Assessing health impacts of hazardous waste: the exposome paradigm

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Connectivity-based workflow for exposome studies

Environmental sensors
Remote sensing
Environmental modeling / data management
Agent based modelling
Environmental analysis
Exposure modelling
Ubiquitous personal sensors
Human biosampling
Fluxomics (dynamic flux balance analysis)
Transcriptomics
Metabolomics
Bioinformatics / systems biology
Pathway analysis

EWAS
Systems Effects / Individual exposome
Community Effects / Cohorts
Cellular/tissue effects
Molecular initiating events

Pathway analysis
Enzyme Kinetics
Connectivity-based workflow for exposome studies

Environmental engineering laboratory
Dep. of Chemical Engineering
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28th Annual Conference International Society for Environmental Epidemiology
31 Aug - 4 Sept 2016
Rome, Italy
The external exposome
External Exposome workflow

Measured data
- Sensors
- Modelled data
- Questionnaires

Data Fusion

- Outdoor
- Indoor
- Food
- Soil
- Water
- Drinking water

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SES
TAMD

Probability framework (MCMC)

Exposure at individual level

Exposure for population groups

Uncertainty

- ABM
- Decision theory
- Kalman filters
- Error reduction
- ANN
Pilot Campaign

Occasionally:
- $\text{NO}_2$, $\text{O}_3$
- Dust fall

- Dylos (PM)
- Netatmo (temperature, humidity, air pressure, $\text{CO}_2$ and noise)
- Vacuum Sample

Fitbit Flex

Sleep

ACTIVITIES

- Smartphone apps
- Paper Log & Questionnaires

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Personal Exposure Assessment

INPUT

- Air Quality Data
- Population Data
- Buildings, Land Use
- Road Network

SIMULATION

Agent Based Modelling

OUTPUT

- Personal Exposure
- Human Agent Trajectories

ACTIVITIES

- Sleeping
- In transit
- Working
- Indoor activities
- Relaxing
- Sports

LAND USE

- Commercial
- Office
- Other
- Park
- Residential
- School
- University

Thessaloniki, Greece

ABM simulation preview
Waste types and pollutants

- Municipal waste
  - PCDDs and PCDFs
  - Heavy metals (Cd, As, Pb, Hg, Cr)
- Agricultural waste
  - VOCs
  - PAHs
  - Other metals and rare earth elements
  - H$_2$S
  - Biogas
  - Pesticides
  - Phthalates
  - PCBs
  - CFCs
  - PHAHs
  - Pharmaceutical
- e-waste
- Hospital waste
- Industrial waste
Environmental mobility and exposure pathways

Leachate substances associated with health risks

- Aniline
- Fluoride
- Organotin compounds
- Arsenic
- Mecoprop
- Pentachlorophenol
- Biphenyl
- Methyl chlorophenoxy acetic acid
- Phenols
- Cyanide
- Methyl tertiary butyl ether
- Phosphorus
- Di(2-ethyl hexyl)phthalate
- Naphthalene
- Polycyclic aromatic hydrocarbons
- Dichloromethane
- Nitrogen
- Toluene
- Ethylbenzene
- Nonylphenol
- Xylenes
Multiple scale interactions of environmental modelling

Detailed micro-environmental concentrations taking into account interactions among different media (gas, particles and dust)

Detailed exposure modelling taking into account multiple pathways and routes of exposure

Consumer products
The internal exposome
Exposure biology workflow
Rendering high dimension biology operational

Whole genome mRNA expression
mRNA Microarrays

Molecular pathways

PoT hypothesis

Targeted proteomics

Targeted DNA Methylation analysis

Functional assays

Phenotypic/endotyptic anchoring

Metabolic pathways

Targeted metabolomics

Targeted (bio)chemical analysis

Untargeted metabolite profiling
LC-MS/MS, MS/MS-ToF, NMR
Exposure biology workflow

- LC-MS/MS
- GC-MS/MS
- Microarrays
- NGS

**Analysis and Software:***
- MassHunter Qual/Quant
- ChemStation AMDIS
- Feature Extraction
- GeneSpring Platform

**Result:**
- Biological Pathways
Methodological transition facilitated by exposome

Congenital anomalies $\rightarrow$ RR 1.01 - 1.08 for various defects (2 km from landfills)
Cancer risk $\rightarrow$ RR 1.035 for all cancer types (3 km from incinerators)

• Which compounds are associated to each endpoint?
• How we can refine exposure to these compounds related to waste disposition?
  ▪ Improved exposure modelling
  ▪ Assimilation of biomonitoring data
• How to improve health associations and identify causalities
  ▪ Identification of molecular markers of exposure and effect
Waste management in Athens
Acute exposure to waste hazards: Cancerogenicity

PCDDs and PCDFs (TEQ)

Concentration (fg/m³)

5%-95%
Median

Rural areas
City centre
Industrial area
Landfield fires
Aspropyrgos fire

Conc. (pg/g lipid_TEQ)

Individuals age (years)

PCDDs and PCDFs (TEQ)

Background levels

Concentration (pg/g lipid_TEQ)

Children
Adults

Blood concentration
Blood concentration (accident)

Fetus - non exposed
Fetus breast fed - non exposed
Fetus - exposed
Fetus breast fed - exposed

Risk

Background risk
Post-accidental risk / adults
Post-accidental risk / neonates
Post-accidental risk / breast fed

Cancer risk

5%-95%
Median

Risk

Background risk
Post-accidental risk / adults
Post-accidental risk / neonates
Post-accidental risk / breast fed
Metabolomics and pathway analysis

Increased levels of unsaturated vs saturated fatty acids, compared to controls → cholesterol homeostasis perturbation → **AhR deregulation**
Chronic exposure to waste hazards
Neurodevelopmental toxicity
Explore causality in EWAS
Conclusions

• Exposome science can overhaul the current environmental health risk assessment paradigm. This requires combination of high dimensional biology and system science aiming at integration using big data analytics and bioinformatics

• The connectivity approach to the exposome elucidates toxicity pathways and assigns causal associations between environmental stressors and health

• Precise prevention towards environmental risks by identifying the susceptible or vulnerable individuals or age-groups
Bertold Brecht’s *Life of Galileo:*
“The main objective of science is not to open the door to infinite wisdom but to roll back the boundaries of infinite error”

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*A connectivity perspective to environmental health*