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## Article

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# A metal-dielectric photonic crystal-based glucose sensor with sensitivity enhancement by using 2D materials

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## ABSTRACT

Metal-dielectric photonic crystals (MDPhCs) that support the excitation of Bloch-like surface waves (BLSWs) at the interface of an MDPhC and the adjacent medium (analyte) have emerged as a very promising alternative for sensing gaseous analytes with high sensitivity. In this theoretical paper we report on an extension of the concept for glucose sensing when the BLSW-based resonances in the Kretschmann configuration are accompanied by narrow dips and are characterized by ultra-high sensitivities. Moreover, one of the possible solutions to enhance the sensitivity represents an MDPhC with a 2D material overlayer, such as black phosphorus or molybdenum disulfide (MoS<sub>2</sub>). For an MDPhC comprising two bilayers of TiO<sub>2</sub>/Au with a termination layer of TiO<sub>2</sub>, we demonstrate that the BLSW-based resonances are resolved for TE waves when simulated glucose solutions are considered, and the glucose analyte refractive index (RI) is in a range of 1.32797–1.32867 at a wavelength of 1.55  $\mu\text{m}$ , corresponding to physiologically relevant glucose concentrations of 0–500 mg/dL. Using the wavelength interrogation, an RI sensitivity of 19.9  $\mu\text{m}/\text{RI}$  unit (RIU), a figure of merit (FOM) of 1047 RIU<sup>-1</sup>, and a limit of detection (LOD) of  $5.0 \times 10^{-6}$  RIU, respectively, were attained. The analysis extended to one monolayer of black phosphorus or MoS<sub>2</sub> on the MDPhC revealed that the RI sensitivity is increased up to 26.9  $\mu\text{m}/\text{RIU}$  for MoS<sub>2</sub>, the FOM reached 1076 RIU<sup>-1</sup>, and the LOD is as low as  $3.7 \times 10^{-6}$  RIU, or equivalently in the glucose concentration domain, the sensitivity is up to 0.0379 nm/(mg/dL), and the LOD is lowered to 2.6 mg/dL. This research is the demonstration of exceptional properties of the BLSW-based sensors employing MDPhCs whose sensitivity can be enhanced by using 2D materials. Such sensors are potentially well suited to a variety of biosensing applications.

## Introduction

Glucose is the principal monosaccharide and the most important source of energy for the majority of cells in the human body. It plays a pivotal role in cellular metabolism and is indispensable for tissues with high energy demands, particularly the central nervous system, skeletal muscle, and erythrocytes. The physiological concentration of blood glucose is subject to rigorous regulation by a sophisticated network of hormonal and metabolic mechanisms. These mechanisms include insulin, glucagon, catecholamines, cortisol and growth hormone<sup>1</sup>.

The global incidence of diabetes mellitus is increasing at an alarming rate<sup>2</sup>. Diabetes mellitus is currently among the most prevalent chronic metabolic disorders and represents a significant medical, social and economic burden. It is well-documented that long-term hyperglycaemia is associated with the development of microvascular and macrovascular complications, including diabetic retinopathy, nephropathy, neuropathy, and cardiovascular diseases<sup>3,4</sup>. Furthermore, the occurrence of hypoglycaemia persists as a grave concern, especially among patients undergoing insulin treatment.

It is imperative that glucose concentrations are accurately determined in order to facilitate diagnosis, to guide therapy, and to monitor diabetic patients over the long term. Glucose analysis has evolved significantly over recent decades, progressing from rudimentary laboratory assays to sophisticated automated analytical systems, point-of-care testing, continuous glucose monitoring, and advanced biosensor technologies<sup>5,6</sup>.

Modern glucose monitoring technologies increasingly combine principles of biochemistry, electrochemistry, optics, photonics, nanotechnology, and materials science. In particular, the development of glucose monitoring systems that are minimally invasive and non-invasive has become one of the major objectives of current biomedical research<sup>7,8</sup>. Optical

and photonic methods are a promising avenue of research due to their potential for rapid, continuous, and painless glucose monitoring. Blood glucose levels are correlated with glucose content in different biological samples, such as blood and urine<sup>2</sup>, and they have advantages in making continuous glucose monitoring (CGM) easier, safer, more accurate and less painful. In glucose monitoring, various techniques have been developed and among them the optical methods have gained considerable attention due to an easy sensor construction.

The development of glucose sensors is driven by key performance parameters, such as sensitivity, figure of merit (FOM), and limit of detection (LOD). Various techniques have been explored to enhance the attributes and improve sensor efficiency and construction<sup>8–10</sup>. These include glucose sensors based on Bloch surface waves (BSWs) excited on a one-dimensional photonic crystal (1DPhC)<sup>11</sup> or Tamm-Fano resonances supported by a PhC<sup>12</sup> with the refractive index (RI) sensitivities reaching  $1.105 \mu\text{m}/\text{RI unit (RIU)}$ <sup>11</sup> and  $14.152 \mu\text{m}/\text{RIU}$ <sup>12</sup>, respectively. An extension to two-dimensional (2D) PhCs enables detections of the disease through analysis of blood, urine, or tears fluid samples<sup>13</sup>. The 2DPhC-based sensors have potential for integration into portable diagnostic devices<sup>14</sup> or enable construction of a highly accurate and sensitive CGM sensor<sup>15</sup> with the RI sensitivities reaching  $20.040 \mu\text{m}/\text{RIU}$ <sup>14</sup> and  $2.592 \mu\text{m}/\text{RIU}$ <sup>15</sup>, respectively. To achieve improved performance of SPR-based glucose sensors, 2D materials have been employed<sup>16–18</sup>, including Transition-Metal-Dichalcogenides (TMDCs) that demonstrate the superior sensitivity. In addition, free-space excited glucose sensors based on either a ternary PhC containing a defect<sup>19</sup> or a hollow-ring cubic structure<sup>20</sup> are also available with the RI sensitivities of  $0.965 \mu\text{m}/\text{RIU}$ <sup>19</sup> and  $2.592 \mu\text{m}/\text{RIU}$ <sup>20</sup>, respectively. From the practical point of view, fiber-optic glucose sensors are mostly preferred<sup>9,10,21–30</sup> with sensitivities ranging from  $0.168 \mu\text{m}/\text{RIU}$ <sup>22</sup> to  $6.709 \mu\text{m}/\text{RIU}$ <sup>26</sup>.

Among the sensors mentioned above, the BSW-based biosensors<sup>31–40</sup> are more advantageous, because they do not rely on the use of metals and exhibit sharp resonances. The sensors employ a periodic structure, which is composed of bilayers of dielectric media of high and low RIs, and a termination layer as well, and is referred to as a truncated 1DPhC<sup>41,42</sup>. A 1DPhC is mechanically and chemically robust, offering the possibility of operation in aggressive environments, which is important for biosensing. 1DPhCs are characterized by photonic band gaps (PBGs), and the optical waves in a 1DPhC are gradually enhanced with the maximum amplitude near the interface with the adjacent medium (analyte) and with high optical field confinement justifying narrow resonance dips within the PBG of the reflection spectrum<sup>43–45</sup>. Contrary to SPR-based sensors, BSWs can be excited by both TE and TM waves<sup>46,47</sup> at any wavelength, including also near-infrared region<sup>11,48</sup>. However, the BSW-based sensors do not outperform SPR sensors in sensitivity.

Recently, a metal-dielectric PhC (MDPhC) has emerged as a very promising alternative<sup>49–52</sup>. In such an MDPhC, the metallic layers instead of low-RI dielectric layers are incorporated into a periodic structure, resulting in an extremely high refractive index contrast within the unit cell. When a truncated 1DPhC contains only a few bilayers, the concept of the BSW, originally developed for a semi-infinite number of bilayers, cannot be used in the obvious way. In addition, when an MDPhC is considered, there can exist some SWs that are localized near the interface with an analyte, and they are referred to as Bloch-like SWs (BLSWs)<sup>52</sup>. Compared to all-dielectric 1DPhCs, MDPhCs are characterized by superior sensitivities for gaseous analytes<sup>52</sup> and this is due to the extremely high RI contrast and field enhancement. By suitably changing the geometry and materials of an MDPhC, high field confinement and long penetration depth can be attained to enhance sensitivity as high as possible with potential applications in biosensing.

In this theoretical paper, an MDPhC supporting the excitation of BLSWs in the Kretschmann configuration is employed for glucose sensing with ultra-high sensitivity. We use the wavelength interrogation and show for an MDPhC, comprising two bilayers of  $\text{TiO}_2/\text{Au}$  with a termination layer of  $\text{TiO}_2$ , that the BLSW resonances are resolved for a TE wave when simulated glucose solutions are considered, and the glucose analyte RI is in a range of 1.32797–1.32867 at a wavelength of  $1.55 \mu\text{m}$ , corresponding to physiologically relevant glucose concentrations of 0–500 mg/dL. The sensitivity to the RI, FOM, and LOD reach  $19.9 \mu\text{m}/\text{RIU}$ ,  $1047 \text{ RIU}^{-1}$ , and  $5.0 \times 10^{-6} \text{ RIU}$ , respectively. The analysis extended to the MDPhC with a 2D material overlayer, namely one monolayer of black phosphorus (BP) or molybdenum disulfide ( $\text{MoS}_2$ ), respectively, revealed the sensitivity enhancement. The RI sensitivity for  $\text{MoS}_2$  is up to  $26.9 \mu\text{m}/\text{RIU}$  and the FOM is  $1076 \text{ RIU}^{-1}$ , while the LOD is lowered to  $3.7 \times 10^{-6} \text{ RIU}$ , or equivalently in the glucose concentration domain, the sensitivity is up to  $0.0379 \text{ nm}/(\text{mg}/\text{dL})$ , and the LOD is as low as  $2.6 \text{ mg}/\text{dL}$ . Thus, the sensing concept based on MDPhCs is very promising for glucose sensing in biological samples. The advantage of the concept is that using a 2D material overlayer leads to substantial sensitivity enhancement, and it may find a variety of biosensing applications. The concept is also potentially well-suited to a fiber-optic implementation of the sensors, similar to that for the BSW-based sensors<sup>38</sup>.

## Theoretical model and basic equations

The experimental setup employing an MDPhC in the Kretschmann configuration is drawn schematically in Fig. 1. It consists of a glass substrate, titanium dioxide and gold layers, and its response to glucose is analyzed by employing the wavelength interrogation. Both a prism and substrate are made from BK7 glass and its refractive index as a function of wavelength can be described by a three-term Sellmeier equation<sup>53</sup>, as specified in a previous paper<sup>52</sup>. In the same paper, the dispersion relation for

the TiO<sub>2</sub> layer<sup>47</sup> and the material dispersion of the Au layer via the complex dielectric function given by the Drude-Lorentz model<sup>54</sup> are present.

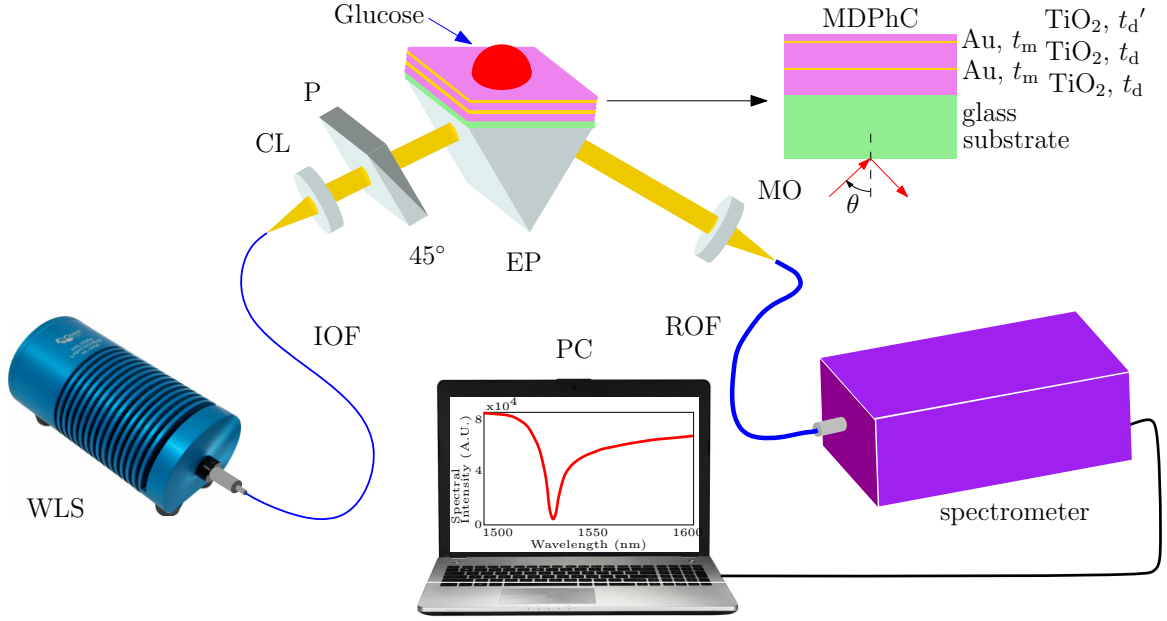


**Figure 1.** Schematic drawing of the experimental setup employing an MDPHC; white light source (WLS), input optical fiber (IOF), collimating lens (CL), polarizer (P), equilateral prism (EP), microscope objective (MO), read optical fiber (ROF) and personal computer (PC).

Light propagation through an MDPHC in the Kretschmann configuration can be analyzed by the transfer matrix method (TMM)<sup>52,55,56</sup>. The method enables to express the spectral reflectances  $R_{s,p}(\lambda)$  for both  $s$ -polarized (transverse electric, TE) and  $p$ -polarized (transverse magnetic, TM) waves, respectively. If  $N$  layers are considered, including both metal and dielectric media, the propagation matrices in different layers and the transmission matrices across different interfaces can be used to express the total transfer matrix  $\mathbf{M}(\lambda)$  at the wavelength  $\lambda$  as

$$\mathbf{M}(\lambda) = \begin{bmatrix} M_{11}(\lambda) & M_{12}(\lambda) \\ M_{21}(\lambda) & M_{22}(\lambda) \end{bmatrix} = \left[ \prod_{j=1}^N \mathbf{B}_{j-1,j}(\lambda) \mathbf{P}_j(\lambda) \right] \cdot \mathbf{B}_{N,N+1}(\lambda), \quad (1)$$

where indices 0 and  $N + 1$  denote the first and last semi-infinite medium, respectively, and  $\mathbf{B}_{j,j+1}(\lambda)$  are the boundary matrices for  $s$ - and  $p$ -polarized waves that satisfy the relations<sup>57</sup>

$$\mathbf{B}_{j,j+1}(\lambda) = \frac{1}{2} \begin{pmatrix} 1 + \tilde{\eta}_{s,p}(\lambda) & 1 - \tilde{\eta}_{s,p}(\lambda) \\ 1 - \tilde{\eta}_{s,p}(\lambda) & 1 + \tilde{\eta}_{s,p}(\lambda) \end{pmatrix}, \quad (2)$$

where  $\tilde{\eta}_s(\lambda)$  and  $\tilde{\eta}_p(\lambda)$  are the complex parameters given by

$$\tilde{\eta}_s(\lambda) = \frac{k_{zj+1}}{k_{zj}}, \quad \tilde{\eta}_p(\lambda) = \frac{\tilde{n}_j^2(\lambda) k_{zj+1}}{\tilde{n}_{j+1}^2(\lambda) k_{zj}}, \quad (3)$$

where  $\tilde{n}_j(\lambda)$  and  $\tilde{n}_{j+1}(\lambda)$  are the complex refractive indices of the media, and  $k_{zj}(\lambda)$  is given as

$$k_{zj}(\lambda) = \frac{2\pi}{\lambda} [\tilde{n}_j^2(\lambda) - n_0^2(\lambda) \sin^2 \theta]^{1/2}. \quad (4)$$

The propagation matrices are given by

$$\mathbf{P}_j(\lambda) = \begin{pmatrix} e^{ik_{zj}(\lambda)t_j} & 0 \\ 0 & e^{-ik_{zj}(\lambda)t_j} \end{pmatrix}, \quad (5)$$

where  $t_j$  is the thickness of  $j$ -th layer.

The total transfer matrix elements enable to express the complex reflection coefficient  $r(\lambda)$  as

$$r(\lambda) = \frac{M_{21}(\lambda)}{M_{11}(\lambda)}, \quad (6)$$

and it can be specified for both  $s$  and  $p$  polarizations as

$$r_{s,p}(\lambda) = |r_{s,p}(\lambda)| e^{i\phi_{s,p}(\lambda)}, \quad (7)$$

with the spectral reflectances  $R_{s,p}(\lambda)$  as

$$R_{s,p}(\lambda) = |r_{s,p}(\lambda)|^2. \quad (8)$$

The sensor performance can be evaluated using simulated glucose solutions. To evaluate the spectral response of an MDPHC to the glucose solution, we approximated the RI of the glucose analyte  $n_a$  as a function of both wavelength  $\lambda$  and glucose concentration  $C$  by a Cauchy relation

$$n_a(\lambda, C) = a + a_0C + \frac{b + b_0C}{\lambda^2} + \frac{c + c_0C}{\lambda^4}, \quad (9)$$

where constants are with values of  $a = 1.3267$ ,  $b = 3 \times 10^{-3} \mu\text{m}^2$ ,  $c = 1 \times 10^{-4} \mu\text{m}^4$ ,  $a_0 = 1.2 \times 10^{-6} (\text{mg/dL})^{-1}$ ,  $b_0 = 0.5 \times 10^{-6} \mu\text{m}^2/(\text{mg/dL})$ ,  $c_0 = 0 \mu\text{m}^4/(\text{mg/dL})$ . It should be stressed here that the extinction coefficient is considered to be negligible.

From Eq. (9), it results that the RI of the glucose analyte at a wavelength of  $1.55 \mu\text{m}$  can be expressed similarly as in<sup>15</sup> and for the glucose concentration  $C$  in a range of 0–500 mg/dL is given by

$$n_a(C) = 1.32797 + 1.408 \times 10^{-6}C. \quad (10)$$

In practical operation, temperature fluctuations may alter both the RIs of the constituent materials and the analyte, leading to additional changes in the spectral reflectances. Therefore, temperature stabilization or compensation strategies will likely be required in future experimental implementations. In addition, the subsequent simulations intentionally consider an idealized single-analyte model in which RI variations are attributed exclusively to the glucose solution. Contributions from proteins, lipids, electrolytes, and other constituents naturally present in biological fluids are not included in the calculations; therefore, the reported sensing characteristics should be regarded as theoretical upper-limit performance estimates.

## Overlayers - 2D materials

To enhance the performance of glucose sensors, overlayers need to be used. The theoretical analyses have revealed that the most effective overlayers are thin films with high RIs. Specifically, 2D materials<sup>16–18, 58–61</sup> such as graphene<sup>26, 34, 62–64</sup>, BP<sup>65–70</sup>, TMDCs<sup>26, 59, 71–74</sup> and franckeite<sup>75</sup> meet the criterion. In addition, 2D materials are advantageous due to their large specific area and excellent adsorption properties towards some biomolecules, especially those with carbon-based ring structures (like ssDNA) that are suitable for graphene<sup>76</sup>. However, some 2D materials, such as graphene, deteriorate the response due to shallow and wide resonance dips. The most appropriate are BP in one of the principal directions and MoS<sub>2</sub>, and Figs. 2(a) and (b) show a schematic drawing of a prism with an MDPHC and BP or MoS<sub>2</sub>.

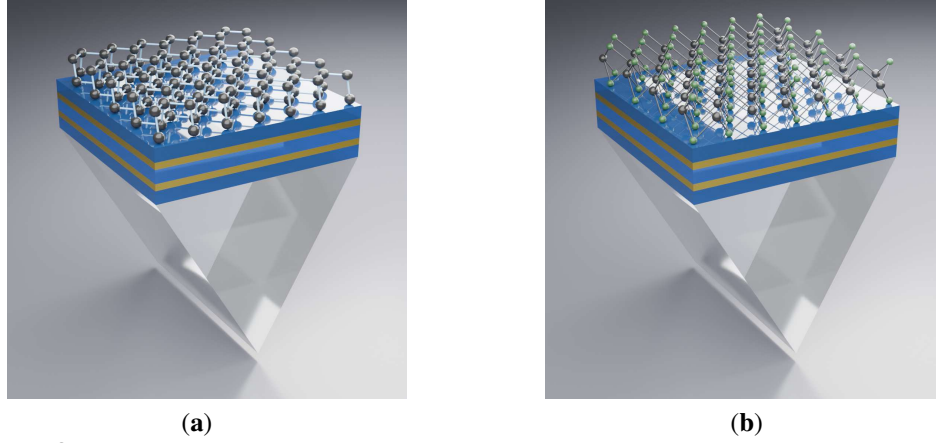


**Figure 2.** Schematic drawing of a prism with an MDPHC and a 2D material: BP (a), MoS<sub>2</sub> (b).

### Black phosphorus (BP)

BP is an anisotropic material with two principal directions - zigzag (ZZ) and armchair (AC) directions<sup>70,77,78</sup>. The optical properties of BP, whose monolayer thickness is 0.53 nm, can be deduced from a rigorous analysis using permittivity tensor<sup>79,80</sup>, and the real and imaginary parts of the refractive indices of BP along the AC and ZZ directions can be described using the Cauchy absorption model<sup>70,78</sup>:

$$n(\lambda) = a + b \frac{10^4}{\lambda^2} + c \frac{10^9}{\lambda^4}, \quad (11)$$

$$\kappa(\lambda) = d \times 10^{-5} + e \frac{10^4}{\lambda^2} + f \frac{10^9}{\lambda^4}, \quad (12)$$

where  $\lambda$  is the wavelength in nm and  $a = 3.57$ ,  $b = 6.79 \text{ nm}^2$ ,  $c = 39.99 \text{ nm}^4$ ,  $d = 3206$ ,  $e = -0.521 \text{ nm}^2$ , and  $f = 10.26 \text{ nm}^4$  are the Cauchy coefficients for the ZZ direction, for which the resonance dips are sufficiently pronounced.

### Molybdenum disulfide (MoS<sub>2</sub>)

The complex dielectric function  $\varepsilon(E)$  of the MoS<sub>2</sub> as a function of photon energy  $E$  can be represented by using the multi-Lorentzian dispersion relation<sup>72,74,81</sup>:

$$\varepsilon(E) = 1 + \sum_{k=1}^5 \frac{f_k}{E_k^2 - E^2 + iE\gamma_k}, \quad (13)$$

where  $f_k$  and  $\gamma_k$  are the oscillator strength and the line-width of the  $k$ -th oscillator, respectively, and  $E_k$  is the resonance energy. For the MoS<sub>2</sub>, whose monolayer thickness is 0.615 nm, these parameters are specified in Table 1.

### Fabrication considerations

Although the present study is purely theoretical, several fabrication-related factors must be considered for experimental implementation of the glucose sensors. The performance of an MDPHC is influenced by the thickness accuracy and uniformity of the TiO<sub>2</sub> and Au layers, since nanometer-scale deviations may induce measurable shifts of the resonance wavelength. Such multilayer structures can be fabricated using electron-beam evaporation, magnetron sputtering, or atomic layer deposition, which provide thickness control at the nanometer level. In addition, the optical response is expected to be sensitive to the quality and uniformity of the deposited MoS<sub>2</sub> monolayer<sup>82</sup>, as grain boundaries<sup>83,84</sup>, defects, and thickness variations can modify its optical properties and consequently affect the BLSW field distribution and resonance characteristics. Surface roughness of the metallic and dielectric layers may further increase scattering losses, broaden the resonance dip, and reduce the FOM.

Furthermore, although the BP can provide substantial sensitivity enhancement, its practical application is limited by its well-known environmental instability<sup>85</sup>. Consequently, BP-assisted implementations would require suitable passivation

**Table 1.** The resonance energy  $E_k$ , the oscillator strength  $f_k$ , and the spectral width  $\gamma_k$  for MoS<sub>2</sub><sup>81</sup>

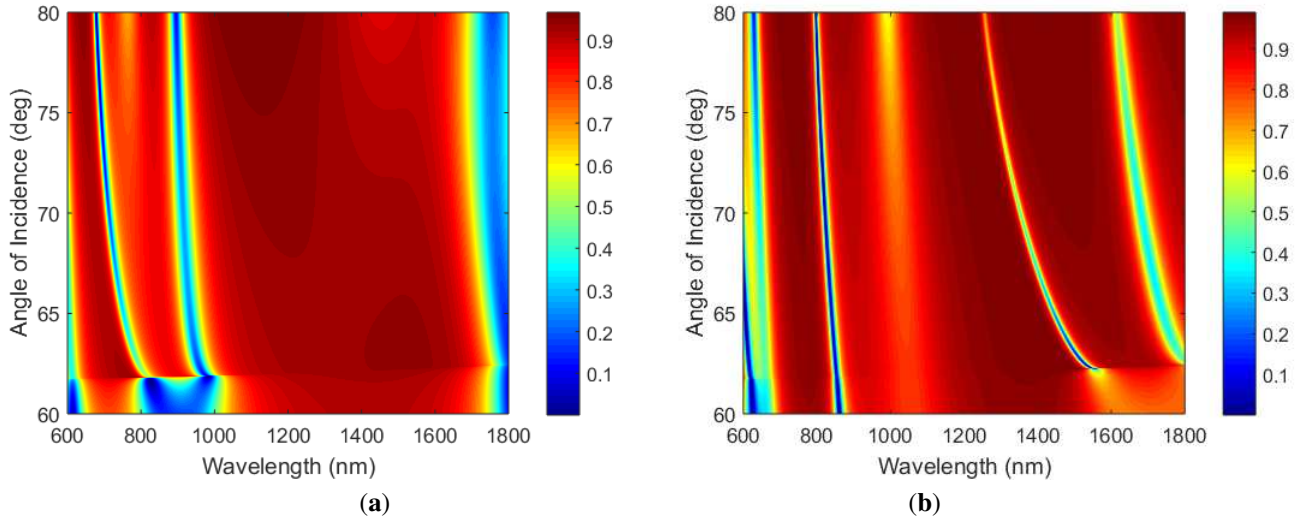
| $k$ | $E_k$ (eV) | $f_k$ (eV <sup>2</sup> ) | $\gamma_k$ (eV) |
|-----|------------|--------------------------|-----------------|
| 1   | 1.866      | 0.752                    | 0.045           |
| 2   | 2.005      | 1.883                    | 0.097           |
| 3   | 2.862      | 36.89                    | 0.383           |
| 4   | 2.275      | 10.00                    | 1.000           |
| 5   | 3.745      | 100.0                    | 0.533           |

strategies, such as dielectric encapsulation (e.g., ultrathin Al<sub>2</sub>O<sub>3</sub> coatings<sup>86</sup>), polymer protective layers, or related stabilization approaches to ensure long-term operation in aqueous environments<sup>87,88</sup>. In comparison, MoS<sub>2</sub> exhibits substantially higher environmental stability and therefore appears to be a more promising candidate for future CGM applications.

## Theoretical results and discussion

We started the analysis by evaluating the spectral response of an MDPHC for different angles of incidence  $\theta$  when the analyte is with the glucose concentration  $C = 0$  mg/dL and the corresponding RI at a wavelength of  $1.55 \mu\text{m}$  is  $n_a = 1.32797$ . The MDPHC, which can be fabricated by different techniques presented in<sup>52</sup>, is composed of two bilayers of TiO<sub>2</sub>/Au with a termination layer of TiO<sub>2</sub>, and the extinction coefficient for TiO<sub>2</sub> is with a value of  $1.6 \times 10^{-3}$ , as specified in previous papers<sup>44,47</sup>. Taking into account the dispersions of the analyte given by Eq. (9), and the prism and materials of the MDPHC, as specified in a previous paper<sup>52</sup>, we calculated the reflectances for the TM and TE waves in a spectral range of 600–1800 nm.

In order to have deeper insights into the reflectance responses of the MDPHC, first we calculated contour plots of both reflectances as a function of the angle of incidence  $\theta$  and the wavelength  $\lambda$  when the thicknesses of the TiO<sub>2</sub>, Au and the termination layer are  $t_d = 400$  nm,  $t_m = 15$  nm and  $t_d' = 200$  nm, respectively. From Figs. 3(a) and (b), it is clear that one of the resonance dips for both the TM and TE waves is with the greatest depth and smallest width. The resonance wavelengths of both dips shift toward the shorter wavelength as the angle of incidence, which is greater than the critical angle, increases and the dips are related to surface waves. The contour plots for both reflectances as the glucose analyte RI increases are shown in the Supplementary Figs. S1 and S2, thus demonstrating that the shift for the TE wave is nearly twice that for the TM wave. This is also shown in detail in the Supplementary Figs. S3 and S4 for the angle of incidence  $\theta = 64^\circ$ .

**Figure 3.** Calculated contour plots of the reflectance as a function of the angle of incidence and wavelength for TM (a) and TE (b) waves when  $n_a = 1.32797$ .

Based on the calculated contour plots of the reflectance as a function of the angle of incidence and wavelength shown in Fig. 3(b), we choose an incidence angle of  $62.3^\circ$ . We calculated contour plots of the reflectance for the TE wave as a function

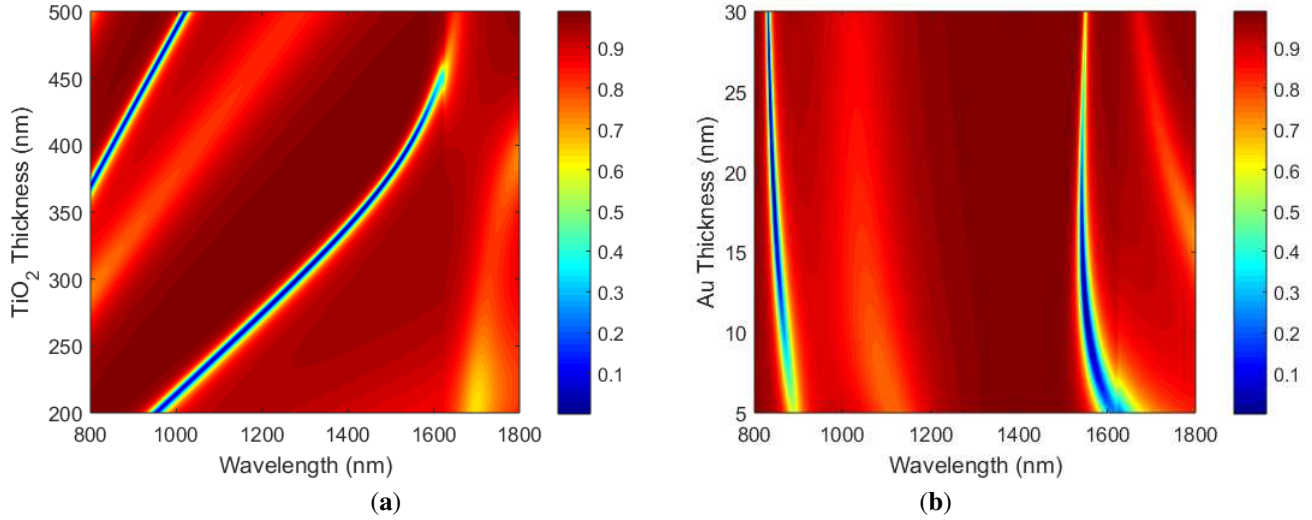


**Figure 4.** Calculated contour plots of the reflectance for the TE wave as a function of the  $\text{TiO}_2$  thickness and wavelength (a) with  $t_m = 15$  nm and  $t_d' = 200$  nm, and as a function of the Au thickness and wavelength (b) with  $t_d = 400$  nm and  $t_d' = 200$  nm when  $\theta = 62.3^\circ$  and  $n_a = 1.32797$ .

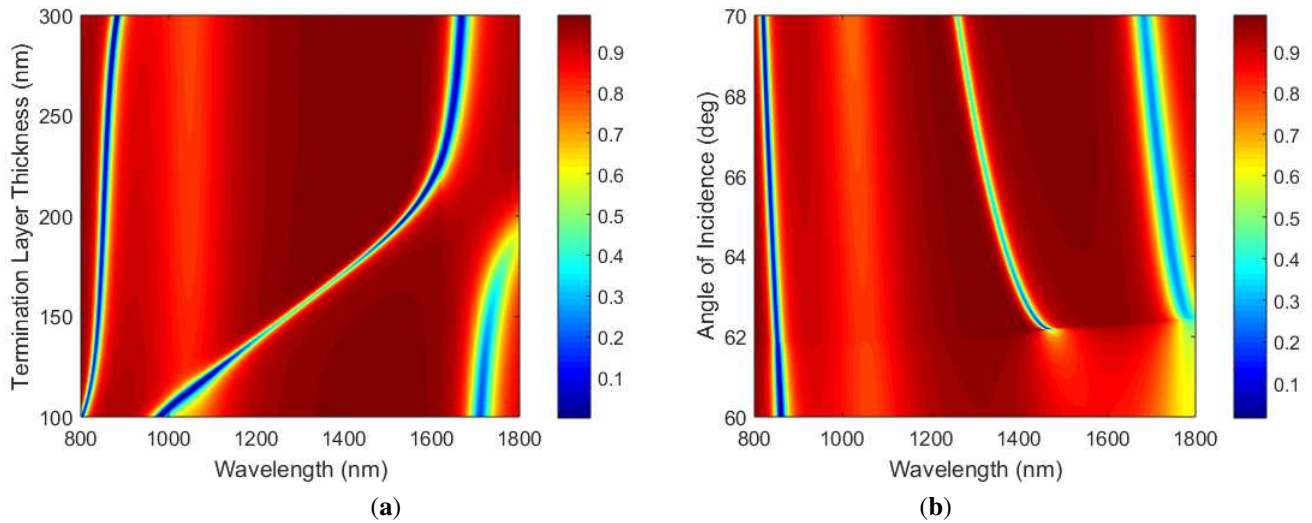


**Figure 5.** Calculated contour plots of the reflectance for the TE wave as a function of the thickness of the  $\text{TiO}_2$  termination layer and wavelength (a) with  $t_d = 400$  nm,  $t_m = 15$  nm, and  $\theta = 62.3^\circ$ , and as a function of the angle of incidence and wavelength (b) with  $t_d = 400$  nm,  $t_m = 14$  nm and  $t_d' = 180$  nm when  $n_a = 1.32797$ .

of the  $\text{TiO}_2$  thickness  $t_d$  when the thicknesses of Au and the termination layer are  $t_m = 15$  nm and  $t_d' = 200$  nm, respectively. From Fig. 4(a), it results that a sufficient dip depth is up to the  $\text{TiO}_2$  thickness of 430 nm. Moreover, we calculated contour plots of the reflectance for the TE wave as a function of the Au thickness  $t_m$  when the thicknesses of the  $\text{TiO}_2$  and the termination layer are  $t_d = 400$  nm and  $t_d' = 200$  nm, respectively. From Fig. 4(b), it results that a sufficient dip depth is up to the Au thickness of 15 nm, and the dip width is smaller as the Au thickness increases.

Furthermore, we calculated contour plots of the reflectance for the TE wave as a function of the thickness of the  $\text{TiO}_2$  termination layer  $t_d'$  when the thicknesses of the  $\text{TiO}_2$  and the Au layers are  $t_d = 400$  nm and  $t_m = 15$  nm, respectively. From Fig. 5(a), it results that the maximum depth and the smallest width are reached for the termination layer thickness  $t_d' = 180$  nm. Consequently, the thicknesses of the  $\text{TiO}_2$ , Au and the termination layer are chosen as  $t_d = 400$  nm,  $t_m = 14$  nm and  $t_d' = 180$  nm (MDPhC 1), respectively. The corresponding contour plot of the reflectance as a function of the angle of incidence  $\theta$  and the wavelength  $\lambda$  is shown in Fig. 5(b), indicating the sufficiently pronounced resonance dip. From Fig. 5(b), it results that the dip shifts toward the longer wavelength as the angle of incidence  $\theta$  decreases. In addition, if the corresponding angle of incidence

is below the critical angle, no dip is resolved.

Figure 6(a) shows the theoretical spectral reflectances for the angle of incidence  $\theta = 62.305^\circ$  when the glucose analyte RI is in a range of 1.32797–1.32867 and the concentration of glucose is in a range of 0–500 mg/dL. This figure demonstrates narrow and sufficiently pronounced dips with the remarkable shift with the RI change. As it results from Figs. 4(a) and 5(a), the resonance dip is red-shifted with the increase of the thicknesses  $t_d$  and  $t_d'$  of both the  $\text{TiO}_2$  and termination layers. Consequently, the penetration depth is also increasing and leading to the sensitivity enhancement. If we consider fabrication tolerances and assume that the thicknesses of the MDPHC layers are with  $\pm 5\%$  thickness variations, the most sensitive MDPHC is characterized by thicknesses  $t_d = 420$  nm,  $t_m = 14.7$  nm and  $t_d' = 189$  nm (MDPhC 2), respectively. Figure 6(b) shows the resonance dips with shifts indicating higher sensitivity to changes in the glucose analyte RI. It is interesting to note that the shape of the dip is distorted by the decrease in the reflectance in the long-wavelength range owing to the wave irradiation through the interface between the termination layer and glucose analyte. This is the reason why we have chosen the angle of incidence  $\theta = 62.305^\circ$  instead of  $\theta = 62.3^\circ$ .

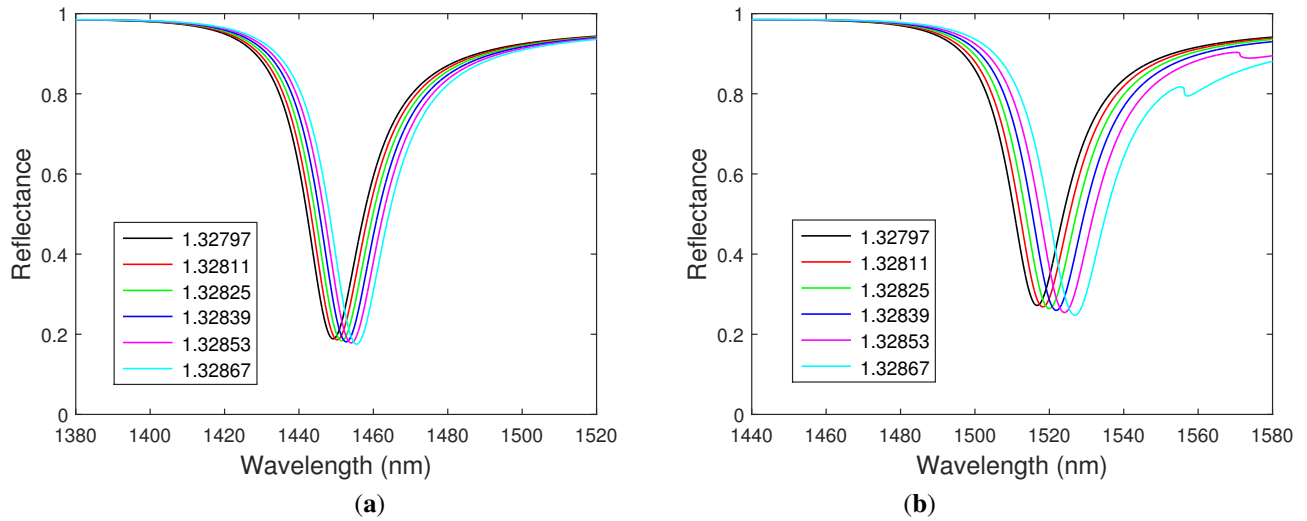


**Figure 6.** Theoretical spectral reflectance for the TE wave and different values of the glucose analyte RI for MDPHC 1 (a) or MDPHC 2 (b) when  $\theta = 62.305^\circ$ .

To demonstrate the sensing properties of the MDPHCs, the computed spectral reflectances for the TE wave shown in Figs. 6(a) and (b) are used to determine the resonance wavelength  $\lambda_r$  as a function of the glucose analyte RI  $n_a$ . These functions are shown in Figs. 7(a) and (b), together with second-order polynomials as the best fits. Such non-linear responses mean that the sensitivity  $S_n$  to the refractive index  $n$  is linearly RI-dependent, as shown in Fig. 7(b). The sensitivity  $S_n$  is defined as

$$S_n = \frac{\delta \lambda_r}{\delta n}, \quad (14)$$

where  $\delta \lambda_r$  is the change in the wavelength position of the dip with respect to the change  $\delta n$  in the glucose analyte RI. The sensitivity  $S_n$  is in a range of 7.0–10.7  $\mu\text{m}/\text{RIU}$  for MDPHC 1, and is enhanced to 8.1–19.9  $\mu\text{m}/\text{RIU}$  for MDPHC 2. These values are substantially higher as compared to a sensitivity of 1.105  $\mu\text{m}/\text{RIU}$  near a wavelength of 1.55  $\mu\text{m}$  for a simple BSW-based sensor<sup>11</sup>.

A quantity similar to the RI sensitivity  $S_n$ , namely the sensitivity  $S_C$  to the glucose concentration  $C$ , can be defined analogously by replacing the RI  $n$  in Eq. (14) with the concentration  $C$ . Consequently, the sensitivity  $S_C$  is in a range of  $(9.9\text{--}15.1) \times 10^{-3}$  nm/(mg/dL) for MDPHC 1, and for MDPHC 2 is enhanced to  $(11.4\text{--}28.0) \times 10^{-3}$  nm/(mg/dL).

The sensor performance is also evaluated in terms of the LOD and FOM. The LOD is defined as the smallest RI that can be reliably detected, and can be expressed by means of the sensitivity  $S_n$  and the smallest spectral shift  $\delta \lambda_{\min}$  that can be accurately measured:<sup>89</sup>

$$\text{LOD} = \frac{\delta \lambda_{\min}}{S_n}. \quad (15)$$

Based on the spectral resolution  $\delta \lambda_{\min} = 0.1$  nm of a spectrometer, the LOD reaches for MDPHC 1 and MDPHC 2 values of  $9.3 \times 10^{-6}$  RIU and  $5.0 \times 10^{-6}$  RIU, respectively. Extending the definition of the LOD to the glucose concentration  $C$ , when  $S_n$

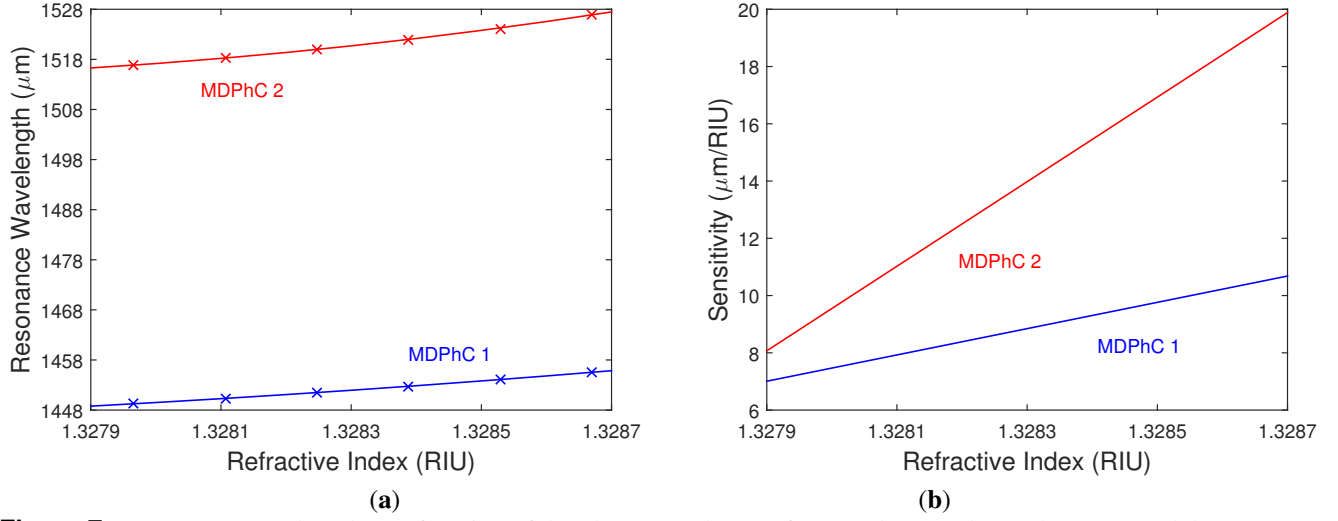


**Figure 7.** Resonance wavelength as a function of the glucose analyte RI for MDPPhC 1 and MDPPhC 2 (a), and the corresponding sensitivity functions (b) when  $\theta = 62.305^\circ$ .

in Eq. (15) is replaced by  $S_C$ , it reaches 6.6 mg/dL for MDPPhC 1 and for MDPPhC 2 is as small as 3.6 mg/dL and outperforms practical limits.

The FOM is defined as the sensitivity  $S_n$  divided by the full-width half maximum (FWHM) of the resonance dip:

$$\text{FOM} = \frac{S_n}{\text{FWHM}}. \quad (16)$$

The FWHMs of the resonance dips shown in Figs. 6(a) and (b) are approximately 18 and 19 nm, respectively, and the FOMs are as high as  $594 \text{ RIU}^{-1}$  and  $1047 \text{ RIU}^{-1}$ , respectively.

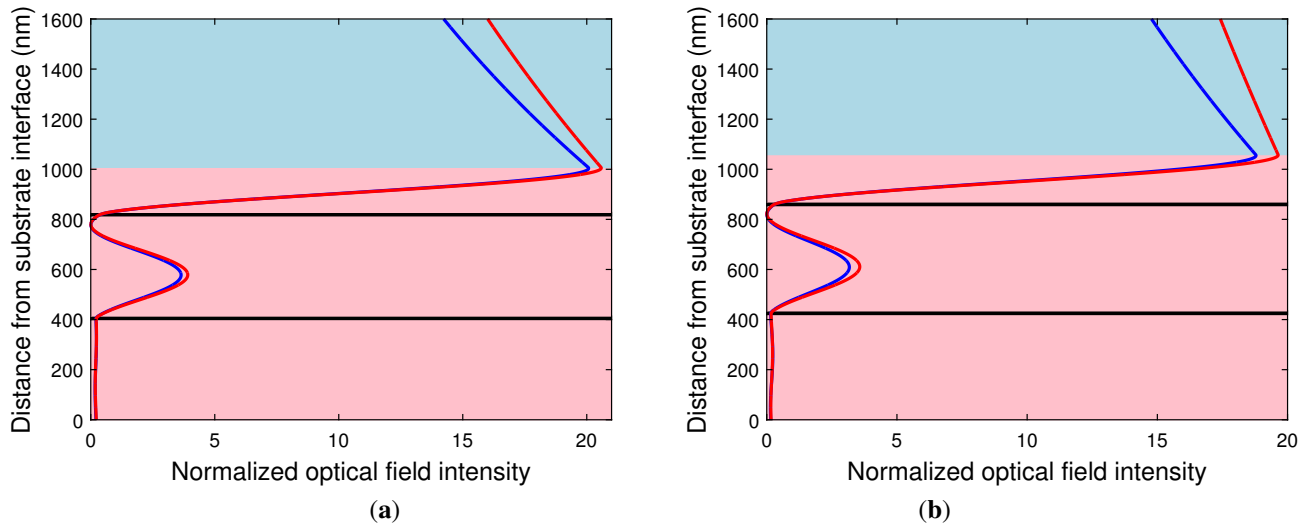


**Figure 8.** The normalized optical field intensity distribution for the TE wave and MDPPhC 1 (a) or MDPPhC 2 (b) when the glucose analyte RI  $n_a = 1.32797$  (blue) and  $n_a = 1.32867$  (red). Au layers are shown in black.

Very high sensitivities to the glucose analyte RI are due to the optical field of the BLSW confined near the surface of the MDPPhC. To support the statement, the optical field intensities normalized to the incident field intensities are computed for the TE wave. In Fig. 8(a), the normalized optical field intensity  $|E_x|^2 / |E_{x0}|^2$  is shown for MDPPhC 1 at wavelengths of 1449.25 and 1455.55 nm, respectively, when the glucose analyte RIs are 1.32797 and 1.32867, respectively. It is clearly seen that the

envelope of the field is exponentially increasing in the MDPHC 1 and exponentially decreasing in the glucose analyte, and thus it is a very good manifestation of the BLSW excitation. The computation was performed using the TMM<sup>90</sup> and  $E_{x0}$  is  $x$  component of the incident electric field, which is perpendicular to the plane of incidence. Similarly, the normalized optical field intensity is shown in Fig. 8(b) for MDPHC 2 at wavelengths of 1516.75 and 1526.9 nm, respectively, when the glucose analyte RIs are 1.32797 and 1.32867, respectively. These fields are of a smaller amplitude compared to that for the MDPHC 1, but are exponentially decreasing in the analyte with a longer penetration depth. These figures clearly demonstrate that for the glucose analyte RIs, the enhanced optical field, characterized by nearly a twenty-fold enhancement of the optical intensity with respect to the incident beam, is confined near the surface of the MDPHCs.

Comparing the fields of the BLSW for the TE wave, as shown in Figs. 8(a) and (b), the penetration depth of the wave in the glucose analyte is much longer for the RI  $n_a = 1.32867$  than for  $n_a = 1.32797$  so that the field concentration in the analyte is higher, thus justifying a higher sensitivity to changes in the glucose analyte RI. In addition, when comparing the fields with those for all-dielectric 1DPhC-based sensors<sup>47</sup>, the amplitude of the optical field at the analyte interface is smaller for the MDPHC-based sensors, justifying the wider resonance dips. However, the extremely high RI contrast between the layers leads to a stronger field confinement and a longer penetration depth, and thus to a higher sensitivity and FOM. Consequently, engineering of the MDPHCs can provide optical glucose sensors with very high sensitivities and FOMs.

We extended the theoretical analysis to include a 2D overlayer material, such as BP or MoS<sub>2</sub>, on the surface of an MDPHC 2. Taking into account the dispersion of the 2D materials specified above, Figs. 9(a) and (b) show the corresponding theoretical spectral reflectances at the angle of incidence  $\theta = 62.305^\circ$  for the glucose analyte RI in a range of 1.32797–1.32867 when a 2D material was one monolayer of either BP or MoS<sub>2</sub>. These figures demonstrate sufficiently pronounced dips with the remarkable shift with the change in the RI of the glucose analyte. By comparing them with dips for the MDPHC 2 alone, as shown in Fig. 6(b), the depths are even slightly higher but the widths increased.

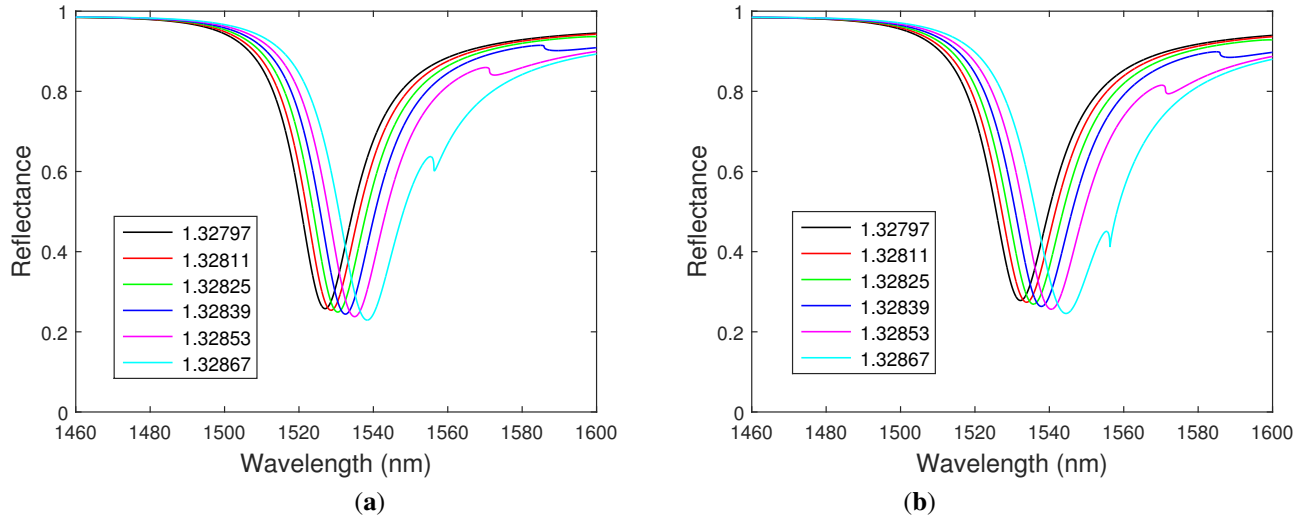


**Figure 9.** Theoretical spectral reflectance for the TE wave and different values of the glucose analyte RI when one monolayer of BP (a) or MoS<sub>2</sub> (b) is on the MDPHC 2 and  $\theta = 62.305^\circ$ .

The sensitivity  $S_n$  to the glucose analyte RI is substantially enhanced, as can be deduced from the resonance wavelength as a function of the glucose analyte RI shown in Figs. 10(a) and (b) for one monolayer of BP and MoS<sub>2</sub>, respectively. Once again, second-order polynomials are the best fits, and the sensitivity  $S_n$  is approximately in ranges of 7.0–23.7  $\mu\text{m}/\text{RIU}$  and 5.8–26.9  $\mu\text{m}/\text{RIU}$ , respectively. Thus, using one monolayer of MoS<sub>2</sub> results in significant enhancement of the maximum RI sensitivity compared to that of the MDPHC 2 alone. Unfortunately, extending the number of monolayers to more than one is accompanied by the dip distortion. Similarly, the sensitivity  $S_C$  to the glucose concentration  $C$  is enhanced and is approximately in ranges of  $(9.9\text{--}33.4) \times 10^{-3} \text{ nm}/(\text{mg}/\text{dL})$  and  $(8.2\text{--}37.9) \times 10^{-3} \text{ nm}/(\text{mg}/\text{dL})$ , respectively. In addition, the LODs for the glucose analyte RI are as low as  $4.2 \times 10^{-6} \text{ RIU}$  and  $3.7 \times 10^{-6} \text{ RIU}$ , respectively. In the glucose concentration domain, the LODs are 4.6 mg/dL and 2.6 mg/dL, respectively. Similarly, taking into account the FWHM of the resonance dip with a value of approximately 20 nm for one monolayer of BP, the FOM is as high as  $1185 \text{ RIU}^{-1}$ . The FWHM of approximately 25 nm for one monolayer of MoS<sub>2</sub> gives the FOM of  $1076 \text{ RIU}^{-1}$ .

The resonance dips depicted in Figs. 9(a) and (b) are due to the excitations of the BLSWs, and Fig. 11(a) shows the computed normalized optical field intensity  $|E_x|^2 / |E_{x0}|^2$  for the TE wave at a wavelength of 1538.4 nm when the glucose analyte RI

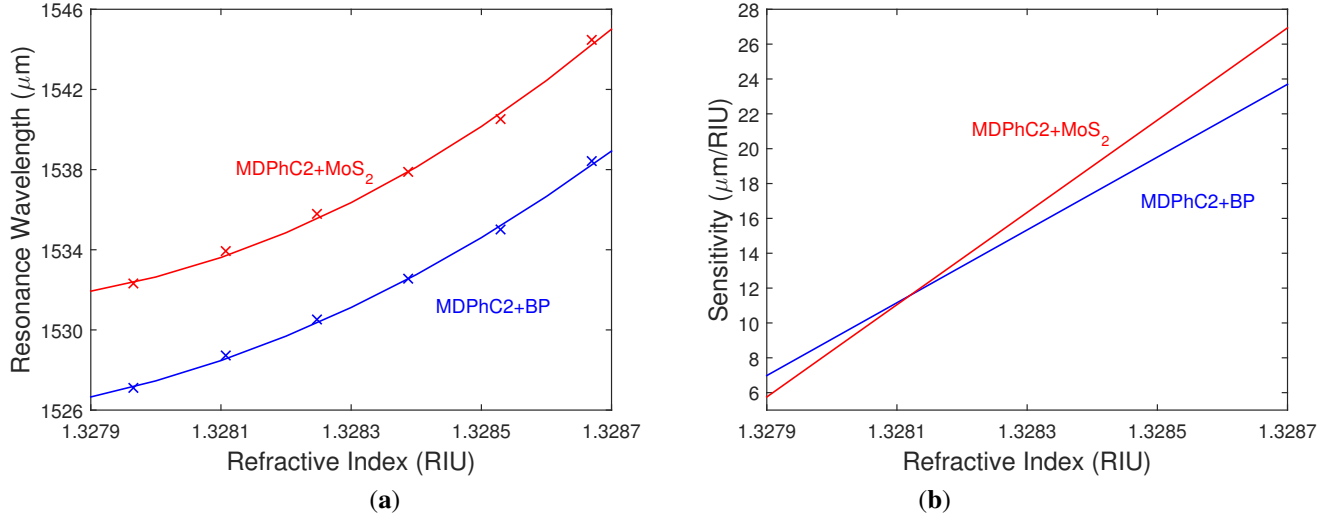


**Figure 10.** Resonance wavelength as a function of the glucose analyte RI for one monolayer of BP or MoS<sub>2</sub> on the MDPHC 2 (a) and the corresponding sensitivity functions (b) when  $\theta = 62.305^\circ$ .

is  $n_a = 1.32867$  and one monolayer of BP is considered. Similarly, Fig. 11(b) shows the same quantity at a wavelength of 1544.5 nm for one monolayer of MoS<sub>2</sub> when the amplitude of the field is smaller. These figures clearly demonstrate that a smaller amplitude of the field and a longer penetration depth are responsible for a wider dip and higher sensitivity, as is the case of MoS<sub>2</sub> in comparison with BP, for which the field amplitude is even slightly higher. Generally, exponential decrease of the field or the penetration depth, and the losses as well, are dependent on the number of monolayers of the 2D material, and are affecting both the sensitivity and FOM of the sensor.

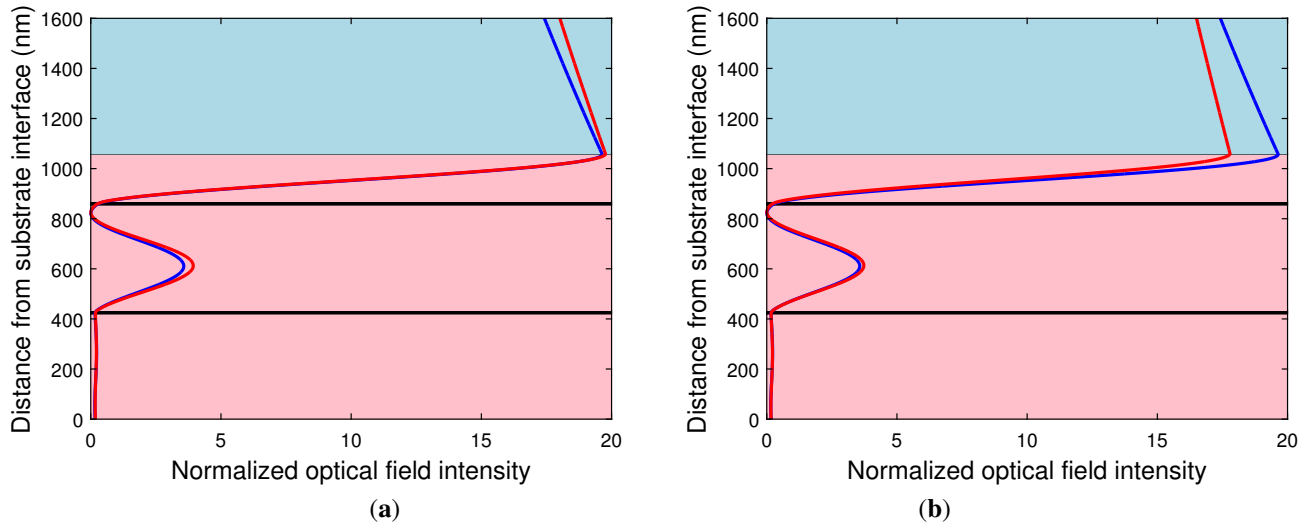


**Figure 11.** The normalized optical field intensity distribution for the TE wave and the MDPHC 2 alone (blue) and including one monolayer of BP (a) or MoS<sub>2</sub> (b) when  $\theta = 62.305^\circ$  and  $n_a = 1.32867$ . Au layers are shown in black.

Next, we compare the performance of our optical glucose sensors with those available chronologically from the point of view of the RI range, the operating wavelength  $\lambda$ , maximum RI sensitivity  $S_n$  and FOM, the glucose concentration range, and the maximum glucose concentration sensitivity  $S_C$ , as presented in Table 2. This comparison highlights the distinctive advantage of the proposed optical glucose sensors based on MDPHCs and supporting BLSWs. The performance is particularly notable in sensitivity when compared to sensors based on a long-period grating (LPG)<sup>21</sup>, a fiber micro probe<sup>24</sup>, a D-fiber with three and one monolayers of MoS<sub>2</sub> and graphene, respectively,<sup>26</sup> a photonic crystal fiber (PCF) and SPR<sup>29</sup>, and a hollow-ring cubic structure (HRCS)<sup>20</sup>.

Although the present work establishes the theoretical sensing performance of the MDPHC-based glucose sensor, any

**Table 2.** Comparison of optical glucose sensors.

| Method<br>Units          | RI<br>(RIU)     | $\lambda$<br>( $\mu\text{m}$ ) | $S_n$<br>( $\mu\text{m}/\text{RIU}$ ) | FOM<br>( $\text{RIU}^{-1}$ ) | C<br>( $\text{mg}/\text{dL}$ ) | $S_C$<br>( $\text{nm}/(\text{mg}/\text{dL})$ ) | Year               |
|--------------------------|-----------------|--------------------------------|---------------------------------------|------------------------------|--------------------------------|------------------------------------------------|--------------------|
| BSW                      | —               | 1.55                           | 1.105                                 | -                            | 10–10,000                      | 0.0017                                         | 2010 <sup>11</sup> |
| LPG                      | —               | 1.55                           | —                                     | -                            | 10–300                         | 0.0081                                         | 2012 <sup>21</sup> |
| Tilted Fiber Grating     | 1.333–1.370     | 1.56                           | 0.168                                 | -                            | 0–150                          | 0.0133                                         | 2014 <sup>22</sup> |
| Fiber Micro Probe        | 1.33250–1.3355  | 1.55                           | 2.180                                 | -                            | 0–300                          | 0.0174                                         | 2018 <sup>24</sup> |
| 1DPhC+defect             | 1.335–1.341     | 2.41                           | 0.965                                 | 757                          | 0–500                          | —                                              | 2023 <sup>19</sup> |
| PCF and SPR              | 1.338–1.358     | 1.05                           | 4.583                                 | -                            | -                              | -                                              | 2024 <sup>29</sup> |
| HRCS                     | —               | 2.29                           | 1.667                                 | 1241                         | 205–289                        | -                                              | 2025 <sup>20</sup> |
| 2DPhC                    | —               | 1.70                           | 20.040                                | -                            | 0–15                           | -                                              | 2025 <sup>14</sup> |
| 2DPhC                    | 1.3280–1.3286   | 1.55                           | 2.592                                 | 12,960                       | 0–500                          | -                                              | 2025 <sup>15</sup> |
| MDPhC 1                  | 1.32797–1.32867 | 1.452                          | 10.7                                  | 594                          | 0–500                          | 0.0151                                         | This work          |
| MDPhC 2                  | 1.32797–1.32867 | 1.518                          | 19.9                                  | 1047                         | 0–500                          | 0.0280                                         | This work          |
| MDPhC 2+BP               | 1.32797–1.32867 | 1.532                          | 23.7                                  | 1185                         | 0–500                          | 0.0334                                         | This work          |
| MDPhC 2+MoS <sub>2</sub> | 1.32797–1.32867 | 1.538                          | 26.9                                  | 1076                         | 0–500                          | 0.0379                                         | This work          |

translation toward practical glucose monitoring will require systematic experimental validation against a traceable laboratory reference method. In the field of blood glucose measurement, the YSI 2300 STAT Plus analyzer (Yellow Springs Instruments, OH, USA) — based on the glucose oxidase electrode principle and traceable to higher-order reference materials — is routinely employed as the comparator in accuracy studies for both self-monitoring blood glucose systems and CGM devices<sup>91,92</sup>. The internationally recognized standard<sup>92</sup> specifies that, when compared against such a reference, at least 95% of results must fall within  $\pm 15$  mg/dL for glucose concentrations below 100 mg/dL and within  $\pm 15\%$  for concentrations  $\geq 100$  mg/dL, with at least 99% of all results lying within zones A and B of a Consensus Error Grid<sup>92</sup>. For integrated CGM systems, the U.S. Food and Drug Administration (FDA) iCGM special controls<sup>93</sup> further define performance thresholds as lower one-sided 95% confidence bounds on the proportions of sensor readings within  $\pm 15$  mg/dL (for sensor values  $< 70$  mg/dL),  $\pm 15\%$  (70–180 mg/dL), and  $\pm 15\%$  ( $> 180$  mg/dL), and these criteria have been shown to be sensitive to study design and reference method choice<sup>93,94</sup>. In this context, future experimental studies of the proposed MDPhC platform should not only confirm the predicted RI sensitivity, FOM and LOD, but also characterize clinical accuracy through standardized metrics — mean absolute relative difference (MARD), %15/15 and %20/20 agreement rates, and Consensus Error Grid analysis versus a YSI reference — across the physiologically relevant glucose range of approximately 40–400 mg/dL. Furthermore, proposed minimum requirements for market approval of CGM systems should be taken into account in designing such future studies<sup>95</sup>. This would facilitate a direct and standardized comparison of the MDPhC optical platform with current invasive and minimally invasive glucose sensing technologies and support its positioning within the contemporary framework of diabetes care, in which CGM-derived metrics such as time in range, time below range and time above range have been endorsed as primary clinical targets<sup>96,97</sup>.

The excellent limits of detection reported in this work are derived under idealized optical and chemical conditions: a stable Kretschmann configuration, a single-component Cauchy RI–concentration relationship for glucose, and negligible extinction of the analyte. In practice, however, a number of additional error sources are expected to affect both the analytical and clinical performance of the sensor. From a physical standpoint, the resonance wavelength and linewidth are sensitive to fluctuations in temperature, any mechanical drift in the angle of incidence and polarization state, spectral instability of the broadband light source, and deviations of the deposited layer thicknesses (TiO<sub>2</sub>, Au, 2D material overlayer) from their nominal values; even sub-nanometer thickness inhomogeneities in the black phosphorus or MoS<sub>2</sub> overlayer can modify the optical field distribution and thereby alter the sensitivity enhancement predicted theoretically<sup>69,70</sup>. From a biochemical and preanalytical perspective, changes in the RI of real biological matrices — blood, plasma, interstitial fluid, urine — are not attributable to glucose alone but are co-determined by total protein concentration, lipids, electrolytes, hematocrit and pH; in whole blood, hematocrit-dependent scattering can introduce systematic errors exceeding the RI-equivalent of several tens of mg/dL of glucose. In addition, sample handling conditions prior to analysis — including the choice of anticoagulant (e.g., EDTA, sodium fluoride), time between collection and measurement, and temperature during storage — significantly influence plasma glucose stability and can introduce pre-analytical biases of clinical relevance<sup>98,99</sup>.

In the context of continuous or minimally invasive sensing, additional challenges include the adsorption of plasma proteins and other biomolecules on the sensor surface (biofouling), non-specific RI contributions from co-analytes, and the long-term chemical and oxidative instability of black phosphorus in aqueous environments; all of these phenomena must be incorporated

into the error budget of any clinically deployed device<sup>69,100,101</sup>. Consequently, future experimental work with the proposed MDPHC platform should systematically quantify the contributions of each of these factors to resonance drift, noise floor and overall measurement uncertainty, and may require active temperature compensation, optimized surface passivation or biochemically selective receptor functionalization — such as phenylboronic acid or enzymatic recognition layers on the 2D material surface — to achieve the analyte selectivity and accuracy required for clinical use<sup>71</sup>.

## Conclusions

In this paper, an MDPHC supporting excitation of BLSWs in the Kretschmann configuration is presented for glucose sensing. For an MDPHC comprising two bilayers of TiO<sub>2</sub>/Au with a termination layer of TiO<sub>2</sub>, the reflectance responses have been analyzed theoretically and an ultra-high sensing ability based on the BLSW-based resonances for the TE wave has been revealed. The analysis has been extended to the MDPHC with different overlayers, such as one monolayer of BP or MoS<sub>2</sub>. Using the wavelength interrogation for simulated glucose solutions when the glucose analyte RI changes in a range of 1.32797–1.32867 at a wavelength of 1.55  $\mu\text{m}$ , corresponding to physiologically relevant glucose concentrations of 0–500 mg/dL, the RI sensitivity and FOM reach 26.9  $\mu\text{m}/\text{RIU}$  and 1076  $\text{RIU}^{-1}$ , respectively, and the LOD is as low as  $3.7 \times 10^{-6}$  RIU for one of the MDPHCs with a monolayer of MoS<sub>2</sub>. In the concentration domain, the sensitivity is up to 0.0379 nm/(mg/dL), and the LOD is as low as 2.6 mg/dL. Thus, the analysis revealed that employing the 2D material affects the penetration depth and for MoS<sub>2</sub> it results that the maximum RI sensitivity is substantially enhanced compared to the MDPHC alone.

This sensing concept, based on the use of MDPHCs that are mechanically and chemically robust, is very promising in the field of ultra-high sensitive monitoring of biomolecules and glucose analytes. Among the main advantages of the concept are the possibility of operation in aggressive environments and the response time of the sensor should be as short as possible because no porous layers are used. In addition, the design of sensors employing an MDPHC with biologically inherent 2D overlayers supporting BLSWs has the potential in sensing with ultra-high sensitivity, and these systems can be optimized to allow for sensing of a wide range of biological samples. Finally, the concept is also potentially well suited to a fiber-optic implementation of the sensors.

Due to the design flexibility of MDPHCs, the sensing concept can be applied to real biological samples containing proteins, lipids and electrolytes, and also in whole blood or interstitial fluid, provided that their RI is known, by employing standard refractometric methods. In addition, long-term operation of the sensor in biological media may also be affected by biofouling due to nonspecific adsorption of proteins and other biomolecules on the sensor surface, resulting in baseline drift and additional measurement uncertainty. Antifouling surface engineering is therefore expected to be important for reliable operation in physiologically relevant fluids<sup>102,103</sup>.

While the present work firmly establishes the theoretical foundation for an MDPHC-based optical glucose sensor with ultra-high RI sensitivity and excellent FOM, the translation of this platform toward real-world glucose monitoring applications will require a structured program of experimental validation and clinical benchmarking. Prototype fabrication should be followed by accuracy testing in physiologically realistic matrices — including whole blood, plasma, serum, and interstitial fluid — across the clinically relevant glucose range of approximately 40–400 mg/dL, with rigorous reporting of MARD, %15/15 and %20/20 agreement rates, and Consensus Error Grid analysis versus a YSI 2300 STAT Plus reference analyzer, in alignment with the internationally recognized standard<sup>92</sup>, and the recently proposed minimum performance requirements for CGM market approval<sup>95,97</sup>. The incorporation of a biochemically selective recognition element — such as a phenylboronic acid receptor or an enzyme-based layer — on the 2D material overlayer represents a critical next step to overcome non-specific RI contributions from co-existing plasma constituents and to achieve the analyte selectivity required for clinical deployment. If these translational challenges are successfully addressed, the MDPHC sensor platform — with its demonstrated mechanical and chemical robustness, fast optical response, absence of porous layers and compatibility with fiber-optic geometries — holds significant promise as a next-generation optical biosensing technology capable of supporting real-time, minimally invasive glucose monitoring within the contemporary clinical framework that increasingly emphasizes CGM metrics as primary indicators of glycaemic control<sup>96,97</sup>.

## Data availability

Data underlying the results presented in this paper are openly available from a Zenodo data repository at <https://doi.org/10.5281/zenodo.20507072>.

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## Author contributions statement

Writing—original draft, J. C., M. G., D. C., P. K., D. S. and P. H.; writing—review & editing, J. C., M. G., D. C., P. K., D. S. and P. H.; methodology, J. C., M. G., D. C. and P. H.; validation, J. C., M. G., D. C., P. K., D. S. and P. H.; Investigation, J. C., M. G., D. C., P. K., D. S. and P. H.; Data curation, J. C. and M. G.; Software, J. C.; Visualization, J. C. and M. G.; Conceptualization, P. H.; Supervision, P. H.

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## Competing interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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