

Diagnostics on Gold by Plasmon Resonance

Evaluating the scene with Ibrahim Abdulhalim, PhotonicSys

An emerging company, PhotonicSys, offers new products based on surface plasmon resonance (SPR) for diagnostics applications. In a discussion with EPIC experts Ana González and Jose Pozo, CEO Ibrahim Abdulhalim explains the benefits and applications for this kind of devices and the challenges that this technology is facing.

PhotonicSys is making great strides in bringing surface plasmon resonance (SPR) technology to academic and research institutions worldwide, next challenge: to move to industrial scale. For this technology report, Ibrahim Abdulhalim, CEO of PhotonicSys and Ben Gurion University professor, discussed the current market and future challenges for SPR with the European

Photonics Industry Consortium's R&D manager, Ana González, and director of technology and innovation, Jose Pozo.

Current market

In the last decade, SPR has emerged as a powerful optical detection technique for setting label-free by molecular interactions in real time within a variety of diverse applications. Yet, despite its

many advantages over traditional techniques, SPR is still largely confined to laboratory research, mainly in the fields of biomedicine and drug development. Unlike ELISA (enzyme-linked immunosorbent assays), SPR is capable of real-time detection and the devices do not require skilled personnel to operate them. SPR also has greater sensitivity and can evaluate bio-molecules in their native state as the molecules don't need labelling. Taken together, these advantages give SPR real added value.

PhotonicSys has recognized the value and potential of SPR. Since 2016, they have been providing academic and research institutions worldwide with photonics based instruments and systems for the rapid detection of small (molecules, viruses) and large (bacteria, cells, proteins) entities both in solutions and in dry forms.

The advantages of PhotonicSys' devices are that they can be standalone or integrated into other systems, such as optical microscopes. Furthermore, being only around three centimeters high, they can be positioned under a microscope or a spectrometer to probe concentration, refractive index, fluorescence, binding kinetics, Raman, surface shape, or other spectroscopic signals. They can detect both gases and liquids, and – as Ibrahim points out –, perhaps the main advantage is that their devices can achieve variable penetration

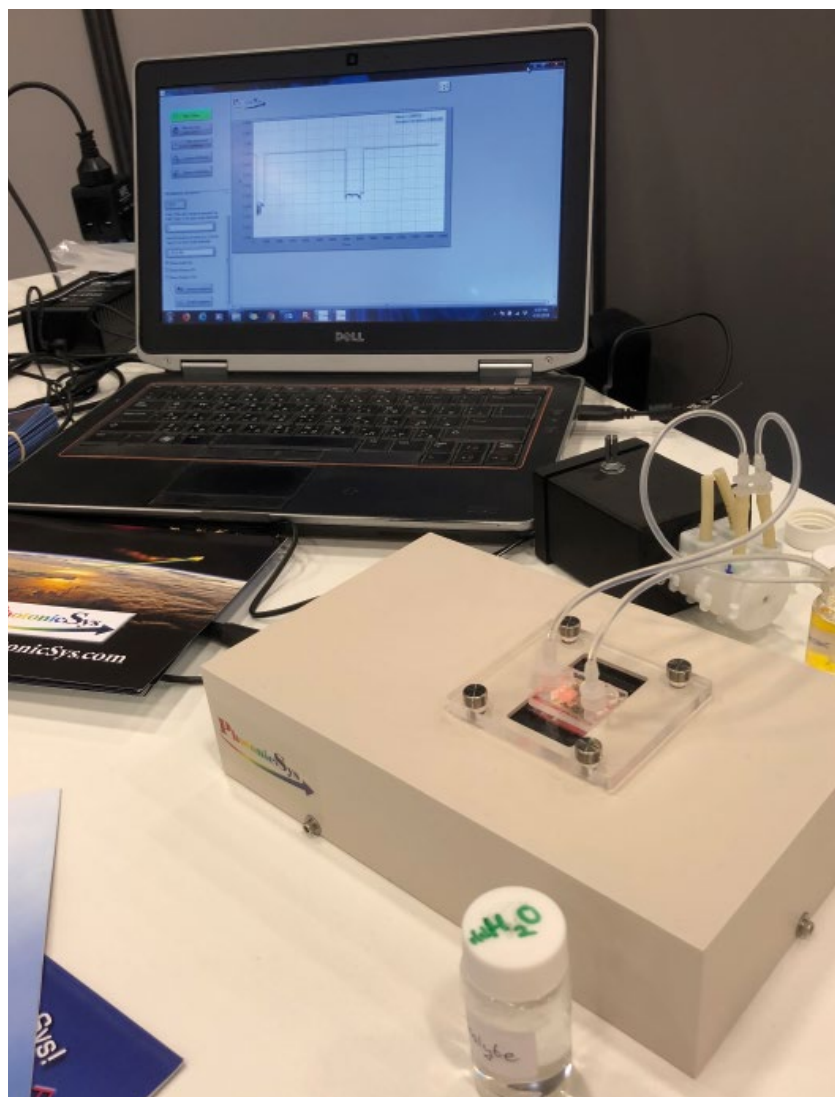


Fig. 1 PhotonicSys SPR system H5 in operation under flow. The name H5 came from its height which is 5 cm. The company is working on H3 future system. Note the dynamic changes of the signal on the screen when changing between two different liquids. (Source: PhotonicSys)

depths from a few hundred nm to a few microns, which makes them suitable both for small and large entities (Fig. 1).

Ibrahim states: “We think our price of around five thousand euros is attractive because in addition to the basic device we offer the option of collaborating with researchers so they can develop their own protocols for specific sensing. We are also happy to consider licensing.”

SPR in the pharmaceutical industry

SPR is an invaluable tool for drug development: In the initial stages, the technique can help determine molecular binding constants while in drug production, it can be used to monitor the concentration of molecules. At this stage, SPR is particularly advantageous as it can detect very low concentrations.

It can also help in the development of new antibiotics for resistant bacteria by rapidly identifying the bacteria causing the infection. Another important area is personalized treatment for cancer. Research has shown that mutations vary according to the individual and by simply placing tumor cells on an SPR substrate, it is possible to determine which drug is able to kill the tumor cells in question.

Technical challenges and bottlenecks

Despite SPR's enormous potential for the betterment of human health and the environment, and the interest shown over many years by the pharmaceutical industry in label-free diagnostics, it has been slow to reach the big industrial labs. If SPR is going to expand from just R&D to an industrial scale, the following technical challenges and bottlenecks will need to be resolved:

Specificity

According to Abdulhalim, one of the biggest challenges is specificity, i.e. how to ensure that the device senses the target particles. Due to the variety of molecules and sample types, this requires the development of different surface treatments to obtain specific receptors for specific biomarkers. Surface treatments can be performed by dropping solutions onto the substrate surface or by printing coatings on different parts of the chip at a wafer scale. Antibodies, aptamers, and molecular imprints are among the fast growing reliable receptors.

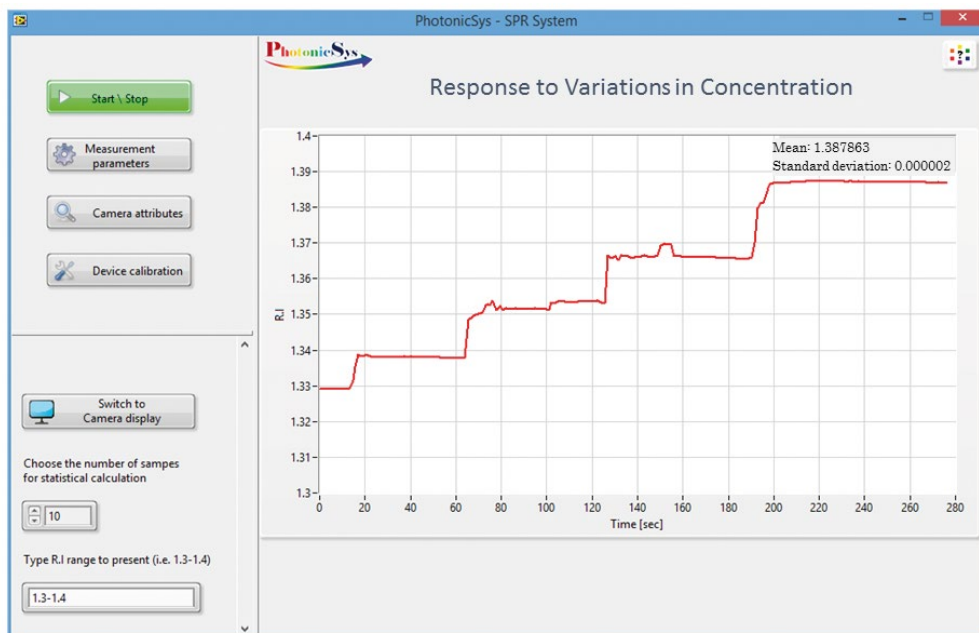


Fig. 2 Sensogram showing video rate speed of following up concentration changes with resolution down to 0.000002 RIU. (Source: PhotonicSys)

But there is also the issue of performing many different assays on the same chip. In this case, while most substrates can be produced in-house, the preparation of more complicated specific binding layers may require partnering with somebody who has the necessary expertise. Moreover, the positioning of various samples in the correct place on the same chip may require robotics. This issue will be addressed at EPIC's 2019 event on automation [1].

For González, as regards functionalization of substrates, gold is a better material than silicon oxide as gold layering is relatively cheap to produce and provides much better reproducibility. Additionally, an important issue in sample preparation is the difficulty of producing non-folding surfaces to ensure that the target (bio)molecule can be detected when real samples such as urine, serum, or even blood are evaluated.

Chemistry

While the SPR technology is already mature, the chemistry needed to attach the bio-recognition molecules on the substrate surface is still challenging in terms of reproducibility. These techniques have taken longer to develop and have proved more difficult than expected.

One way to resolve this problem would be to facilitate greater collaboration between the chemical and the photonics R&D key players, respec-

tively. This would create synergies in photonics and chemical knowledge and enable chemists and bio-researchers to become more familiar with and aware of the potential of optical techniques.

Component bottlenecks

To date, PhotonicSys has not experienced any significant supply chain problems as they mostly use standard components, i.e. metallic and dielec-

Professor Ibrahim Abdulhalim

is with the Department of Electro-optics and Photonics Engineering at Ben Gurion University. He worked in academic institutions and companies such as the OCSC in UC at Boulder, the ORC at Southampton University, the Thin Films Center of the University of Western Scotland, in KLA-Tencor, Nova, and GWS Photonics. He published more than two hundred articles, two books, ten chapters, and is an inventor with twenty filed patents. He is a fellow of IoP and SPIE and an associate editor for the Journal of NanoPhotonics, the Journal of Imaging, and the Journal of Sensors. His research activities involve optical and plasmonic bio- and chemical sensors, liquid crystal devices for photonic applications, and fast 3D interference microscopy. In 2014, he established PhotonicSys Ltd. to commercialize the different innovative plasmonic techniques for bio- and chemical sensing.



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European Photonics Industry Consortium (EPIC)

EPIC is the European Photonics Industry Consortium, a membership-led not-for-profit industry association that promotes the sustainable development of organizations working in the field of photonics. Our members encompass the entire value chain from LED lighting, PV solar energy, silicon photonics, optical components, lasers, sensors, displays, projectors, optic fiber, and other photonic related technologies. We foster a vibrant photonics ecosystem by maintaining a strong network and acting as a catalyst and facilitator for technological and commercial advancement. EPIC works closely with related industries, universities, and public authorities to build a more competitive photonics industrial sector, capable of both economic and technological growth in a highly competitive world-wide marketplace.



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tric substrate coatings, standard light sources, camera, pumps, laser diodes. One exception are the micro-channels that are specially made in China.

Fluidity

In González' experience, a potential component bottleneck is in the handling of fluids inside the device. For example, a bubble in the middle of a measurement area can have disastrous effects on the refractive index and produce unusable results. Consequently, it would be very useful to have a device capable of removing bubbles from fluids that are going to be introduced into the sensor area. Degassing and noise removal software

are developed by PhotonicSys to tackle this problem.

Sensitivity

A key factor in the marketing of SPR devices is penetration depth of the evanescent field that the device can provide. While small structures like molecules can be detected by an evanescent field of around 200 nm, larger structures, such as cells and bacteria, require a larger penetration depth of up to a few microns. Abdulhalim agrees and stresses that sensitivity must be tuned for each application as a too high sensitivity would make it very difficult to produce a stable device. The unique technology of

PhotonicSys enables detecting both the small (nanoscale) and large (microscale) entities using the same instrument. In one case the SPR substrate even provides self-referencing while in another case the reference is introduced in a micro-channel nearby the sample channel (Fig. 2).

Future Applications

Abdulhalim believes that in the near future, various health monitoring SPR based devices will become available. Most of these will use fluorescence and color parameters based on nano-plasmonics, as used in currently available pregnancy tests. But the detection capabilities will be much more sophisticated, for example, enabling users at home to determine the age of a pregnancy, to detect the type and severity of a virus, and to carry out a variety of blood analytics. González also sees potential for health monitoring and prevention, for example, the daily detection of the C reactive protein, an indicator of cancer. One of the main advantages of SPR devices is that unlike more traditional techniques e.g. OCT, the results are analytical and do not require interpretation. In addition, SPR-based biosensors could provide many other applications including specific cancer biomarker detection, fast identification of resistant bacteria and DNA mutation detections among others. González and Pozo agree that it is time for SPR biosensors to reach the hospitals and primary care points and to revolutionize the healthcare, and they are very glad to see an EPIC member in the lead of it.

Authors

Ana González is R&D manager at EPIC. Her expertise relies on the development of systems based on integrated photonic circuits, packaging, and assembly, and the investigation of applications such as chemical / biological sensing and datacom. In addition, she has been involved in technology transfer and business development processes. She received her bachelor's degree in chemistry from the University Autonomous of Barcelona (UAB) and her PhD degree from the Catalan Institute of Nanoscience and Nanotechnology (ICN2).



Jose Pozo is director of Technology and Innovation at EPIC. As EPIC's CTO, he represents 400-plus leading corporate members active in the field of photonics. His job consists on actively engaging with them and provide them with tools to strengthen their position in the supply chain. He has 20 years' background in photonics technology, market knowledge, and a large network within the industrial and academic photonics landscape. Dr. Pozo holds a PhD in electrical engineering from the University of Bristol, UK, and a MSc and BEng in telecom engineering from Spain and Belgium.



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- [1] EPIC's 2019 Event on Automation (23 – 24 May 2019 at Amicra) www.epic-assoc.com/epic-meeting-on-automation-tools-for-packaging-and-testing-at-amicra/