Photonic Integrated Biosensors

Introduction

Our Photonic Integrated BioSensor platform has unparalleled sensitivity and reproducibility and finds application in drug discovery and development, companion diagnostics, therapeutic drug response monitoring and early diagnostics. Measurements show a sensitivity improvement of 2 orders of magnitude over conventional techniques.

Personalized Medicine and Diagnostics

An important area in the pharmaceutical application field is Personalized Medicine, which is characterized by a change in the whole value chain of drugs, from discovery to production, leading to a shift from big pharma to high-tech SMEs as the innovation leaders, such as LioniX International. This paradigm shift opens many opportunities for innovations based on Lab-on-a-Chip technology, especially in drug development and Companion/Complementary Diagnostics (CDx) as well as in the emerging area of Organ-on-a-Chip.
Our photonic integrated biosensor platform will have a major impact in instrumentation in which optical detection is being exploited in order to reveal more information on drug efficacy and toxicity.

Competences and Platform Technologies

Our photonic integrated biosensor platform combines key competences: proprietary (TriPleX™) integrated photonics (micro-photonics), micro/optofluidics and related surface functionalization for application in Lab-on-a-Chip based analysis and detection systems.

Examples of platforms are:

• Label-free photonic biosensor-array platform based on a proprietary asymmetric Mach-Zehnder Interferometer (aMZI) (see figure 1);

• Fully integrated chip-based Light Induced Fluorescence (LIF) micro-array (100 spots) for handheld and Point-of-Care diagnostics [1];

• Absorbance VIS-NIR spectroscopy-on-chip, including a proprietary tunable, ultra-narrow linewidth laser.

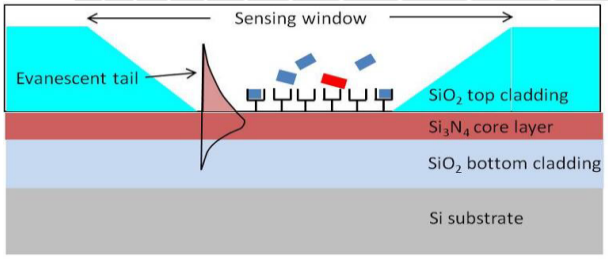

Fig 1 Basic principle of label-free detection by an integrated optical waveguide on a chip. The evanescent tail of the light wave in the Si_3N_4 core (red) detects tiny mass changes by capturing of analyte by surface-bound receptors [2]. In our platform these changes are sensed with the ultra-sensitive asymmetric Mach-Zehnder Interferometer (aMZI) [3].

Label-free Biosensor-Array Chip-Module with World-Record Sensitivity

We have developed world's first fully (hybrid) integrated and wafer scale manufacturable photonic interferometric biosensor-array chip-module (figure 2). This biosensor-array platform shows an unparalleled sensitivity and reproducibility, and is applicable in both drug screening/lead optimization and all kinds of diagnostics.

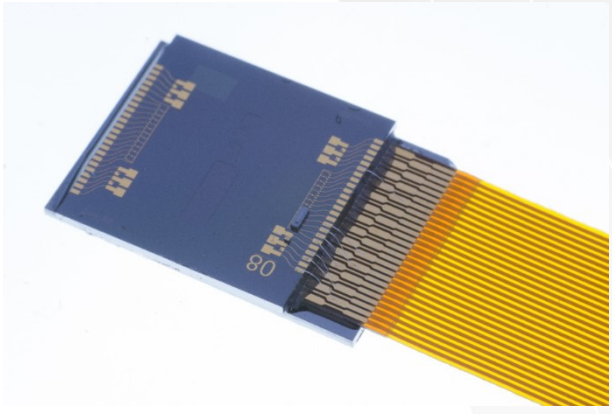

Fig 2 Label-free photonic aMZI biosensor-array module with flip-chip bonded laser and detector-array, and connected flex cable.

The fully integrated module is produced cost-effectively and therefore allowing mass production for high volume Point-of-Care applications.

The platform supports selective functionalization of the sensor surface (figure 3) in a co-development with partner Surfix. With this, the sensitivity of the biosensor is enhanced substantially. The nanochemistry based functionalization shows excellent selectivity with different kinds of receptors such as antibodies and aptamers.

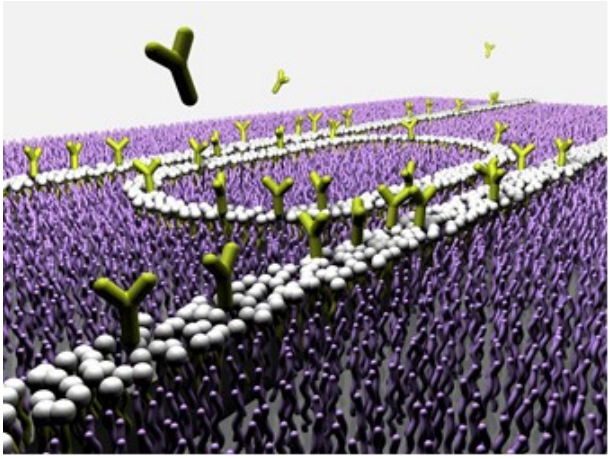

Fig 3 Selectively antibody (green) functionalized sensing area (white) avoiding analyte depletion by a surrounding repelling surface (purple) and allowing for orders lower limit-of-detection (LOD) on the ultra-sensitive, optical waveguide-based sensor.
Courtesy of Surfix BV (www.surfix.nl)

Examples of Product Developments

At present, this platform is being applied in a number of medical diagnostic equipment developments for (OEM) customers and in the framework of EU funded projects [4]. One of these is dedicated to a drug (fragments) and to lead optimization instrument based on the ultra-sensitive optical detection feature proven to be one to two orders higher than state-of-the-art Surface Plasmon Resonance (e.g. Biacore of GE Healthcare) and Micro Ring Resonator based equipment, such as exploited by Genalyte (USA) [5]) (figure 4).

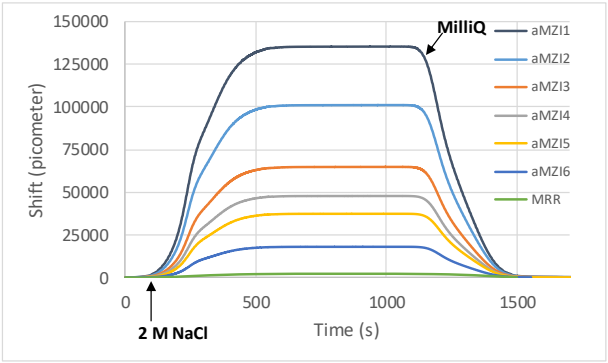

Fig 4 Sensitivity testing of a series of LioniX International proprietary aMZI sensors by stepping from demineralized water to 2 Molar NaCl and back, showing the sensitivity enhancement of nearly two order of magnitude.

Another application of the photonic integrated biosensor platform exploits the fully (hybrid) integrated and wafer scale manufacturable biosensor-array chip-module platform for a clinical, therapeutic response monitoring tool in a co-development with a class of new, proprietary cancer drugs of a pharma partner company (see https://biocdx.eu).

[1] R. Duer, R. Lund, R. Tanaka, D. A. Christensen and J. N. Herron, In-plane parallel scanning: a microarray technology for point-of-care testing Anal. Chem. 82, 8856 (2010)
[2] Besselink GAJ, Heideman RG, Schreuder E, Wevers LS, Falke F and Van den Vlekkert HH, Performance of Arrayed Microring Resonator Sensors with the TriPleX Platform, J Biosens Bioelec-tron 2016, 7: http://dx.doi.org/10.4172/2155-6210.1000209
[3] Patent pending
[4] H. Leeuwis et al., IDDST-2018 presentation in Session 2201: Novel Analytical Technology for Drug Discovery
[5] Sasi Mudumba et al, Photonic ring resonance is a versatile platform for performing multiplex immunoassays in real time, Journal of Immunological Methods 448 (2017) 34–43