



Mohamad Ali Nasri, I. F., Mbomson, I., Sharp, G.J., De La Rue, R.M. , Johnson, N.P., Sorel, M. and Gauchotte-Lindsay, C. (2019) Biomedical optical sensing using nano-/micro-structured metamaterials. In: 21st International Conference on Transparent Optical Networks (ICTON 2019), Angers, France, 9-13 July 2019, ISBN 9781728127804 (doi:[10.1109/ICTON.2019.8840143](https://doi.org/10.1109/ICTON.2019.8840143))

There may be differences between this version and the published version. You are advised to consult the publisher's version if you wish to cite from it.

<http://eprints.gla.ac.uk/202354/>

Deposited on 05 November 2019

Enlighten – Research publications by members of the University of
Glasgow

<http://eprints.gla.ac.uk>

Biomedical Optical Sensing Using Nano-/Micro-Structured Metamaterials

I. F. Mohamad Ali Nasri, I. Mbomson, G. J. Sharp, R. M. De La Rue, N. P. Johnson, M. Sorel,
and C. Gauchotte-Lindsay

University of Glasgow, School of Engineering, Glasgow G12 8LT, Scotland, UK

1. INTRODUCTION

Work on optical sensing techniques continues to advance – and optical sensing techniques and related technologies are becoming a well-established approach for, *inter alia*, applications in biomedical and environmental sensing. Both structured surfaces and arrays of integrated devices that are fabricated by means of classical planar technologies are likely to have a central role in the development of low-cost and reliable bio-sensors, at both the molecular and cell levels. One approach that has been demonstrated as viable in biomedical sensing is the use of fluorescent labelling, e.g. for carrying out competition immunoassays to identify the possible presence of specific analyte molecules in suitably prepared fluid samples. Many bio-materials exhibit a finite level of fluorescence that could possibly be exploited in sensing, but is also potentially problematic when it forms an undesired background, thereby limiting sensitivity. But the alternative approach of *label-free* biomedical sensing seems likely to be favoured in future applications. A ‘standard’ approach to label-free sensing exploits the detection of changes in the (complex) refractive index that occur when bio-material is added to the local environment of a designed resonant structure, thereby changing its *resonance frequency*. Designed tuning of reflection, transmission and absorption resonances can be used to help identify specific molecules, through selection of the known bond resonances of the molecules of interest. Since it is typically possible to organise resonant structures in arrays that consist of thousands of individual resonant ‘atoms’, thereby forming a *metasurface*, it has become possible to select and quantify various characteristic molecular bond resonances simultaneously – and to identify possible molecular compositions in composite bio-material.

2. SURFACE PLASMON RESONANCE (SPR)

One approach that has been successful in biomedical applications is surface plasmon resonance (SPR) based sensing [1, 2]. The use of SPR in sensing relies on the precise detection of typically small changes in the angle at which a light beam that is incident on a plasmonic guiding surface couples to the plasmonic propagation mode. Characteristically, the plasmonic surface is a thin film of a noble metal, most obviously gold. The presence, for example, of a thin layer of deposited bio-analyte can be detected by the consequent change in the refractive index of the medium immediately ‘above’ the surface and the resulting change in the coupling angle for the guide layer. For operation at a single chosen optical wavelength, it is the coupling angle that exhibits the resonance that is known as SPR. The alternative of detecting changes in the SPR wavelength at a fixed coupling angle has also been exploited. The narrowness of the SPR is strongly determined by the area of the surface that is illuminated, as well as the uniformity of the deposition of the analyte material. Sharp resonance in the SPR coupling angle requires the illumination of a relatively large area. Furthermore, achieving large values of sensitivity requires accurate mapping of the light beam angular variation, so that the resolution obtained is much smaller than the Rayleigh resolution criterion that is often used. Alternatively, a well collimated beam is focused onto a small area of the plasmonic waveguide surface – and the reflected beam is allowed to expand, passes through collimating optics – and is refocused onto a detector array [2].

3. BIO-ANALYTES, FLUORESCENT LABELLING AND RESONANT DETECTION

Analytes of interest in biomedical sensing may take the form of weak solutions containing a variety of specific protein molecules – or they may take the form of layers, down to the mono-layer level, deposited from solution onto a suitably prepared surface. The protein molecules that are present in an analyte solution – and their relative amounts – can, in the right circumstances, identify (or help to identify) the health condition of the individual from which the analyte has been extracted. This applies, for instance to major events such as a stroke (in the brain) or a heart attack. The classic antigen-antibody binding process is often exploited to lock known antigens of interest on to regions that have been prepared with specific antibodies fixed of a test surface, via well-established chemical binding layer technologies. *Fluorescent labelling* has been demonstrated as a viable approach in biomedical sensing, e.g. for carrying out *competition immunoassays* to identify the possible presence of specific analyte molecules in suitably prepared fluid samples. An example of a fluid sample of interest in bio-sensing is readily generated by diluting, with pure water, a sample of blood/serum extracted (e.g. using a hypodermic needle) from a human being or animal. But the alternative approach of *label-free* biomedical sensing seems likely to be favoured in future applications. Label-free sensing is favoured because it avoids the need to attach known fluorescent molecular labels to, for instance, carefully chosen antigens (haptens) before

initiating the detection and identification processes. Provided that the binding process for the protein(s) of interest is reliably specific, label-free sensing can be used over a wide range of bio-analytes – with small changes in refractive index producing measurable shifts in, e.g., the resonance frequency of an electromagnetically resonant test structure.

4. PLANAR METASURFACES

The application of various planar technologies has led to the development of a wide variety of different optical device structures that provide alternative possible approaches to biomedical sensing, at both the molecular and cell levels. Designed tuning of reflection, transmission and absorption resonances can be used to help identify specific molecules, through selection of the known bond resonances of the molecules of interest. Since it is typically possible to organise resonant structures in arrays that consist of thousands of individual resonant ‘atoms’, thereby forming a *metasurface*, it has become possible to select and quantify various characteristic molecular bond resonances simultaneously – and to identify possible molecular compositions. Reasonably typical metasurfaces are produced as uniform arrays of individual metallic film patterns, e.g. split-ring resonators (SRRs) and asymmetric split-ring resonators (ASRRs) [3-7], FRAMMs [8] (Fano-resonant asymmetric metamaterials) and split-H structures (ASHs) [9,10], on dielectric substrates. Such dielectric substrates should, of course, be transparent at the operating wavelength, for situations where the observation is based on resonant changes (e.g. sharp dips) in the transmission of the ‘light’. (We remark that such metasurfaces can operate over a wide range of electromagnetic wavelengths/frequencies – from the visible, through the whole of the infra-red spectrum and on into the terahertz spectral region). The spacing and the resonator dimensions used in the array are typically small compared with the free-space wavelength of the light used, so the structuring can be described as *sub-wavelength*. Furthermore, it is not essential for the array elements to be uniformly spaced, since the resonance properties of the metasurface array are those of the individual ‘atoms’, provided that the coupling between adjacent atoms is weak. In passing, it should be noted that metasurfaces of interest do include metallic film patterns, e.g. fishnet structures, where the periodicity is a characteristic feature. Another useful point that arises from some recent publications is that ‘purely’ dielectric-based metasurfaces, e.g. designed thickness multi-layers of silica and silicon [11], are now available – and potentially out-perform metasurfaces that are based on metallic films.

The metasurfaces mentioned in the paragraph above, may be regarded as particular examples of *structured surfaces*. Such structured surfaces can often legitimately be considered as (nano-)structured or (micro-)structured surfaces, if only because the precision at which they should be fabricated can be as small as a few nanometres. Examples of structured surfaces of interest include the *photonic crystal waveguide slabs* that can provide valuable increases in signal strength and signal-to-background (noise levels) for optical microscopy, e.g. as exploited in photonic crystal-enhanced microscopy (PCEM) [12-14]. PCEM is of particular interest because of its demonstrated application to observation of the structure of cells – in particular bacterial cells.

5. PLANAR WAVEGUIDE DEVICE STRUCTURES

As already said above, the application of various planar technologies has led to the development of a wide variety of different optical device structures that provide a variety of alternative possible approaches to biomedical sensing, at both the molecular and cell levels. Integrated devices that are fabricated by means of classical planar technologies have a central role in the development of low-cost and reliable sensors – and this role is potentially dominant. Thin-film optical waveguides provide the base for a variety of device concepts and realisations that enable very high sensitivity in biomedical and environmental sensing applications. High sensitivity can result from the designed and controlled resonance of, for instance, waveguide ring resonators [15,16] and photonic crystal micro-cavities [17]. High sensitivity is also obtainable in suitably designed stripe waveguide Mach-Zehnder interferometer (MZI) structures [18], particularly where a large path length difference between the two arms of the structure, e.g. in the form of a folded spiral structure in one arm of the interferometer, but not the other. While thin-film waveguides most typically use materials that are transparent at the operating wavelength, alternative forms of waveguide are of interest, e.g. ‘purely’ plasmonic waveguides based on materials with both significant real and significant imaginary parts to their (complex) refractive index and dielectric constant functions – and hybrid plasmonic/dielectric waveguide structures. Characteristically, waveguide structures in which the absorption length is small (i.e. typical plasmonic waveguide structures) provide correspondingly small useful interaction lengths for sensing purposes – but a potential advantage of this behaviour is that the interaction region is correspondingly strongly localized. With a sufficiently symmetrical dielectric material distribution and geometry, plasmonic waveguides can exhibit a characteristic fundamental mode, the long-range plasmonic (LRP) mode [19] that exhibits lower propagation losses and gives characteristically longer interaction lengths. The LRP mode has an interesting inherent behaviour: as the core dimension reduces, the modal volume increases, with progressively more of the modal energy/power being supported in the external ‘exponential tail’ regions. In some situations of interest, the ability to extend the volume of the guided mode enables significant increases in the sensitivity.

6. ASYMMETRIC SPLIT H-STRUCTURE (ASH) ARRAYS

One emphasis in our presentation will be on the use of ASH structures [9, 10] for bio-sensing – applied to hormones that are of interest in both biomedicine and in the environment. Recent work on estradiol, an important hormone for human health and animal welfare, will be reviewed. An important aspect of this work is the ability to distinguish between different forms of estradiol, via differences between their characteristic spectra in the mid-infrared that are matched to the dimension-controlled resonances of the ASH array metasurface. This work can be categorized under the general heading of surface-enhanced infrared absorption (*SEIRA*) spectroscopy.

REFERENCES

- [1] J. Homola and M. Piliarik, “Surface Plasmon Resonance (SPR) Sensors,” *Springer Series on Chemical Sensors and Biosensors*, **4**: pp. 45-67, Springer-Verlag Berlin Heidelberg, 2006.
- [2] M. Piliariuk and J. Homola, “SPR Sensor Instrumentation,” *Springer Series on Chemical Sensors and Biosensors*, **4**: pp. 95-116, Springer-Verlag Berlin Heidelberg, 2006.
- [3] B. Lahiri *et al.*, “Asymmetric split ring resonators for optical sensing of organic materials,” *Optics Express*, **17**(2), pp. 1107-1115, 19th Jan. 2009.
- [4] B. Lahiri *et al.*, “Resonance hybridization in nanoantenna arrays based on asymmetric split-ring resonators,” *Applied Physics Letters*, **98**, 153116, 2011.
- [5] B. Lahiri *et al.*, “Enhanced Fano resonance of organic material films deposited on arrays of asymmetric split-ring resonators (A-SRRs),” *Optics Express*, **21**(8), pp. 9343 - 9352, 22nd Apr. 2013.
- [6] G. J. Sharp *et al.*, “Mapping the sensitivity of split ring resonators using localized analyte,” *Appl. Phys. Letts.*, **108**, 25105, 2016.
- [7] L. Dong *et al.*, “Nano-gapped Au antennas for ultrasensitive surface-enhanced infrared absorption spectroscopy,” *ACS Nano Letters*, **17**, pp. 5768-5774, 8th Aug. 2017.
- [8] C. Wu *et al.*, ‘Fano-resonant asymmetric metamaterials for ultrasensitive spectroscopy and identification of molecular monolayers’, *Nature Materials*, **11**, pp. 69-75, Jan. 2012.
- [9] I. G. Mbomson *et al.*, “Asymmetric H-shape nanoantennas for molecular sensing,” *Biomedical Optics Express*, **8**(1), pp. 395-406, 1st Jan. 2017.
- [10] I. G. Mbomson *et al.*, “Dual polarization operation of nanostructure arrays in the mid-infrared,” *Appl. Phys. Lett.*, vol. 112, no. 7, p. 073105, Feb. 2018.
- [11] C. Wu *et al.*, “Spectrally selective chiral silicon metasurfaces based on infrared Fano resonances,” *Nature Communications*, **5**, 3892, 27th May 2014.
- [12] W. Chen *et al.*, “Photonic crystal enhanced microscopy for imaging of live cell adhesion,” *Analyst*, **138**, 5886, 2013.
- [13] Y. Nazirizadeh *et al.*, “Material-based three-dimensional imaging with nanostructured surfaces,” *Applied Physics Letters*, **102**, 011116, 2013.
- [14] D. Threm, Y. Nazirizadeh, and M. Gerken, “Photonic crystal biosensors towards on-chip integration,” *J. Biophotonics*, **5**(8-9), pp. 601-616, 2012.
- [15] D.-X. Xu *et al.*, “Folded cavity SOI microring sensors for high sensitivity and real time measurement of biomolecular binding,” *Optics Express*, **16**(19), 15th Sep. 2008.
- [16] A. Yalcin *et al.*, “Optical sensing of biomolecules using microring resonators,” *IEEE Journal of Selected Topics in Quantum Electronics*, **12**(1), Jan./Feb. 2006.
- [17] Y.-F. Chen *et al.*, “Controlled photonic manipulation of proteins and other nanomaterials,” *Nano Letts.*, **12**, pp. 1633-1637, 2012.
- [18] A. Densmore *et al.*, “Silicon photonic wire biosensor array for multiplexed real-time and label-free molecular detection,” *Optics Letters*, **34**(23), pp. 3598 -3600, 1st Dec. 2009.
- [19] P. Berini, “Long-range surface plasmon polaritons,” *Advances in Optics and Photonics*, **1**, pp. 484-588, 2009.