PhD Report – 1st semester

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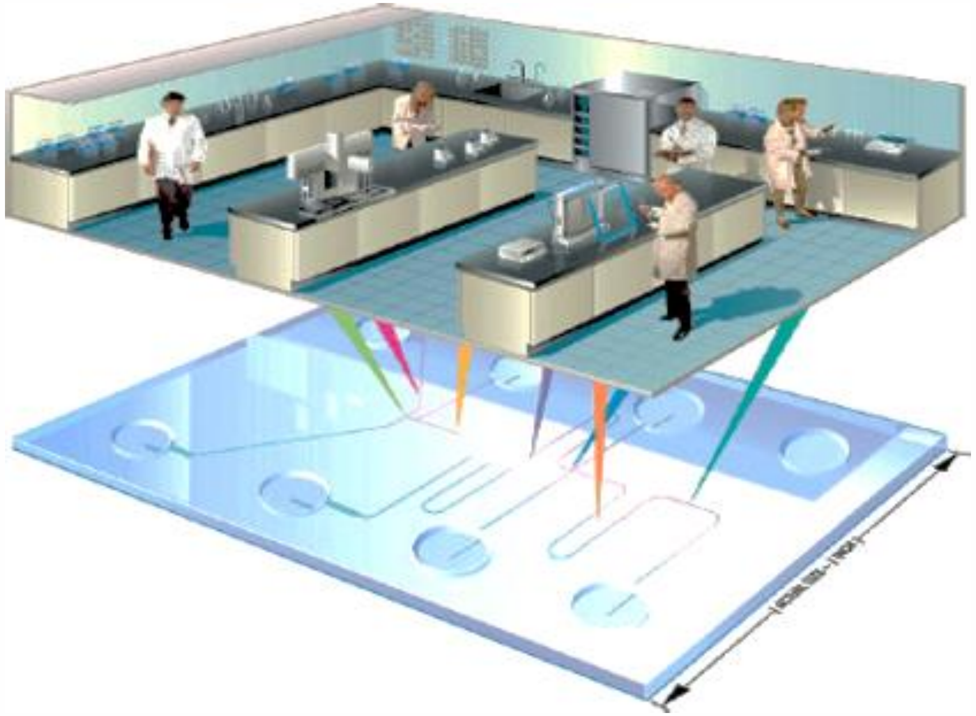
Introduction

- Microfluidics: precise control and manipulation of fluids on a micrometer scale
- Small Reynolds number: viscous forces, laminar flow
- Capillary flow, autonomous flow
- Advantages of size: portability, low consumption (sample, reagents)
- Lab-on-a-chip: miniature version of a complete laboratory
- Organ-on-a-chip: cell cultures, tissues on a microchip
- Generating chemical gradients
- Cell-trapping and behaviour monitoring
- Measurements with bacteria and antibiotics

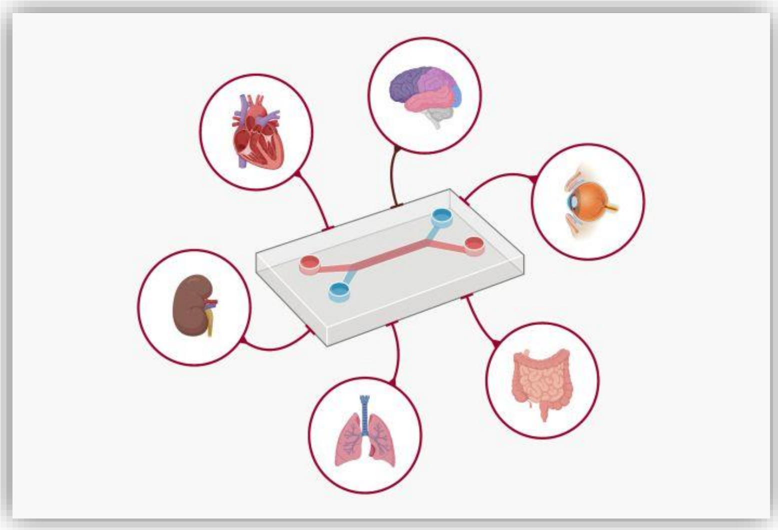
Goal: chemical gradient generation, cell-trapping, electrode integration, impedance spectroscopy based measurements, rapid antibiotic resistance measurements

Lab-on-a-chip

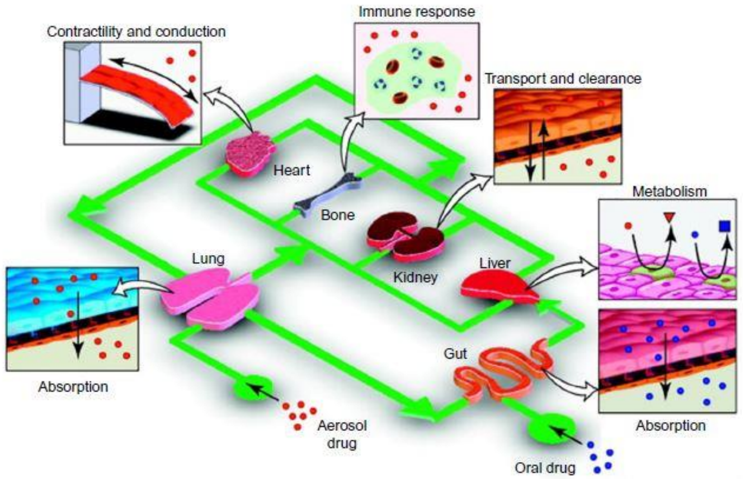


Polimer alapú mikrofluidikai eszközök technológiája, Holczer Eszter

Organ-on-a-chip



https://www.ufluidix.com/microfluidics-applications/organ-on-a-chip/



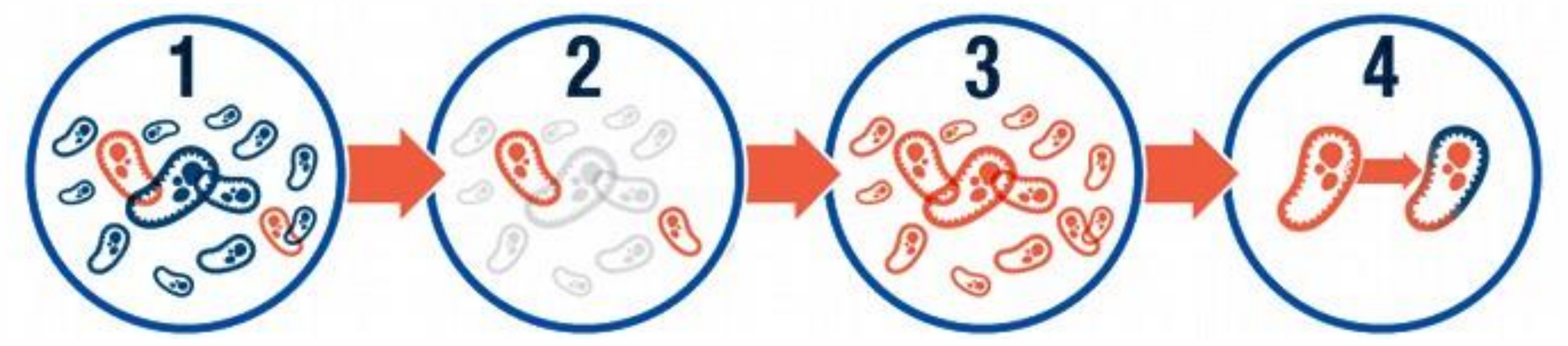
Lab-on-a-chip technology and microfluidics: Antonio Francesko, Vanessa F. Cardoso, Senentxu Lanceros Mendez, 2019

<u>Advantages</u>:
- Low consumption, reduced waste
- Point-of-care
- Fast, precise, controllable
- Low cost, disposable

<u>Advantages</u>:
- Reduce or replace animal testing
- Drug development and tests
- Cancer research

Antibiotic resistance

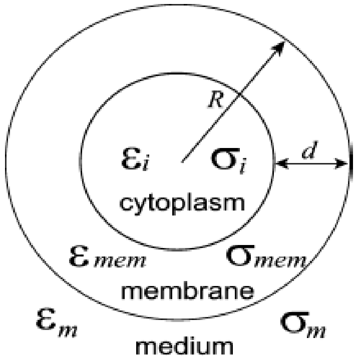
- Overuse of antibiotics
- Broad-spectrum antibiotics
- Multiresistant bacteria
- In need of fast and accurate diagnosis
- Antibiotic susceptibility testing (AST) is slow (16-20 h)
- Solution: microfluidic devices

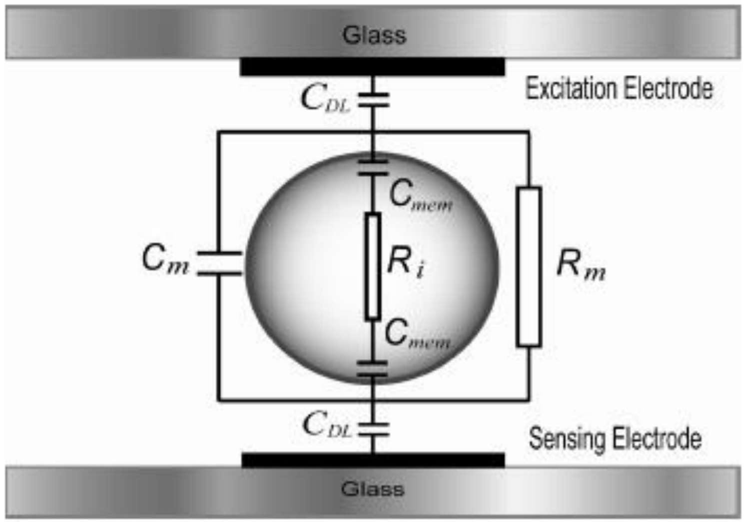


https://2019.igem.org/Team:CSU_Fort_Collins/Description

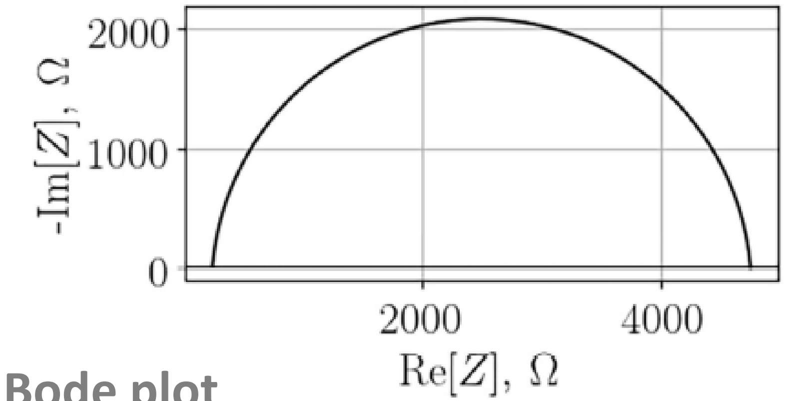
Impedance spectroscopy

$$Z(f) = \frac{V(f)}{I(f)} = Re(Z) + i \cdot Im(Z) = |Z|e^{i\varphi}$$

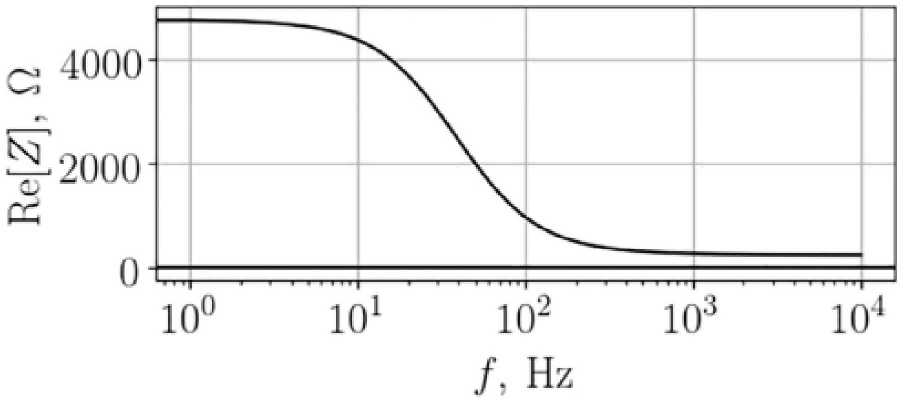


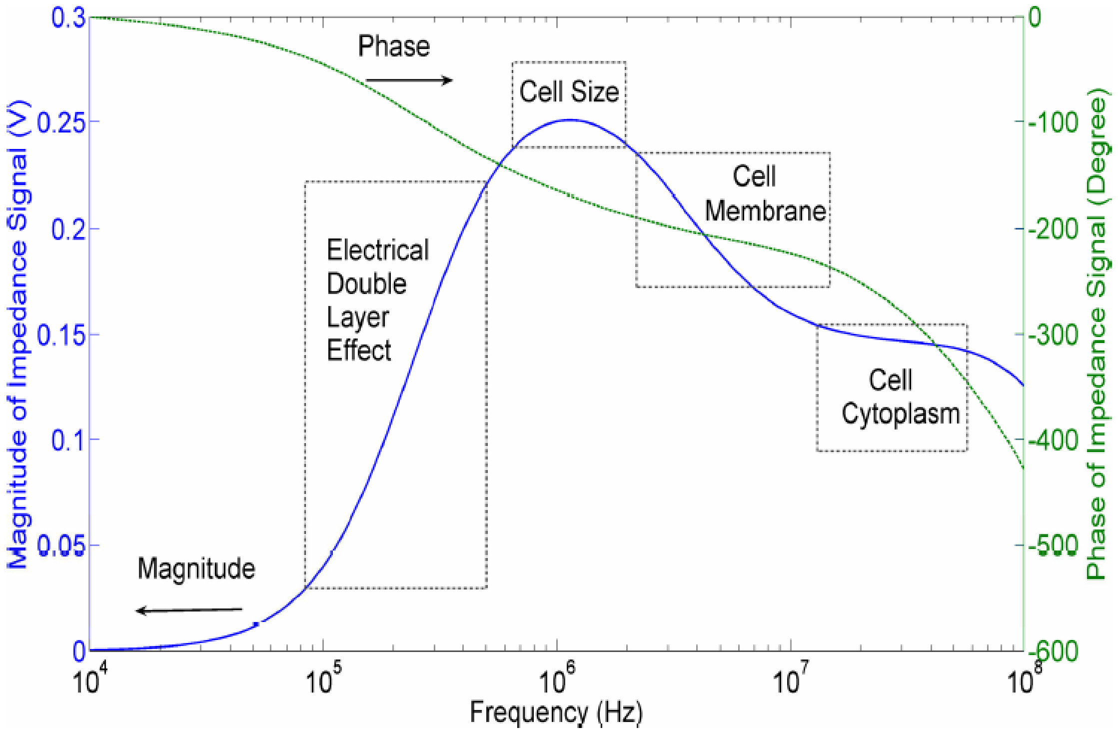


Nyquist plot



Bode plot





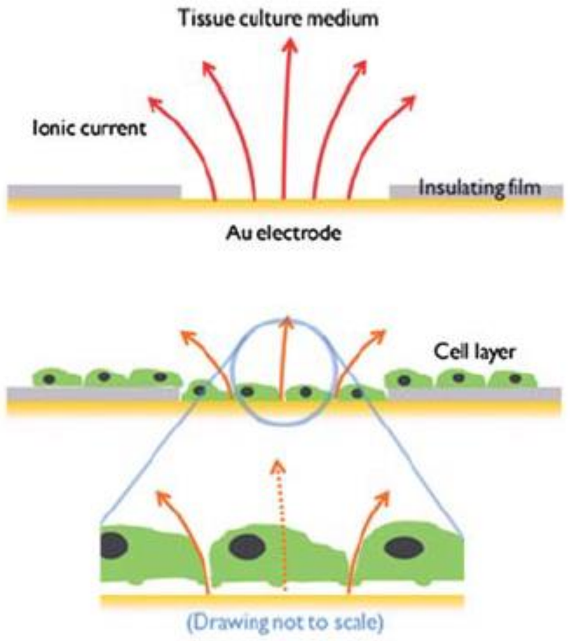
T. Gerasimenko et al. “Impedance spectroscopy as a tool for monitoring performance in 3D models of epithelial tissues,” Frontiers in Bioengineering and Biotechnology, vol. 7, 2020

T. Sun, N. G. Green, and H. Morgan, “Analytical and numerical modeling methods for impedance analysis of single cells on-chip,” Nano, vol. 03, no. 01, pp. 55–63, 2008

Impedance spectroscopy methods

Electric Cell-Substrate Impedance Sensing - ECIS

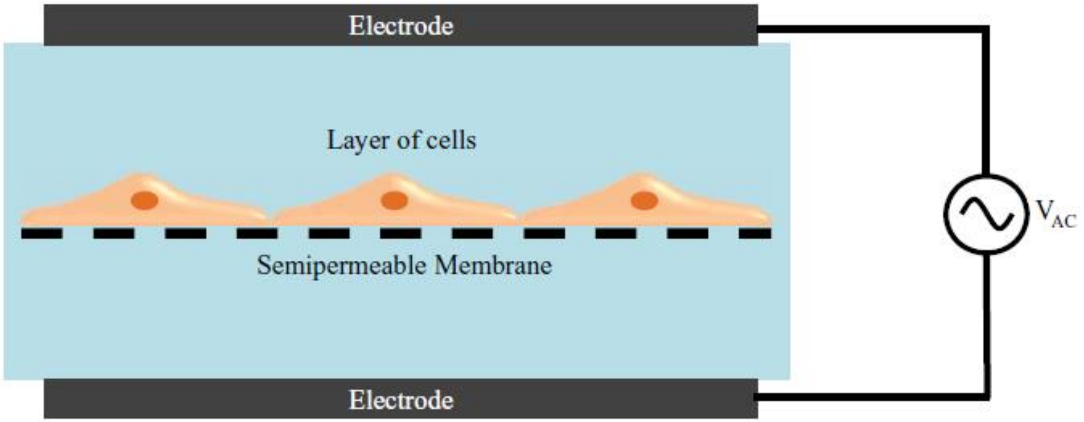
- Impedance changes when cells attach to electrode surface
- Changes due to motion, morphology
- Cell viability, toxicity, proliferation



J. Hong, et al. „Electrical cell-substrate impedance sensing as a non-invasive tool for cancer cell study," The Analyst, vol. 136, no. 2, pp. 237–245, 2010.

Transepithelial / Transendothelial Electrical Resistance - TEER

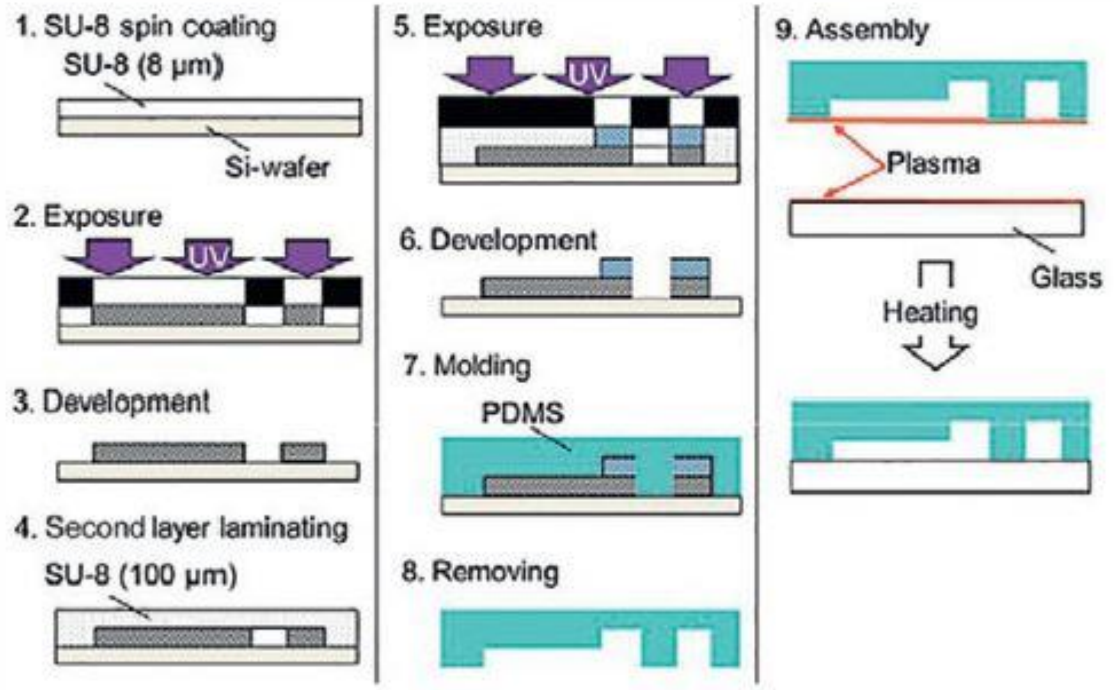
- Impedance across semi-permeable membrane
- Monolyaer formation, barrier integrity
- Permeability to chemical agents



B. Srinivasan et al. „TEER measurement techniques for in vitro barrier model systems," Journal of Laboratory Automation, vol. 20, no. 2, pp. 107–126, 2015.

Research

Method: Soft Lithography



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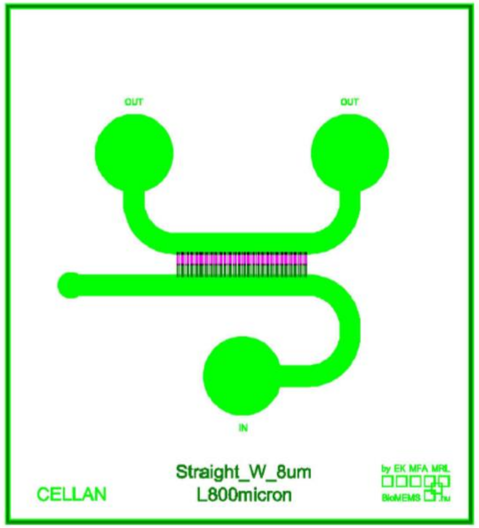
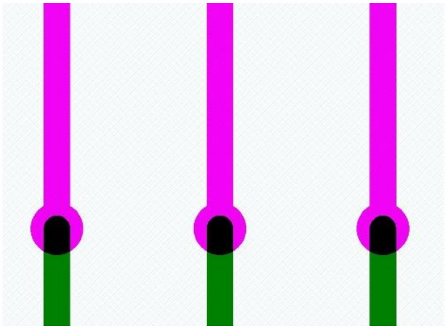
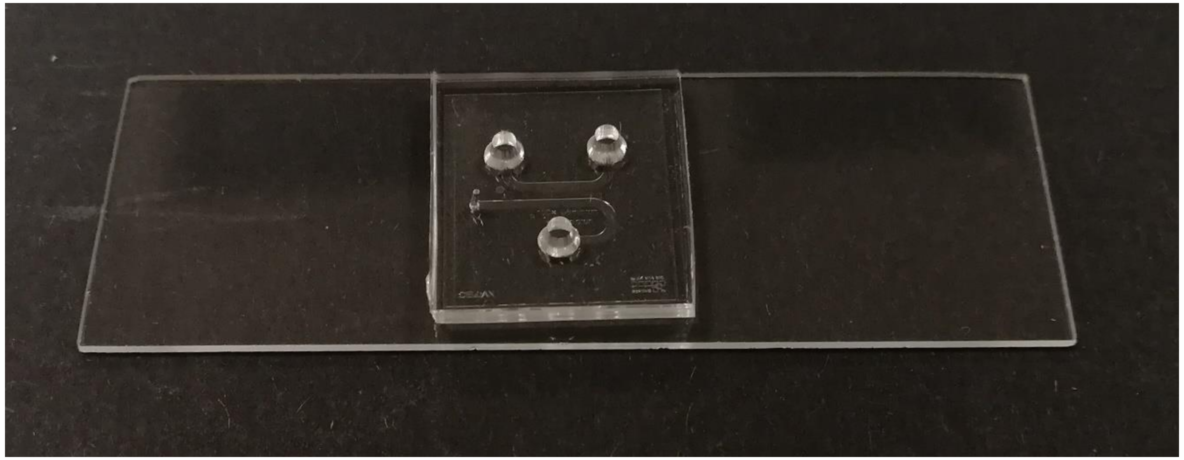
Antonio Francesko, Vanessa F. Cardoso, Senentxu Lanceros-Mendez, 2019

Chip Layout



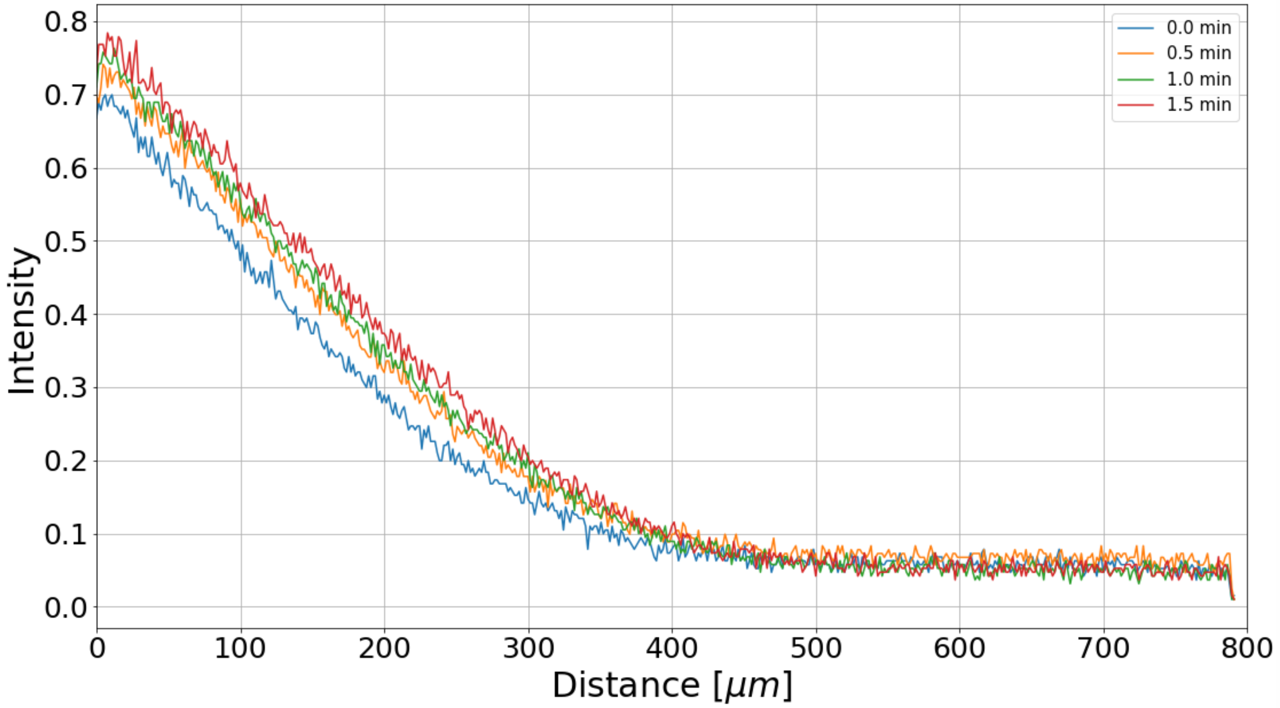
Channel height: ~45 µm
Vertical narrowing: 10 µm → 5 µm
5 µm → 10 µm





Research

Protein Diffusion: IgG

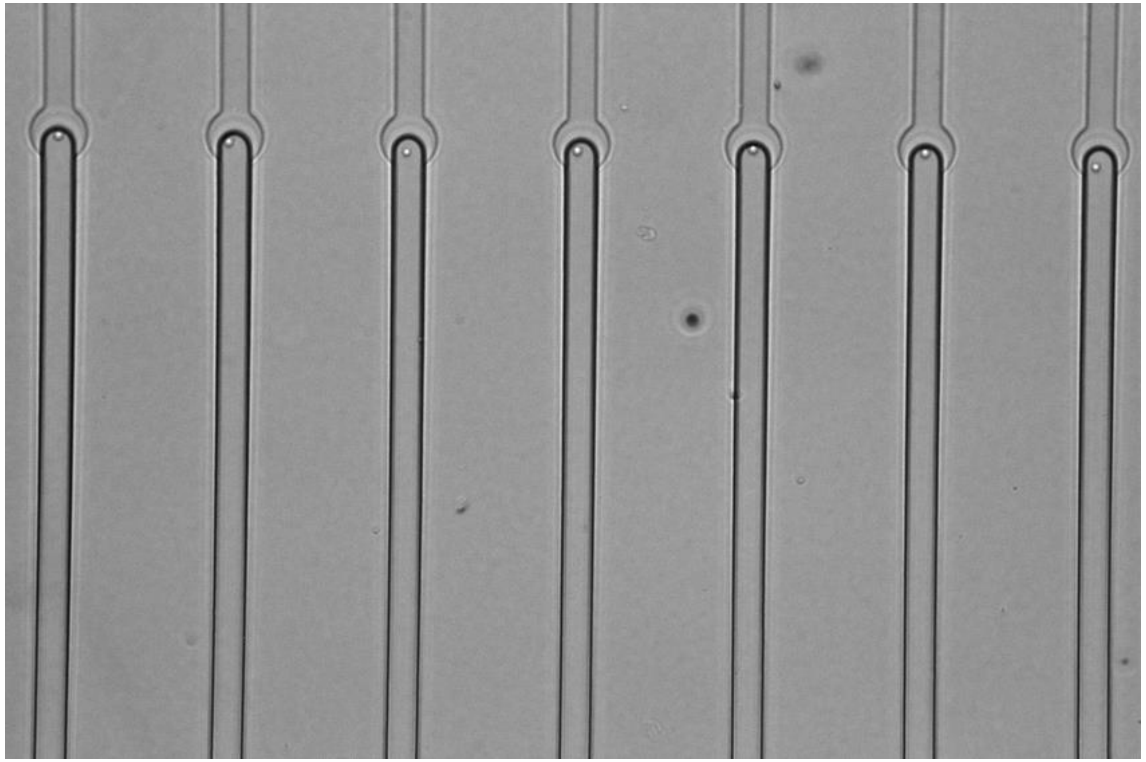


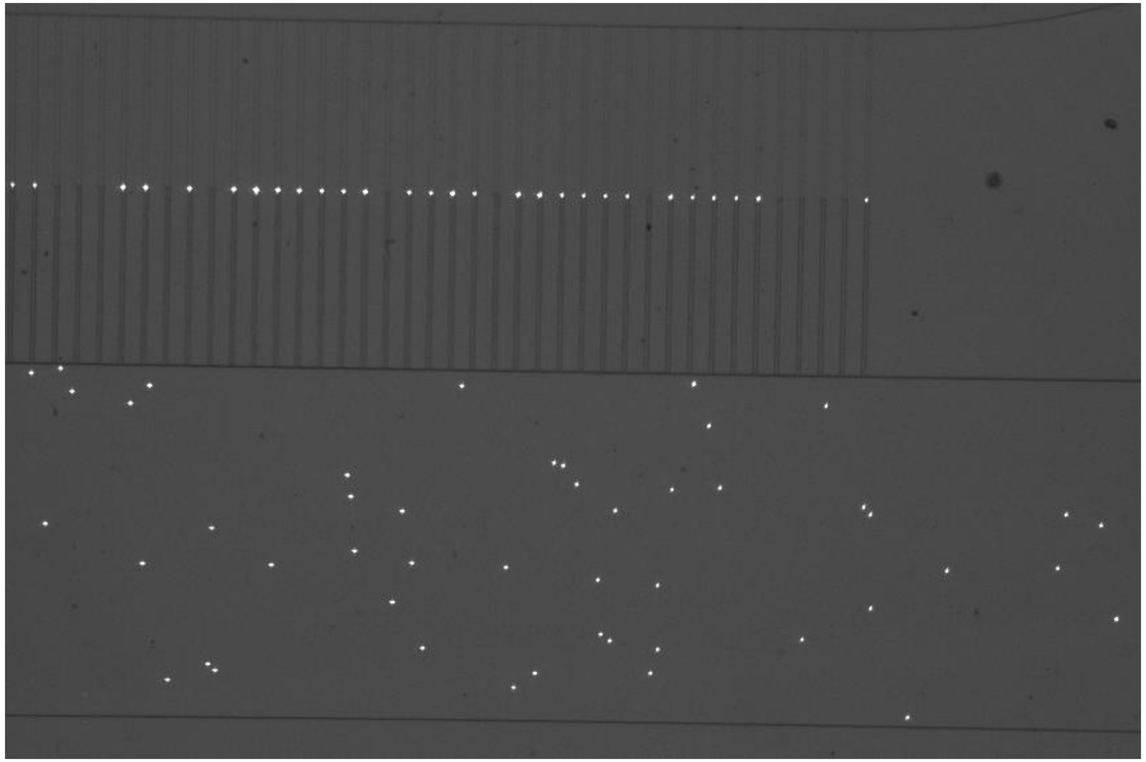
Diffusion coefficient from profile, fitting with a self-written custom Python program

Literature: D= ~50 µm^2/s Measurement: ~40/50/60 µm^2/s

Research

Cell trapping: Yeast, Fluorescent Nanoparticles



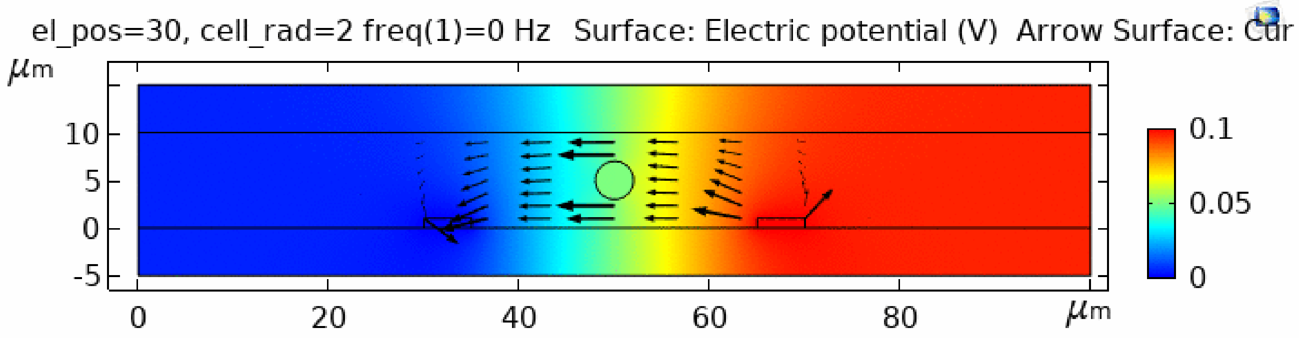


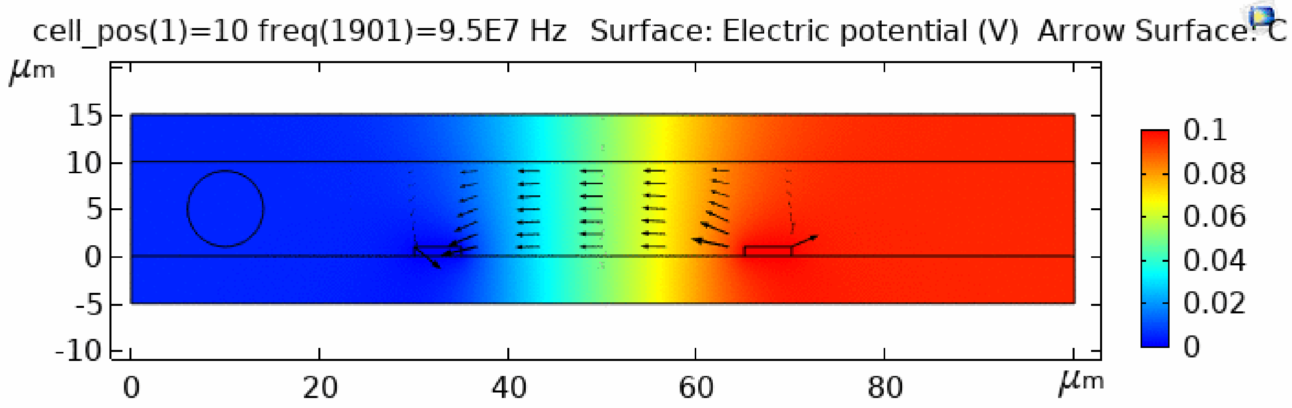
Individual trapping, fluorescent detection

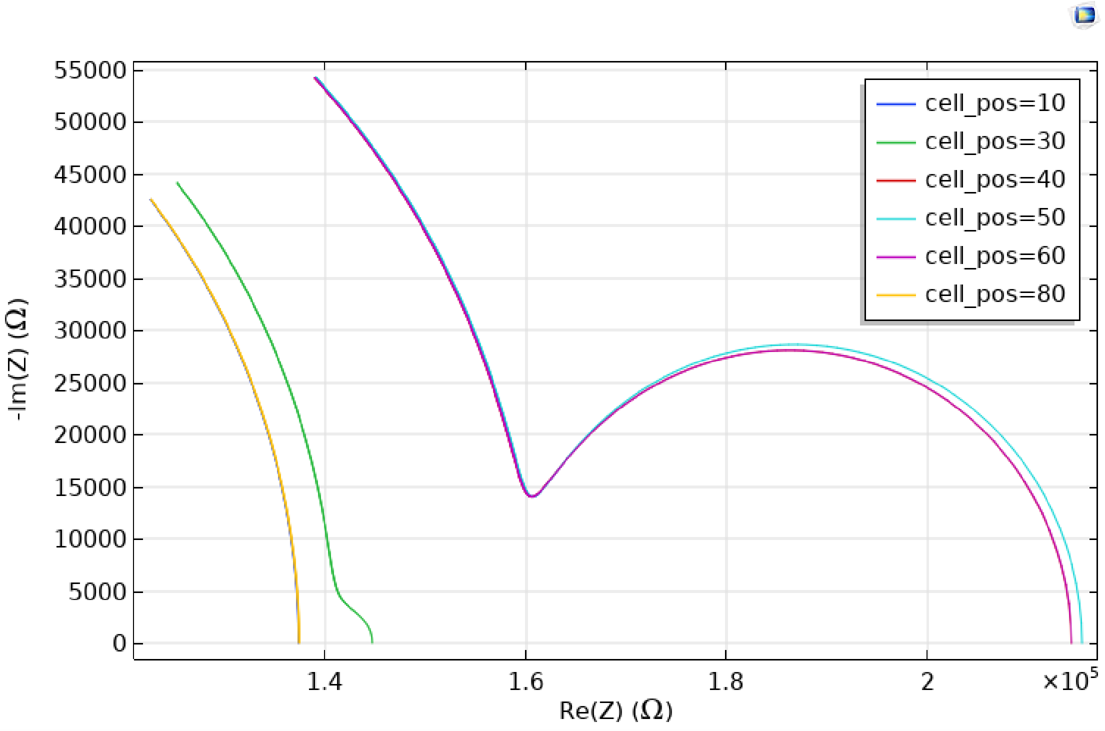
Research

Comsol simulation

Impedance spectrum of cells in microfluidic channels







Courses completed:

- BioMEMS: Miniature Biosensors
- Measurement of bioelectrical activities

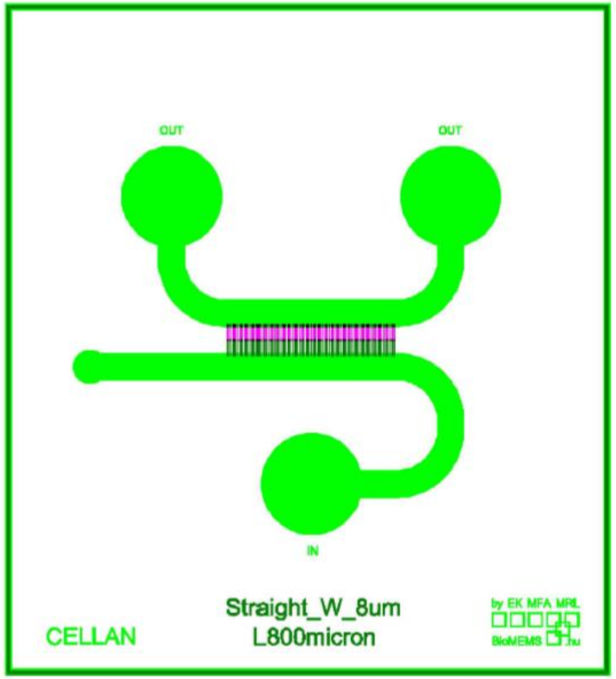
Future plans

Research

- Diffusion measurements with BSA, GFP, Fluorescin, Rhodamin B
- Electrode integration
- Impedance spectroscopy measurements on trapped yeast cells
- Rapid antibiotic resistance measurements (E. Coli)

Publication

- Protein diffusion measurements and results



Thank you for your attention!