Integrated bio-photonics to revolutionize health care enabled through PIX4life and PIXAPP

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ABSTRACT

Photonics has become critical to life sciences. However, the field is far from benefiting fully from photonics' capabilities. Today, bulky and expensive optical systems dominate biomedical photonics, even though robust optical functionality can be realized cost-effectively on single photonic integrated circuits (PICs). Such chips are commercially available mostly for telecom applications, and at infrared wavelengths. Although proof-of-concept demonstrations for PICs in life sciences, using visible wavelengths are abundant, the gating factor for wider adoption is limited in resource capacity.

Two European pilot lines, PIX4life and PIXAPP, were established to facilitate European R&D in biophotonics, by helping European companies and universities bridge the gap between research and industrial development. Through creation of an open-access model, PIX4life aims to lower barriers to entry for prototyping and validating biophotonics concepts for larger scale production. In addition, PIXAPP enables the assembly and packaging of photonic integrated circuits.

Keywords: Pilot line, PIX4life, PIXAPP, bio-photonics, silicon nitride photonics, life sciences, visible wavelength, foundry, packaging

1. INTRODUCTION

In the life science industry, many devices rely on the use of light for different applications. In these devices, relatively large optical components such as lasers, lenses and rectifiers are used. Biophotonics makes it possible to produce miniaturized versions of these components, such as lasers, waveguides, modulators, photodetectors, filters, ring resonators and others. By integrating these photonic components in a single chip, a miniature system can be developed that often also works faster and more reliable than its larger counterpart. Moreover, the possibility of including all these building blocks into the same monolithic circuit, enables system architectures combining tens, hundreds or even more blocks, opening the door to novel complex applications that could otherwise not be conceived using assemblies of discrete optical components. Photonic circuits, produced on silicon wafers, in a standardized and automated production flow, also makes this integration technology inexpensive and scalable.

Different applications in biophotonics are nowadays benefiting from PICs:

e.g.,

- Medical instrumentation: confocal and multiphoton imaging, DNA sequencers, optical coherence tomography, respiratory gas monitors, Raman spectroscopy, glucose monitors, flow cytometry, etc.

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- Photonic Lab-on-a-chip: rapid and automated analysis of small volume samples, in vitro and in vivo monitoring, implantable bio-fluoro-imaging, digital electrowetting, drug discovery, etc.
- Optical sensors to measure chemical properties such as pH changes and trace gas, indirect biosensors using fluorescence, phosphorescence or colorimetric measurements, and direct biosensors of metabolites, enzymes, environmental toxins, etc.

A major feature for many of these applications is the short wavelength used, from the visible, 400-700 nm, to the lower near-infrared, 700-1100 nm. However, most PICs platforms, traditionally proposed for telecom (e.g., silicon, InP), strongly absorb light at those wavelengths. Recent advances in silicon nitride (SiN)-based PICs are also achieving very low propagation losses at visible wavelengths.

There are currently two major hurdles for developing SiN PICs for biophotonic applications: the maturity of the manufacturing process, including design tools and device libraries, foundry processes, and packaging options, and secondly, the high cost that prototyping and pilot production still entails for taking an idea into the market. The PIX4life and PIXAPP pilot lines aim to solve these issues, and are described in detail below.

2. PIX4LIFE, THE EUROPEAN PILOT LINE FOR SILICON NITRIDE PHOTONICS

In PIX4life we aim to mature a high performance, high yielding and CMOS-processing compatible SiN Photonic IC pilot line together with the accompanying supply chain for applications in the visible range (405 nm, 455 nm, 530-562 nm, 625-660 nm and 785-850 nm) in order to become the world's premier pilot line for integrated biophotonic applications. To lower the cost barrier, the SiN PIC technology will be offered via multi-project wafer (MPW) runs, where multiple designs from different end-users are combined into a single wafer, sharing thus area and cost.

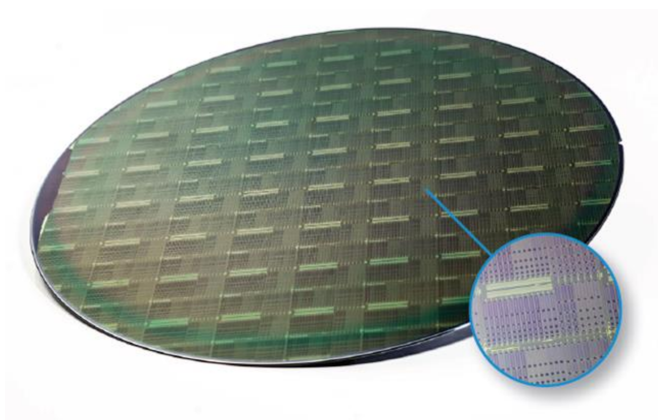

Figure 1. Several designs from various end-users are combined into one multi-project wafer (MPW).

The two manufacturing platforms will be implemented in an industrial foundry (TriPleX at LioniX) and a R&D CMOS pilot line (BioPIX at IMEC) and will provide a superior quality, highly reliable technology platform in the visible range using the accuracy and yield of microelectronic CMOS fabrication processes. Moreover, they will be using generic photonic building blocks and interfaces to commercial design software tools like PhoeniX and Luceda.

The goal is to mature SiN waveguide platforms with very low propagation losses, low autofluorescence and a high level of integration to realize compact systems at low cost targeted towards the visible spectrum. PIX4life will ensure that adequate process in-line metrology tools, photonic chip validation methodologies, process statistics and design software tools are ported and extended to control the quality and reliability of SiN photonic ICs in the visible range. We will build passive components with best-in-class performance, including waveguides, splitters, filters, multiplexers and couplers based on optimized ultra-low loss SiN material. Furthermore, we will improve state of the art active modulators, exploring the best suited tuning options using additional materials combined with SiN.

We will improve accessibility to the technology, not only for photonic end users, but also for system houses and pioneering life science companies willing to try out photonic components to address miniaturization needs in life science instrumentation. We will develop an end-to-end supply chain reaching from consultancy and design services to packaged and characterized chip components by aligning and extending existing European expertise in source and detector coupling, and microfluidic integration, achieving functional photonic components in the visible range. PIX4life will extend design tools capabilities including process design kits (PDKs), simulation tools, layout tools and design libraries of building blocks optimized for the visible wavelength range.

PIX4life will combine already mature laser sources (GaN and GaAs edge emitting laser diodes and VCSELs) and CMOS imager technology with the SiN PIC technology, to enable a complete platform in the visible range. Some of these integration technologies are still at an early development stage and need to be matured in the framework of PIX4life, with life science applications and open access in mind.

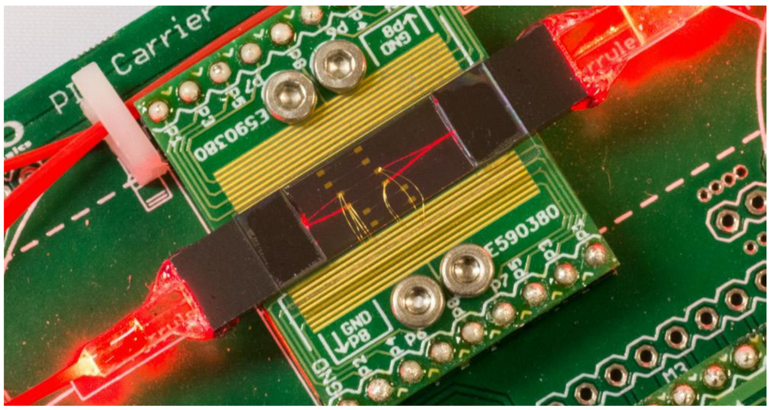

Figure 2 A photonic integrated circuit integrated with optical and electrical connections

While the whole service offering of the pilot line will be open to selected end-users during its maturing stage until 2019, the development of the complete value chain of technologies and services will be guided and validated by four well-chosen applications coming from European industrial customers aiming to launch new products in the life sciences area. These are described below.

2.1 Toptica: a multispectral light source on chip

Life science applications in the field of e.g. microscopy or flow cytometry require multiple wavelengths to excite the dyes of interest. To move away from the bulky optics, Toptica is developing a fully integrated multispectral light source by combining different wavelengths in a SiN chip. This not only reduces the physical dimensions but also the cost, and it improves robustness.

2.2 Medlumics: an OCT-on-chip for ophthalmologists

Medlumics aims to use the SiN photonic pilot line to produce an OCT-on-chip system operating in the near infrared, thus paving the way towards compact and cost-effective medical devices to be used in the daily practice, for example by ophthalmologists. The company's current OCT systems are based on SOI technology and use light at larger wavelengths. While this is perfect for its use, among others, in cardiology, gastroenterology or dermatology, in other applications like oftalmology, light in the near infrared is preferable. This is only possible using SiN technology, and will be explored in PIX4life.

2.3 Miltenyi: flow cytometer with innovative laser

Miltenyi is a German company that makes flow cytometers with a chip-based sorting module. At the moment it uses standard lasers to illuminate the fluorescent labels attached to the cells that flow past in the microfluidic channel and to identify them. The company now wants to start using integrated biophotonics so that this laser light can be better targeted and controlled, and hence enhance the sensitivity and robustness of their flow cytometer.

2.4 Bosch: lower cost sensors for monitoring health parameters

Bosch wants to start using photonic sensors for monitoring health parameters such as body temperature, the composition of sweat, heartbeat, respiration rate, etc. Interaction between light and the body at the nanoscale, either by absorption or diffraction, will provide valuable information about these parameters. For engineering such a system and in order to create a reliable device, the SiN platform offers the best compromise between chemical resistance and optical performance, enabling the detection of the desired physical and chemical properties, while maintaining the small size and low power. Open-access platforms and services

In PIX4life, 14 European partners collaborate to make biophotonics accessible for innovative life science companies and start-ups, providing both a technology platform and supporting services such as consultancy, design services, chip testing and assembly.

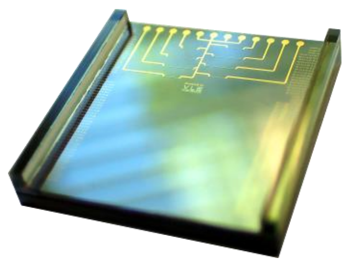

Figure 3 TriPleX photonic circuit with test structures for visible wavelengths designed by VLC Photonics.

PIX4life will have 4 MPW runs that will be accessible to external customers through an early access scheme. Design tools and design support and services will also be available, including the later chip characterization service too.

Table 1. PIX4life MPW offering in 2018.

	imec	**LioniX International**
Dates[1]	April 2018	June 2018
Cell size	5.3 x 4.8 mm	25 x 8/16 mm
Cell copies	20 dies	4 dies
Cell fabrication cost	10.000€ / 17.000€[2]	8.500€ / 16.000€[2]

[1] Exact design submission, tape-out and chip delivery dates will be detailed at the website: www.pix4life.eu

[2] Cost for non-EU users.

3. ASSEMBLY AND PACKAGING THROUGH PIXAPP

PIXAPP is the world's first open access PIC (Photonic Integrated Circuit) assembly and packaging supply chain, with capacities from early stage prototyping to low-to-medium volumes. It is funded by the European Union, and is a Public Private Partnership with Photonics21. PIXAPP combines an interdisciplinary team of Europe's leading industrial and research organizations, providing users with state-of-the-art PIC assembly and packaging technologies, including optical, electrical, thermal and mechanical packaging capabilities, along with standardized test protocols and packaging equipment. Target markets include communications, healthcare, sensors and security. PIXAPP provides users with a single easy access point-of-contact called the Pilot Line Gateway, which is located at the Tyndall Institute. The Gateway staffed by packaging experts and project managers, will ensure users, including non-photonics experts, get fast access to PIXAPP's extensive range of advanced assembly and packaging technologies. Furthermore, PIXAPP will implement a comprehensive user training programmed, including training PIC designers and those involved in the application of PIC technologies.

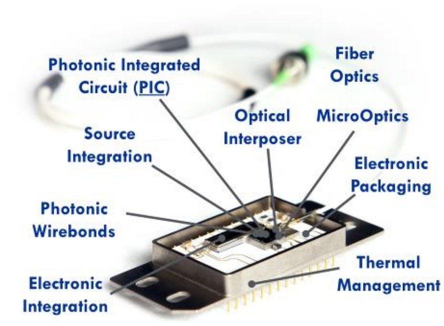

Figure 4. a PIC assembled in a multifunctional package by PIXAPP

4. SUMMARY

Two European pilot lines are addressing the main challenges for the adoption of photonic integration technologies by biophotonic applications at a larger scale: PIX4life and PIXAPP.

PIX4life focuses on developing a pilot line to support the development of visible and short near-infrared SiN PICs, the most relevant wavelength ranges for bio- and life-science. To reduce the cost of design and fabrication of new PICs, manufacturing processes and libraries of building blocks are being validated at those wavelength ranges, and they are starting to be offered through different PDKs for two different foundries. Open-access MPW runs and custom dedicated runs are offered to external end users interested in prototyping and scaling up into larger volumes.

PIX4life and PIXAPP are intensively working together, since a PIC requires a robust package. PIXAPP focuses on developing a pilot line enable assembly and packaging of PICs for prototyping and up-scaling volumes.

Detailed information of both pilot lines can be found at www. PIX4life.eu and https://pixapp.eu/.