2010 Concertation and Consultation Workshopon Micro-Nano-Bio Convergence Systems

NanoEngineered Monolithic Optoelectronic transducers for highly Sensitive and LAbel-free Biosensing

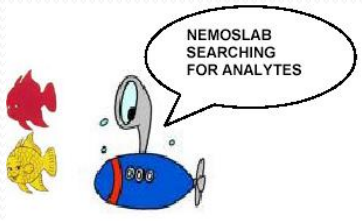
NEMOSLAB

Panagiota Petrou

Immunosensors/Immunoassay Lab.

Institute of Radioisotopes & Radiodiagnostic Products

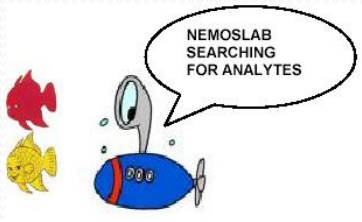
NCSR "Demokritos"



Start date of the project: 1-1-2006
End date of the project : 30-06-2009

Partners

- NCSRD (Coordinator, EL)
- FhG/IBMT (D)
- Technobiochip (TB) (I)
- STMicroelectronics (I)
- University of Copenhagen (DK)
- Biomedica L.S. (EL)
- IMTEK (D)
- Dortmund IVF (D)



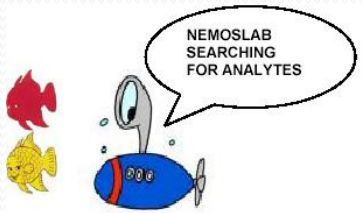
Project objective:

Lab-on-A-chip based on **monolithic soliucon optoelectronic transducers** for **protein and DNA detection**

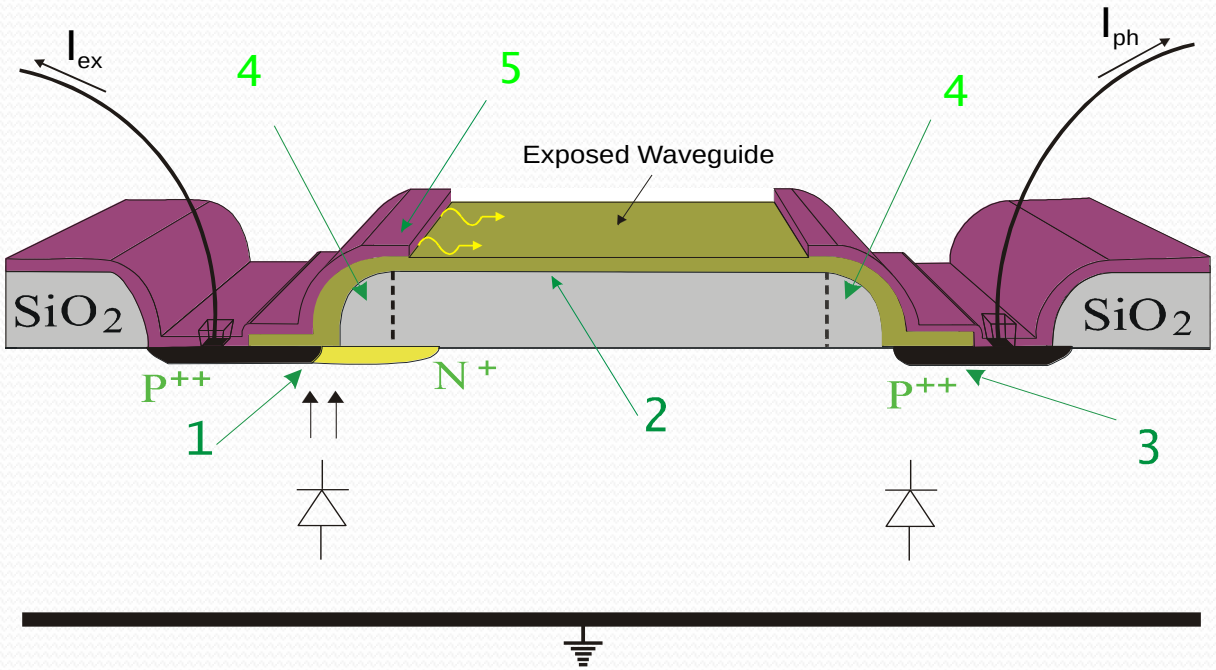
Targeted applications:

Label-free detection of BRCA1 gene mutations associated with breast/ovarian cancer predisposition diagnosis.

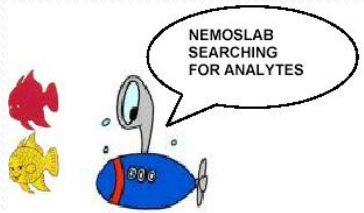
Highly sensitive determination of a panel of hormones (glycoproteins and steroids) related to diagnosis of female fertility disorders for in-vitro fertilization applications.



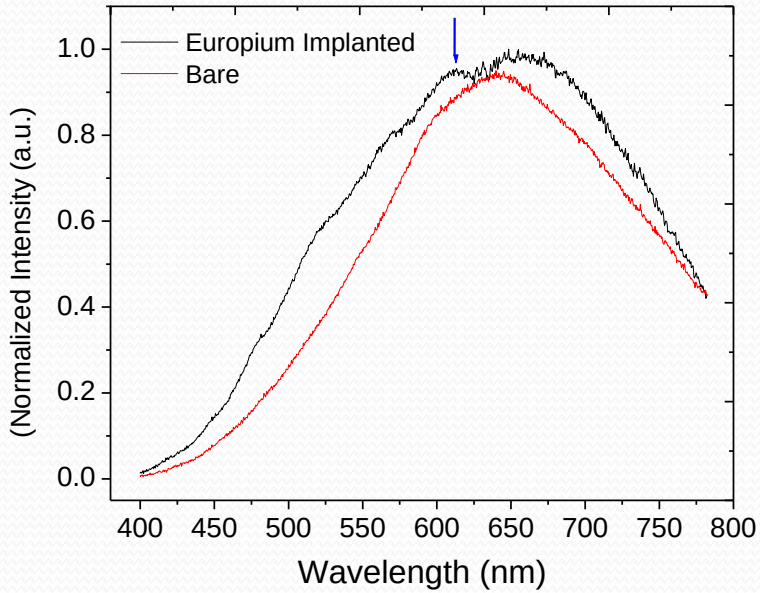
Monolithic Silicon Optoelectronic Transducers based on silicon avalanche diodes self-aligned to optical fibers and detectors



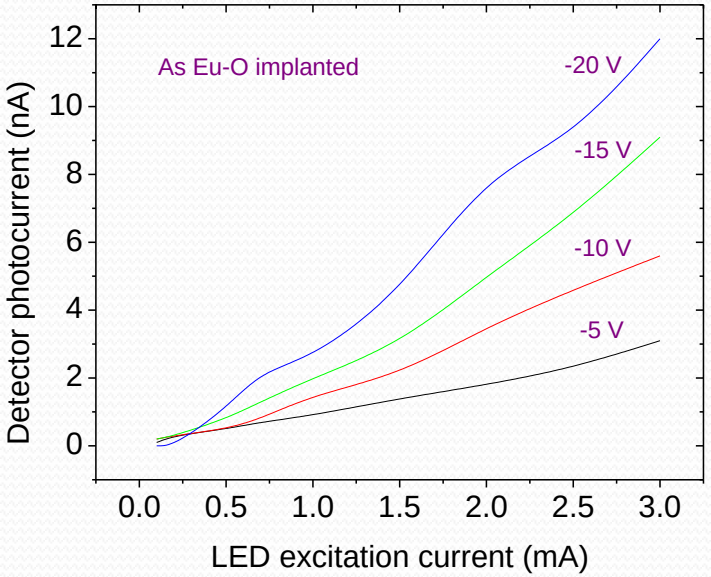
Three dimensional representation of the optocoupler device.
The recognition biomolecules are immobilized on the exposed waveguide surface.
Shown are: (1) the emitting avalanche junction, (2) the waveguide, (3) the p/n junction detector, (4) the SiO2 spacers and (5) the cladding layer.



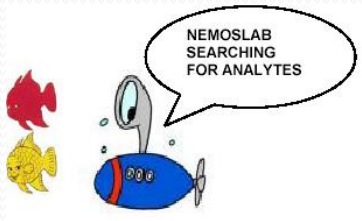
Major achievements:
Enhancement of silicon-based light emitters
Eu-O implanted silicon avalanche diode emitters



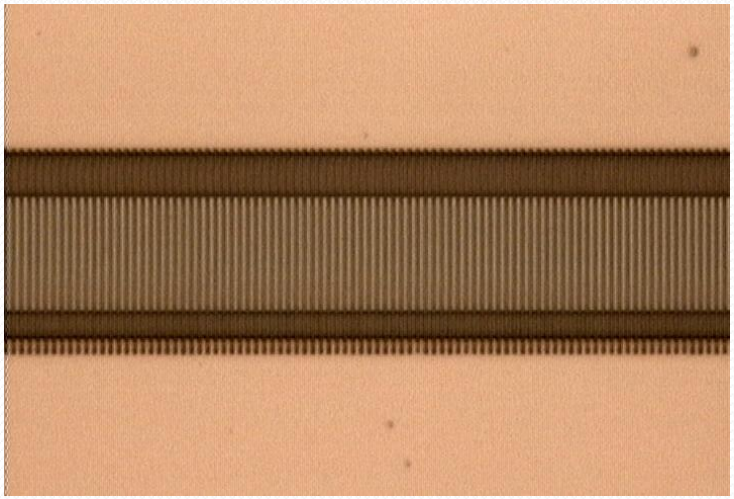
Spectrum emitted by the Eu-O implanted optocoupler compared to the one by a plain junction optocoupler. The arrow indicates an emission peak at 613 nm characteristic of Europium.



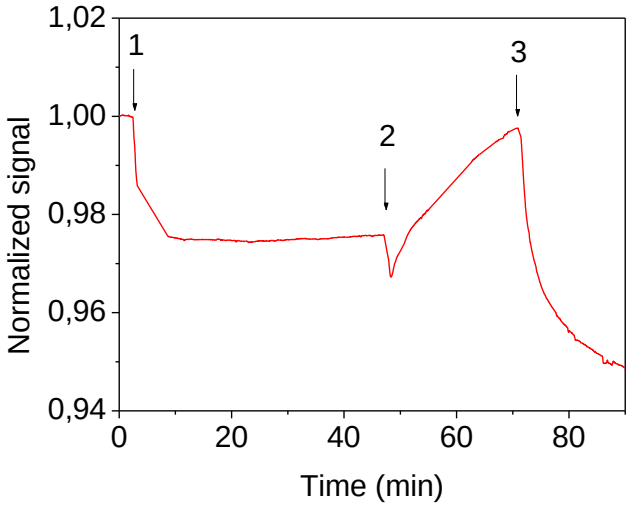
Optocoupler photocurrent for three different bias voltages on the detector for the as implanted device.



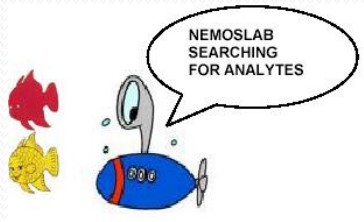
Label-free detection by patterning of the waveguide surface to create a latent photonic crystal



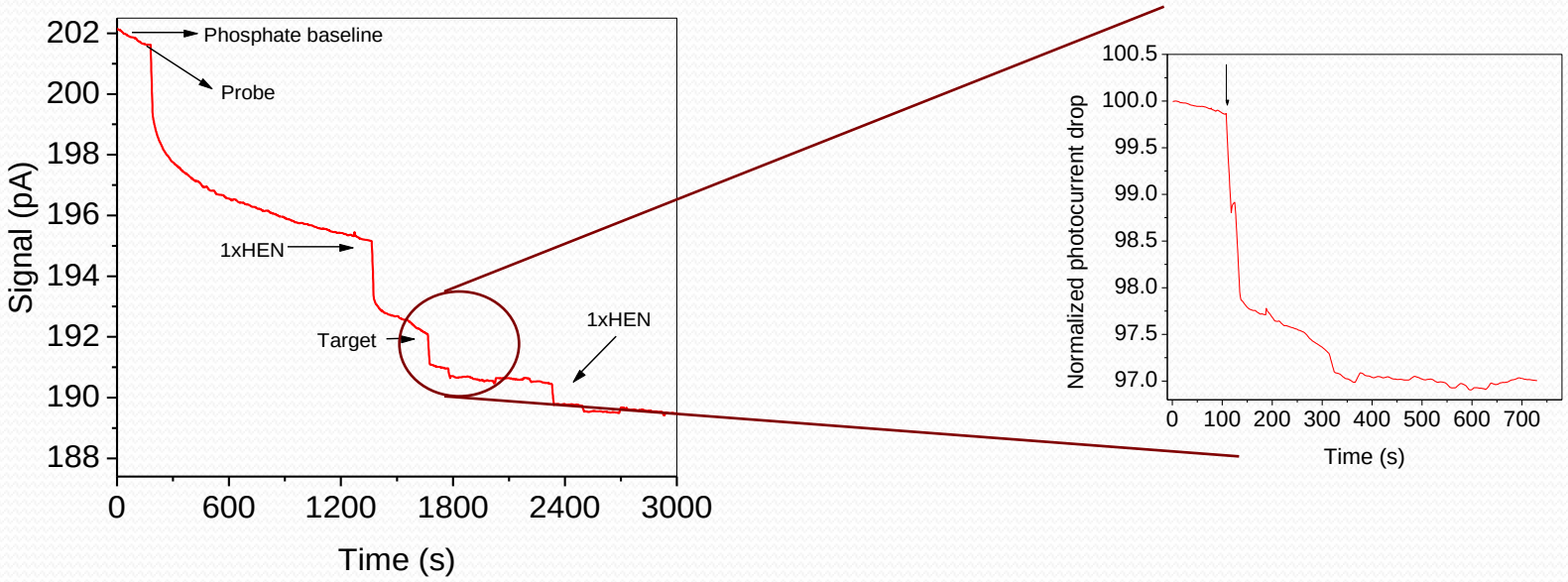
1 micron pitch pattern



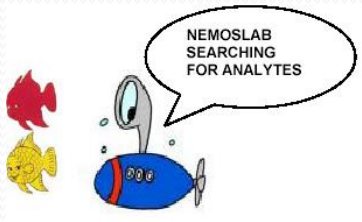
Normalized signal response obtained by reacting biotinylated BSA immobilized on 1 μm wide lines (2 μm period) with 10 nM streptavidin.
Up to 1: coating buffer
1-2: coating with biotinylated BSA
2-3: blocking
3 to end: reaction with 10 nM streptavidin



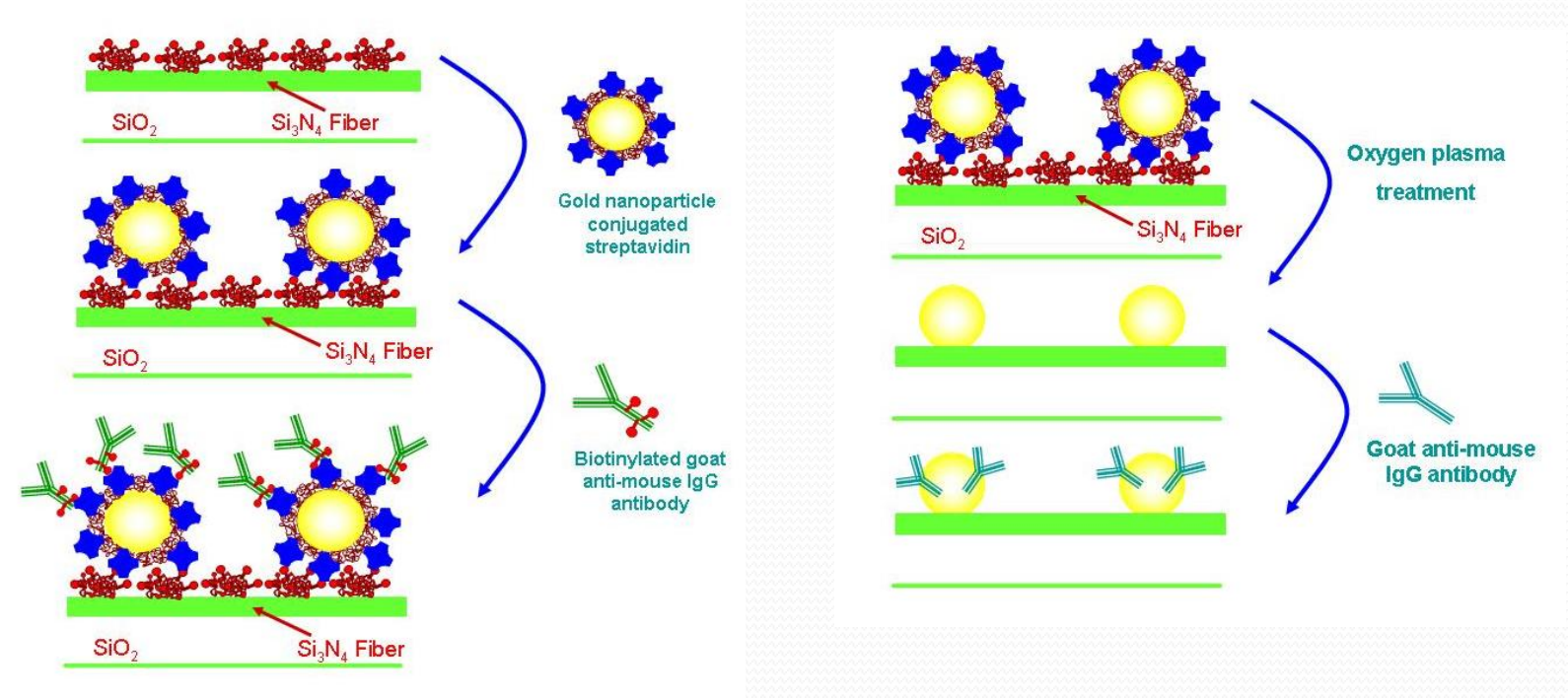
Label-free detection of BRCA1 gene mutations



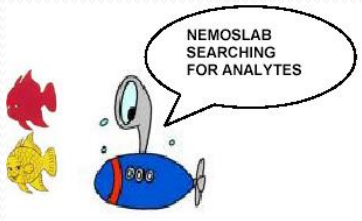
Real time monitoring of signal on fibers engineered by photonic crystal upon immobilization of pre-formed streptavidin-biotinylated oligo conjugate (PROBE), hybridization with the non-labelled complementary oligo (TARGET).



Waveguide engineering with noble metal nanoparticles for label free detection



Schematic presentation of approaches used for immobilization of distinct of gold nanoparticles on top of the fiber for label free detection of biomolecular reactions.



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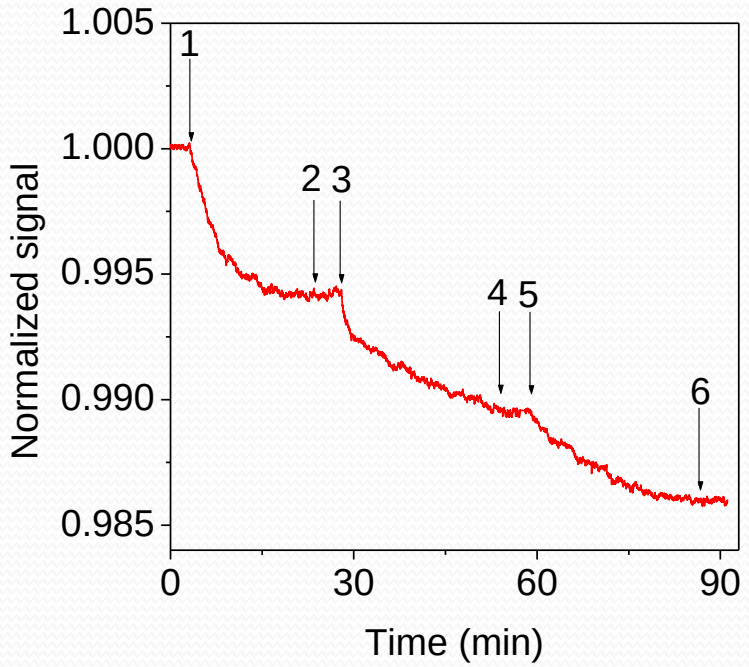
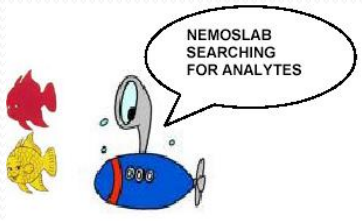
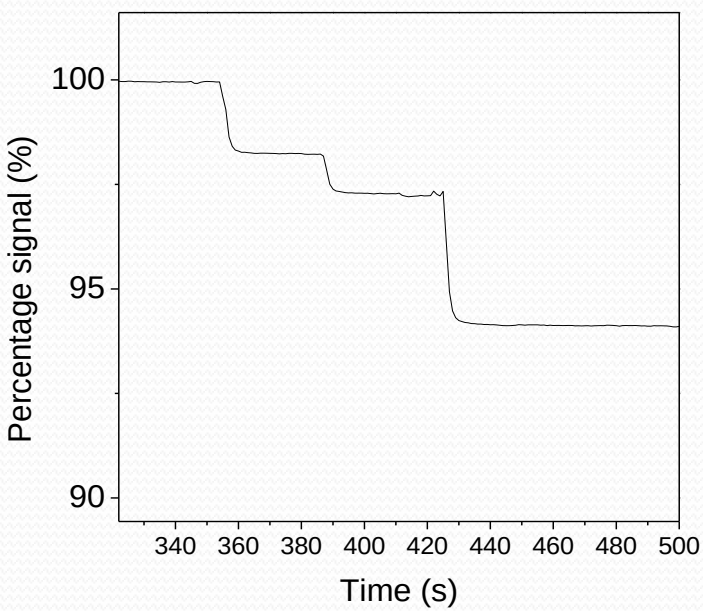


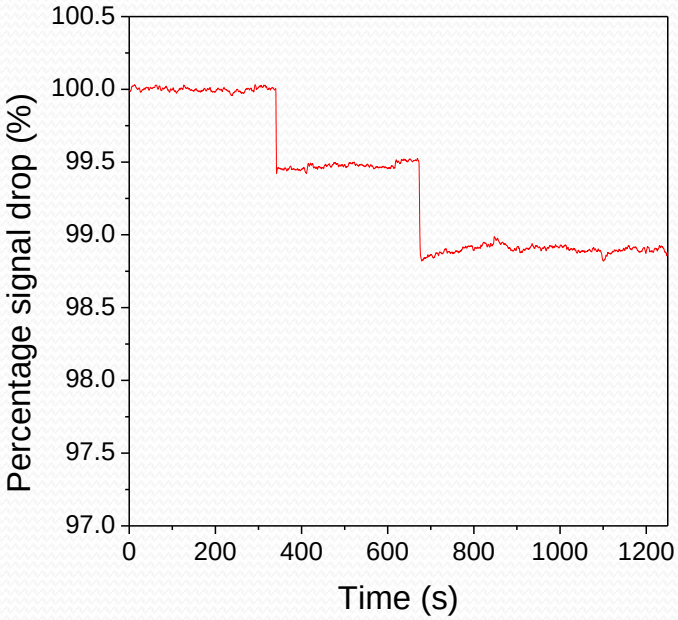
Real time signal monitoring from a waveguide modified with bare gold nanoparticles during:
immobilization of anti-mouse IgG antibody (150 nM) onto the surface (arrow 1-2),
washing (arrow 2-3),
immunoreaction with mouse IgG (10 nM; arrow 3-4),
washing (arrow 4-5), and
binding of anti-mouse IgG antibody (10 nM) onto mouse IgG (arrow 5-6).



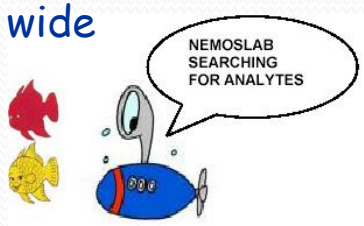
Single binding event detection on narrow fibers



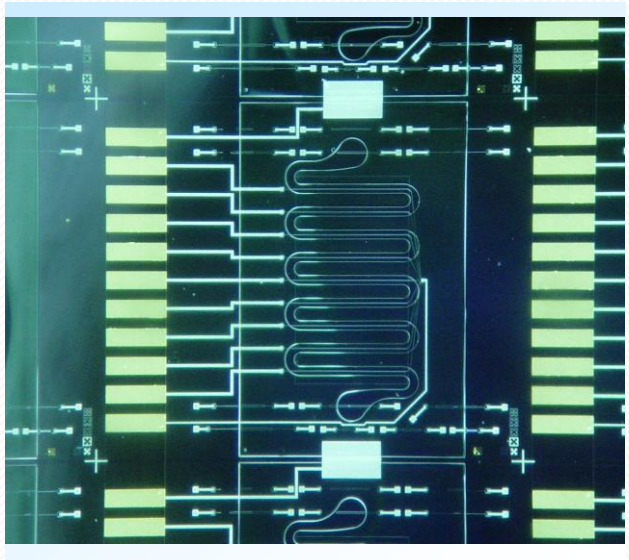
Binding of streptavidin labeled with 1-μm polystyrene beads onto biotinylated BSA spotted on a 2-micron wide waveguide

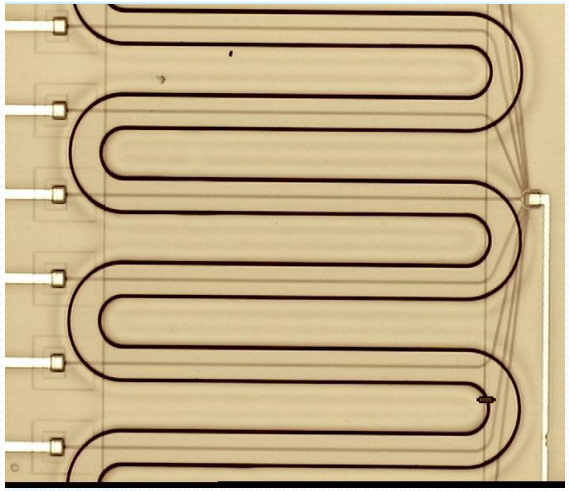


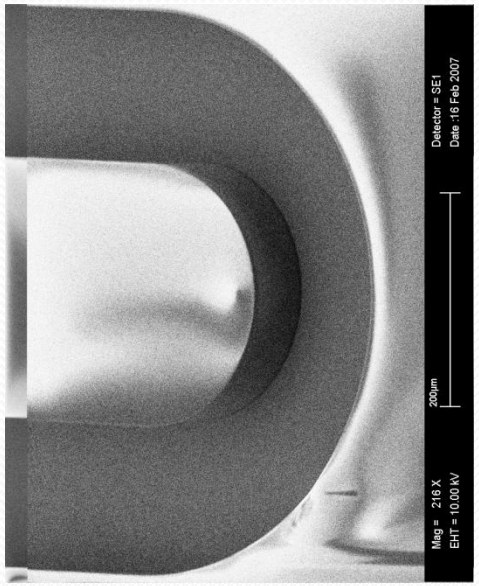
Binding of biotin modified fluorescently labeled vesicles (100 nm in diameter) onto streptavidin spotted on a 2-micron wide waveguide



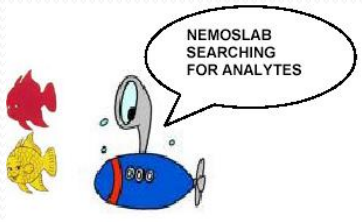
Integrated SU-8 microchannels







Spotting of different binding molecules onto different waveguides of the same chip was achieved using standard microarray spotters.

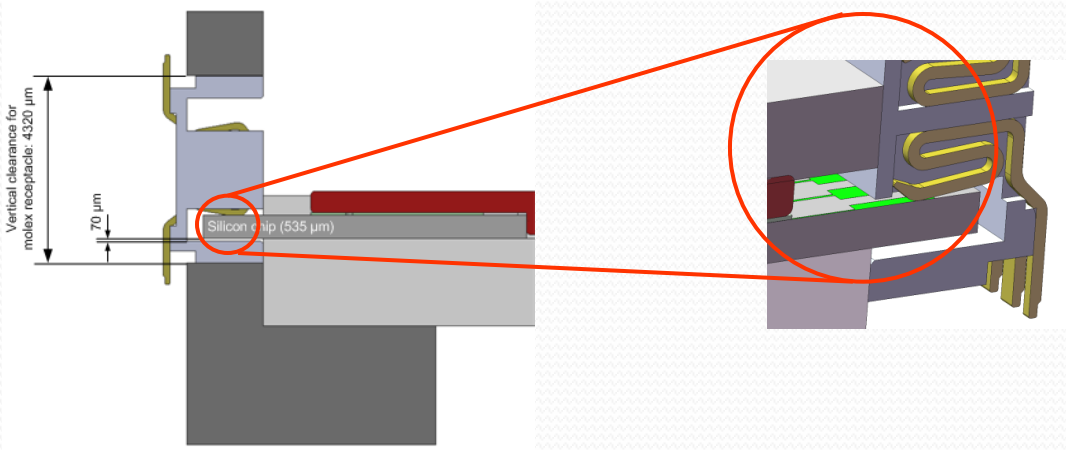


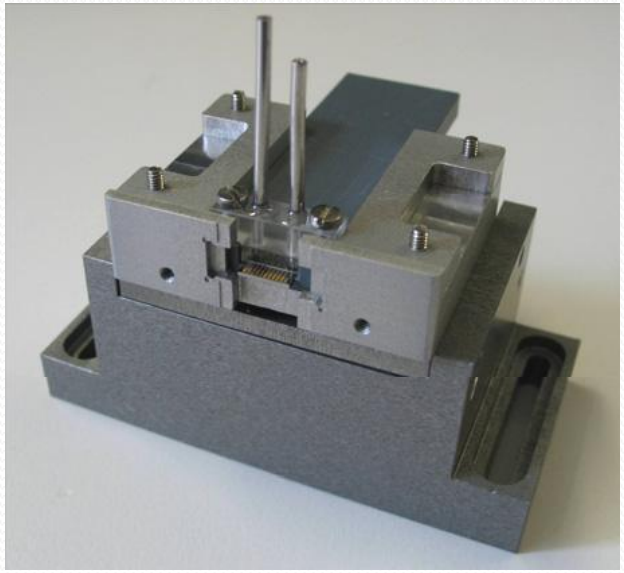
Direct contact scheme:

no bonding wires

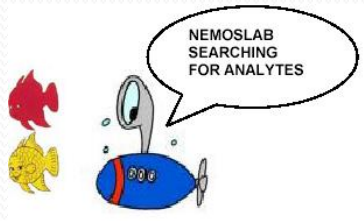
no additional PCB or ceramic package

sharp reduction in packaging cost

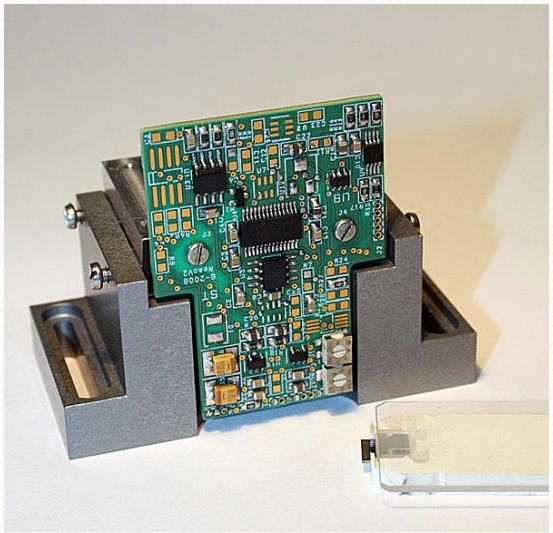


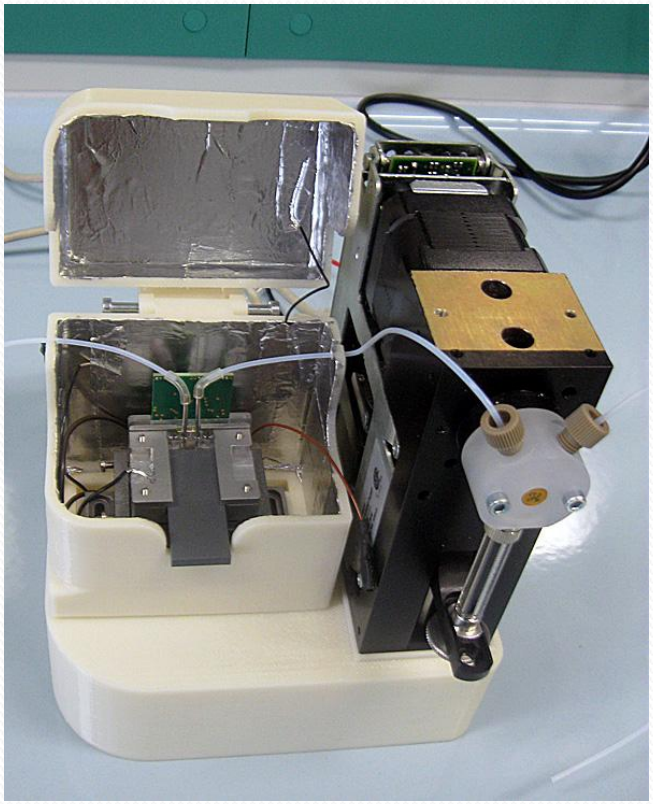


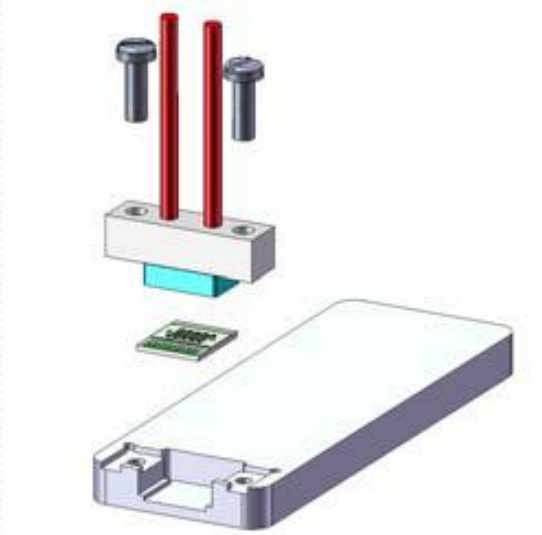
Moulded disposable cartridge

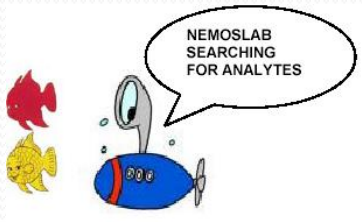


NEMOSLAB read-out microsystem-board and instrument

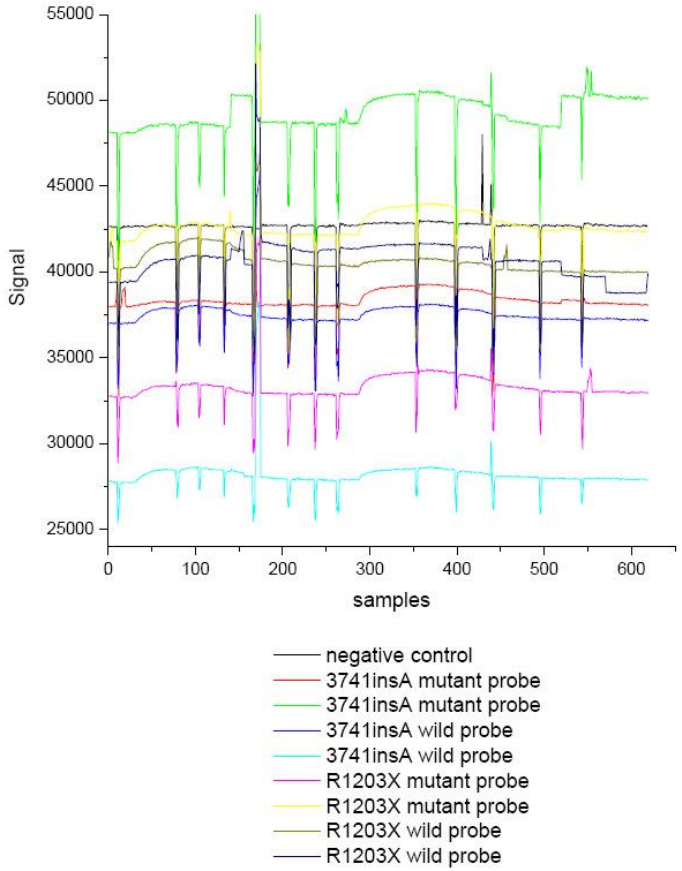


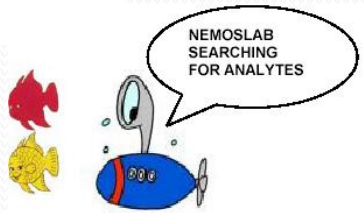






Real time detection of multiple BRCA1 mutations in PCR products using NEMOSLAB instrument

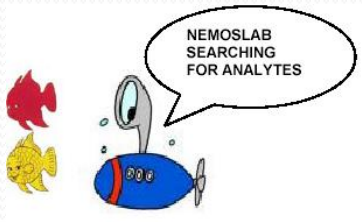




Limitations, future challenges and possible topics for cluster collaborations

Long-term stability of immobilized antibodies.
On chip stabilization of immobilized biomolecules was complicated by the fact that:
Salts and/or stabilizing agents had to be washed-out with water in order not to compromise the waveguiding properties of the transducer
There was a long "way" between functionalization and testing.

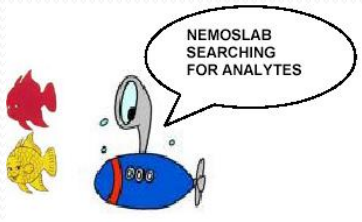
Reliability of individual chip packaging.
Fluidic connections not always achieved.



Limitations, future challenges and possible topics for cluster collaborations

Repeatability of results especially for label-free detection.

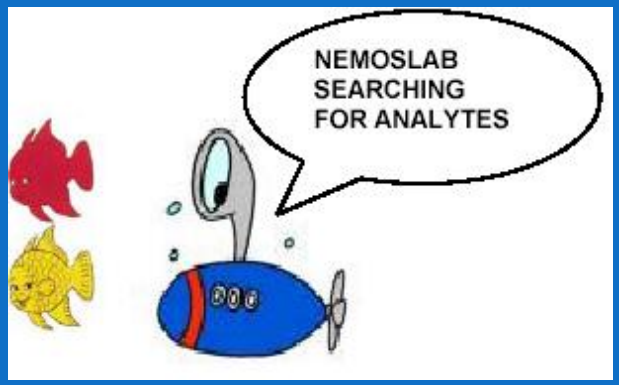
Lack of labels with wide absorption spectrum (Vis to near-IR) that can be readily conjugated to biomolecules.
Due to the wide emission spectra of the LED conventional fluorescent labels had limited efficiency in absorbing the waveguided modes.
Particulate labels seemed to bind reversibly possibly due to reduced affinity and to high flow rate during the experiments.



IMTEK

imel NCSR Demokritos

STMicroelectronics



IBMT

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