MRC-HPA Centre for Environment & Health
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"Systems perspectives of the exposome"

IARC 50th anniversary, Lyon June 2016

Imperial College London

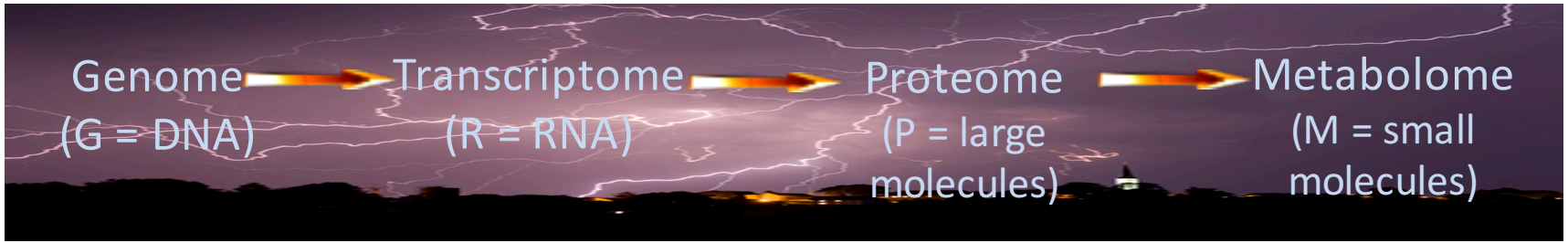
Epidemiology has reached a limit? Examples of open questions that imply large attributable risks but also large measurement error:

Air pollution and disease at low levels of exposure
Bladder, colon cancer and exposure to disinfection by-products
Socio-economic differentials and biological determinants of ageing

Biomarker research supports causal reasoning by linking exposures with disease *via* mechanisms and emphasizing causality as a process ("meet-in-the-middle").

In **Salmon's view** (Salmon 1984, 1997; Vineis et al, submitted), processes are conceptualized as ***world lines of objects***. An airplane flying in the sky is a world line, but so is its shadow on the ground.

How do we discriminate between world lines, or processes, that are causal and those that are not? In the Salmon-Dowe approach, causal processes are capable of transmitting **conserved quantities**, such as mass-energy, linear momentum, or charge. **Shadows do not transmit conserved quantities (as demonstrated when two airplanes collide).**



Transmission of conserved quantities is also transmission of information via molecules (=the internal exposome).

The exposome concept refers to the totality of environmental exposures from conception onwards. The ***internal exposome*** is based on measurements in biological material of complete sets of biomarkers of exposure, using ***repeated biological samples*** especially ***during critical life stages***.

The EXPOsOMICS Project

This project aims to develop a novel approach to the assessment of exposure to high priority environmental pollutants by characterizing the **external and the internal components of the exposome (Wild 2012),** focusing on air and water contaminants during **critical periods of life**. A life-course approach is used.

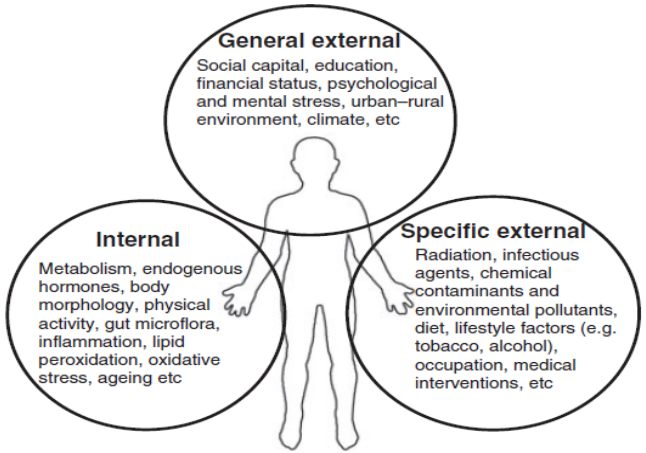
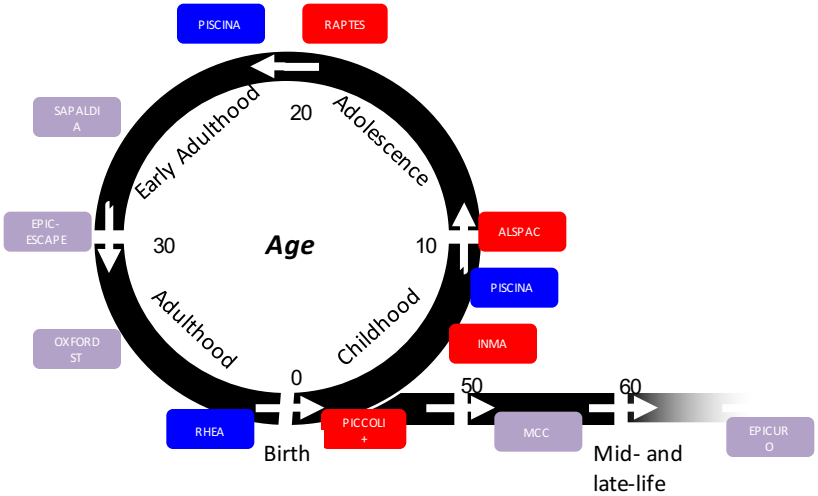


Figure 1 Three different domains of the exposome are presented diagrammatically with non-exhaustive examples for each of these domains



MRC-PHE Centre for Environment & Health

The EXPOsOMICS Project

Aims: develop a new approach to assess environmental exposures

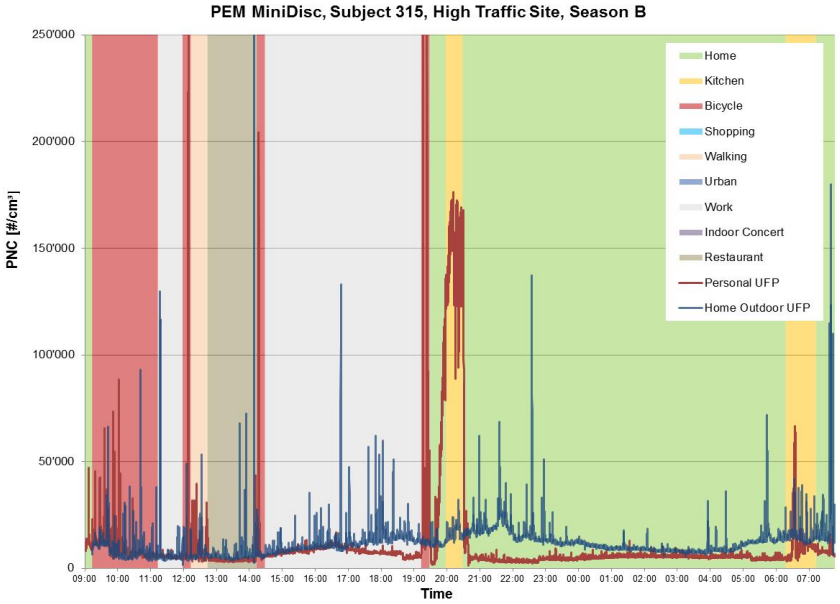
Predict disease risk

Characterize the exposome for common exposures during critical periods

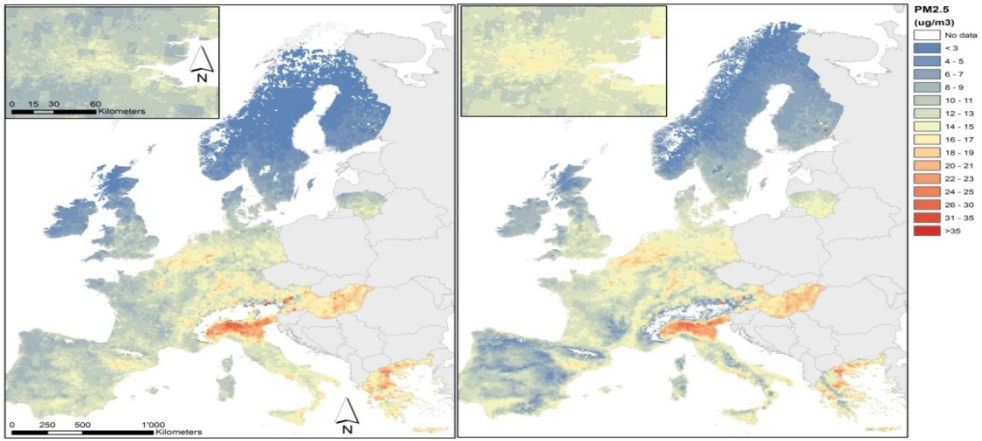
Using omics: link exposure to biochemical and molecular changes – help to improve understanding of molecular pathways (**adductomics, proteomics, transcriptomics, metabolomics, epigenomics for about 3,000 samples overall**)

Type of effect	Timescale	Design	Exposures
Acute effect	<2 hours	Intervention study	Pre-post experiment meas.
Short-term effect	24 Hours	Personalised Exposure Measurement Campaigns (PEM)	Real-time monitoring (e.g., backpack)
Long-term effect	Years	Cohort Studies	Modelled exposure (LUR...)

External exposome: from personal monitoring to satellite integration



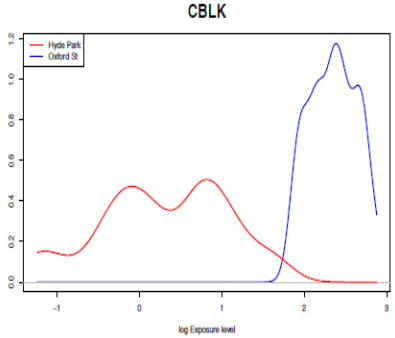
Personal UFP monitoring (outdoor and home) (courtesy of N Probst-Hensch)

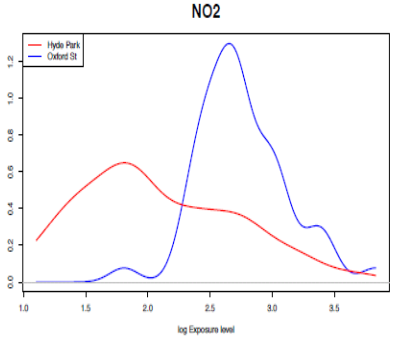


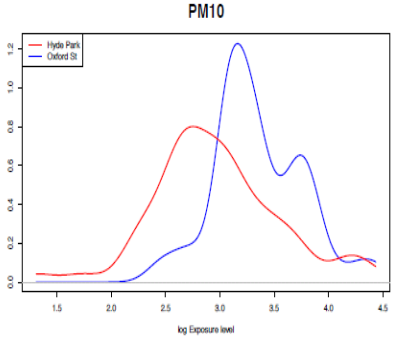
"Hybrid LUR" models including satellite data (AOD) and data from chemical transport models developed using ESCAPE (A) and AIRBASE (B) sites (courtesy J Gulliver)

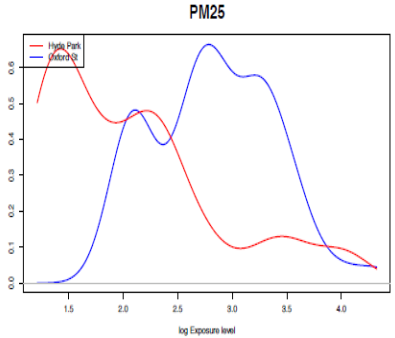
Oxford Street and Hyde Park cross-over study

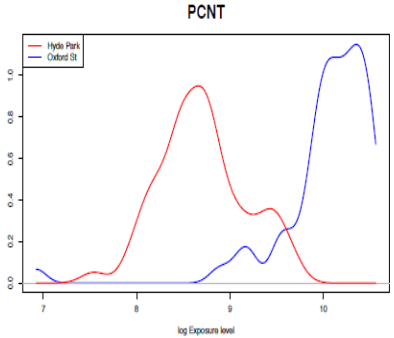
Total 354 samples (6 samples per person). Air pollution measurements (at both sites): PM10, PM25, NO2, UFP, Black carbon. Outcomes: COPD, IHD, Healthy
Metabolomics and adductomics measured 3x (before, 2h and 24h after) at 2 time points

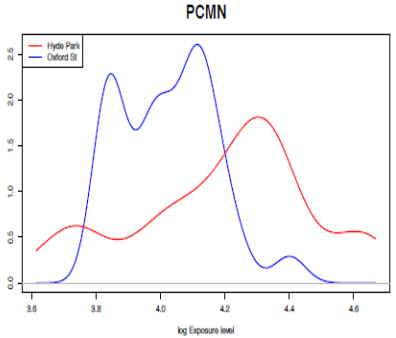






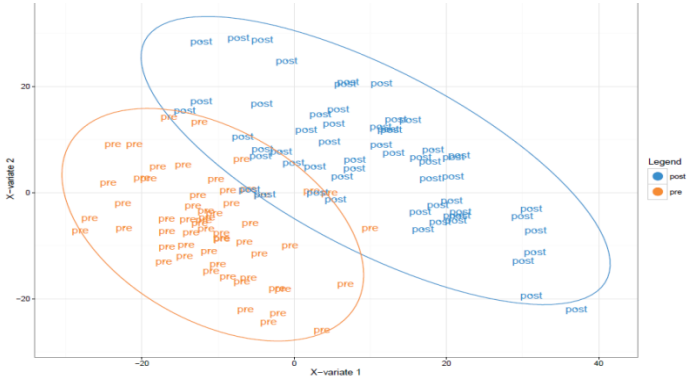






Glimpses on the internal Exposome

PISCINA study - Metabolomic analysis (PLS-DA and top hits) - Exposure to disinfection by-products and their short-term effects in swimmers - Untargeted metabolomics of blood samples, using UHPLC-QTOF mass spectrometer. N= 6,471 metabolomic features identified (courtesy K van Veldhoven)

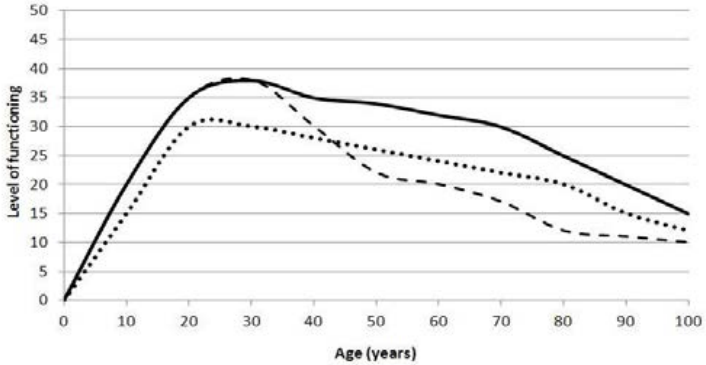


Exposure	Smallest *p*-value	Significant Bonferroni
CHCl3	5.50E-18	245
BDCM	1.80E-17	267
DBCM	5.17E-15	217
CHBr3	2.27E-12	147
TTHM	4.63E-18	255

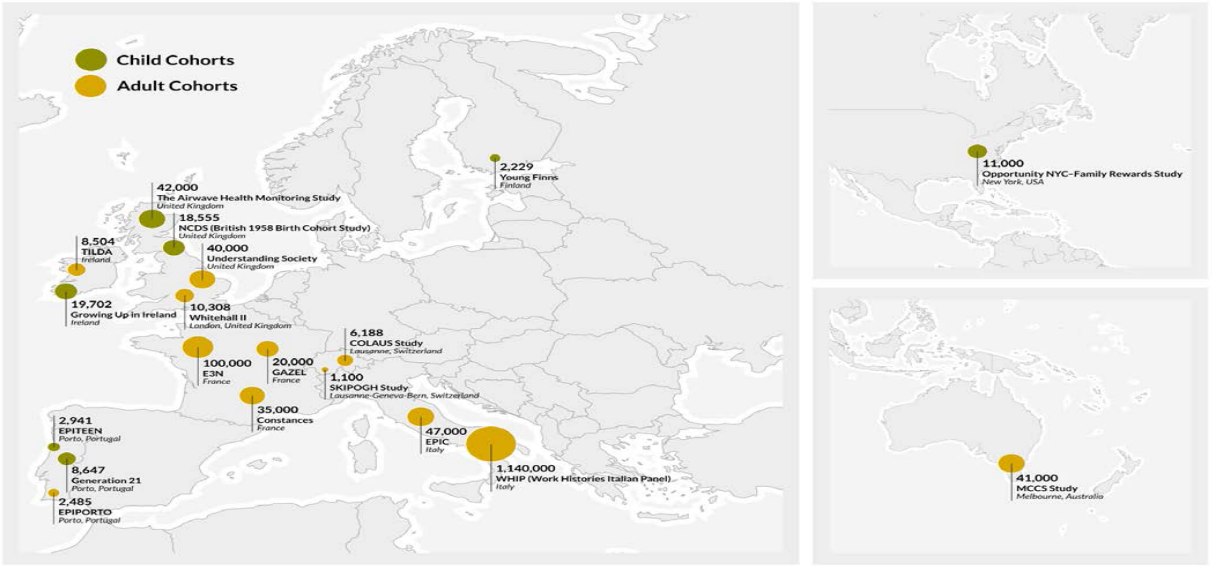
Socio-economic status and omics

Goals of H2020 Lifepath

- To provide updated, relevant and innovative **evidence for healthy ageing policies** (particularly “health in all policies”)
- To improve the understanding of the mechanisms through which healthy ageing pathways diverge by SES, by investigating **life-course biological pathways using omic technologies**.
- To examine the consequences of the current **economic recession** on health and the biology of ageing (and the consequent increase in social inequalities)**.**

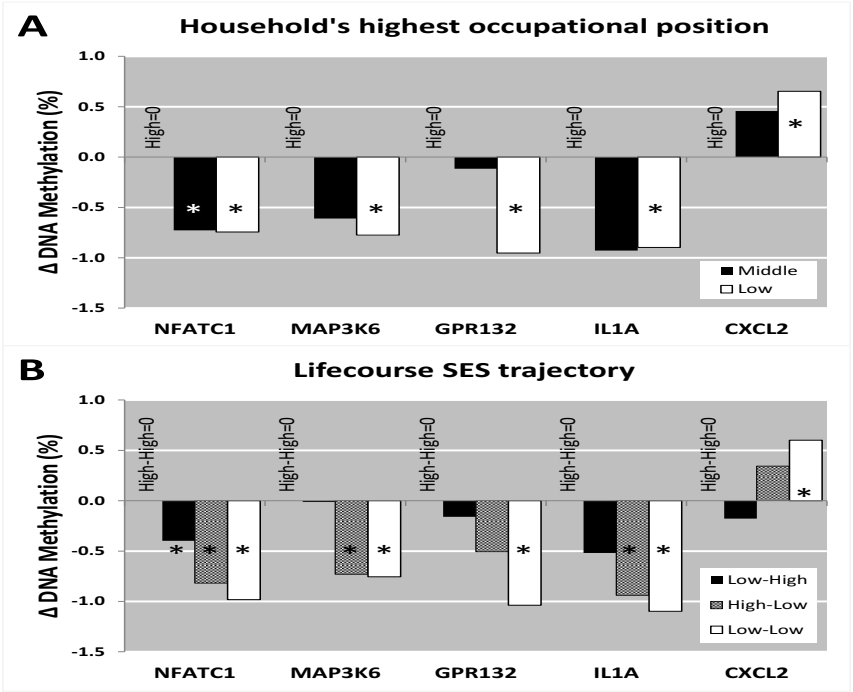


The life-trajectory model of ageing implies a «build-up» phase and a «decline» phase



Methylation as a marker of socio-economic differentials

Methylation as a marker of socio-economic differentials in EPIC-Italy (Stringhini et al, IJE 2015)



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