Interaction of SARS – CoV2 and Influenza Viruses with Particulate Matter Air Pollution

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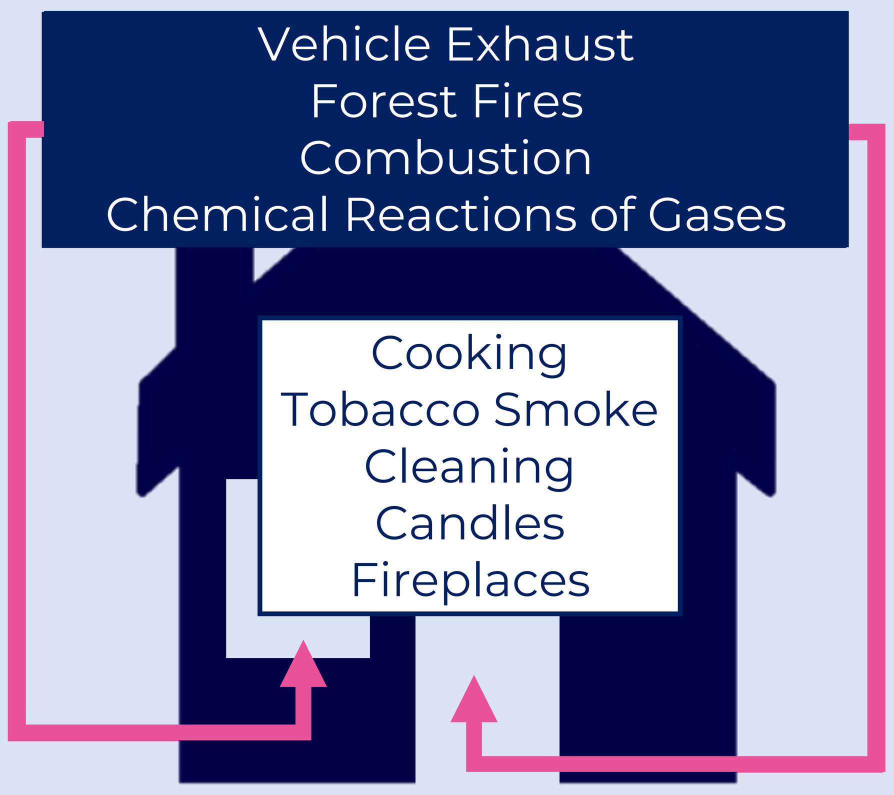
There is evidence of higher transmission rates and worsening of disease outcomes for viral infection in more heavily polluted areas[1]. We hypothesise that fine and ultrafine Particulate Matter (PM) acts as a vector for viruses, which increases their infectivity and boosts the cellular inflammatory response, with varying PM chemistries triggering different inhibitory or protective immune responses.

1. Background

Indoor Ambient PM

With people spending ~80% of time indoors[2], **viral transmission is more likely to occur inside.** But indoor PM activity is poorly characterised.



- Up to 95% of indoor PM can originate outdoors, so indoor PM composition and number concentration is fluid[3].
- PM2.5 in the home >65% of WHO guidelines[3]. This is likely to increase in polluted environments.

INHALE Project: London Underground

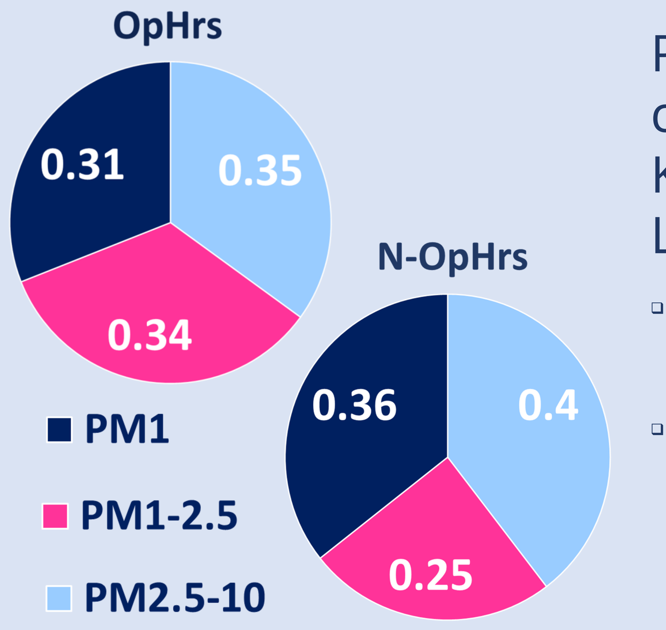


Figure. 1. Particle size fractions between operating and non-operating hours[4]

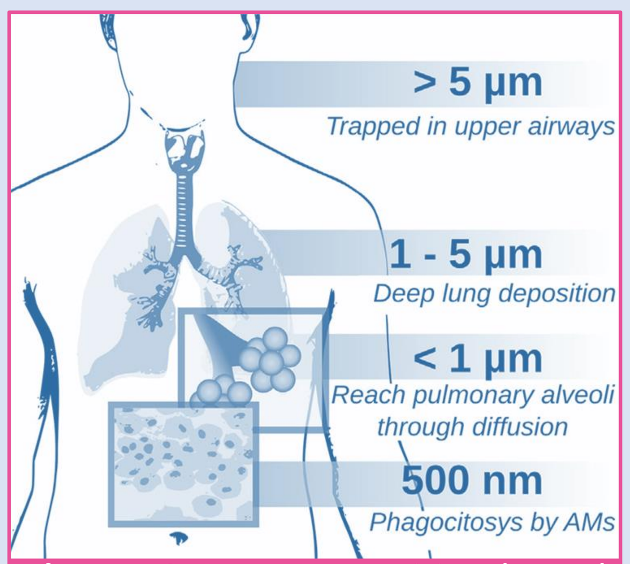


Figure. 2. Lung Deposition based on particle size [5]

PM size and chemical characteristics from South Kensington tube station in London[4] :

- PM2.5 (<2.5um) increased during operating hours
- **Alveolar respiratory dose deposition (mass) was dominated by fine and ultrafine PM**. Course PM mainly deposited in extra thoracic region (Fig. 2).
- **Particles reaching the deep lung are difficult to clear** and more likely to be internalised to cells or penetrate the bloodstream.
- **High Fe** atomic percentage – Redox active → toxicity

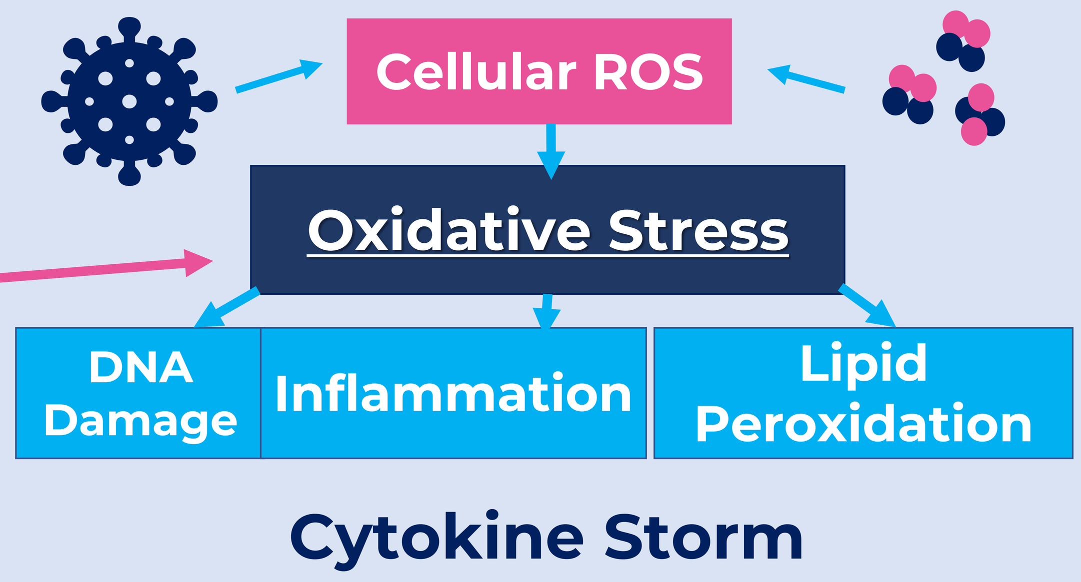
Clearly, potentially high levels of harmful metal traces can reach the deep lung during commuter times.

How Might PM Affect Viral Infection?

Virus Survival: Evidence that influenza can be deactivated by diesel emission particles[6]

Viral Cell Entry: PM known to upregulate expression of SARS-CoV-2 receptor, ACE-2. PM may also inhibit protective proteins in lung secretions[7].

Inflammatory Response: Persistent inflammation from chronic PM exposure, weaken immune response to viral infection. Overstimulation of immune response may occur through reactive oxygen species (ROS) and oxidative stress



2. Statement of The Problem

- Direct visual evidence of interactions between virus and PM is yet to be demonstrated, as is the cellular inflammatory response to virus and PM acting together.
- The effects of specific PM chemical components on viral infectivity could be delineated.

3. Objectives

- To determine whether PM effects viral cell entry and intracellular trafficking
- To visualise virus and PM interactions within lung secretions
- To determine how PM affects viral cell entry and cellular inflammation in *in vitro* cell culture

4. Methodology

1. **Transmission Electron Microscopy (TEM)** will be used to visualise virus and PM localisation within pre-prepared samples of **VeroE2 cells exposed to SARS-CoV-2 and London Underground PM**.
2. **PM** (from INHALE project) will be mixed with surrogate virus, **Psuedovirus, in a model of Airway Surface Liquid** to look for interactions
    - Developing and adapting new ***in situ* Liquid TEM** protocols (Fig.3) to image the mixtures of virus and PM in these media **real time**
3. Using *in vitro* cell culture techniques, **VeroE2 cells will be exposed to both PM and Pseudovirus** to measure:
    - **Virus/PM localisation and intracellular trafficking** (TEM)
    - **Cell death** (flow cytometry, plaque assay)
    - **Biomarkers of oxidative stress and inflammation** (Immunofluorescence, Reverse Transcription Polymerase Chain Reaction)

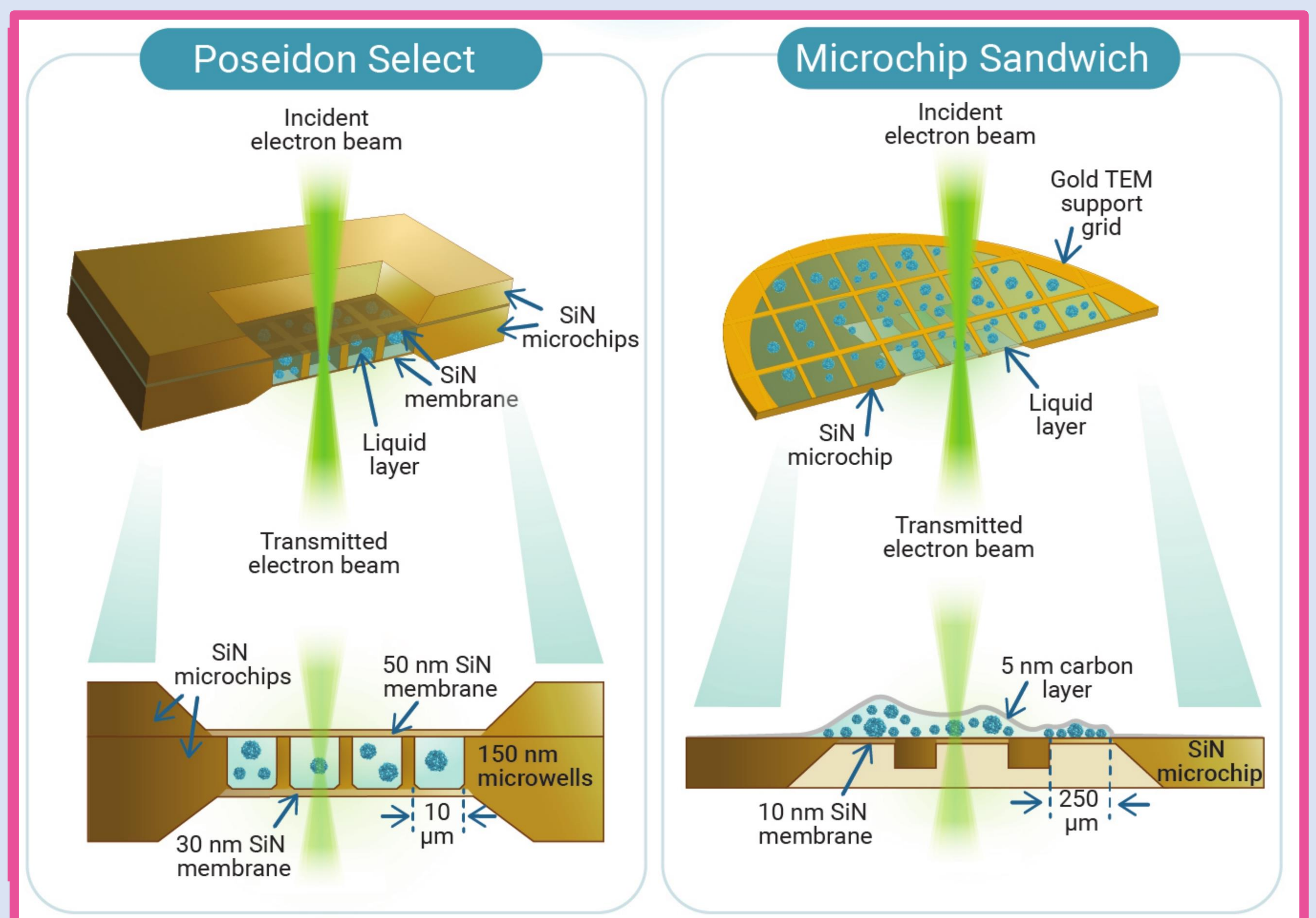


Figure 3. Liquid TEM techniques. From [8]

5. Significance

- The outcomes will provide guidance around which polluted microenvironments are potentially most unsafe for infection
- Could shed light on new therapeutic interventions.

6. Responsible Innovation

- What research avenues should future work follow?
- How can the outcomes of these become entangled politically?

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