Biosensor based on hollow-core metal-cladding waveguide

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A new hollow-core metal-cladding waveguide (HCMW) has been proposed in order to design and realize biooptical sensor for the direct liquid probing. Two peculiar properties are exhibited with respect to the current evanescent wave sensors. First, the effective index of the HCMW can exist in the region of \(0 < N < 1\), which is usually prohibited for the conventional guided modes and the surface plasmon resonance modes. Second, the analyte to be detected does not locate in the evanescent field but in the oscillating field. Glucose solution is utilized to characterize the device performance. According to the reflectivity changes and the signal-to-noise ratio, the new biosensor has been shown to be capable of directly detecting concentration of glucose as low as 0.5 ppm, which corresponds to a high resolution of \(1.4 \times 10^{-7}\) RIU units. This new biosensor improves the detection limitation and shortens the analysis time significantly.

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1. Introduction

The need for rapid and sensitive detection of microorganisms and their interactions is very important in areas of food safety, medical care, environmental protection, and biological warfare [1–7]. Among various detecting approaches, biosensors based on optical resonant mode are the subject of growing interest due to their peculiar properties, such as relatively high sensitivity, fast response, small dimensions, and high mechanical stability. Techniques reported include surface plasmon resonance (SPR) [8,9], long-range surface plasmon resonance (LRS) [10], resonant mirror (RM) [11], leaky mode waveguide (LMW) [12], reverse symmetrical waveguide (RSM) [13] and metal-clad leaky waveguide (MCLW) [14–16]. The common feature of these current sensors is that the analyte to be detected is located in the region where the evanescent wave of the resonant modes propagates. According to the sensitivity analysis, the use of such evanescent wave biosensors is problematic due to the limited sensitivity resulting from several reasons [4]. These include (1) the limited power portion propagating in the sensing region where the analyte is located; (2) the refractive index of the analyte must be always less than the effective index of the resonant modes; (3) the short penetration depth of the evanescent field makes the large analytes, such as bacteria, outside the sensing region, resulting in further insufficient sensitivity of the system.

To achieve a high sensitivity, it is essential to get as much of the optical power as possible to propagate in the sensing region. Investigation of the mode power distribution suggests us to design a configuration that contains the sample in the guiding layer of the waveguide, where oscillating wave is located and most of the mode power concentrates. Addressed this issue, a sensor structure based on porous silicon (PS) waveguide [17] is proposed, in which the target material is filled inside the porous silicon where the oscillating field propagates. Theoretical calculations indicate that the PS sensor shows a greater sensitivity than the conventional SPR sensors. However, sensitivity enhancement is also limited due to the limited volume of the analyte locates in the region of oscillating field. Recently, several chemical and biological sensors based on liquid-core waveguides (LCW) have been proposed to improve the detection efficiency [18]. Unfortunately, this idea is severely blocked by conventional waveguiding, since water-based solvent has a lower index than almost all the solids which acts as the clad layer of the waveguide.

Facing the above challenge in the biosensors, we proposed a hollow-core metal-cladding waveguide (HCMW) structure in which the hollow-core of sub-millimeter scale is surrounded by metal claddings. In this design the use of double metal claddings which exhibit negative dielectric constant implies that the effective index of the guided modes can exist in the region of \(0 < N < 1\) [19], which is usually prohibited for the conventional guided modes and the surface plasmon resonance modes [20]. Analyte of interest
contained in the hollow core serves as guiding medium where oscillating wave propagates. Furthermore, in the HCMW structure, the thickness of guiding layer can be expanded to sub-millimeter scale, which makes it easy to inject the aqueous sample into the guiding layer and to excite the sensitive ultrahigh-order modes [21]. It is expected that guiding both light and liquid through the same physical volume maximizes their interaction and should allow for extremely sensitive and rapid sensing. In order to characterize the device performance, a significantly lower concentration of glucose is utilized in our experiment. In the conventional biosensor [22,23], glucose usually is present in relatively high concentrations so that most assays have been developed for a rather high concentration range. Nevertheless, analytical methods for relatively small concentrations of glucose are needed as well, for example when analyzing body fluids that do contain low concentrations (such as tear, sweat and urine). Owing to (1) light power concentrated in the guiding region can enlarge the interaction with the analyte of interest; (2) using of the ultrahigh-order modes with smaller effective index further increases the interaction distances, concentration of glucose as low as 0.5 ppm has been unambiguously identified in our experiment within a several minutes assay. The proposed HCMW sensor exhibits a minimum refractive index variation of $\Delta n = 1.4 \times 10^{-7}$. Aside from higher detection efficiency, the proposed platform offers additional benefits: such as small analyte volume, label-free and real-time detection, and enables environmentally stable, compact, and inexpensive sensing.

2. Hollow-core metal-cladding waveguide

The schematic diagram of hollow-core metal-cladding waveguide (HCMW) in our experiment is illustrated in Fig. 1. Excepting a glass prism with a big vertex angle which serves as a coupling element, HCMW is basically a three-layered optical waveguide, where solution confined in hollow core acts as the guided medium, while the two metal films serve as the claddings. For simplicity in sensitivity analysis, we neglect the effects resulting from the limited thickness of the metal film due to the weak coupling [24]. Dispersion equation of the HCMW can then be written as [21]

\[
\kappa_1 h_1 = m \pi + 2 \arctan \left( \frac{\rho \varepsilon_2}{\kappa_1} \right), \quad (m = 0, 1, 2, \ldots),
\]

where $\rho = 1$ for TE modes, while $\rho = \varepsilon_1/\varepsilon_2$ for TM modes. $\varepsilon_1 = n_1^2$ and $\varepsilon_2$ represent dielectric constants of the analyte and the metal films, respectively. $h_1$ is the thickness of the analyte and $m$ is mode-order number. The vertical propagation constant $\kappa_1$ in the guiding medium and the decay coefficient $\alpha_2$ in the metal claddings are defined by

\[
\begin{align*}
\kappa_1 &= \left( k_0^2 n_1^2 - \beta^2 \right)^{1/2}, \\
\alpha_2 &= \left( \beta^2 - k_0^2 \varepsilon_2 \right)^{1/2},
\end{align*}
\]

$k_0 = 2\pi/\lambda$ is the wavenumber with light wavelength $\lambda$ in free space, and $\beta = k_0 N$ is the transverse propagation constant with the effective index $N$ of the guided modes. For most commonly used noble metals in the visible and near-infrared regions, since the imaginary part of its dielectric constant is much less than its real part, it is often convenient to neglect the imaginary part in the analysis. The dispersive curves of the HCMW are shown in Fig. 2. When the thickness of the guiding medium is extended to sub-millimeter scale (see the dashed line $h_1 = 700 \mu m$), the waveguide can accommodate thousands of guide modes ($m > 1000$), in our terminology, we denote these modes as ultrahigh-order modes [21]. Since the real part of the dielectric constant of the coupling film (metal) is negative, the allowed range of the effective index of both TE and TM modes of proposed HCMW is $0 < N < n_1$ [20]. It is quite different from the conventional guided modes and the surface plasmon

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Fig. 1. Schematic diagram of hollow-core metal-cladding waveguide (HCMW): (a) stereogram, (b) plan view, (c) graphical representation of field distribution in HCMW.

Fig. 2. Dispersive curves of the HCMW with the parameters: $n_1 = 1.330$, $\varepsilon_2 = -16.2$, $\lambda = 632.8$ nm. The blue transverse dashed line denotes $h_1 = 700 \mu m$, the red and green curves indicate the ultrahigh-order modes and low order modes, respectively. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article).
resonance, in which the effective index $N$ must be greater than that of the cover medium, the region of $0 < N < 1$ is absolutely prohibited.

HCMW sensor is operated with the attenuated total reflection scheme in which a polarized laser beam is incident from the prism-side and the reflectance $R$ is measured as a function of the angle of incidence. During the angle scanning, a series of resonance dips with respect to the excitation of the guided modes are then produced a so-called attenuated total reflection (ATR) spectrum. Position of the resonance dip indicates the effective index of the guided mode and is very sensitive to the change of refractive index of the guiding layer. A minute variation in the concentration of the aqueous solution will consequently cause an angular shift of the resonance dip. By monitoring the angular shift of the resonance dip, the change in solution concentration can be measured. The resonance excitation of the guided mode occurs at [21]

$$\beta = k_0 n_3 \sin \theta,$$

(3)

where $n_3$ represents refractive index of the prism, and $\theta$ is the angle of incidence. As shown in Fig. 3, if $\theta$ is small, ultrahigh-order modes with $N \to 0$ will then be excited under the condition of resonance excitation.

3. Sensitivity analysis

ATR spectrums for one and a small number of the ultrahigh-order modes are shown in Fig. 3. It is shown that the falling edge and the rising edge of a reflection dip exhibit quite favorable linearity. In this case we fix the angle of incidence near the mid point of the falling edge of a reflection dip and monitor changes in the reflectivity $\Delta R$ caused by shift of the resonance angle $\Delta \theta$, which is resulted from changes of the analyte concentration. In this intensity interrogation mode [25], the sensitivity can be defined as:

$$S = \left( \frac{\Delta R}{\Delta n_{\text{guide}}} \right)_{\theta = \theta_0} \cdot \left( \frac{\partial n_{\text{guide}}}{\partial \Delta R} \right) = S_1 \cdot S_2.$$  

(4)

Obviously, $S_1$ represents the slope of the falling edge at the operation angle $\theta_0$, it is strongly dependent on the full-width-half-maximum (FWHM) of the dip. The narrower of the dip, the bigger of $S_1$. Theoretical comparisons of the FWHM for HCMW, SPR, LRSRP, and MCLW are demonstrated in Fig. 4. As is shown, the FWHM of the reflectivity curves is broadest in the conventional SPR and gets narrower one by one in the MCGW, LRSRP and HCMW configurations. It is clear that the HCMW sensor relative to the other three types of sensor has a FWHM at least an order of magnitude less.

Meanwhile, $S_2$ represents the detect efficiency or the sensitivity in angular exploration mode of the HCMW sensor. To be clear, we use $n_{\text{guide}}$ as the refractive index of the analyte confined in the hollow core. Without loosing any generality, we neglect the effect of a less important factor $1/(n_3 \cos \theta)$ and consider TE modes only here. After a rather lengthy derivation, $S_2$ can be expressed as [26]

$$S_2 = \frac{\partial N}{\partial n_{\text{guide}}} = \frac{n_{\text{guide}}}{N} \frac{p_{\text{guide}}}{p_{\text{total}}},$$

(5)

and

$$\frac{p_{\text{guide}}}{p_{\text{total}}} = \frac{h_1 + 2 \alpha_2 / (\alpha_1 + \alpha_2^2)}{h_1 + 2 \alpha_2},$$

(6)

where $p_{\text{guide}}$ represents the power flowing in the sensing medium, and $p_{\text{total}}$ is the total power flowing in the whole waveguide. Noting that in a HCMW sensor, since $h_1$ is sub-millimeter scale, while $1/\alpha_2$ is wavelength scale, it is obvious that $p_{\text{guide}}/p_{\text{total}}$ approaches to 1 without any question. As to another factor in Eq. (5), since $n_{\text{guide}}$ is the refractive index of the guiding medium, and $N \to 0$ when ultrahigh-order modes are used as sensor's probe, therefore, $(n_{\text{guide}}/N) \gg 1$ is fulfilled in any case. It means that $S_2$ can easily be greater than 1.

In the evanescent field sensors, taking a reverse symmetrical waveguide (RSW) as an example, the analogous equations are cast in the form [13,27,28]

$$S_2 = \frac{\partial N}{\partial n_{\text{cover}}} = \frac{n_{\text{cover}}}{N} \frac{p_{\text{cover}}}{p_{\text{total}}},$$

(7)

and

$$\frac{p_{\text{cover}}}{p_{\text{total}}} = \frac{k_1^2}{\alpha_2^2 (\alpha_1^2 + \alpha_2^2) (h_1 + 2 \alpha_2)},$$

(8)

where $n_{\text{cover}}$ and $p_{\text{cover}}$ represent the refractive index and the power in the cover medium where the sensing analyte is located, respectively. Investigating Eq. (8), it is found that $p_{\text{cover}}/p_{\text{total}}$ is hardly to attain the value of 1, even at the cut-off thicknesses of the guiding layer. Moreover, since $N$ is always great than $n_{\text{cover}}$ in the conventional optical waveguides or the surface plasmon structure. Consequently, $n_{\text{cover}}/N < 1$ and $S_2 < 1$ in turn are hold under any circumstance. Simulations for sensitivity and the compositions of four type biosensors are listed in Table 1 and Table 2 respectively. Theoretical analysis indicates that both $S_1$ and $S_2$ of the HCMW biosensor are considerably higher than that of the other.
three biosensors. The integration improvement of the sensitivity and the detection limit by a few orders of magnitude are completely possible.

4. Experimental

4.1. Materials

In the sample fabrication, the required glucose injection was purchased from Hunan Zhongnan Kelun Pharmaceutical Co., Ltd, China. A set of glucose solution with concentrations change of 2 ppm (0.011 mmol/L) were obtained by calculating the ratios of glucose and de-ionized water in weight percentage. An 8-mm equilateral glass prism with a big vertex angle of 150° was coated with a thin gold film via DC sputtering to serve as the coupling layer. Two layers of light incident on the prism at a small angle to excite the ultrahigh-order modes. A relative thicker gold film was sputtered on a polished glass chip to act as the substrate. A glass gasket of 5 mm in radius and about 0.7 mm in depth which was glued together with the substrate by using a UV-curable epoxy. The glass prism was then placed on the gasket to form a hollow cell to work as the sample room. With the help of a peristaltic pump, analyte solution to be detected flow into the cell through the inlet and the outlet tubes embedded in the substrate glass plate. Before the detection, a test experiment has been performed to precisely determine the parameters of the HCMW, and the result is given as follows: $h_1 = 688 \, \mu m, \varepsilon_2 = -28 + 1.8i, n_3 = 1.503, h_{thick}^{film} = 38 \, nm$ and $h_{thick}^{film} = 300 \, nm$. The incident wavelength is adjusted to be 860.00 nm. The thickness and the complex dielectric permittivity of the thin gold film are determined by the double-wavelength method [29] and the thickness of the guiding layer (hollow core) is determined by the m-line spectroscopy technique [24]. Since the thick gold film is used as the substrate, it is thick enough and its thickness is evaluated by the sputtering time.

4.2. Measurement

The schematic diagram of the experimental setup is shown in Fig. 5. To excite the ultrahigh-order mode of the HCMW, a TE polarized laser beam from a tunable laser (DL100, Topica Photonics) with a divergence angle of 0.4 mrad is induced to impinge upon the thin gold film of the HCMW biosensor which is located on a computer controlled 0°/20° goniometer. Two apertures with a diameter of 1 mm and a distance of 0.5 m between them are inserted to further confine the divergence of the incident light. The reflected light is detected by a photodiode PD2. Another part of the beam, which comes from a beam splitter BS1, irradiates the second beam splitter BS2 and splits into two beams. One is detected by PD1 as a reference in order to remove the intensity fluctuation. The remaining light is fed to a wavelength meter (COHERENT, WaveMaster) connected to a computer. In the experiment, the actual reflectivity is the product of the coupling ratio of PD2 to PD1 and the split ratio. In order to monitor the concentration variation of the analyte solution which is injected into the alyte room with the rate of 50 µL/s, a recoded ATR spectrum for one of the ultrahigh-order modes produced by angle scanning is shown in the inset of Fig. 6. It is demonstrated that a shift of the ATR spectrum occurs with the increasing of the analyte concentration of 10 ppm. In this angular exploration mode, the concentration change of the analyte solution is determined by detecting the position shift of the ATR dip. In order to further enhance the sensitivity, the HCMW biosensor is operated with intensity interrogation scheme. The incident angle is fixed near the midpoint of the falling edge of a selected dip. As the glucose concentration was changed subsequently from 0 to 2, 4, 6 and 8 ppm in the steps, the operation position moves from the midpoint to the upside of the probing curve, which results in the increases of the reflectivity.

<p>| Table 1 | Sensor’s sensitivities for different optical biosensor: SPR, LRSPR, MCWG and HCMW. |
|---------|-------------------------------|-----------------|-----------------|-----------------|-----------------|</p>
<table>
<thead>
<tr>
<th>Sensor types</th>
<th>FWHM</th>
<th>$S_1$</th>
<th>$S_2$</th>
<th>$S_3$</th>
<th>$S_4$</th>
<th>$S_5$</th>
</tr>
</thead>
<tbody>
<tr>
<td>SPR</td>
<td>6.76</td>
<td>13</td>
<td>2.57</td>
<td>33</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LRSPR</td>
<td>0.19</td>
<td>301</td>
<td>0.45</td>
<td>135</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MCWG</td>
<td>0.52</td>
<td>189</td>
<td>0.92</td>
<td>174</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HCMW</td>
<td>0.02</td>
<td>3675</td>
<td>6.01</td>
<td>22086</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<p>| Table 2 | Parameters chosen for the four biosensor types being studied [10,16,27]. |
|---------|---------------------------------|-----------------|-----------------|-----------------|-----------------|</p>
<table>
<thead>
<tr>
<th>Sensor</th>
<th>HCMW</th>
<th>SPR</th>
<th>LRSPR</th>
<th>MCWG</th>
<th>SPR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polarization</td>
<td>TE</td>
<td>TM</td>
<td>TM</td>
<td>TE</td>
<td>TM</td>
</tr>
<tr>
<td>Prism ($n_1$)</td>
<td>1.517</td>
<td>1.517</td>
<td>1.517</td>
<td>1.517</td>
<td></td>
</tr>
<tr>
<td>Buffer ($n_0, n_n$)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Metal ($\varepsilon_2, \varepsilon_3$)</td>
<td>$-10.2 + i10.0, 50 , nm$</td>
<td>$-16.0 + i0.52, 56 , nm$</td>
<td>$-10.2 + i10.0, 15.2 , nm$</td>
<td>$-16.0 + i0.52, 60 , nm$</td>
<td>–</td>
</tr>
<tr>
<td>Guiding ($n_1, n_1$)</td>
<td>1.330, 700 , µm</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Substrate ($\varepsilon_0, n_0$)</td>
<td>$-10.2 + i1.0$</td>
<td>1.330</td>
<td>1.330</td>
<td>1.330</td>
<td></td>
</tr>
</tbody>
</table>

Fig. 5. Experimental set up of the HCMW biosensor.

Fig. 6. Changes of reflectivity with variation of glucose concentration. (a) deionized water, (b) 2 ppm glucose solution, (c) 4 ppm glucose solution, (d) 6 ppm glucose solution, and (e) 8 ppm glucose solution. Insert is angular interrogation in which the glucose concentration is increasing with 10 ppm.
5. Discussion

Fig. 6 illustrates the performance of the HCMW device when used with low concentrations of glucose. The step-change concentration of 2 ppm, with the average 2.3% change in the reflectivity. According to noise level [30–32] and the assumption that the photodiode detection limit of the reflected light is 0.5%, the new biosensor has been shown to be capable of directly detecting concentration of glucose as low as 0.5 ppm, which corresponds to a high resolution of $1.4 \times 10^{-7}$ RI units [22]. The reason for the obtained relative high sensitivity maybe that our detect probe is the oscillating field (see Fig. 1(c)) not the evanescent field. The sensitivity of biosensor is closely related to the ratio of light energy interacted with the analyte, the bigger ratio, the higher sensitivity [4]. The ratio of energy of evanescent field is far less than that of the oscillating field, thus the performance of the oscillating field is better. The strong confinement of the light power in the guiding region could result in a sufficient interaction between light and the analyte solution. Owing to the sensor’s high sensitivity, the temperature variation of the system becomes one of the major noise sources. In our experiment, the room-temperature is held constant at 22.4°C and is monitored by a thermal couple. More, both the biosensor and the samples are placed in a thermal shield box made of the polymethyl methacrylate. Temperature change in the thermal shield box is constant to about 0.1°C in a short time duration. Since the temperature coefficient of the refractive index of water sample between 20 and 30°C, on average [33], is $1.0 \times 10^{-4}$ °C, the repeatable experiment result demonstrates that variation of temperature in the thermal shield box is less than 0.01°C within several minutes detection.

Another important parameter of an HCMW biosensor is its operating range. It is noted that the zone of linearity with intensity interrogation scheme is limited, and this mode is suit for the measurement of extremely lower concentration. In the case of a relative higher concentration, an angular interrogation scheme is recommended, which exhibits a large linear region of detection.

6. Conclusion

In conclusion, a novel biosensor based on a hollow core metal cladding waveguide has been proposed and characterized. The measurements performed have shown that a refractive-index change of $1.4 \times 10^{-7}$ can be unambiguously identified. This study has also revealed that strong confinement of the light power in the guiding region results in a sufficient interaction between light and the analyte solution, which makes the response time greatly reduced. Aside from higher detection efficiency, the proposed biosensor platform is simple to fabricate by conventional technology and enables label-free and real-time detection.

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