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Design of highly sensitive biosensors using hollow-core microstructured fibers for plasma sensing in aids with human metabolism

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Abstract
Detection of low index liquid analytes in real-time, in-situ, and with high accuracy is of great importance in various scientific fields, particularly in medicine and biology. Accurate detection of plasma concentration in blood samples is one of the most significant usages of biosensors in medicine. In this paper, we report a highly sensitive biosensor using hollow core microstructure optical fibers (HC-MOFs) to detect low index liquid analytes with a particular focus on detection of plasma concentration in blood samples. We demonstrate how variations in plasma concentration in blood can change transmission spectra of the HC-MOF due to the photonic bandgap mechanism. We use the finite element approach to explore how the biosensor's performance depends on the number of capillary rings encircling the hollow core of the fibre. An average spectral and amplitude sensitivity of 8928.57 nm/RIU and 1.21 dB/RIU is reported for the optimized design of HC-MOF for five capillary rings with a refractive index detection range of 1.333 to 1.3385 for different ratios of plasma in blood serum. The proposed biosensor can have potential application in liquid analyte detection in medicine, chemistry, and biology where real-time and accurate data about liquid analytes are necessary for human metabolism.

Keywords Photonic crystal fiber (PCF) biosensor · Hollow-core fiber · Transparent medium · Microstructured fiber, Fiber-optic sensor

1 Introduction

In recent years, there have been various investigations on the optical properties and usage of microstructured optical fibers (MOFs) either as a light matter interaction platform for nonlinear optics (Russell et al. 2014) or in optical functional devices like biosensors (Malinin et al. 2010). Compared to conventional optical fibers, MOFs have a lot of important characteristics including flexibility in the design, controllable effective

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area and nonlinearity, and adjustable dispersion (Chau et al. 2010). In particular, HC-MOFs have opened the door to effectively control the interaction between light and matter (Cubillas et al. 2013). In HC-MOFs, photonic bandgaps will be generated via microstructured cladding. When the incident light wavelength overlap with the HC-MOF bandgaps, the light will be reflected by the cladding and guided in the fiber core (Russell 2003; Rahaman et al. 2022). HC-MOFs have been used extensively in various applications including nonlinear optics (Azhar et al. 2013), imaging and spectroscopy (Stawska and Izabela 2018; Andreana et al. 2019), high-intensity laser transmission (Couny et al. 2007), and biosensing (Islam et al. 2021; Hossain et al. 2020). In specific, HC-MOFs are used for numerous bio sensing applications such as Cancer Cell sensing (Ahmed et al. 2019), Pregnancy sensing (Jabin et al. 2019), hemoglobin detection (Mitu et al. 2021) and Covid-19 detection(Patel et al. 2022).

While conventional optical fibers or photonic crystal fibers (PCFs) demonstrated great potential for sensing and biosensing applications including their miniature probe size and immunity to EMI interference, there are some inherent issues associated with these fibers in biosensing applications, particularly liquid biosensing. The main problem is the way scientists infiltrate liquids in the fiber structure which is either the fiber core or fiber air holes (Liu et al. 2014a, b). Detecting a liquid sample often requires a plasmonic or interferometric setup, both of which is complicated, costly and has limited sensing capabilities. For example, it is difficult to sense low-index liquids in the fiber core as the total internal reflection mechanism does not work with low index liquids. In contrast to complete internal reflection, which occurs in ordinary optical fibres and solid-core photonic crystal fibres, the bandgap guiding mechanism in HC-MOFs makes it feasible for low-index light to be guided through the material. In applications involving the sensing of liquid, HC-MOFs provide a number of advantages over typical optical fibres, including a reduction in the amount of light that is lost, increased flexibility, and simpler selective liquid filling. Because of these factors, optical fibres may be used in previously unexplored fields of study, such as gas sensing (Senthil et al. 2021) and low-index liquid sensing in the fiber core which can have important applications in the fields like medicine and biology in which liquid sensing is of a great importance (Malinin et al. 2011a, b; Hossain 2019; Podder et al. 2020).

Interestingly, while detection of low index and high index liquid analytes using conventional optical fibers or photonic crystal fibers have been investigated in detail (Podder et al. 2022; Islam et al. 2020; Monfared and Qasymeh 2021; Monfared et al. 2021), detection of low index liquid analytes via HC-MOFs is not investigated in detail. Between various liquid analytes, blood plasma detection is one of the transformative areas of research in medicine and biology. Plasma is the liquid component of blood which incorporates blood cells and proteins (Liu et al. 2014a, b). Detection of plasma concentration in blood via HC-MOFs can provide important advantages over the conventional methods of plasma detection like accuracy, in-situ, and almost real-time detection (Horan et al. 2011). In this paper, we will study various HC-MOF structures with varying numbers of cladding rings, and a hollow-core filled with liquid sample to detect various concentrations of blood plasma. We will measure changes in the bandgaps and transmission spectra of the proposed HC-MOFs as a means of studying the biosensor's performance over a wide variety of analyte refractive indexes. This will allow us to show that the biosensor is an effective way to detect changes in blood plasma.

2 Design of HC-MOF sensor

To design the HC-MOF, we used soft glass as the background material with a RI of n_{glass}=1.519 at the excitation wavelength of 550 nm (Ermatov et al. 2020). We simulate the HC-MOFs using finite element method (FEM) while perfectly matched layer (PML) boundary condition as well as strict convergence analysis has been done to make sure about the accuracy of the results. The schematic representation of the proposed HC-MOF is presented in Fig. 1. To obtain maximum sensitivity, we performed extensive numerical simulations to obtain the optimized design parameters for the HC-MOF. The design parameters agree well with the approximate dimensions of realistic fabricated HC-MOF in our previous works (Skibina et al. 2008, 2011; Malinin et al. 2011a, b; Nikolelis et al. 2013). In the simulations, the HC-MOF that has been suggested is made up of five layers of capillaries that are arranged in a concentric pattern and an exterior PML layer. In every simulation, the diameter of the core is made to measure d = 172 micrometres. The capillary walls are made from the soft glass with variable thicknesses depending on the number of layers. The thickness of capillary wall layers are t_1=1.9 µm, t_2=2.6 µm, t_3=3.0 µm, t_4=3.4 µm and t_5= 4.1 µm. The diameters of the capillaries, which are shown by the letters m and n and range from 1 to 5, are given below: m_1= 14 µm, n_1=16 µm, m_2=19 µm, n_2=20 µm, m_3=22 µm, n_3=24 µm, m_4=26 µm, n_4=29 µm, m_5=31 µm and n_5=35 µm, respectively. In conclusion, we assumed that the RI of air was equal to 1. In Fig. 2, the electric field distribution across the cross section of HC-MOFs with various numbers of rings (two rings to five rings) is demonstrated at 550 nm excitation wavelength. It is clear that most of the light energy will remain inside the fiber core due to the photonic bandgap guiding mechanism.

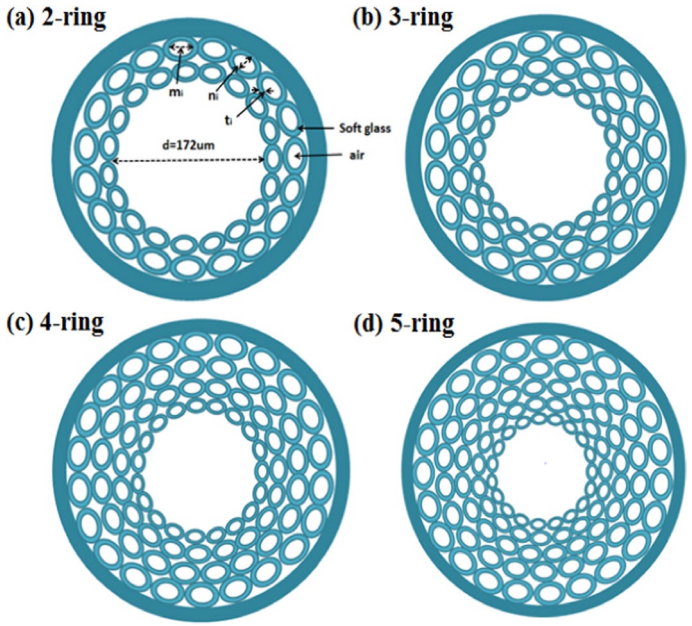

Fig. 1 Cross section of the HC-MOF with different design parameter including thickness of capillary walls (t_i), width and height of capillary walls (m_i and n_i), and various number of capillary rings: **a** two rings, **b** three rings, **c** four rings, and **d** five rings

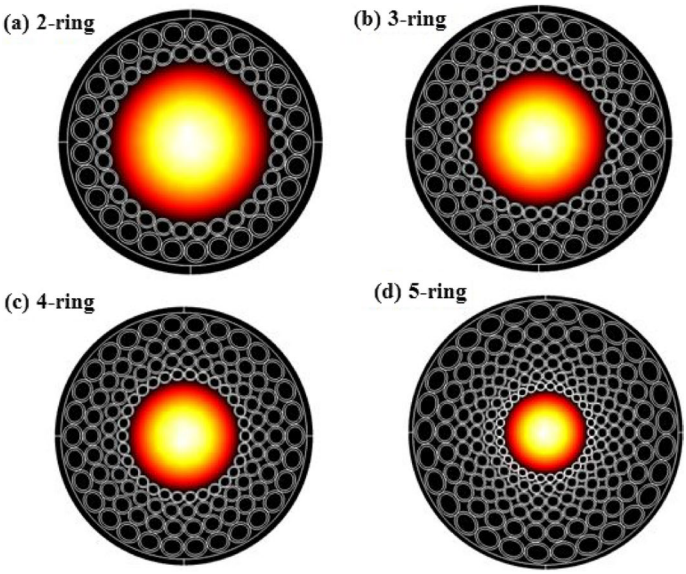

Fig. 2 Cross Section view of Electrical field distributions of the proposed HC-MOF with various number of capillary rings: **a** two rings, **b** three rings, **c** four rings, and **d** five rings

The proposed HC-MOF can be used to detect various biomolecules and biological samples as its transmission spectra (band gaps) are strongly dependent on the analyte refractive index inside the hollow core of the fiber. For this specific research, we choose to consider plasma in blood serum as a biological sample and analyze and calculate the sensing performance of our HC-MOF as a biosensor. Figure 3 illustrates the correlation that exists between the amount of plasma present in the blood serum and its specific RI value.

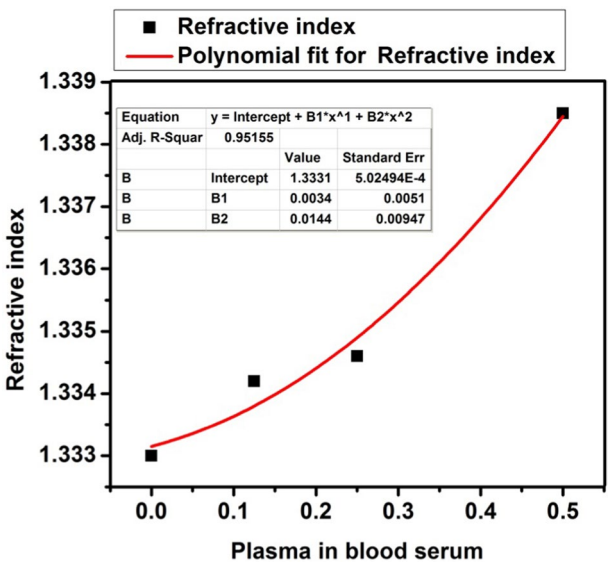

Fig. 3 The relationship between plasma concentration in blood serum vs. the refractive index (RI) of the analyte. Note that the black squares are experimental data points using a pocket refractometer (Atago PAL-RI)and red line is a polynomial fit for the experimental data

According to Fig. 3, as the concentration of plasma in blood serum increases from nearly 0 to 0.5, RI of the analyte increases from 1.3330 to approximately 1.3385. This means to detect the variations of plasma concentration, one need a highly sensitive biosensor to be able to differentiate between small variations in analyte RI. By using a pocket refractometer (Atago PAL-RI), the RI of the plasma in the blood serum was tested and found to be 1.3342, 1.3346, and 1.3385 for 1/8, 1/4, and 1/2 plasma dilution with.

water ratios, respectively. The mixing of raw plasma serum with distilled water is actually specified as having a ratio of 1/2, 1/4, and 1/8. For instance, 1/2 indicates a mixture of 1 component plasma serum and 2 parts purified water. Similar to this, 1/4 and 1/8 are equal parts of plasma serum and distilled water (4 parts for 1/4 and 8 parts for 1/8), respectively. Additionally, it is established that water's RI is 1.333.

We have investigated at the layer-by-layer (LBL) assembly method for the consistent modification of the fibre capillaries using a combination of diamagnetic and nondiamagnetic polyelectrolytes. The HC-MOF is made up of five concentric layers of capillaries and an external buffer layer, which gave the drawing process structural wholeness. The five circular layers of glass tubes with various sizes that make up the fibre preform each contain 30 identical cells. Each individual tube has an inner diameter to an exterior diameter ratio of 0.85. This structure is suspended in a cylindrical tube with a greater diameter using an outside buffer layer. The electro-vacuum glass, a soft optical glass made up of 72% silica, 16% Na_2O, and lower amounts, is used to make the whole fibre structure. The outstanding thermo-elastic qualities of this glass and its adaptability for the fibre drawing process are the major reasons it was chosen.

3 Sensing performances

The position of the photonic band gap as well as the location of the transmission maximum in HC-MOFs is heavily dependent on the geometrical structure of the cladding as well as the RI of the biological analyte in the hollow core region of the fibre. In order to prove that HC-MOFs may be used for biosensing, the sensing performance of these materials has been quantitatively examined for the detection of plasma concentration in blood serum. Here, we take a close look at how different design factors, and in particular the total number of capillary rings, affect the sensing performance of HC-MOFs that have been rigorously adjusted. In Fig. 4, we show the transmission spectra of HC-MOFs with a different number of capillary rings from two rings in Fig. 4a to five rings in Fig. 4d for various concentrations of plasma in blood serum (1/2, 1/4 and 1/8). We also demonstrate the transmission spectra of HC-MOFs with water as the analyte for the reference. As seen in Fig. 4, depending on the plasma concentration in blood serum we will get different transmission spectra with various peak wavelengths.

By increasing the plasma concentration and consequently analyte RI in the hollow core of HC-MOF, transmission peak wavelength red shifts to larger wavelengths as demonstrated in Fig. 4. This trend is also demonstrated in detail in Fig. 5 for the reference. By increasing the analyte RI from 1.333 to 1.385, a clear shift to longer wavelength in transmission peak can be observed in Fig. 5a and d. However, the amount of these variations strongly depends on the number of capillary rings in HC-MOF design. It is clear that the variations are much larger in HC-MOF with a larger number of capillary rings. For example, the transmission peak wavelength shift is 50 nm for HC-MOF with five capillary rings while the transmission peak wavelength shift is only 25 nm for

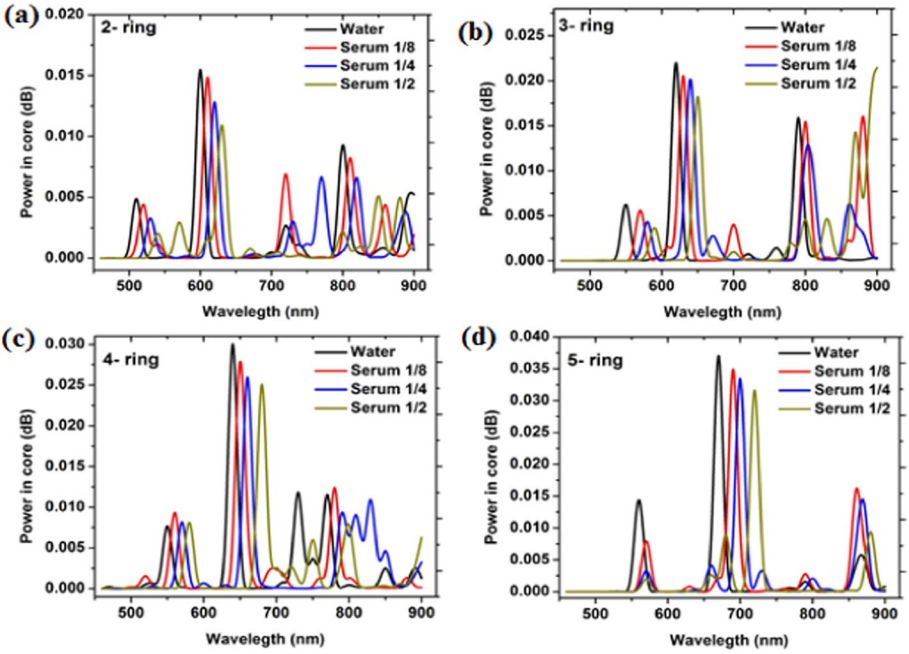

Fig. 4 Transmission spectra of the proposed HC-MOFs filled with water and various concentration of plasma in blood serum (1/2, 1/4 and 1/8) for different number of capillary rings: **a** 2 rings, **b** 3 rings, **c** 4 rings, and **d** 5 rings

HC-MOF with two capillary rings (where analyte RI varies between 1.333 and 1.385). It means by increasing the number of capillary rings from two to five, we can double the wavelength sensitivity of the designed HC-MOF. The wavelength sensitivity (S_w) of the HC-MOF can be calculated as,

$$S_w(nm/RIU) = \frac{\Delta\lambda_{peak}}{\Delta n_{analyte}} \tag{1}$$

where, λ_{peak} is resonance peak and $n_{analyte}$ is analyte or blood plasma sample. Using the above formula, the wavelength sensitivity of the 5-ring and 2-ring HC-MOF is 8928.57 nm/RIU and 4464.28 nm/RIU respectively.

Furthermore, one can see that the transmitted power in HC-MOF core increases significantly by raising the number of capillary rings in the design of the HC-MOFs. By increasing the number of capillary rings from two to five, transmitted power increases from 0.015 to 0.0375 for an analyte RI of 1.333. This means the transmitted power is more than two times larger for the 5-ring HC-MOF than the 2-ring HC-MOF. It should also be noted that the shift in transmitted power for 4-ring HC-MOF is significantly larger than that of the 2-ring HC-MOF while one increases analyte RI from 1.333 to 1.385 as demonstrated in Fig. 6. For instance, the transmitted power shift for the 5-ring HC-MOF is 0.0068 dB while the transmitted power shift is only 0.003 dB for the 2-ring HC-MOF (more than two times larger sensitivity). This is an important factor to

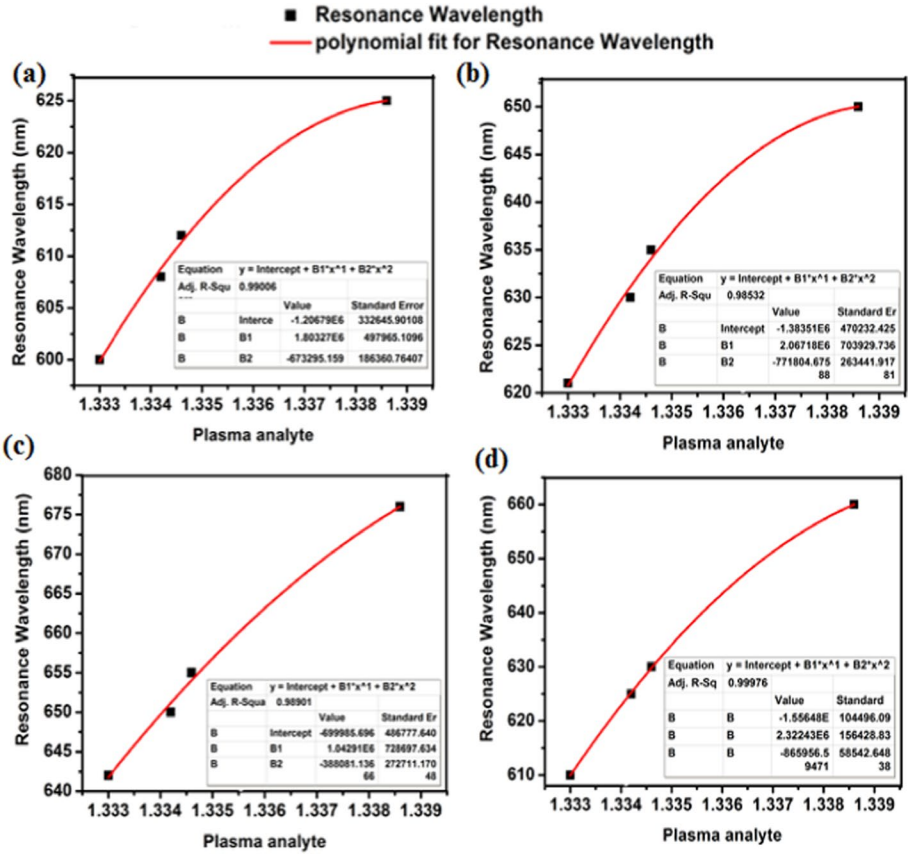

Fig. 5 Transmission peak wavelength as a function of plasma analyte RI for **a** 2-ring HC-MOF, **b** 3-ring HC-MOF, **c** 4-ring HC-MOF, and **d** 5-ring HC-MOF. Note that the black squares are data points and red solid lines are polynomial fits for these simulated data points

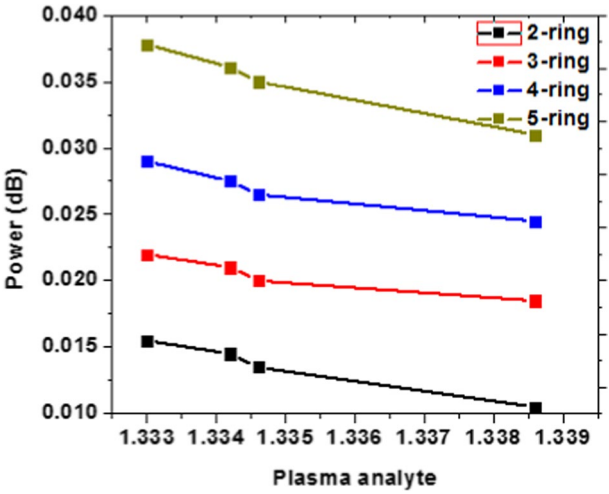

Fig. 6 Transmission power in the fiber core as a function of plasma analyte RI for the HC-MOFs with various number of capillary rings. Note that the squares are data points and solid lines are polynomial fits for these simulated data points

Table 1 Performance Analysis of designed HC-MOFs

Number of rings/sensing parameters	2-ring	3-ring	4-ring	5-ring
Wavelength shift (nm)	25	29	34	50
Wavelength sensitivity (nm/RIU)	4464.28	5178.57	6071.42	8928.57
Power shift (dB)	0.003	0.0035	0.0045	0.0068
Amplitude sensitivity (dB/RIU)	0.53	0.62	0.80	1.21

consider for biosensing applications based on amplitude sensitivity. The amplitude sensitivity (S_a) of HC-MOFs can be obtained from,

$$S_a(dB/RIU) = \frac{\Delta \lambda_{peak}}{\Delta n_{analyte}} \tag{2}$$

where, T_{power} is maximum peak power or resonance peak wavelength power in core region and $n_{analyte}$ is analyte or blood plasma sample. Using Eq. 2, the amplitude sensitivity of the 5-ring HC-MOF is determined to be 1.21 dB/RIU while the wavelength sensitivity of the 2-ring HC-MOF is only 0.53 dB/RIU.

Table 1 compares the sensing performances of the proposed HC-MOF with various number of capillary rings (two rings to five rings) including wavelength sensitivity and amplitude sensitivity of the proposed biosensors. Based on the results of our numerical investigation, increasing the number of capillary rings can significantly improve the sensing performance of the HC-MOF in both spectral detection method and amplitude detection method. Our findings can demonstrate the importance of the HC-MOFs in biosensing applications, and the importance of the design parameters and particularly, number of capillary rings in obtaining the best sensing performances.

4 Conclusions

An ultra-sensitive HC-MOF biosensor for detection of blood plasma is reported here. Using a finite element method, the transmission spectra of HC-MOFs filled with various concentrations of plasma in blood samples have been investigated. The results indicated that transmission spectra of HC-MOFs are more sensitive to small variations in liquid analyte refractive index and consequently, the concentration of plasma in blood samples. We demonstrated that the spectrum sensitivity and amplitude sensitivity of HC-MOFs for low-index liquid analyte detections may be improved by increasing the number of capillary rings around the hollow core. We demonstrated that an average spectral and amplitude sensitivity of 8928.57 nm/RIU and 1.21 dB/RIU respectively can be obtained using the optimized design parameters. The proposed biosensor can have important applications in medicine, chemistry and biology where detection of liquid analytes in real-time is of particular interest.

Author contribution Conception and Design: MKA, KV, AN, MGS, KKG, KCS, SN, YK. Data and Investigation: MKA, KV, AN, MGS. Manuscript Initial draft: MKA, KV, AN, MGS, KKG, KCS, SN, YK.

Manuscript final draft: MKA, KV, AN, MGS, KKG, KCS, SN, YK. Approval: MKA, KV, AN, MGS, KKG, KCS, SN, YK.

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Data availability Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

Declarations

Competing interest The author declares that they do not have any conflict of interest. The author of this research acknowledges that they are not involved in any financial interest.

Ethical approval Not applicable.

Consent to participate Author certifies that this material or similar material has not been and will not be submitted to or published in any other publication before. Furthermore, the authors certify that they have participated sufficiently in the work to take public responsibility for the content, including participation in the concept, design, analysis, writing, or revision of the manuscript.

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