Project III. 3

BIO-MICROSYSTEMS

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Graduate Students : Maria Zavali

Objectives:

- Development of bioanalytical lab-on-a-chip devices based on monolithic optoelectronic transducers (bioactivated optocouplers). Development of white light interferometric setup for label free monitoring of biomolecular reactions.
- Develop highly sensitive and/or label free assays suitable for point of care applications
- Develop microfluidic channels integrated on transducer silicon chips
- Use soft lithography, Deep Plasma Etching, and plasma assisted bonding to fabricate PDMS, PMMA (and other organic polymer) based microfluidic devices
- Fabricate capillary electrophoresis, and chromatography devices
- Develop open microfluidics using electrowetting actuation
- Develop novel plasma based micro array technologies

Funding:

- EU, IST, STREP, “NEMOSLAB”, NanoEngineered Monolithic Optoelectronic transducers for highly Sensitive and LAbel-free Biosensing (coordinated by K. Misiakos start 1-1-2006, end 31-12-2008)

RESEARCH RESULTS

A. Single binding event detection

Label-free protein detection through one dimensional monolithic photonic crystal engineering

SU-8 microchannel integration on optocoupler chips.

Lithography and plasma processes for microfluidics fabrication

Optocouplers employing fibers of 2 μm in width can demonstrate the effect of single binding event detection if big enough labels are used. Such a demonstration is outlined in Fig. III.3.1 where the Biotin-Streptavidin model assay is employed and 1 μm polystyrene beads as labels. Each binding event introduces an identifiable step downwards in the detector photocurrent.

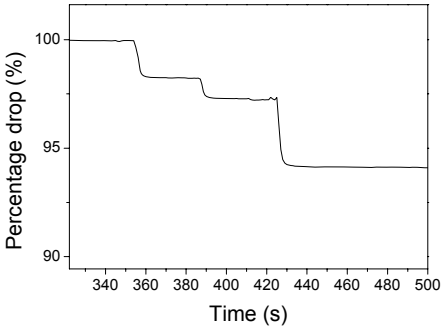


Fig. III.3.1: *Single binding event detection assay. Biotinylated BSA was spotted on a 2 micron wide fiber. Streptavidin labeled with polystyrene coated paramegnetic beads (one micron in diameter) was introduced in a dilute solution (10^8/cm^3) so that at each moment only one bead (on average) was present in the fluidic channel above the fiber. Each binding event introduces a significant and identifiable drop in the photocurrent due to scattering of waveguided photons .*

The optocoupler chips can be applied to label free detection by grafting on the waveguide a latent photonic crystal through APTES pattering. Biomolecular coating and binding on the patterned waqveguide surface induces wavelength filtering and subsequent signal transduction as shown in Fig. III.3.2.

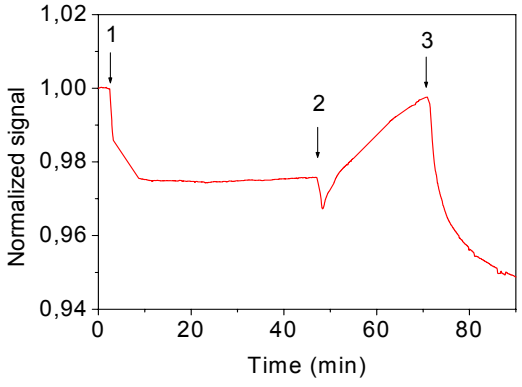


Fig. III.3.2: *Representative real time monitoring of reactions performed onto fibers engineered with photonic crystals. The sequence is as follows: up to arrow 1: washing with coating buffer; arrows 1-2: coating a with 400 nM biotinylated BSA solution (0.0025 %); arrows 2-3: blocking solution (1% BSA); arrow 3 to end: 10 nM streptavidin buffer in blocking solution. The signal was normalized in respect to its initial value.*

Microfluidic channels are nessacary in biosensing microdevices to supply sample and reagents. They are made by SU-8 photoresist coating (Fig. III.3.3) and form channels after being covered with elastomeric covers and pressed.

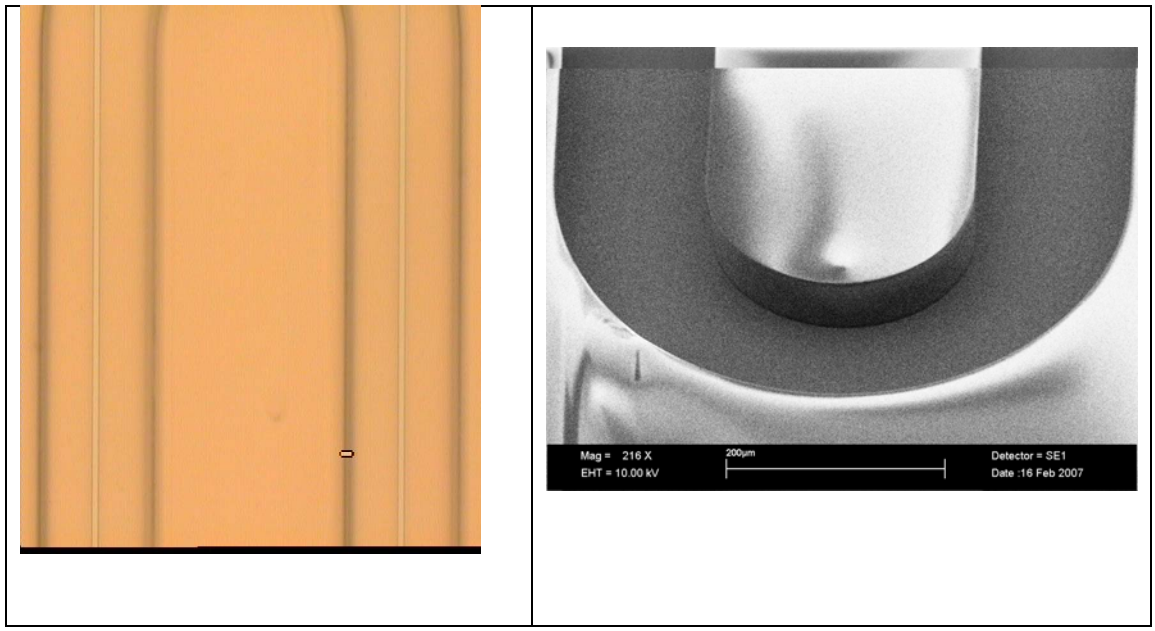
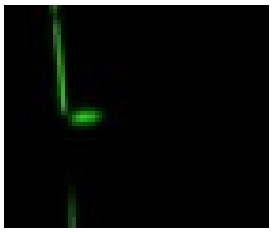


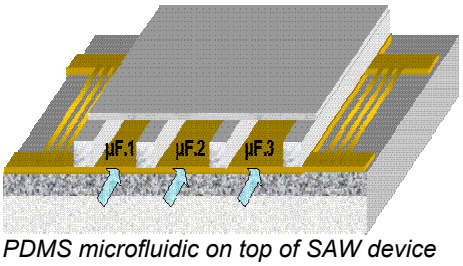
Fig. III.3. 3: *Open fluidic channels. Left: A view of 150 µm fluidic channels with the 8µm waveguide within. The fluidic walls are 50 microns high. Right: A SEM picture on a test wafer showing how vertical the fluidic walls are. The artifacts on top of the SU-8 film are charging effects.*

B. Lithography and plasma processes for microfluidics fabrication Results:

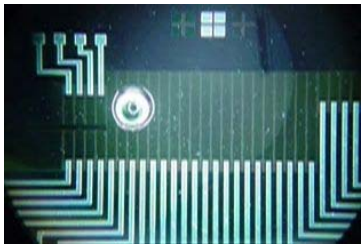
Development of fabrication processes for PMMA and PDMS microfluidics: soft lithography, deep plasma etching, bonding
Fabrication of capillary electrophoresis devices on PMMA using plasma etching. Investigation of the effect of superhydrophilic, or superhydrophobic wall on electroosmotic flow.
Fabrication of a gas chromatography microcolumn and multi-channel microfluidic modules integrated on a biosensor
Development of actuation technology for microfluidics based on electrowetting. Electrowetting-based transport of liquid droplets was demonstrated on open microfluidic devices.
Development of methodology for fabrication of protein micro-arrays based on selective plasma-based surface modification of patterned Si/SiO_2 substrates



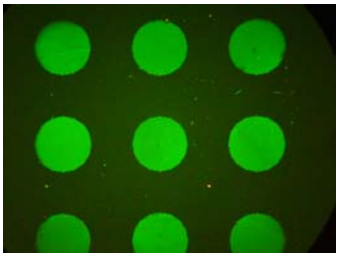
Electrophoresis in PMMA microfluidic



PDMS microfluidic on top of SAW device



Electrowetting-based droplet transport on open microfluidic device



Protein micro array by novel technology

For details on the above, please see **Project I. 2: LITHOGRAPHY and PLASMA PROCESSES for ELECTRONICS, MICROFLUIDICS, and SURFACE Nano-ENGINEERING** (Part **B**)

PROJECT OUTPUT in 2007

Publications in International Journals

1. "Electrowetting on plasma-deposited fluorocarbon hydrophobic films for biofluid transport in microfluidics", Bayiati, P., Tserepi, A., Petrou, P.S., Kakabakos, S.E., Misiakos, K., Gogolides, E. Journal of Applied Physics 101 (10), 2007
2. "Biofluid transport on hydrophobic plasma-deposited fluorocarbon films", Bayiati, P., Tserepi, A., Petrou, P.S., Misiakos, K., Kakabakos, S.E., Gogolides, E., Cardinaud, C., Microelectronic Engineering 84 (5-8), pp. 1677-1680, 2007
3. "A biomolecule friendly photolithographic process for fabrication of protein microarrays on polymeric films coated on silicon chips", Petrou, P.S., Chatzichristidi, M., Douvas, A.M., Argitis, P., Misiakos, K., Kakabakos, S.E. Biosensors and Bioelectronics 22 (9-10), pp. 1994-2002, 2007

Conference Papers

1. "Real-time and label-free determination of analytes using a bioanalytical microsystem based on a monolithic silicon optoelectronic transducer", P.S. Petrou, E. Mavrogiannopoulou, S.E. Kakabakos, K. Misiakos, 4th pHealth Conference, Porto karras Chalkidiki, Grrece June 20-22, 2007
2. "Detection of BRCA1 gene mutations in real-time using a monolithic optoelectronic transducer", P.S. Petrou, E. Mavrogiannopoulou, S.E. Kakabakos, K. Misiakos 5th International Conference on Instrumental Methods of Analysis Modern Trends and Applications, IMA 2007, Rio, Patras Greece, 30 September-4 October, 2007.