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

EK MFA

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The aim of my research

- design and development of integrated microfluidic systems for sample transport and preparation
- screen for urine bacterium / Project - RUBA - **(Rapid urine bacteria analyzer)**
- study and determine the geometry and material structure of the microfluidic system

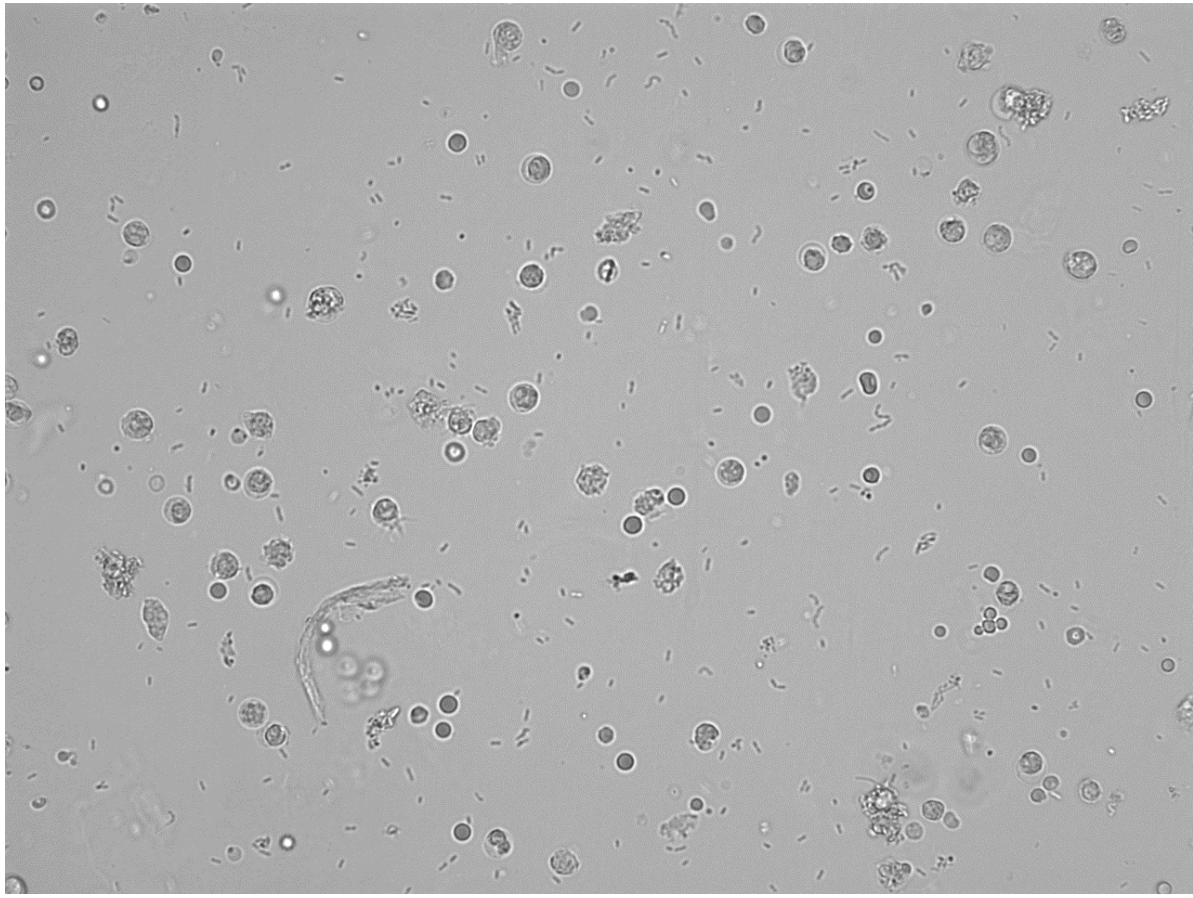
Main tasks of this semester

size and morphology based separation of bacteria (< 6 um)

- **DLD** – Deterministic Lateral Displacement (previous semester)
- **Crossflow filtration**
- **Lateral focusing** over the sensing area

Cell separation

- Red blood cell (7-10µm)
- White blood cell (8-15µm)
- Squamous cell (~ 40-60µm)
- Small round epithelial cell (~ 10-40µm)
- Hyalin cylinder (~ 10-40-60µm)
- Pathological cylinder (~ 10-40-60µm)
- **Bacteria**
  - **Wand (BACr) (~ 2-4µm)**
  - **Coccus (BACc) (~ 1-2µm)**
  - **E.coli (~ 1-3µm)**
- Crystals (~ 5-20-40µm)
  - CaOxd
  - CaOxm
  - Tripple phosphate
  - Uric acid crystal
- Fungii (~ 7-50µm)
- Neck
- Sperm (~ 20-30µm)



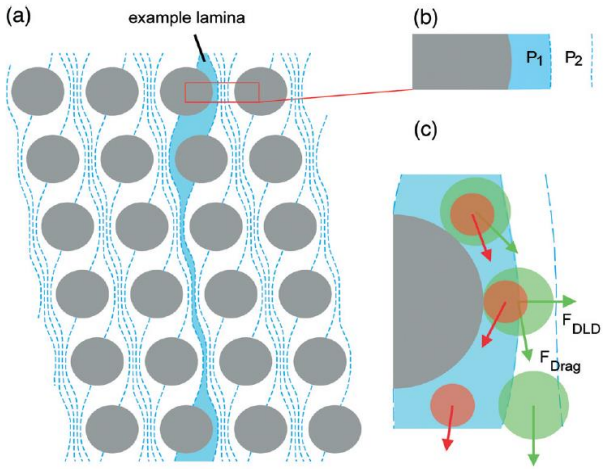
LABORATORY SINGLE CHANNEL MICROFLUIDIC CARTRIDGE

(theoretical summary)

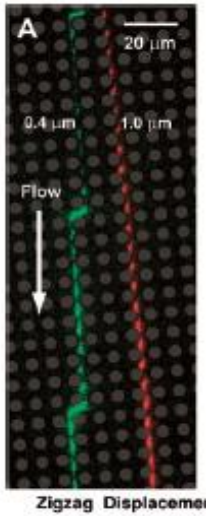
I. Particle separation (DLD, Crossflow)

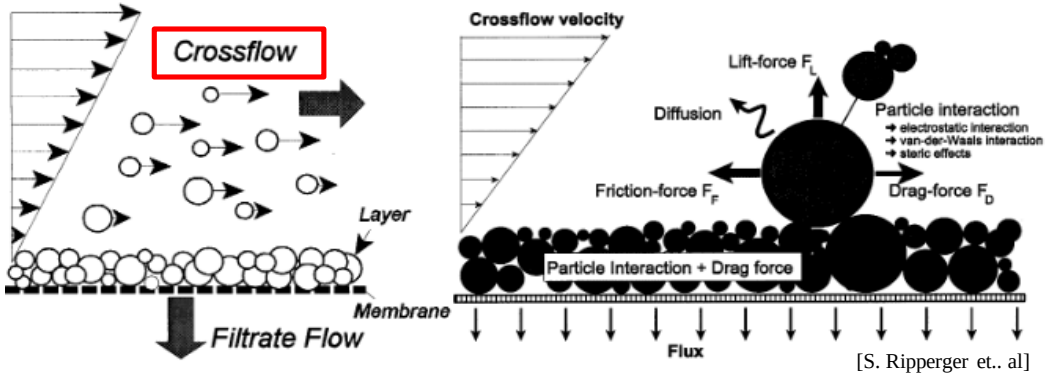
DLD

[Lotien Richard Huang et.al.]



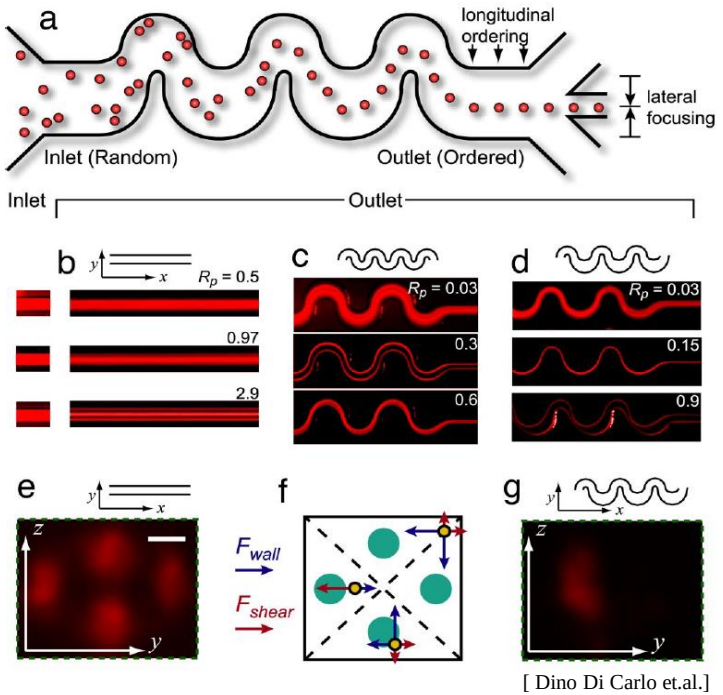
[J. McGrath et al. (2014)]



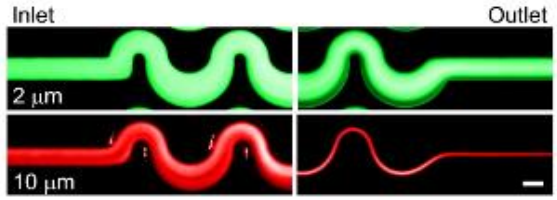


[S. Ripperger et.. al]

II. Lateral focusing



[Dino Di Carlo et.al.]



[D. Di Carlo et.al.]

I. Particle separation-> DLD

(summary – last semester)

$$Dc = \alpha G \varepsilon^{\beta}$$

[E. Pariset et al. (2017)]

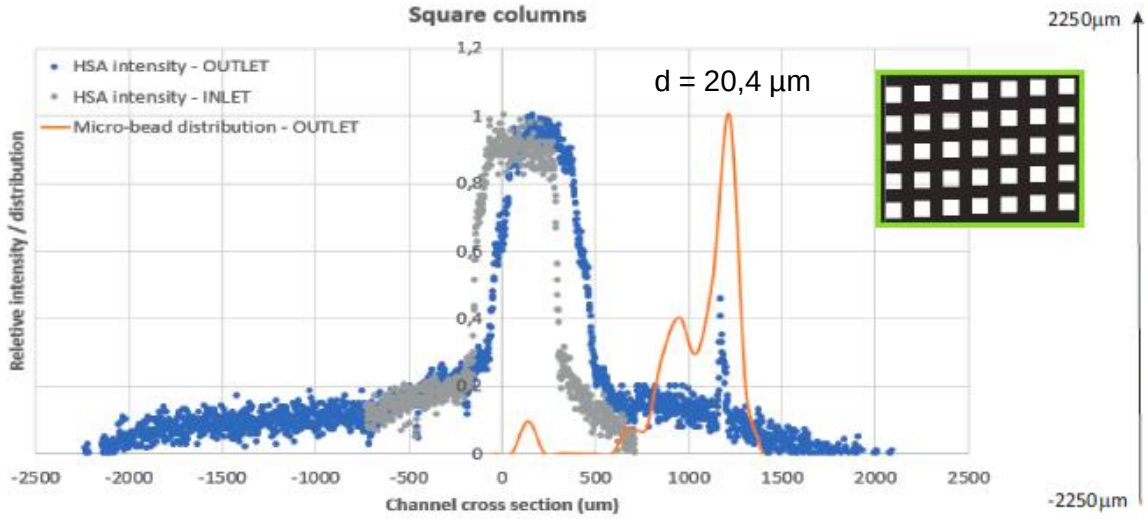
G: gate diameter
ε : reciproc of the period number
α,β: column shape specific parameters

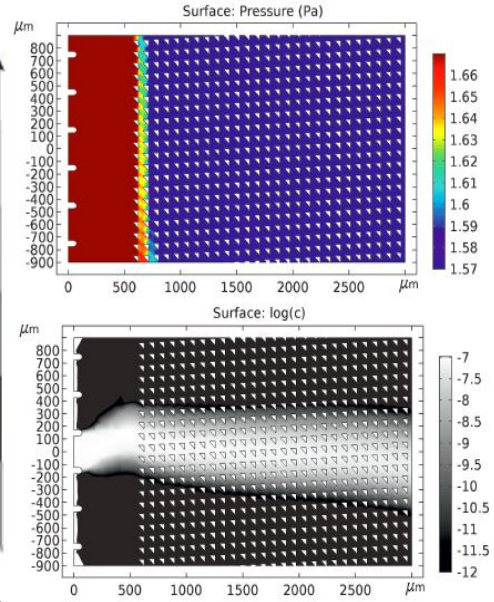
Buffer (from two sides): 1,8 µl/s
FITC-HSA + Beads (focused): 0,2 µl/s

Circle | Square | Triangle (+) | Triangle (-) | Right-angled Triangle (+) | Right-angled Triangle (-)

N	21
G	40 µm
Dp	50 µm
λ	90 µm
Θ	2,8624
h	50 µm

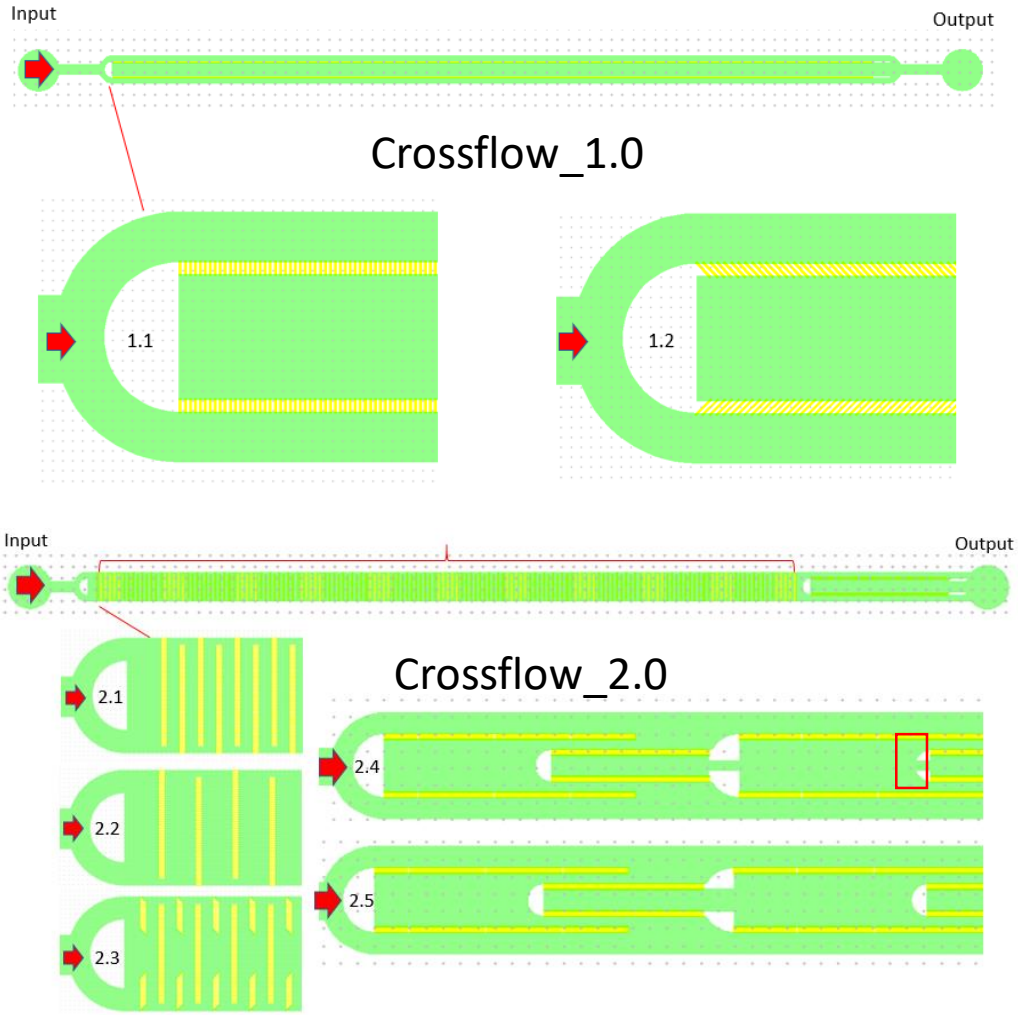
	Dc (µm)
Circle	13,30
Tri. +	11,11
Tri. -	12,90





A. Bányai, P. Hermann, O. Hakkel, Z. Hajnal, P. Fürjes, Shape design dependent performance of DLD (deterministic lateral displacement) based particle separation systems - FEM modelling and validation, Lab-on-a-Chip Europe Conference, Rotterdam, The Netherlands, 2019

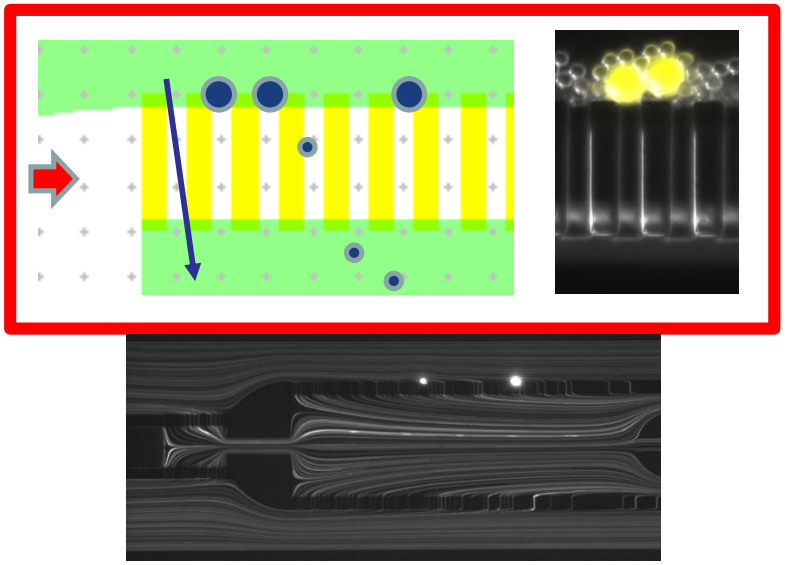
I. Particle separation-> CFM – Crossflow microfiltration



d=4,8 µm Beads – Green [FITC]
d=15,8 µm Beads – UV [DAPI]

CFM flow velocity: 0,5-1µl/s; 3µl/s

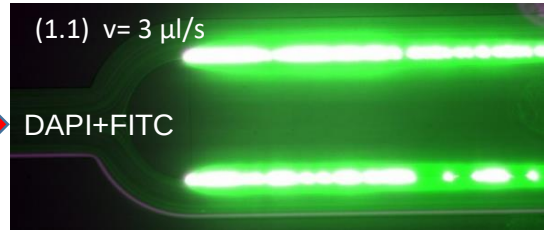
- first: pressurized flow from the input,
- later: fluid suction from the output

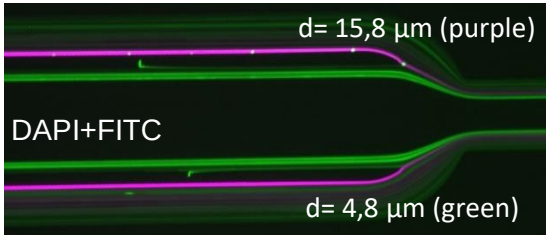


I. Particle separation-> CFM – Crossflow microfiltration (pressurized flow)

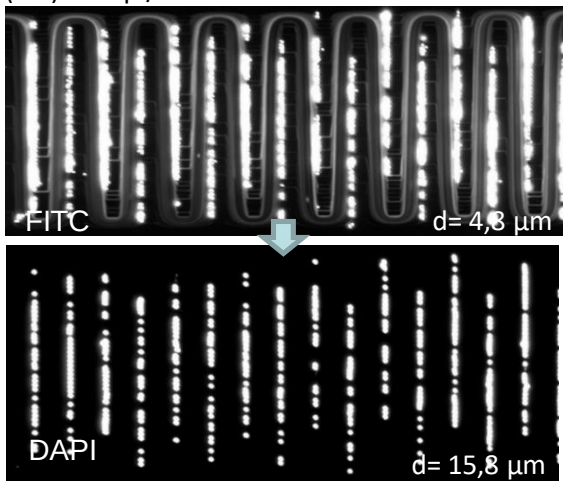
- Parallel filters are better at lower fluid flow rates.
- The perpendicular filters trapping the bigger beads, filter better at higher flow rates.

A.

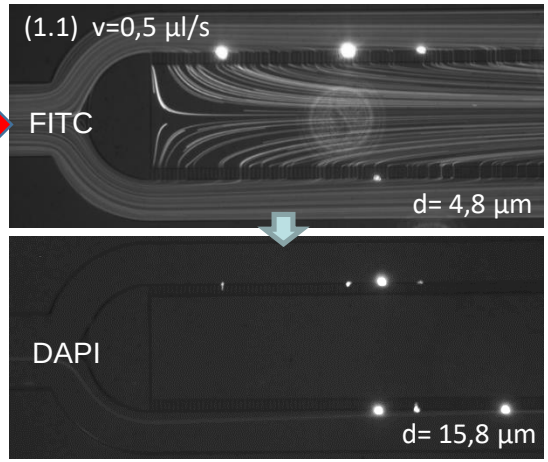


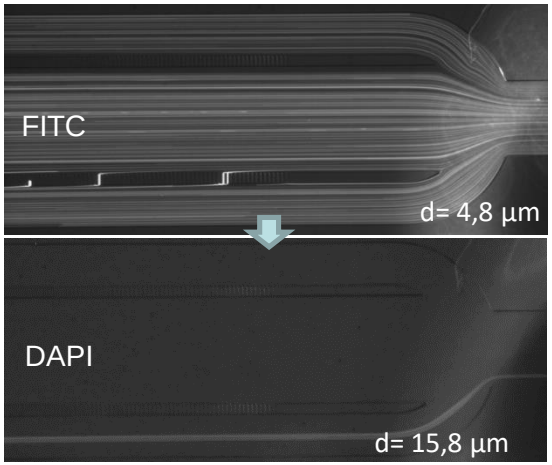


(2.1) v=3 µl/s

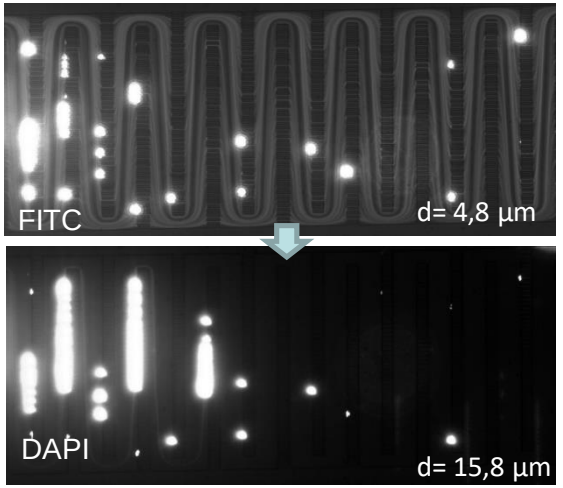


B.





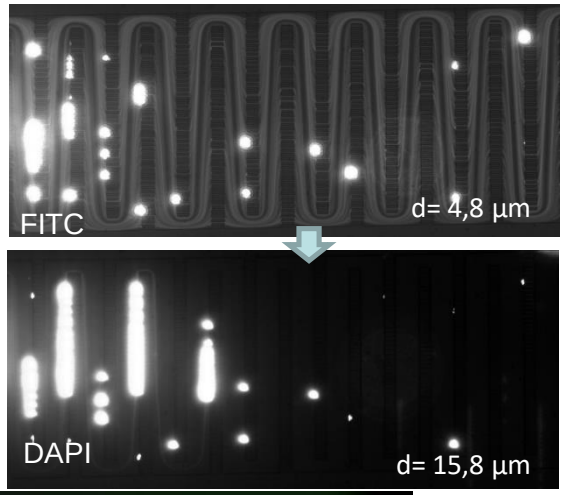
(2.1) v=0,5 µl/s



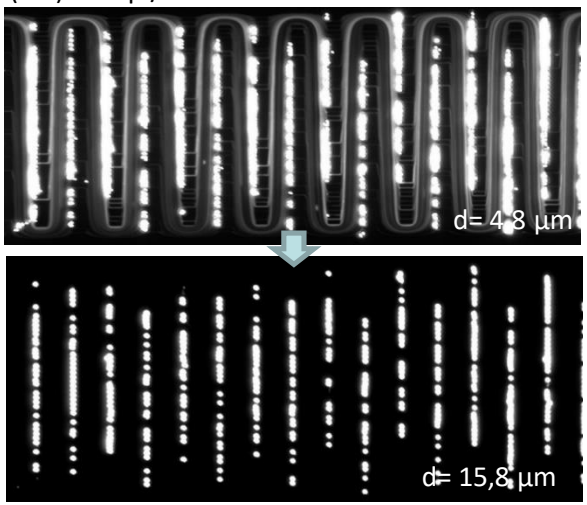
I. Particle separation (fluid flow)

Pressurized flow

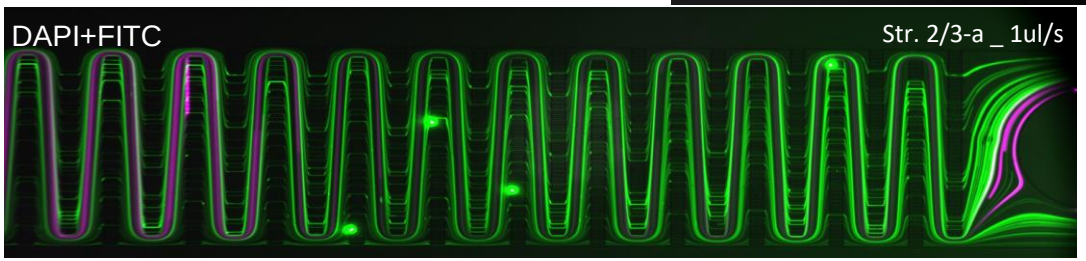
(2.1) v=0,5 µl/s

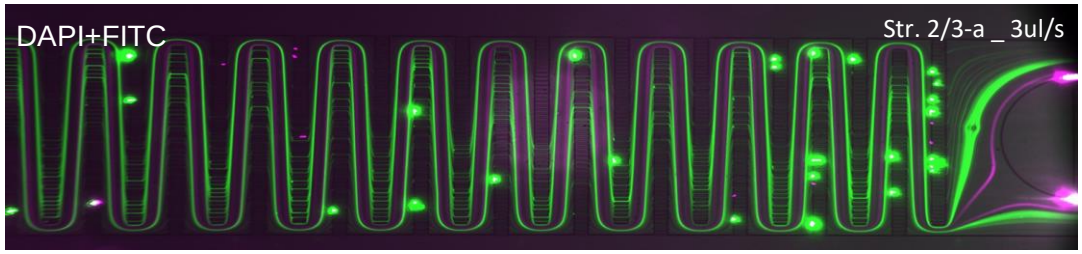


(2.1) v=3 µl/s



Purple – d=15,8 um Beads
Green – d=4,8 um Beads

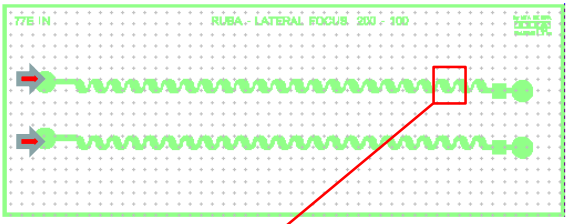


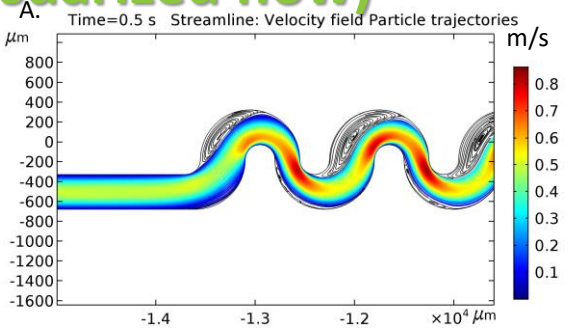


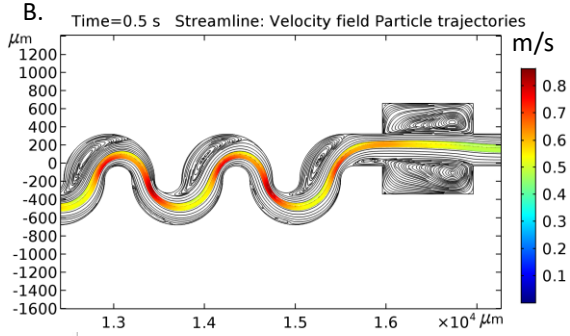
Fluid suction

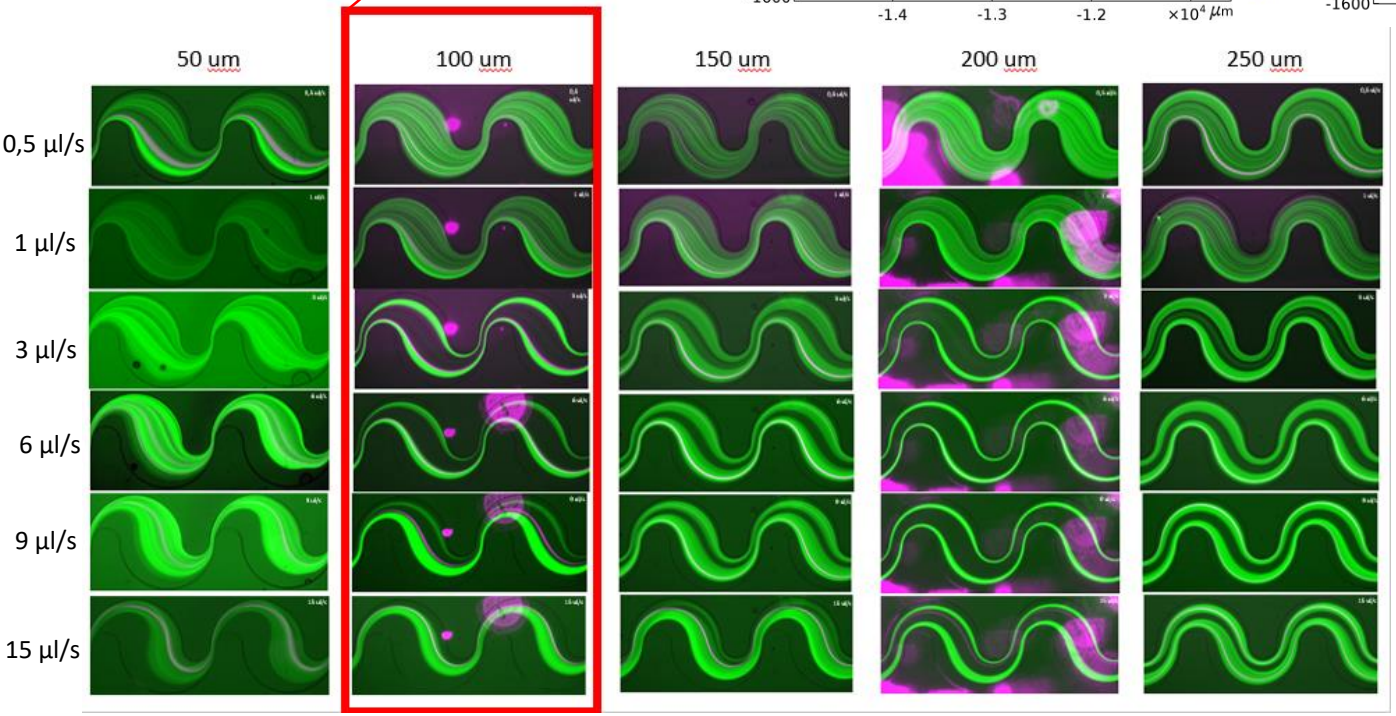
Conclusion:
- In a pressurized system, separation can be "forced" by increasing speed due to increased pressure conditions, but in a suction system this arrangement does not work.

II. Lateral focusing (presuarized flow)



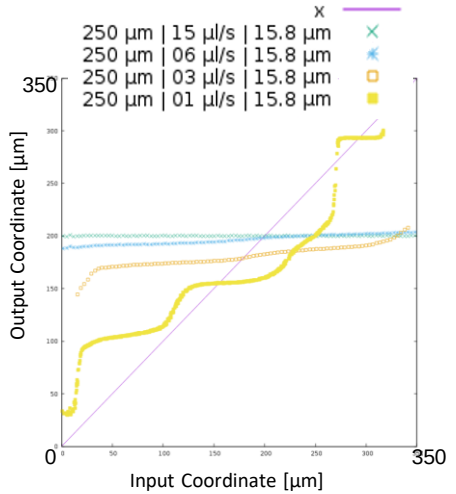






d= 15,8 µm (purple)

d= 4,8 µm (green)



$a/D_h > 0,07$ [D. Di Carlo et.al.]

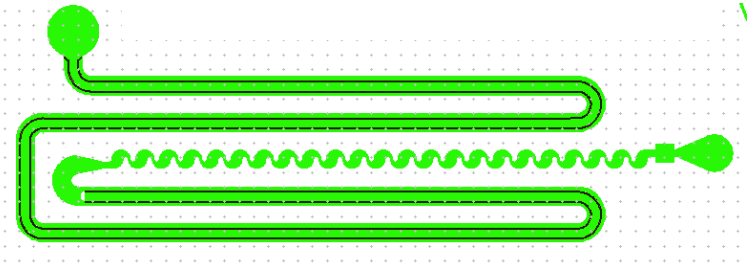
w (µm)	4,8 µm/Dh	15,8 µm/Dh
50	0,096	0,316
100	0,072	0,237
150	0,064	0,211
200	0,06	0,1975
250	0,058	0,1896

Summary

- ~~DLD~~, Crossflow at various flow rates/ flows
- perpendicular filters -> at higher flow rates
- suction system the parallel filtering layout better at lower flow rates
- Lateral focusing of 4.8 µm diameter beads at 15 µl / s

Plans

- Further optimization of lateral focusing unit -> for lower flow rates
- Build and test existing components in a suction system
- Begin biological measurements in DLD, Crossflow and Lateral Focusing Unit
- Publication of the results from DLD structures



Completed courses

- Surface characterization and modification of polymeric materials (Éva Kiss)
- Semiconductor devices (Zsolt József Horváth)

Publications

[1] D. Petrovszki, S. Valkai, E. Gora, M. Tanner, **A. Bányai**, P. Fürjes, A. Dér, Dielectrophoretically enhanced detection of E. coli cells by an integrated optical biosensor system, 45th International Conference on Micro & Nanoengineering, Rhodes, Greece, 2019

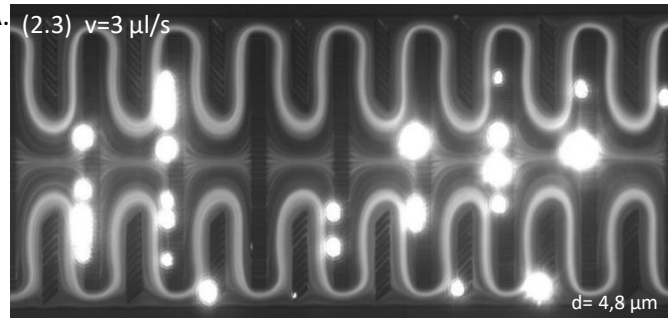
[2] Petrovszki D., Valkai S., Gora E., Tanner M., **Bányai A.**, Fürjes P., Dér A., E. coli sejtek dielektroforetikusan erősített detektálása integrált optikai bioszenzorral, a Magyar Biofizikai Társaság XXVII. Kongresszusa, Debrecen, Magyarország, 2019

[3] P. Fürjes, O. Hakkel, **A. Bányai**, P. Hermann, E. Holczer, E. L. Tóth, K. Papp, J. Prechl, Autonomous microfluidic systems for sample transport and flow characteristics based diagnostics, Matrafured 2019 International Meeting on Chemical Sensors, Visegrad, Hungary, 2019

I. Particle separation (fluid flow)

Pressurized flow

A.



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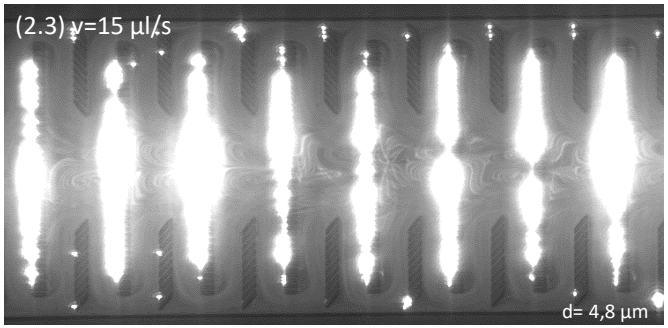
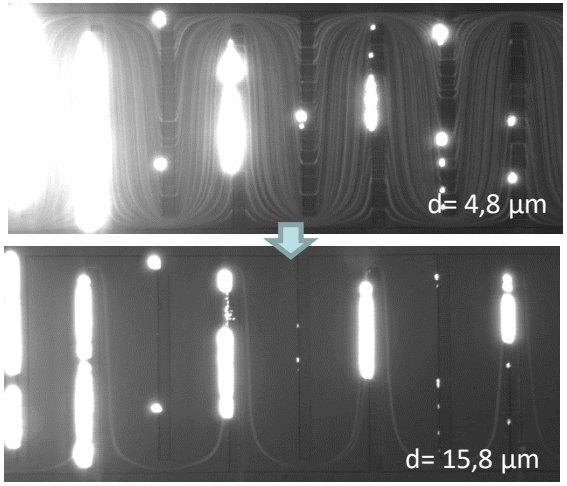
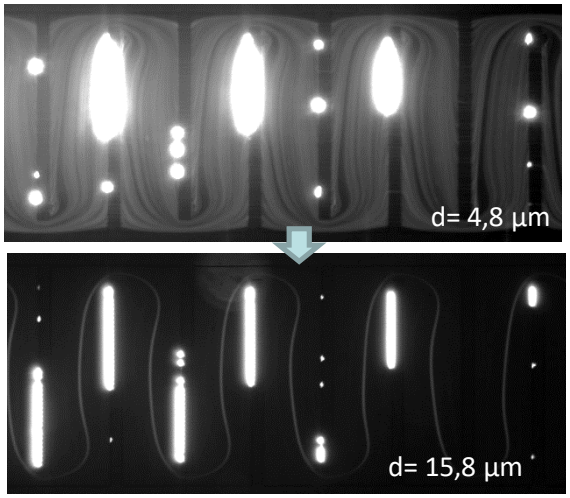
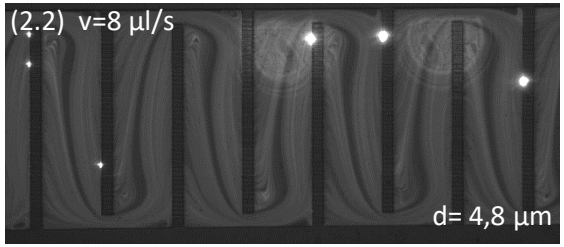


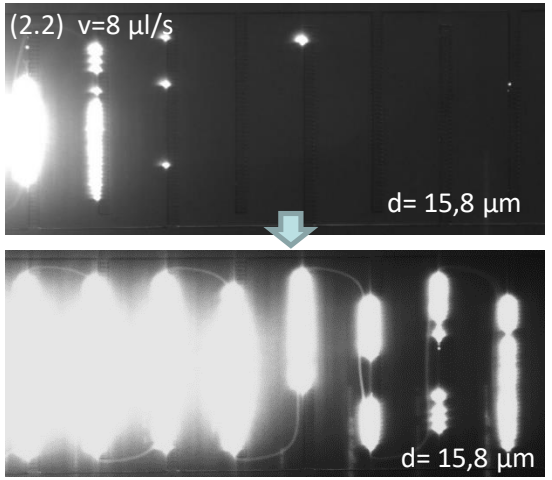
(2.2) v=0.5 µl/s



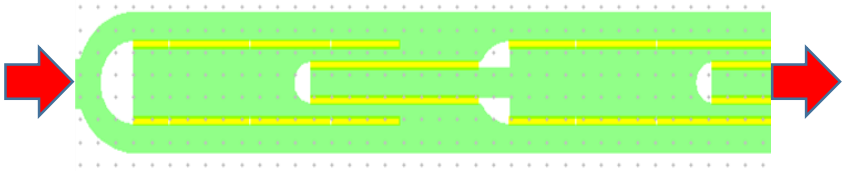
(2.2) v=3 µl/s



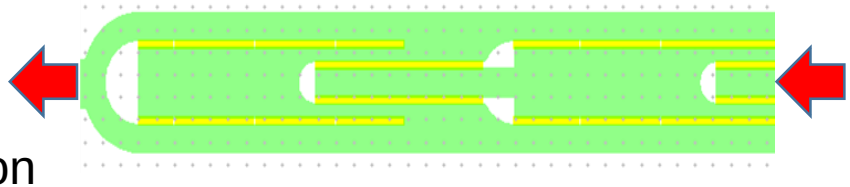




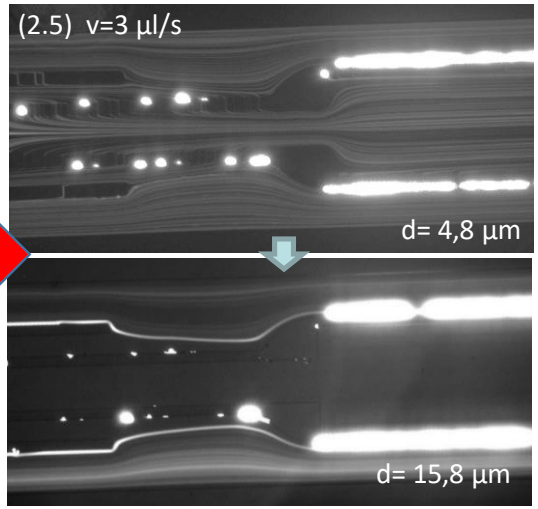
I. Particle separation (potentional solution)

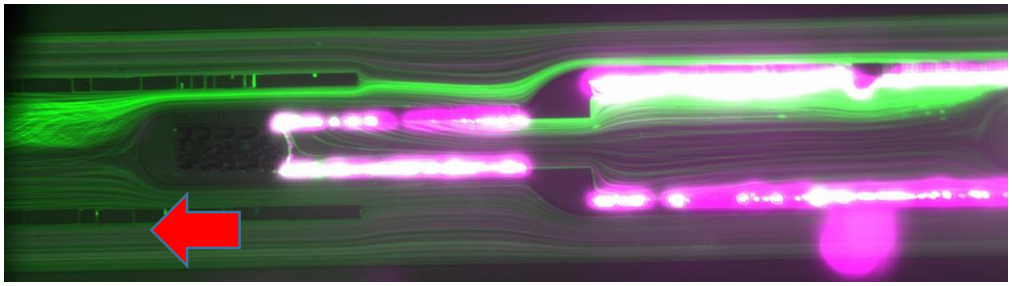


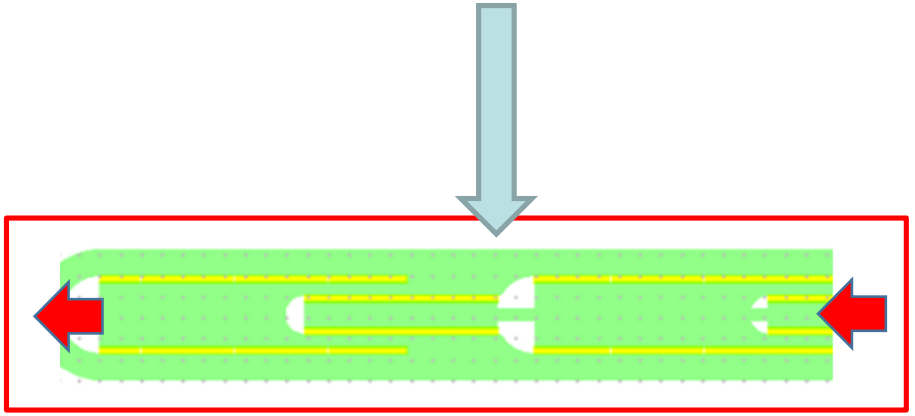
Fluid suction



Pressurized flow







Conclusion:
-Parallel filters work at lower pressures.
-Retesting a previously rejected structure -> trapping a larger particle doesn't have to worry about draining a waste.