Towards Continuous Cytokine Monitoring in Organ-based Platforms

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Introduction

Cytokines are cell signaling molecules that can give an indication of cell status. One cytokine of interest is **Interleukin-6 (IL6)**, a small protein (22 kDa), with both pro- and anti-inflammatory effects.

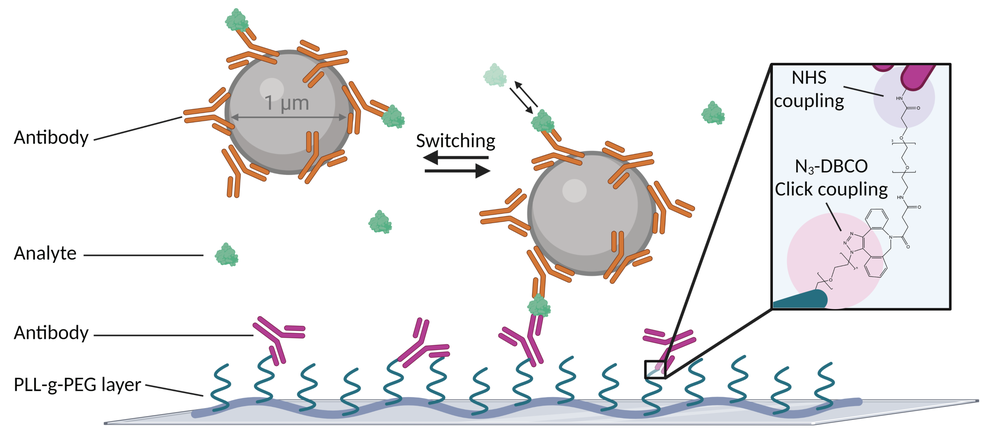
Continuous monitoring of cytokines in organ platforms can give insight in

- Organ platform status
- Effect of cell stimulation
- Drug screening

Biosensing by Particle Motion (BPM) is a sensor platform which can be used for continuous monitoring.

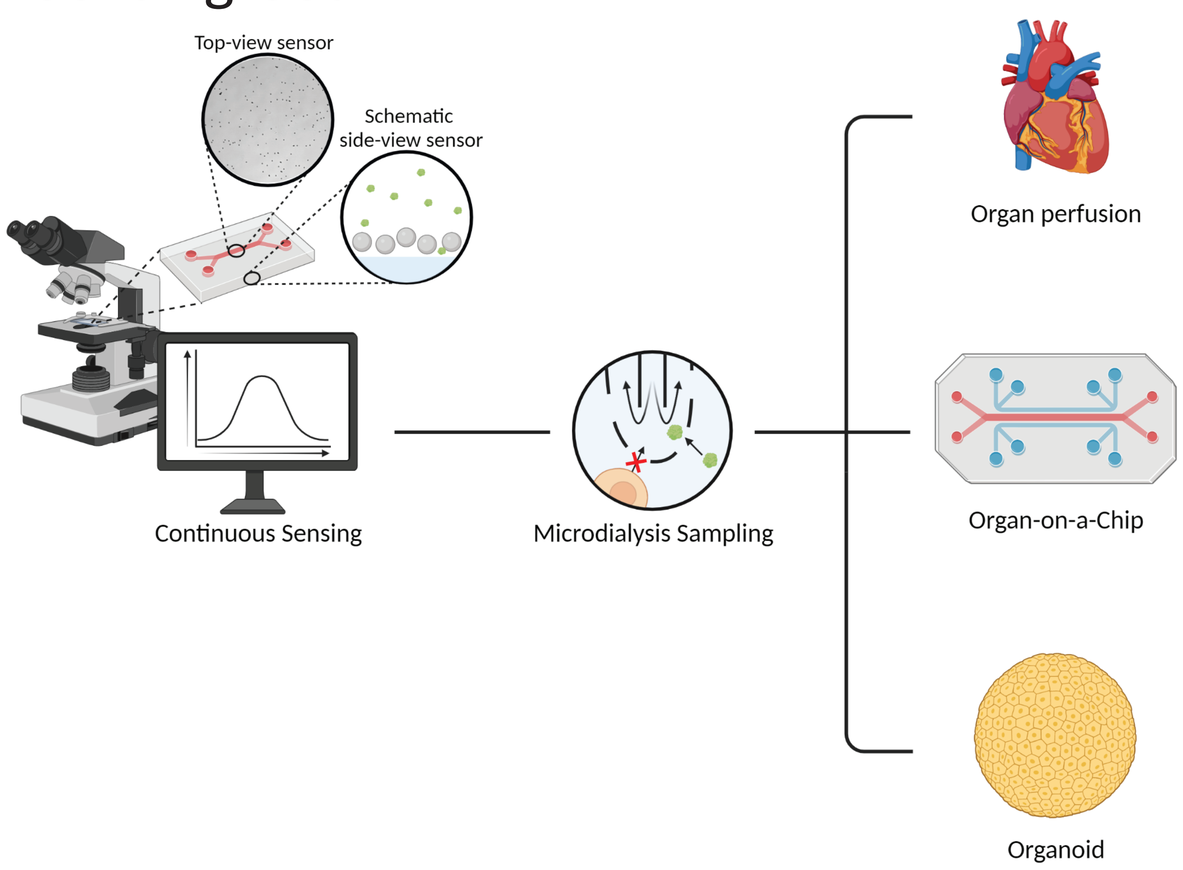
Here we describe the development of an interleukin-6 biosensor to achieve continuous sensing in organ-based platforms.

Biosensing by Particle Motion (BPM)



Scheme 1 | Overview of BPM sensor for Interleukin-6. Particles show free brownian motion (left particle) or confined brownian motion (right particle). The motion of thousands of particles are tracked simmultaniously over time via video microscopy.

Sensing Goal



Scheme 2 | Continuous sensing in various organ-based platforms by microdialysis sampling.

Interleukin-6 Sensing

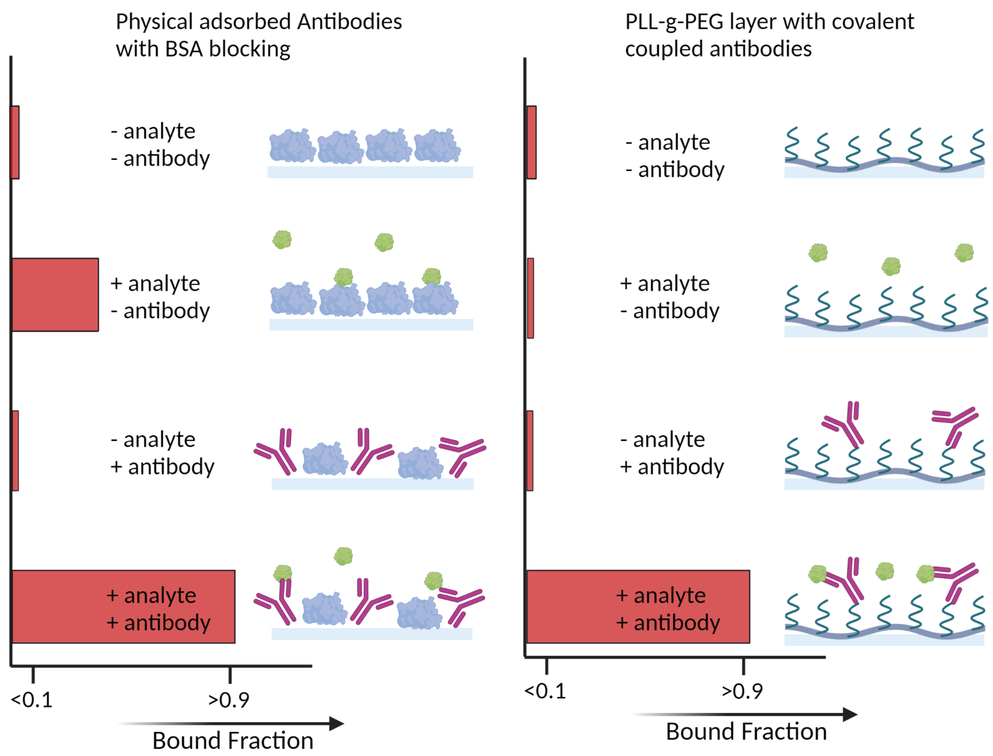


Figure 3| Fraction of bound particles for varying surface functionalizations for the IL-6 assay when using physical adsorbed antibodies and BSA blocking (left) and antibodies bound to the low-fouling PLL-g-PEG layer (right).

- PLL-g-PEG shows very low non-specific background binding. IL-6 binds to BSA (not all data shown), which influences assay signal.

Measurement Principle

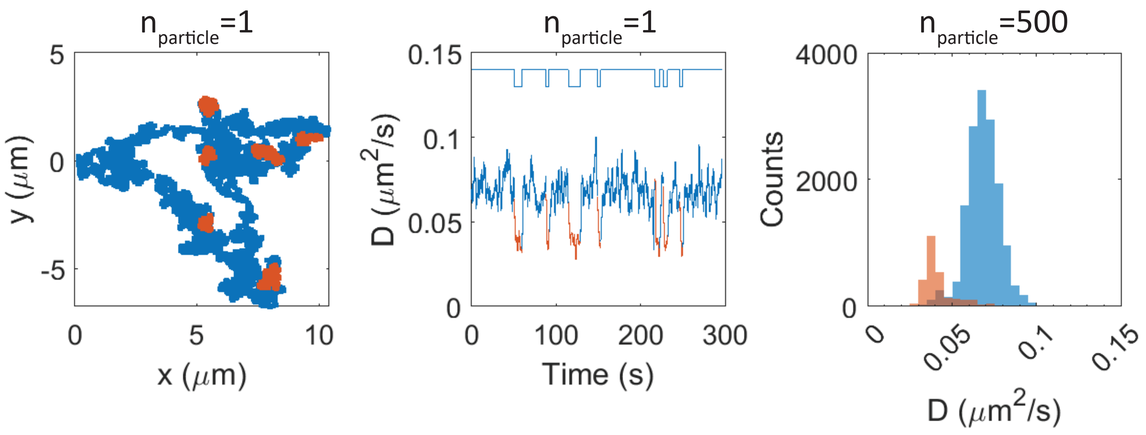


Figure 1 | Example of signal read-out for particles. The first graph shows the **trajectory of a single particle in the xy plane**. The orange traces indicate confined brownian motion and the blue traces indicate free brownian motion. The **effective diffusivity (D) of a single particle over time**, shown in the second graph, is derived from the particle trajectory. Differentiation between free (blue) and confined (orange) brownian motion is preformed by tresholding based on diffusivity of the particles. A **distribution of D from 500 particles** is shown in the right image. Orange indicates confined brownian motion, and thus stuck particles. Blue indicates free brownian motion, and thus freely moving particles [1].

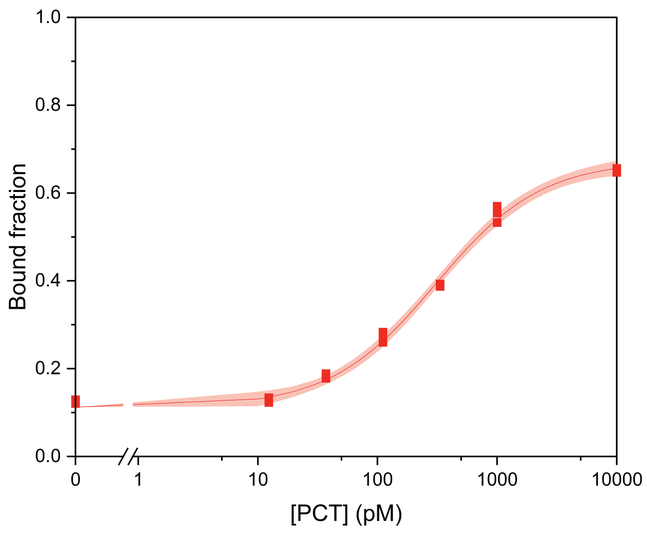


Figure 2 | Typical response optained from measuring increasing analyte concentrations in a sandwich BPM assay. Data shown for Procalcitonin assay.

- The sensor signal increases with increasing analyte concentration, resulting in an S-shaped response curve.
- The sensor shows sensitivity in the picomolar range.

Outlook

IL-6 assay on PLL-g-PEG surface coating gives low background. Reversibility of the assay needs to be evaluated. This will be executed by

- Comparing different particle functionalizations
- Evaluate alternative binders

The sensor will be tested in organ platforms

- Development of microdialysis probe for sampling of cytokines
- Sensor performance in different matrices (perfusate, hydrogel, etc.)
- Sensor performance in organ platforms (Organ-on-a-chip, transplanation heart, etc.)

Molecular Biosensing (MBx)
Department of Biomedical Engineering & Department of Applied Physics

[1] Buskermolen et al., Nature Communications (2022)

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Schemes were created using BioRender.com