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PHOTONICS21

AmbrosIa

A MULTIPLEXED PLASMO-PHOTONIC BIOSENSING PLATFORM FOR RAPID AND INTELLIGENT SEPSIS DIAGNOSIS AT THE POINT-OF-CARE

AMBROSIA factsheet

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Consortium:
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Catalan Institute of Nanoscience & Nanotechnology, ES
University of Bourgogne, FR
X-Celeprint, IE
Vall d'Hebron Research Institute, ES
Argotech, CZ
Biopix DNA Technology P.C., GR
microLIQUID, ES
University of Ioannina, GR
Smart Photonics BV, NL
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THE CHALLENGE

Sepsis is a life-threatening whole-body inflammatory reaction caused by a severe infection. With mortality rates around 35%, sepsis is responsible for 11 million deaths worldwide every year. The window of opportunity for sepsis management is in hours: the chance of survival drops by 7.6% each hour of disease progression until an appropriate treatment is started. Early and accurate sepsis detection and stratification is essential for enhancing survival rates. This is challenging, due to: i) complex diagnostic criteria requiring screening of multiple targets including both biomarkers and pathogens, (ii) time-consuming laboratory methods for identifying the bacterial causes of sepsis. Even worse, these conventional immunoassay techniques are performed in centralized laboratories, causing extra delays due to specimen transfers.

MISSION STATEMENT

This is exactly where AMBROSIA steps in to transform integrated plasmo-photonic refractometric sensors into a disruptive solution for sepsis diagnosis at the point of care that will offer multiplexed quantification of multiple protein biomarkers and bacteria within a few minutes, providing also real-time disease stage classification and enabling a rapid and precise decision making for therapy and medical actuation. Specifically, a

total number of 4 sepsis-related protein biomarkers (CRP, PCT, IL-6, MR-proADM) and 3 bacteria (E. coli, S. aureus, P. aeruginosa) will be simultaneously detected, targeting the successful experimental classification into four different sepsis stages (No Inflammation, Inflammation, Sepsis and Septic Shock). The unique AMBROSIA PoC diagnostic platform will be validated with clinical samples from the Hospital Vall d' Hebron Sepsis Biobank together with samples from healthy donors.

PROJECT OBJECTIVES

The overall objective of AMBROSIA is to develop a portable diagnostic unit for intelligent diagnosis of sepsis. This will be accomplished by label-free plasmo-photonic sensor technology in multi-channel configuration able to detect 4 sepsis related biomarkers and the 3 bacteria, within a single test. The sensor array will be integrated on a disposable SiN photonic sensor chip that will contain multiple sensing areas with such arrays. On top of that, the disposable chip will be equipped with on chip lasers and photodiodes heterogeneously integrated by means of the high-throughput micro-transfer printing technology. Based on the detection results, a photonic deep neural network will provide disease severity classification. Finally, the whole AMBROSIA technology is going to be validated in real clinical environment.

The individual objectives of AMBROSIA are to:

- **Develop high-sensitivity and noise-resilient ultra-compact CMOS plasmo-photonic sensors**
- **Deploy an InP-on-SiN cost-efficient integration platform through micro-transfer printing (µTP)**
- **Develop and demonstrate multi-channel label-free plasmo-photonic sensors for sepsis diagnosis**
- **Develop an AI-based electro-optical read-out system for real-time sepsis detection and classification exploiting ultra-low power photonic Deep Neural Networks (DNNs)**
- **Develop a Point-of-Care sepsis diagnostic and classification system**
- **Validate experimentally label-free and real-time sepsis detection and classification**

TECHNOLOGY BREAKTHROUGHS

Slow-light enhanced CMOS plasmo-photonic sensors: AMBROSIA aims to develop high-sensitivity and noise resilient ultra-compact CMOS plasmo-photonic sensors. Two different routes will be followed for the sensor configuration: (i) an optically-balanced Mach-Zehnder Interferometric (MZI) sensor with identical plasmonic waveguide segments in both arms that offers resilience to noise, (ii) a single-arm, bimodal interferometer that minimizes footprint. Sensitivity enhancement will be pursued leveraging dispersion engineered designs and utilizing slow-light phenomena through the adoption of Bragg grating decorated plasmonic stripes. Sensitivity is expected to reach the unprecedented values of 130000 nm/RIU with Limit-of-Detection (LoD) <10-8 RIU within ultra-compact designs utilizing <70 um sensing lengths.

Hetero-integration of InP-on-SiN through micro-transfer printing (µTP): AMBROSIA will transform its plasmo-photonic sensing technology into self-contained and completely electrically-interfaced sensor chips with on ***chip light generation and photodetection*** at 1550 nm avoiding complicated fiber alignment processes. This will be accomplished through the high-throughput ***micro-transfer printing*** technology where multiple InP coupons with pre-fabricated active structures (lasers and photodiodes) will be transferred onto the host SiN platform.

Ultra-low power photonic Deep Neural Networks (pDNN) for real-time sepsis detection and classification: AMBROSIA aims to develop a real-time identification and disease classification system minimizing misdiagnosis and saving time towards optimal medical treatment. Sepsis medical protocols will be translated into ***Deep Learning models*** that will train a ***SiN-based pDNN*** comprising 7 inputs (corresponding to the different biomarkers and bacteria) and 4 outputs (corresponding to the different sepsis stages). Within the pDNN, the matrix multiplication will be accomplished via a photonic ***Crossbar (Xbar) architecture*** while the ***weighting elements*** will be based on zero-power electrically programmable ***non-volatile Phase Change Material (PCM)-based modulators***.