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Route Towards a Label-free Optical Waveguide Sensing Platform Based on Lossy Mode Resonances

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Abstract: According to recent market studies of the North American company Allied Market Research, the field of photonic sensors is an emerging strategic field for the following years and it is expected to garner $18 billion by 2021. The integration of micro and nanofabrication technologies in the field of sensors has allowed the development of new technological concepts such as lab-on-a-chip which have achieved extraordinary advances in terms of detection and applicability, for example in the field of biosensors. This continuous development has allowed that equipment consisting of many complex devices that occupied a whole room a few years ago, at present it is possible to handle them in the palm of the hand; that formerly long duration processes are carried out in a matter of milliseconds and that a technology previously dedicated solely to military or scientific uses is available to the vast majority of consumers. The adequate combination of micro and nanostructured coatings with optical fiber sensors has permitted us to develop novel sensing technologies, such as the first experimental demonstration of lossy mode resonances (LMRs) for sensing applications, with more than one hundred citations and related publications in high rank journals and top conferences. In fact, fiber optic LMR-based devices have been proven as devices with one of the highest sensitivity for refractometric applications. Refractive index sensitivity is an indirect and simple indicator of how sensitive the device is to chemical and biological species, topic where this proposal is focused. Consequently, the utilization of these devices for chemical and biosensing applications is a clear opportunity that could open novel and interesting research lines and applications as well as simplify current analytical methodologies. As a result, on the basis of our previous experience with LMR based sensors to attain very high sensitivities, the objective of this paper is presenting the route for the development of label-free optical waveguide sensing platform based on LMRs that enable to explore the limits of this technology for bio-chemosensing applications.

Keywords: Lossy mode resonances, Optical fiber sensor, Thin-films, Sensing platform, Refractive index.

1. Introduction

Photonic sensor detection systems are attracting a great deal of interest and investment owing to their superior performance [1-3] and the utilization of intimate light-matter interactions is becoming more and more attractive for both chemical and biological detection of different species in size (from nm to microns) at surprisingly low concentrations (attomolar or parts per trillion or even further) [4] capable to cope with very challenging applications, such as cell activity or volatile compounds detection in aqueous or gaseous environments respectively [5]. So, there is a need for the development of cheap, portable and real time detection devices, such as the one represented schematically in Fig. 1, applicable in various fields like food quality, discovery of novel biomarkers and early diagnosis in medicine, the recognition of chemical substances at very low dilutions in chemical sciences, trace detection of air pollutants at very low concentrations associated to the more and more restrictive regulations in harmful gases emissions or other applications.

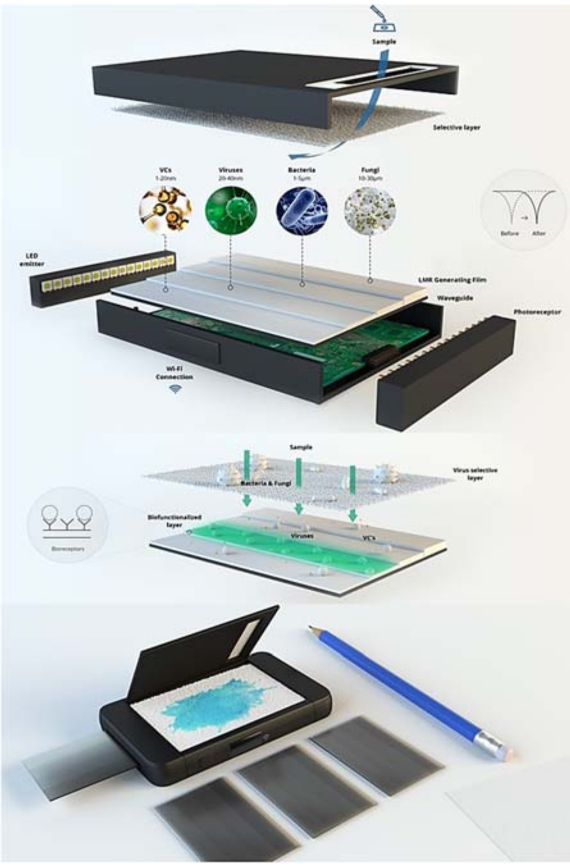

Fig. 1. Setup of the label-free multipurpose sensor. At the top, a schematic of the sensing platform. In the middle, a practical application of the platform towards detection of a type of virus. At the bottom, an infographic of the final device with the detection cartridges.

Currently, photonic sensing systems are far from being exploited to their full potential and there is still a long way to go in the understanding of these phenomena in order to achieve so. For example, the first SPR based sensor developed in 1982 was a scientific breakthrough [6]. It used the Kretschmann-Raether configuration [7], which basically consisted of an optical prism with a metallic overlay of tens of nanometres fabricated on one facet (see Fig. 1-top), which can be simplified using an optical fiber configuration (see Fig. 1-bottom) that removes the prism while reduces the size of the setup. Both setups presented in Fig. 2 permit surface plasmon polaritons to be generated at the metal-dielectric interfaces and to couple light at specific wavelength ranges as a function of the surrounding medium conditions. This configuration can be adjusted for biological or chemical applications adding a selective coating for the selected target on top of the metallic layer, then a biosensor or a chemical sensor is obtained [8].

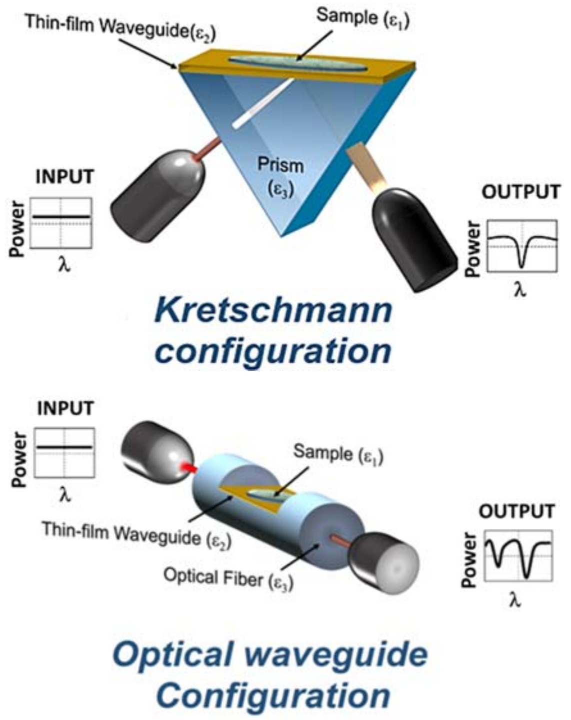

Fig. 2. Resonance generation with a nanocoated optical prism (SPR, Kretschmann configuration, top) and a nanocoated D-shaped fiber optic, LMR (bottom). Reprinted from [9] with permission from Elsevier.

Since SPR-based sensing devices working principle remains the same, the technological platforms have evolved in terms of stability, robustness and applicability with the possibility to detect different analytes at different concentrations at the same time. As a result, SPR based sensors are expected to reach in 2025 a business of more than 1 billion dollars [10].

The interest in this kind of devices has been already proven by commercial developments of SPR-based devices such as GE-healthcare Biacore systems for screening and quality characterization of molecular interactions from ions to viruses [11]. In the same manner, other devices based on different optical principles have emerged, such as Research International RAPTOR, a 4-channel optical waveguide system for rapid, automatic, portable fluorometric assay for monitoring toxins, viruses, bacteria, spores, fungi and other diverse targets [12] or Fortebio OCTET that performs quantitation and kinetics characterization assays at high speed and throughput [13]. However, previous devices are mainly intended for analysis in aqueous environments, the size of the equipment prevents in most cases from any portable measurement or in-field usage and they do not enable analysis in gaseous media, which is an important question that must be addressed for a versatile analytical tool.

The solution to previous concerns might come by exploiting lossy mode resonances (LMR), a phenomenon that emerges from the promising combination of nanotechnology (a thin-film with nanometer thickness deposited onto a substrate) and photonics (light transmitted through a waveguide is coupled to the thin-film generating a resonance).

The first reported experimental LMR demonstration was performed by Dr. Carlos Ruiz Zamarreño in his PhD thesis followed by a complete theoretical explanation of the phenomenon by Dr. Ignacio Del Villar in [14], the corresponding diffusion by Professor Ignacio Raúl Matias in an invited talk at Optical Fiber Sensors Conference 2009 followed by the invited talk given by Dr. Carlos Ruiz Zamarreño at SEIA conference in 2019 [15]. During that time, this technology has been cited more than 3,000 times in different projects related to LMR-based devices for the detection of pH [9], VCs [16], IgGs [17], proteins [18] or DNA [19] just to mention a few. In addition, other research groups from United Kingdom, Poland, India or China have explored the potential of LMRs for sensing applications in both experimental and theoretical works [20-27].

LMR technique has been proposed as an alternative sensing platform that competes with SPR. Both phenomena occur when the magnitude of the real part of the thin-film permittivity is greater than both its imaginary part and the permittivity of the material surrounding the thin-film (dielectric medium). However, unlike in SPRs, where the real part of the thin-film permittivity is positive (that is, metallic material) in LMRs it is negative (dielectric or semiconductor material) [28]. As a result, LMR based sensors broaden the range of materials that allow attaining a resonance and the associated chemistry possibilities.

Moreover, LMRs overcome SPRs in optical waveguide configurations (typically fiber optic where the incident angle is close to 90º), where the resonances are induced when a mode guided in the waveguide experiences a transition to guidance in a thin-film with losses. LMRs offer other important differences in the way they operate, which is advantageous for sensing purposes: LMRs can be obtained with both transverse electric (TE) and transverse magnetic (TM) polarized light while SPRs are only obtained with TM polarized light [29], which permits to obtain reference measurements as well as override the utilization of polarized light if necessary. Moreover, the position of the resonance in the optical spectrum can be precisely tuned in a simple way by controlling the thin-film thickness (tens to hundreds of nm thick). An additional way to tune the LMR is through the dielectric properties of the thin-film and the optical waveguide as it is described in [30].

Among the LMR potential application domains, probably the most important ones, from the point of view of their multiplicity of possibilities, are volatile compound detection and biosensing. On one side, the detection of VCs in air could enable detecting explosives and distinguishing specific biomarkers in human breath or other body fluids for volatolomic applications towards early diagnosis and detection of acute pathologies and data mining [31]. On the biosensing side, the rapid and real time detection of DNA/RNA towards DNA methylation and DNA mutation identification to viruses, proteins and cell activity monitoring are of extreme importance.

2. Previous Results

Obtained results in this field rely on one of the key parameters of LMRs, "the sensitivity", which can be improved in a very simple way by controlling the thin-film thickness, the thin-film refractive index and the surrounding medium refractive index. These basic rules, described in one of our works [30], have allowed us to obtain a major advance in LMR with a record sensitivity below 10^{-9} refractive index units (RIU) per nanometer [32] (see Fig. 2), which permits for example to detect concentrations in the order of femtomolar or even lower, [17]. This record sensitivity was achieved in the vicinity of the refractive index of the substrate (~1.45) because, as stated in [30], the sensitivity increases exponentially as the surrounding medium refractive index approaches the refractive index of the substrate. Therefore, the adequate matching between the dielectric properties of the substrate and the surrounding medium as well as the optimization of the LMR generating layer or layers in terms of thickness and dielectric permittivity might open a full range of possibilities in the improvement and applications of these devices throughout an intensive study of material properties, fabrication procedures and technology integration.

In the case of Fig. 3, the substrate was optical fiber made of fused silica (refractive index~1.45). However, as stated before, the device has not been optimized for operation in the aqueous domain with a surrounding medium refractive index ~1.33 (it has applications in oil industry though [33]), which still presents an opportunity for a sensitivity improvement of several orders of magnitude. Concerning the application of these devices for biosensing applications the two most interesting regions are the refractive index region of water-based solutions (~1.33) and the refractive index region of air (~1) for aqueous and gaseous media respectively. Most of the chemical and biological reactions take place in aqueous media, whereas many other applications can be found in air, (detecting VCs for example). Therefore, from [30], the development of optical sensors using the adequate LMR generating thin-films and waveguide substrates with a refractive index of 1.33 or 1 is expected to satisfy the conditions for maximum sensitivity, which is not trivial to come through or straightforward to prove experimentally due to the difficulties to design or handle such a thin-films as well as to find suitable waveguide substrates with that properties towards the fabrication of a multipurpose label-free LMR-based platform.

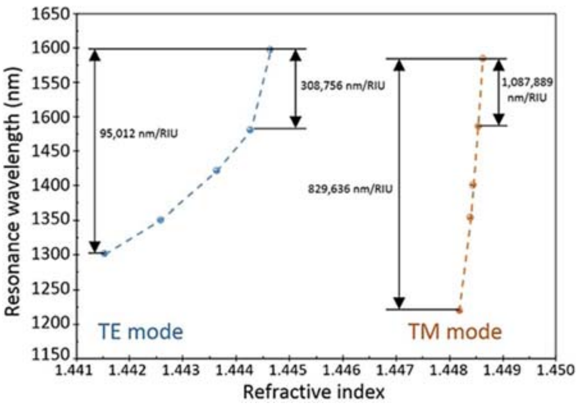

Fig. 3. LMR wavelength shift as a function of the surrounding medium refractive index using a D-shape fiber coated with a SnO2 thin-film. Reprinted from [32] with permission from Scientific Reports-Nature.

3. Discussion

The idea behind a label-free LMR-based sensing platform basically consist of exploiting the LMR phenomenon towards a wide range of applications in a simple and versatile manner by means of the combination of thin-film multi-pattern structures of different materials.

In particular, thin-film material dielectric properties enable to position the resonance within a defined working range that satisfies LMR generation conditions among other things [30]. Concerning the thin-film thickness, thicker coatings will excite LMRs at longer wavelengths and they will be more adequate for the detection of bigger size targets in the NIR spectrum, whereas thinner coatings will excite LMRs at shorter wavelengths and will be more adequate for the detection of small size targets in the UV spectrum. Fig. 4 gives an idea of the corresponding detection wavelength and thickness of the nanocoating for each target size (VCs, DNA, virus or cells).

Moreover, thin-film patterning permit to enhance the sensitivity and selectivity capabilities of the devices, which are mainly associated to the penetration depth of the evanescent wave (shorter for UV and larger for NIR) and the surface area. LMR properties can be predicted roughly using material theoretical models and waveguide propagation theory. However, there is little work done in this field, the models are not complete and often do not cover a broad spectral range (UV-VIS-NIR) or complex patterns, which requires a continuous experimental feedback to adjust correctly these models in order to obtain accurate calculations for the fabrication of LMR-based devices matched with the application.

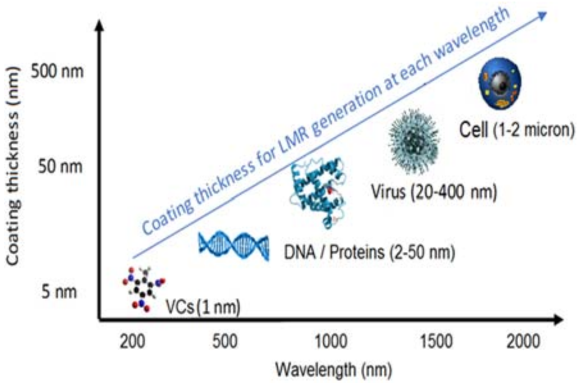

Fig. 4. Wavelength versus adequate coating thickness for detecting different targets: VCs, DNA, Proteins, viruses and cells.

Finally, the adequate selection of the optical waveguide geometry and material (the refractive index of the optical waveguide should be similar to that of the surrounding medium as it was mentioned before) and interrogation method enable to improve the signal to noise ratio and increase the resolution of the device. Here, the utilization of transmission and reflection configurations in both cylindrical and planar waveguides should be evaluated in order to opt for what it is called as “lab-on-fiber”, “lab-in-fiber” [34] or “planar waveguide” [35] configurations (see Fig. 5).

Fig. 6 shows some simulation results for a substrate of refractive index 1.45 (silica) where a coating of refractive index 2, like that of SnO_2 [32], has been used as LMR generating thin-film. In a simple manner, Fig. 6 shows the LMR relative wavelength shift as a function of the thickness of the LMR generating thin-film when a second coating representing the size of VCs (5 nm), viruses (20 nm) or cells (100 nm) are attached to the thin-film. Depending on whether the surface is covered by any of them, the resonance wavelength associated to each coating thickness will experience a different relative wavelength shift.

As it is depicted in Fig. 6, small molecules, such as VCs (in the order of a few nanometers) will lead to a measurable relative wavelength shift for thin LMR generating coatings. However, for thick LMR generating coatings the resonance wavelength shift will be very low for VCs. In view that the absolute wavelength resolution is smaller at longer wavelengths, the effect of VCs will not be detected at long wavelengths, where LMRs induced by thick coatings are located. On the opposite side, the relative wavelength shift induced by thick biolayers (cells) when a thin LMR generating coating is used, exceeds 100 % and it is difficult to track, whereas for thicker LMR generating coatings this relative wavelength shift is smaller and adequate for the absolute resolution of the equipment. In other words, thin films are more appropriated for small feature detection while thick films are appropriated for larger size targets. All in all, the position of the resonance also takes an important role and is dependent on both the refractive index of the substrate (silica in the simulation) and the surrounding medium as well as the LMR generating material dielectric properties, which requires a profound knowledge of the application and the final performance of the device for a proper design.

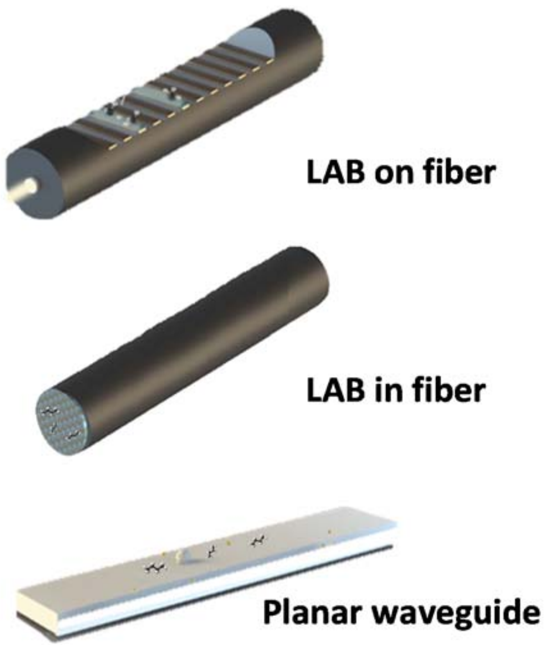

Fig. 5. Schematic representation of proposed optical waveguide configurations: lab on fiber (top), lab in fiber (center) and planar waveguide (bottom).

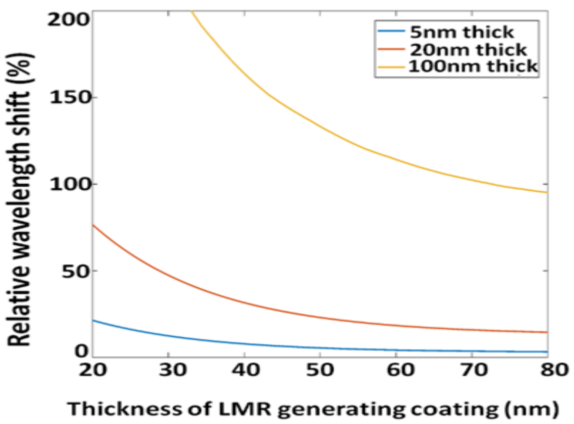

Fig. 6. LMR relative wavelength shift as a function of the coating thickness when a second coating representing the size of VCs (5 nm), viruses (20 nm) and cells (100 nm) is attached.

4. Challenges

It is important to remark that the development of the label-free LMR-based sensing platform proposed in Fig. 1 should also overcome many drawbacks concerning the utilization of broadband excitation light sources (covering the entire working range). At the same time, the light coupled through the optical waveguides should be collected by the corresponding detectors in the entire working range. In addition, the profile (thickness) and pattern of the device should be chosen according to the desired target size (from nm to microns), which might require the utilization of a porous membrane or filter that prevent particles that exceed the objective target size to be detected and avoid interferences and undesirable resonance shifts produced by bigger particles attached to thinner resonance generating thin-films as it was mentioned before when discussing the simulations of Figure 6. Finally, the chemistry of the sensitive layers used as receptors should be compatible with the LMR generating material in order to form strong bonds that enable an effective target particle capture.

5. Outlook

The achievement of this ambitious purpose could open infinite possibilities in science and knowledge generation, such as early diagnoses that are not possible nowadays either for the low concentration of target analytes, such as VCs and gases (volatolomics) in breath or proteins in urine for example or for the necessity to perform target detection in air and liquid at the same time. Additionally, the utilization of the proposed system could be helpful for the discovery of unknown biomarkers in other body fluids, such as tears, skin secretions or flatulencies that were not possible to detect before, due to their low concentration or the difficulties in the application of standard detection methods. Health and safety are some of the most important sectors that could benefit from these achievements.

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