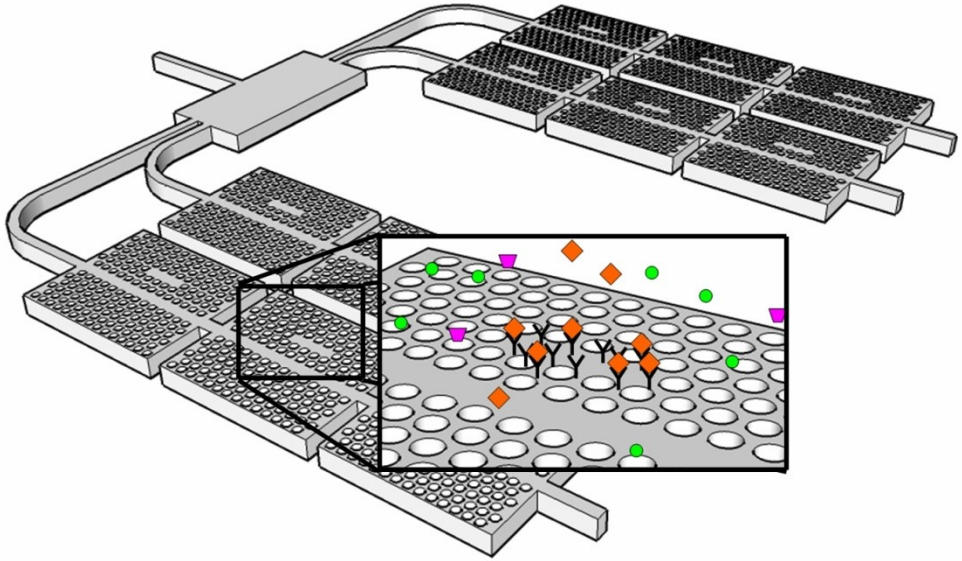

P3SENS

« **P**olymer **P**hotonics multiparametric biochemical **SENS**or for **P**oint of care diagnostics »

R&D project funded by the European Commission through FP7-ICT Call 4 – Objective – 2009.3.8 Organic Photonics and Other Disruptive Photonics Technologies

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- Consortium and project description
- Main achievements
- Photonic Crystals (PhC): principles
- Targeting low-cost production techniques
- Low and high-index materials for PhC chip fabrication
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- Sensor biofunctionalisation
- Integration and validation of the final chip
- Project's opportunities and challenges
- Dissemination & Exploitation of technical advances

The consortium

Identifier: ICT-2009-248304
Starting Date: January 1st, 2010
Duration: 36 months
Total Budget: 3,6 M€
EU Grant: 2,6 M€

University of Glasgow

stratophase

Multitel

UNIVERSITÉ DE GENÈVE

VTT

MFA

Bayer Technology Services

Project's abstract

- P3SENS will design, fabricate and validate a **multichannel polymer based Photonic Crystal (PhC) biosensor** (label-free and disposable) for detecting ultra-small concentrations of analytes (< 1 ng/mL) in solution

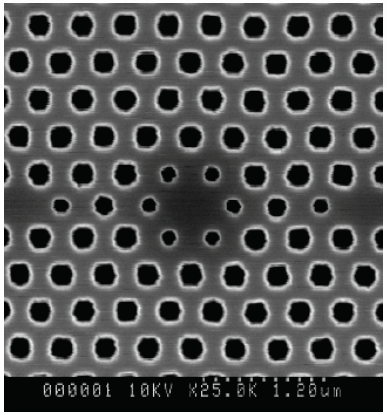
- The photonic sensor chip, based on polymer PhC micro-cavities coupled on a planar waveguide optical distribution circuit, shall be produced by using **low-cost, high-volume production technologies**, such as Nano Imprint Lithography (NIL)

- The biosensor will be tested for early screening of **cerebrovascular diseases (stroke)** via direct detection of more prevalent antigens (or antibodies), which are specific to the targeted pathology, in blood or plasma/serum (volume of ~25 µL or smaller)

Project description

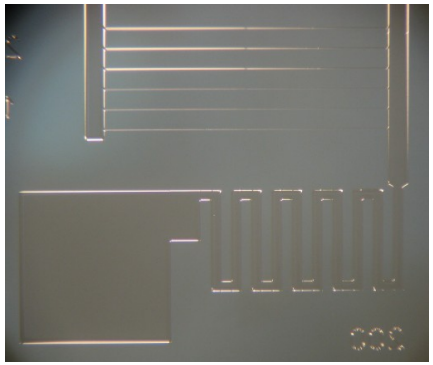
- Multidisciplinary project (including photonics, microfluidic, material, biochemistry, etc.)
- PhC based biosensor for label-free biomolecular recognition
- State of the art concentration detection-limit for highly integrated biosensor at < 1 ng/mL
- Multichannel (around 50 channels) for multiple detection of analytes
- Disposable and low-cost measurement chip
- Portable device for direct reading of diagnostically relevant information
- Low-cost large scale production
- Validation of the biochip with different bioassays simultaneously

A multidisciplinary project

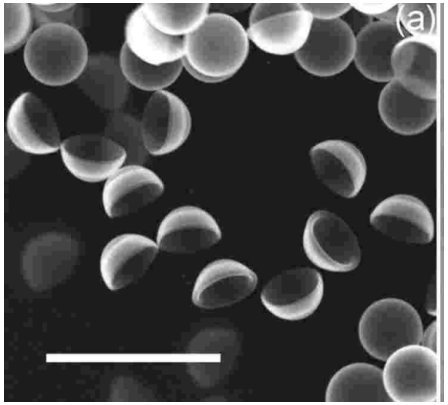


PHOTONICS

MICROFLUIDICS

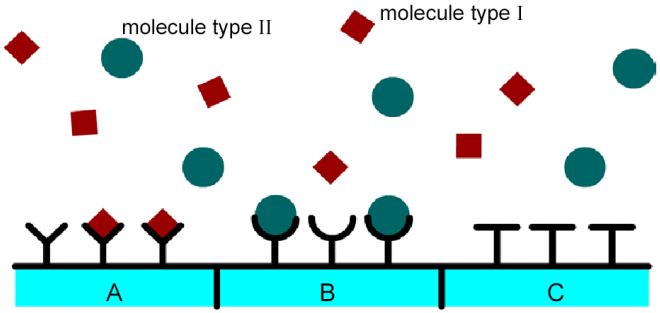


MEDICAL TRIALS



MATERIALS

BIOCHEMISTRY



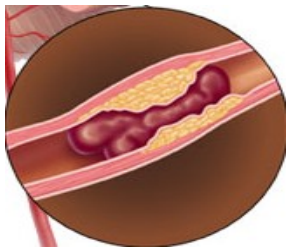
PHYSICAL REVIEW E **78**, 051401 2008

Main technical innovations

- High sensitivity, multi-channel sensor for protein detection
- Development of polymers with enhanced optical properties
- Development of low-cost techniques for mass production of photonic chips
- Novel optical sensor design based on photonic crystals
- Integrated approach (photonics, fluidics, biochemistry)
- Development of a portable optical interrogation platform
- Point-of-Care diagnosis device

Diagnostic needs for stroke

- Stroke is caused either by the occlusion (ischemic stroke, about 80% of the cases) or rupture (hemorrhagic stroke, 20% of the cases) of a large blood vessel in the brain reducing blood supply to the affected brain tissue, which can lead to hypoxia and irreversible tissue damage
- Stroke produces a measurable and reproducible change in concentration of some marker proteins in the blood → the measured concentration of these proteins can be used to detect stroke at an early stage
- Since no single marker has been found so far, which by itself has enough power to distinguish stroke patients from mimics or controls, the use of a panel of good candidate markers demonstrates better sensitivities and specificities than a single biomarker

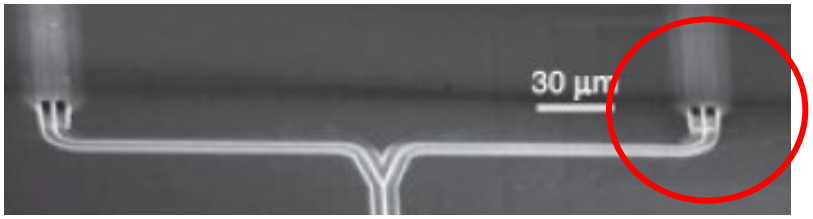


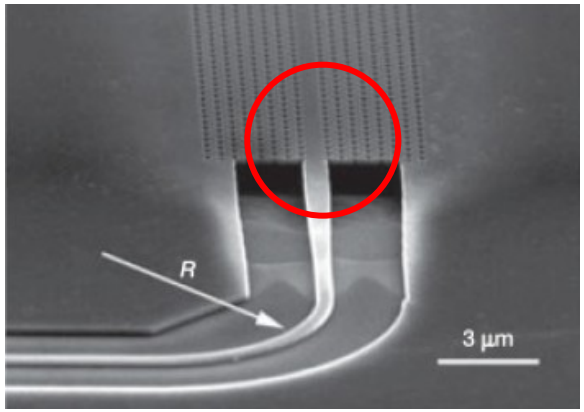
Photonic crystals: principles

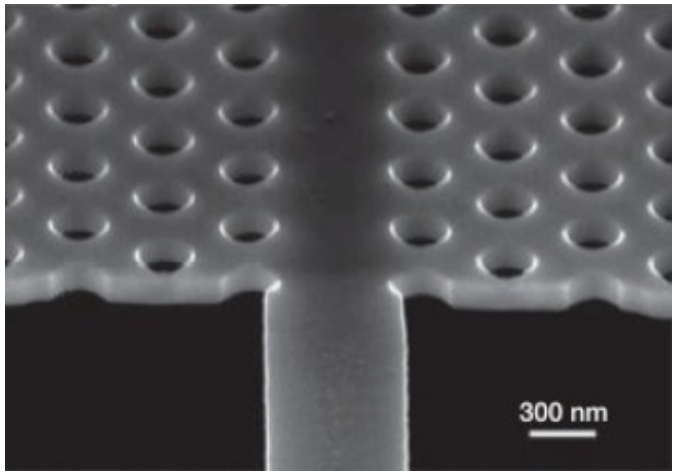
- Photonic crystals (PhCs) are structures in which the refractive index varies periodically on the wavelength scale in one, two or three dimensions
- Due to interference effects light propagation is forbidden over a large spectral range (the so-called photonic bandgap)
- Using PhCs in integrated optics enables the manipulation of an optical signal to realise filters, lasers, waveguides and multiplexers
- Typically photonic crystal structures used in integrated optics consist of periodic arrays of holes etched through classical semiconductor based planar waveguides
- The intrinsic sensitivity of the device to the surrounding medium makes it an ideal candidate for bio-chemical sensing

Photonic crystal distribution circuit

Complex functionalities can be integrated directly into photonic chips by using special design and the intrinsic properties of photonic crystals



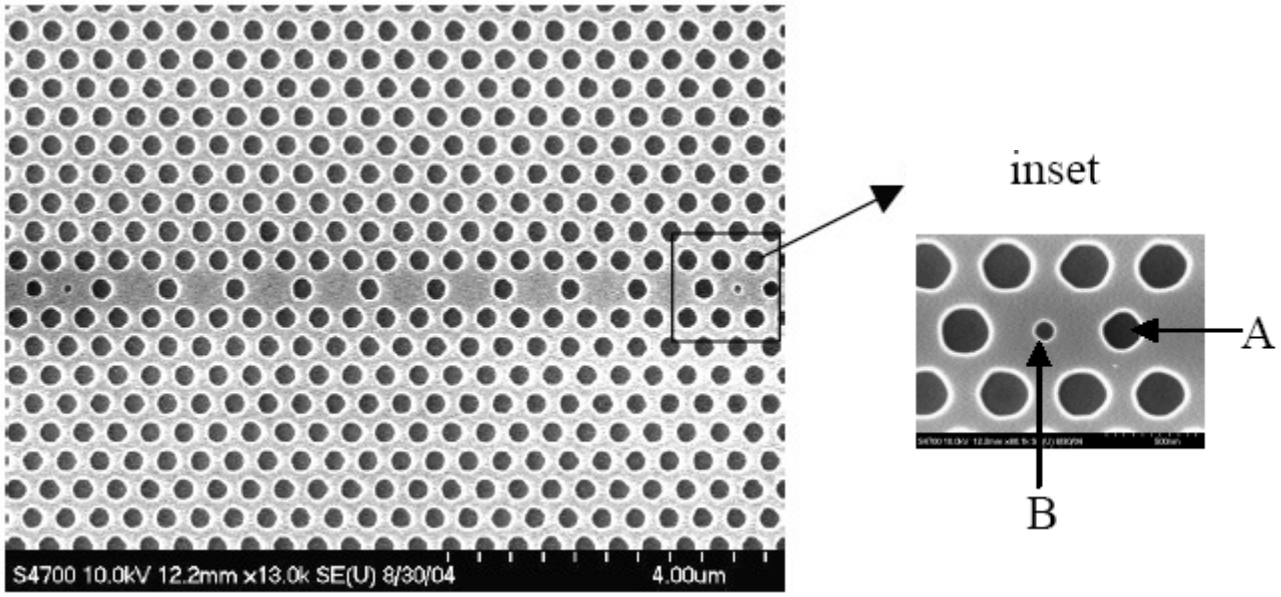




Source: Romuald Houdré, 2009 Photonics Summer School, EPFL (Lausanne, Switzerland)

Technological approach

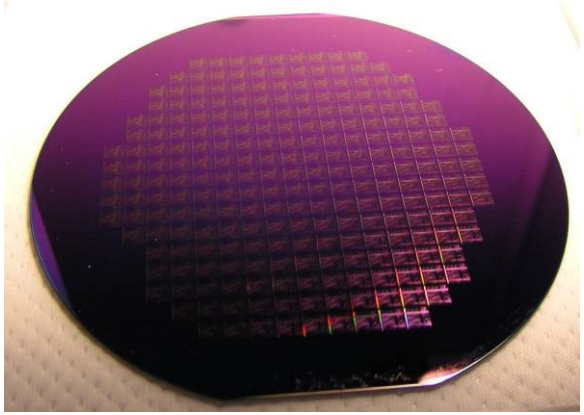
- Example of Fabry-Perot cavities: cavities having at each end a small additional hole in their centre – and an intermediate size hole at each of entry and exit → this helps taper the guided wave into the cavity



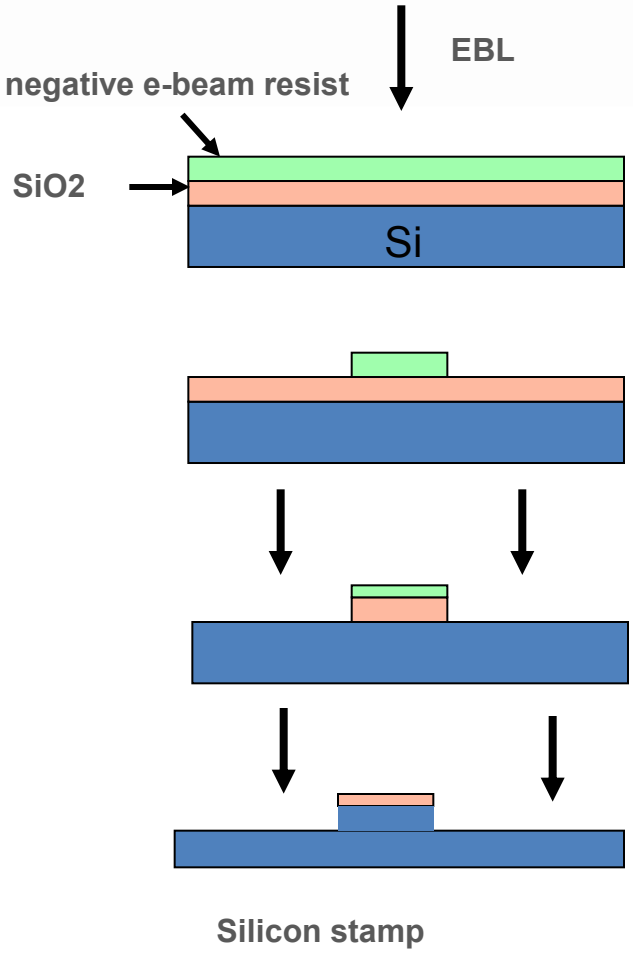
C. Jin et al., Optics Express, 13, (7), 2295-2302, April 2005

Low-cost production techniques: NIL

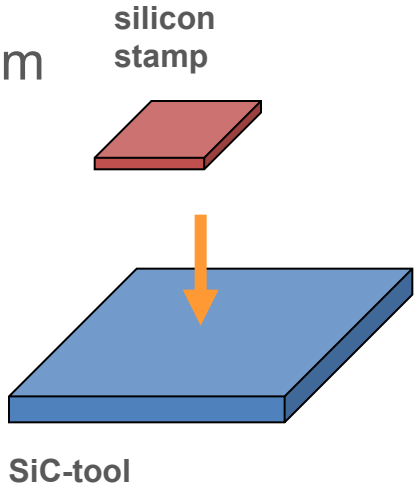
- Electron beam lithography (EBL) is suitable for R&D, but too slow and expensive for commercial manufacturing in large volumes
- Nanoimprint lithography (NIL) will be used and further developed for the patterning of waveguides and PhC sensors into polymer
- NIL has the potential for enabling high-volume, good quality manufacturing of photonic crystal based polymer chips
- NIL provides a future-path towards roll-to-roll manufacturing
- In this project NIL will be studied on both silicon and polymer substrates, and several NIL options will be tested

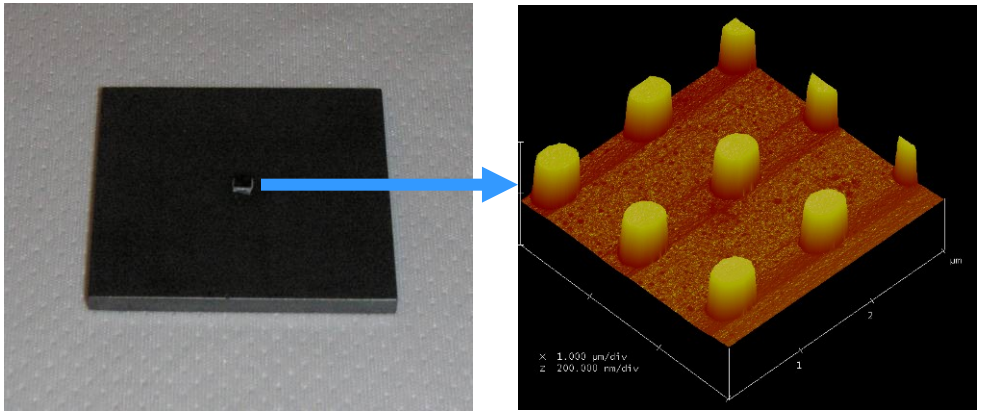


NIL implementation



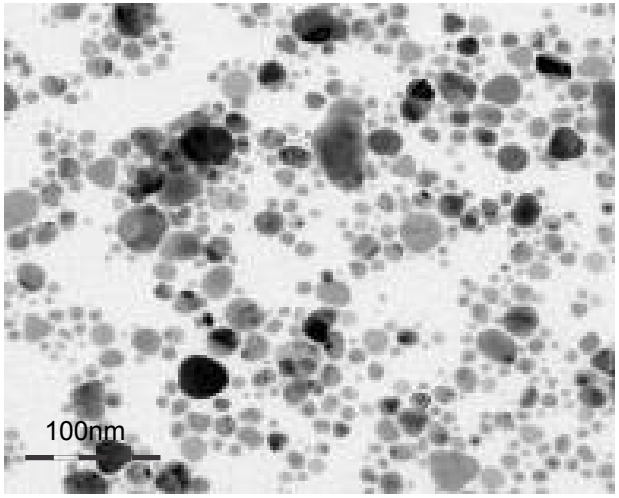
- Stamp size < 10 mm x 10 mm
- Material typically silicon
- Patterning by EBL or UV-lithography and dry etching
- Stamp attachment to a SiC-tool by glue or vacuum





High- and low-index materials for photonic chip fabrication

- In order to have the desired refractive index contrast between the sample fluid being sensed and the polymer of the photonic sensor chip, new composite materials will be designed and produced
- Nanoparticles of appropriate size and nature are to be integrated in the polymer
- The transmission and absorption characteristics of the material are important in determining the operational wavelength for the photonic chip
- As the surrounding transport material is aqueous media this places a high index constraint on the polymer



Ag nanoparticles

Nanocomposite materials

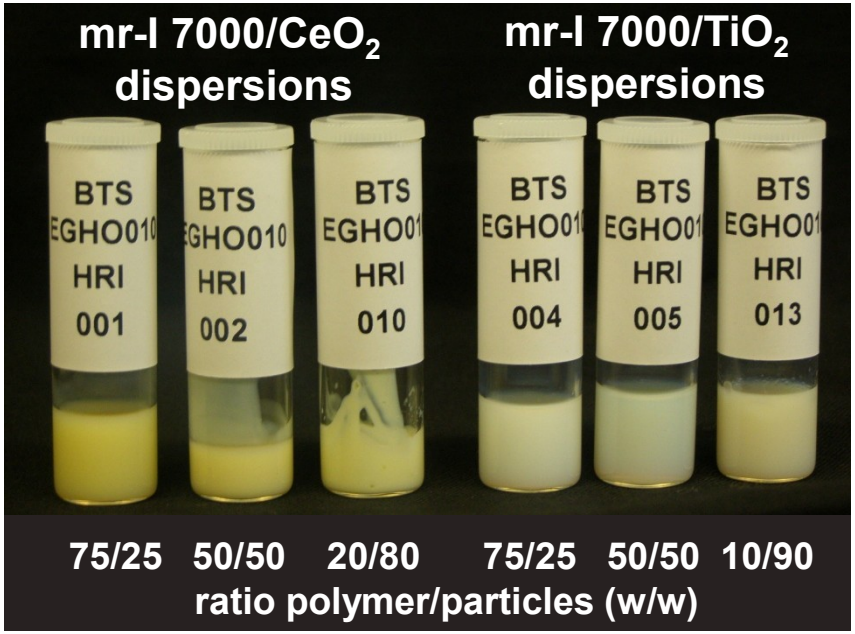
Modified polymers will be initially produced by using:

- **Polymer**: mr-I 7000E, a thermoplastic polymer developed for NIL
- **Nanoparticles**:

  - Particle size < 50 – 100 nm

  - High refractive index, e.g. Ag, TiO_2, CeO_2,…

  - Stabilized in organic solvents (ideally butyl acetate)
- Stable dispersions up to very high particle concentrations could be prepared with special TiO_2- and CeO_2-particles

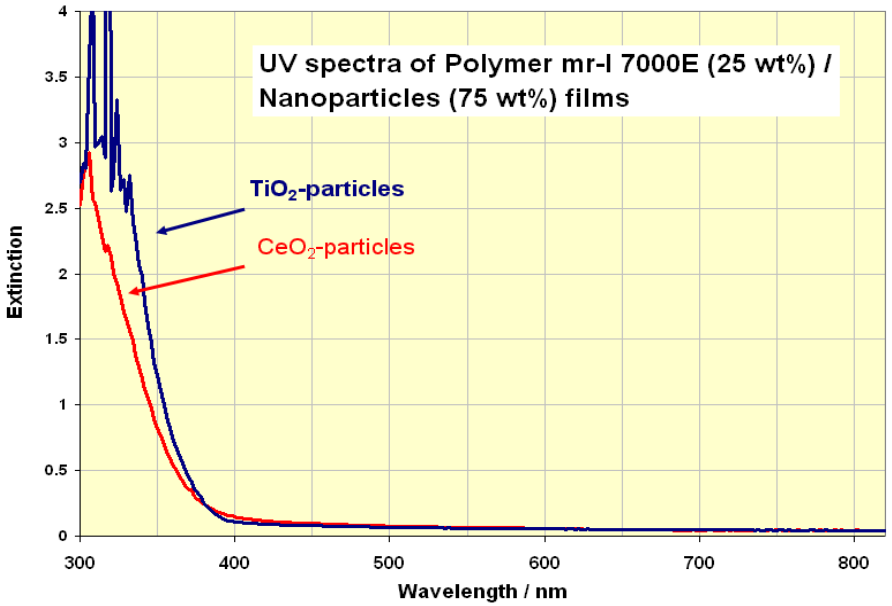


Optical properties of nanocomposite materials

- Transparent films up to a high nanoparticle content (at least 75 wt%) can be prepared
- UV-spectrum

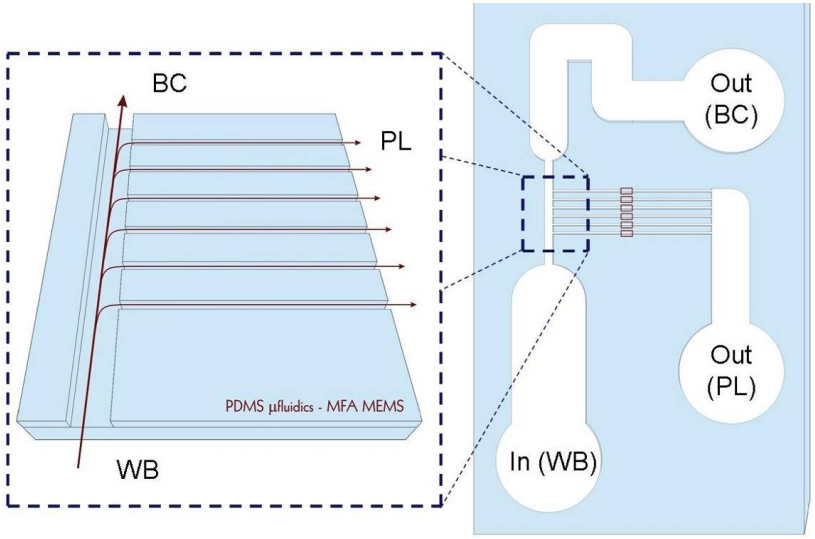
  Ag: very broad plasmon peak, maximum around 470 nm

  CeO_2 and TiO_2 : no absorption above approx. 400 nm
- Samples will be prepared to check influence on refractive index and compatibility with NIL



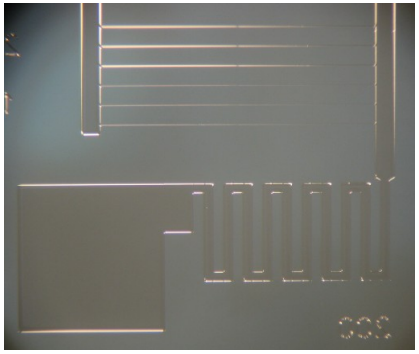
Microfluidic devices

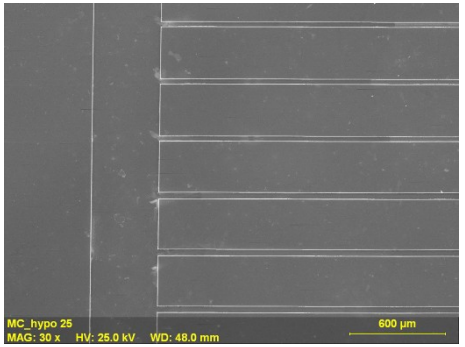
- The microfluidic chip enables high throughput, quick and low-cost design with direct manipulation of the biological samples: transportation, dilution, separation etc.



Example of Characteristics

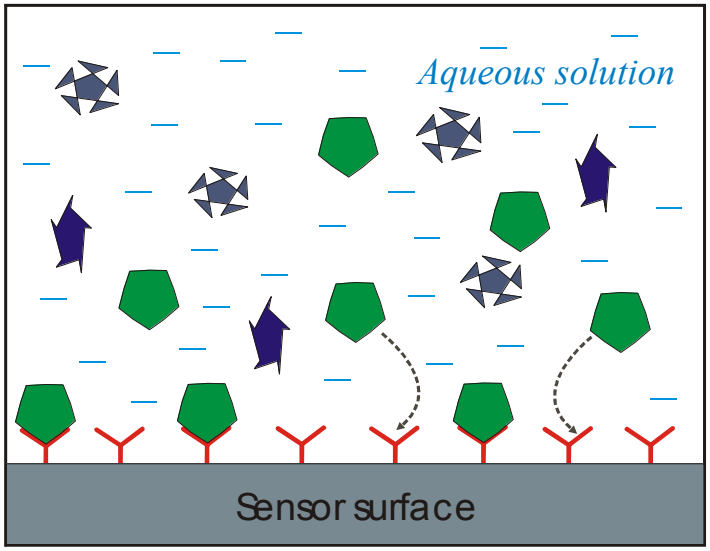
- Sealed channels with high aspect ratio vertical walls
- Connectivity to external, macroscopic flow systems
- Integrability in sensing systems
- Biocompatibility
- Relatively simple and cheap
- Decreased sample volume
- Accelerated clinical tests





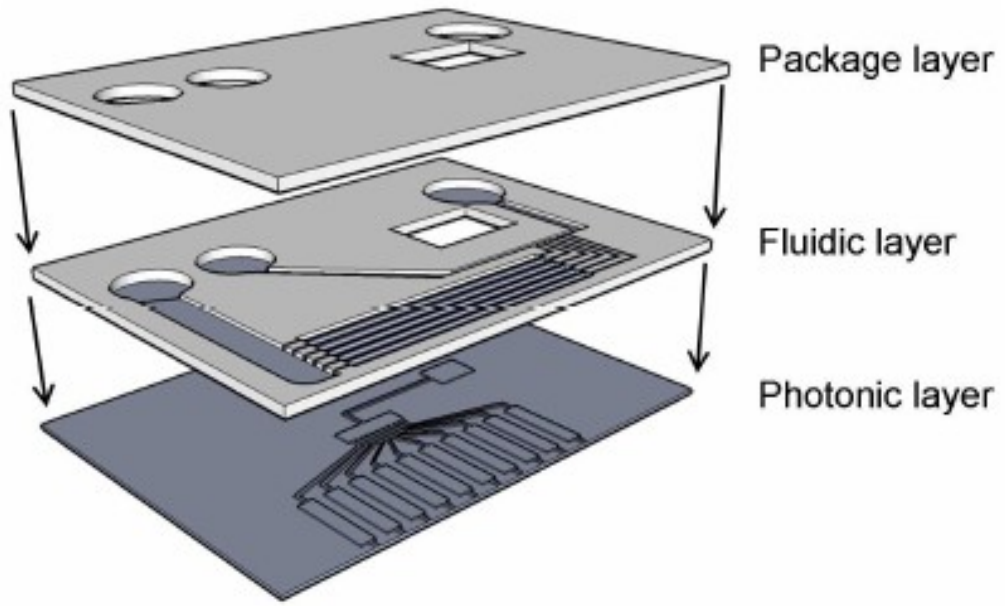
Surface biofunctionalisation

- Biochemical treatment of the sensor surface will permit precise detection of specific proteins by means of an antibody/antigen mechanism
- The various sensor surfaces are functionalised with different receptors capable of binding on one specific analyte only
- The receptors are tested with state of the art Optical Waveguide Lightmode Spectroscopy and the best possible configuration is integrated in the final device



Chip integration

- The photonic chip with the polymer PhC sensors and biofunctionalised surfaces will be integrated with the fluidic chip and packaged into a compact module
- The module also includes optical and fluidic input/output connections



In laboratory sensor validation (IVD validation)

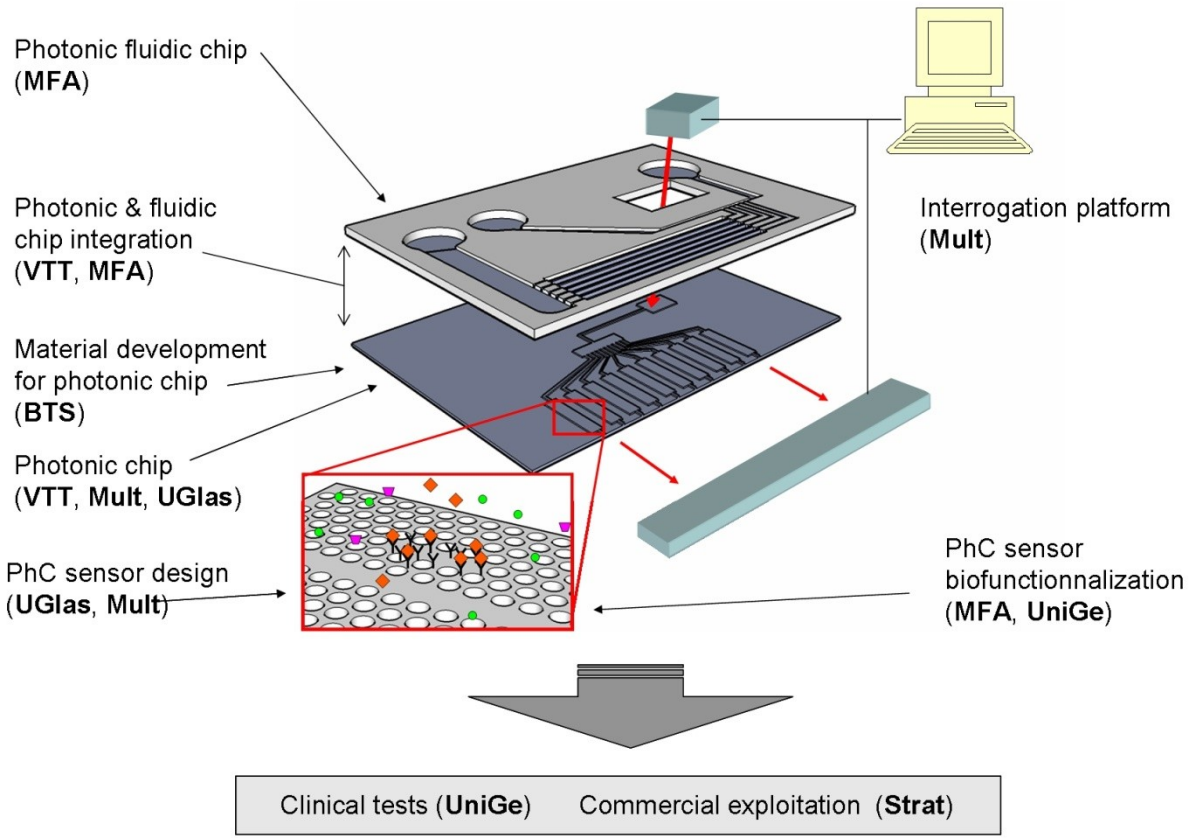
- Goal 1: detection of BSA binding interactions on the biochip and determination of device sensitivity, reliability and performance

- Goal 2: validation of the biochip with a multi-analyte panel for the diagnosis and prognosis of ischemic brain damage as a result of stroke using 6 well-known vascular associated analytes (S100b, H-FABP, NSE, Troponin I, BNP and CRP)

a. Comparison of the biochip performances with classical ELISA for the 6 biomarkers in a first small cohorts (n=20) and a larger cohort of stroke patients (n=100)
b. The study population comprises a total of about 100 individuals, separated into two distinct groups. Group 1 is the stroke cohort, which includes 45 patients, while group 2 is the control cohort, includes 100 subjects

Portable interrogation platform

- P3SENS will deal with the design and implementation of a compact measurement platform for the fabricated biochip that will be used to perform measurements without the need of additional optical/fluidic equipments (the platform will contain all optical, electrical and mechanical elements)

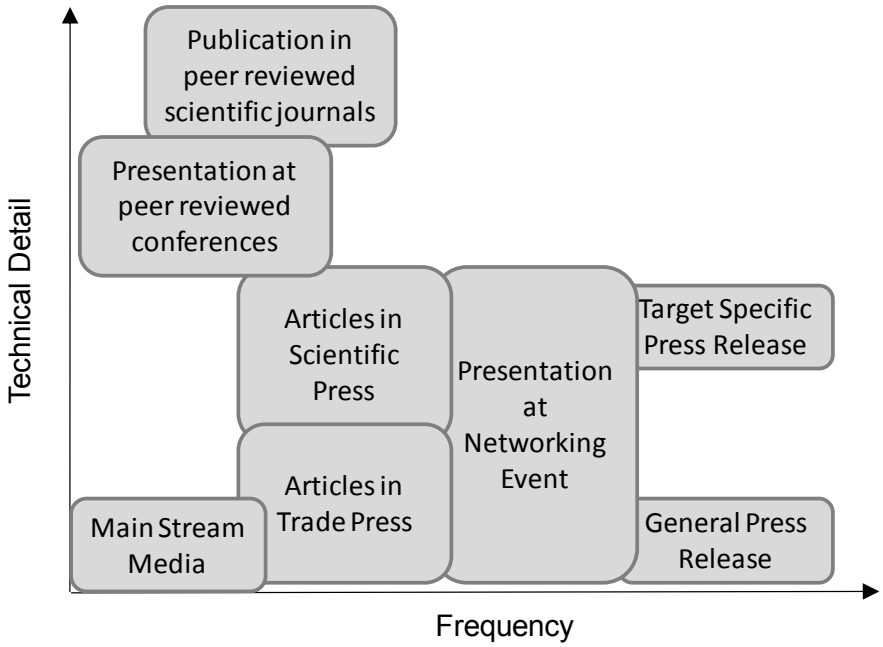


Opportunities and challenges

- Low-cost manufacturing: NIL-patterning of polymers enables very low fabrication costs, but achieving the targeted sensitivity is a challenging task.
- Biofunctionalization: Attain the highest sensitivity, keep the immobilized receptor molecules in an active state, avoid nonspecific binding.
- Biofunctionalization selective to only the PhC cavities will increase sensitivity, but this requires precise alignment
- Microfluidics: Effectively remove cell components from blood samples, Avoid blood clogging

Dissemination & Exploitation

- A multi-facetted approach to communication is intended to maximise the visibility of the developing P3SENS technology, thus:
  - Informing current and future stake holders
  - Building a strong media presence to aid further dissemination and exploitation activities.



- Press releases will be circulated to relevant publication, ~3-4 per year
- Contribution to editorial articles is an expected outcome of press release circulation, ~1-2 per year
- Ongoing communication is expected to attract mainstream media opportunities (Television/ Radio/ Newspapers)
- High technical detail communication will occur via peer reviewed journals and conferences
- Attending exhibitions and topical networking events will allow continuing assessment of the market for the P3SENS technology and the identification of exploitation opportunities