Nanoscale Analysis of London Pollutant Particles and their Interaction with Airway Epithelial Cells

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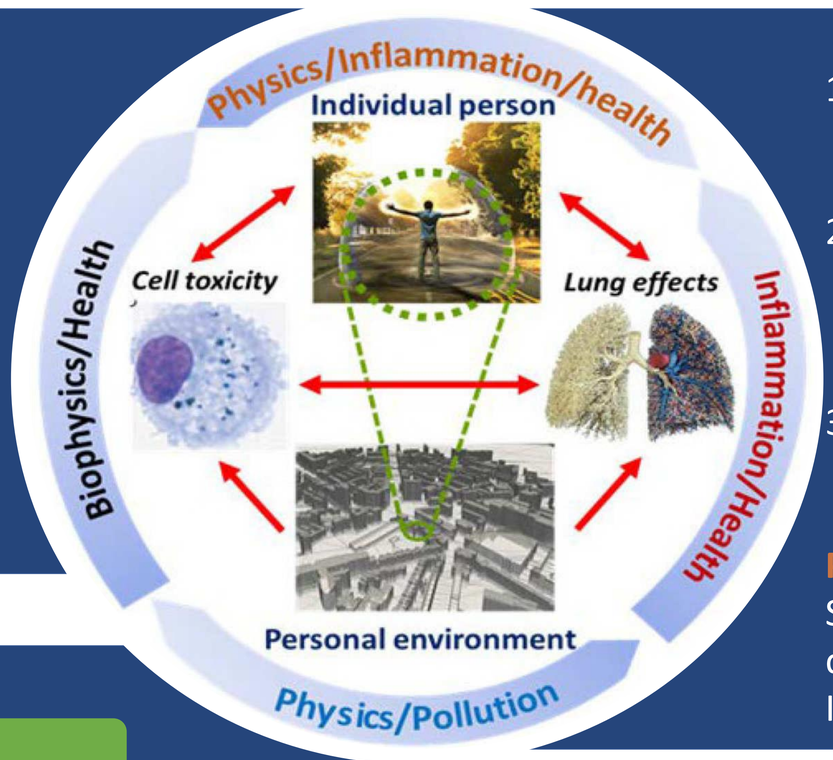
INHALE

UKRI Engineering and Physical Sciences Research Council

Motivation

Statement of the Problem:

- Exposure to respirable air pollution leads to 9 million excess deaths each year.
- The contribution of $PM_{0.1}$ to this figure is unknown, as is the composition and differential toxicity of PM constituents.
- Current air quality guidance only limits mass fractions of total PM_{10} and $PM_{2.5}$.



Objectives

1. To measure the sizes, size distributions and chemistries of $PM_{2.5}$ PM_1 & $PM_{0.1}$ at different sites around London.
2. To relate intracellular $PM_{2.5}$ and $PM_{0.1}$ size distribution, chemistry and location to altered metabolism of organelles in nasal epithelial cells.
3. To determine biochemical response of nasal epithelial cells from INHALE cohort.

Placement:
Statistical and machine learning approaches to develop a personal predictive toxicity profile for INHALE subjects.

Research Stages

1. Capture and Monitoring
2. Materials Characterisation / Compositional analysis
3. Respiratory Toxicology
4. Machine Learning for Personal Toxicity Profile

Stage 1

1. Pair online time-resolved PM **size distribution data** with
2. Offline gravimetric analysis (filter weight) of PM **mass concentration**
   - using electrical low-pressure and cascade impactors respectively

Table 1: Explanation of impactor selection for ultrafine particle collection

a **Type of microenvironment** (concentration; μgm^{-3})	b **Instrument** (Flow rate, LPM)	c **Mass extracted** ($\mu gmin^{-1}$)	d **Time for physicochemical assessment** (hrs)	e **Time for toxicity assessment** (hrs)
		= (b × (60/1000) × a/(60))	**(100 µg of mass needed)** (d) = 100/(a × b × (60/1000))	**(1000 µg of mass needed)** (e) = 1000/(a × b × (60/1000))
Roadside (3.2 ± 2.2) Parks (1.6 ± 0.9) Indoors (4.1 ± 3.5) Traffic intersections (5.6 ± 4.1) Green infrastructure roadside (behind vegetation) (1.0 ± 0.4)	Harvard Compact Cascade impactor (HCCI) (30 LPM)	0.1	17.4	173.6

Stage 2

Choosing the right technique:

- Destructive vs non-destructive
- Detection limit
  - Bulk/micro/nano-scale
- Quantity required for operation
- Target material / properties

Table 2: Workflow and available techniques for PM characterisation

Metal Content		
Technique	Used For	Destructive/Processed
TEM & SEM	Imaging (down to individual particles), Agglomeration State, Morphology	Processed
↳ with EDX/EELS	Elemental Composition, map metal valence to predict oxidative potential	
↳ with XRD/e^-D	Crystallinity	
ICP-MS	Bulk Analysis of Trace metal content	Destructive
Volatile Organic Compounds		
Technique	Used For	Destructive/Processed
GC-MS	Identification of VOC's/PHC's/PAH's	Destructive
GC-C-IRMS	Isotopologue distribution of VOCs/PAHs	Destructive

Abbreviations:
TEM/SEM: Transmission/Scanning Electron Microscopy
EDX: Energy Dispersive X-ray Spectroscopy
EELS: Electron Energy Loss Spectroscopy
e^-/XRD: electron/X-ray Diffraction
ICP-MS: Inductively Coupled Plasma-Mass Spectrometry
GC-MS: Gas Chromatography-Mass Spectrometry
GC-C-IRMS: Gas Chromatography-Combustion-Isotope Ratio Mass Spectrometry

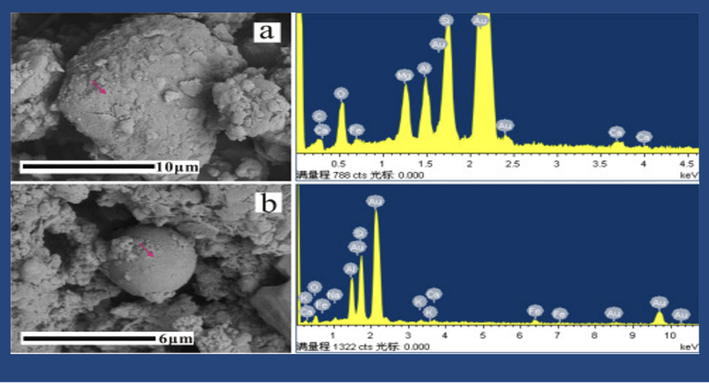


Figure 5: Representative of imaging and data acquisition from SEM-EDX chemical mapping of elemental composition

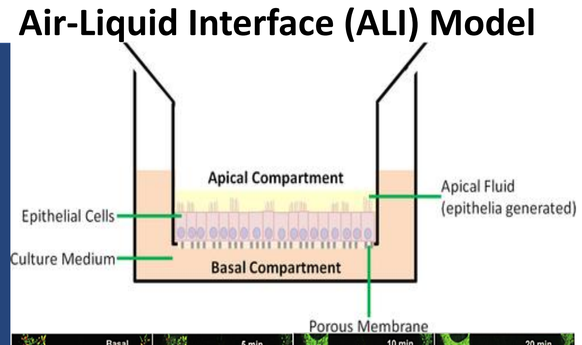
Stage 3

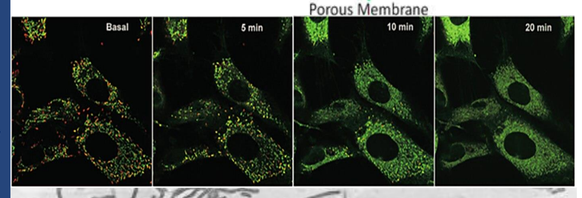
Cells exposed to $PM_{2.5}$ and $PM_{0.1}$:
- Nasal Epithelial (INHALE subjects)

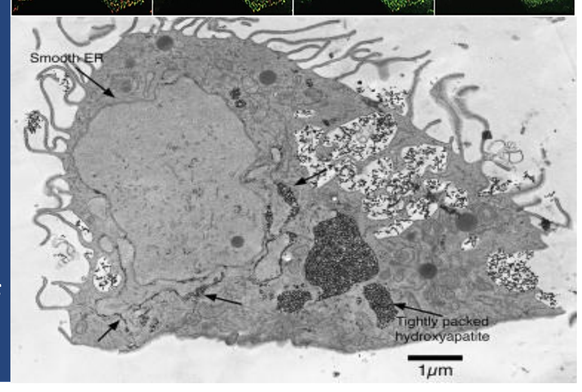
Toxicological Assays
- ROS: CellRox dye
- Mitochondrial ROS: MitoSOX
- Membrane potential: JC-1
- ELISA: detection of pro-inflammatory markers
  e.g. IL-6/8, alarmins IL-25/33/TSLP

Intracellular compartmentalisation:
- TEM: imaging
- SEM-EDX: chemical mapping
- ICP-MS: uptake; metal content of intra/extra-cellular PM

Air-Liquid Interface (ALI) Model



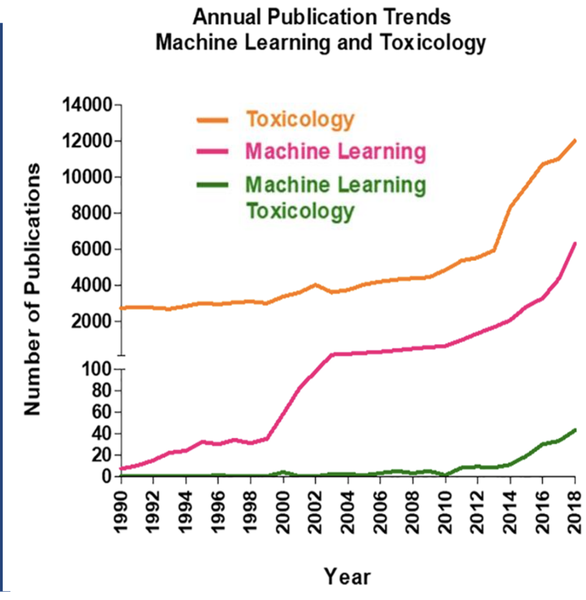




Stage 4

Question:
- How to relate material properties and composition of PM to cellular toxicity and clinical symptoms?

End goal:
- **Predictive toxicity index** for subject exposure to each fraction and component of air pollution



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