



Integrated microfluidics / lab-on-chip systems for point-of-care medical diagnostic applications

EK MFA



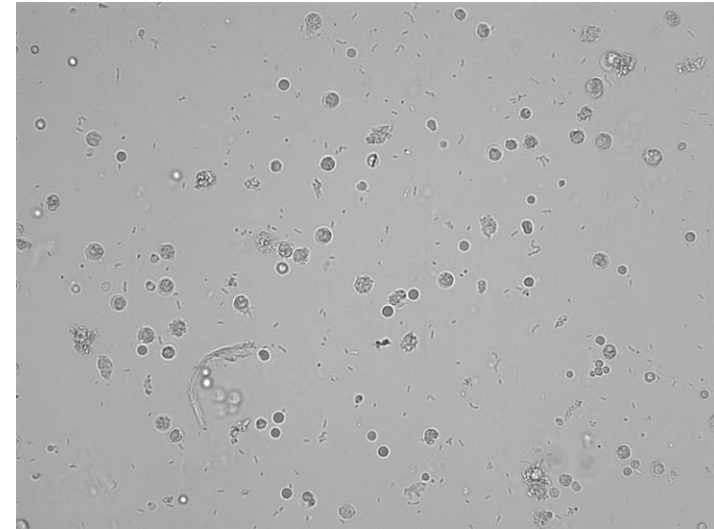
Anita Bányai, dr. Péter Fürjes

www.biomems.hu, www.mems.hu



The aim of my research

- design and development of integrated microfluidic systems for sample transporters to be used in fast and reliable diagnostic tools
- screening for urine bacteria on a targeted microfluidic platform
- study and determine the geometry and material structure of the microfluidic system; promoting compatibility with industrial technologies



Main tasks of this semester

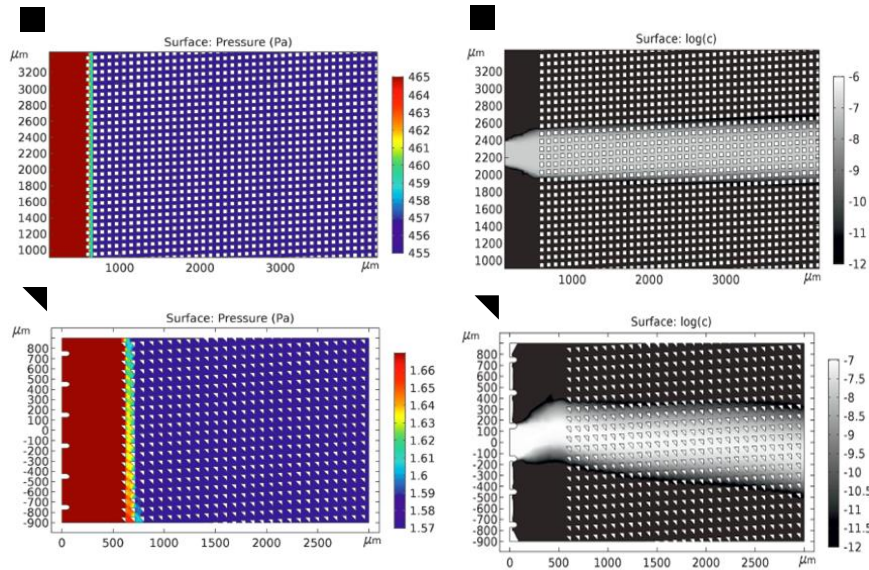
Until now passive separation methods were tested: **Crossflow filtration (CF)** and **Lateral focusing (LF)** but in this semester investigation was made in the active separation methods, especially in:

- **Magnetoforetic separation**



Previous semesters – passive separation

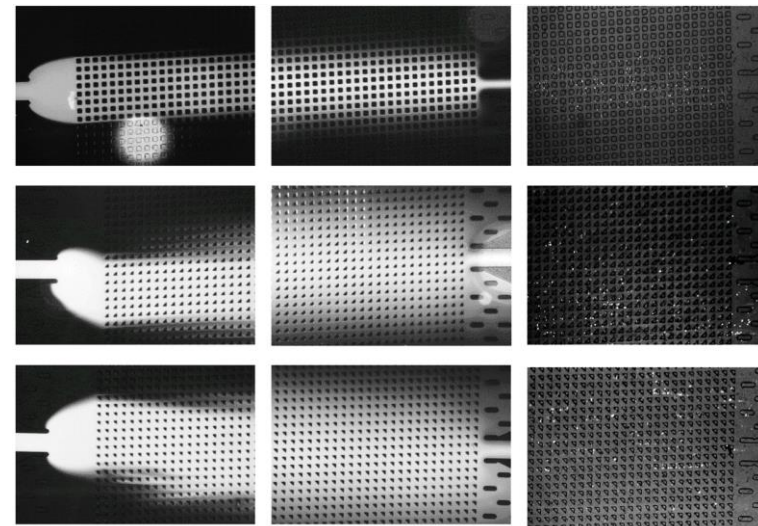
DLD



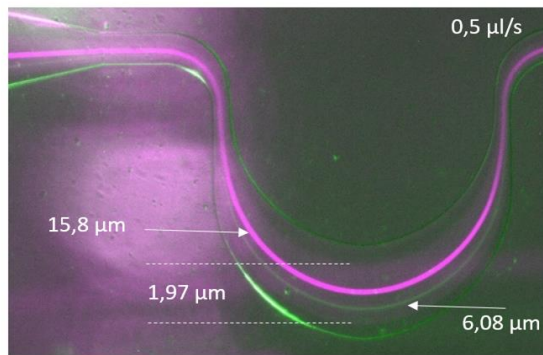
Alexa Fluor 350 (DAPI) - INLET

Alexa Fluor 350 (DAPI) - OUTLET

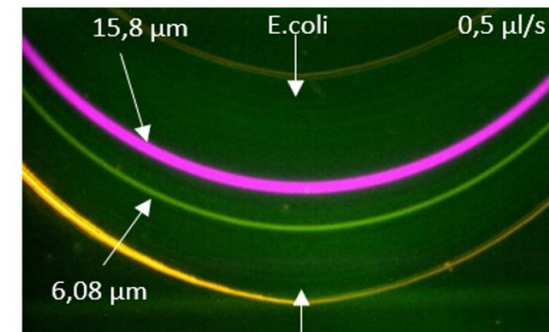
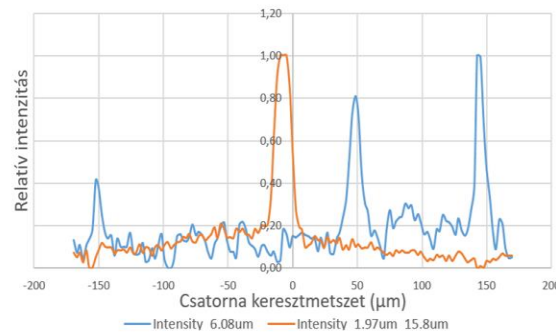
GFP-E.coli (FITC) - OUTLET



LF

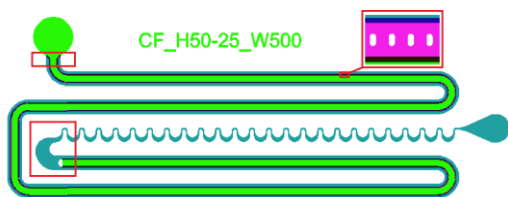


1.97 um fókuszálás_Crossflow után_M50_S50_Nyom. rsz.

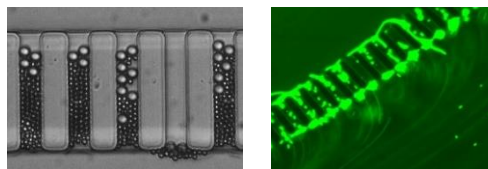


Previous semesters – passive separation

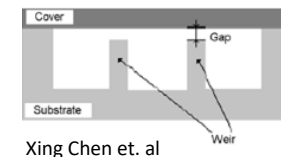
CF



Design change:

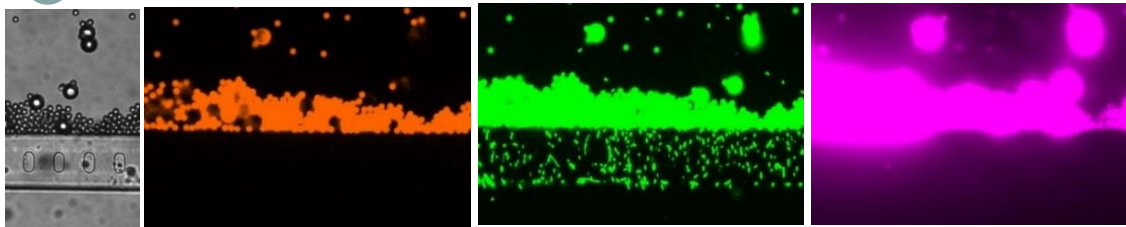
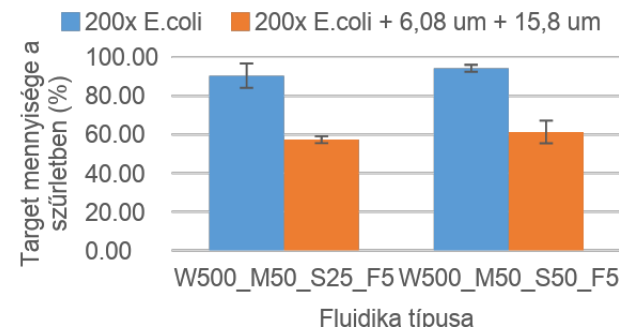
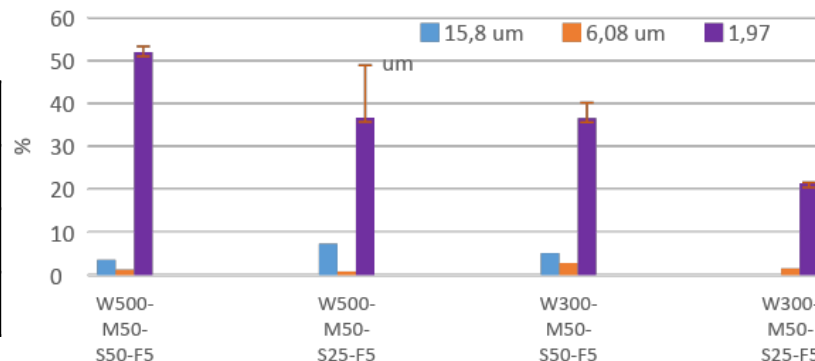


Weir-type



%-os jelenlét a szűrletben

	15,8 μm	6,08 μm	1,97 μm
W500-M50-S50-F5	3,57	1,28	51,99
W500-M50-S25-F5	7,33	0,85	36,71
W300-M50-S50-F5	5,13	2,82	36,61
W300-M50-S25-F5	0,00	1,56	21,44



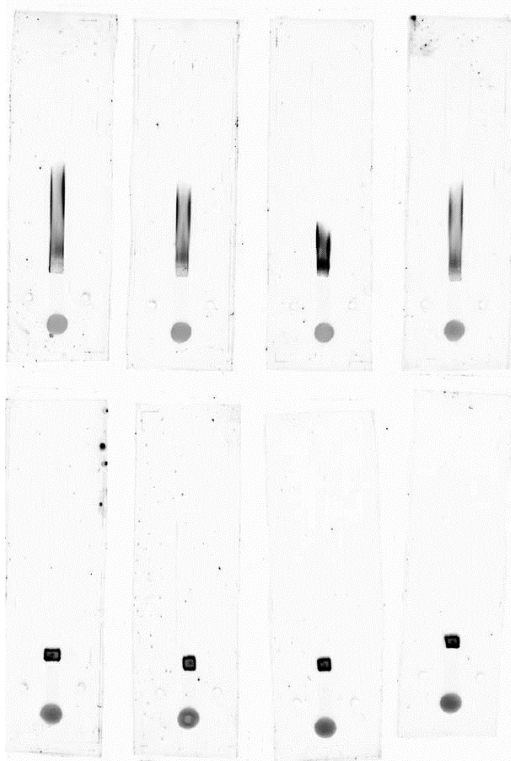
Current semester – active separation, IVD

- Paper writing for Lateral focusing -> comparing experimental data with COMSOL simulations
- Winning a tender in Cooperative doctoral program, and starting the work at 77 Elektronika Kft; on a theme of in vitro diagnostics (IVD) based on Lab-on-a Chip device
- Learning of new technological equipments:
 - DRIE: Deep Reactive Ion Etching
 - SEM: Scanning Electron Microscope
- Investigation in Magnetoforetic separation
 - Magnetic separation efficiency at different channel height and flow rates
 - Development of new design of microfluidic system (MMS – micromagnetic separation) with efficient corporation of the size of the ordered neodymium magnet

Work at 77 Elektronika Ltd.

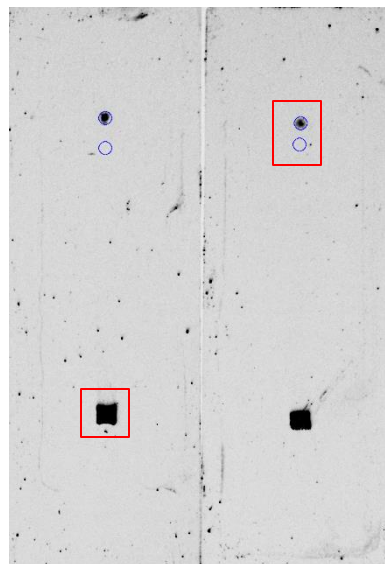
IVD in combination with LOC

- Immunoassay preparation on COP
- Special microfluidic structure for sample preparation
- Aim: detect the exact concentration of biomarker from blood (NT-proBNP, CRP)
- Conclude the presence of cardiac disease or inflammation in patient



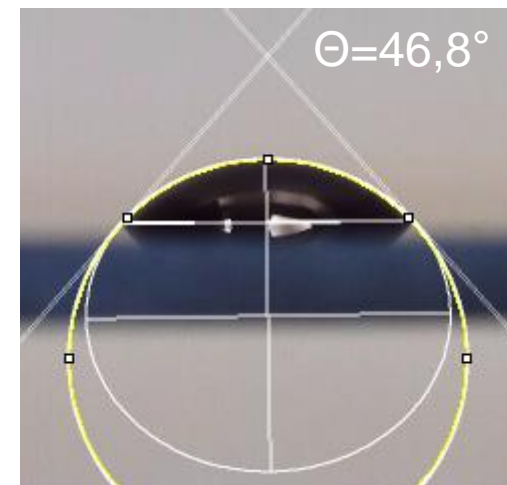
Antigen spike in blood sample

Rapid test evaluation

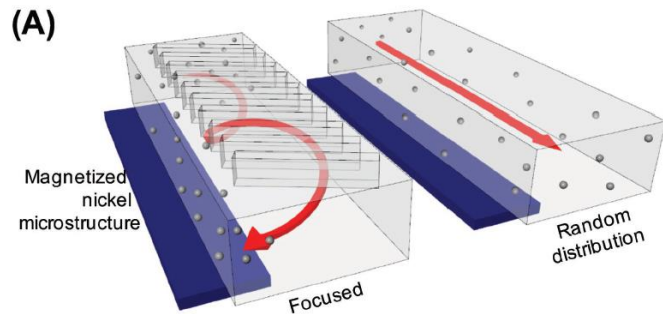
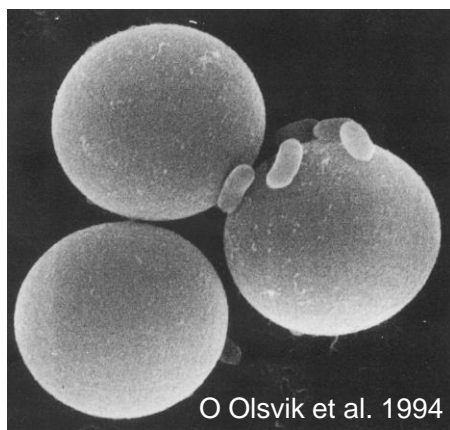
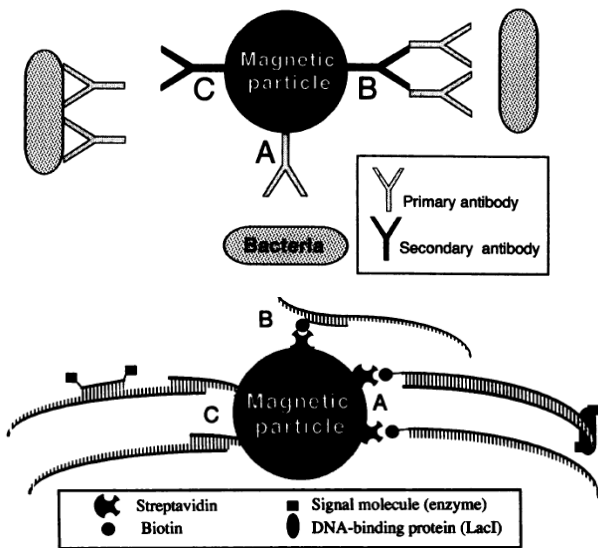


Antibody coated microbeads

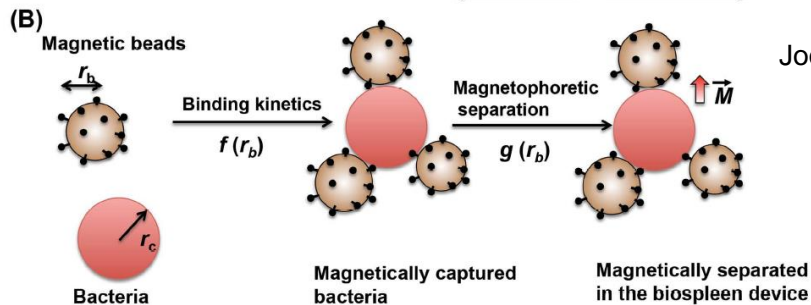
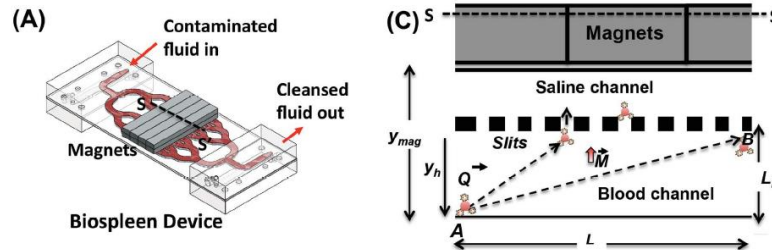
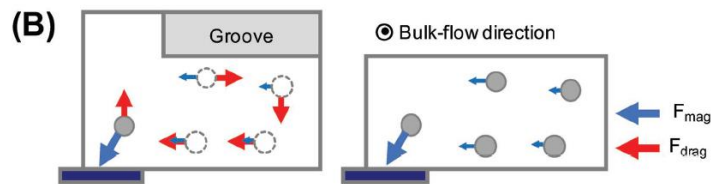
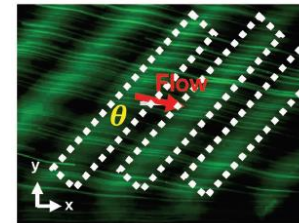
Signal to noise ratio



Magnetic separation



Su Hyun Jung et al. 2018



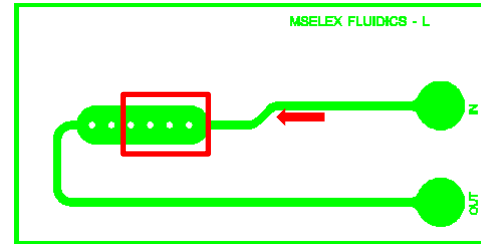
Joo H. Kang et al. 2015



Magnetic separation in practice

5x5x5 mm³
neodymium

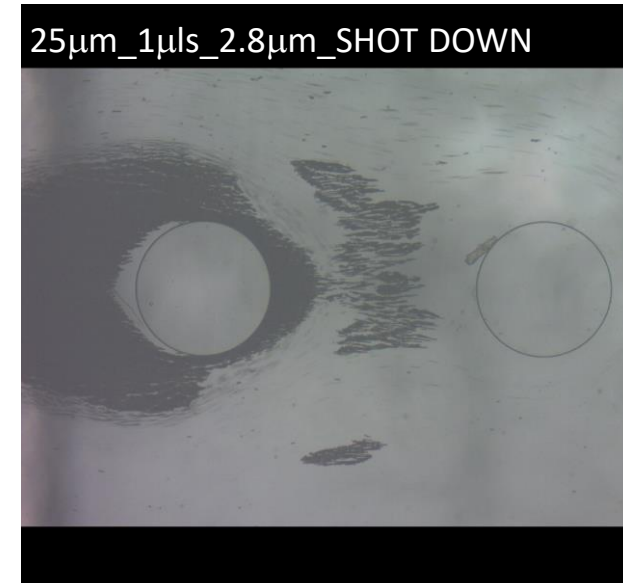
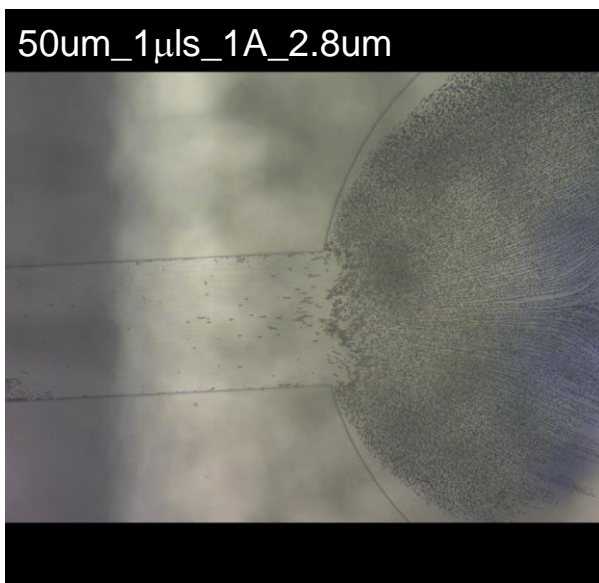
Bead type	Volume	Concentration	Buffer	Bead diameter
M-280 Streptavidin	1 mL	10 mg/mL (6-7 × 10 ⁸ beads/mL)	PBS, pH 7.4 0.1% BSA 0.02% Sodium azide	2.8 μm
M-270 Streptavidin	1 mL	10 mg/mL (6-7 × 10 ⁸ beads/mL)	PBS, pH 7.4 0.09% sodium azide	2.8 μm



- Two different channel heights: 50 μm, 25 μm
- Three different flow rates: 0.5 -1-2 μl/s

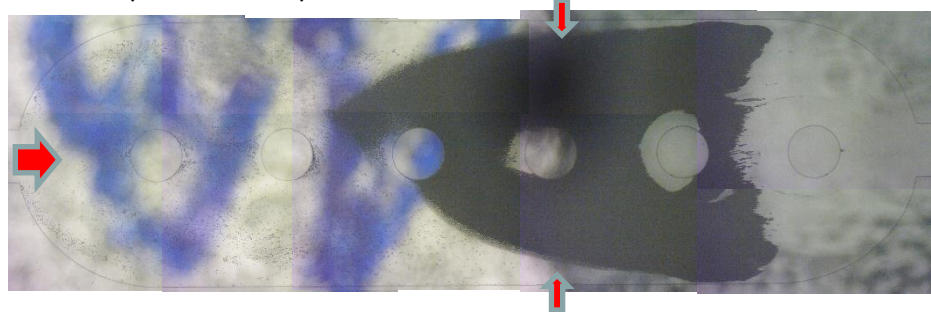


Measurement of filtration efficiency

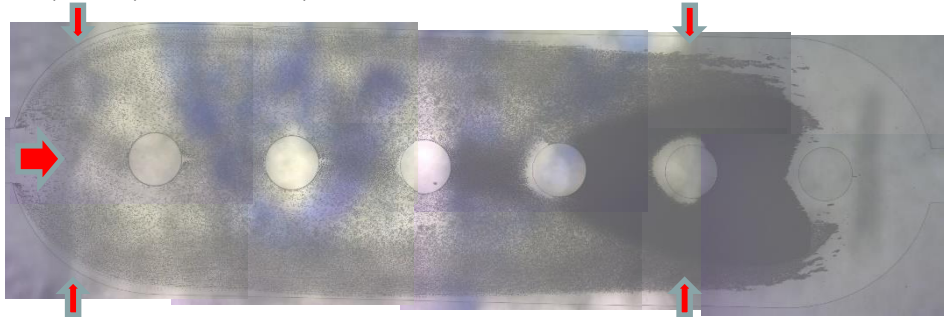


Magnetic separation in practice

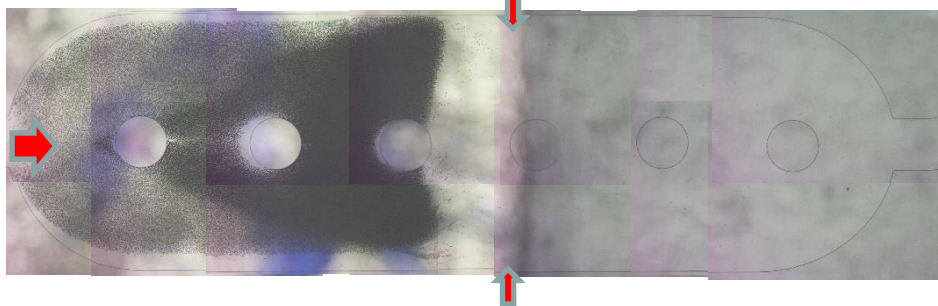
50um_2µl/s_1B_2.8µm



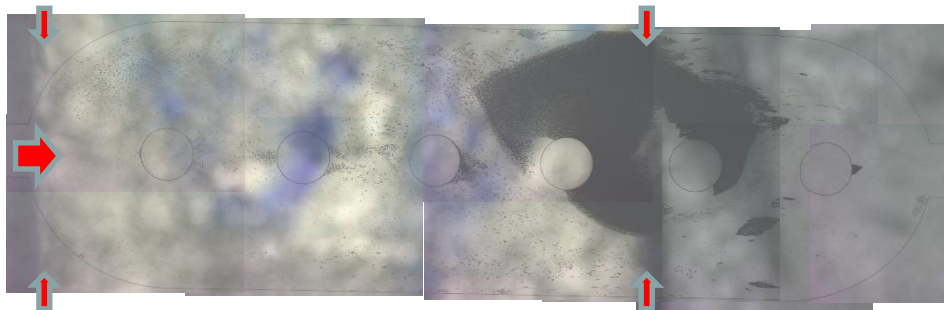
25µm_2µl/s_1B_2.8µm



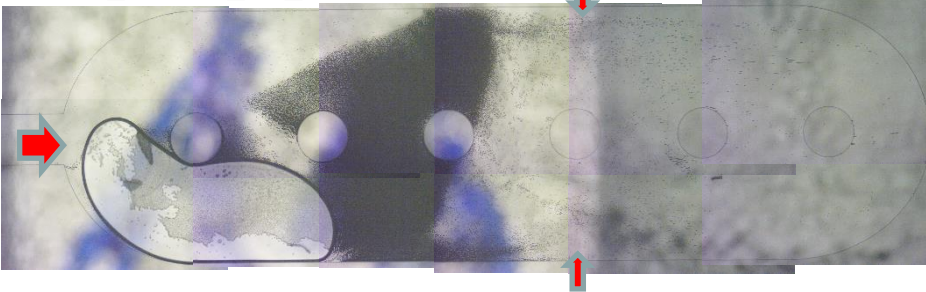
50um_1ul/s_1A_2.8um



25um_1ul/s_1A_2.8um



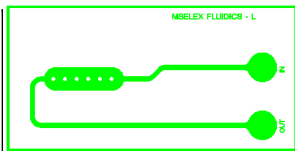
50um_0.5 ul/s_1B_2.8um



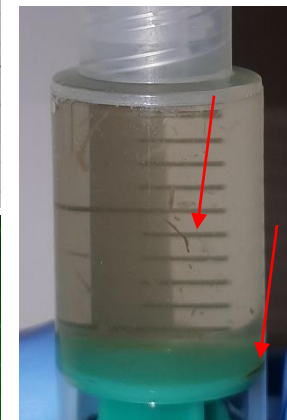
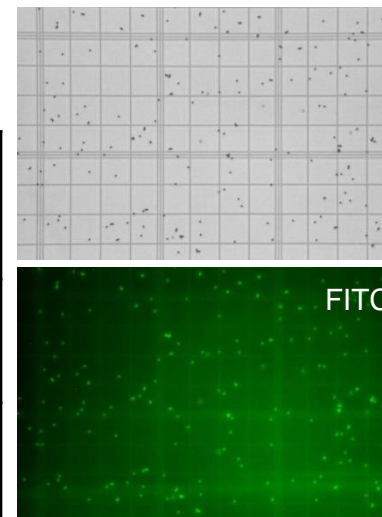
25um_0.5 ul/s_1_2.8um



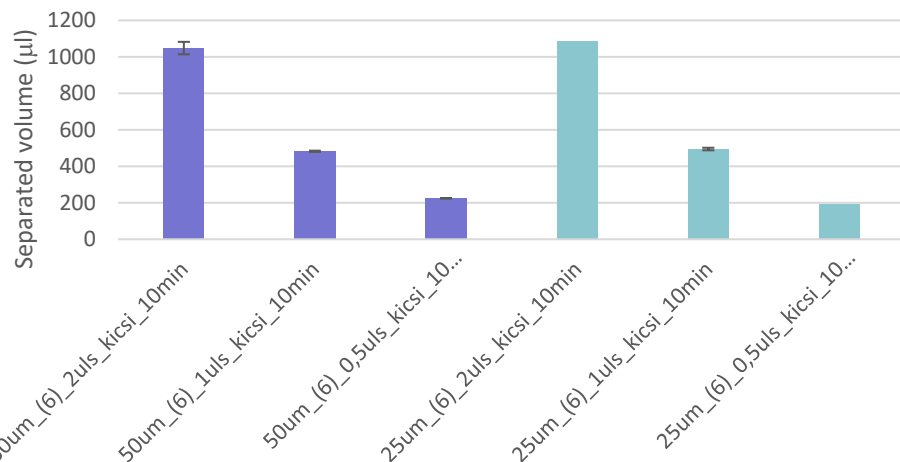
Magnetic separation in practice



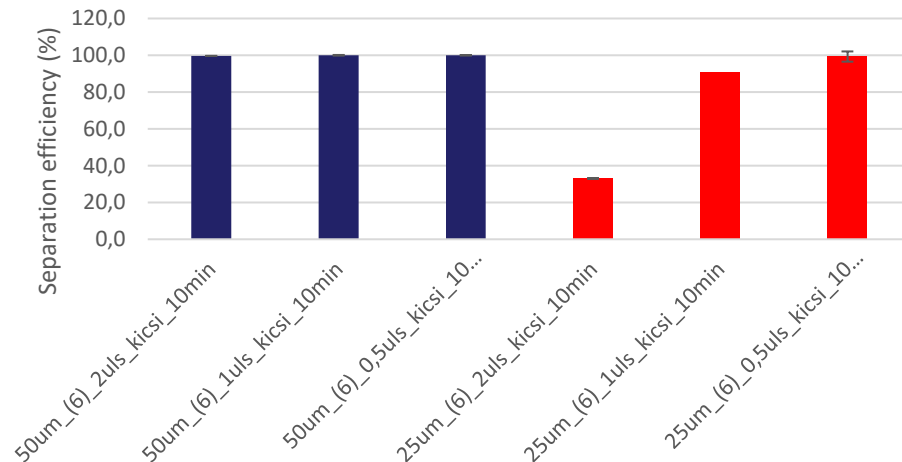
	Filtration volume AVERAGE (ul)	DISPERSION	Filtration efficiency (%)	DISPERSION
50um_(6)_2uls_kicsi_10min	1049,25	34,29	99,6	0,19
50um_(6)_1uls_kicsi_10min	481,5	3,54	100,0	0,00
50um_(6)_0,5uls_kicsi_10min	224	1,41	100,0	0,00
25um_(6)_2uls_kicsi_10min	1088		33,0	-
25um_(6)_1uls_kicsi_10min	494,5	6,36	90,6	2,76
25um_(6)_0,5uls_kicsi_10min	190		99,4	-



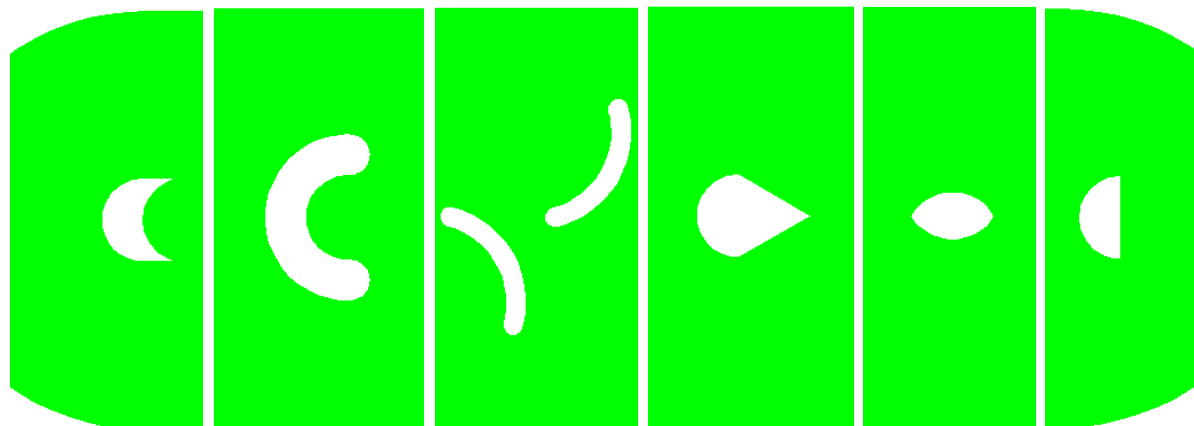
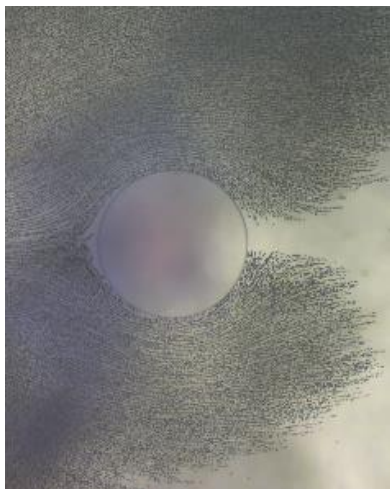
Filtration volume AVERAGE (μl)



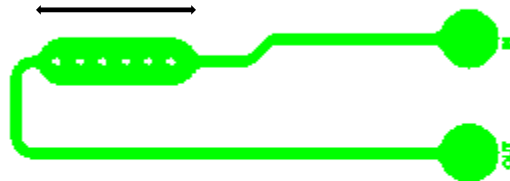
Filtration efficiency (%)



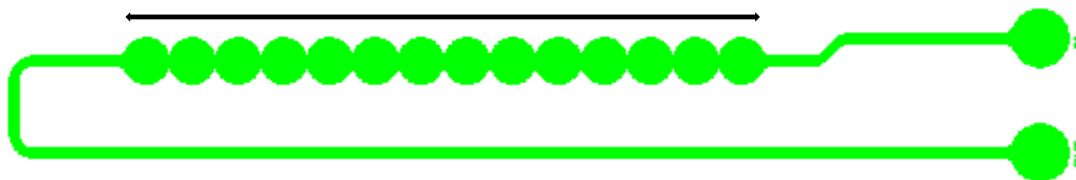
Consideration of new design



6,9 mm



28 mm



Summary

- In magnetic separation 2.8 μm magnetic beads were used.
- Better filtration efficiency was measured in the 50 μm height microchannel at 1 $\mu\text{l/s}$ flow rate.
- Too small channel height and high flow rate result in a drastic target loss
- An optimal balance need to be found for high throughput at short time, but with less loss

Plan

- Finish the articles in this summer for DLD, Lateral focusing
- To continue magnetic separation with the new design (smaller beads, E.coli or aptamers)
- Futher investigation in DRIE methodes

This semester - article

- An integrated electro-optical biosensor system for rapid, low-cost detection of bacteria

(D. Petrovski D, S. Valkai, E. Gora, M. Tanner, A. Banyai, P. Furjes, A. Der,/ Microelectronic Engineering, Volumes 239–240, 2021, 111523/
<https://doi.org/10.1016/j.mee.2021.111523/> Q2 / SJR 2020: 0,55)