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Microliquid S.L. (Arrasate)

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microLIQUID

experts in microfluidics

Photonic Lab-on-a-Chip: Integration of Optical Spectroscopy in Microfluidic Systems

microLIQUID

experts in microfluidics

Microliquid Assets

Unique Microfluidic State-of-the-art-assets under one roof

2020-2021

Adding more than > 25000 ft²

to new manufacturing lines and product development laboratories.

→ **State-of-the-art cleanroom facilities from prototyping to mass-manufacturing**

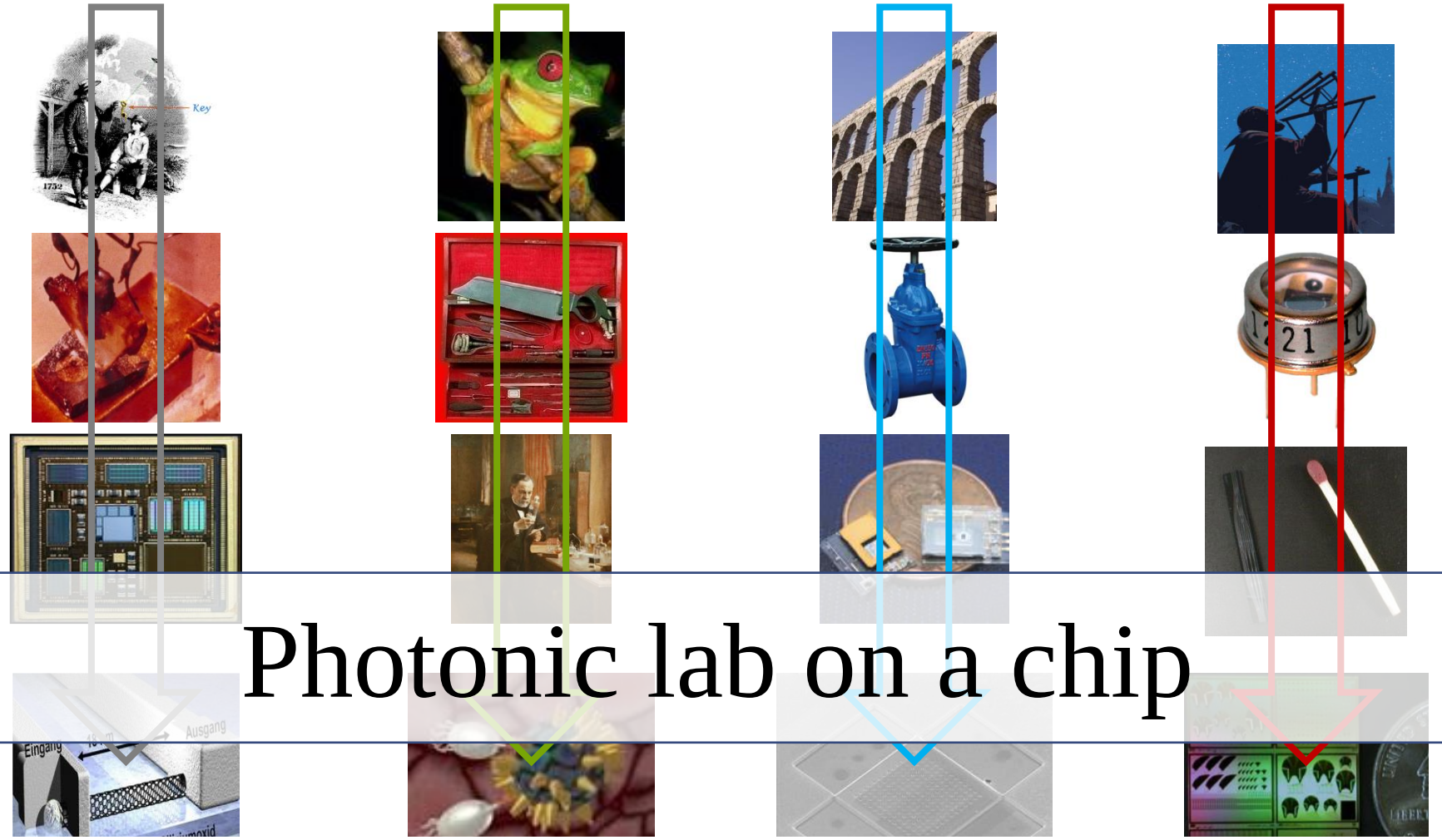
- Polymer Microfluidic (ISO5 to 7)
- Silicon Microfluidic (ISO5)

Mold and microinjection production lines

→ **Safety 2 level Biolaboratories**

- Reagents (Integration & Preparation)
- Sample Processing
- Molecular dx
- Cell culture

Development of new analysis tools

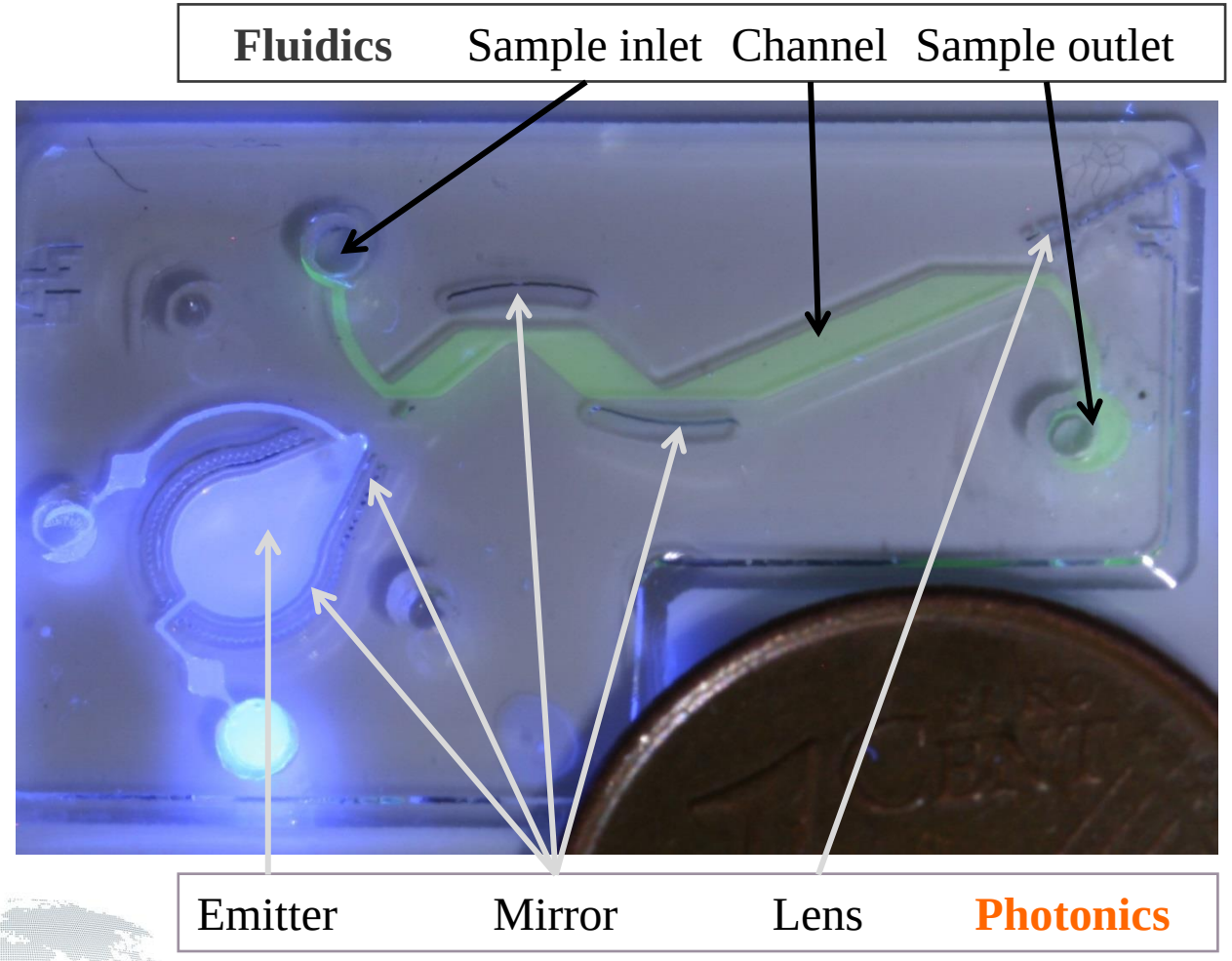


Photonic lab on a chip

Nanoelectronics **Nanomedicine** **Nanofluidics** **Nanophotonics**

Photonic lab on a chip (PhLoC)

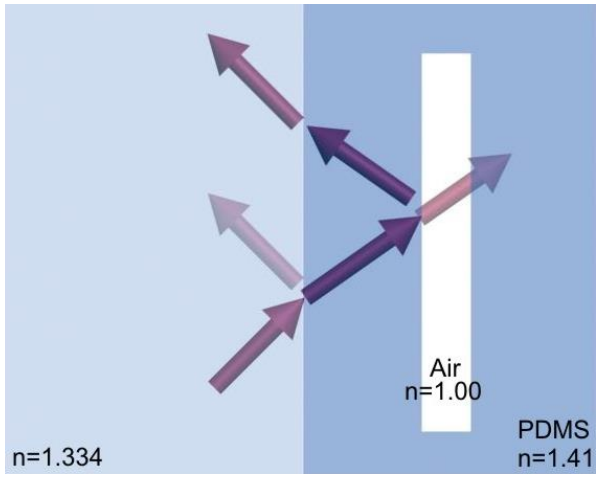
Integration of photonic elements in the vicinity of a LoC. Use of light as interrogation mechanism

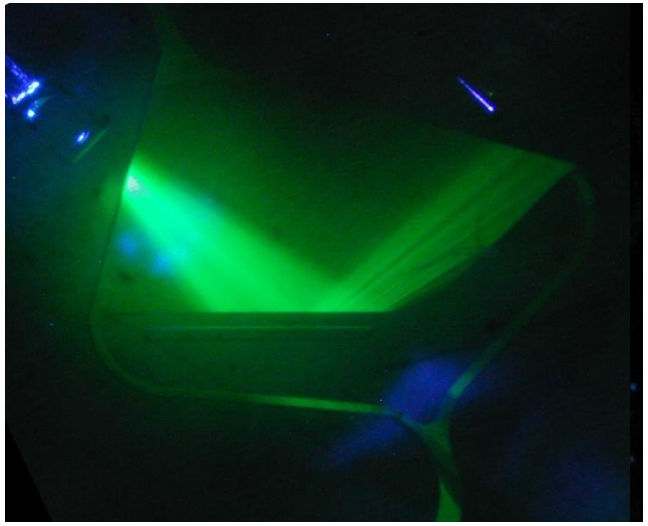


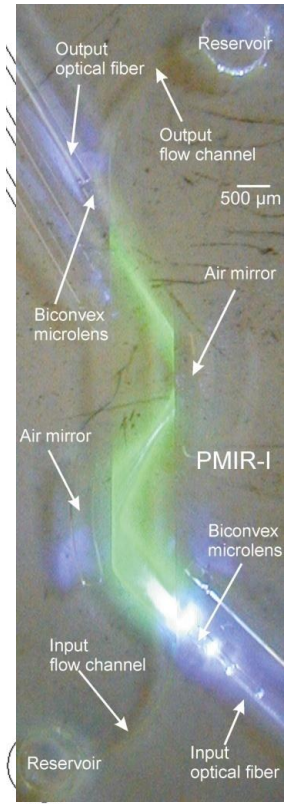
Optical transduction possibilities compatible with PhLoC:

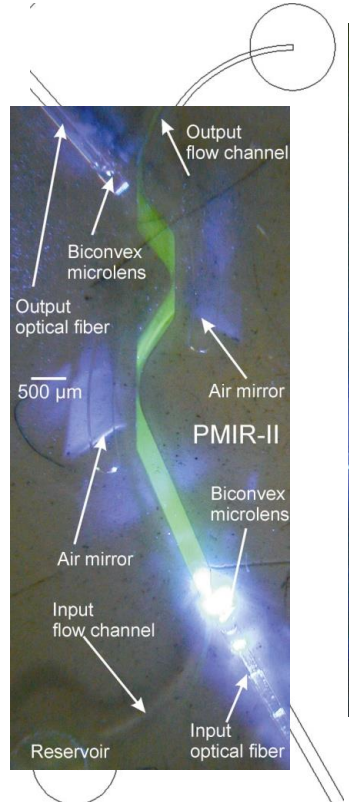
- Absorbance
- Fluorescence
- Interferometry
- Scattering
- Raman
- Plasmonics
- Correlation spectroscopy
- ….

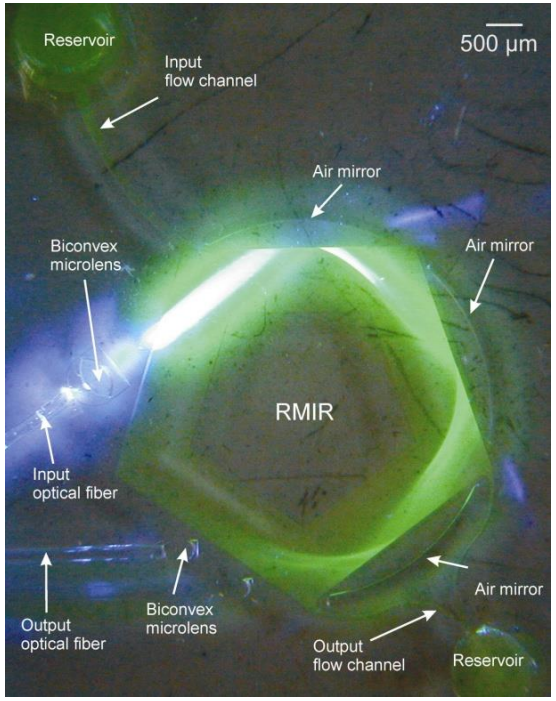
Integration: Mirrors







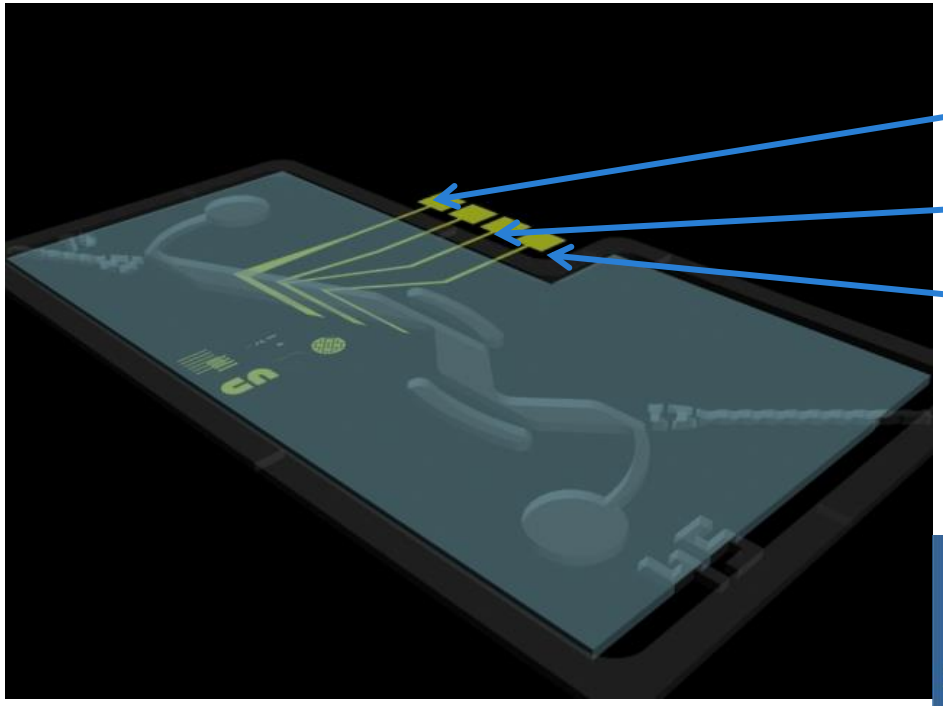




Suitable to be used mainly in absorbance measurements to lengthen the optical path

	LOD [nM]	Sensitivity [AU/mM]	Integration time [sec]	SNR [dB]
PR-90 (no mirror)	1830	5.19	2.5	12
PR-90 (mirror)	1080	6.90	0.08	19.5
PMIR-I	93	16.0	0.3	17
PMIR-II	110	13.6	0.3	17
RMIR	41	21.8	0.4	17

Dual optical-electrochemical LOC

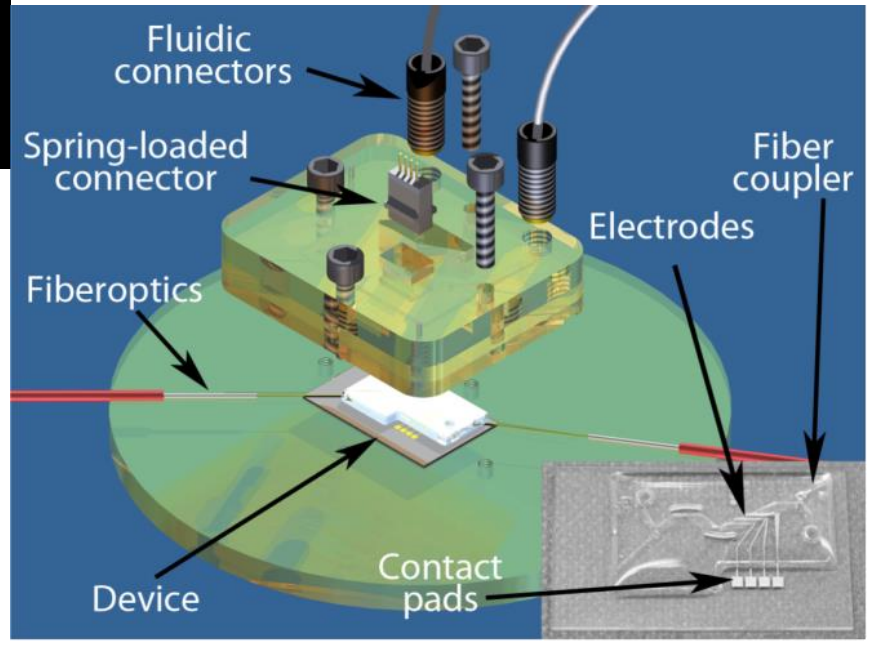


Counter electrode

Working electrode

Reference electrode

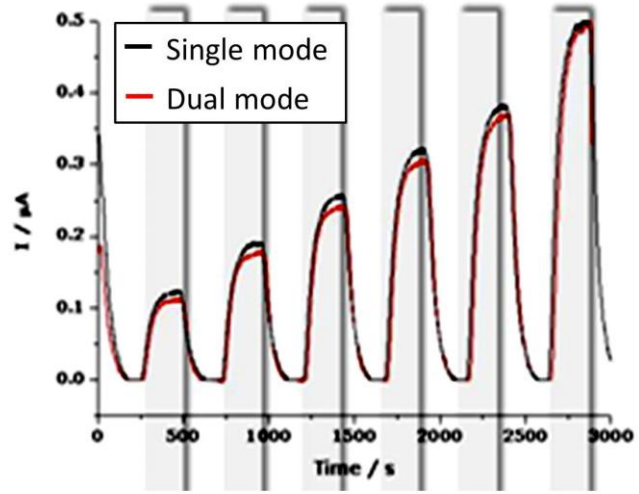
Simultaneous optical and electrochemical detection working in continuous flow regime



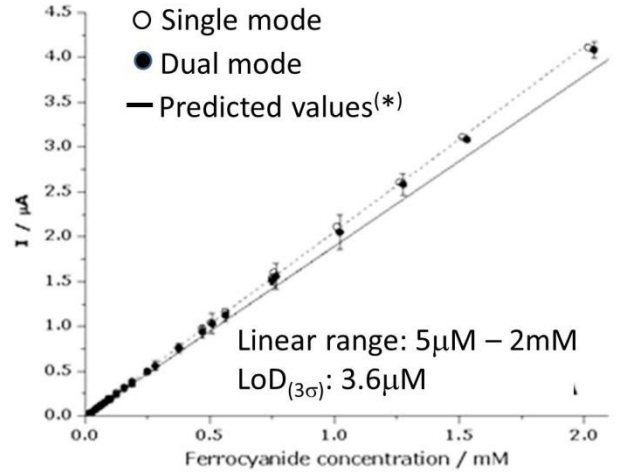
Dual optical-electrochemical LOC

Ferro/ferricyanide solutions

Electrochemical: +0.4V

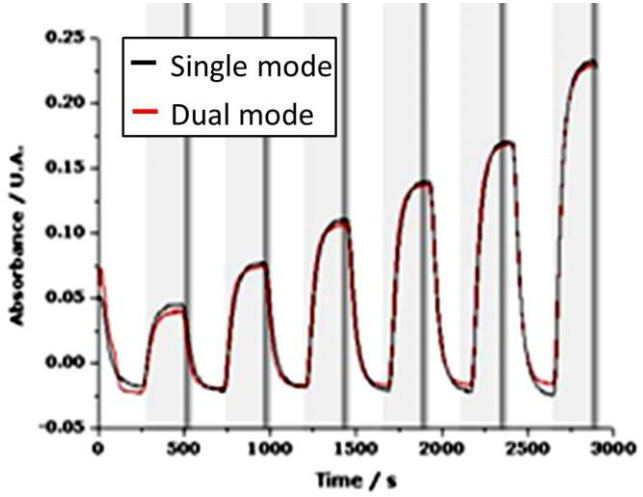


Response time: 4 min

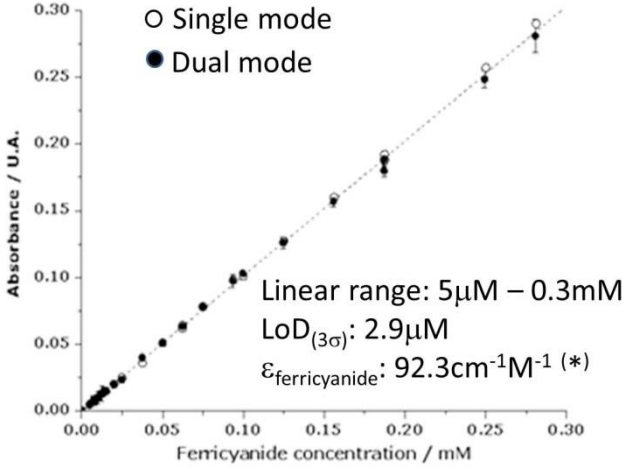


(*)From Levich equation

Optical: Abs_{420nm}



Response time: 4 min

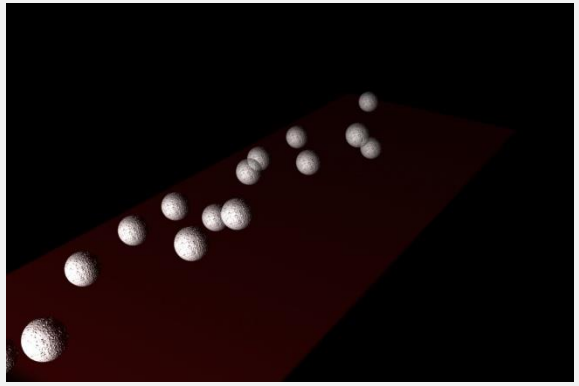


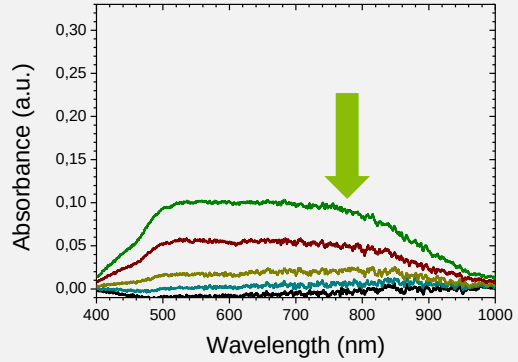
(*)From Beer-Lambert expression

PhLoC for scattering measurements

B. Ibarlucea et al. Anal. Chem 82 (10), (2010), 4246
J. Vila-Planas et al. Nat. Prot. 6(10), (2011), 1642

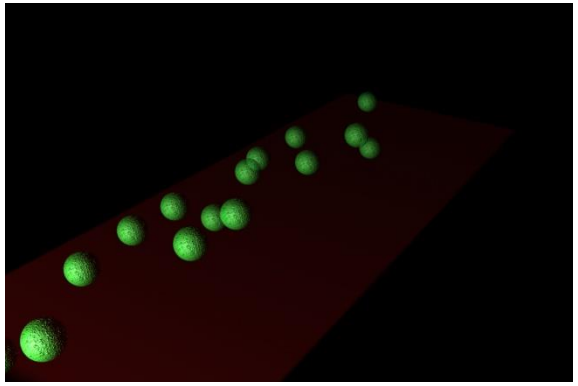
Case #1: Particles without absorption bands

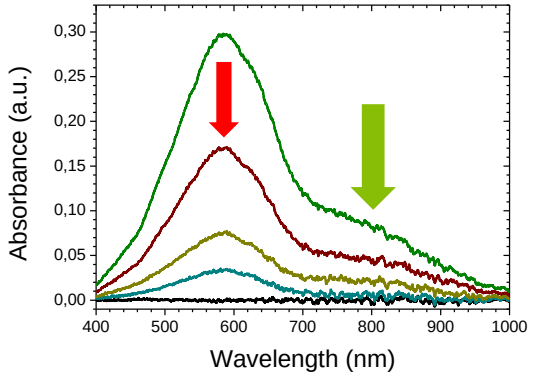




Variation of the **scattering band** with the particle concentration

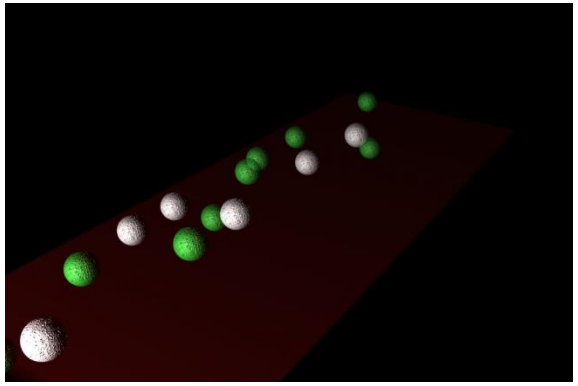
Case #2: Particles with absorption bands

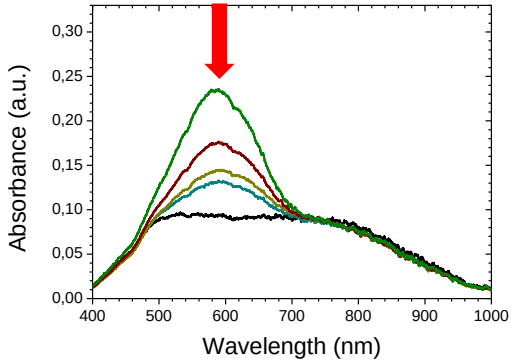




Variation of the **scattering** and **absorption** bands with the particle concentration

Case #3: Mixed particles at a constant total concentration





Variation of the **absorption** band with the labelled/non-labelled particle ratio

PhLoC for scattering measurements

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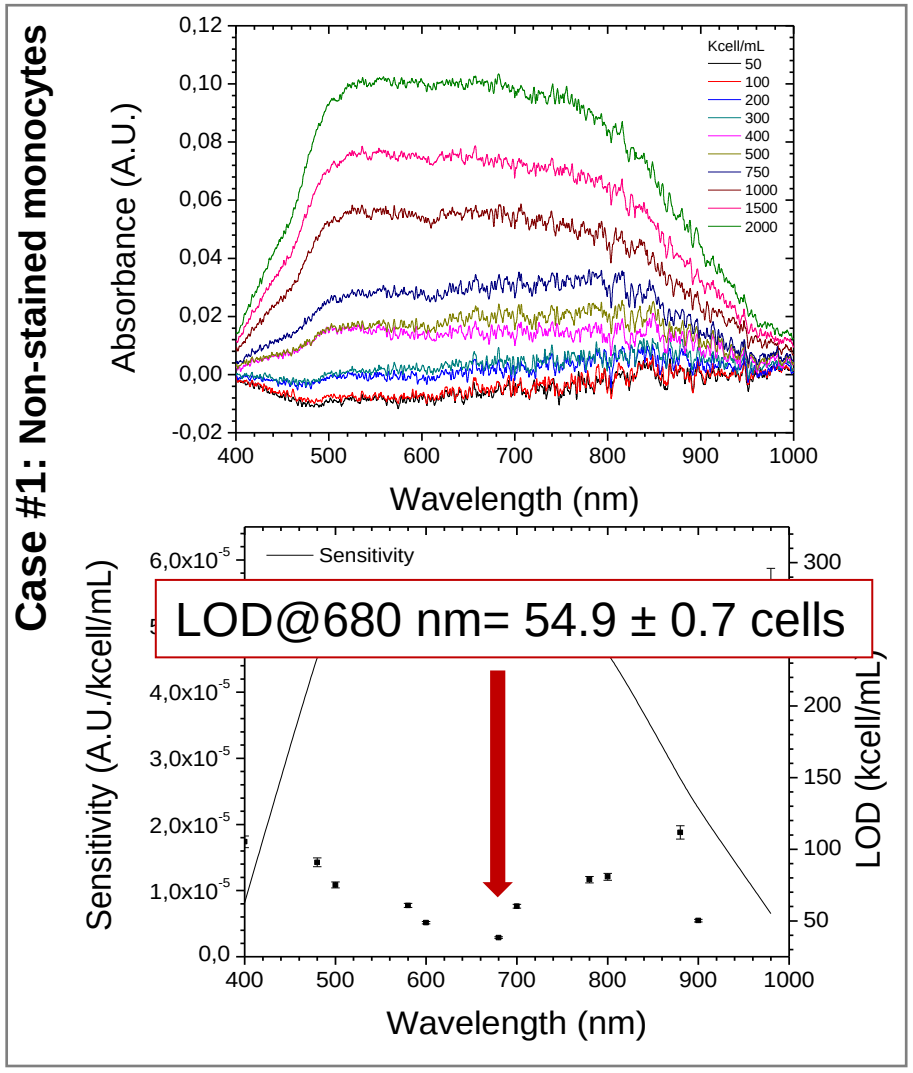
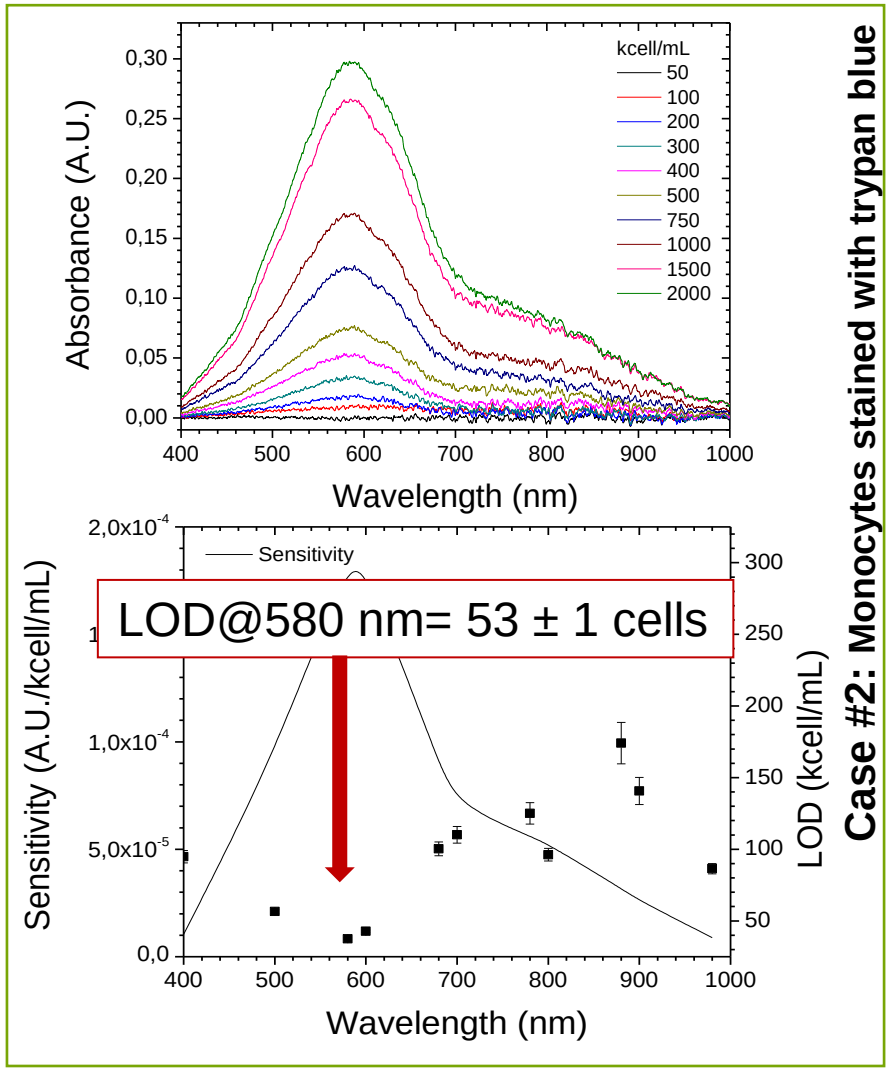
J. Vila-Planas et al. Nat. Prot. 6(10), (2011), 1642

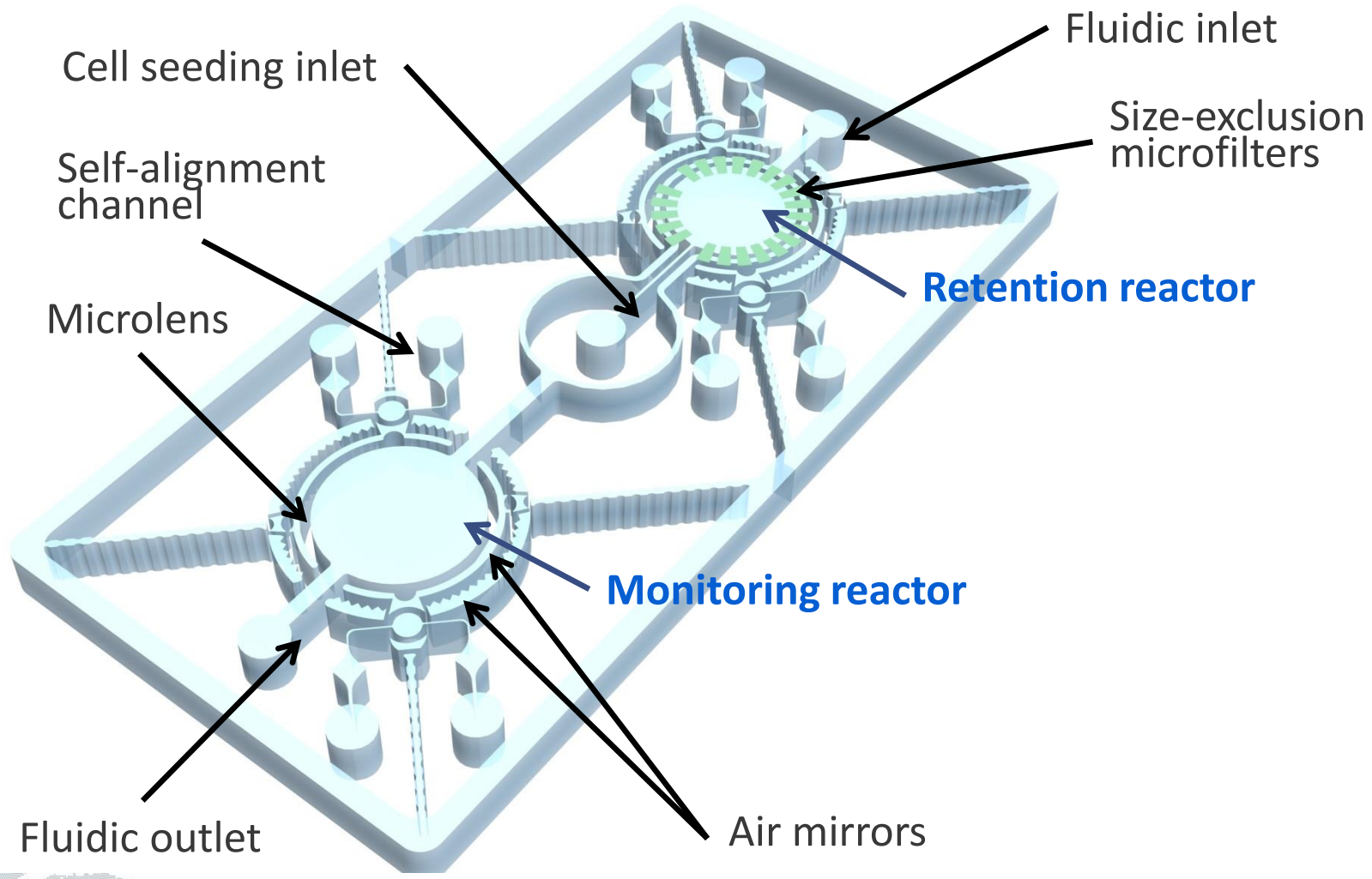


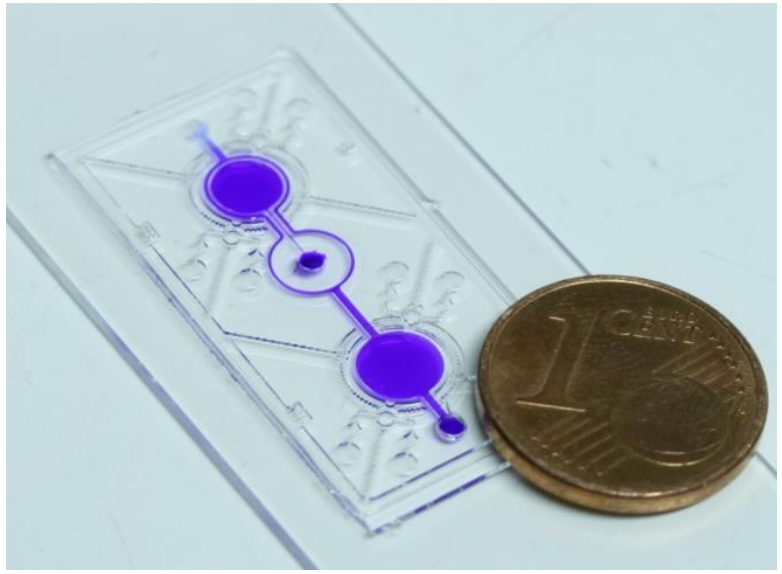


And this means…..

X. Muñoz-Berbel et al. Lab Chip 13(21), (2013), 4239

PhLoC for real time cell screening and separation



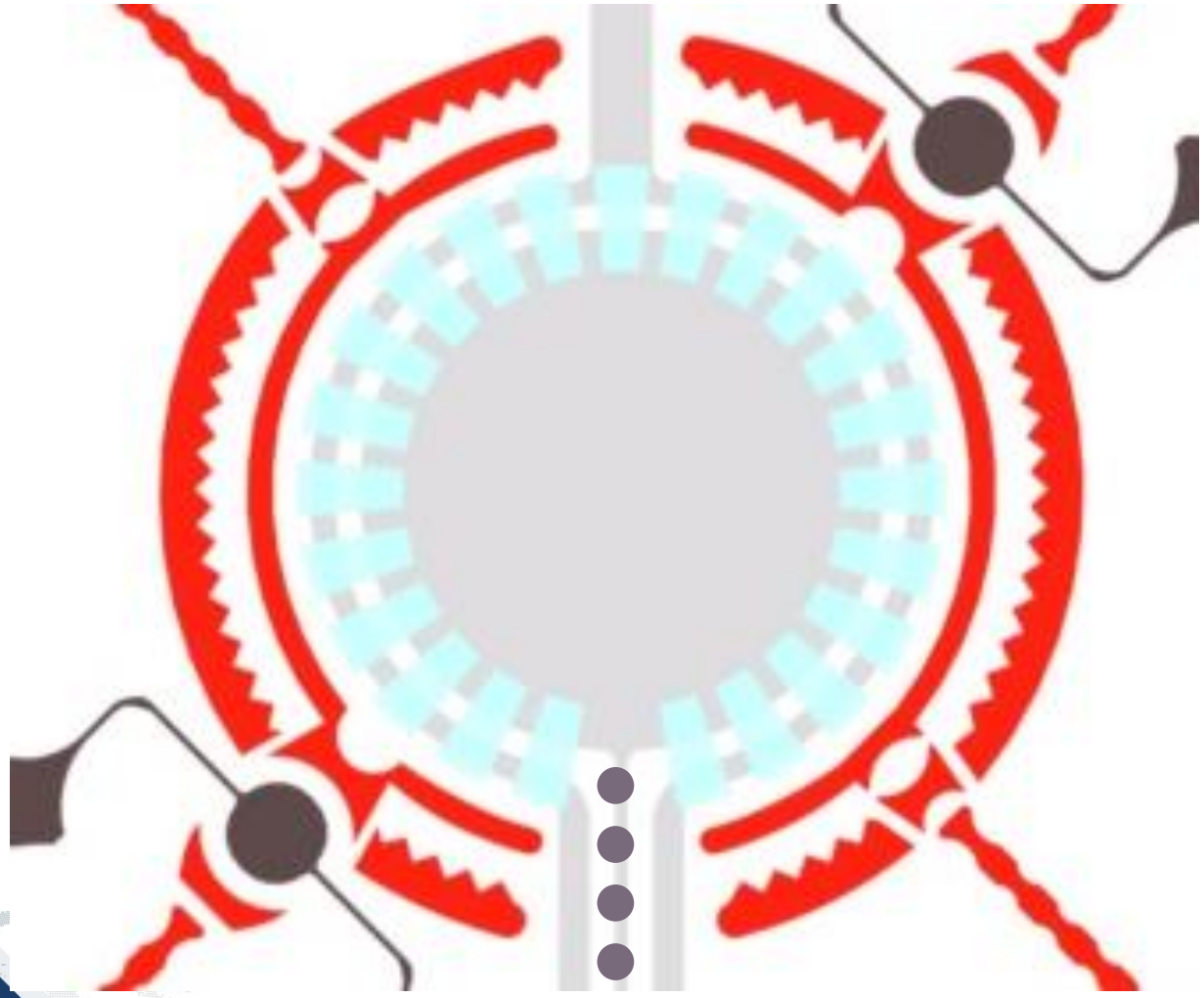


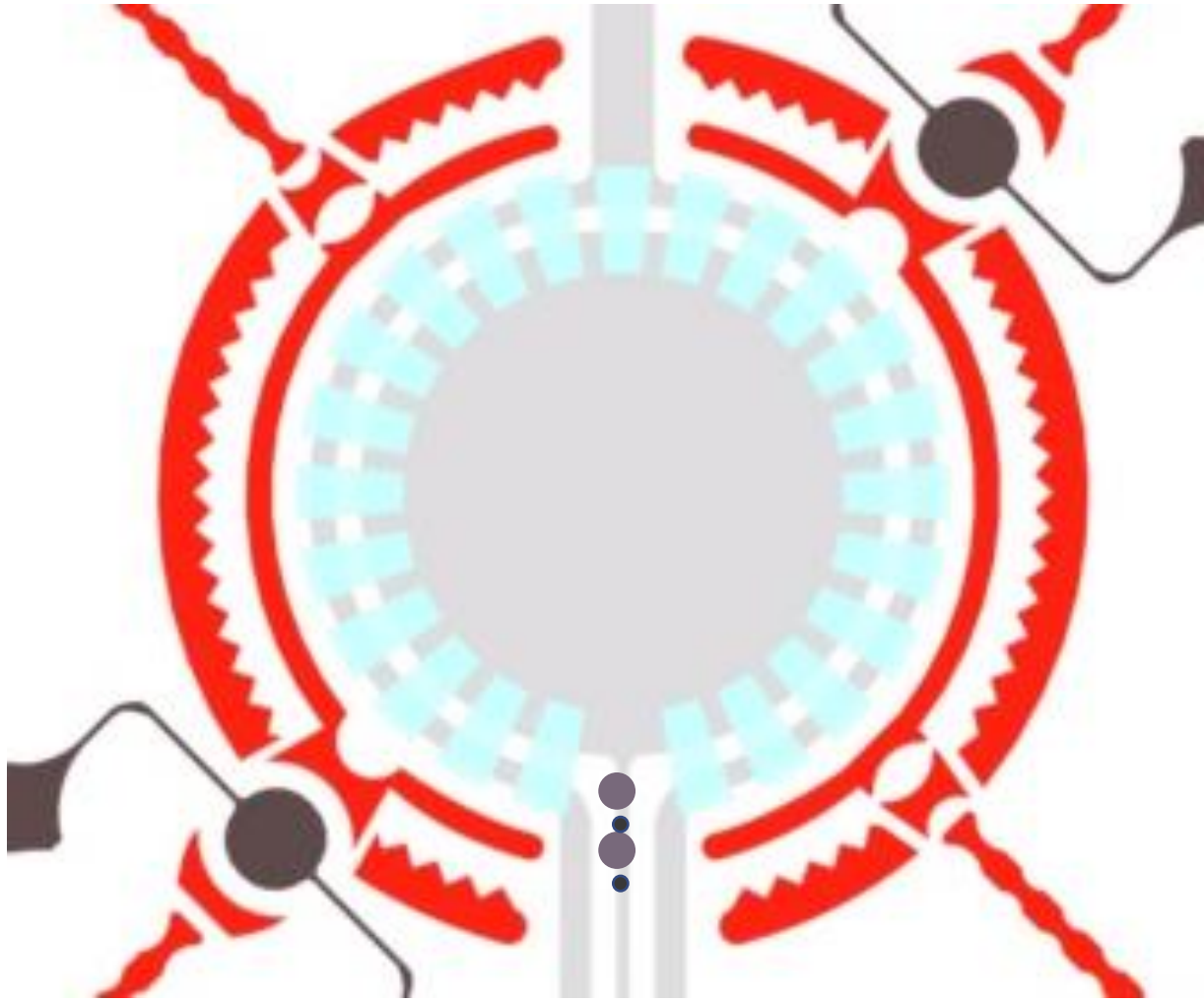
- Twin Reactors
- Independent cell seeding inlet
- Size exclusion microfilter (< 3µm)
- Reconfigurable
  - Absorbance
  - Fluorescence

X. Muñoz-Berbel et al. Lab Chip 13(21), (2013), 4239

PhLoC for real time cell screening and separation

Integrated size-exclusion microfilters





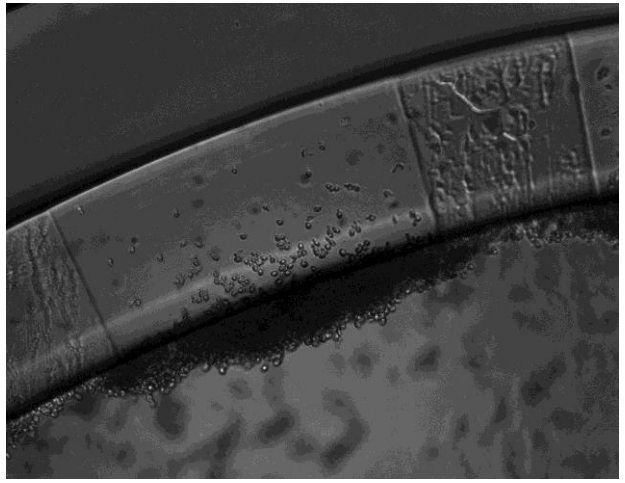
X. Muñoz-Berbel et al. Lab Chip 13(21), (2013), 4239

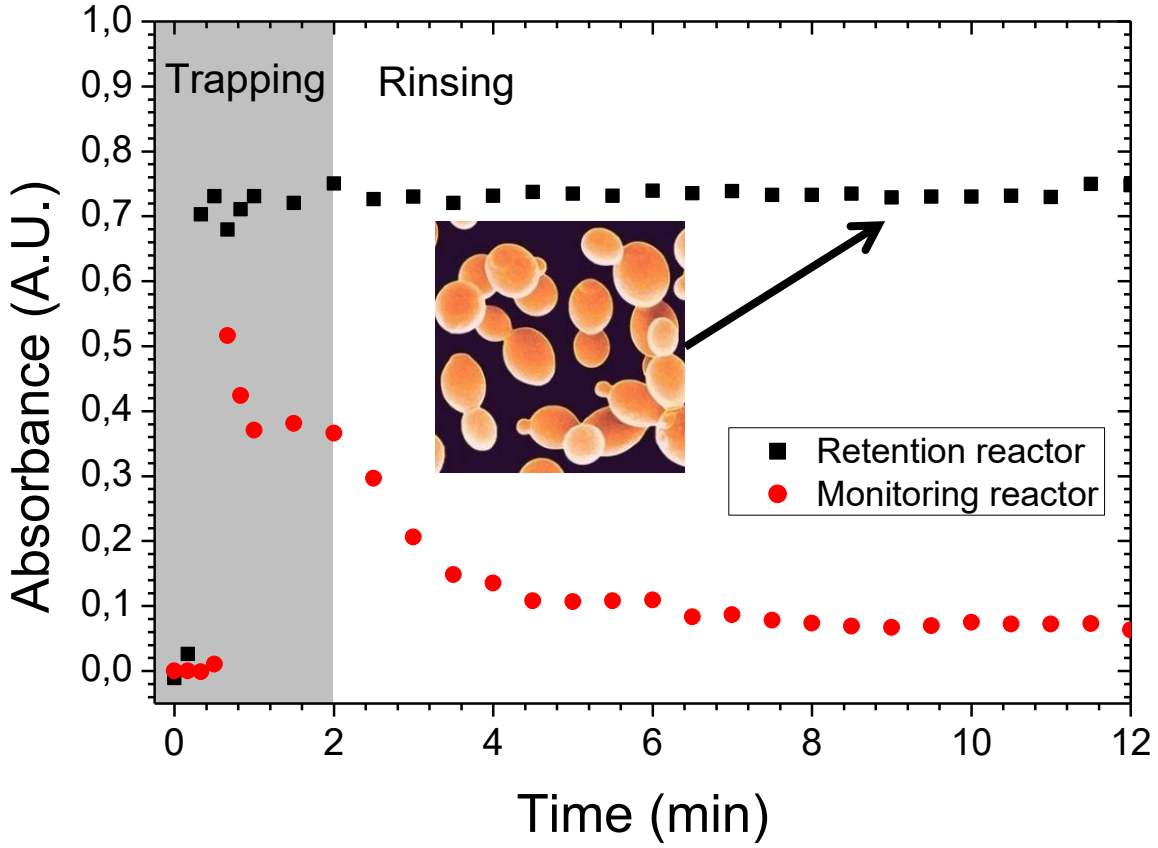
PhLoC for real time cell screening and separation

Biophotonic LoC

Saccharomyces cerevisiae

10^7-10^8 CFU
Round shaped
5-10 µm diameter
Re-suspended in PBS
100 µL/min





- Effective yeast cell entrappment
- Real time measurement

X. Muñoz-Berbel et al. Lab Chip 13(21), (2013), 4239

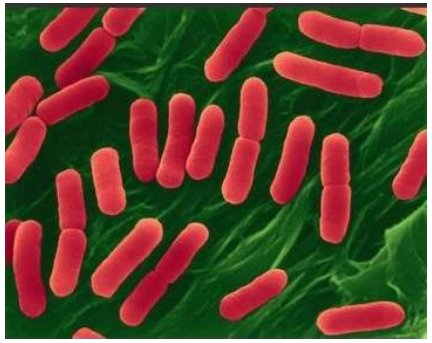
PhLoC for real time cell screening and separation

Size-dependent microorganism separation

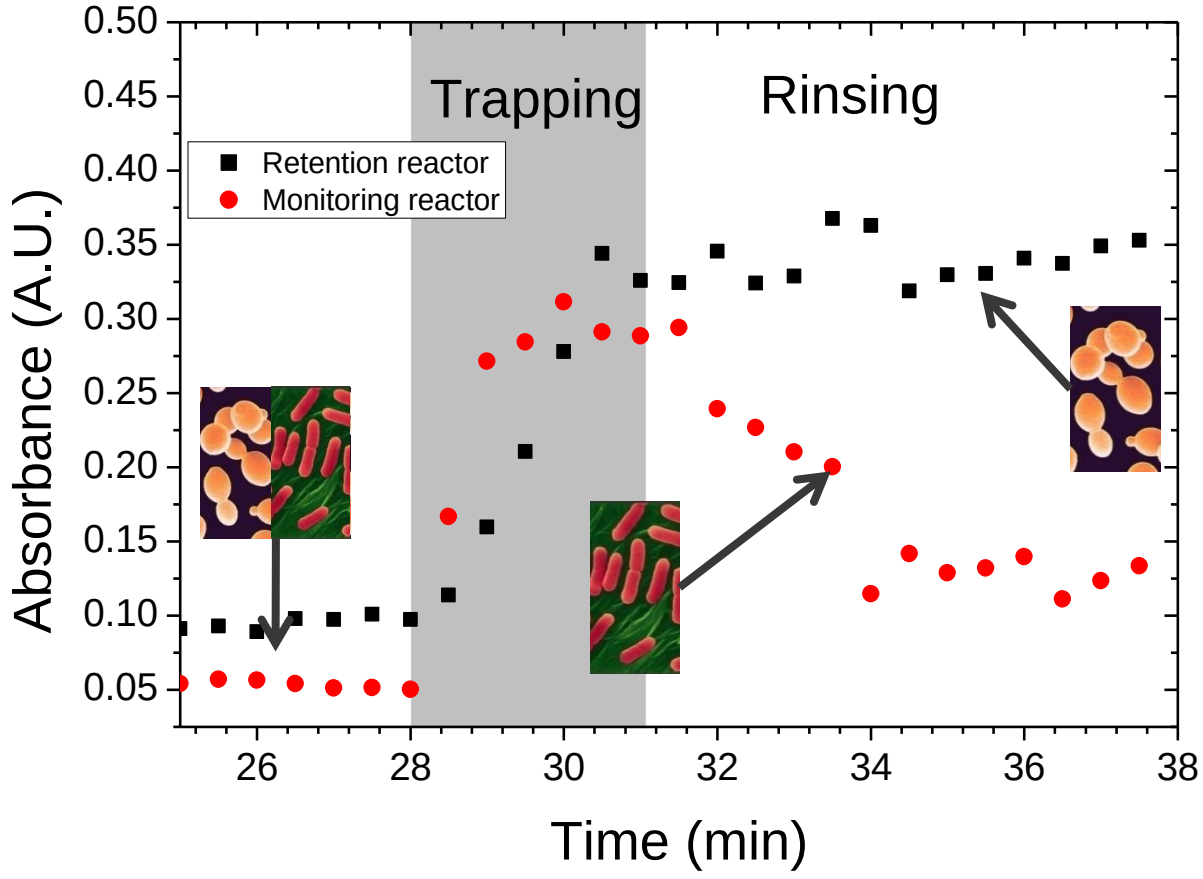
Saccharomyces cerevisiae

10^7-10^8 CFU
Round shaped
5-10 µm diameter
Re-suspended in PBS
100 µL/min

Escherichia coli



10^7-10^8 CFU
Rod shaped
1.5 x 0.5 µm (L:W)
Re-suspended in PBS
100 µL/min

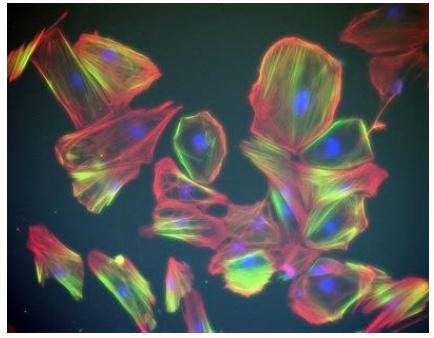


- Cell culture purification, microorganism separation…
- Real time measurement

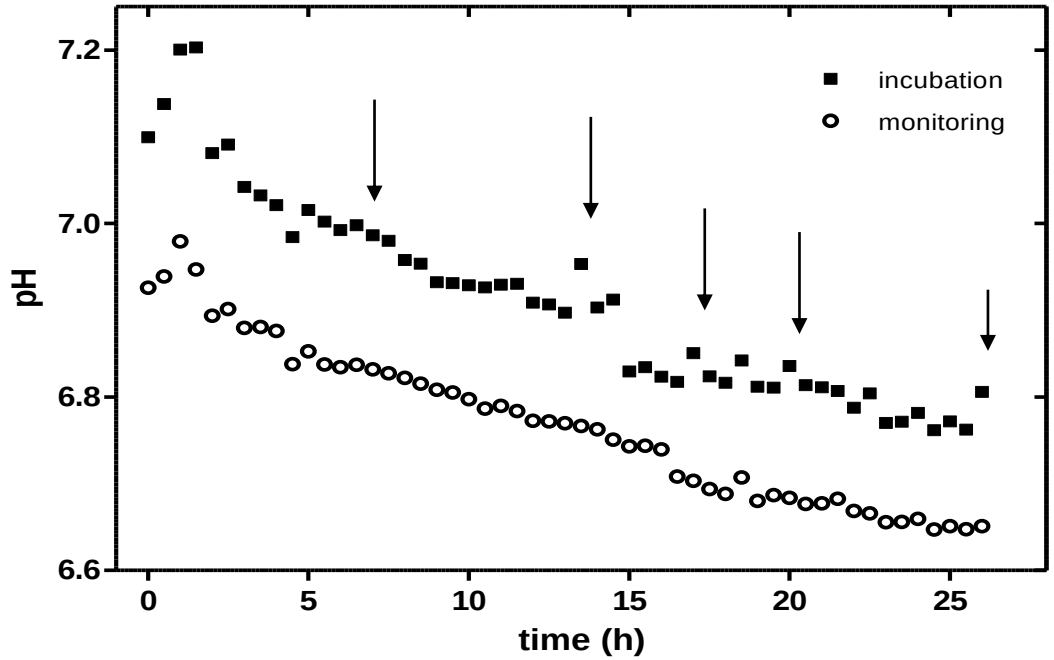
PhLoC for real time cell screening and separation

pH monitoring: phenol red (pH indicator present in DMEM)

Vascular smooth muscle cells (VSMC)



Rat aorta VSMC
10^4 cells/mL
Spindle shaped
Non-adhered: 5 -10 µm diameter
Adhered: 80 - 100 µm
Re-suspended in DMEM
Proliferation in typical hill-and-valley phenotype
Inoculation:100 µL/min
Measurement: 0,5 µL/min



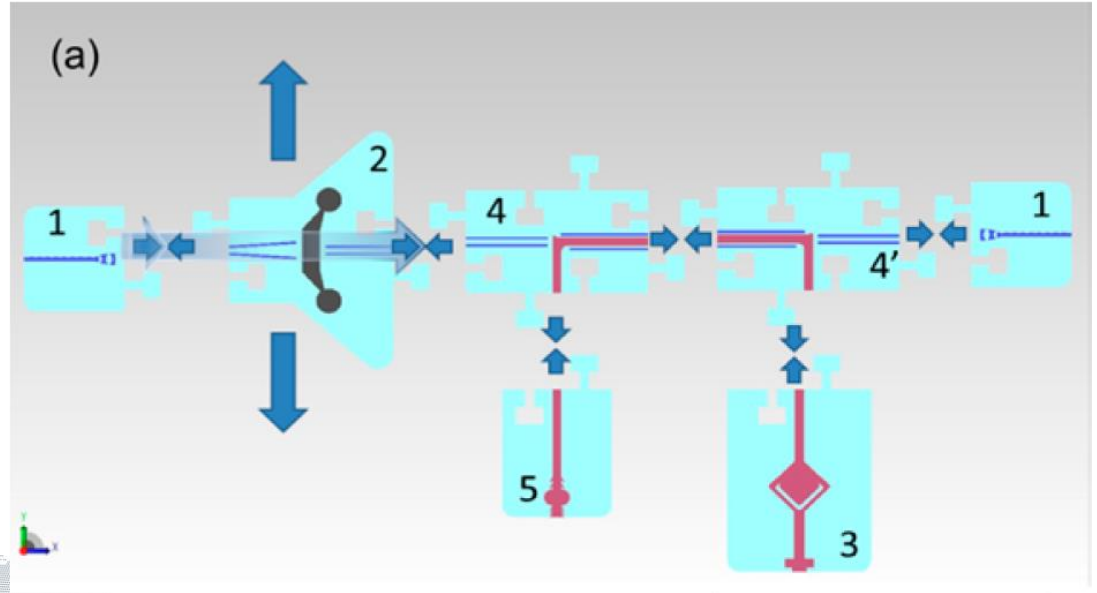
pH changes due to cell metabolism can be monitored with time without interference of cell attachment/detachment in the monitoring reactor (uncoupling the cell culture from the cell metabolism)

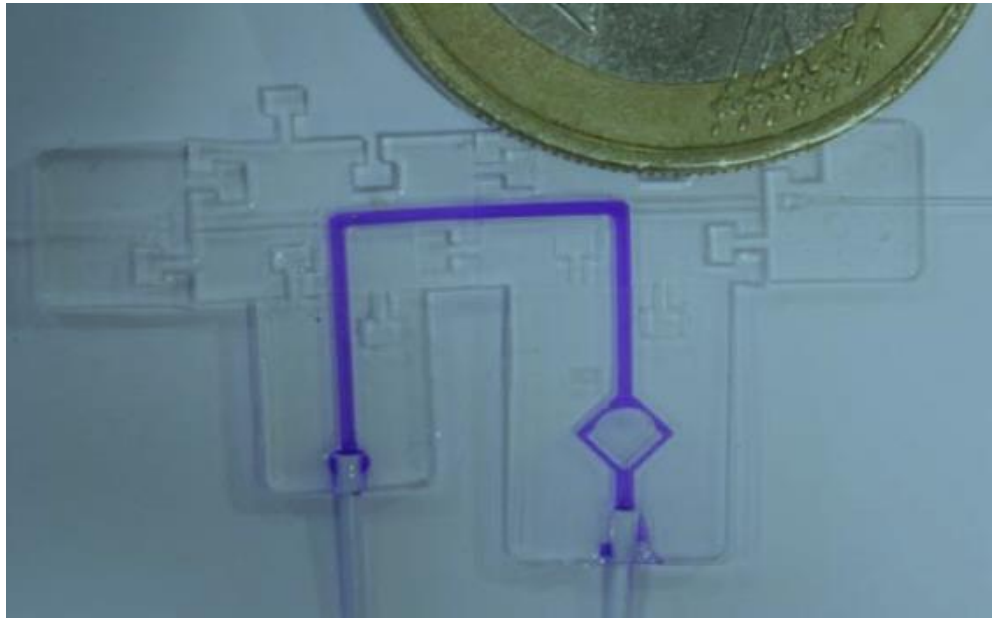
	seeding	trapping
incubation	7.3	8.2
monitoring	7.1	7.7
pH-meter	7.1	7.8

T. N. Ackermann et al. Proc. SPIE 10013, SPIE BioPhotonics Australasia, 100131C 2016;

Monolithic vs lego-like building blocks

(1) two fiber optics connections
(2) Absorbance filter (filled with a colorant or a doped sol−gel) which can be included or excluded as required,
(3) a fluidic inlet port with an internal air bubble based pressure regulator
(4/4′) two waveguides directed to a microchannel which is shielded with air mirrors to prevent optical cross-talk,
(5) Fluidic outlet port.





Redesign/replacement and improvement on-the-go

Acknowledgements

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