"PYTHIA"

Monolithically Integrated interferometric biochiPs for labelfree earlY deTection of Human dlseAses, FP7-ICT-224030

MAIN OBJECTIVE: ON CHIP INTERFEROMETRY FOR MULTIPLEXED BIOMOLECULAR REACTION MONITORING

Duration: 01/05/2008-31/10/2011

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CONSORTIUM



PLTHIP

BB-MZI chip: Layout & WaveGuide Engineering MONOMODAL WAVEGUIDES



Resolve mono-MZI Issues: signal fading+ Phase ambiguity SiO₂ (top cladding) Si₃N₄ waveguide SiO₂ (bottom cladding) 150 nm Silicon Nitride WG1.25 µm waveguide width,600 microns exposed arm



Monolithically Integrated Optoelectronic Platform





•K. Misiakos, S.E. Kakabakos, P.S. Petrou and Hans H. Ruf, "A Monolithic Silicon Optoelectronic Transducer as a Real-time Affinity Biosensor", *Anal. Chem.* 2004, 76, 1366-1373
•K. Misiakos, S. Kakabakos "Integrated optoelectronic silicon biosensor for the detection of biomolecules labeled with chromophore groups or nanoparticles", PCT WO2007/074348, US7319046
•K. Misiakos, S. Kakabakos, I. Raptis, E. Makarona, "Integrated optoelectronic silicon biosensor for the detection of biomolecules labeled with chromophore groups or nanoparticles", OBI, 1006509 2008



SPECTRAL SHIFTS IN MONOMODAL MZI

150 nm Silicon Nitride Thickness 1.25 μm waveguide width, 600 microns exposed arm





TRANSITION REGION IN MONOMODAL MZI

Increasing protein thickness





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watertoprop new.avi



BB-MZI chip: Layout & WaveGuide Engineering





Fully Integrated Configuration

Semi Integrated Configuration



Chip features

10 transducers in <40mm² area

Two Modes of Operation (Semi-integrated, Fully Integrated)



Demonstration of Operation



PYTHIA Semi-integrated chip: The ten monolithically integrated LEDs are activated sequentially through an external multiplexer. Each LED is coupled to one Mach-Zehnder interferometer and the light emitted at the edge of the chip is monitored through a standard optical microscope. Silicon nitride waveguides are 1.25microns wide and 150nm thick each and have period of 6microns.

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TE-TM MODE CCD IMAGE





SIMULTANEOUS MONITORING OF TE-TM MODES





Chip size: <40mm² 150 operational dies per 4"- wafer



MNBS 2012 Athens Greece

Si-LED



Spotting of the different binding biomolecules to the ten MZIs per chip for the preparation of protein sensor array. 11



Encapsulation & Electrical-fluidic docking station



Wafer-scale encapsulation





PYTHIA electric-fluidic docking station for Semi-Integrated chips



Multi-Analyte detection with model assays (SI)



Sequential detection of mouse-IgG and biotinylated BSA through reaction with anti-mouse IgG and streptavidin



Detection of Total-PSA with Fully Integrated chips

Cover medium RI changes (1.2x10⁻²)





start to 1: assay buffer (1% (w/v) BSA in 50 mM phosphate buffer, pH 7.4; 1 to 2: total-PSA zero calibrator in horse serum diluted 1:6 in assay buffer; 2 to 3: 1 ng/ml total-PSA calibrator in horse serum diluted 1:6 in assay buffer; and 3 to end: assay buffer.



PYTHIA Approach: FI configuration







- Transducer with monolithically integrated light source
- Broad-Band Mach-Zehnder Interferometry resolves the Single Wavelength Mach-Zehnder Interferometry limitations
- Wafer-scale encapsulation
- Two configurations of operation (semi-integrated, fully-integrated)
- Successful detection of Protein markers down to a few pM Concentrations
- FUTURE PROSPECTS: ON-CHIP SPECTRAL ANALYSIS





- Interferometric Chip Suppliers: Silicon foundries, MEMS foundries
- Selection of analyte panel and probe spotting: Kit manufacturers, Biotech-diagnostic companies. Provide encapsulation-packaging, too.
- Users-Applications: Real Time monitoring of a number of molecular binding events, of RI changes as a function of position, cell binding events: Research Labs, Bioanalytical companies, Pharmaceutical companies





- Molecular Probe Stability
- Lack of standards (also lack of common units-RIU in Optical devices, other units in different transducers). Multianalyte chips provide on chip zero calibrators
- Lack of unified view-language: Different disciplines develop distinct interests (Physists, Engineers, Biologists, Medical personnel).

THANK YOU !