety Agency (AFSSA). Food consumption patterns disaggregated for age, gender, educational level and geographical region were derived from the INCA 2 study which was carried out by AFSSA between 2006 and 2007 and included 4,079 individual subjects (2,624 adults aged from 18 to 79 years and 1,455 children aged from 3 to 17 years). By way of example, population daily exposure to arsenic for different gender and age classes and educational level are reported below.

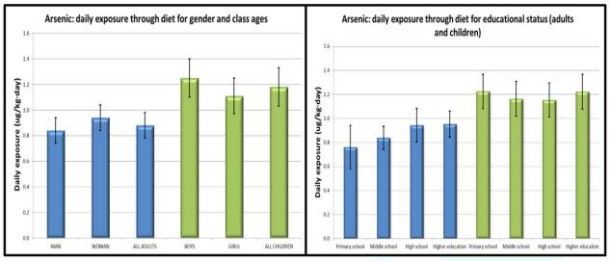


Figure 14. Arsenic daily exposure for some population groups

For the second application we used the individual food consumption data collected in the pilot study carried out in Athens in the frame of the FP7 project HEALS. Thirty mothers and their children were followed for one week and their individual food consumption habits were collected through the Fatsecret app.

Individual daily intake to trace metals (As, Cd, Cr, Hg and Pb) and persistent organic pollutants (PCDDs, PCDFs, PCBs, PFOS and PFOA) are reported below.

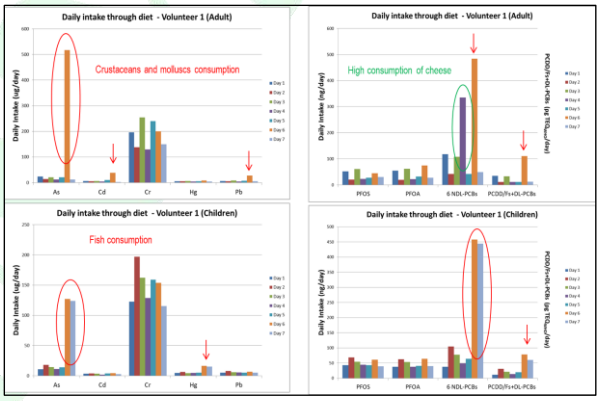


Figure 15. Individual daily exposure of adult (above) and children (below) to trace metals (left) and POPs (right)

Results of the two applications showed that both in adults and in children fish and seafood (e.g. crustaceans and molluscs) are the main contributors to POP and to most of trace metal (As, Cd, Hg and Pb) exposure.

The main contributors to chromium intake are bread and dried bread products and alcoholic beverages. In children, the main contributors to chromium intake are milk and pasta. Generally, cheese and dairy products are significant contributors to dioxin and PCB exposure. For children, the most consumed foodstuff is milk; the latter has a vector rate equal to that of ultra-fresh dairy products and cheese, which have more fat content and thus higher concentrations of POPs.

People with higher educational level show higher exposure to POPs and to most of the trace metals (As, Cd, Hg and Pb) due to the higher average consumption of fish and seafood. Children show higher exposure level to all the contaminants investigated due to their lower body weight with respect to the adult one.

Pathway analysis of prenatal exposure to phthalates and child motor development

Phthalate prenatal exposure was determined by targeted metabolomics measuring 11 phthalate metabolites in urinary samples from (n=165) mothers during the third trimester of pregnancy (prenatal exposure) and from their children at the 24th month of age (postnatal exposure), using HPLC–MS/MS. Psychomotor development was assessed in children at the age of 2 years by the Bayley Scales of Infant and Toddler Development.

Child motor development was inversely associated with natural log concentrations (µg/g creatinine) of 3OH-MnBP (β = − 2.3; 95% CI − 4.0 to − 0.6), 5OH-MEHP (β = − 1.2; 95% CI − 2.2 to − 0.3), 5oxo-MEHP (β = − 1.8; 95% CI − 3.3 to − 0.2) and sum of DEHP metabolites (β = − 2.2; 95% CI − 3.6 to − 0.8), DnBP metabolites (β = − 1.9; 95% CI − 3.4 to − 0.4), and high molecular weight phthalates (β = − 2.5; 95% CI − 4.1 to − 0.9) in the urine collected from mothers during pregnancy after adjustment for a variety of potential confounders. Postnatal child exposure to phthalates was not associated with any of the measured scores of child psychomotor development. To further elucidate the potential mechanism that relates phthalates exposure with child motor development, untargeted metabolomics analysis (using a 600 MHz NMR) of the mother urine samples was carried out. A typical metabolites profile is illustrated in Figure 16.

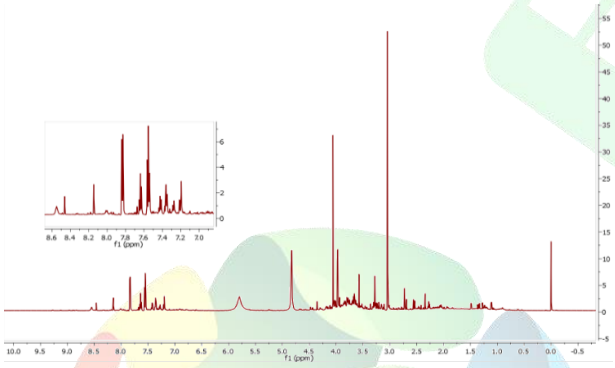


Figure 16. Typical metabolites profile

Meta-analysis revealed that mothers with higher exposure to phthalates have completely different metabolic profiles compared to the ones with lower exposure levels (Figure 19). Metabolic pathway analysis using Agilent GeneSpring revealed that alterations in urine metabolites are related to the TCA cycle, suggesting impaired mitochondrial respiration; the latter is central to energy metabolism and cellular signalling and plays fundamental roles in synthesis of nucleotides and active transport processes. Inhibition of mitochondrial oxidative phosphorylation could also cause defective mitochondrial energy production during the process of fetus formation and development that are reflected in early life motor development.

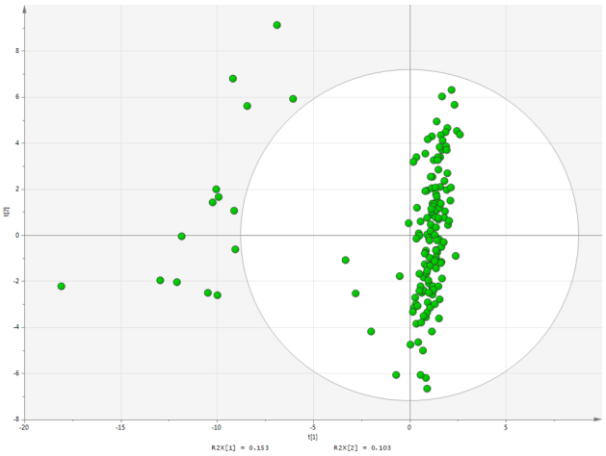


Figure 17. Multivariate analysis of metabolic profile

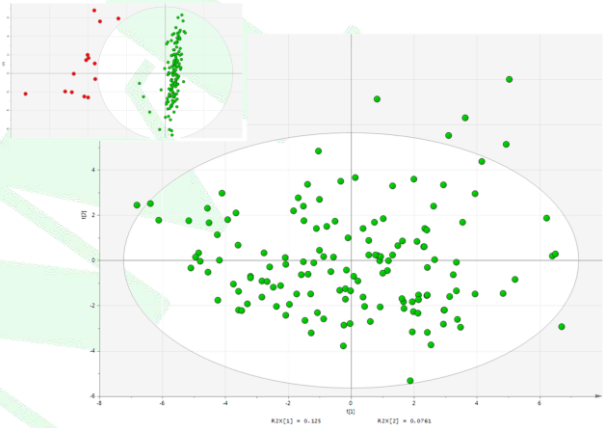


Figure 18. Meta-data of multivariate analysis excluding outliers

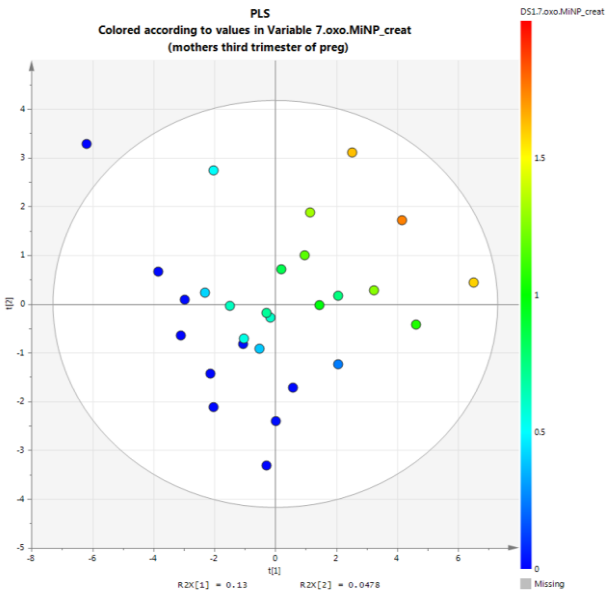


Figure 19. PLS scores plot in correlation with the variable 7.oxo.MiNP in urine of mothers in the third trimester of pregnancy. Blue shows lower values for urinary 7.oxo.MiNP, whereas red shows higher values of the same variable.

.

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 20):

- 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.

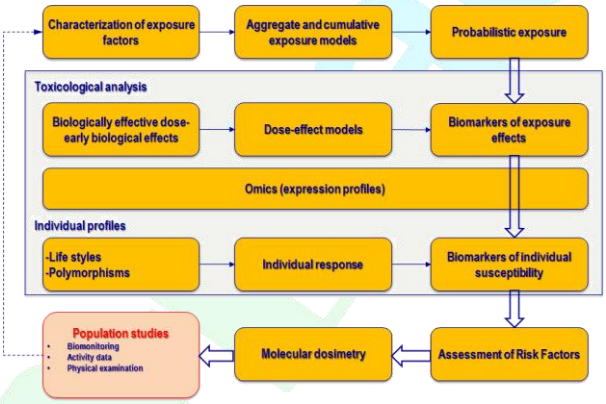


Figure 20. Connectivity – a multi-layered approach

Additional elements towards the implementation of the connectivity approach is the integration of multiple factors that determine the exposome, genetics (e.g. susceptibility) and epigenetic alterations, as well as dietary and other behavioral factors that affect overall exposure through metabolic profiling and systems biology integration (Figure 21). By understanding the individual exposome we have a better understanding of the causal associations of individual disease, paving the way towards more precise prevention strategies, as well as treatment of the disease. Precision prevention and treatment are more efficient, thus improving overall health status and well-being, in addition to reducing the socioeconomic burden from morbidity and mortality.

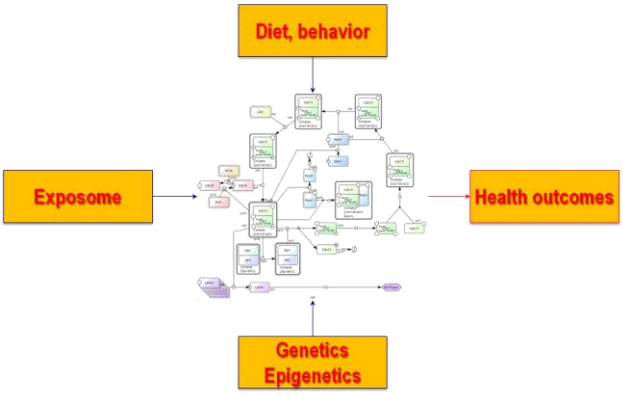


Figure 21. Metabolic profiling and systems biology integration

Cross-Mediterranean Environment and Health Network (CROME)

The concept

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

The main objective of CROME-LIFE is to demonstrate a technically feasible integrated methodology for interpreting 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 tools are being applied in 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.

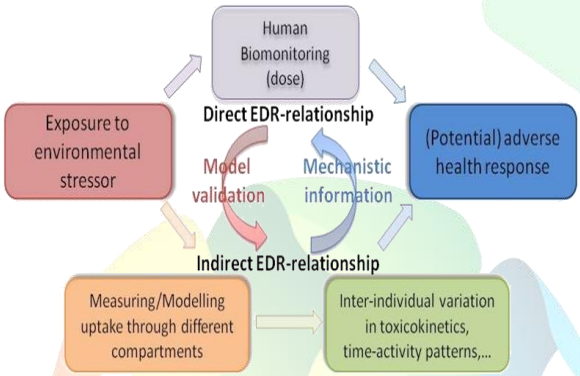


Figure 22. CROME methodological framework "middle out approach"

Re-evaluation of existing cohort data

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 land use at the participant residence and workplace, 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).

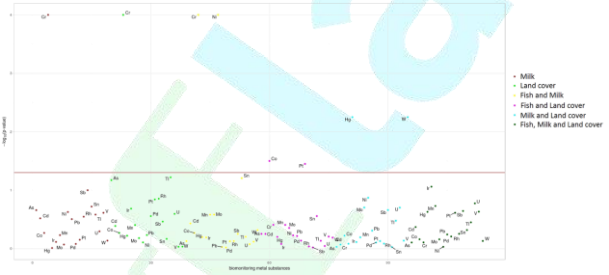


Figure 23. Manhattan plot of associations of the environmental factors with HBM levels of metals ($p < 0.05$). The red line represents a $p < 0.02$, which means a more robust association.

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 country-specific case studies (one for each participating Country) and one common case study in all 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.

Assessment of PAHs exposure and genotoxic effects

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 24).

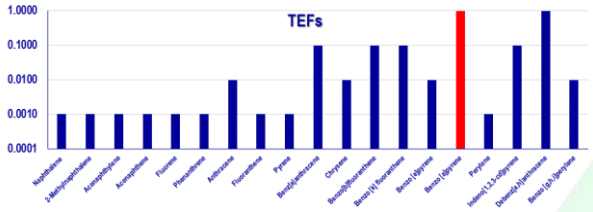


Figure 24. Toxic Equivalent Factors (TEFs) for the different PAHs, on the assumption that the TEF for B[a]P is equal to 1

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 25). Therefore, practically, most of the PAHs are adsorbed in fine particles (PM2.5 and finer).

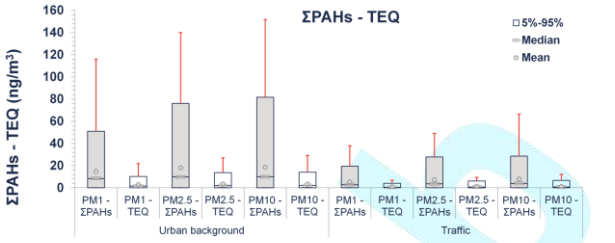


Figure 25. Total PAHs concentrations for the two monitoring stations

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 25). 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.

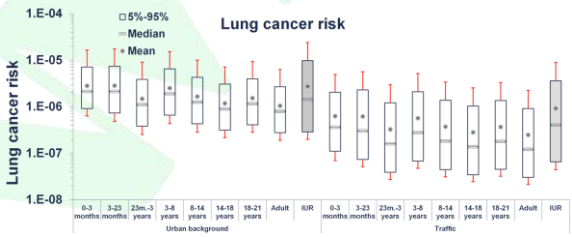


Figure 26. ICR calculated for each age group

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.

Waste and health

Athens, the capital of Greece, is populated with around 5 million inhabitants. The average amount of municipal solid waste is equal to 6 ktn/d (Hellenic Statistical Authority 2008). The average composition of the waste in Attica ***Figure 27***includes organics (42%), paper (29%), plastic (14%), metal (3%), and other material (6%).

Figure 27. The main waste management site in the area of Athens (landfill in Fili) and the respective waste composition

The average transportation distance of the MSW is 19 km. Two of the main MSW facilities in Athens are the landfill in Fili. The HERACLES (Waste Management) Greek cohort, is a study aiming at assessing the contribution of environmental contamination due to waste management practices in the urban and periurban environment associated to children neurodevelopment. The study has been established in 2012. Around 350 children aged 3 to 8 living in the proximity between 0.5 to 12 km were enrolled. For the association, several exposure factors have been investigated, including exposure to heavy metals, such as Cd, Hg and As in urine, Pb in blood, Mn and Hg in hair (Figure 28), exposure proxies, such as distance from the contaminated sites, concentration of heavy metals in the soil of the child address, additional factors considered as exposure and effects modifiers such as sociodemographic parameters (socioeconomic status, mother education, father education, stress events) as well as child anthropometric parameters and post-delivery factors (child body mass index, child gender, breastfeeding, presence of micronutrients, minerals and vitamins, Se in the mother plasma during pregnancy, delivery and in cord blood).

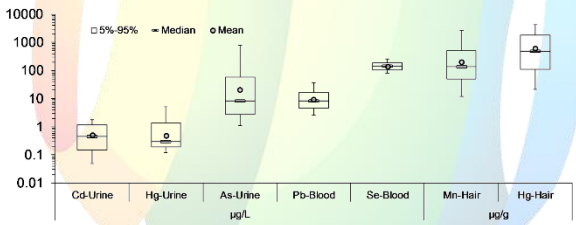


Figure 28. Levels of heavy metals in the various human biospeciments

Finally, detailed dietary habits, such as consumption of meat products (pork meat, beef, lamb, sausages), fish, sea food, poultry (eggs, chicken), dairy products (milk, yogurt), nuts, fruits, vegetables and snacks (biscuits, chocolates) were also recorded. Neurodevelopmental progress in children was estimated with (a) the Child Behavior Checklist, also called the Achenbach System of Empirically Based Assessment, is a report form to screen for emotional, behavioral, and social problems and (b) Wechsler Intelligence Scale for children – Fourth Edition (Wechsler, 2003), which is an individually administered measure of intelligence intended for children. WISC-IV yields measure of general intelligence as reflected in both verbal and nonverbal (performance) abilities and specific indices including verbal comprehension, perceptual reasoning, working memory and processing speed. Auto-correlations of the various parameters, are illustrated in the correlation globe (***Figure 29***).

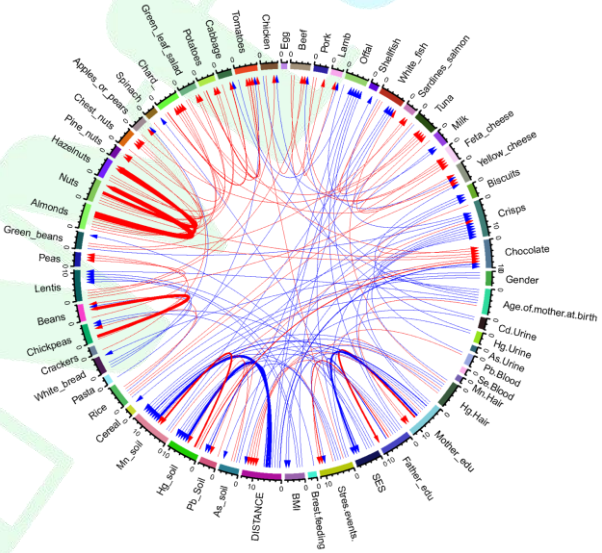


Figure 29. Correlation globe of environmental, dietary and exposure factors in the HERACLES study

EWAS analysis results relevant to the Child Behavioral CheckList (CBCL) test battery results show that socio-cultural factors are strongly associated with children behavior. More specifically the mother school title and the age of the mothers at birth show both a robust statistical association (p-value<0.05 and in some cases p-value <0.01) with most of the CBCL indices considered. Looking at the volcano plots both parameters show a negative association with the CBCL scores indicating that lower educational level of the mothers as well as a lower age of the mother at the children birth may have negative impact on the children behavior.

The stress index was derived by merging the total number of stressful events detected by the mother and their average intensity is also playing an important role on the children behavior (p-value<0.05 and in some cases p-value<0.01) showing a negative effect on both internalizing and externalizing problems indices such as anxiety and depression, withdrawal and depression and somatic complaints, aggressive and rule-breaking

behavior. The concentration of lead in blood shows a strong statistical significance (p-value <0.05) with most of the CBCL indices analyzed. In this case the association shows a positive direction revealing a negative impact of higher blood concentration of lead on the on cognitive functions in children. This result is confirmed by a number of research studies which indicate exposure to lead as one of the most environmental determinants of neurodevelopmental disorders in children. Of opposite sign but still with robust statistical significance is the association of the concentration of selenium in blood which appears to beneficially, especially with regard to Internalizing Problems and ADHD as measured by CBCL battery indices. These results confirm the antioxidant properties of selenium which is a well-known regulator of brain function.

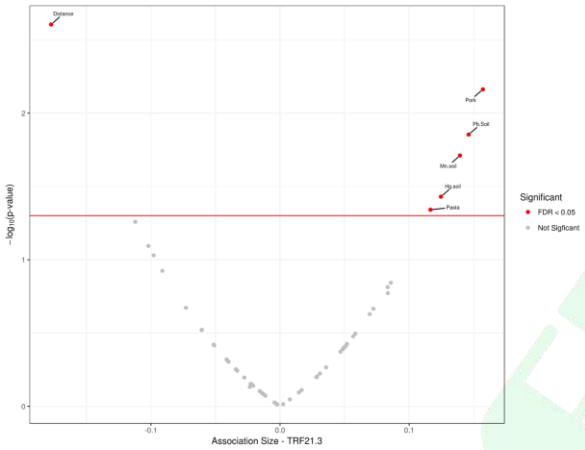


Figure 30. Associations of attention deficit / hyperactivity problems (from the CBCL test battery) with the environmental, dietary and exposure factors

Distance of the residence address from the waste management site was found also to be a key factor associated with almost all the indices of the WISC IV test. More specifically, this variable showed a robust statistical association (p-value <0.001) with the Intelligence Quotient (IQ), Verbal Comprehension index, Perceptual Reasoning index, Working Memory index. Analysis of the results shows a positive association with the WISC IV scores indicating that living far from the waste management site has a positive impact on the children cognitive functions. Interesting conclusions can be drawn from the analysis of food consumption patterns. Tomato consumption appears to be statistically (p-value <0.05) associated with intelligence quotient (Figure 31), Verbal Comprehension index and Working Memory index while cereal consumption reveals a strong association (p-value < 0.01) with the Perceptual Reasoning index. Both food items are positively associated with cognition indices meaning that their consumption has potential positive effects on the cognitive functions of the children. Epidemiological evidence suggests that consumption of lycopene, a natural antioxidant present in tomatoes, is able to reduce the risk of chronic diseases such as cancer, cardiovascular diseases as well as psychiatric syndromes. In another study reported that low serum levels of lycopene have been associated with increased risk of psychiatric disorders.

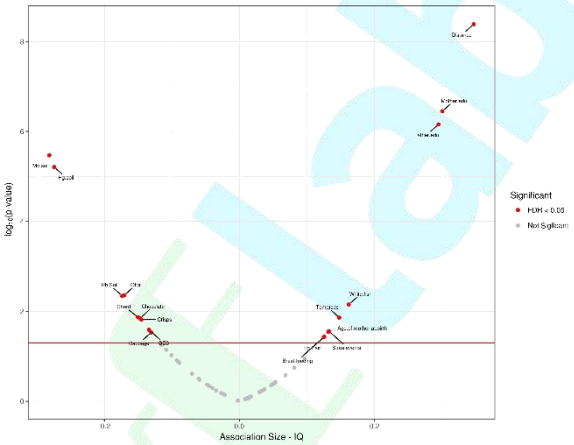


Figure 31. Association of intelligence quotient (from the WISC-IV test battery) with environmental, dietary and exposure factors

Consumption of fish showed a hybrid behavior depending on the type of fish and the neurodevelopmental indicator considered: higher consumption of white fish appears to have positive effects on the IQ and Verbal Comprehension index (p-value <0.001) while higher consumption of white fish reveals a negative effect (p-value <0.01) on Perceptual Reasoning index and Working Memory index.

A key finding of the study is that concurrent evaluation of environmental, societal and nutrition factors, allowed the identification of the most critical parameters. Distance of the family residence from the landfill was identified as the most important parameter, highlighting the contribution of the area contamination to child neurodevelopment. However, the beneficial effect of parental education and of children/family socio-economic status need to be underlined. Additional beneficial effects arise from specific dietary patterns such as consumption of white fish and tomatoes, while the same occurs for breast feeding. White fish is rich in omega 3 fatty acids. Direct actions of omega-3 polyunsaturated fatty acids on neuronal composition, neurochemical signalling and cognitive function constitute a multidisciplinary rationale for classification of dietary lipids as "brain foods." The validity of this conclusion rests upon accumulated mechanistic evidence that omega-3 fatty acids actually regulate neurotransmission in the normal nervous system, principally by modulating membrane biophysical properties and presynaptic vesicular release of classical amino acid and amine neurotransmitters. On the other hand, tomatoes are considered as strong antioxidants, providing protection against the reactive oxygen species (generated by heavy metals) that affect neuronal mitochondria and eventually children neurodevelopment.

he Integrated External and Internal Exposure Modelling Platform (INTEGRA)

The concept

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 main component of INTEGRA is a flexible and user-friendly web-based computational platform that integrates environmental fate, exposure and internal dose dynamically in time allowing us to differentiate between biomonitoring data corresponding to steady exposure patterns as opposed to acute, one-off exposures (Figure 32). The platform is largely validated using human biomonitoring data from Europe and the USA.

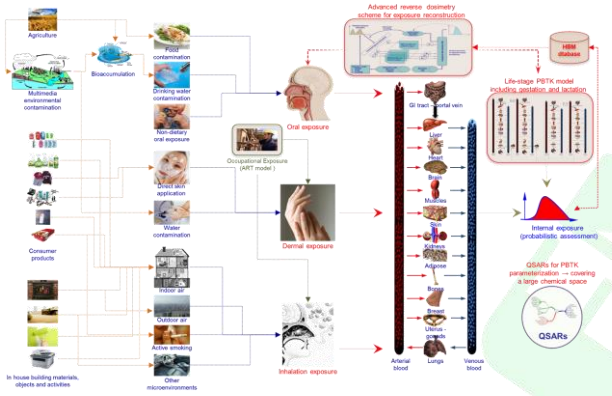


Figure 32. INTEGRA conceptual representation

The project started on January 1, 2013 and has a total budget of 299 K€ entirely funded by CEFIC for a duration of 36 months with the participation of four leading Institutions in Europe coordinated by EnvE Lab.

The INTEGRA methodology (and the relevant computational platform) brings about clear advances in terms of indoor micro-environmental interactions (contamination exchange between gaseous, particles and dust phases, chemical reactivity), towards an integrative exposure assessment framework that captures the dynamics of biological processes involved and reduces 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.

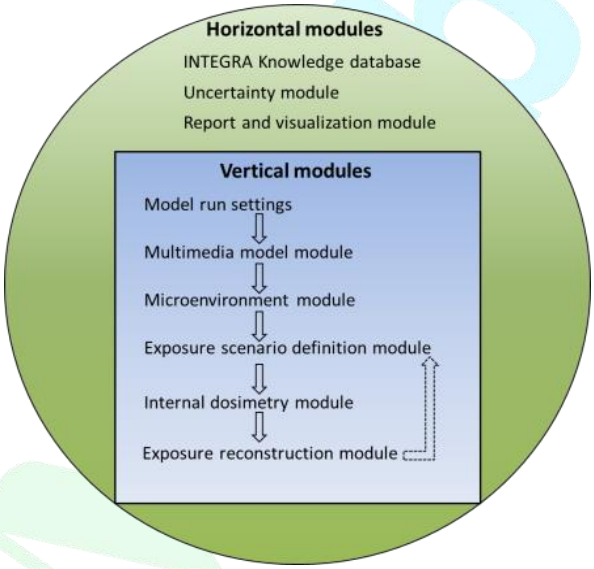


Figure 33. Modules of INTEGRA computational platform

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 to better embed the work of the project within international efforts towards improved risk assessment of chemicals. The INTEGRA platform is a multimodular software following the open architecture paradigm especially designed to execute aggregate exposure assessment. The platform enables 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 encompasses three horizontal modules and six vertical modules, each addressing a step along the source-to-dose (external and internal) continuum (Figure 33).

QSARs

A major area of work within the INTEGRA project is the development of Quantitative Structure – Activity Relationship (QSAR) models. QSARs are regression or classification models, included in "in silico" approaches that form a relationship between the biological effects and the chemical structure of a chemical compound, Y = f (X). QSAR models comprise three parts:

a. the activity data to be modeled (Y),

b. the descriptors with which to model (X) and

c. a method to formulate the model.

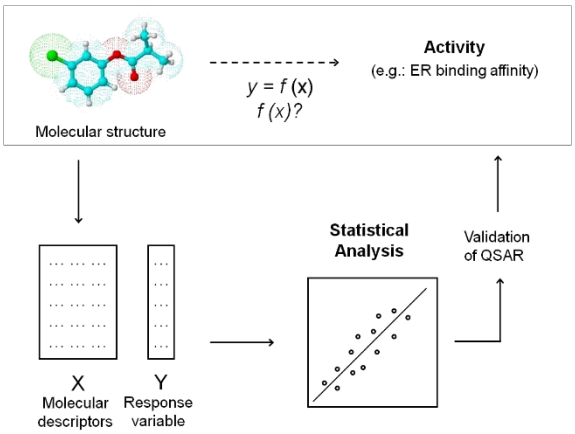


Figure 34. Basic methodological scheme for QSAR development.

QSARs are widely used in order to estimate the required inputs of Physiologically Based Bio – Kinetic (PBBK) models. PBBK models provide quantitative descriptors of Absorption, Distribution, Metabolism and Excretion (ADME) of an environmental or pharmaceutical chemical and their application is of major importance in toxicity testing and health risk assessment.

EnvE – Lab research focuses on the development of a simple and unified QSAR model, which could be used to predict both major physicochemical and biochemical properties of a large group of environmental chemical compounds. The activity data to be modeled (Y) includes the tissue/ blood partition coefficients for different human tissues (kidney, heart, muscle, adipose, brain, lung, liver) as well as the metabolic parameters, V_{max} and K_m.

Up until now, several approaches incorporating QSARs have been proposed for the prediction of partition coefficients for PBBK modeling, including the Peyret, Poulin and Krishnan algorithm and the molecular fractions algorithm proposed by Béliveau et al.

In this study, particular emphasis is being given to the development of QSAR models using two different descriptor sets (X):

1. Linear Free – Energy Relationship (LFER) Descriptors

$$logSP = c + e \cdot E + s \cdot S + a \cdot A + b \cdot B + v \cdot V$$

Where ***SP***: biological property of the examined chemical, ***E***: excess molar refractivity, ***S***: chemical's dipolarity/polarizability, ***A***: solute effective or summation hydrogen-bond acidity, ***B:*** solute effective or summation hydrogen-bond basicity, ***V:*** McGowan characteristic volume of the chemical.

2. PaDEL Descriptors

1D, 2D, 3D molecular descriptors and fingerprints of the chemical.

The first step for the development of QSAR models was the preparation of the collected data. This process included prereduction of the initial descriptors in order to avoid the semi-constant (>80%) and intercorrelated (>95%) ones, distribution and categorization of the chemicals using Principal Component Analysis (PCA), data splitting into training, validation and test set.

The data was, then, analysed using three statistical methods:

a. Artificial Neural Networks (ANN)

- Multi-Layer Perceptron (MLP) model using the scaled conjugate gradient back-propagation algorithm.

b. Non Linear Regression (NLR)

- Least Squares (LS) coupled with the Levenberg-Marquardt algorithm.

c. Multiple Linear Regression (MLR)

- Ordinary Least Squares (OLS) model
- Genetic Algorithm (GA) for descriptors' selection.

A comparison of experimental and predicted values of tissue/ blood partition coefficients and metabolic constants, using the ANN, NLR and MLR methods is presented at the following figures.

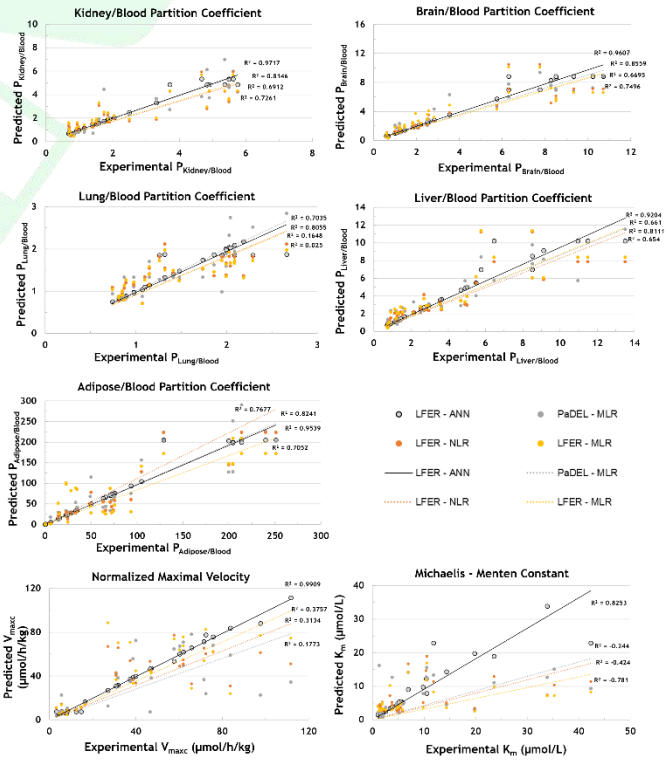


Figure 35. Predicted vs experimental values of tissue/ blood partition coefficients and metabolic constants, using the ANN, NLR and MLR methods.

The results indicate that the molecular descriptors of LFER can be suitable for the estimation of the parameters which characterize the physicochemical and biochemical phenomena. The use of ANN provides the essential flexible mathematical framework for describing the non-linear biological interactions.

Specifically, a major breakthrough came from the use of LFER coupled with ANN for predicting biochemical properties such as Maximal Velocity (V_{max}) and Michaelis – Menten constant (K_m). This was a remarkable advance, since till now, the prediction capability of Michaelis – Menten constant was rather poor (R^2 up to 0.35); with our coupled LFER – ANN method for the investigated group of chemicals, R^2 went up to 0.82 (Figure 35), which is by far higher to any other existing methodology.

Exposure reconstruction from HBM data

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 36).

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.

MCMC simulation (Figure 37) 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.

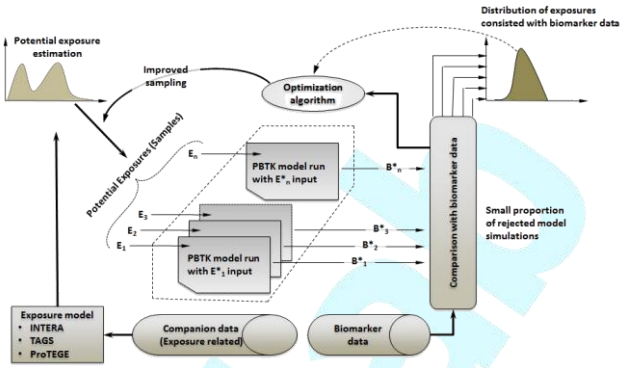


Figure 36. Optimization-aided exposure reconstruction based on HBM data using time-evolving PBPK models

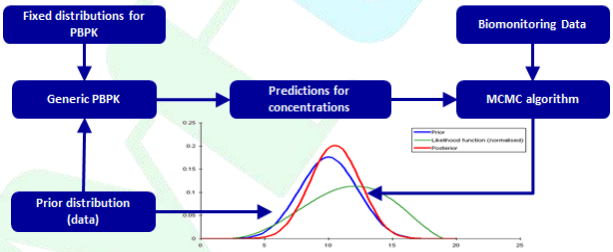


Figure 37. Conceptual/computational framework for the exposure reconstruction

Moreover, Differential Evolution (DE) and MCMC algorithms have been combined to solve 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 38).

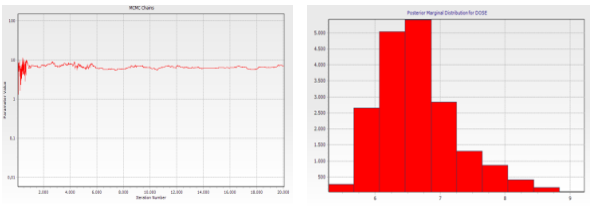


Figure 38. MCMC simulation convergence and Posterior Distribution for dose

Validation of the computational tool using real life HBM data

Exposure reconstruction of trichloromethane (TCM)

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.

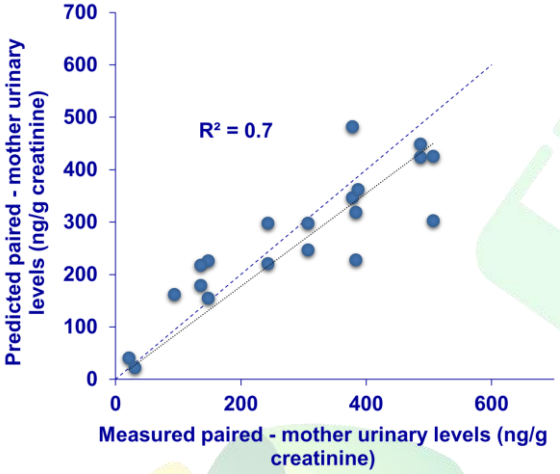


Figure 39. Measured vs. predicted urinary chloroform levels for the paired mothers, based on indoor concentrations derived from exposure reconstruction of paired-children data

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 $\mu g/m^3$, 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.

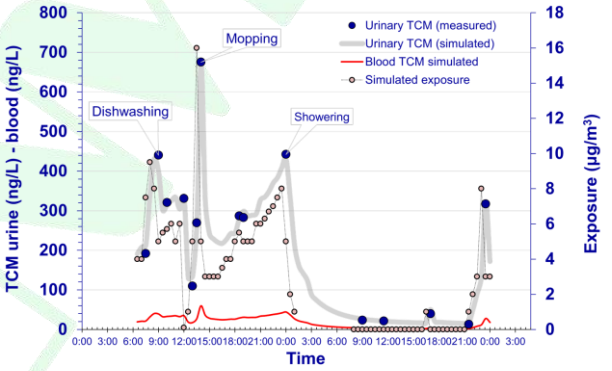


Figure 40. Measured urinary TCM (blue dots) and modelled chloroform levels in urine (grey line), blood (red line) and ambient air (dashed line)

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.

Exposure reconstruction of triclosan

Another application of validating the computational platform of INTEGRA was the estimation of triclosan exposure levels during teeth brushing. Seven volunteers were writting in a time-activity diary the time of teeth brushing and the amount of toothpast used, while all day urinary voids were collected and analyzed. Based on the urinary triclosan concentrations, and knowing the timing that exposure events occurred, the amount of triclosan

intaken per brushing was successfully estimated. The results of the simulation for a typical individual are illustrated in Figure 41. Starting from the measured urinary triclosan (black dots) and knowing the moment that the individual was exposed to triclosan, the dose received in each brushing was estimated (green dots). The accurate prediction of the dose is shown by the very good fit of the measured urinary concentrations against the ones predicted by the model. This further allows us to estimate the actual internal dose, meaning the concentration of triclosan in blood (red line) and eventually to potential target tissues.

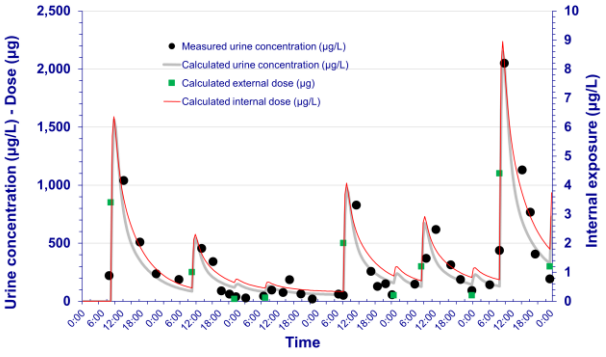


Figure 41. Measured (black dots) and modelled (grey line) urinary triclosan levels, modelled levels in blood (red line) and predicted dose (green dots)

Exposure reconstruction of bisphenol A

Similarly, diurnal exposure to bisphenol A through food and drink items was estimated starting from urinary biomonitoring data. The results indicated that overall daily exposure to bisphenol A remains below 0.1 µg/kg_bw/d, while internal dose of free plasma bisphenol A was in the range of few pg/L.

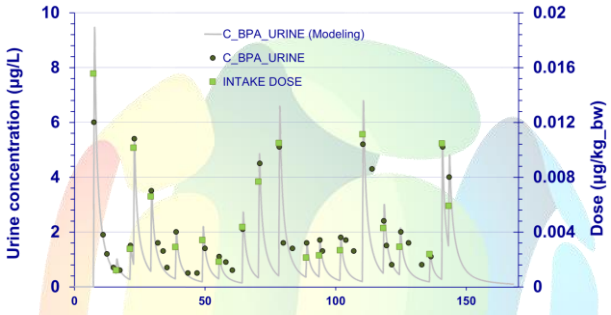


Figure 42. Measured (black dots) and modelled (grey line) urinary bisphenol A levels, and predicted dose (green dots)

External and internal exposure assessment to PAHs from multiple sources

Exposure to PAHs has became of particular scientific and regulatory interest the last year, especially in view of the potential for petroleum substances to be included in the different REACH processes (notably Evaluation and Authorisation). In order to meet the requirements of REACH, it is of particular importance the capability of models to predict direct (arising from the use of substances) and indirect (e.g. fuel combustion) PAH exposures. The capabilities of the INTEGRA platform for addressing integrated multi-source, multi-route (MSMR) exposure to PAHs was demonstrated in a workshop organized by CONCAWE. A typical scenario that was demonstrated, dealt with the prediction of the environmental fate and exposure of annual emissions of 400 tones B[a]P in air within EU, and for regional emissions of 15 tons. Distribution across different environmental media and the contribution of different pathways and routes to the overall exposure were estimated (Figure 43) both for adults and children.

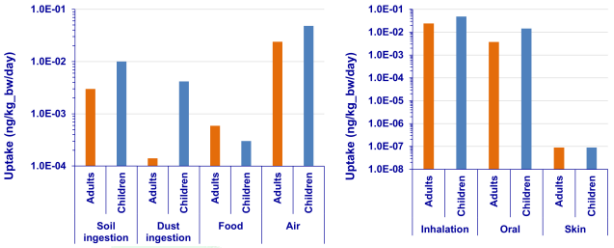


Figure 43. Contribution of pathways and routes in aggregate PAHs exposure

Moreover, internal exposure to B[a]P and urinary concentration of 3-OH-B[a]P (the most specific B[a]P metabolite) was also estimated.

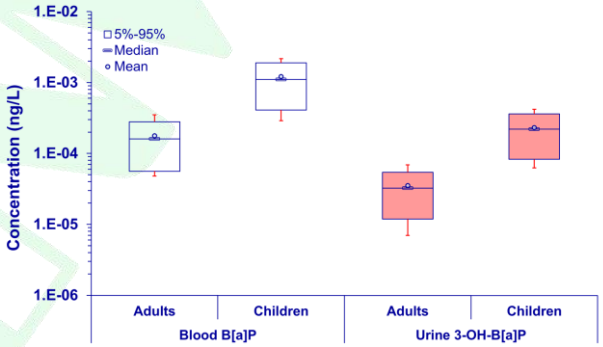


Figure 44. Internal exposure and urinary concentrations of major B[a]P metabolite

The time-dynamic nature of the INTEGRA computational platform, allows also to capture environmental, exposure and internal dose dynamics in high temporal resolution, quantifying the effect of real-life different exposure conditions (such as driving, eating smoked fish or operating an open fireplace) in actual uptake, internal dose and expected biomarker urinary levels (Figure 45).

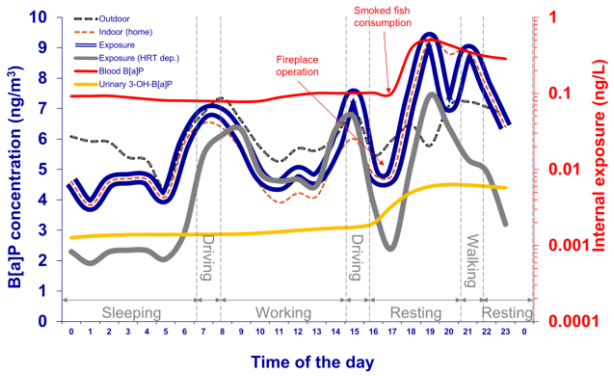


Figure 45. Diurnal variability of environmental, exposure and internal dose dynamics

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 titled "***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.

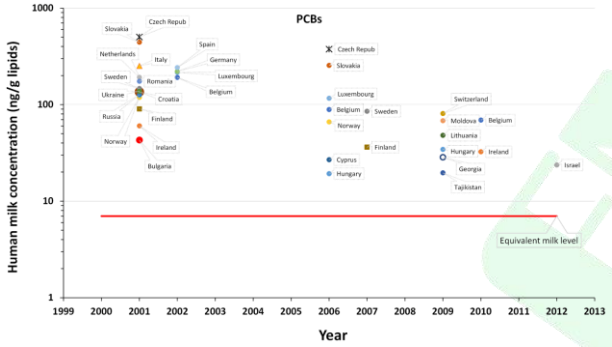


Figure 46. Time trend of PCBs in human milk for several countries of the European region

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.

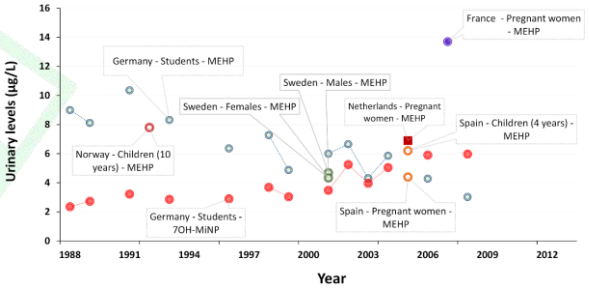


Figure 47. Time trend for the urinary concentrations of MEHP (DEHP metabolite) and MiNP (DiNP metabolite). The German ESB data indicate that MEHP (blue dots) is decreasing due to the continuous restrictions in DEHP use. On the contrary, MiNP levels tend to increase, reflecting the progressive replacement of DEHP by other phthalates such as DiNP

As a result, monitoring efforts should be continued under a more hamonized way. It is also of equal importance to use thenecessary 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.

Climate change, air pollution and human health

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 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 48); 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.

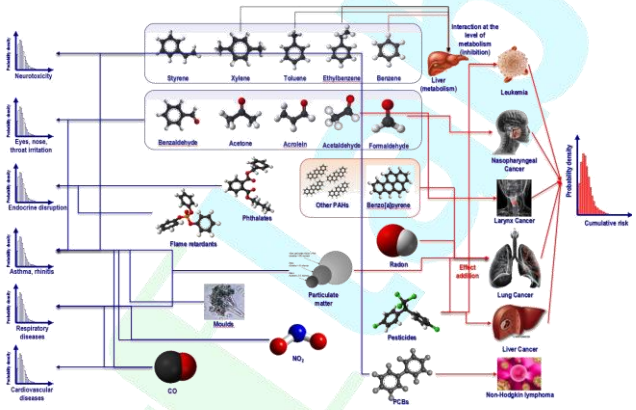


Figure 48. Multiple ways of interaction for chemicals

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).

Chemical and Radiological Risk in the Indoor Environment (CheRRIE)

The Chemical and Radiological Risk in the Indoor Environment (CHERRIE) is a 20-month project funded under the European Territorial Cooperation Programme Greece- Bulgaria 2007-2013 INTERREG IV programme. Cherrie started officially on February 28, 2014. Four Greek and two Bulgarian partners participate; the lead beneficiary is the Bulgarian Academy of Sciences and EnvE Lab assumes the scientific coordination of the project.

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

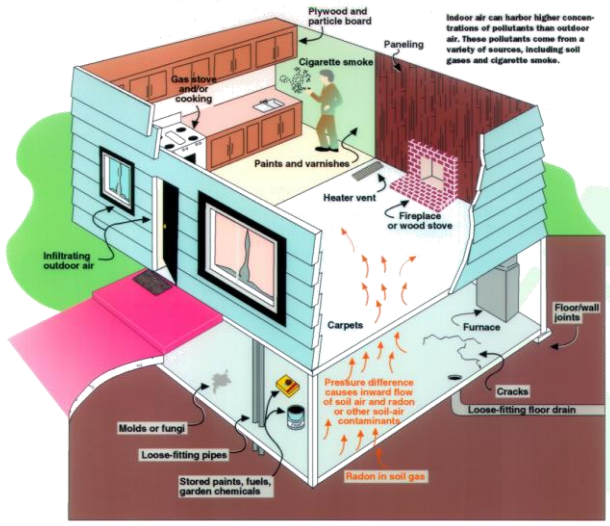


Figure 49. Typical sources of air pollution within a residential building

Quantitative health impact related to the use of building materials was 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 system for human exposure to indoor physical and chemical stressors/ health impact assessment and management is 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.

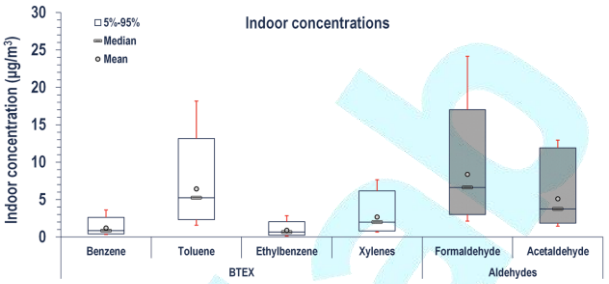


Figure 50. Indoor air levels of BTEX, formaldehyde and acetaldehyde attributed to building materials

Based on the chemical compounds and radon measurements, as well as on the γ-radiation emissions of the various building materials used in the residential places in Thessaloniki, cumulative cancer risk was estimated for the various indoor stressors.

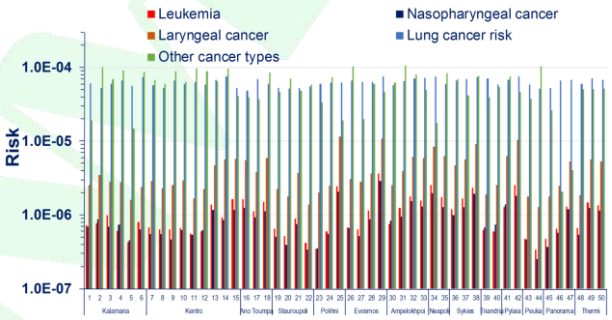


Figure 51. Risk estimates associated to the various indoor stressors for the 50 locations in Thessaloniki.

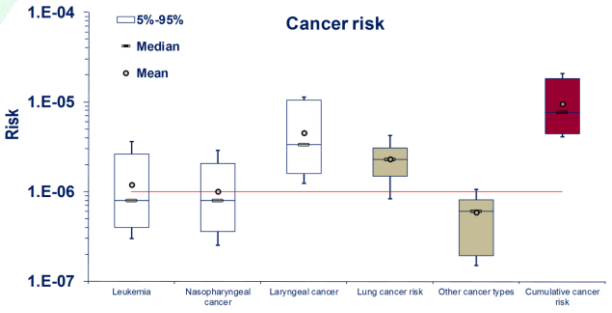


Figure 52. Estimated cancer risk in the residential area of Thessaloniki

Cancer risks associated to indoor locations are mainly driven by radiological risk factors. Calculated risks are on the order of 10^{-6} related to benzene and formaldehyde exposure, and around 10^{-5} regarding exposure to acetaldehyde. Radon and γ-radiation result in cancer risks in the order of magnitude of 10^{-4}. Considering that radon emissions are not anthropogenic, it is advisable to avoid combination of materials that result in high levels of indoor air VOCs concentrations and materials with high levels of γ-radiation, aiming at minimizing the contribution of indoor stressors to the cumulative cancer risk.

Detection of Indoor Airborne Chemical & Biological Agents Thematic Group

The European Reference Network for Critical Infrastructure Protection (ERNCIP) will provide a framework within which experimental facilities and laboratories will share knowledge and expertise in order to harmonize test protocols throughout Europe leading to better protection of critical infrastructure against all types of threats and hazards and to the creation of a Single Market for security solutions. The ERNCIP Detection of Indoor Airborne Chemical & Biological Agents Thematic Group which is led by EnvE Lab, will define scenarios for indoor, airborne contamination (threat, contamination area, topology, conditions of use for the equipment, etc.), which are realistic/are considered important in the EU or have been used in other projects. This activity will be supported by the use of the state-of-the-art on flow and dispersion 3D modelling/simulation and source term evaluation from detector network measurements.

Figure 53. ERNCIP Detection of Indoor Airborne Chemical & Biological Agents Thematic Group logo

The overall aim of this thematic group is to investigate issues that can be addressed on the EU level regarding Detection, Identification and Monitoring (DIM) of airborne, chemical and biological threats in enclosed spaces. Towards this aim, three main activities have been foreseen during the next months for accomplishing the TG objectives. In order to evaluate the applicability of the current sensor technologies and what has to be done, it is critical to evaluate what are the actual needs that have to be addressed i.e. what we expect from the sensors against CB threats in enclosed spaces. Thus, a critical starting point of the overall approach will be the definition of relevant scenarios of indoor airborne threats (chemical and biological) in critical infrastructures. The needs that have to be addressed will define the criteria for performing a critical review on the existing sensors available in the EU and used either for chemical or for biological agents. Computational simulations will provide the spatial and temporal gradients of contamination within indoor critical infrastructures. Finally, evaluation of capabilities of existing sensors based on their capability to give early warning will allow us to identify gaps and define requirements for next generation detectors in the EU.

More in detail, specific questions have to be answered, such as:

- Define the criteria and usage scenarios, suitable for chemical and biological DIM of contamination by airborne substances in enclosed spaces.
- Gather information from the relevant stakeholders and from the literature on the potential chemical and biological threats.
- Define typical threat scenarios, as most relevant
- Perform a critical review on the existing sensors available in the EU, based on the criteria and usage scenarios identified in Task 1. This will allow us to evaluate the suitability of the existing technologies for early and accurate identification of indoor airborne chemical and biological threats. Parameters to be examined, include whether to add a commercial off-the-shelf product or not, products under development/close to release or prototype - Technology Readiness Levels (TRL) level should be taken into account.
- To challenge the existing technologies against quantitative results, to identify gaps, future areas and emerging technologies. Specific considerations include:

The main scope of sensor use, is the (as possible as early) detection, identification and monitoring of the contamination with a toxic agent within an enclosed indoor location. The capability of a sensor to (a) early detect and (b) to identify a threat is of major importance. The importance of these capabilities are graphically illustrated in Figure 1, where the difference in the capability of detection (detector 1 and detector 2, with different detection limits) and eventually the identification of a hypothetical threat agent X, results in significant differences in actual exposure and internal dose, defined as the Area Under the Curve (AUC), that represents the integral of internal dose in time. These differences in actual dose will result in completely different casualty patterns. This comprehensive exposure and toxicokinetics and toxicity framework provides a robust analysis to be used for the assessment of the suitability of sensors and sensoring systems.

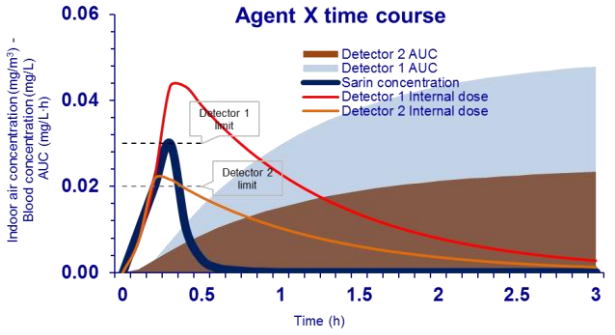


Figure 54. Agent X environmental and toxicokinetic time dynamics following a hypothetical attack under two different detection capabilities scenarios

Urban Reduction of GHG Emissions in China and Europe (URGENCHE)

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.

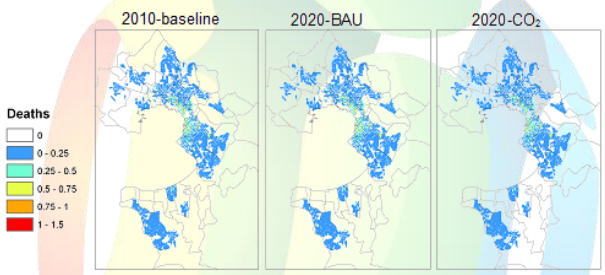


Figure 55. Spatial distribution of annual number of deaths attributed to PM_{10} in 2010, 2020-BAU and 2020-CO_2

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 55).

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 56).

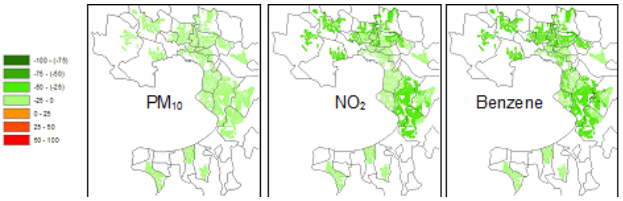


Figure 56. Decrease (%) in the annual number of deaths for the GHG scenario

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.

Monitoring air quality in Charilaos Trikoupis bridge

The Charilaos Trikoupis bridge, known as bridge of Rio-Antirrio (Figure 57), is one of the world's longest cable-stayed bridge of multiple openings in the world, with a total length of 2,252 meters. It connects Western Greece with the rest of the country.

Figure 57. Charilaos Trikoupis bridge

Six monitoring campaigns were realized in the course of the last three years. The exact periods of the two annual campaigns were selected taking into account the high traffic seasons according to a careful examination of the bridge traffic patterns. In each of the campaigns $PM_{2.5}$, PM_{10} and TSP were sampled every 24 hours near the edges of the bridge located in the urban areas of Rio and Antirrio respectively, using low (for PM2.5 and PM10) and high (for TSP) volume automatic sequential samplers. Dynamic measurements of CO, NO_x, SO_2, $PM_{2.5}$ and PM_{10} were also performed continuously during the 10-day periods. TSP were collected on quartz filters (203 mm × 254 mm) in order to determine lead (Pb). Lead concentrations were measured using an inductively coupled plasma mass spectrometer (ICP-MS). Moreover, meteorological data (wind speed and direction, temperature, cloud cover and humidity) were recorded. The pollution data were analyzed statistically and the quality of the air was characterized according to the US Environmental Protection Agency indicators and the European Common Air Quality Index framework.

The results indicated that air pollution levels are in generally below the regulatory thresholds. Across the three summer sampling sessions (N = 10 days) the average PM_{10} daily concentrations at the Rio site were 19.7 μg/m^3, 20.1 μg/m^3, 19.2 μg/m^3 only slightly higher than that at the Antirrio site that were 17 μg/m^3, 17.5 μg/m^3 and 12.6 μg/m^3 (for the 1st, 3rd, 4th periods respectively). The $PM_{2.5}$ were 8.7 μg/m^3, 10.61 μg/m^3, 8.9 μg/m^3 at Rio site while at Antrirrio were 7.8 μg/m^3, 9.22 μg/m^3, 7 μg/m^3 (for the 1st, 3rd, 4th periods respectively). Moreover, the traffic emissions from the bridge are not the main source of air pollution in the area. During the winter period of sampling (2nd) $PM_{2.5}$ and PM_{10} levels were below 25 and 50 μg/m^3 on both sides of the bridge almost every day. These limits were exceeded only one day (5/12/2013) on the side of Antirrio (26.4 and 52.2 μg/m^3 for $PM_{2.5}$ and PM_{10} respectively). However, during the winter period, $PM_{2.5}$ and PM_{10} levels are higher due to the use of light oil and biomass burning for space heating. Pb levels were very low; the average daily value recorded (2.6 ng/m^3) is two orders of magnitude lower than the regulatory limit of 0.5 mg/m^3. Hourly average concentrations of CO, SO_2, NO and NO_2 for the both sides were below the regulatory thresholds. Overall the contribution of the Charilaos Trikoupis bridge to the surrounding air pollution levels is very low. This is the result of the relatively low daily volume of vehicles (~10000 vehicles per day), the respective traffic fleet composition (~80% of the traffic fleet are passenger vehicles) and the speed limit (80 km/h) which does not favor traffic emissions. In addition, the strong and frequent winds further contribute to the rapid dispersion of the emitted pollutants. The air pollution data was also characterized according to the United State (US) Environmental Protection Agency (EPA) indicators and the Common Air Quality Index framework.

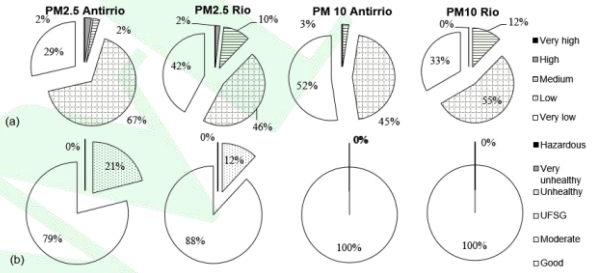


Figure 58. (a) European Common Air Quality Index framework, (b) US Environmental Protection Agency indicators

The US EPA AQI was calculated for NO_2, PM2.5 and PM10 and the results showed that the main driver of associated health risks in Rio-Antirio Bridge was PM2.5 at both locations. Figure 58 illustrates that during the 4 periods of measurements the daily air pollution was characterized as "moderate" with 21% and 12% for the Rio and Antirrio, respectively. But it has to be noted that the 87% of these measurements was observed the winter period. Simultaneously, CQAI showed that in Rio and Antirrio PM2.5 was also again the dominant pollutant. It was highlighted that the 2% of the measurement was at level of the high pollution and this percentage was observed during the winter. The highest concern is that ambient air PM levels in the urban environment are greatly affected by seasonal effects of emissions patterns and deposition processes occurring in the different regions of the human respiratory tract, which are related to the physiology/morphology of the respiratory system and the PM size distribution. Despite the lower level of traffic during the winter period, higher levels of PM were observed then. That could be related to the relative increase in all-size fraction of PM emissions in Greece, especially during the cold months of the year due to biomass combustion for space heating. Yet, the results of the AQI calculations indicate that care has to be taken to cater to the needs of susceptible individuals. US EPA remarks that "moderate" level of pollution can be alarming for a very small number of people.

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 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.

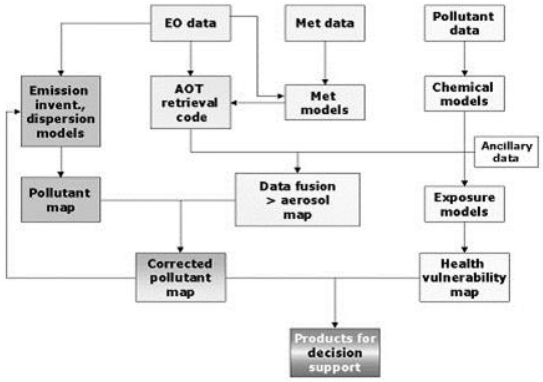


Figure 59. Conceptual representation of the advanced satellite data fusion system

Earth observation (EO) from satellite, in fact, may provide an additional information layer through the calculation of suitable air pollution indicators, such as atmospheric turbidity as measured by the atmospheric aerosol optical thickness (AOT). This calculation is based on the knowledge that the optical atmospheric effects of pollution on High Resolution Sensors (HRS) EO data are more pronounced in certain spectral bands than in others; this permits a first delineation of polluted areas and localization of emission sources, through computer assisted photo-interpretation of satellite imagery.

More specifically, fusing processed EO HRS data such as the ones obtained from the LANDSAT TM and the SPOT family, with ground-based measurement data, atmospheric dispersion modelling results and meteorological information (mixing height, relative humidity) can provide full spatial coverage of the area of interest at very high spatial resolution (up to 10 by 10 meters) allowing quantitative assessment of the PM pollution levels also at street level covering a domain as large as 80-100 x 80-100 km^2.

The methodology we developed was applied in Athens and the region of Western Macedonia (Greece), Munich (Germany), Rome and Lombardy (Italy) and Budapest (Hungary) 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.

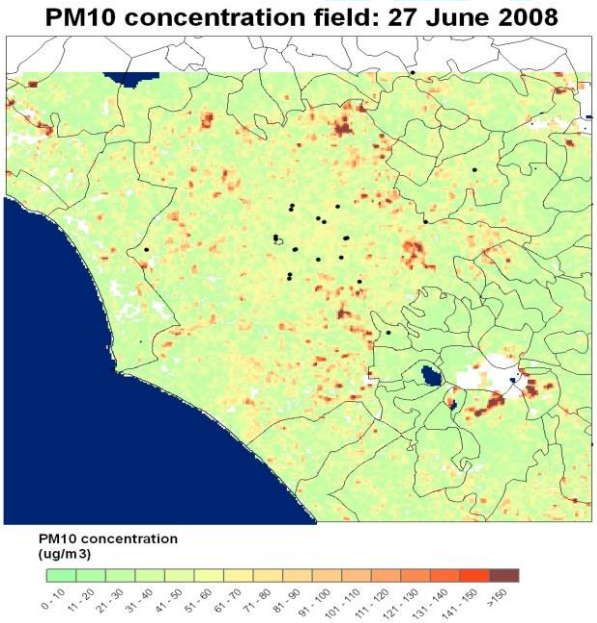


Figure 60. Application of the fusion system in Rome

Results showed that the computational model developed allows highly accurate estimates of particulate pollution and their health effects at high 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.

This allows the accurate spatial identification of hot-spot areas where air quality and public health managers need to concentrate their efforts.

Moreover, the derivation of high resolution estimates of PM mass concentration can support the optimization of air quality monitoring networks; using EO 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.

.

Industrial contamination, waste and human health

Industrially Contaminated Sites and Health Network (ICSHNet)

The concept

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.

Figure 61. 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.

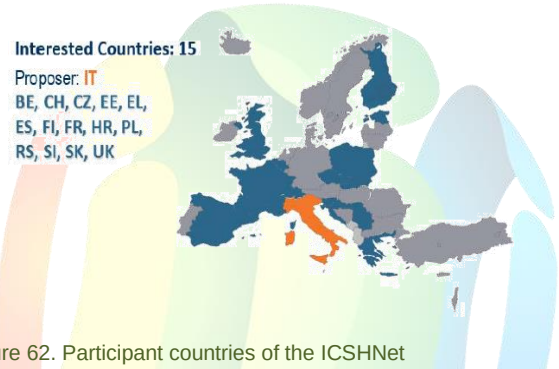


Figure 62. Participant countries of the ICSHNet

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.

Contaminated sites in Greece

Asopos basin – Cr(VI)

A major local environmental issue in Greece is related to the presence of hexavalent chromium Cr(VI) in drinking water of the Oinofyta municipality (50 km North of Athens, Greece), within the wider area of Asopos basin and the related cancer mortality. In 1969, a ministerial decision gave permission for depositing processed industrial waste in the Asopos river, which runs through Oinofyta. This decision, furthered by a presidential decree in 1979, permitted free disposal of processed liquid industrial waste into the river. Initial concerns were raised after Oinofyta area citizens complained about the discoloration and turbidity of their drinking water. Regular protests ensued from the 1990s onward. In 2007, the Ministry of Environment, Regional Planning and Public Works of Greece imposed fines on 20 industries for disposing industrial waste with high levels of hexavalent chromium into the Asopos river. Since 2007, three independent sets of hexavalent chromium measurements are available for the Oinofyta area, indicating that public drinking water Cr(VI) conentrations were above 8 μg/l. According to official Oinofyta municipality authorities, in early 2009 the main drinking water supply of Oinofyta was diverted to receive water from Mornos lake (reservoir) which is part of the drinking water supply network of the city of Athens. Therefore, more recent measurements made by the Oinofyta municipality (June 2009- July 2010) record relatively lower levels of Cr(VI) (<0.01-1.53 μg/l). A measurement made by the Oinofyta municipality in 1996, showed Cr(VI) levels of 54 μg/l in the public drinking water supply. Association to health effects was based upon existing epidemiological data already published by Linos et al1. [1]. The SMR for all cancer deaths over all the years was slightly increased but not statistically significantly (SMR = 114, 95% CI 94-136). For primary liver cancer, the observed deaths were eleven fold higher than the expected number of deaths (SMR 1104, 95% CI 405-2403, $p < 0.001$); statistically significant SMRs for primary liver cancer were observed among both males and females. Observed deaths associated with kidney and other genitourinary organ cancers (five deaths with ICD-9 code 189, and one death with ICD-9 code 184) were more than threefold higher than expected in women (SMR 368, 95% CI 119-858, $p = 0.025$). The SMR for lung cancer was also statistically significantly elevated (SMR 145, 95% CI 101-203, $p = 0.047$).

[1] Linos, A., A. Petralias, C.A. Christophi, E. Christoforidou, P. Kouroutou, M. Stoltidis, A. Veloudaki, E. Tzala, K.C. Makris, and M.R. Karagas, Oral ingestion of hexavalent chromium through drinking water and cancer mortality in an industrial area of Greece - An ecological study. Environmental Health: A Global Access Science Source, 2011. 10(1).

Accidental Aspropyrgos recycling plant fire - dioxins release

Calculating the health burden due to increased exposure to dioxins and furans of the Aspropyrgos area (Close to Athens) residents by an accidental fire in a plastics recycling plant in June 6, 2015 was the challenge of this case study.

Figure 63. Snapshot of the recycling plant fire in Aspropyrgos

For this purpose, several type of data were combined mechanistically, including: a) dioxins and furans biomonitoring data of previous years to determine the background exposure of the population (equal to 7,3 pg/g_lipids) and b) exposure to environmental media as shaped the days of the fire. The equivalent potential toxic dioxins in the air was found to be 1.8 pg/m^3 TEQ WHO (in accordance with measurements of NCSRD Demokritos), a value that is significantly greater than the 0.1 pg/m^3 TEQ WHO atmospheric background concentration of an industrial area.

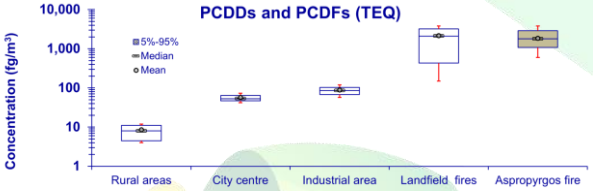


Figure 64. Levels of dioxines and furans at various Athens sub-areas, as well as during the fire in the recycling plant

In various parts of the food chain calculated values were less than 1 pg TEQ / g_fat. The change of the internal exposure of the population as to the background is then calculated using a validated Physiology Based BioKinetic (PBBK) model for dioxins and furans.

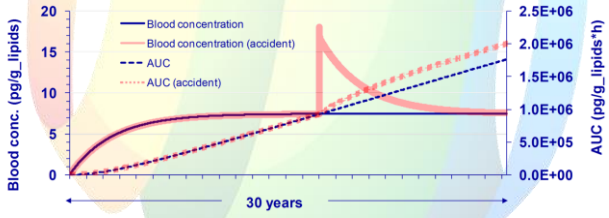


Figure 65. Internal exposure to dioxines under (a) usual conditions (continous line) and (b) under accidental release (doted line)

Considering bioaccumulation, for 6 days exposure to dioxins / furans smog, additional burden of internal exposure for the exposed population is about 13%. Cancer risk increases similarly, and is estimated equal to $3 \cdot 10^{-7}$.

Goldmining in Skouries Halkidikis – heavy metals contamination

In Skouries of Halkidiki (Northern Greece), a mining company want to establish an open-pit mine in the middle of the Skouries forest on the Kakavos mountain, which happens to be the main freshwater source for the entire region. By the company's own estimates, the open pit will generate 3,000 tons of toxic dust per hour. Galleries will be dug at 700 meters deep, taking the mine below sea level, so that even water that is not contaminated with heavy metals and other toxic materials from the mine will surely be contaminated by seawater. A 9 kilometre long tunnel aimed at connecting two mining sites will cut through a geological fault line that caused a devastating earthquake in the area in 1932. Finally, an ore processing factory will be built in the mountain where gold will be separated from other substances. The company claims this will be done without using cyanide, but this method has not been shown to be effective on Skouries ore. This raises additional concerns about the possible disposal of cyanide inside the forest. Major environmental compartments are expected to be contaminated, including:

- Water resources: The Kakkavos mountain supplies water to the entire N.E. Halkidiki. The proposed mining activity will directly and irreversibly affect the region's water resources. The EIA does not meet any of the goals of the Framework Directive 60/2000/EK - "Establishing a framework for Community action in water policy" which has been incorporated into Greek law.
- Air pollution. Only in "Skouries" the particulate emissions are estimated to 430 t/y PM10, with high concentrations of heavy metals, particularly arsenic. The ore dust production sums up to 4.324 t/h with high concentrations of sulfur compounds such as heavy metals antimony, arsenic, barium, cadmium, chromium, lead, mercury, etc. The emission of carbon monoxide, nitrogen oxides, volatile organic compounds, sulfur dioxide and particulate matter PM10 and PM2,5, is in total 715 t/y in the first two years of operation and over 950 t/y over the next years.
- The decrease in soil pH due to acidic runoff and the high heavy metal concentration makes the soil unsuitable for organisms and plant growth. The mining activity will cause drying topsoil within kilometers of the open pit and severe soil erosion with subsequent catastrophic flood events.

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.

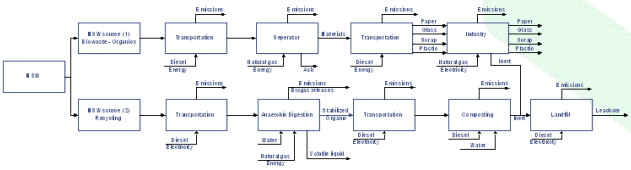


Figure 66. Waste management scenario: Waste is pre-treated and pre-sorted into biodegradable and non-biodegradable material for further anaerobic digestion and composting. Residues end in landfill. Plastic, paper and ferrous material are recycled.

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.

This integrated framework was applied in the case of MSW management in the two larger cities in Greece, 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. Public health impacts were assessed based on adverse effects on respiratory health, congenital malformations, low birth weight and cancer incidence.

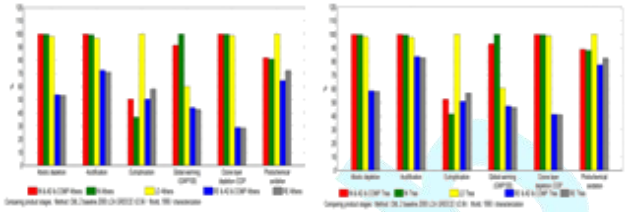


Figure 67. Impact categories of life cycle assessment for Athens and for Thessaloniki

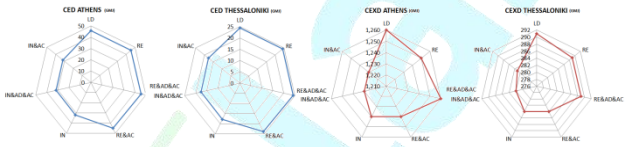


Figure 68. Cumulative Energy and Exergy Demand for Athens and for Thessaloniki

A significant and non-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 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.

However, not all options are benign on the local environment and on the local population health, since both can be influenced by non-negligible local emissions.

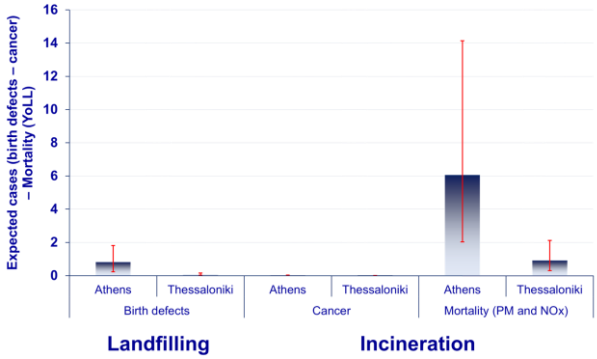


Figure 69. Health impact assessment among the various waste management options

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.

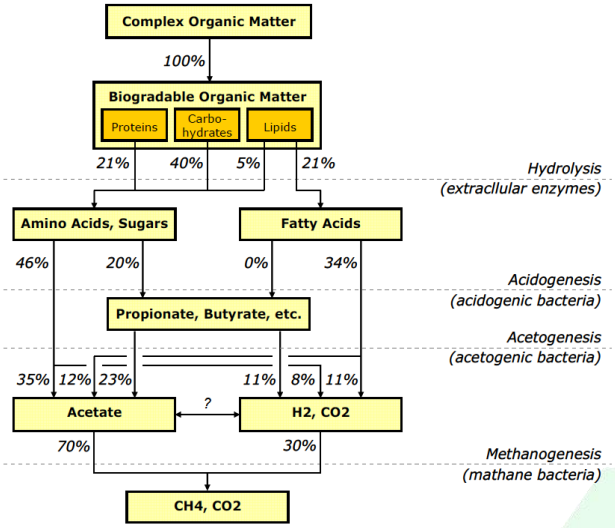


Figure 70. Anaerobic digestion process

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 CSTR and batch reactors.

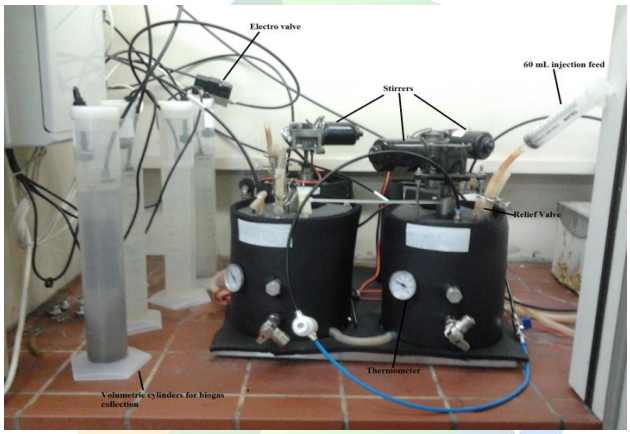


Figure 71. Anaerobic bioreactors

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.

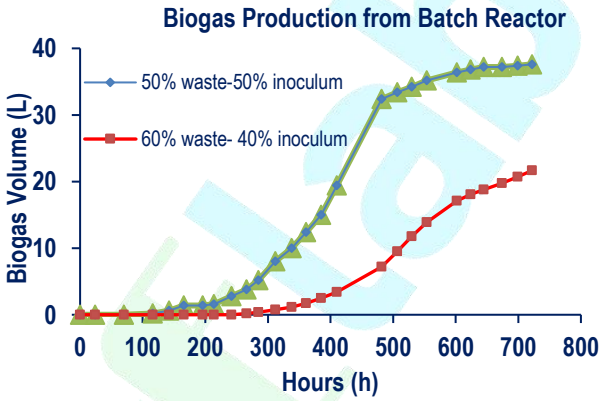


Figure 72. Biogas production from a batch work bioreactor using as feedstock the OfMSW 50% and inoculums 50%

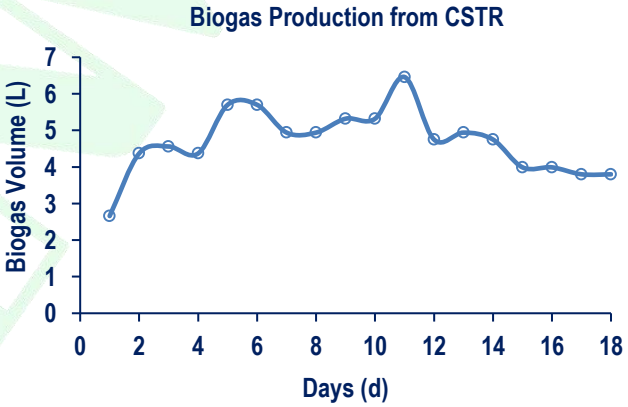


Figure 73. Biogas production from a CSTR bioreactor using as feedstock 0.2L/d of optimal waste

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 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 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 microorganisms are able to valorize different waste streams, they have a number of inherent limitations which through appropriate management can be bypassed or ever used in advantage of another biological process in a win-win process scheme. One of these limitations is the inefficiency of anaerobic microorganisms to convert a

number of natural macromolecules into biogas mainly due to slow hydrolysis.

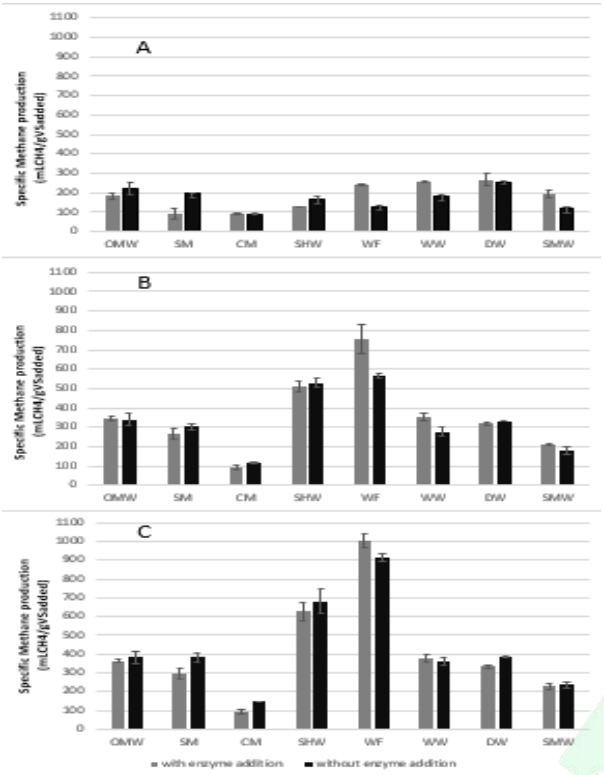


Figure 74. Specific methane production (mL/gVS$_{added}$) on days 5, 12 and 30 for the enzymatically pretreated and not pretreated substrates (Olive Mill Waste, Sterilized Mass, Cattle Manure, Slaughterhouse Wastes, White Fat, Winery Wastes, Distillery Wastes, Slaughterhouse, Solid Mill Wastes)

In order to improve the efficiency of the process toward these macromolecules, in the last couple of years a number of small scale digestion experiments took place in our laboratory where we assessed the effectiveness of initial enzymatic pretreatment 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 or negligible effect, as is the case of olive mill and distillery waste.

B) Positive effect on the process with the methane production taking place faster and the organic matter exhausts more rapidly. This category includes white fat and olive mill solid waste.

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 cattle manure and sterilized mass.

Photo bioreactors

Another inherent limitation of anaerobic digestion is the generation of carbon dioxide during anaerobic respiration. This in some cases can be volumetrically equal to the generated methane. The presence of carbon dioxide in the biogas is undesirable as it is reducing the heating value of the gas while increasing storage and management costs. In order to reduce the concentrations of carbon dioxide from the biogas, we designed and constructed a bench-scale anaerobic digestion system coupled to photo-bioreactors where algae are employed for the valorization of the carbon dioxide, hydrogen sulfide and ammonia available in the biogas.

Figure 75. The photo-bioreactors within the temperature controlled cabinet

After harvesting algal 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 algae has been explored in order to identify pathways through which the application of these species can reduce the environmental burden of human activities. Algae are an important carbon sink and their cells can contain more than 50% of fats and oils, sometimes rich in ω-3, from where pharmaceuticals or raw material for biodiesel production can be extracted. It noteworthy 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 anaerobic digesters.

Fur farming by-product bio-methanation

European fur production is a dynamic and well established industry with long tradition in the production of quality products. The European Union is the main exporter of pelts worldwide accounting for the 64% of the total production with the States of Denmark, Netherlands, Finland and Greece being the main producers.

The waste generated from mink breading facilities includes manure and waste feed. Both are collected under the animal cages in small piles of up to 50cm in height. The waste management options for this waste stream are constrained by high solids, organics and nitrogen content that hamper significantly the ability of aerobic biological processes to treat or valorize them.

A waste management option which can be employed for the valorization of fur farming waste is anaerobic digestion (AD). AD is a biomass bio-conversion process disengaged from weather conditions which offers the advantages of self-sustainability, income generation and waste valorization with limited material requirements.

The substrates evaluated in this work were fresh and weathered mink manure (FMM, WMM respectively), waste mink feed (WF) and bone and meat meal (BMM) that is being generated by the mink carcasses after pelting.

The substrates were assessed in batch vials under mesophilic conditions mainly due to the known problems related to the inhibition of the process by elevated concentrations of unionized ammonia. This inhibitory process is driven by the bio-conversion of protein into ammonia and it is assisted by the high temperature and pH experienced in thermophilic systems.

The ranching derived substrates were found in the solid state with TS higher than 33%. The solids are composed mainly of organic matter with VS levels higher than 83%. They have significant nitrogen content with TKN concentrations ranging between 14 and 93 g/kg, while the pH of manure is alkaline. This is in contrast to that of the WF, which is acidic and that of BMM, which is neutral. Finally the theoretical methane production of the substrates ranges between 545 and 705 $mLCH_4/gVS_{added}$.

The highest production from the substrates assessed (Figure 76) observed by BMM with 591 ± 38 mL/gVS_{added}, a value corresponding to the 83.7% of the theoretical methane production for this substrate. The second highest yield offered by the waste mink feed with 548±33 $mLCH_4gVS_{added}$ corresponding to 91% of the theoretical bio methane potential with a significant daily productivity of 65.0 $mLCH_4gVS$-d. The production level offered by mink manure is significantly lower compared to the mink derived by-products with 365 and 428$mLCH_4/gVS_{added}$ for the fresh and weathered mink manure respectively.

Based on our system analysis the total annual manure streams generated by the Greek mink ranches are calculated at 8100 tons of solids. While this value seems low, this waste stream corresponds to around 160.000 tons of pig slurry (5% TS) or 100.000 tons of cattle manure (8% TS).

In all four assessed substrates, pH had shown a small reduction up to 0.4 units during the first days of the experiments in response to the increasing concentrations and primary accumulation of the volatile fatty acids. This process however got reversed as the acids were consumed and converted into biogas by methanogens.

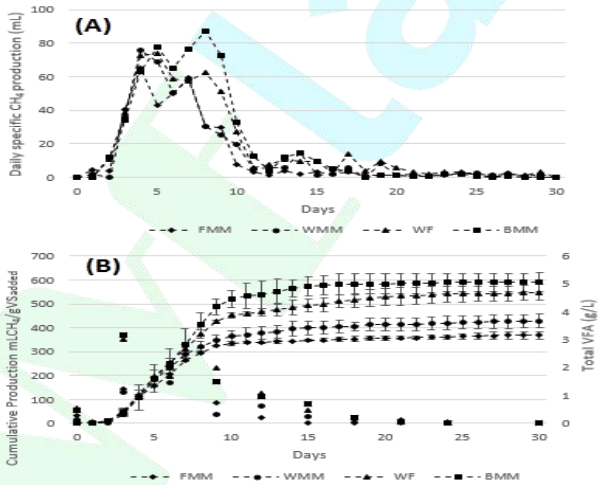


Figure 76. Daily (A) and cumulative (B) specific methane production for the four substrates assessed

According to mink farmers the generated mass of waste feed is approximately the 6% of the feed provided. Thus, the generated mass was calculated at 268 tons of solids per year. According to rendering facility managers out of 1000kg of raw minks slaughtered, 290kg of BMM and 60kg of mink fat are recovered. The total mink bodies produce 160 tons of BMM product per year.

Based on the above calculated total mass of substrates, the volume of CH_4 that can be generated through management of the mink-derived byproducts in Greece, reaches 2.85 million m^3, which equals to approximately 2600 m^3 of fuel oil in terms of lower heating value equivalents.

Experimental results indicated that in contrast to pig and cattle manure, minks generate waste which may offer very high specific and volumetric methane productions. Thus, we deem that with proper management the economic viability of bio-methanation plants can be ensured. The anaerobic digestion process lends itself toward mink-derived waste and byproducts offering a robust process from where significant volumes of biomethane can be recovered while at the same time environmental sustainability is safeguarded.

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

Redirection of organic municipal waste 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 waste 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.

Anaerobic digestion provides a waste management option for OFMSW, while offering the opportunity to recover marketable products both in the forms of biogas and slow release bio-fertilizers. As a result, less waste is dumped into landfills, 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 types of waste-wastewater can be mixed and treated together in co-digestion schemes. Mixing of different substrates is not only desirable for improving methane recovery rates and reducing life cycle costs; 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 were performed under thermophilic conditions in batch and large volume laboratory digesters, with the feed rate of food waste to manure reaching levels as high as 70% based on VS loading, the total solids levels at 15.7% and the OLR at 6.85kgVS/m3/d. At the higher feed rate the digestion process was slightly inhibited, probably due to sugar accumulation. In contrast waste mixtures containing up to 65.3% food waste with the OLRs as high as 6.2 kgVS/m3/d with the influent TS levels up to 14.3% can be accepted by CSTR systems with no signs of inhibition.

Our results show that the addition of food waste 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 (3000m^3, HRT 21-d) the addition of food waste can result in a fourfold increase of cash flow by only slightly increasing operational costs due to pasteurisation requirements. Additionally, gate fees and carbon credits can further improve the financial performance of treatment facilities.

Valorization of semi solid pickling wastes, through bio-methanation pathways

Vegetable and fruit pickling and the subsequent canning is a multibillion Euros industry presenting great export potential with the gross European pickle production reaching the 1.6 million tons per annum. Pickling is a traditional method of preservation employed for the long term storage of vegetables and fruits under either an acidic brine solution or an acidic oily solution.

The waste assessed in the present work were:

a) pickled green peppers in brine,

b) pickled red peppers marinated with olive oil and

c) mixed green olives stuffed with red pepper and cheese based cream in brine.

These substrates have high total solids, significant fat and NaCl concentrations and acidic pH as an effect of the addition of acetic acid during pickling. The theoretical specific production of the substrates fluctuates between 435 and 561 $mlCH_4/gVS_{added}$. The experiments performed in batches and under thermophilic conditions with a retention time of 30 days.

The highest specific production offered by the green stuffed olives with 519 $mlCH_4/gVS_{added}$, followed closely by red peppers in oil with a yield of 488 $mlCH_4/gVS_{added}$. These values correspond to 92.4 and 99% of the theoretical production for these substrates. In contrast to the high yields exhibited by red peppers and stuffed olives, the bio-methane yield offered by the green pepper in brine was only 149 $mlCH_4$/gVSadded, i.e. the 34% of the theoretical production for this substrate. In order to overcome the inhibition of the monodigestion of the green peppers, these were assessed under co-digestion conditions together with cattle manure. Under these conditions the efficiency of the process improved by 32% with the yield reaching the 270$mlCH_4/gVS_{added}$.

Anaerobic digestion and co-digestion of pickling solid waste and cattle manure was performed successfully with significant volumes of biogas recovered. The red peppers and the stuffed olives, thanks to their high content in fats and organic acids, offer very high specific and volumetric methane productions. Unfortunately, green peppers assessed contain significant concentrations of NaCl that is a known inhibitor of methanogenesis. The successful application of co-digestion reveals the merits of the combined treatment of substrates for minimizing inhibitor stress and improving the chances of success.

Biomethanation of cellulose rich agro-waste

Cereal farming is the main agricultural activity worldwide generating 1-3 tons of cellulose rich waste per ton of grain product. The main wastes of this process are the two straw types as well as the husk in the case of rice. While a small proportion of the agrowastes are used as feed for ruminants, a significant volume is burned on the fields prior to the new agronomic year. Recently, the exploitation of cellulose-rich waste has started to gain momentum as a possible substrate in biorefineries. Toward this target, the wheat and rice straws as well as the rice husk were selected and assessed as substrates to anaerobic digestion process. The substrates underwent milling in a hammermill and three fractions were generated, these were the 2 cm, 1 cm in length as well as in a powder form. In addition, the enzymes cellulase and xylanase were added into the substrates in order to evaluate the effect of the biological pretreatment methods. The enzymatic cocktails evaluated were these composted by 10, 50 and 100 mg /gVS_{added} per enzyme. The mechanical and biological pretreatment of the substrates was investigated in batch as well as continuous CSTR type reactors.

Figure 77. Cellulose rich agro-waste anaerobic digestion

According to the results, the highest methane production 370 mLCH_4/ gVS_{added} offered by the wheat straw when it was pretreated through milling into 1 cm fractions with the addition of 10mg/gVS_{added} of cellulase and xylanase.

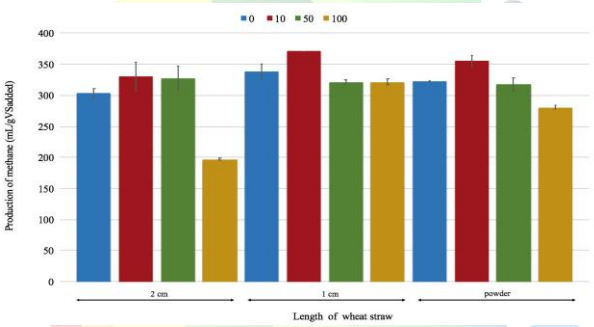


Figure 78. Methane production

It was found that the mechanical or biological pre-treatments in a number of cases inhibited the process. It seems that the type of pretreatment and required enzyme is a substrate specific method and significant pretreatment experimentation should be used before a pretreatment method becomes standardized within a biogas production facility.

Microalgae cultivation for biofuel production

Microalgae cultivation for biofuel production is a promising economic activity toward sustainable development. Biofuels derived from algae biomass offer several advantages compared to the biofuels generated at the first and second generation biorefineries. An advantage of microalgae is their ability to utilize carbon in closed systems. Although, algae cultivation it seems as an easy and first class solution to a number of environmental and economic issues, the availability of sustainable carbon dioxide sources is limited. Biogas is known for its high carbon dioxide concentration which can be considered as a substrate for microalgae cultivation. Thus, microalgae biomass is recovered and the concentration of carbon dioxide in the biogas is reduced, improving its heating value. Furthermore, through photosynthesis, microalgae generate organic compounds, such as lipids, proteins and carbohydrates, which can be valorized for biogas production generating in this way a closed carbon circle system. During the experimentation period batch photoreactors were used and different concentrations of biogas was added into the systems. The aim was to evaluate the effect of pH and to assess the growth potential of the microalgae *Chlorella vulgaris* with biogas as substrate. In order to evaluate acceptance and growth rate of the algae the batches were fed with 1.1, 2.3 και 3.4 g CO_2/L·d. Furthermore, the biomethanation of the generated biomass was also studied. For the biomethane potential tests a similar biogas test was used with organic loadings ranging between 6.25 and 18.75 gVS/L.

Figure 79. Biogas production under different organic loadings

According to the results the highest biomass concentration of 2.3 g/L, in a 10-day cultivation circle, achieved for the feeding rate of 2.3 g CO_2/L·d while the highest bioconversion efficiency of CO_2 offered by the 1.1 g CO_2/L·d with approximately 26%. Moreover, the highest methane production was offered by the anaerobic digestion of microalgal lipids and measured at 669 mL CH_4/gVS. Growth of *Chlorella vulgaris* on biogas is a possible and sustainable method for biogas polishing. The results of anaerobic digestion suggest that microalgae biomass offers a high quality substrate that can be used for biomethane production.

New projects

Integrated Climate forcing and Air pollution Reduction in Urban Systems (ICARUS)

The ICARUS main objective is to develop integrated tools and strategies for urban impact assessment in support of air quality and climate change governance in EU Member States leading to the design and implementation of appropriate abatement strategies to improve the air quality and reduce the carbon footprint in European cities. We will develop detailed policies and measures for air pollution and climate control for the short and medium term (until ca. 2030). For the long term perspective (2050 and beyond) we will develop visions of green cities and explore pathways on how to start realizing these visions. The specific project objectives are to:

- quantitatively assess the impact of current and alternative national and local policies on reducing greenhouse gas (GHG) emissions and improving air quality through a full chain approach and evaluate the future public health and well-being impacts of these policies in European cities.
- evaluate (using source apportionment and atmospheric modelling) the current contributions of the different pollution sources linked to urban activities including heat and power use in the urban building stock, urban traffic and transportation needs, energy production, industrial activities including energy production, agriculture and trans-boundary pollution with respect to GHG-emissions, air quality loading, public health and well-being of the population.
- propose measures of technological (i.e. measures that will lead to a reduction of emissions at the source) and non-technological (i.e. measures that induce behavioural changes) nature to reduce both carbon footprint and air quality burden (win-win solutions). Techno-economic analysis of possible scenarios for the introduction of such measures will result in the definition of cost-effective environmental and climate protection and air quality management plans adapted to the specific needs of different EU cities and regions. The effect of these measures will be evaluated jointly taking into account the socioeconomic drivers related to the existing and projected scenarios.
- develop visions of green cities with clean air, close to zero or negative carbon footprint and maximal wellbeing
- develop a pathway for the realization of these visions in the next 50 years and propose first steps down that road in the form of a concrete plan towards achieving these visions in the participating cities.
- raise awareness of the citizens about the impacts on public health and climate change caused by their activities or with changes in their activities.

The policy analyses results mwill allow us to determine the most sustainable GHG mitigation and air quality (AQ) improvement strategies. The latter will be proposed to the authorities competent for atmospheric pollution and climate protection management and to the main industrial end-users as guidance for decision making that would lead towards maximizing the net public health and wellbeing benefits while taking into consideration the costs associated with air pollution and climate change in the EU.

We will employ state-of-the-art technologies for fusing the necessary environmental and ancillary information to allow for cost-effective air pollution monitoring and assessment. The tools developed will allow the analytical accounting of the main industrial and area emission sources in the area and the creation of precise and updated emission inventories. An **integrated approach** will be used for air pollution monitoring combining ground-based measurements, atmospheric transport and chemical transformation modelling and air pollution indicators derived from satellite, airborne and personal remote sensing. Thus, air quality will be readily assessed across different spatial scales in the participating cities. Based on the advanced monitoring activities outlined above, a **cloud-based solution** will be developed to inform citizens of environmental friendly alternatives that may have a positive impact on their health, motivate them to adopt these alternative behaviours by offering them refundable coupons and controlling them either instantly or over a period of time for the application of the alternative actions. Citizens would use web or smartphone/tablet-based applications to be informed about actions, collect and redeem coupons from the participating organisations. Our findings will be translated into a **web-based guidebook** that will provide an estimate of the effects of a number of policies in every participating city and will also give guidance to other European cities.

ICARUS will develop a vision of a future green city: a visionary model that will seek to minimize environmental, climate and health impacts in the participating cities. To this aim we will develop a **transition pathway**, which will demonstrate how current cities in Europe could be transformed towards green cities within the next 50 years. To raise citizen awareness regarding the impacts of their activities on air pollution and climate forcing and increase societal acceptance of emission reduction policies, a **web- and smartphone/tablet-based tool** will be developed to inform citizens in participating cities about how their life style affects their carbon footprint and the health impacts of their actions/consumer choices.

Linking Up Environment, Health and Climate for Inter-sector Health Promotion and Disease Prevention in a Rapidly Changing Environment (BlueHealth)

The BlueHealth Consortium will, for the first time, bring together leading research, public health and policy institutes at the forefront of understanding the relationships between the environment and human health across Europe to address opportunities for BlueHealth interventions with interactive cross-sector stakeholder engagement. Key questions to be addressed include: a) How are the unexplored benefits of urban blue infrastructure (e.g. promotion of physical activity and stress reduction) distributed across the EU and will address the public health challenges of the 21st Century?; b) Which social groups derive the most benefit, and are there pockets of good practice that promote more equitable distribution?; c) Can these benefits of blue infrastructure programmes be assessed in ways that inform good design (e.g. through the use of prospective longitudinal evaluation of ongoing and planned environmental interventions)?; d) Can some of these benefits to health and well-being be used in settings without direct exposure to urban blue spaces (such as hospitals and care-homes) through the use of virtual reality technology?; e) How might different climate and environmental futures influence the ability of urban blue infrastructures to deliver these benefits to public health and well-being?; f) How can existing health and planning policies be built upon to best ensure that these benefits to health and wellbeing are factored into the policies for maintenance and retrofitting of existing, and the development of future, urban blue infrastructures; and g) What innovation and commercial, as well as public health prevention, opportunities exist to best utilise the increased knowledge the BlueHealth project will provide?'

The Aim of the 4.5 year BlueHealth project is to quantify the impacts on population health and wellbeing of existing and novel interventions and policy initiatives connected to urban blue infrastructure, and to identify opportunities and obstacles for cross-sectoral collaboration in this area. Assessments of the health and wellbeing (and environmental) benefits, risks, trade-offs, and costs will improve our understanding of the role of urban blue infrastructures, both positive and negative, on cross-sector health promotion and disease prevention. Many of these infrastructures were originally designed for other policy goals (e.g. transport, flood prevention). However, innovative design and planning can promote health by ensuring that the co-benefits are captured. For example, walking and cycle paths can become integrated features of existing and future blue infrastructures; promoting better access to water bodies for recreation can foster better mental health and increases in physical activity; and blue infrastructure can also aid sustainability and connectivity with other transport networks. Given peoples' preferences for blue spaces and their willingness to visit them, the evidence suggests that the population uptake of blue infrastructure initiatives that encourage, for instance, greater levels of active recreation, will be particularly high, and thus important for disease prevention and health promotion at the individual, community and populations levels. On the other hand, the predicted increased use of water in urban areas introduces new challenges for improving human health and wellbeing (e.g. as exposures to known and unknown environmental stressors such as flooding, pathogens and chemical pollutants increase), as well as making the attainment of the long term sustainability of urban blue ecosystems more difficult.

To fully understand the unique role of blue infrastructures for health and wellbeing, wherever possible we will compare relevant 'blue' interventions to similar interventions located in 'grey' infrastructures (i.e. highly built environments with little to no natural environment) and 'green' infrastructures (e.g. parks, woodland, street trees), as well as 'mixed' infrastructures. This will enable us to identify both the direct and opportunity costs of the blue infrastructure interventions, as well as examine urban blue infrastructure design and planning as a means for adaptation to climate change. For example, by comparing the uptake of a new cycle path along a river (blue infrastructure) instituted as part of a larger flood control plan with similar projects on an urban road (grey infrastructure) or through a park (green infrastructure), we can directly examine the potential synergistic benefits of blue infrastructure investment in a cross-sectoral setting (e.g. health, transport, planning, tourism, engineering, environment, fisheries and aquaculture, recreation, and climate).

Throughout the project, we will utilise innovative indicators and other measures which demonstrate the health, economic, environmental, and social impacts of Case Study interventions, policies and best practices. In addition to building on existing methodologies, we will use mobile phone technologies (e.g., GPS tracking with point-to-point location-based questionnaires, environmental monitoring) to assess indices of health and environment both 'on-line' and in situ. Highly innovative work will be dedicated to different but complementary forms of state-of-the-art virtual reality technology to provide therapeutic intervention, planning and communication opportunities to increase physical and/or virtual accessibility to blue environments among key populations (e.g. hospital patients, care home residents, disabled persons, deprived persons) normally without access; and to explore the underlying mechanisms of how blue infrastructures can act positively on health and wellbeing.

Post-Emergency, Multi-Hazard Health Risk Assessment in Chemical Disasters (PEC)

Analysis of health impacts associated with accidental release of chemicals from industrial sources is currently based on knowledge of inherent properties of individual agents (toxicity, flammability, explosivity, etc.) and the predictable response to a given dose of the chemical determined by classical health risk assessment methods. Limited information exists on health risks that may result from absorption of complex chemical mixtures or from combined accidents, natural and technological (NaTech), for example an earthquake or terroristic attack that devastates chemical installations causing environmental release and dispersion of toxic chemicals in the primary disaster area.

A consolidated methodology for risk assessment of chemical mixtures and combined NaTech hazards is currently not available. In this project an integrated multi-hazard risk assessment toolkit will be developed and the validity of this model will be evaluated on a case study (sample area) by considering the effects on plant structures and infrastructures of hypothetic natural and manmade disasters, such as earthquake, flood or terroristic attack leading to accidental release of large amounts of toxic chemicals into the environment. Immediate and long-term population health impacts of the toxic chemicals absorbed either individually of in combination will be determined and quantified according to (i) characteristics (type and intensity) of the initial disaster, (ii) degree of vulnerability of buildings and infrastructures, (iii) quantity of chemicals stored/handled in the plants, magnitude of their dispersion into the environment and levels of chemical contamination in the disaster area. The key receptors considered in simulations will include employees present in the affected plants during the incident, emergency responders, and the local population. A risk prioritisation matrix based upon damage level attainable in the infrastructures and potential public health risks will be developed to provide strategic risk information for public health planning.

PEC aims at (a) implementing an integrated model for rapid multi-hazard health risk assessment applicable to chemical release incidents occurring during major natural or man-made disasters; (b) developing a composite risk matrix, considering both severity and probability of identified hazards, to prioritize disaster-related public health risks from clusters of industrial facilities handling toxic chemicals.

Specific objectives are: (a) to develop an operational approach toward the implementation of a model applicable to contamination and health risks assessment in connection to natural and manmade disasters (b) to estimate pathways, levels and time course of environmental contamination, human exposure profiles and health damage (acute and chronic) that may result, at various time intervals after a disaster, from acute or prolonged absorption of a mixture of model hazardous chemicals selected among those listed in the EU inventory of high-risk toxic industrial substances;

(c) to develop a series of risk mitigation guidelines for characterisation of “multi-hazard and multievent-related” health risks in chemical exposures following natural or man-made disasters, namely guidelines for early warning systems, risk mitigation of buildings and plants, population exposure, environmental and human health monitoring and proper design of post-disaster populations surveys; (d) to provide evacuation distance estimates based on acute chemical exposure indicators for different toxicant combinations, and different types of disasters and incidental release scenarios ; (e) to develop an integrated computational platform supported by a GIS system which covers the full chain from chemical releases to internal doses in human tissues in order to build a functional and ready-to-use software operated by local authorities responsible for civil safety and public health protection.

Although the research-oriented nature of the proposal, the guidelines and tools developed by the project could be promptly adopted by chemical manufacturers and industries. This is confirmed by the expression of interest of the Cluster “Smart Cities and Communities”, a regional cluster located in Lombardy (Italy), with the participation of more than 80 industries that could be potential beneficiaries of the risk management and safety procedures that will be implemented by the project. Interest in the results of the project has been also expressed by the GEM Foundation, which coordinates an international forum where organisations, stakeholder groups, major reinsurance, insurance and brokering companies and people come together to develop, use and share tools and resources for transparent assessment of earthquake risk.

Potential beneficiaries and end-users of the results obtained in the project would include cities and communities, public authorities and control agencies responsible for disaster prevention and risk management with special emphasis to organizations involved in the assessment of medium- and long-term health consequences of major multi-hazard incidents.

The Civil Protection personnel will also benefit from the ready-to-use software developed during the project. Other potential end-users would be the European Poison Information Centres, Chemical Emergency Centres established by chemical manufacturer associations, health professionals, organisations involved in studies of natural or man-made disasters, and organisations responsible for preparing evaluated data on chemicals, health and safety guides, chemical safety measures, and environmental criteria documents.

European Human Biomonitoring Initiative (HBM4EU)

Problem to be addressed: European citizens of all ages are exposed to a wide range of chemicals through their diet, their environment, the use of consumer products and at the work place. Exposure to chemicals (including combinations of chemicals) takes place through a variety of pathways and exposure routes, notably via dermal and oral uptake and by inhalation, with the combined exposure via all routes being the aggregate exposure. Despite the existence of human biomonitoring (HBM) programmes at national level and the large number of research and development projects ongoing both at national and European Union (EU) level, there is a clear lack of data on aggregate exposure to single substances and to combinations of chemical substances, as well as insufficient evidence-based knowledge on the link between external exposure via different routes, internal levels and human health. This knowledge is essential to inform effective policy-making to protect the EU population from the impacts of chemical exposure on health. HBM data that represent national populations or vulnerable/highly exposed subgroups exist in many European countries and these data can be used to inform chemical regulations aiming to protect human health. However, a number of factors prevent the use of these data at EU level to gain a pan-European perspective. Firstly, the data were not collected according to harmonised protocols and might therefore not be comparable, secondly differences in the metadata characterising the datasets impede cross-dataset analyses, and finally available data are not representative of the European population.

Overarching objectives: In order to address these issues there is a clear need to:

i) Harmonise procedures and tools for HBM at EU level;

ii) Provide and, where missing, generate internal exposure data and link this data to aggregate external exposure and the relevant exposure pathways;

iii) Develop novel methods to identify human internal exposure to environmental and occupational chemicals and establish the causal links with human health effects;

iv) Provide policy-makers and the general public with science-based knowledge on the health risks associated with chemicals exposure; and

v) Improve chemical risk assessment in the EU through the effective use of HBM data.

HBM4EU solution: The European Human Biomonitoring Initiative (EHBMI) will establish and implement an ambitious European Joint Programme (EJP) and will provide policy makers with comparable and validated chemical exposure and health data at EU level. This will be done by integrating and building on previous and ongoing EU initiatives, national HBM programmes and studies (including cohorts, epidemiological studies and health surveys). In contrast to former projects, the proposed programme will involve national programme owners and/or the national managers of those programmes, and include policy makers at national level. This inclusive approach, combined with the integration of HBM and environmental health research, will strengthen the EJP, enhance the sustainability of the initiative and amplify the impacts of the results. In order to ensure that the knowledge to be generated is targeted, timely and fit for purpose, we will establish a sustained dialogue with EU policy makers responsible for assessing and managing the risks to human health from chemical exposure via the environment, diet, consumer products and occupational exposure. Through effective communication and dissemination to policy makers, we will actively promote the exploitation of our results by policy makers in such a way as to impact positively on human health.

Specific goals:

The overarching objectives will be achieved via the following specific goals, to be accomplished during the 5 year programme:

- **Objective 1**: Laying the foundations for a pan-European HBM platform that builds on national hubs and existing expertise;
- **Objective 2**: Developing a common methodology for the interpretation and use of HBM data in policy-making;
- **Objective 3**: Harmonising and optimising the practices of national HBM programmes, including sample collection, quality assurance and data management;
- **Objective 4**: Identifying gaps where further data are needed to inform current policy questions and design new, targeted studies to address these knowledge gaps;
- **Objective 5**: Including new HBM data and, where possible, existing HBM data in the European Commission´s Information Platform for Chemical Monitoring (IPCheM);
- **Objective 6**: Linking external to internal exposure in order to improve exposure models for risk assessment;
- **Objective 7**: Developing, validating, and applying exposure and effect biomarkers to improve our understanding of the health risks associated with aggregate exposures;
- **Objective 8**: Identifying chemicals of concern through novel methods for the holistic analysis of HBM samples and improving the use of HBM data in assessing exposure to and the risks of chemical mixtures;
- **Objective 9**: Enhancing our understanding of the causal association between chemical exposure and adverse health outcomes by combining mechanistic studies with existing cohort data;
- **Objective 10**: Promoting capacity building at national level through training and exchange programmes;
- **Objective 11**: Engaging with stakeholders, including the general public, throughout the programme to ensure the credibility, accountability and legitimacy of activities and results.

Green Infrastructures for disaster risk management (GRIN)

The damage and losses caused by natural hazards in Europe over the period 1980-2013 amounted to 480 billion Euros in 2013 prices. More than 80% of the losses, 393 billion Euros, were caused by extreme weather events (i.e., on average 11.6 billion Euros per year). Without concerted action and long-term adaptation planning, future risks are likely to be amplified by on-going human-induced climate change and socio-economic change. To improve the resilience of society, both structural and non-structural measures and grey and green infrastructure will be needed. In particular, a greater deployment of nature-based solutions such as green infrastructures (GIs) is being increasingly advocated by European institutions NGO's, governments and financing bodies as a part of flexible, effective and efficient, and no-regret measures for disaster risk reduction and adaptation to climate change. The rationale behind the promotion of GI-based solutions is that they have the potential to contribute to both risk reduction (including, for example, flood and drought risk) as well as providing ancillary benefits such as positive effects on water quality, recreational amenities, economic resilience in agriculture and the provisioning of a wider range of other ecosystem services. Despite this recognized potential grey solutions have often prevailed over green solutions; primarily because grey infrastructure is often perceived to be more effective, efficient and easier to implement. Although there is plenty of research indicating the potential benefits of GI, demonstration of its practical value for DRR and role in both adaptation planning and sustainable development is lagging behind compared to other solutions and take up has been slow. This is primarily due to lack of actual applications, experience and coherence in the evidence base showing the direct and indirect benefits of GI solutions. In particular there is a lack of experience and coherence in implementation (including financing) and monitoring of GI solutions, including a lack of tools and methods supporting these processes. GREEN addresses these shortcomings and provides the necessary innovation in methods, tools, and solutions to appropriately promote the role of GI for DRR, climate change adaptation (CCA) and sustainable. In doing so, GREEN responds to the challenge transversally proposed by the three pillar of Action 1. To give a proper value to ecosystem services will drive towards smart, sustainable and inclusive growth. As an innovation action, GREEN will improve existing and develop new assessment tools and services that are able to capture the multiple benefits of nature-based solutions; design and test business and policy models fostering innovative GI projects and services; and elaborate instruments for upscaling and monitoring the performance of GI strategies.

The specific objectives of the innovation actions are to:

[1] Collect, critically review, and enhance the evidence that enables a sound and thorough assessment and monitoring of the functions and worthwhileness of green infrastructure-based solutions and ecosystem services for protecting economic, social and environmental assets and infrastructures in a representative number of regional, national and supra-national case/pilot studies;

[2] Review the established and develop new business and policy strategies that foster realization of green infrastructure-based solutions; and to identify the regulatory 'enablers' and novel financial schemes that foster greater efficient deployment of GI-solutions;

[3] Build a greater awareness about, and boost support for the practical application of green infrastructure-based solutions through ample engagement of stakeholders and businesses in designing innovative strategies, projects and services; and through systematic and tailor-made consultations and dissemination activities;

[4] Develop criteria and instruments for mapping the potential of a large scale deployment of green infrastructures throughout Europe, and by doing so promote their uptake; and to demonstrate the value and feasibility of green infrastructures-based solutions for the scope of regional, national and supranational DRR/CCA planning and nature conservation;

[5] Foster market replication of the demonstration pilots through developing training, guidance documents and capacity building; making available large scale mapping outputs and well-documented generated datasets; and fostering business oriented knowledge products and services.

[6] Develop methodologies able to extrapolate and/or up-scale the empirical evidence supporting the value of GI-based solution to regional and Pan-European level using also novel earth observation based services.

[7] Provide guidance on and demonstration of the possibilities for large scale deployment of GI supported by structural and investment funds.

The GREEN consortium will build upon and will exploit and further advance the knowledge produced in many past and ongoing international and national projects in which the consortium members (beneficiaries) are or have been directly involved. The range of these backbone projects have addressed both or either of the disaster risk reduction and climate change adaptation themes from various perspectives including risk and impact assessment, vulnerability and resilience measurement, performance assessment of structural and non-structural measures, policy analysis, innovation, market replicability, and capacity development. In many from among these projects the GREEN consortium members have already worked together.

EnvE Lab international profile

International collaborators network

EnvE Lab has a broad network of collaborators in each thematic area. In total, EnvE Lab collaborates with 56 research and academic institutions covering 18 different countries across the world in the frame of the six projects running in 2016.

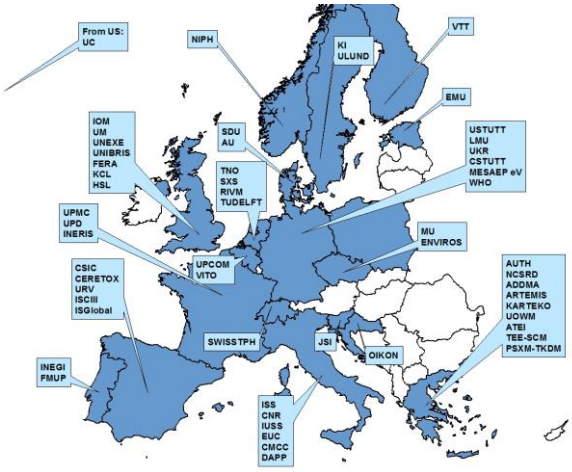


Figure 80. EnvE Lab collaborator network

In 2016 these collaborations gave rise to 55 presentations given in international fora. During the same period ten joint papers were published in international peer-reviewed journals and two book chapters were prepared.

World Health Organization (WHO)

Over the last five years 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 legacy in integrated health impact assessment from previous projects such as HEIMTSA, HEREPLUS, INTARESE, 2FUN. In the frame of 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. Knowledge exchange between EnvE Lab and WHO was strengthened by the close collaboration on expanding the methodologies to other cities/case studies in China involved in the project;
- 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[2].
- 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.
- Assessment of current state of play in human biomonitoring focusing on optimal design of biomonitoring campaigns, as well as on the exploitation of biomonitoring data through internal dose modelling.
- Overview of human exposure to endocrine disruptors in Europe through a combination of environmental and consumer product monitoring and biological monitoring of the human population.
- Waste and human health; this forth collaboration axis entails the development of refined exposure assessment tools for the exploitation of exposome capabilities on public health assessment of risks related to industrially contaminated sites. The contribution of EnvE Lab on the topic, was clearly demonstrated by Prof. D. Sarigiannis; based on the outcomes of CROME-LIFE, made clear proposals on waste management policy actions in Europe to ensure health and sustainability in his capacity as WHO advisor on integrated health impact assessment. This will be used as input to the forthcoming Ministerial Conference of the WHO (13-15 June 2017 @Ostrava, Czech Republic). inated sites and waste management. For the needs of this collaboration scheme, Prof. Sarigiannis was invited speaker in the respective workshop organized by the World Health Organization on “Waste, health, sustainability: what way forward”, held in Bonn, Germany, on October 5-6, 2016. The respective invited lecture was entitled “Integrated assessment of waste-related health impacts”.

On the basis of the extended and long-standing collaboration of EnvE Lab with WHO, we have now started the process of making EnvE Lab an official Collaborating Center of WHO on integrated environmental health risk. That process is expected to be completed in 2017.

[2] 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.

ICARUS Project kick-off meeting in Thessaloniki

The ICARUS project launch event & scientific workshop were held on 1, 2 and 3 June 2016 at the Research Dissemination Centre of the Aristotle University of Thessaloniki (AUTH). The ICARUS kick-off scientific workshop was part of the Green Week 2016, the biggest annual occasion to debate and discuss European environment policy. Professor Denis Sarigiannis, Director of the Environmental Engineering Laboratory (EnvE-Lab) and Scientific Coordinator welcomed the project partners and marked the beginning of this ambitious 5-year project, a flagship European-funded project in the area of climate change mitigation and air pollution reduction.

This event provided a great opportunity to debate and enhance the common understanding of the multiple interactions between air quality, carbon footprint, policy measures and human behaviour in defining a transition pathway towards greener, healthier and smarter cities within the next 50 years. Avenues of further research in the years to come were identified, such as the need to take into account social and cultural factors, socio-economic status (SES) and societal dynamics to assess overall policy impact, or the quest for win-win solutions tackling jointly air pollution and climate change mitigation.

Figure 81. ICARUS Project kick-off meeting in Thessaloniki

At the same time innovation and stakeholders engagement (including citizens) was considered as a central theme in the project which is aiming at assisting stakeholders in the selection, application and evaluation of the available datasets and tools for urban impact assessment in support of air quality and climate change governance at different spatial and temporal scales and taking into account the specific regulatory context. ICARUS will therefore improve innovation capacity by putting a special emphasis on stimulating a dialogue between policy makers/ implementers with the citizens and the main stakeholders in order to allow for a better involvement in planning and decision-making processes.

Media and the press were also invited to the event for wide publication and dissemination coverage and a press release was given by the project Coordinator Prof. Sarigiannis.

CROME project closing event

On 20 December, the Environmental Engineering Laboratory (EnvE-Lab) of the Aristotle University of Thessaloniki hosted the CROME-LIFE Closing Conference at the Athens Music Hall, Greece. The event garnered nearly 40 participants from the scientific, academic and policy community. At the event, international experts presented insights and novel tools for improved environmental health impact assessment and governance, making use of human biomonitoring data. Experts also outlined preventive strategies and policy measures to minimize the environmental burden of disease and protect public health. The conference was chaired by Assoc. Prof. Dimosthenis Sarigiannis. EnvE-Lab director. In particular, Assoc. Prof. Sarigiannis welcomed the participants, introduced the project consortium and kicked started the first session of the conference on “Environment and health risk: a multi-dimensional perspective”. Prof. Sarigiannis explained the exposome and stressed that it is very important to keep an unbiased agnostic stance to coupling chemical exposure to health status. He also referred to the CROME Environment & Health paradigm that proposes targeted innovation steps, including: a) the operational use and demonstration of the validity of biology-based modeling tools that allow to mechanistically link environmental exposure to biomonitoring and epidemiological data; b) the operational use of an integrated approach to biomonitoring that combines the use of state-of the-art biomarkers with reverse dosimetry and environmental data to reconstruct the effective dose human population is exposed to. The results will allow moving towards an improved environmental health risk assessment in the EU and the world; and c) the development of new and validation of existing biomarkers for environmental health risk assessment and environmental human biomonitoring.

Figure 82. CROME project closing event

The second session of the conference was dedicated to the CROME-LIFE legacy: “Synthesis of the main results obtained for the management of environmental burden and its consequences to health”. At this session, the project team showcased the project final findings regarding the impact of exposure to environmental chemicals on health across the Mediterranean basin.

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 and positive regulatory change.

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 (Table 2).

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€.

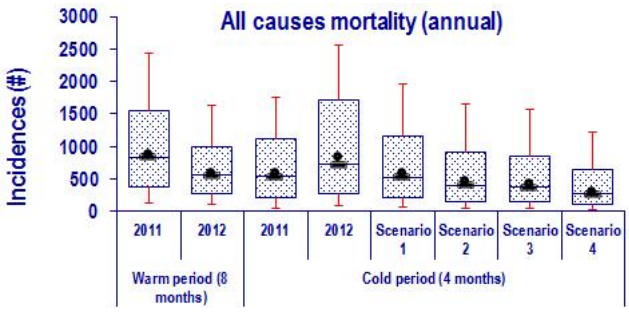


Figure 83. Estimated annual mortality due to PM exposure under current situation and "what if" scenarios

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

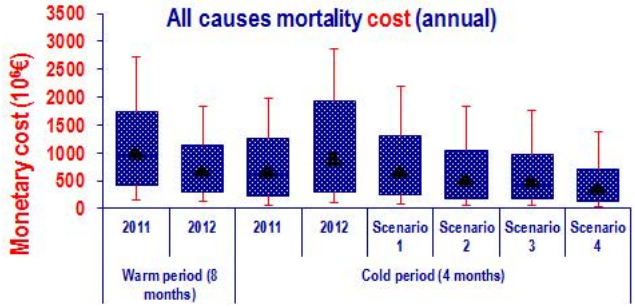


Figure 84. Estimated socioeconomic cost of PM attributed mortality based on total welfare change

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 survey 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 non-oxidised 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.

EnvE Lab in the news – TV interviews

Figure 84. A comprehensive interview at Vergina TV Channel with Associate Professor Dimosthenis Sarigiannis, EnvE Lab director, talking about the main environmental health problems that Greece is facing nowadays. **Watch the video at: https://youtu.be/weGNZiQeBEU**.

Figure 85. An interview at EPT3 TV Channel with Associate Professor Dimosthenis Sarigiannis, EnvE Lab director, talking about traces of arsenic element in potable water and its implications on human health. **Watch the video: https://youtu.be/lOWReJ9hJ2q**.

Figure 86. An interview at EPT3 TV Channel with Associate Professor Dimosthenis Sarigiannis, EnvE Lab director, talking about lifelong ionizing and non-ionizing radiation exposure and human health, taking into account the issue of combined or multiple exposure to health stressors. **Watch the video at: https://youtu.be/hox__0254QA**.

Figure 87. An interview at PONTOS TV Channel with Associate Professor Dimosthenis Sarigiannis, EnvE Lab director, presenting ICARUS, a Horizon 2020-funded project led by EnvE Lab, that aims to develop tools and propose policy measures for climate change mitigation and management as well as reduction of air pollution in cities. **Watch the video at: https://youtu.be/9HpH2fSCqRs**.

Figure 88. Assoc. Prof. Dimosthenis Sarigiannis explains the health and environmental implications from biomass burners used for heating in Greece at an interview for the EPT3 TV Channel. **Watch the video at: https://youtu.be/SCVj4TTNzGY**.

Figure 89. Assoc. Prof. Denis Sarigiannis discusses about the use of wood burning as a domestic heating source at an interview for the EPT3 TV Channel. This particulate air pollution may lead to as significant health implications as monetary costs on the public healthcare system - environmental injustice and inequity. **Watch the video at: https://youtu.be/EDXwqsieeQk.**

Publications & Conferences

Journal Publications

Sarigiannis D, Karakitsios S, Handakas E, Simou K, Solomou E, Gotti A. **Integrated exposure and risk characterization of bisphenol-A in Europe**. Food and Chemical Toxicology 2016; doi:10.1016/j.fct.2016.10.017.

Sarigiannis DA, Kontoroupis P, Nikolaki S, Gotti A, Chapizanis D, Karakitsios S. **Benefits on public health from transport-related greenhouse gas mitigation policies in Southeastern European cities**. Sci Total Environ 2016. DOI:10.1016/j.scitotenv.2016.11.142

Tobollik M, Keuken M, Sabel C, Cowie H, Tuomisto J, Sarigiannis D, Kunzli N, Perez L, Mudu P. **Health impact assessment of transport policies in Rotterdam: Decrease of total traffic and increase of electric car use**. Environ Res 2016; 146: 350-358.

Manrai A.K., Cui Y., Bushel P., Hall M., Karakitsios S., Mattingly C.J., Ritchie M., Schmitt C., Sarigiannis D.A., Thomas, D., Wishart, D., Balshaw, D.M., Patel, C.J. **Informatics and data analytics to support exposome-based discovery: a report from the 2015 NIEHS Exposome Workshop**. Annual Reviews of Public Health (2016). (accepted)

Sabel CE, Hiscock R, Asikainen A, Bi J, Depledge M, van den Elshout S, Friedrich R, Huang G, Hurley F, Jantunen M, Karakitsios SP, Keuken M, Kingham S, Kontoroupis P, Kuenzli N, Liu M, Martuzzi M, Morton K, Mudu P, Niittynen M, Perez L, Sarigiannis D, Stahl-Timmins W, Tobollik M, Tuomisto J, Willers S. **Public health impacts of city policies to reduce climate change: findings from the URGENCHE EU-China project**. Environmental Health 2016; 15: 5-21.

Vitkina TI, Yankova VI, Gvozdenko TA, Kuznetsov VL, Krasnikov DV, Nazarenko AV, Chaika VV, Smagin SV, Tsatsakis AM, Engin AB, Karakitsios SP, Sarigiannis DA, Golokhvast KS. **The impact of multi-walled carbon nanotubes with different amount of metallic impurities on immunometabolic parameters in healthy volunteers**. Food and Chemical Toxicology 2016; 87: 138-147.

Sarigiannis D, Karakitsios S, Gotti A, Handakas E, Papadaki K. **The exposome and Health Impact Assessment**. Dimosthenis A Sarigiannis 2016; 26: DOI: http://dx.doi.org/10.1093/eurpub/ckw172.048.

Sarigiannis, D., Kyriakou, S., Kermenidou, M., Karakitsios, S. **The reactive oxidative potential from biomass emitted particulate matter (PM10, PM2.5 & PM1) and its impact on human health**. Fresenius Environmental Bulletin (2016) (accepted).

Sarigiannis D., Nikolaki S., Zikopoulos D., Kermenidou M. **Determination of 19 PAHs in air samples using gas chromatography-mass spectrometry**. Fresenius Environmental Bulletin (2016) (accepted).

Handakas E., Chapizanis D., Sarigiannis D., Karakitsios S. **Study of in-vehicle particulate matter exposure in Thessaloniki, Greece**. Fresenius Environmental Bulletin (2016) (accepted).

Handakas E., Sarigiannis D., Manariotis I., Yannopoulos P., Zarkadas I. **Decision support tool for urban solid waste management**. Fresenius Environmental Bulletin (2016) (accepted).

Zarkadas I., Georgopoulos N., Kaldis F., Pilidis G., Sarigiannis D. **Assessing the Biomethane potential of three pickling and canning semi-solid wastes under thermophilic conditions**. Fresenius Environmental Bulletin (2016) (accepted).

Books

Sarigiannis D.A. and Karakitsios S.P. **Complex exposure modeling**. Chapter in: Mixtures toxicology and risk assessment. J.E. Simmons and C. Rider, Springer (2016).

Sarigiannis D.A., S. Karakitsios, E. Handakas, K. Papadaki, D. Chapizanis, A. Gotti. **Informatics and data analytics to support exposome-based discovery Part 1: Assessment of external and internal exposure**. Chapter in: Applying Big Data Analytics in Bioinformatics and Medicine. P. Papadopoulou and D. Lytras (eds.), IGI Global (in print).

Sarigiannis D.A., A. Gotti, E. Handakas, S. Karakitsios. **Informatics and data analytics to support exposome-based discovery Part 2: Computational exposure biology**. Chapter in: Applying Big Data Analytics in Bioinformatics and Medicine. P. Papadopoulou and D. Lytras (eds.), IGI Global (in print).

Conference presentations

D. Sarigiannis, D. Chapizanis, S. Karakitsios. **Emerging Methodologies for Environmental Exposure Assessment: Coupling Personal Sensor Data and Agent Based Modelling (ABM)**. 2016 AIChE Annual Meeting, San Francisco (CA), USA, 13-18/11/2016.

D. Sarigiannis, S. Karakitsios, A. Tsatsakis, K. Golokhvast. **Real Life PM Emissions from Traffic and Human Exposure Implications**. 2016 AIChE Annual Meeting, San Francisco (CA), USA, 13-18/11/2016.

K. Papadaki, S. Karakitsios, D. Sarigiannis. **Advanced Modeling of Tissue:Blood Partition Coefficients for Industrial Chemicals**. 2016 AIChE Annual Meeting, San Francisco (CA), USA, 13-18/11/2016.

D. Sarigiannis, S. Karakitsios, E. Handakas, A. Gotti. **Exposome Analysis of Polyaromatic Hydrocarbons**. 2016 AIChE Annual Meeting, San Francisco (CA), USA, 13-18/11/2016.

D. Sarigiannis, S. Karakitsios, A. Tsatsakis, K. Golokhvast. **High Dimension Biological Analysis of Carbon Nanotube Toxicity**. 2016 AIChE Annual Meeting, San Francisco (CA), USA, 13-18/11/2016.

D. Sarigiannis, F. Kaldis, I. Zarkadas. **Biomethane Potential Determinants of Different Agro Industrial Substrates**. 2016 AIChE Annual Meeting, San Francisco (CA), USA, 13-18/11/2016.

D. Sarigiannis. **Assessing health impacts of hazardous waste: the exposome paradigm**. 9th European Public Health Conference, Vienna, Austria, 9-12/11/2016.

D. Sarigiannis. **The exposome and Health Impact Assessment**. 9th European Public Health Conference, Vienna, Austria, 9-12/11/2016.

D. Sarigiannis, S. Karakitsios, M. Kermenidou. **Health impact assessment of urban ultrafine and nano particles**. International Conference on Health & Safety issues related to Nanomaterials - Nanosafe 2016, Grenoble, France, 7-10/11/2016.

D. Sarigiannis, S. Karakitsios, A. Tsatsakis, K. Golokhvast, A. Engin. **High dimension biological analysis of carbon nanotube toxicity**. International Conference on Health & Safety issues related to Nanomaterials - Nanosafe 2016, Grenoble, France, 7-10/11/2016.

D. Sarigiannis, S. Karakitsios, M. Kermenidou. **The reactive oxidative potential of pm associated with sources and its impact on human health**. International Conference on Health & Safety issues related to Nanomaterials - Nanosafe 2016, Grenoble, France, 7-10/11/2016.

D. Sarigiannis. **Multiscale connectivity in HEALS - a high dimension biology approach to unravel the exposome**. 2016 Annual International Society of Exposure Science Meeting, Utrecht, The Netherlands, 9-13/10/2016.

D. Chapizanis, D.A Sarigiannis, S. Karakitsios, A. Gotti. **Personal exposure assessment fusing multi-sensor data and Agent Based Modelling (ABM)**. 2016 Annual International Society of Exposure Science Meeting, Utrecht, The Netherlands, 9-13/10/2016.

S. Karakitsios, D. Sarigiannis, A. Gotti, E. Handakas. **The importance of internal dosimetry in unravelling the exposome**. 2016 Annual International Society of Exposure Science Meeting, Utrecht, The Netherlands, 9-13/10/2016.

D. Sarigiannis. **Early observations from HEALS**. 2016 Annual International Society of Exposure Science Meeting, Utrecht, The Netherlands, 9-13/10/2016.

D. Sarigiannis, D. Chapizanis, S. Karakitsios, A. Gotti. **Using agent-based modelling for interpreting the individual exposome**. 2016 Annual International Society of Exposure Science Meeting, Utrecht, The Netherlands, 9-13/10/2016.

E. Handakas, A. Gotti, S. Karakitsios, D. Sarigiannis. **Exposure assessment of multiple chemicals starting from biomonitoring data**. 2016 Annual International Society of Exposure Science Meeting, Utrecht, The Netherlands, 9-13/10/2016.

D. Sarigiannis, S. Karakitsios, A. Gypalis, E. Handakas, A. Gotti. **INTEGRA LCA: An innovative tool for health risk assessment of plastic waste**. 5th International Conference on Industrial and Hazardous Waste Management, Chania, Greece, 27-30/9/2016.

D. Sarigiannis, S. Karakitsios, A. Gotti. **Assessing health impacts of hazardous waste: the exposome paradigm**. 5th International Conference on Industrial and Hazardous Waste Management, Chania, Greece, 27-30/9/2016.

D. Sarigiannis, S. Karakitsios, E. Handakas, A. Gotti. **Cancer risk from exposure to dioxins and furans after accidental fire in an urban waste recycling facility**. 5th International Conference on Industrial and Hazardous Waste Management, Chania, Greece, 27-30/9/2016.

D. Sarigiannis, G. Dontis, I. Zarkadas. **Biomethanation and valorisa-tion of mink droppings and byproducts**. 5th International Conference on Industrial and Hazardous Waste Management, Chania, Greece, 27-30/9/2016.

D. Sarigiannis, A. Gotti, S. Karakitsios, A. Pino, G. Calamandrei, L. Chiarotti, A. Alimonti. **Human Biomonitoring Data Analysis for metals in an Italian Adolescents Cohort: an Exposome Approach**. 8th International Conference On Children's Health and the Environment, Barcelona, Spain, 14-16/9/2016.

D. Sarigiannis, S. Karakitsios, E. Handakas, A. Gotti **Internal dosimetry metrics for risk assessment of endocrine disruptors – the case of bisphenol A**. 8th International Conference On Children's Health and the Environment, Barcelona, Spain, 14-16/9/2016.

D. Sarigiannis, S. Nikolaki, M. Kermenidou, D. Zikopoulos, S. Karakitsios. **Children exposure to PAH and potential carcinogenic risk assessment from biomass burning incorporating internal dosimetry metrics**. 8th International Conference On Children's Health and the Environment, Barcelona, Spain, 14-16/9/2016.

D. Sarigiannis. **Assessing the impact of hazardous waste on children's health: the exposome paradigm**. 8th International Conference On Children's Health and the Environment, Barcelona, Spain, 14-16/9/2016.

D. Sarigiannis, K. Polanska, G. Theodoridis, C. Xatziioannou, W. Hanke. **Pathway analysis of prenatal exposure to phthalates and child motor development**. EUROTOX 2016 Seville, Spain 4-7/9/2016.

D. Sarigiannis, S. Karakitsios, A. Tsatsakis, K. Golokhvast, A. Engin. **High dimension biological analysis of carbon nanotube toxicity**. EUROTOX 2016 Seville, Spain 4-7/9/2016.

D. Sarigiannis, S. Karakitsios, E. Handakas, A. Gotti. **Exposome analysis of polyaromatic hydrocarbons**. EUROTOX 2016 Seville, Spain 4-7/9/2016.

D. Sarigiannis, K. Papadaki, S. Karakitsios. **Development and evaluation of QSAR models for use in**

toxicokinetic modelling of "data poor" industrial chemicals. EUROTOX 2016 Seville, Spain 4-7/9/2016.

D. Sarigiannis, P. Kontoroupis, E. Solomou, S. Nikolaki, A. Karabelas. **Cancer risk attributable to inhalation of plant protection products in the EU**. EUROTOX 2016 Seville, Spain 4-7/9/2016.

D. Sarigiannis. **Industrially contaminated sites in Greece: use of biomarkers and the exposome paradigm**. 28th Annual Conference International Society for Environmental Epidemiology, Rome, Italy, 31/8-4/9/2016.

D. Sarigiannis. **Assessing health impacts of hazardous waste: the exposome paradigm**. 28th Annual Conference International Society for Environmental Epidemiology, Rome, Italy, 31/8-4/9/2016.

D. Sarigiannis, S. Nikolaki, M. Kermenidou, D. Zikopoulos, S. Karakitsios. **Cancer risk of PAHs in particles emitted from biomass combustion**. 28th Annual Conference International Society for Environmental Epidemiology, Rome, Italy, 31/8-4/9/2016.

D. Sarigiannis, I. Zarkadas. **High dimension biological processes for the valorization of agro-industrial waste towards a circular bioeconomy**. Circular Economy and Sustainable Use of REnewable REsources in the context of Climate Change and Social Upheavals, Nisyros, Greece, 20-22/7/2016.

D. Sarigiannis, S. Karakitsios, A. Gotti. **Combined exposure to indoor air pollutants in Europe**. SIDISA 2016 - X International Symposium on Sanitary and Environmental Engineering, Rome, Italy, 20-22/6/2016.

D. Sarigiannis, S. Karakitsios, D. Chapizanis, E. Handakas, A. Gotti. **The ICARUS paradigm for air pollution exposure management in cities**. SIDISA 2016 - X International Symposium on Sanitary and Environmental Engineering, Rome, Italy, 20-22/6/2016.

D. Sarigiannis, S. Karakitsios. **Health and monetary impact of biomass burning for space heating**. SIDISA 2016 - X International Symposium on Sanitary and Environmental Engineering, Rome, Italy, 20-22/6/2016.

D. Sarigiannis, S. Karakitsios, A. Gotti. **Cancer risk from exposure to dioxins and furans after accidental fire in an urban waste recycling facility**. SIDISA 2016 - X International Symposium on Sanitary and Environmental Engineering, Rome, Italy, 20-22/6/2016.

D. Sarigiannis, M. Antonakopoulou, E. Handakas, A. Gotti, S. Karakitsios. **Life cycle assessment of municipal waste management options as strategic tool for decision making**. SIDISA 2016 - X International Symposium on Sanitary and Environmental Engineering, Rome, Italy, 20-22/6/2016.

I. Zarkadas, E. Handakas, D. Sarigiannis. **The benefits of food waste biomethanation in farm-scale systems**. SIDISA 2016 - X International Symposium on Sanitary and Environmental Engineering, Rome, Italy, 20-22/6/2016.

D. Sarigiannis. **Multi-omics for exposome analysis**. 4th Workshop on Holistic Analytical Methods for Systems Biology Studies, Thessaloniki, Greece, 17-19/4/2016.

D. Sarigiannis, P. Kontoroupis, C. Schieberle, B. Miller, V. Singh, R. Sokhi. **Integrated uncertainty evaluation in air pollution health impact assessment**. 10th International Conference on Air Quality – Science and Application, Milan, Italy, 14-18/3/2016.

D. Sarigiannis, M. Kermenidou, D. Zikopoulos, S. Nikolaki, S. Karakitsios. **Health and monetary cost attributed to aerosol and gaseous emissions from biomass use for space heating**. 10th International Conference on Air Quality – Science and Application, Milan, Italy, 14-18/3/2016.

D. Sarigiannis, S. Nikolaki, M. Kermenidou, D. Zikopoulos. **Determination of 19 PAHs in air samples using gas chromatography - mass spectrometry**. 10th International Conference on Air Quality – Science and Application, Milan, Italy, 14-18/3/2016.

D. Sarigiannis, D. Chapizanis, P. Kontoroupis, S. Karakitsios. **Personal exposure assessment to air pollutants using portable sensors and agent based modelling**. 10th International Conference on Air Quality – Science and Application, Milan, Italy, 14-18/3/2016.

D. Sarigiannis, M. Kermenidou, S. Kyriakou, Roxani Tzimou – Tsitouridou, S. Karakitsios. **Reactive oxygen species found in urban PM2.5 and PM10: chemical analysis and source apportionment**. 10th International Conference on Air Quality – Science and Application, Milan, Italy, 14-18/3/2016.

D. Sarigiannis, E. Handakas, M. Kermenidou, P. Charisiadis, K. Makris, A. Gotti, S. Karakitsios. **Air pollution at the Charilaos Trikoupis bridge (Greece)**. 10th International Conference on Air Quality – Science and Application, Milan, Italy, 14-18/3/2016.

K. Golokhvast, V. Chernyshev, V. Chaika, S. Ugay, E. Zelinskaya, A. Tsatsakis, S. Karakitsios, D. Sarigiannis. **Size-segregated emissions and metal content of particles emitted by vehicles with low and high mileage: implications to population exposure**. 10th International Conference on Air Quality – Science and Application, Milan, Italy, 14-18/3/2016.

D. Sarigiannis, K. Polanska, G. Theodoridis, C. Xatziioannou, W. Hanke. **Pathway analysis of prenatal exposure to phthalates and child motor development**. The Society of Toxicology 55th Annual Meeting and ToxExpo, New Orleans (Louisiana), USA, 13–17/3/2016.

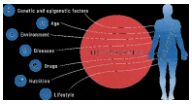
D. Sarigiannis. **Mixtures Assessment: the exposome paradigm**. EEA workshop on activities on mixtures under the EHBMI, Copenhagen, Denmark, 11/2/2016.

Invited talks

Invited talk in the European Environmental Agency (EEA) workshop on "Activities on mixtures under the European Human Biomonitoring Initiative" held in Copenhagen, Denmark, February 9. Lecture titled "**Mixtures Assessment: the exposome paradigm**".

Invited talk in the Cyprus University, Department of Biological Sciences / Department of Chemistry in Nicosia, Cyprus, March 23. Lecture titled "**Unravelling the exposome through integrated exposure biology**".

Invited talk in "ENMF 2016 - Exploring Novel Medical Frontiers", held in Thessaloniki, Greece, April 10. Lecture titled "**Cosmic ray exposome**".



Invited talk at the 4th Workshop on "Holistic Analytical Methods for Systems Biology Studies" in Thessaloniki, Greece, April 17. Lecture titled "**Unravelling the exposome through integrated exposure biology**".

Invited talk at the Emory Exposome Summer Course, in Hercules Exposome Center, Atlanta, US, on June 13-17. Lecture titled "**The exposome in Europe"**.

Invited talk at the workshop on "Environment and Health in Urban Agglomerations, held in Cyprus Technical University in Limassol, Cyprus, on July 4. Lecture titled "**The exposome in Thessaloniki**".

Invited talk at the 12th Conference of Greek inter-municipality Network of Healthy Cities, held in the Municipality of Milos, Greece, on July 4. Lecture titled "**Environment and Health**".

Invited talk in WHO, at the workshop "Waste, health, sustainability: what way forward", held in Bonn, Germany, on October 5-6. Lecture titled "**Integrated assessment of waste-related health impacts**".

Invited talk in the 2016 Annual International Society of Exposure Science Meeting, held in Utrecht, The Netherlands, on October 9-13. Lecture titled "**Multiscale connectivity in HEALS - a high dimension biology approach to unravel the exposome**".

Invited talk in the 6th Panhellenic conference of Public Health and Social Medicine Forum, held in Athens, Greece on October 31 - November 1. Lecture titled "**Environmental Health Inequalities associated biomass emitted PAHs exposure**".

Invited talk at the Workshop "The role of scientists to inform and limit the impact on health and the environment from exposure to pesticides" held in Heraklion, Crete, on November 4. Lecture titled "**Environmental pesticide exposure and impact on public health**".

Invited talk at the European Public Health Conference, in Vienna, Austria, on November, 9-12. Lecture entitled "**Assessing health impacts of hazardous waste: the exposome paradigm"**.

Laboratory Personnel

Dimosthenis A. Sarigiannis, Director

M.Sc., PhD (University of California, Berkeley, USA) is Associate Professor specialising on environment and health engineering at the Department of Chemical Engineering of the Aristotle University of Thessaloniki and the institute for Advanced study of Pavia. He is visiting Professor at the Master's Program on Toxicology of the University of Thessaly and at the Master's Program on Toxicology and Environmental Risk at the Medical School of the University of Pavia. He is also 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 President of MESAEP. He leads the projects ICARUS, HEALS, PEC, CROME, INTEGRA CheRRIE and TAGS. He has also 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 21 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 several projects.

Dr. Spyros Karakitsios is an environmental health scientist, with studies in physics (B.Sc.), environmental and computational chemistry (M.Sc.) and applied biology (PhD) of the University of Ioannina.

Dr. Ioannis Zarkadas is an Environmental Engineer from the University of Leeds (UK), his research activities focus on waste management, anaerobic digestion, Life Cycle Analysis.

Marianthi Kermenidou (PhD Student Researcher) is Environmental Engineer, graduated from Democritos University of Thrace, Greece with a MSc degree. Her scientific field is indoor air pollution, chemical analysis, source apportionment and redox activity of airborne particulate matter.

Evangelos Handakas is a PhD Student Researcher, Chemical Engineer and civil infrastructure engineer with 2 M.Sc. degrees (MMAths and M.Eng). His research activities focus on the fields of biological systems modelling, health impact assessment and exposure reconstruction.

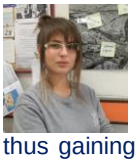
Krystalia Papadaki (PhD Student Researcher) is a Chemical Engineer, graduated from Aristotle University of Thessaloniki, Greece. Her research activities focus on Quantitative Structure Activity Relationship modelling.

Dimitrios Chapizanis is a PhD Student Researcher. He holds a diploma in Chemical Engineering and his research activities focus on atmospheric pollution, exposure assessment and environmental risk.

Evelin Matiaki MBA, MSc Civil Engineer is a European Projects Manager and a PhD Candidate at the Environmental Engineering Laboratory of the Department of Chemical Engineering, Aristotle University of Thessaloniki (AUTH).

Maria Andrielou is a Communications Adviser. With more than 10 years of experience in the industry, policy and education field, Maria is responsible for building communication, dissemination and stakeholder engagement strategies with a focus on research and innovation topics.

Nafsika Papaioannou is a chemical engineer. Her expertise lies in metabolic engineering, bioinformatics and metabolomics analysis.



Irini Furxhi holds and Msc in Toxicology. She has worked in "Etablissement Francais du Sang" (EFS) – France Compte in the diagnostic Molecular-Oncology laboratory, thus gaining experience in molecular technical methods such as DNA and RNA extraction, PCR, RTqPCR, Sanger sequencing, Chimeris and -omics.