Photonic Crystal Fiber Sensor Design for Enhanced Tumor Detection: Structural Optimization and Sensitivity Analysis

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Abstract—This paper introduces an advanced Photonic Crystal Fiber (PCF) sensor tailored for the sensitive detection of tumor cells in cerebrospinal fluid (CSF), particularly relevant for leptomeningeal spread diagnosis. The PCF sensor leverages guided mode resonance (GMR) for its unique optical properties, with the resonant wavelength being highly sensitive to refractive index variations. A comprehensive sensitivity analysis is conducted, considering key structural parameters such as pitch and diameter, material properties including the refractive index of the core and liquid filling, and environmental factors like temperature and pressure. The proposed approach integrates a specific biomarker, the refractive index variation induced by the presence of tumor cells (Δn), into the PCF sensor design. The calibration curve, developed through experimental data, correlates observed changes in resonance wavelength ($\Delta\lambda_{res}$) with varying concentrations of tumor cells in the CSF. The PCF's dynamic response is optimized for rapid and precise detection while ensuring uniform sensing depth and volume sensitivity. These findings demonstrate the potential of the proposed PCF sensor for accurate and early-stage tumor detection, contributing to the advancement of photonic sensing technologies in medical diagnostics.

The exploration of advanced sensing technologies in medical diagnostics has led to the development of a novel Photonic Crystal Fiber (PCF) [1] sensor designed for the susceptible detection of tumor cells in cerebrospinal fluid (CSF). This innovative sensor is particularly tailored to address the challenges associated with leptomeningeal spread diagnosis, offering a promising avenue for early detection and precise monitoring of brain tumors. The PCF sensor's unique optical properties make it exceptionally sensitive to variations in refractive index, a key biomarker indicative of the presence of tumor cells. Integrating a biomarker—refractive index variation induced by tumor cells (Δn)—into the PCF sensor design becomes paramount. The calibration curve, derived from experimental data, establishes a robust correlation between changes in resonance wavelength ($\Delta\lambda_{res}$) and varying concentrations of tumor cells in the CSF, laying the foundation for accurate and reliable detection. Signal processing techniques are suggested to enhance the sensor's precision in varying conditions. Figure 1 presents the proposed PCF sensor. This journey is fundamental to understanding optical sensing [2] in the near-infrared spectrum (700–1100 nm), where optimal interactions with biological tissues occur.

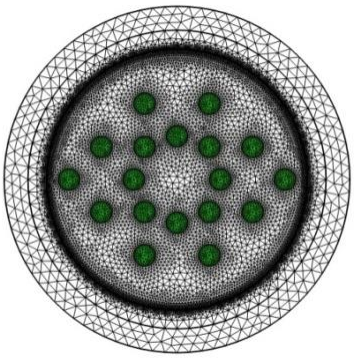

Fig. 1. Proposed PCF Sensor.

The theoretical foundation of PCF structures is established, with the light propagation within these fibers governed by Maxwell's equations. A pivotal starting point involves the mathematical formulation of wave equations, where the interplay of wavelength, refractive index, and geometric parameters sets the stage for designing PCF structures. In the context of PCF structures, these equations lay the groundwork for the wave equation, providing profound insights into how light waves interact with the periodic microstructure inherent to PCFs. The grating equation, a linchpin in PCF design, emerges organically from Maxwell's equations. It articulates the intricate relationship between the pitch (Λ) of the PCF and the wavelength (λ) of the incident light:

$$\Lambda = 2n_{eff}\,\lambda^{-1}, \tag{1}$$

here, n_{eff} signifies the effective refractive index, a parameter intricately linked to the geometric and material properties of the PCF. Concurrently, the choice of the core material assumes pivotal importance, introducing a refractive index (n_{core}) that significantly influences n_{eff}. This relationship is encapsulated in the formulation:

$$n_{eff} = n_{eff}(n_{core}, D, \Lambda), \tag{2}$$

where D represents the diameter of the PCF.

Venturing further into the intricacies of PCF design, a dynamic element is introduced – a liquid filling within the PCF core. This introduces tunability, influencing the effective refractive index and, consequently, the sensor's

sensitivity [3]. The mathematical expression for this interplay is articulated as:

$$n_{eff} = n_{eff}\,(n_{core}, n_{liquid}, D, \Lambda). \quad (3)$$

Sensitivity analysis quantifying how changes in parameters impact the sensor's performance. The culmination incorporates meticulous choices in dimensions, including a diameter of 2 micrometers and a pitch of 1 micrometer, aligning the PCF with the targeted wavelength range and optimizing its interaction with biological tissues. Identify specific biomarkers that are known to be associated with the presence of tumors. Figure 2 represents the selection procedure of biomarker for identification of tumors.

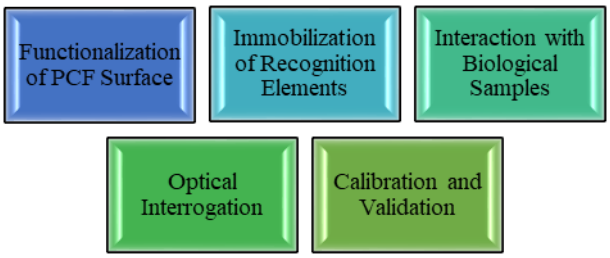

Fig. 2. Biomarker selection process.

Cerebrospinal fluid (CSF) analysis, particularly through CSF cytology, is crucial in identifying tumor cells, especially in cases involving leptomeningeal spread. This diagnostic approach gains further precision and sensitivity when integrated with the capabilities of a Photonic Crystal Fiber (PCF) sensor. The PCF sensor is strategically employed to enhance the detection and characterization of tumor cells within the CSF. The PCF's unique optical properties, such as its ability to transmit light through its core and interact with surrounding substances, become instrumental in this context [4]. As CSF contains cellular components shed by the central nervous system, including potential tumor cells in cases of leptomeningeal involvement, the PCF sensor is designed to detect subtle variations in optical signals induced by the presence of these cells. The functionalized surface of the PCF, equipped with recognition elements specific to tumor cell markers, facilitates the selective binding of these elements to the tumor cells within the CSF. This binding event induces changes in the PCF's optical properties, such as alterations in refractive index or resonance wavelength shifts, which can be accurately monitored and analyzed. The PCF sensor, thus, provides a real-time and highly sensitive means of identifying and quantifying tumor cells in the CSF, offering a valuable tool for the early diagnosis and monitoring of brain tumors with leptomeningeal involvement. This innovative integration of CSF cytology with PCF sensing underscores the potential for advancing diagnostic capabilities in the realm of central nervous system disorders.

One suitable mode for this application is based on the resonant coupling of light with the PCF, explicitly using the guided mode resonance (GMR) phenomenon. Additionally, the biomarker of interest is the presence of abnormal cells in the CSF, which can be detected through variations in refractive index.

In the GMR mode, the PCF is designed to support specific guided modes that resonate at certain wavelengths when the conditions for constructive interference are met. The resonance wavelength is highly sensitive to changes in the refractive index of the surrounding medium, making it an ideal mode for detecting variations associated with the presence of abnormal cells in the CSF.

Mathematical Formulation:

· Effective Refractive Index (n_{eff}) Calculation:

The effective refractive index of the PCF is calculated based on its structural parameters, core material properties, and any additional materials in the core. This is a crucial parameter influencing the resonance conditions.

· Resonance Wavelength (λ_{res}) Calculation:

The resonance wavelength is determined using the grating equation in the GMR mode: $\Lambda = \lambda_{res}/2n_{eff}$, where Λ is the pitch of the PCF, and λ_{res} is the resonance wavelength. Any change in the refractive index of the CSF alters λ_{res}.

· Variation in Refractive Index (Δn) due to Tumor Cells:

The presence of tumor cells in the CSF introduces a change in the refractive index (Δn) surrounding the PCF. This change is directly proportional to the density and refractive index of the cells.

· Shift in Resonance Wavelength ($\Delta\lambda_{res}$):

The change in refractive index (Δn) induces a shift in the resonance wavelength ($\Delta\lambda_{res}$), which can be calculated as: $\Delta\lambda_{res} = \lambda^2_{res}\Delta n/2\pi n_{eff}$. This shift is a measurable parameter indicating the presence and concentration of tumor cells in the CSF.

Detection Mechanism:

The PCF sensor is exposed to CSF containing normal or tumor cells. The resonance wavelength of the PCF is monitored, and any shift from the baseline indicates changes in the refractive index. An algorithm or calibration curve is employed to correlate the observed resonance wavelength shift with the presence and concentration of tumor cells in the CSF. This approach helps GMR in PCF sensors and offers a highly sensitive and specific method for detecting the refractive index variations associated with the presence of abnormal cells in cerebrospinal fluid, providing a potential avenue for early and accurate diagnosis of leptomeningeal spread in brain tumors.

Sensitivity analysis:

Sensitivity analysis is crucial in assessing the performance and reliability of Photonic Crystal Fiber

(PCF) sensors for detecting tumor cells in cerebrospinal fluid (CSF). It involves quantifying how changes in various parameters impact the sensor's response, particularly in terms of detecting variations in the refractive index associated with the presence of tumor cells. The objective is to understand the sensor's sensitivity to different factors and optimize its performance. Here's a breakdown of the sensitivity analysis presented in Fig. 3 for the proposed PCF sensor.

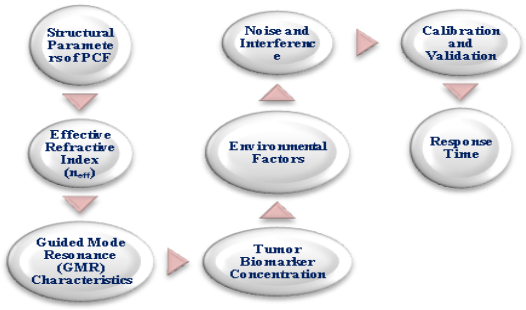

Fig. 3. Breakdown for sensitivity analysis.

Based on this breakdown, an analysis was performed and presented in Table 1 for different parameters of the proposed PCF sensor.

Table 1: Sensitivity Analysis with different parameters

Parameter	Base Value	Variation	Impact on Sensor Response	Optimization Strategy
Pitch (Λ)	1 µm	±0.1 µm	Shifts resonance wavelength	Optimize pitch for sensitivity
Diameter (*D*)	2 µm	±1 µm	Influences mode confinement	Optimize diameter for sensitivity
Refractive Index (n_{core})	1.45	±0.01	It affects the effective refractive index	Optimize core material for sensitivity
Refractive Index (n_{liquid})	1.33	±0.005	Influences effective refractive index	Optimize liquid for sensitivity
Concentration of Tumor Cells (Δ*n*)	-	Low to High	Impacts refractive index variation	Calibrate sensor for various concentrations
Temperature	25°C	±2°C	Alters material properties	Implement temperature compensation
Pressure	1 atm	±0.1 atm	It affects the refractive index of air	Correct for pressure variations
Calibration Curve	-	-	Correlation between $\Delta\lambda_{res}$ and Δn	Validate with known concentrations.

This table provides a structured overview of the critical parameters, their base values, potential variations, impact on the PCF sensor's response, and suggested optimization strategies. The sensitivity curve is plotted and shown below in Fig. 4.

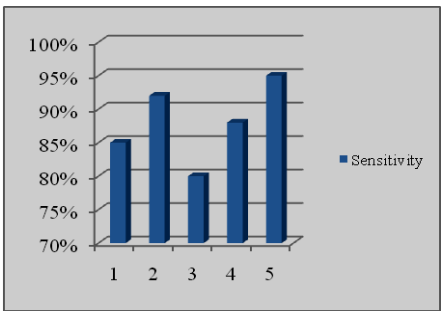

Fig. 4. Sensitivity analysis of the proposed PCF sensor.

Sensitivity analysis shows the sensor's response to different concentrations of tumor cells in the CSF is analyzed. This sensitivity to varying concentrations is crucial for developing a calibration curve that can accurately correlate resonance wavelength changes with different tumor cell presence levels.

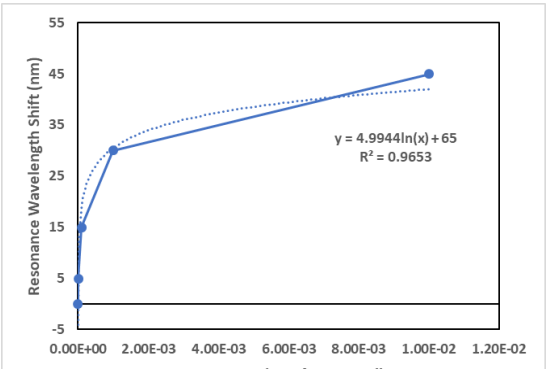

Fig. 5. Derived concentration curve.

The concertation curve presented in Fig. 5 presents a robust correlation between changes in resonance wavelength ($\Delta\lambda_{res}$) and varying concentrations of tumor cells in the biomarker.

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