MICROFLUIDIC DEVICE FOR THE DYNAMIC CHARACTERIZATION OF CELL ADHESION USING CELL ADHESION DOT ARRAYS (SCADA)

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INTRODUCTION

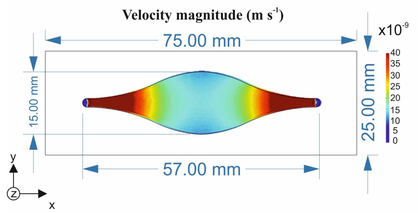
The use of **single cell arrays** to evaluate the degree of **affinity between a certain cell type and a given substance** provides a simple yet high-throughput tool for molecular and cellular biology as well as the development of biocompatible devices. A method to isolate cells is the generation of **cell adhesion spots with single cell size**, which is the basis of the **SCADA** technology. SCADA assays have proven to be useful for the characterization of integrin profiles and cell-biomaterial interactions[1]. Moreover, they have been used for cytotoxicity assays[2], confirming their versatility. This method has previously been exploited **on culture plates**. However, the handling and analysis of culture plates is time-consuming and leads to low time accuracy, therefore, it could greatly benefit from automation**. In this work, we present the integration of SCADA substrates within microfluidics to enable dynamic cell adhesion assays**.

EXPERIMENTAL

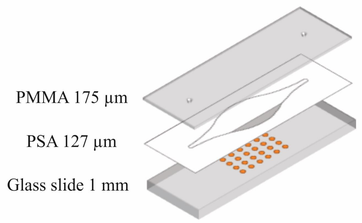
The **microfluidic chamber** was designed to render a homogeneous velocity of the cell suspension and promote adhesion to the patterned substrate. This was checked through **COMSOL multiphysiscs © simulation** of the flow in the device.

The bottom of the device (made of glass) was patterned by **Alvéole's PRIMO®** micropatterning device. The pattern consisted of **20 µm diameter dots** developed as "holes" in an adhesion-blocking layer of polyethylene glycol (PEG), hence revealing a base layer of laminin (LAM) or poly-L-lysin (PLL).

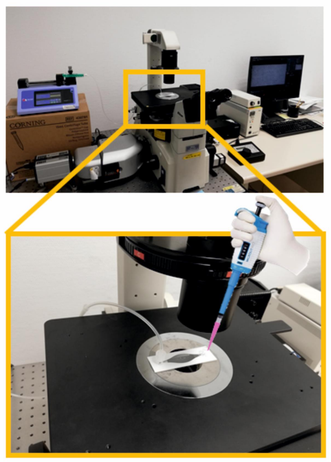
COMSOL simulation



Layer-by-layer device



Microfluidic and observation set-up



Holes of 20 µm were left with the base layer, **fibronectin (FN)** and BSA-TAMRA**.**

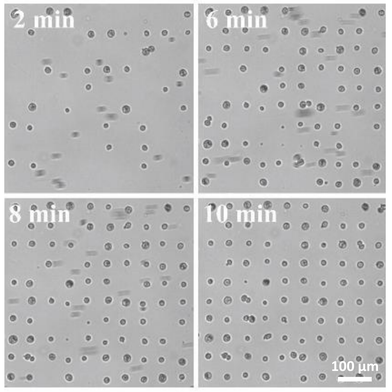
Hf-MSCs: 2 10^5 cells mL^{-1}
Flow rate: 50 µL min^{-1}.

Adhesion was monitored in real-time through **direct microscopic observation**.

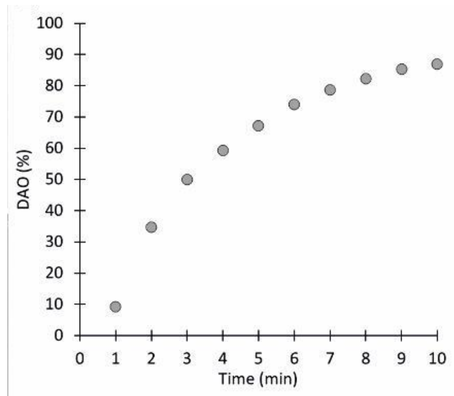
Quantification:
percentage of potential adhesion dots occupied by a cell.
Dot Array Occupancy or **DAO.**

RESULTS AND DISCUSSION

Scale bars: 100 µm



Brightfield images of the evolution of the single cell array after 2, 6, 8 and 10 min of flowing cells over the patterned substrate



Adhesion kinetics of hf-MSCs in the SCADA-on-chip device

CONCLUSIONS

SCADA assays into a microfluidic device (**SCADA-on-chip**) reduces the usage of materials, reagents and cells, and **decreases the assay time by a 6-fold**.
The dynamic monitoring of a single chamber in real-time drastically improves time resolution (which is only limited by the time resolution of the camera), directly enhancing the precision of our analysis.
SCADA-on-chip devices are useful tools to evaluate the degree of **affinity between a certain cell type and a given substance** in a very short time and using already-available equipment and analysis resources.

[1] Gonzalez-Pujana et al., *Sensors and Actuators B: Chemical*, 299, 126954, 2020.
[2] Garcia-Hernando et al., *Analytical Chemistry*, 92, 9658-9665, 2020.

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