A digital microfluidic-based electrochemical impedance spectroscopy for cell-based immunoassay in a dynamic mode

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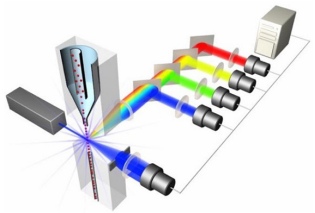
Abstract

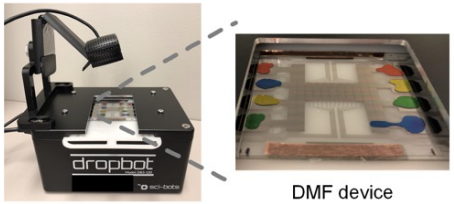
- The dynamic immune response to various diseases and therapies is a promising indicator of disease status and therapeutic effectiveness.
- Human peripheral blood mononuclear cell (PBMC), as a major player in the immune system, is an important index of a patient's immune function.
- Establishing a simple yet sensitive tool that can frequently assess the immune system during the course of disease and treatment can prompt the most effective treatment strategies.
- This study introduced an integrated system that includes an electrochemical impedance spectroscope (EIS)-based biosensor in a digital microfluidic (DMF) device, to quantify the PBMC abundance with minimally trained hands.

Our Method

Standard: Flow cytometry



Our method: Digital microfluidics (DMF)-based electrochemical impedance spectroscopy (EIS)



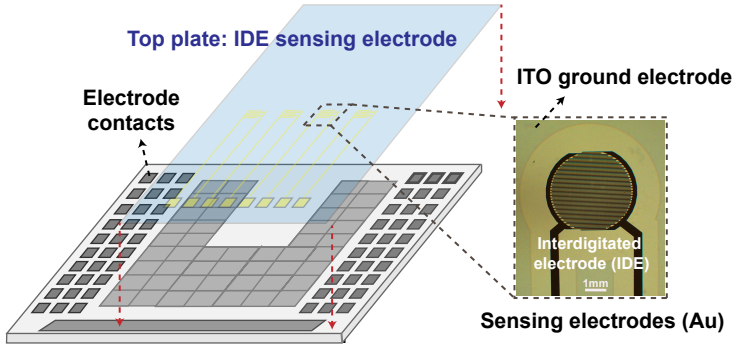
Dropbot system

DMF device

- √ Sensitive and reliable
- ✗ Relies on highly specialized and bulky equipment
- ✗ Tedious sample preparation
- ✗ Can hardly monitor on a regular basis

- √ Sensitive and simple
- √ Portable and cost-effective
- √ Minimal human intervention: automated and parallel operation
- √ Ideally for point-of-care (POC) testing

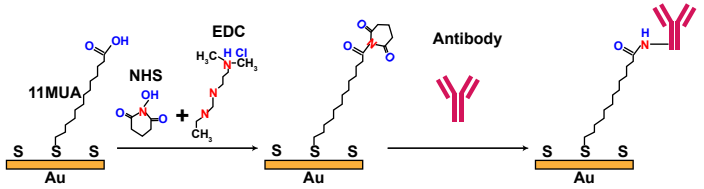
Layout of the integrated DMF device



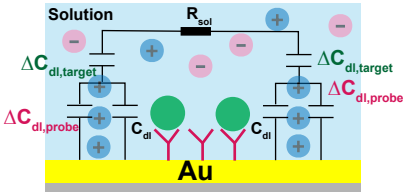
Bottom plate: actuation electrode array (Electrowetting-on-dielectric)

Results

Electrochemical impedance spectroscopy (EIS): label-free and real-time detection

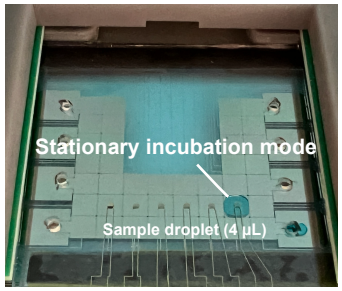


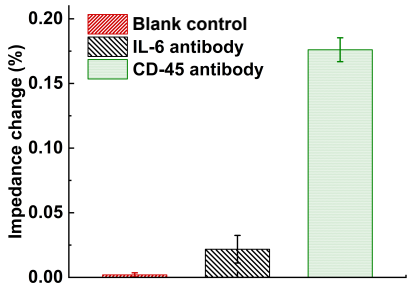
Thiol-carboxyl self-assembled monolayer (SAM)



Capacitance increase is **proportional to** the amount of target cells adsorbed on the surface

PBMC-immunoassay detection in a dynamic mode





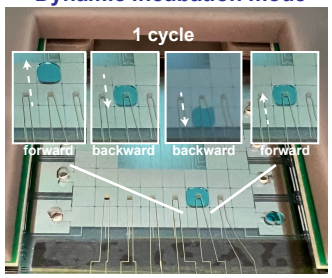
Impedance change (%)

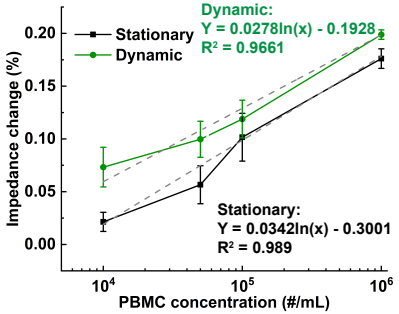
$$= \frac{Z_{cell} - Z_{base}}{Z_{base}} * 100$$

Specificity:

1. **Blank control: 0.19%**
2. **Non-specific binding: 2.2%**
3. **Target binding: 17.6%**

Dynamic incubation mode





Comparison of impedance increment (dynamic vs stationary)

PBMC (#/mL)	Impedance increment (%)
10^4	242.7%
$5*10^4$	64.4%
10^5	26.9%
10^6	12.9%

Conclusions

- **Low sample volume (4 μL)** and **rapid detection (20 min).**
- **Quantitative detection** of PBMC abudance in **dynamic incubation modes** showed **2.4-fold enhanced detection signal** and detected **as low as 10^4 PBMCs/mL**, approximately **two orders of magnitude less** than the biological relevant range.
- Overall, the integrated system presented the technical feasibility of detecting immune cells in a simple and sensitive manner.

Acknowledgements

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Reference: Zhang, Yuqian, and Yuguang Liu. 2022. "A Digital Microfluidic Device Integrated with Electrochemical Impedance Spectroscopy for Cell-Based Immunoassay" Biosensors 12, no. 5: 330.