EMAIL SUBJECT:

INTOPSENS NEWSLETTER 2 - **Recent progress in SEPSIS diagnostic test development.**

Introduction:

This Newsletter overviews the recent results in the European INTOPSENS Project. Intopsens develops nanophotonic biosensors for the fast identification of septic bacteria strains and their antibiotic resistance from whole blood.

Highlights of technology developed in first 12 months:

- The most important and frequent etiological organisms causing sepsis are being focused upon as the target strains for the project: *S. aureus*, coagulase negative staphylococci and *E. coli* .

- Protocols have been developed for the purification, amplification and identification of the selected targets that can be implemented in lab-on-chip system as well as performed a first round validation

- Quantitative PCR protocols for *S. aureus* and *E. coli* were established for the characterization of the assay and the microfluidic devices

- A microfluidic device was developed that achieves selective blood cell lysis in less than 10 seconds while keeping bacteria intact.

- A novel lab-on-chip system has been developed for the online gas bubble removal during micro-PCR. Our system simplifies previous procedures by enabling debubbling when needed and by not requiring excessive pre-treatments of the chip or the sample.

- An uncomplicated single-step method has been developed for the fabrication of large scale integrated (LSI) 3D microfluidic networks in polydimethysiloxane (PDMS). PDMS is the most used construction material in the lab-on-chip community, and our specific invention relates to a robust manufacturing method for the dense integration of vertical fluidic vias between fluidic channel layers, in a high yield fashion and over a large area, without modifying its beneficial mechanical, physical and chemical material properties.

- Photonic crystals designed, fabricated and characterized for biosensing based on the refractive index sensitivity of the polarization resonance. Initial measurements show an increased sensitivity compared to previous photonic crystal sensing measurements.

- A technology for direct linking of photobiotin onto Si-O-H and Si-H bonds on the silicon surface by exposing to UV light has been developed.

- A more stable read-out mechanism of our ring resonator sensors was developed to enhance their detection limit. Additionally, more sensitive ring resonators with a higher light-matter interaction were designed, fabricated and characterized.

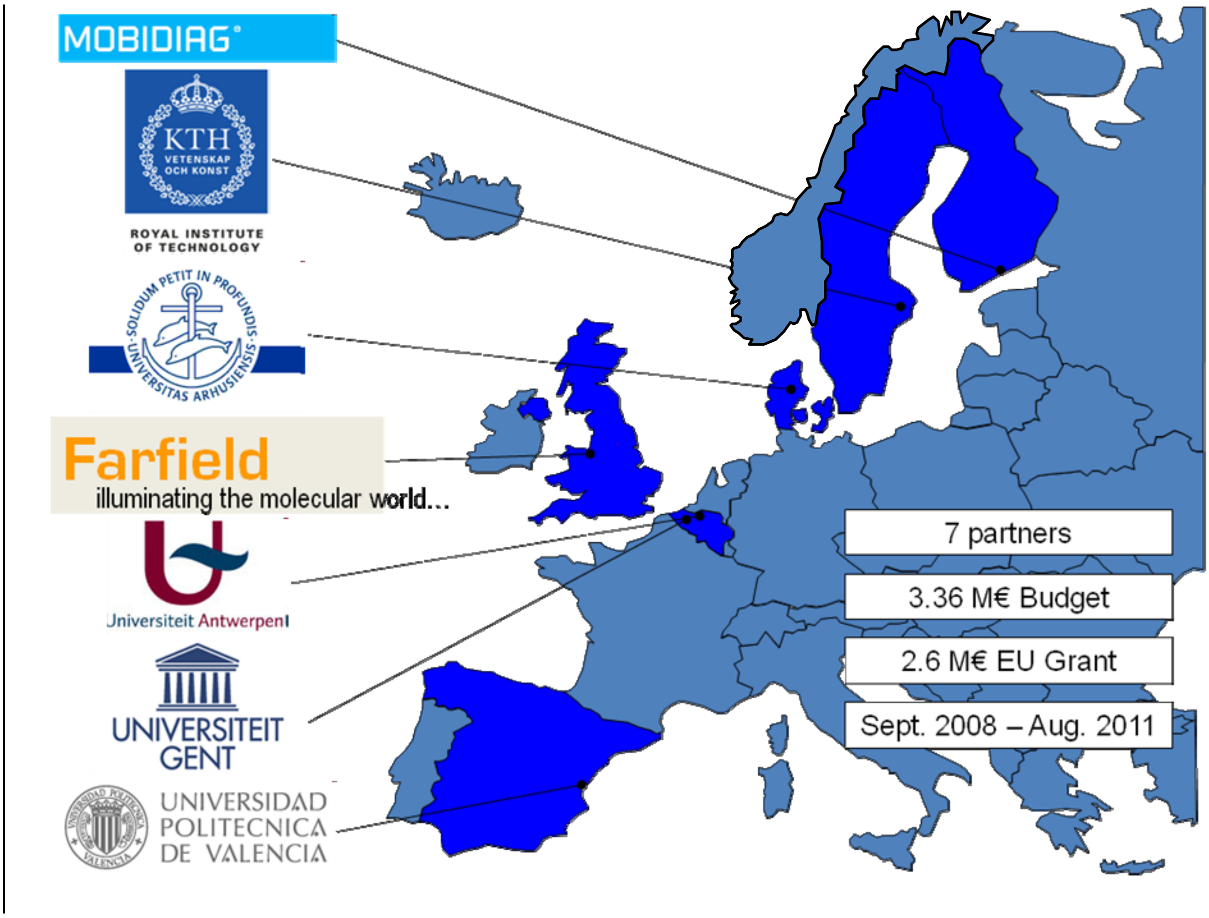
- To achieve even higher detection limits, Mach-Zehnder based sensors with folded waveguides were designed and are being fabricated.

- The project has resulted in five papers to conferences and one journal publication.

About Intopsens and its collaborators:

Intopsens (project number 223932) is an EC 2.6M€ funded three year FP7 ICT call 2 multidisciplinary project that began in September 2008, involving the emerging fields of photonics structures, electronics, fluidics and bio-chemistry, to contribute to the development of high value sensor technology.

The seven partners within the project, consisting of both SME and academic institutes, are distributed amongst 6 European countries and are fully complementary for such a project. The project's setup and partners' background ranges from physics through to microfluidics and to medical science. This multidisciplinary mixture has the potential to work as a key accelerator for novel, ground-breaking scientific development. The management structure of the consortium is designed to ensure the maximum participation between partners from the disparate backgrounds without the need for each partner to become experts in each other's fields.



More information can be found on the Intopsens website www.intopsens.eu.

Intopsens project manager and main contact person:
Dr. Daniel Hill, KTH – the Royal Institute of Technology - Microsystem Technology Lab (http://www.ee.kth.se/mst).
Visiting address: Osquldas väg 10, 100 44 Stockholm, Sweden
Email: danhill@kth.se

Other partners:

- Farfield Group Ltd (www.farfield-group.com): Dr. Gerry Ronan, CEO
- Mobidiag Ltd (http://www.mobidiag.com/): Dr. Antti Vuolanto
- KTH – the Royal Institute of Technology - Cell Physics Lab

(http://www.cellphysics.kth.se/): Dr. Aman Russom Microsystem Technology Lab (http://www.ee.kth.se/mst) Assoc. Prof. Wouter van der Wijngaart

- Universiteit Antwerpen (http://www.ua.ac.be/): Prof. Herman Goossens
- Universidad Politécnica de Valencia - Nanophotonics Centre (http://www.ntc.upv.es/): Dr.Jaime Garcia Ruperez - Grupo de Señal y Medida en Química - SYM (http://carta.cc.upv.es/knl/carta/grupo.jsp?aux=272): Prof. Angel Maquieira
- Århus University - Interdisciplinary Nanoscience Center (http://www.inano.dk/): Prof. Martin Kristensen
- Universiteit Gent (http://www.photonics.intec.ugent.be/): Assoc. Prof. Peter Bienstman

Partner feature:

Interdisciplinary Nanoscience Center (www.inano.dk)

The Interdisciplinary Nanoscience Center (iNANO) is a major research and education centre based at the University of Aarhus, Denmark. The centre currently undertakes interdisciplinary research involving scientists from relevant areas in physics, chemistry, molecular biology, biology, engineering, and medicine. iNANO offers a dynamic, interdisciplinary research environment with many national and international collaborators. The group lead by Professor Martin Kristensen is experienced in photonic crystal waveguides and also working on the immobilization of specific biomarkers onto sensor surfaces. The work concerns SOI (silicon on insulator)-based optical biosensors using crystal waveguides and cavities. Currently, it is working on the design and characterization of the biosensor components. The work also includes immobilization of sensor proteins on SOI-based components in order to achieve high selectivity for specific biological agents such as proteins. In the middle of 2008 the construction of its clean-room facilities will be completed. Until then it will be performing silicon fabrication at the Danchip clean-room at DTU (Technical University of Denmark) Planar integrated photonic crystal components are fabricated using clean-room processes originally developed for the microelectronics industry and further specialized for optical components. We use silicon-on-insulator (SOI) wafers as platforms for the components. The fabrication-processes include electron beam lithography or deep-UV lithography, and inductively-coupled plasma (ICP) etching. In conclusion our competences most relevant to the project are to design and characterise planar photonic crystal waveguide components and to functionalize the sensor surface for immobilisation of organic molecules.

Primary contact person

Martin Kristensen
Department of Physics and Astronomy
University of Aarhus
Ny Munkegade, Building 1520
DK-8000 Aarhus C
Tel: +45 8942 5532
Fax: +45 8612 0740

Participants

Dr. Martin Kristensen is a professor of nano-photonics at iNANO and Department of Physics and Astronomy at University of Aarhus since November 2004. Before this he worked more than 10 years at the Technical University of Denmark (DTU) where he was heading a group specializing in waveguide components for telecommunications. He has a long experience in design, clean-room fabrication and characterization of optical components and has published more than 250 scientific research journal and conference papers within optics and supervised 26 Ph.D. students. During the time at DTU his research has directly led to the formation of two spin-off companies (Koheras and Ignis Photonyx). He has participated in four EU projects and acted as workpackage leader for the largest workpackage in two of these (PICCO and GLAMOROUS).

Photonics development feature:

Photonic crystal waveguide sensors are envisioned as one of the sensor structures to be used in the final sepsis diagnostic device. Previous experiments have shown that these sensors can detect binding of biomolecules through a shift in the transmission band edge of TE polarised light reaching a sensitivity of 10 μg/mL concentration. In the Intopsens project a sensitivity increase is aimed in order to allow faster detection times. By adjusting the input polarisation to the photonic crystal waveguide element it is possible to launch a mixture of TE and TM and produce a narrow band-pass filter with more than 40dB signal contrast in air due to polarisation-mixing-induced interference. This exploits the high dispersion available from the TE eigenmode of the waveguide and allows the generation and tuning of optical resonances by adjusting the polarisation. Such narrow resonances can be exploited for sensing, since they shift at approximately the same rate as the TE band edge as a function of refractive index changes in the add-layer on top of the chip. The sensitivity is greatly enhanced as the resonances are much narrower than the band edge. In recent experiments we have been able to reproduce the effect under water, proving that the method works under realistic conditions for the Intopsens project. Initially the main limitation was to get stable performance under water. We solved this by embedding the crystal waveguide section in a closed-loop water circulation system so that the conditions remain stable without influence from air turbulence and evaporation.

For more details about the project please visit the website www.intopsens.eu where both the photonic and all the other aspects of the project are described.

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