



Introduction to the feature issue: Advances in Optical Biosensors for Biomedical Applications

**SANTOSH KUMAR,^{1,*} AGOSTINO IADICICCO,² SEUNGHYUN KIM,³
DANIELE TOSI,⁴ AND CARLOS MARQUES⁵**

¹Department of Electronics and Communication Engineering, Koneru Lakshmaiah Education Foundation, Vaddeswaram, Andhra Pradesh 522302, India

²Department of Engineering, University of Naples "Parthenope", 80143 Naples, Italy

³Department of Electrical and Computer Engineering, Baylor University, Waco, TX 76798, USA

⁴Department of Electrical and Computer Engineering, Nazarbayev University, 010000 Astana, Kazakhstan

⁵CICECO – Aveiro Institute of Materials, Physics Department, University of Aveiro, 3810-193 Aveiro, Portugal

*santosh@kluniversity.in

Abstract: The feature issue of *Biomedical Optics Express* titled “Advances in Optical Biosensors for Biomedical Applications” presents a comprehensive collection of cutting-edge optical biosensor research. With the growing demand for sensitive, label-free, and real-time detection of biological analytes, optical biosensors have emerged as important devices in a wide range of biomedical applications, including medical diagnostics, bioanalysis, and personalised healthcare. This collection of 26 papers highlights recent advances and innovations in the development, design, and implementation of optical biosensors. The feature issue serves as an opportunity for disseminating ground-breaking findings, promoting new ideas, and inspiring further developments in optical biosensors for medical applications. The authors provide breakthrough technology, innovative approaches, and practical clinical applications that have the potential to revolutionize healthcare and biomedical research.

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1. Introduction

Optical biosensors have emerged as essential devices in biomedical research, providing novel answers to a wide range of healthcare applications. Optical biosensors have transformed medical diagnostics, bioanalysis, and personalized healthcare by allowing for the sensitive, label-free, and real-time detection of biological analytes. The special issue “Advances in Optical Biosensors for Biomedical Applications,” hosted by *Biomedical Optics Express*, provides a venue to highlight the most recent advancements and accomplishments in this rapidly growing field. This special issue intends to promote interdisciplinary interactions among researchers in optics, photonics, biology, medicine, and related topics. Its goal is to foster the exchange of ideas, promote new research, and spur future developments in optical biosensors for healthcare applications by bringing together professionals from many disciplines. This feature issue covers a wide range of subjects, including optical fiber biosensors, plasmonic biosensors, photonic crystal biosensors, whispering gallery mode biosensors, and nanomaterials for biosensing. It also covers topics like optical microcavities, wearable and implantable biosensors, point-of-care diagnostics, signal processing, data analysis, biofunctionalization, and sensing mechanisms. Now a days, WaveFlex biosensors utilize plasmon wave properties and flexible optical fiber structures to detect biological analytes, providing improved sensitivity and adaptability for real-time monitoring in biomedical applications. These cutting-edge biosensors employ the flexibility of optical fiber to adjust to different sample conditions, allowing for reliable and precise detection of biomolecules. Furthermore, the feature issue investigates the integration of optical biosensors with upcoming technologies as microfluidics and lab-on-a-chip systems. It

also discusses biosensors' uses in neurological research, personalized medicine, environmental monitoring, medication development, and food security. We hope that this feature issue will give researchers with a thorough overview of the most recent advances in optical biosensors, inspiring more study and innovation in the field of biomedical optics.

2. Overview of contributions

Following a thorough peer-review process, published 26 articles for publication in this special feature issue. The following summary provides an overview of the outstanding contributions found within.

2.1. *Diffuse and fluorescence tomography*

In this technology, Yin et al. [1] presented a unique approach to rotational fluorescence sectioning imaging that combines dynamic speckle illumination wide-field fluorescence microscopy (DSIWFM) with line optical tweezers (LOTs). LOTs trap large polystyrene fluorescent microspheres and carefully manipulate them to rotate around a certain axis. During the rotation, dynamic speckle illumination captures several raw fluorescence images. The root-mean-square (RMS) technique is then used to extract fluorescent signals and generate fluorescence sectioning images from different angles. The effect of speckle granularity on image quality is assessed by experimental study. The combination of LOTs and DSIWFM enables non-contact handling and imaging of large samples, making this a potential approach for biological imaging applications.

2.2. *Endoscopy and fiber optics*

Using this technique, Luan et al. [2] introduce an innovative in-situ background-free Raman fiber probe based on double-cladding anti-resonant hollow-core fibers (AR-HCFs). When compared to typical multi-mode silica fibers, the probe significantly decreases Raman background noise by two orders of magnitude. A specialized fiber coupling optics device is developed to work with a commercial confocal Raman microscope, allowing enabling in-situ Raman detection. The AR-HCF claddings have a high numerical aperture (NA), that improves Raman signal collection efficiency at the probe's distal end. The probe's performance is proved by characterizing a variety of samples, including ABS plastics, alumina ceramics, and ethylene glycol solutions. Overall, this study successfully employs double-cladding AR-HCFs in Raman sensing through the development of a specialized fiber probe. Despite mediocre laser quality, the probe successfully eliminates silica Raman background noise. With a distal end diameter of less than 0.4 mm, the probe has high promise for *in-vivo* Raman endoscopic applications. However, more study is needed to solve issues such as continuing to minimize silica background noise and improving AR-HCF NA performance.

2.3. *Optical biosensors*

Arrow et al.'s [3] new study on heart failure, which is related with a rehospitalization rate of up to 50% within six months, highlights the importance of early warning symptoms. While invasive techniques for measuring central venous pressure are common in hospitals, they become impractical once discharged. A non-invasive approach is available; however, its reliability is limited. This review looks at camera-based approaches for jugular vein assessment, highlighting design considerations and suggesting future research directions. It emphasizes the neck's extensive imaging potential beyond the jugular veins, discusses factors influencing signal quality, and offers minimum reporting criteria for future investigations. Similarly, Rashidova et al. [4] develop a sensor for healthcare application because detecting biomarkers for illness progression is critical, and saliva provides a safe, inexpensive, and non-invasive diagnostic medium. Salivary interleukin-8 levels indicate a variety of disorders, however typical diagnostic procedures are

complicated and time-consuming. This paper describes an optical fiber-based biosensor for label-free IL-8 detection that achieves an ultra-low limit of 0.91 fM and a wide concentration range of 273 aM to 59 fM, with good sensitivity and little signal changes. Furthermore, Chen et al. [5] proposed Fano resonance-based sensor with a high Q-factor for refractive index (RI) sensing. Their research investigates a RI sensor with numerous Fano resonances of high Q-factor, that is accomplished by introducing an asymmetry parameter to establish a quasi-bound state in the continuum. Analyzing resonant modes such as toroidal dipole, magnetic quadrupole, and magnetic dipole, its metastructure has exceptional sensing properties with a Q-factor of 3668, sensitivity of 350 nm/RIU, and FOM of 1000. Experiments have confirmed its potential in biosensors, nonlinear optics, and lasers.

Mamontov et al. [6] developed an imaging plethysmograph (IPG) to assess the sympathetic vasomotor response, crucial for autonomic regulation of circulation. This study, conducted on congestive heart failure (CHF) patients pre- and post-heart transplantation, compared IPG with the classical air plethysmograph (APG). Results showed a significant decrease in vasomotor response in CHF patients, with an increase post-transplantation. Both techniques correlated in assessing changes, but IPG demonstrated greater artifact resistance, promising for clinical evaluation of vasomotor response. Peng et al. [7] introduced a real-time optical phase sensing method for ultra-sensitive detection of calreticulin (CRT) levels in human serum. By employing weak amplification within weak measurements, they monitored CRT response continuously, enabling precise determination at the picomolar level. This advancement could establish CRT as a diagnostic biomarker for various medical applications, including rheumatoid arthritis. Teng et al. [8] proposed a cascaded plastic optical fiber-based surface plasmon resonance (SPR) sensor for simultaneous measurement of RI and temperature. By connecting side-polish plastic optical fiber and FONTEX optical fiber with UV glue, they achieved broader RI measurement range with low crosstalk. The sensor exhibited high RI sensitivity and temperature sensitivity, making it promising for biochemical sensing applications. Lin et al. [9] developed a non-invasive and extremely sensitive terahertz wave detector for detecting sugar concentrations using a thin $\text{Co}_3\text{Sn}_2\text{S}_2$ semimetal screen. They developed a method for real-time, highly sensitive blood sugar testing by analysing the terahertz wave responses of various sugar concentrations. This innovation not only demonstrates the potential for 6 G edge intelligence in non-invasive and real-time blood sugar monitoring, but it also adds to the evolution of 6 G technology. Zhang et al. [10] proposed a high-precision glucose sensor based on active multidimensional feature THz spectroscopy. They successfully identified glucose concentrations and detected adulteration by combining terahertz time-domain spectroscopy (THz-TDS) with multidimensional feature spectrum identification and linear discriminant analysis (LDA) techniques. This technology provides a cost-effective, quick, and safe alternative for blood sugar monitoring, sweetness assessment, and food safety, with promising applications in a variety of industries. Ullah et al. [11] demonstrated a fiber cavity ring-down biosensor for lipoarabinomannan (LAM)-based tuberculosis (TB) detection. They accomplished rapid, portable, and cost-effective LAM detection in urine samples by applying phase shift-cavity ring-down spectroscopy (PS-CRDS) to an optical fiber cavity and functionalizing the tapered fiber surface with anti-LAM antigen CS-35. With a detection limit of 10 pg/mL and great sensitivity, this sensor shows promise for tuberculosis diagnosis in low-resource settings, addressing a significant need in global healthcare.

Bekmurzayeva et al. [12] offered valuable information on all-fiber label-free optical fiber biosensors, emphasizing their potential applications in biomedicine and environmental monitoring. These biosensors provide benefits such as affordability, exceptional sensitivity, and resistance to electromagnetic interference by utilizing fiber optic technology. The paper examines contemporary methodologies for fabricating optical fiber sensors that do not require labels and investigates their utility in identifying a wide range of substances, such as soluble cancer biomarkers, hormones, viruses, bacteria, and cells. Whitaker-Lockwood et al. [13] developed a novel device for

direct frequency comb spectroscopy to analyze CO₂ generated during microbial metabolism, with *Saccharomyces cerevisiae* serving as the model organism. The apparatus successfully distinguished between different forms of CO₂ with great accuracy by manipulating ambient factors and providing yeast with sugar that had been enriched with isotopes. In addition, the spectrometer quantified the ratio of carbon in the initial sugar that was transformed into CO₂ and approximated the quantity that was assimilated into the yeast biomass. Yang et al. [14] examined the integration of portable optical fiber biosensors with cellphones, specifically focusing on the technology, applications, and issues associated with this integration. These biosensors provide convenient and portable solutions for a range of analytical tasks, such as monitoring the environment, diagnosing medical conditions, and ensuring food safety. The paper examines the incorporation of optical fiber biosensors onto smartphone platforms, which allows for instantaneous data analysis, remote monitoring, and improved accessibility in various environments. Chen et al. [15] developed a method to measure haemoglobin levels without the need for intrusive procedures. They achieved this by employing a wearable system that utilizes diffuse reflectance spectroscopy. This cutting-edge system consists of control and sensor boards equipped with photodiodes and light-emitting diodes, allowing for the non-invasive measurement of haemoglobin levels without the requirement of drawing blood. By utilizing neural networks and chromophore fitting techniques, the system is able to precisely measure haemoglobin levels. This measurement shows a significant correlation with invasive approaches. This gadget effectively mitigates the impact of melanin interference and shows potential for incorporation into wearable technology, enabling uninterrupted monitoring of haemoglobin levels in different groups of people.

Xiao et al. [16] developed wearable FBG sensors integrated in Polydimethylsiloxane (PDMS) for the purpose of gesture detection and communication support. The sensors, which are integrated inside PDMS silicone elastomer, precisely detect complex gestures such as wrist rotation, finger flexion, and mouth motion. The study showcases the long-term durability of the sensors over a period of four months. It also highlights their potential in aiding those who have suffered from a stroke or other disabilities, by improving their capacity to engage with their environment. A team led by Arcadio and his colleagues [17] developed three-dimensional (3D) printed biosensors specifically designed for biomedical purposes. These biosensors utilize plasmonic phenomena and antibody self-assembled monolayers. The biosensor, constructed using a silver-gold bilayer, was modified using antibodies that specifically bind to the p27Kip1 protein. The biosensor exhibits excellent selectivity and a highly sensitive detection limit, making its performance comparable to that of ELISA kits. The modular and simple-based architecture of this system allows for flexible deployment in experimental and biomedical research. Plasmonic nano-bowls were developed by Das et al. [18] to observe changes within liposomes and DNA-based nanocarriers that occur within the cell membrane. The paper showcases the sensitive characterization of liposomes and DNA specimens, including drug-loaded DNA micelles, using surface-enhanced Raman spectroscopy. The nano-bowls being proposed passively capture particles, resulting in consistent augmentation of SERS signals. This allows for useful observations of molecular complexes and chemical morphology in their original condition. In their study, Li et al. [19] investigated the use of single-fiber probes to simultaneously perform fluorescence-based sensing and imaging in biological tissue. Although there are difficulties in sensitivity and resolution, these probes provide possibilities for studying intricate physiological phenomena and enhancing disease diagnosis and monitoring. Cao et al. [20] developed a versatile sensor using an all-dielectric metastructure to detect both temperature and RI, simultaneously. The sensor demonstrates remarkable Q-factor and modulation depth, together with high sensitivity and figure of merit for RI sensing. The work emphasizes the potential of the metastructure for diverse applications in biological and chemical sensing. Saiko et al. [21] examined the detection of blood flow in the internal jugular vein using photoplethysmography during physiological testing. The work showcases the capacity of photoplethysmography to analyze the movement of fluid in the venous system, providing

valuable information for monitoring venous blood flow in remote patient monitoring applications. Piretta et al. [22] introduced a chemical sensor on a silicon chip that utilizes an interferometer to measure changes in the RI of liquid substances upon contact. The sensor, which necessitates a laser with a certain wavelength and immediate data processing, demonstrates improved sensitivity and cost-effective analysis, rendering it appropriate for a wide range of chemical sensing tasks.

2.4. *Optical coherence tomography*

Cornelio et al. [23] proposed a method for precisely aligning optical coherence tomography (OCT) volumes in secondary analyses. Utilizing its ability to achieve micron-level precision, OCT is extensively employed in the field of ophthalmology, resulting in the generation of large quantities of picture data. The objective of this procedure is to improve the quality of images and the ability to see important features by aligning and averaging several OCT scans. Their pipeline employs surface feature and entire volume data to align previously obtained 3D OCT volumes, resulting in a unique and straightforward method that effectively reduces speckle noise and enhances the examination of retinal tissue.

Similarly, Li et al. [24] developed a precise 3D segmentation method for wet age-related macular degeneration (AMD) utilizing optical coherence tomography (OCT) with a high level of accuracy. Wet AMD is a primary factor in vision impairment among older individuals, and OCT allows for precise imaging of retinal structures. Their deep-learning network utilizes multi-scale and cross-channel feature extraction, as well as channel attention methods, to accurately segment wet AMD lesions in 3D. This method offers valuable information about the precise structure of lesions in three dimensions, which enhances comprehension and medical treatment of wet AMD.

2.5. *Molecular imaging and nanoparticles*

Zhang et al. [25] presented a new method to improve the photoluminescence of Tb/Eu co-doped PMMA film by utilizing plasmonic Au nanorods-PVA nanocomposite films. The study utilized plasmonic nanostructures to uniformly boost the photoluminescence within small micro-regions, hence increasing the radiation characteristics of emitters. When stimulated with light at a wavelength of 292 nm, the emission at 612 nm was amplified by a factor of 37.2, while the emission at 545 nm was amplified by a factor of 21.6. The experimental results were analyzed using finite difference time domain simulations. These simulations showed that the modulation of luminescence was caused by two factors: the increase in the local density of optical states due to the Purcell effect, and the improvement in energy transfer efficiency between Tb and Eu ions. Additional experiments conducted with excitation at a wavelength of 360 nm revealed a maximum enhancement factor of roughly 71.5 times. The primary effect of Au nanorods was observed in the modulation of the emission process at a wavelength of 612 nm, resulting in a higher enhancement factor at that specific wavelength. This study offers valuable insights into the interactions between materials co-doped with rare earth ions and plasmonic nanostructures. These findings provide the groundwork for a wide range of applications, including the development of detectors and sensors based on thin films.

2.6. *Tissue optics and spectroscopy*

Lazaro-Pacheco [26] conducted a study that investigated the application of *in-vivo* infrared spectroscopy for the purpose of non-invasively screening for diabetes using nail tissue. Conventional diabetes screening methods are frequently burdensome and intrusive, necessitating intricate processes for sample collection. This study aims to utilize near-infrared spectroscopy (NIR) for the detection of glycated keratin, a crucial marker for assessing the risk of type 2 diabetic mellitus (T²DM), in nail tissue. The study encompassed a total of 200 participants, consisting of 100 individuals diagnosed with diabetes and 100 individuals without diabetes. The effectiveness of NIR was compared to that of a point-of-care HbA1c analyzer. The results showed that the

assessment of diabetes risk had a specificity of 92.9%. The results indicate that the suggested NIR system has the capacity to function as an uncomplicated and dependable instrument for early detection of diabetes and the management of associated risks in different healthcare environments.

The introduction of feature issue presents a summary of the 26 articles chosen for publication, organizing them into six thematic sections: Diffuse and Fluorescence Tomography, Endoscopy and Fiber Optics, Optical Biosensors, Optical Coherence Tomography (OCT), Molecular Imaging and Nanoparticles, and Tissue Optics and Spectroscopy. These papers showcase notable progress in advances in optical biosensors for biomedical applications especially, optical imaging and sensing technologies, covering a wide range of applications including biological imaging and medical diagnostics. I've also incorporated several high-quality advancements in optical biosensors, as recently published in *Biomedical Optics Express* [27–54]

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