Portable optical fiber bio-sensing device for detection and quantification of biomolecules in bodily fluids

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Abstract

Bio-sensing plays an important role in the determination of bio-target molecules in medical applications. Tapered Optical Fibers Sensor (TOFS) as a biosensor has the required higher sensitivity, and real-time specimen measuring capabilities. The sensitivity of a typical TOFS is 0.00001 RIU (Refractive Index Units) meaning TOFS can detect 0.00001 minute change in refractive indices in the tarped region. Thus molecular-level interactions are detectable. The detection mechanism involves the evanescent electromagnetic (EM) field that enables the detection of minute changes in the refractive index close to the surface of the fiber.

Introduction

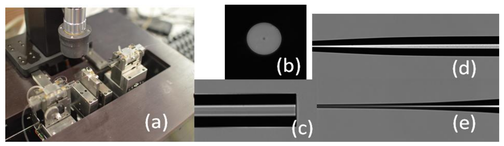
When a laser beam is passed through the fiber from left to right, multiple cladding modes are excited simultaneously in the tapered region. The transmission intensity in the output end of the fiber is given by the equations below.

$$I_T = \Sigma_n I_n + 2\Sigma_{n>m} (I_m I_n)^{1/2} cos\Delta\phi_{nm}(\lambda) \quad (1)\ ,\ \text{where}$$

$$\Delta\phi_{nm}(\lambda) = (\beta_n(\lambda) - \beta_m(\lambda))L \quad (2)$$

the sum is over the core and cladding modes of the fiber. The sinusoidal signal leaving fiber with wavelength λ that is analyzed. In Eq. (1), $\Delta\phi_{nm}(\lambda)$ is the phase change and $\{\beta_n(\lambda)\}$ is the propagation constants of each mode in the fiber and L is the length of the waist or tapered region along the direction of propagation.

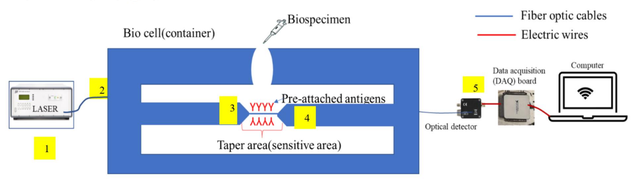
Materials and method



a).Glass processing system b,c,d,e). fiber and tapered fiber.

The tapered region or the sensitive area of a TOFS is obtained by stretching single-mode fiber cables to desired dimensions. Typical dimensions of a tapered region are 20-25 mm.

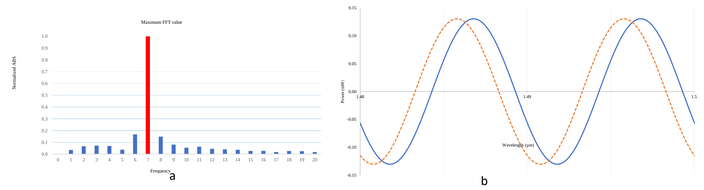
A wavelength-swept laser beam is launched at one end of the at infrared wavelengths λ ~ 1.48 to 1.56 μm, passing through the tapered region, and then is collected at the other end.

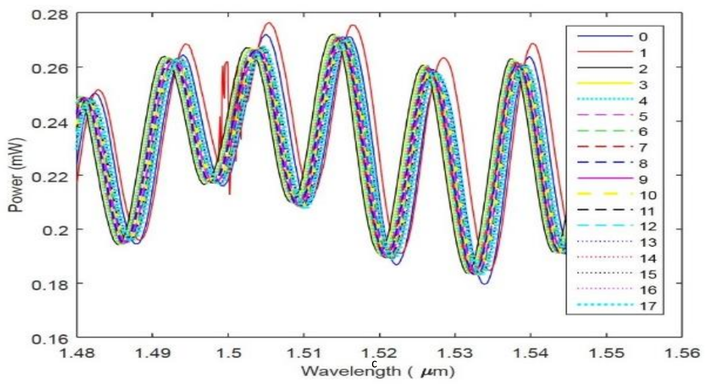


The complete TOFS system

The modes excited at the tapered region have evanescent components in the surrounding medium.

In the tapered region (3), multiple cladding modes are excited simultaneously. These modes have evanescent components in the surrounding medium and are sensitive to the concentration of a bimolecular antigen-antibody pair. These modes revert to a single mode as they pass through the up-taper region (4). The in-phase or out-of-phase with the single-mode, provides an interference spectrum as a function of wavelength. Fourier analysis, and the phase change related to maximum amplitude is used.





a). Dominant frequency plot b,c).Phase alterations for each scan

To achieve high resolution, the signal-to-noise ratio (SNR) must be maximized. This is achieved by optimizing fiber parameters, including the waist diameter and length of the up-and-down-taper regions. In our experiment, optimized dimensions were used to obtain higher SNR.

First, tapered fiber is placed in a Teflon cell and prepared specifically for label-free detection. As a proof of concept,

(1) The cell was tested for water and methanol- the cell was first filled with water and methanol was added to see the phase alterations.

(2) For bio-sensor testing HCoV-OC43, which is a viral surrogate of SARS-CoV-2 was tested. This requires the attachment of a molecular detecting element, such as antigen-antibody binding interactions. This allows us to detect target molecules on the femtomolar level. Anti-HCoV OC43 Spike Polyclonal antibody (CABT-CS063, Creative Diagnostics, United States) was tethered to the tapered fiber. This step was processed at the Sinha labs at the University of Southern California.

Results

(1) First cell was filled with water and 100 μL methanol was added to the cell at sampling 16. A clear step function-like phase change is observed. The minute RIU change between water and methanol was clearly visible. The output signal was stable and repeatable.

(2) The first 100 μL of saliva passed the filter (without virus as a control input) was added to the reaction chamber for background signal calibration. After removing the control input from the chamber and removing the filter from the syringe, another 100 μL of saliva (from the same sample) with viral particles was added for binding to TOFS (for 5 min). The phase shift of light was calculated and processed for HCoV-OC43 detection.

HCoV-OC43 viral antigen in our experiments. Due to the covalent binding of these antigens to the tapered fiber surface, fibers must be stripped between uses with a 2.4 pH glycine solution to remove antigens between uses.

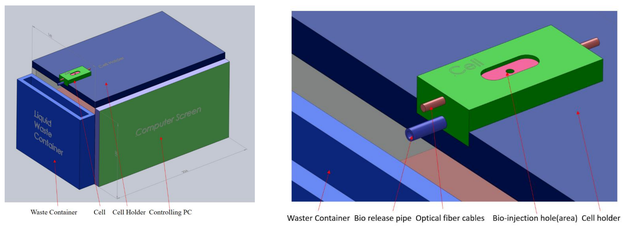
Phase change for a).water-methanol and b).HCoV-OC43

Conclusion

The developed TOFS system was experimentally tested for practical use and yielded repeatable results with high resolution. It had been tested using various liquids, such as PBS, water, and saliva. The system utilized for head and neck squamous cell carcinoma (HNSCC), through IL-8 virus in saliva and Covid variant called HCoV-OC43. Experiments showed success with resolutions of 50 viruses/ ml for HCoV-OC43.

Future work

The long-term goal of the TOFs system is its use as a point-of-care (POC) technology for detection, monitoring, and surveillance in the clinical setting. POC devices must exhibit high sensitivity and specificity, system stability, rapid results, and low cost.



The proposed complete portable sensing system