A physiological circulation-mimicking microdevice to study protein corona formation on nano-pollutants

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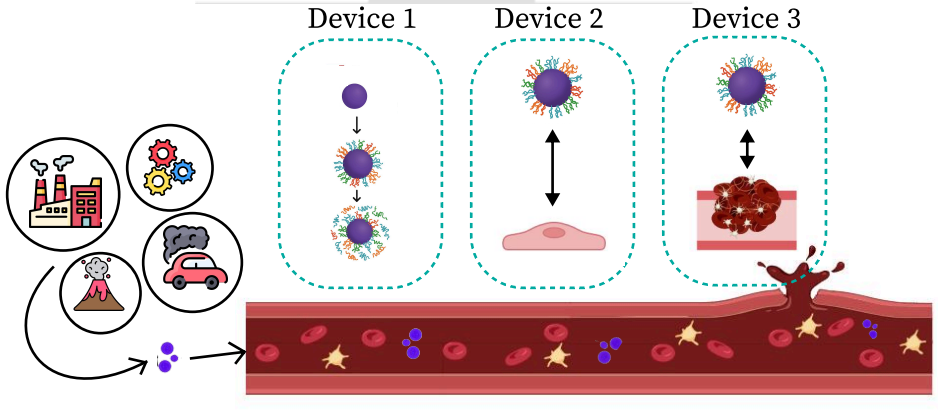
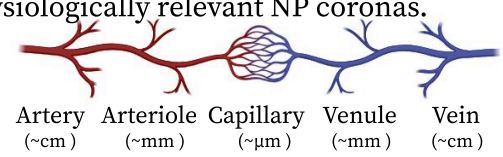
Introduction

Airborne nanopollutants (NPs) emitted by combustion processes or industrial activities, are increasingly recognized for their potential impact on human health [1-2]. Due to their small size and high surface reactivity, these NPs can translocate from the lungs into the bloodstream [2]. Once in biological fluids, a **protein corona** forms, alters their surface properties and governs interactions with the **vascular endothelium** and **haemostasis mechanisms**. The biological effects of NPs remain elusive due to the complexity of the protein corona and the lack of standardized models. To address these challenges, **a microphysiological platform is being developed** to form NPs coronas under flow, monitor endothelial responses, and assess effects on primary haemostasis.

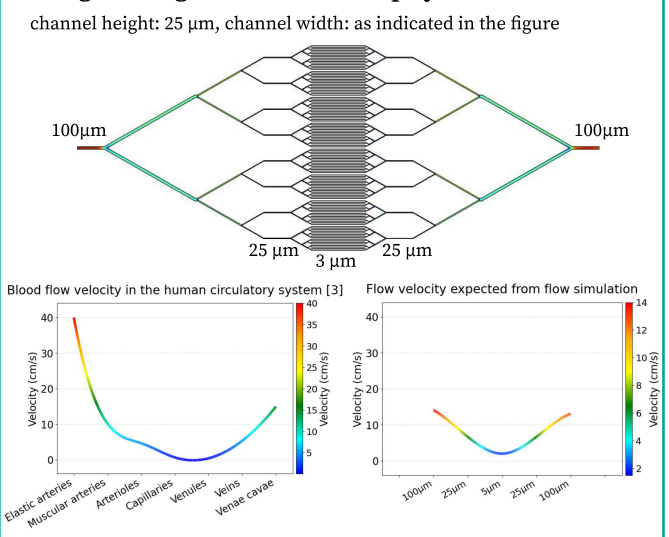


Device 1: Physiologically relevant circulation

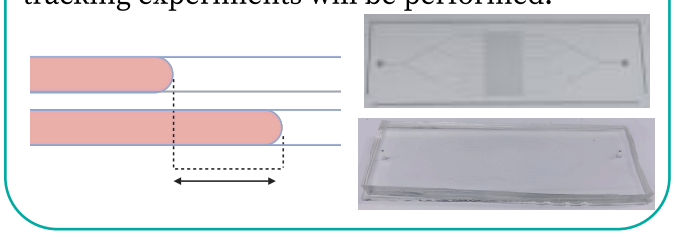
Purpose:
Simulate the human circulatory system to form physiologically relevant NP coronas.



Design and Simulations:
Validation of flow velocities in the first device design using COMSOL multiphysics.



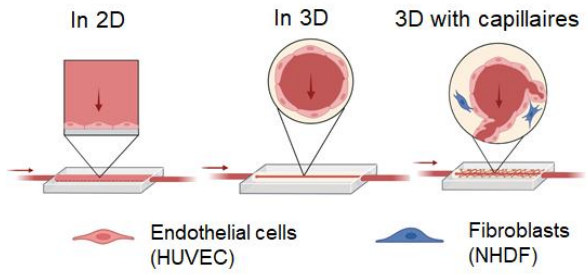
Device Characterization:
To verify whether the velocity profiles in the device correspond to those calculated, front tracking experiments will be performed.



Device 2: Endothelium-on-Chip

Purpose:
Investigate endothelial responses to exposure of NPs with protein corona.

Design:
A microfluidic device lined with endothelial cells, developed in 3 levels of complexity:

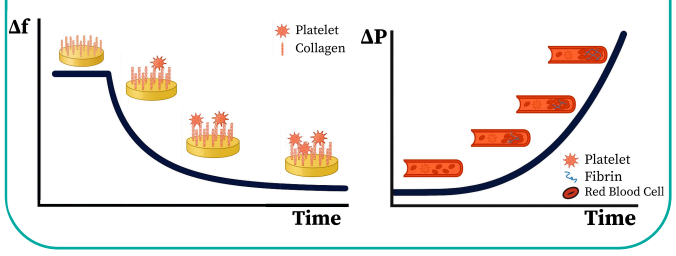


Planned Analysis:
Different tests to indicate endothelial response to NPs with protein corona: Viability, barrier integrity, inflammation, cytotoxicity.

Device 3: Heamostasis-on-Chip

Purpose:
Evaluate the impact of NPs with protein corona on heamostasis.

Design:
Based on previous work from the Interreg project BLOODE and ANR project GHOST.

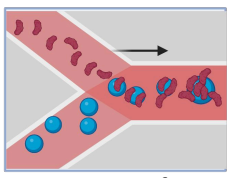


Method development: Protein Corona Formation

Choice of NPs:
There are many different types of airbone nanopollutants originating from different sources. In this project the focus will be on:

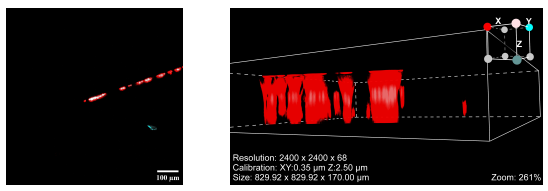
- Silica (SiO2) NPs
- Carbon based NPs
- Metal oxide NPs

Confocal Microscopy:
The observation of a single protein on a NP can be performed using confocal microscopy.

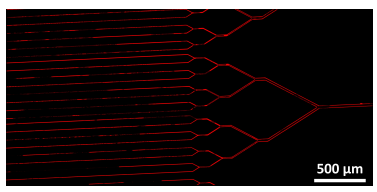


- 10µm blue fluorescent silica particles
- Red fluorescent Albumin

When imaging for multiple heights, the distribution of protein and particle is obtained.



The observation can also be performed for **Device 1**. Here 1µm red fluorescent MF particles were observed.



Next steps:

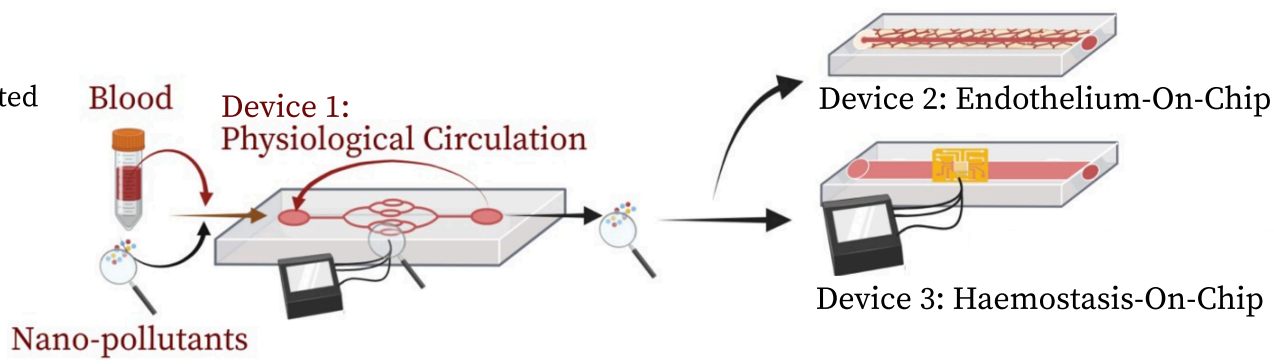
- Continue method development for complex media
- Optimization to avoid channel blocking and particle aggregation.

Integration of components

The three modules —protein corona formation, endothelium-on-chip, and haemostasis— will be integrated to simulate the biological interactions of NPs.

With incorporation of **on-flow sensing** of:

- Particle Size
- Zeta Potential
- pH



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References
[1] European Environment Agency (n.d.).
[2] H.-S. Kwon, M. H. Ryu, and C. Carlsten, Exp. Mol. Med. 52, 318 (2020).
[3] J. G. Betts et al., (2022).

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