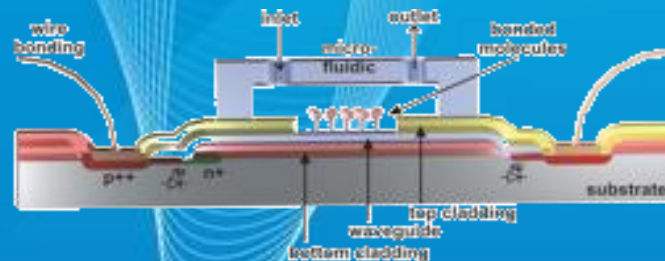


# PYTHIA: Monolithically integrated interferometric biochip for label-free early detection of human diseases



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[www.pythia-project.eu](http://www.pythia-project.eu)

# The Problem

The development of miniaturized and more powerful analytical and diagnostic tools for the early detection of diseases & for point-of-care monitoring systems is of very high priority for the whole healthcare sector.

**Photonic biosensors** are considered as very promising solutions towards this objective. Despite their attractive attributes, the existing optical biosensors are burdened with the need of external optical components and the final systems are bulky regardless of the miniaturization level of the biosensors themselves.

For the fabrication of the next generation of compact, portable, cost-efficient biosensors which will allow for the label-free, real-time detection of biomolecules (like proteins and DNA strands) at very low concentrations in small-volume samples, “smarter” designs are directly required. These designs should also result into biosensing devices able to be mass-produced and used in any size clinical center or even private praxis by non-specialized personnel.

# PYTHIA Objective

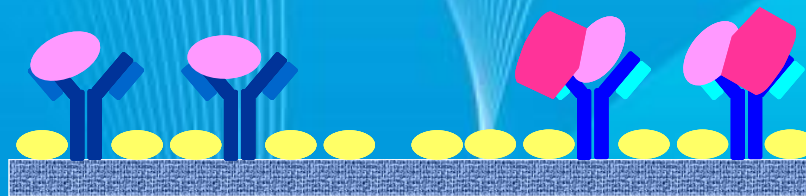
Development of *Monolithically Integrated  
Broad-band Mach-Zehnder Interferometer*  
for label-free detection  
(protein and DNA mutations)

Start Date: May 1<sup>st</sup> 2008

Duration: 36Months

# Targeted Applications for Demonstration

- Prostate cancer (Total & Free PSA quantitative antibody assay)

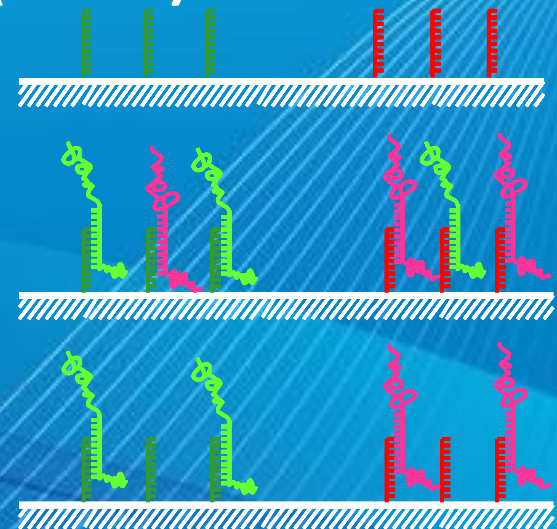


Sensor A:  
specific anti-free PSA antibody

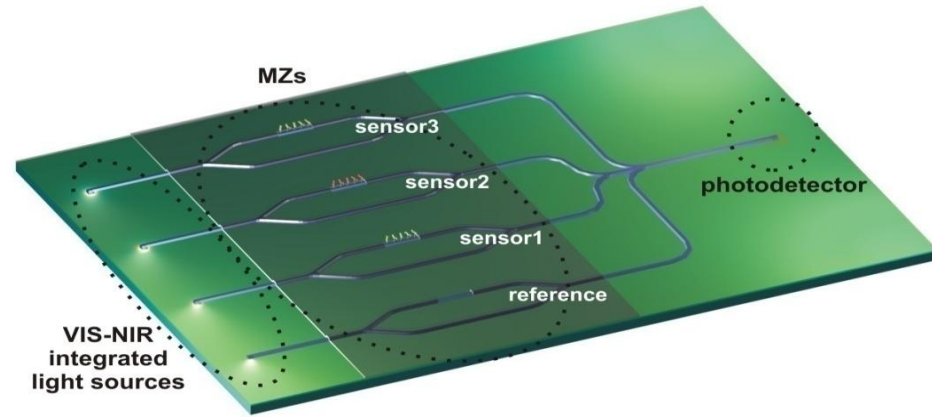
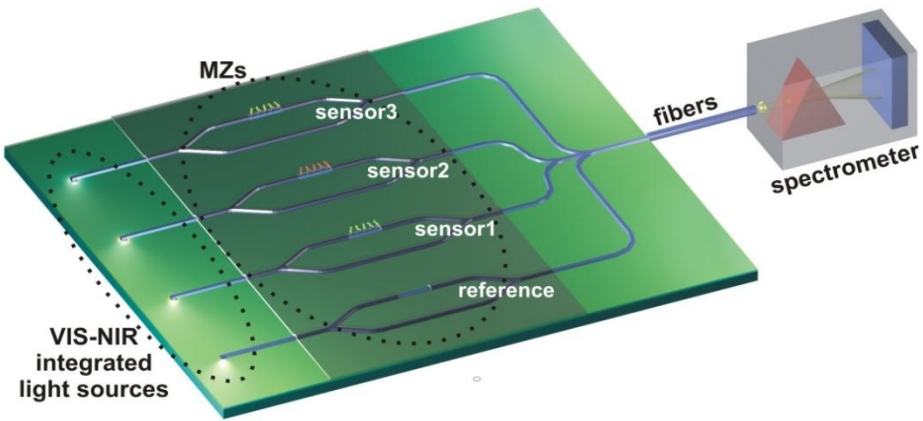
Sensor B:  
specific anti-PSA/ACT complex antibody

- Multiple Endocrine Neoplasia type 2 (MEN2)  
/ Familial Medullary Thyroid Carcinoma (FMTC)

- Retinitis Pigmentosa (RP)  
(mutated oligonucleotide detection)



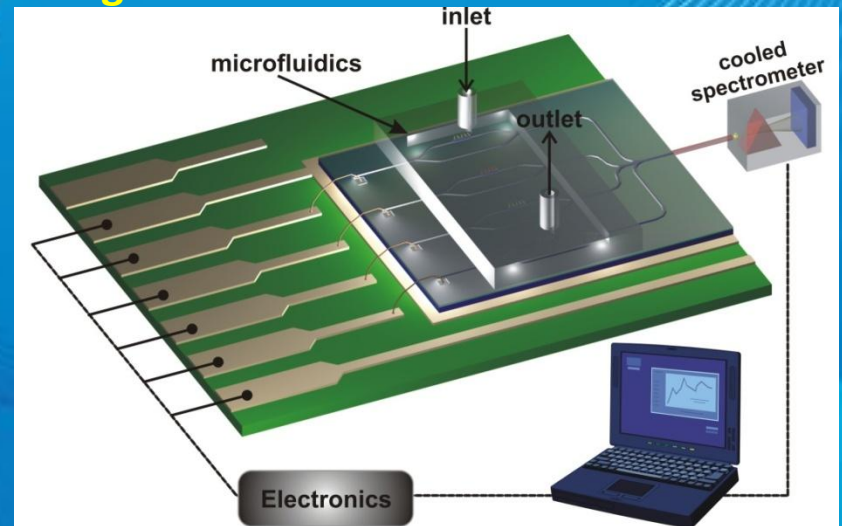
# The PYTHIA concept: Si optoelectronic biochip



The MZI array is coupled to an external spectrometer through a pre-aligned optical fiber. **Semi-integration configuration.**

MZI array coupled with one monolithically fabricated photodetector. **Full-integration configuration.**

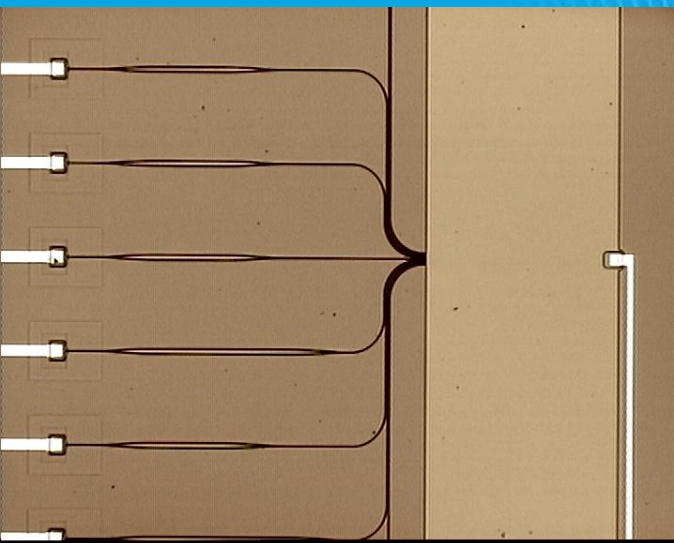
## Electrical connections of the PYTHIA biochip



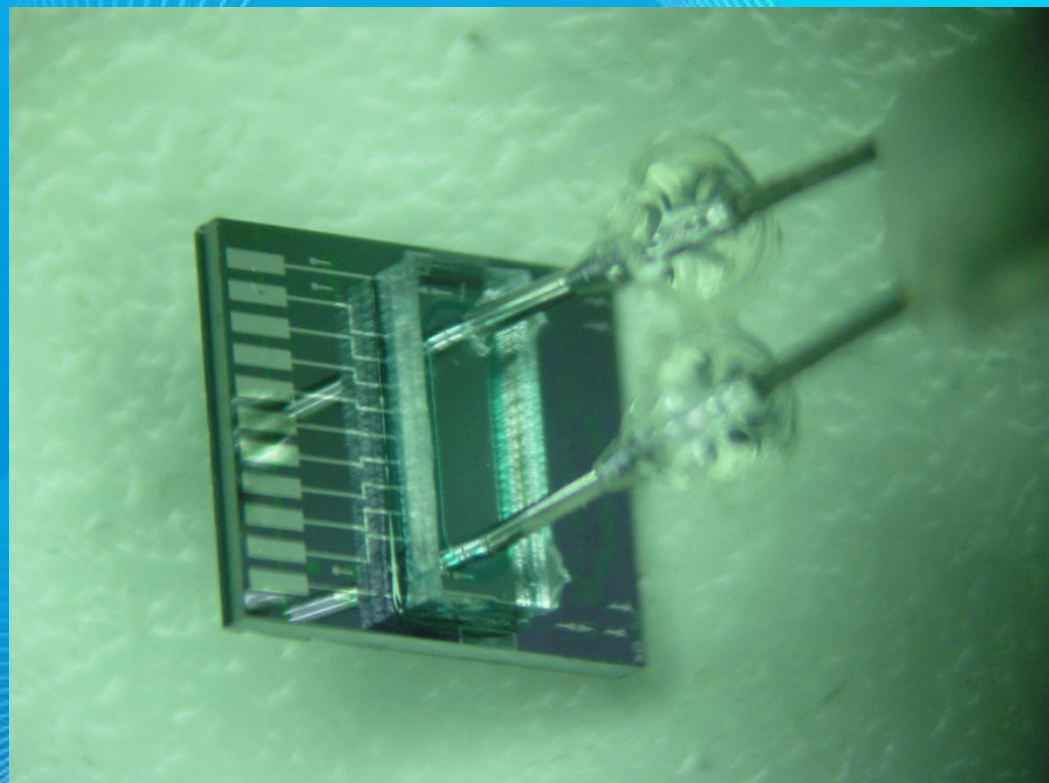
# Mid Term Major achievements

- ✓ Fabrication of truly monolithically integrated optoelectronic transducer by standard Si processing
- ✓ Experimental validation of transducer's Proof of Concept
- ✓ Successful detection of model analytes and of very low concentration
- ✓ Assay development for PSA
- ✓ Assay development for DNA mutation detection
- ✓ Validation of wafer-scale Assembly & packaging

# PYTHIA biochip



PYTHIA transducer array



Encapsulated PYTHIA biochip

10 sensors per chip (<math>60\text{mm}^2</math> area)

For the Biotin-Streptavidin model assay, the detection of streptavidin in the **pM range** was easily demonstrated, which is comparable with the state of the art values for label-free biosensors.



# Technological Issues

## Solved

Monomodal waveguiding

Broadband MZI readout principles

Experimental validation of BB-MZI proof of concept

## In Proof Stage

Encapsulation methods to preserve the functionality of probe molecules

Multi-analyte detection

Detection of single base-pair mutation

# Technology Offer

## Fully integrated photonic platform for *LoC* applications

Broad-Band Mach-Zehnder Interferometry Concept (patented) for improved performance and higher sensitivity

## Real-time label-free optical biosensor array with high sensitivity and dynamic range

**Antibody assay**

**Oligonucleotide based detection**

can be used in applications in the food & agricultural industry and in clinical applications : quick and accurate screening in genetic testing to application in virology

# Potential Collaboration with other projects

## Technical

- Standardization of functionalization protocols
- Biocompatible microfluidics integration in large scale
- PCR integration

## Dissemination

- International workshop of multi-analyte optical biosensors (2011)
- Notification on publications and press-releases
- Public awareness of the microsystems advantages on pHealth

# LoC application in Genetic testing & Personalized Medicine

Need for high throughput of DNA testing enabling fast and economically efficient genome-wide analyses in order to understand the genetics of diseases through high throughput deep sequencing.

Significant market for early-fast diagnosis of diseases through specific Protein detection. Need for operation with the minimum possible sample pre-treatment.

If the LoC sensitivity will increase by an order of magnitude over the standard analysis level at medical labs will be a significant powerful tool in the clinical hands (example: will be a life-saving instrument in the case of metastate prostate cancer).

# Who We Are



**NCSR 'Demokritos', Greece**

Optoelectronic sensor chip fabrication & functionalization



**PhoeniX BV, Netherlands**

Optical sensor simulation and design



**LioniX BV, Netherlands**

Optical sensor chip fabrication



**Jobst Technologies GmbH, Germany**

Microfluidics & encapsulation



**Jagiellonian University, Poland**

Sensor surface characterization



**VTT, Finland**

Read-out electronics and measuring system



**Biogenomica SA, Greece**

Biochip & system evaluation



**University College London, UK**

Biochip & system evaluation

# Contact Info

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