Microfluidic devices

I. Bernacka-Wojcik[1], F. Perreira[1; 2], P. U. Alves[1], V. Rodrigues[1], M. Soares[1], D. Matos[1], M. T. Lobato[1], B. Veigas[1]; [3], F. Carlos[3], P. Lopes[4], L. Hillou[5], A. Oliva[2], R. Igreja[1], P. Baptista[3], E. Fortunato[1], H. Aguas[1], R. Martins[1]

[1]Departament of Materials Science and I3N, FCT-UNL, Campus de Caparica, 2829-516 Caparica, Portugal
[2]Biomolecular Diagnostics Laboratory, ITQB, Av. da República - Qta do Marquês, Apartado 12, 2781-901 Oeiras, Portugal
[3]CIGMH, Departamento de Ciências da Vida, Faculdade de Ciências e Tecnologia, Universidade Nova de Lisboa, Campus de Caparica, 2829-516 Caparica, Portugal
[4]Department of Physics and I3N, University of Aveiro, Campus Santiago, 3810-193 Aveiro, Portugal
[5]Institute for Polymers and Composites and I3N, University of Minho, Campus de Azurém 4800-058 Guimarães, Portugal
Corresponding details: H. Águas hma@fct.unl.pt and R. Igreja rni@fct.unl.pt; tel: +351212948564

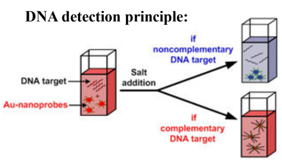
www.cenimat.fct.unl.pt

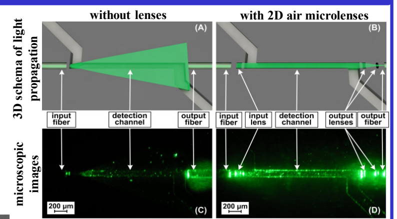
Abstract

Miniaturization is a recent trend in analytical chemistry and life sciences due to the possibility of performing sophisticated analysis within a hand hold size, faster sample analysis, higher throughput, portability, reduced reagent use, all of which are associated with decreased cost. We have developed microfluidic devices (μFL) for: (A) colorimetric DNA detection based on gold nanoparticles; (B) micromixing; (C) electro-optical biosensor for characterization of single cells; (D) cell trapping in Quantum Dots assays. In parallel, digital microfluidic devices for digital control of single μL droplets and impedance analysis for DNA detection based on gold nanoparticles are under investigation.

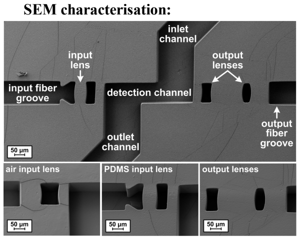
Colorimetric DNA detection

DNA detection principle:



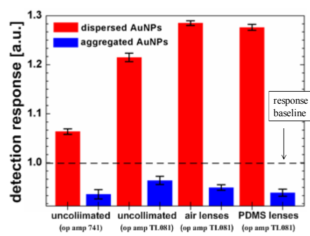


SEM characterisation:

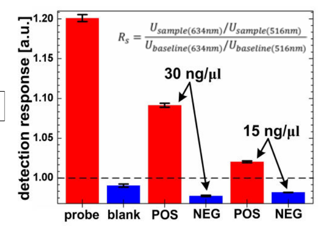


- ✓ Optimized optoelectronic acquisition system yielded increased accuracy and reduced noise.
- ✓ The proper light collimation resulted in a 6 times higher signal-to-loss ratio.
- ✓ The μFL platform coupled to the non-cross-linking colorimetric assay enabled detection a single nucleotide mismatch associated with increased risk of obesity (*FTO*) using target DNA concentration below the limit of detection of the conventionally used microplate reader with 10 × lower solution volume.

[Bernacka-Wojcik I. et al. Biosens Bioelectron, 2013, 48, 87-93.]



The detection response (R_s) of the microfluidic platform for dispersed (in red) and aggregated (in blue) AuNPs solutions.



Results of the colorimetric DNA detection of the *FTO* single nucleotide polymorphism (SNP).

Digital microfluidics

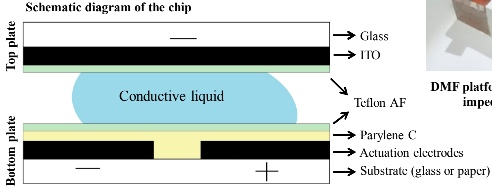
Digital microfluidics is variation of microfluidics in which individual droplets are controlled, instead of a continuous flow. This control is achieved not through micropumping systems, but through voltage application on an electrode array, by the electrowetting on dielectric (EWOD) phenomena.

This approach allows further reduction of solution volumes to the nL scale and can greatly reduce the complexity of the system, since drops can me mixed, moved, merged and cut, through the control of the applied voltage on each electrode, instead of using mechanical structures. It also allows an additional detection method, through the drop's impedance variation measurement.

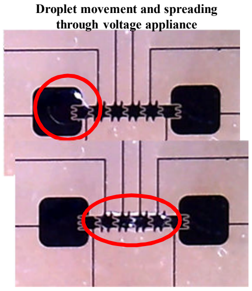
Efforts are also being made towards making a functioning device on a paper substrate.

DMF platform for droplet control and impedance variation tests.

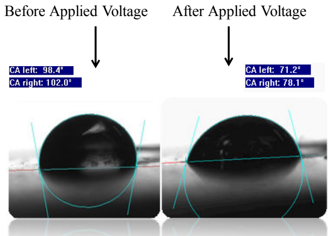
Schematic diagram of the chip



Droplet movement and spreading through voltage appliance

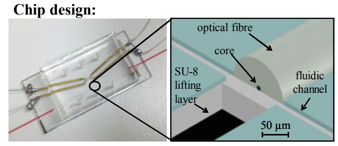


EWOD of buffer solution with Au probes on paper substrate

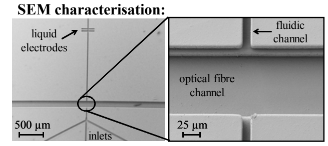


Electro-optical chips for single cells

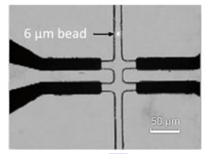
Chip design:

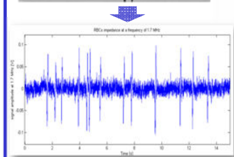


SEM characterisation:



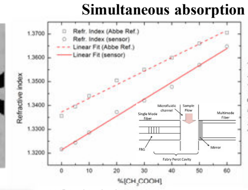
Electrical properties:



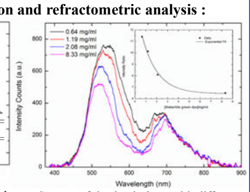


Particles were counted and sized by applying the AC Discrete Frequency System and analysed in LabView and MatLab.

Simultaneous absorption and refractometric analysis :

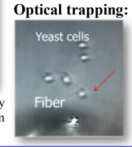


Refractive index measured by the Abbe refractometer and the uFL platform.



Spectra of dyed solutions with different concentration of Malachite Green dye.

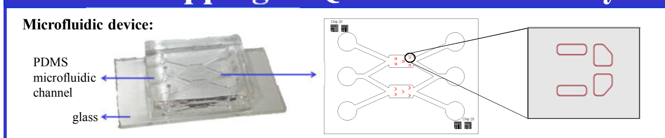
Optical trapping:



- ✓ Particles were successfully identified and counted by electrical impedance and also by fluorescence analysis.
- ✓ Simultaneous measurement of refractive index and absorption **spectroscopy** of dyed acetic acid solutions
- ✓ Measuring the Refractive index of beads and cells requires stopping of the cell in the fiber optic. Work is in progress to implement in chip optical trapping.

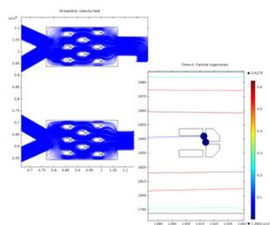
Cells trapping in Quantum Dots assays

Microfluidic device:



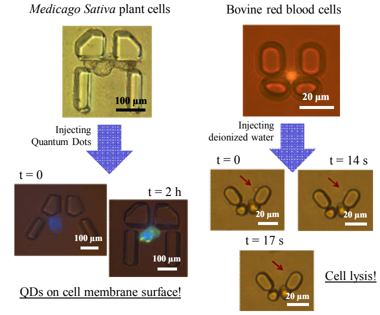
Example of a chip conformation with "U" shape structures for cell trapping. This chip allows to modify the surrounding medium and monitor the cell responses through the time while they are trapped.

Theoretical results:



COMSOL simulations of streamlines profile and particle trajectories.

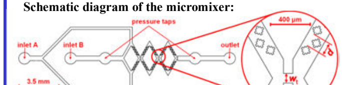
Experimental assays:



QDs on cell membrane surface!

Micromixer

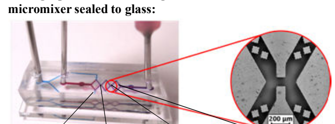
Schematic diagram of the micromixer:

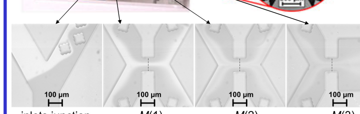


Mixing unit:
rhombic (60º) with diamond-shape obstacles and rectangular contractions

Variables:
w_t = 100–400 μm; d = 60–140 μm; Re = 0.1–117.6

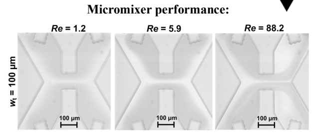
Photograph and SEM image of PDMS micromixer sealed to glass:



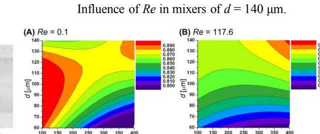


Optical microscopy images taken at different locations along the micromixer with w_t = 100 μm and d = 140 μm at Re = 8.2.

Micromixer performance:



Influence of Re in mixers of d = 140 μm.



The contour plots of the overall desirability to obtain the highest M values with dP as low as possible.

Statistical analysis:
1. data sieving
2. fitting a mathematical model: 2[nd] order polynomial for $M(1)$; $M(2)$; $M(3)$ and dP
3. significance analysis:
   for M: Re > number of rhombi > w_t > d
   for dP measured after three rhombi: Re > d
4. desirability

Characteristics:

Mixing efficiency (M):	80% (can be considered as full mixing)
Pressure drop (dP):	6 Pa (Re = 0.1); 5.1×10⁴ Pa (Re = 117.6)
Mixer length:	2.5 mm (one of the shortest planar passive micromixers to date)

UNINOVA
i3N INSTITUTE FOR NANOSTRUCTURES, NANOMODELLING AND NANOFABRICATION
FACULDADE DE CIÊNCIAS E TECNOLOGIA UNIVERSIDADE NOVA DE LISBOA