Refractometric Sensors for Lab-on-a-Chip Based on Optical Ring Resonators

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***Abstract*—We demonstrate refractive index measurement of liquids using two sensor system designs, both based on microring resonators. Evanescent sensors based on microrings utilize the resonating nature of the light to dramatically decrease the required size and sample consumption volume, which are requirements of lab-on-a-chip sensor systems. The first design, which utilizes an optical microsphere, exhibits a sensitivity of 30 nm/RIU and a resulting detection limit on the order of 10^{-7} RIU. The second approach is a novel design called a liquid core optical ring resonator (LCORR). This concept uses a quartz capillary as the fluidics and as the ring resonator and achieves a sensitivity of 16.1 nm/RIU. The detection limit of this system is around 5×10^{-6} RIU. Both of these systems have the potential to be incorporated with advanced microfluidic systems for lab-on-a-chip applications. In particular, the LCORR combines high sensitivity, performance stability, and microfluidic compatibility, making it an excellent choice for lab-on-a-chip development.**

***Index Terms*—Label-free sensing, optical ring resonator, refractive index, whispering gallery modes.**

I. Introduction

ADVANCES in microfluidic technology are enabling the lab-on-a-chip concept to become a reality. Micrometer-scale fluidic channels are enabling picoliter sample volumes, and functions such as miniature valves and pumps are being integrated into small silicon or polymer chips [1]. It is envisioned that sensor technology will be integrated densely with the microfluidics to construct a device that can quickly and simultaneously perform an array of tests on a tiny sample volume, resulting in lower cost and higher throughput analysis. Thus, today, there is a need for economical sensor platforms that are compatible with microfluidic technology and that can perform an array of functions.

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Photonics technology is readily adaptable to miniaturized sensor arrays and, thus, has been investigated actively for integrated sensor systems [2]–[12]. Optical detection in these systems usually takes place through the depth of the microfluidic channels, which has led to a large body of work reporting on the fabrication of high aspect ratio channel structures. One of the most common optical techniques used is the measurement of fluorescence, due to inherent sensitivity and selectivity. However, fluorescence detection is generally costly and not applicable for the majority of molecular systems. Among the optical methods, measurement of the change in the refractive index is one that has been successfully coupled to many analytical techniques, including liquid chromatography (LC) and capillary electrophoresis (CE) [2]–[8], [12], [13]. Refractive index detection methods have useful characteristics that make them attractive alternatives to more conventional luminescence techniques. In particular, refractive index detection affords the generation of a signal for a wide variety of analytes that lack useful chromophores. Furthermore, the analytical signal is concentration rather than mass sensitive, and the technique is nondestructive [7]. Concentration sensitivity makes the application of refractive index measurement suitable for ultra-small volumes [14].

Recently, a number of evanescent wave optical sensors have been developed and used for refractive index detection in sensing systems [2]–[7], [9], [10], [15]. Examples of such devices include the resonant mirror [6], [16], [17], metal and absorbing material-clad leaky waveguide [14], [18], the differential interferometry sensor [19]–[21] grating coupler, and the integrated optical waveguide [13], [22]–[25]. Though evanescent wave sensors are effective for measuring the refractive index, they typically require a relatively long physical length to achieve sufficient light-matter interaction in order to provide the necessary sensitivity. This is in contradiction to the requirements of lab-on-a-chip systems.

In this work, we show highly sensitive refractive index measurement using optical ring resonators as evanescent field-based sensors. The resonating nature of the ring cavity enhances the light that interacts with the sample volume by hundreds to thousands of times, thus reducing the required interaction length as compared with typical evanescent sensors. We discuss a variety of approaches of ring resonator sensors and identify the advantages and disadvantages. We then present experimental demonstrations of two approaches that both take advantage of extremely high Q-factors. The first design uses, as the resonating cavity, a fused silica sphere, which is submerged in the sample fluid. In the second design, a quartz capillary acts as both a fluidic channel for the sample fluid and as a ring resonator.

II. Ring Resonator Sensors

In a dielectric ring, light will circulate continually at the inner surface due to total internal reflection. For rings that are much larger than the wavelength, resonant modes exist for wavelengths that meet the following condition [26]:

$$\lambda = \frac{2\pi r n_{eff}}{n} \tag{1}$$

where r is the sphere radius, n_{eff} is the effective refractive index experienced by the mode, and n is the angular momentum term. These resonating modes are called the whispering gallery modes (WGMs). As with any wave guiding medium, an evanescent field extends beyond the dielectric surface and into the surrounding medium. As indicated by (1), refractive index changes in the surrounding medium near the surface cause a change in the resonant condition. Thus, changes in the spectral positions of the WGMs convey quantitative and kinetic information about the refractive index of the surrounding medium. Therefore, this technique can be used to detect changes in the surrounding solution, or the binding of molecules at the surface, as was first proposed in [27].

Ring resonator sensors have an advantage over typical evanescent wave sensors because in a ring resonator, the light continually circulates at the surface, increasing the light-matter interaction. The quality factor, or Q-factor, is the parameter that indicates the strength of the resonance and, thus, the enhancement in light-matter interaction. Q-factors as high as 10^9 have been demonstrated in microsphere resonators [28], which can result in an effective sensing length on the order of hundreds of centimeters, despite the sub-millimeter dimensions of typical microspheres.

A few different types of ring resonators have been demonstrated, including microspheres and planar disks/rings. Additionally, we have demonstrated a novel ring resonator design called a liquid core optical ring resonator (LCORR), which utilizes a quartz capillary as the fluidic channel and the ring resonator. All three designs leverage the recirculating light to achieve high sensitivity, even though there are advantages and disadvantages in terms of the Q-factor and the ability to be integrated with microfluidic systems.

Microsphere resonators such as bio/chemical sensors are well known and have been demonstrated several times [29]–[34]. The sensor concept is illustrated in Fig. 1. Captured molecules affect the effective refractive index of the WGMs, resulting in a measurable spectral shift. Low detection limits have been achieved, primarily because of the high Q-factor. Furthermore, the high Q-factor results in a very narrow mode linewidth, which improves measurement precision.

An alternative approach for ring resonators is to use planar technology to form a disk or ring coupled to a planar waveguide on a substrate, as illustrated in Fig. 2. The disk or ring and the waveguide features are formed by advanced lithographic techniques and etching [35]–[37]. The advantage of this approach, as compared to the microsphere approach, is the use of integrated device technologies, which is amenable to mass production, and allows for stable performance because the components are integrated onto a substrate.

However, although the manufacturing process enables dense integration and economical mass production, it also decreases

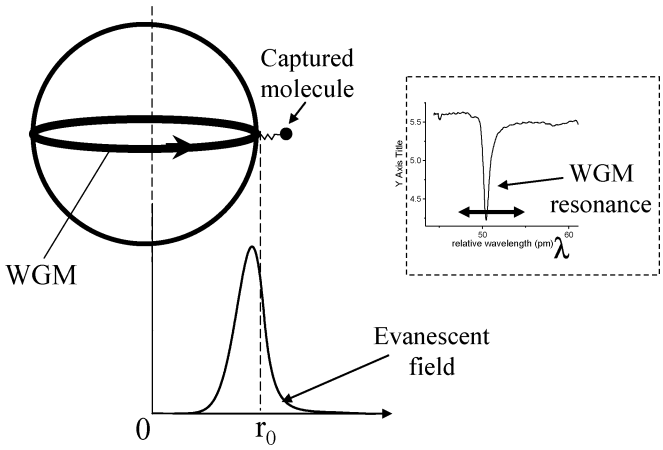

Fig. 1. Evanescent field interacts with matter near the surface of the sphere, and thus, the WGM spectral position shifts when the bulk refractive index of the solution change or when molecules bind at the surface.

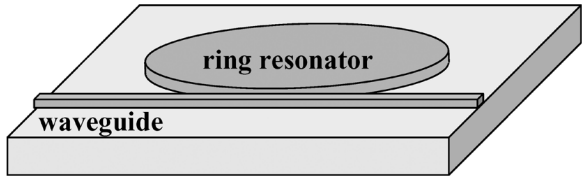

Fig. 2. Planar microdisk with a waveguide to deliver the excitation light.

the typical performance of planar ring resonators. The etching process yields a rougher surface as compared to the discrete microsphere. As a result, the Q-factor of ring resonators is on the order of 10^4, which is anywhere from two to three orders of magnitude lower than microsphere resonators [35], [36]. Furthermore, the fluidic channel must be manufactured separately and then assembled onto the ring resonator chip. Therefore, although the planar ring resonators can be easily mass produced, the practical device may have a complicated assembly procedure.

We have developed a novel sensing architecture that delivers the stable performance of the integrated planar approach while not sacrificing performance. This design, which is diagrammed in Fig. 3, uses a thin-walled quartz capillary as a fluidics channel and as a ring resonator. A waveguide is brought into contact perpendicularly with the capillary, which enables light to couple into the WGM of the ringed cross-section. An evanescent field exists both on the outside and the inside of the capillary wall. The interior evanescent field interacts with the sample as it passes through the capillary, similar to the exterior evanescent field in the microsphere and the planar ring. Thus, as the refractive index of the sample fluid changes, or as molecules bind to the inner surface of the capillary, the WGMs shift spectrally.

As shown in Fig. 3, this design is easily scalable to a 2-D array. Multiple capillaries can be arranged along a single waveguide. Meanwhile, each capillary can be patterned with different immobilization treatments [38], and thus, a single capillary can be used to detect multiple analytes. This multiplexed integration of fluidics and photonics is a promising concept for lab-on-a-chip technology.

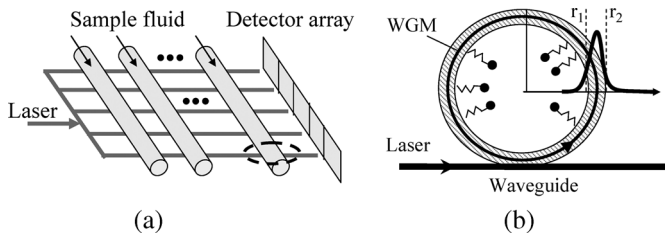

Fig. 3. (a) Two-dimensional arrangement of LCORRs. Each LCORR is in contact with several waveguides or fiber tapers, and each LCORR is patterned with the desired surface functionalization at each waveguide/taper connection point. (b) Cross section of a single LCORR, as circled in (a).

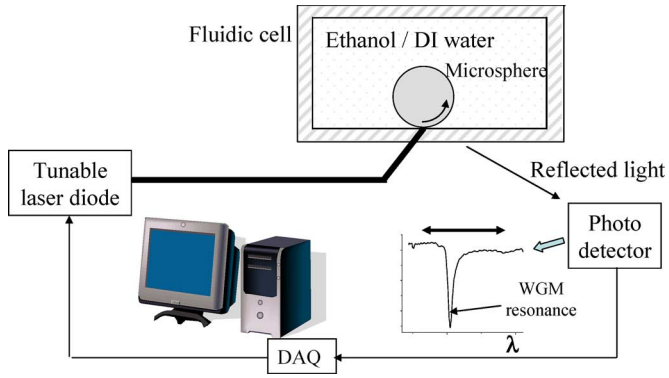

Fig. 4. Experimental setup for the microsphere resonator sensor system.

III. Experimental Setup

In this work, we demonstrate experimentally the microsphere resonator and the LCORR for refractive index measurement. The setups are similar in function but differ in the sensor head and the fluidics. The experimental setup of the microsphere sensor is illustrated in Fig. 4. The microspheres are created by melting the tip of a standard single mode fiber optic cable with a CO_2 laser. The sphere used in this experiment is 110 μm in diameter. The light from a tunable diode laser (New Focus, $\sim$ 980 nm) is coupled into the microsphere through an angle-polished fiber prism [39]. In the experiments presented here, the prism is polished at an angle of 74°, which is designed for optimal mode coupling, as described in [39].

To observe the WGM, the laser repeatedly scans across a spectral range of approximately 100 pm at a frequency of about 3 Hz. Light reflected by the prism is collected by a photodetector and monitored with a data acquisition card and computer. When the wavelength of the tunable laser is on resonance with the WGM of the sphere, the power of the light reflected at the prism decreases, and a spectral dip indicating the WGM spectral position is recorded.

The microsphere is submerged into a fluidic cell and brought into contact with the fiber prism, which is polished into one wall of the cell. The well initially contains de-ionized (DI) water. To vary the refractive index, a solution of ethanol and water is incrementally added to the fluidic cell with a digital syringe. Following each injection, the WGM modes are monitored until equilibrium is reached, and then, the subsequent injection is made.

This method is also used to characterize the refractive index sensitivity of the LCORR system. The experimental setup is illustrated in Fig. 5. The LCORR is positioned in contact with a fiber optic cable that is tapered to about 3 μm in diameter. Light from a distributed feedback laser (JDS Uniphase, $\sim$1550 nm) is coupled into the LCORR through evanescent coupling at the exterior surface [40]. The laser is scanned in wavelength by approximately 50 pm by varying the current into the gain section of the laser. The signal from a photodetector at the output of the fiber taper is recorded by a computer, where the spectral dips are monitored, just as in the microsphere setup. During the experiment, the varying concentrations of ethanol in water are pumped through the LCORR using a peristaltic pump.

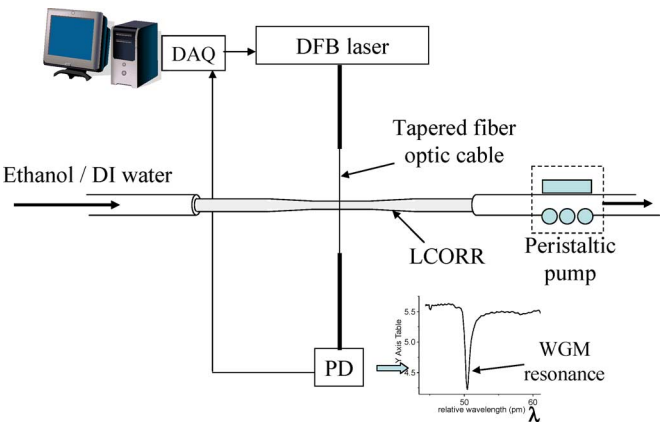

Fig. 5. Experimental setup for the LCORR sensor system.

In order to create an evanescent field at the interior surface of the LCORR, the capillary walls must be very thin. The LCORR capillary is formed by stretching a quartz tube (outer diameter = 1.2 mm, inner diameter = 0.9 mm) under an H_2O flame until the outer diameter at the center of the tube is less than 100 μm. Then, to further reduce the wall thickness, diluted concentrations of HF are pumped through the interior of the capillary, while the WGM spectral shift is monitored.

IV. Experimental Results

The sensitivity to refractive index changes of the microsphere sensor system is determined by monitoring the magnitude of the WGM spectral shift when a known quantity of ethanol is added to the solution in the well [41]. The change in refractive index for a given addition of ethanol solution is computed from the formula in [42]. The steady-state values of WGM spectral shift for a change in refractive index are plotted in Fig. 6 and exhibit excellent linearity. The expected WGM spectral shift can be computed from the theoretical relation between wavelength and refractive index, given by the asymptotic formula presented in [43]. The wavelength shift calculated from that expression is plotted in Fig. 6 with the experimental data.

The results show that the sphere has a sensitivity of approximately 30 nm/RIU. The detection limit of our system can be calculated from this sensitivity. Because the laser linewidth is extremely narrow (<300 kHz), it is expected that we can resolve 1/20th to 1/50th of the WGM linewidth. For a Q-factor of 5×10^6, this results in a refractive index detection limit of on the order of 10^{-7} RIU, which is comparable to or even better than surface plasmon resonance or waveguide-based sensors [44], [45].

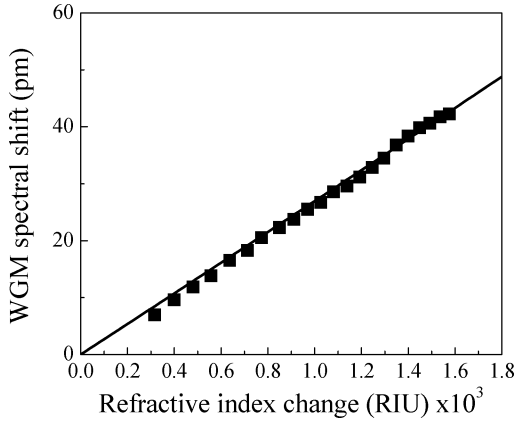

Fig. 6. WGM spectral shift versus change in refractive index for the microsphere sensor. Experimental data: (■); calculated data: (−). The slope is 30 pm/RIU.

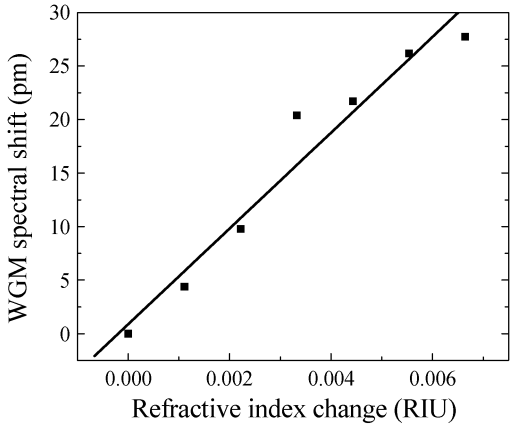

Fig. 8. WGM spectral shift versus change in refractive index for the LCORR sensor. The slope is 4.5 nm/RIU.

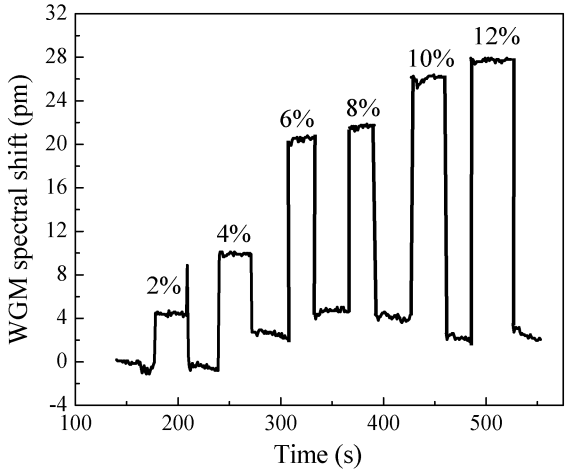

Fig. 7. Sensorgram when various concentrations of ethanol are pumped through the LCORR. Red shifts in the WGM spectral position indicate the moment when the ethanol solution entered the LCORR.

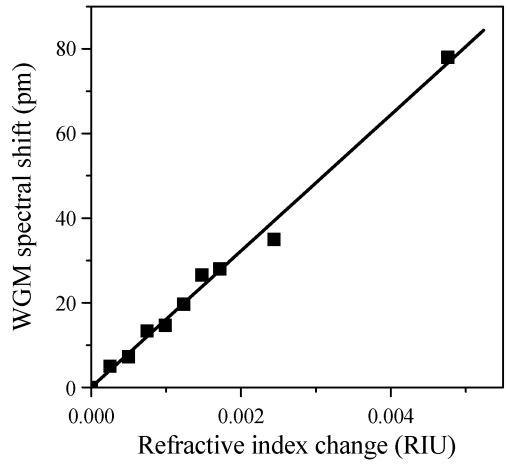

Fig. 9. WGM spectral shift versus change in refractive index when methanol is added. The slope is 16.1 nm/RIU.

The LCORR sensor system was characterized with a similar procedure. Fig. 7 shows the WGM spectral shift when various concentrations of ethanol in DI water are pumped through the LCORR. The abrupt red shifts coincide with the entrance of the ethanol solution into the capillary, whereas the blue shifts indicate a water-rinsing period. The sensorgram data is compiled into a graph in Fig. 8, showing the WGM shift versus refractive index change. As before, the change in refractive index for a given addition of ethanol solution is computed from the formula in [42]. The results show that the LCORR has a sensitivity of approximately 4.5 nm/RIU.

Similar LCORR sensing performance has been confirmed in other experiments as well [46]. Furthermore, the experiments have been repeated with another LCORR using a methanol/water solution. The resulting WGM spectral shift versus refractive index change using a 980–nm laser is given in Fig. 9. The change in refractive index per 1% (w/w) change in methanol is 0.0002 RIUs, as was characterized in [47]. This LCORR exhibits a sensitivity of 16.1 nm/RIU. Just as with the microsphere, the detection limit of the LCORR system can be calculated from this sensitivity. The linewidth of the mode tracked in this experiment is 1.55 pm, which results in a Q-factor of 6.3×10^5. Assuming again that we can resolve 1/20th of the mode linewidth, the spectral resolution of the system is 0.08 pm. This precision results in a refractive index detection limit of around 5×10^{-6} RIU. Similar results to these above have been further duplicated in our lab, which shows that these novel sensing devices can be reproduced with regularity.

Intuitively, the sensitivity is highly dependent on the thickness of the capillary wall. Fig. 10 shows the cross section of the LCORR used in the ethanol measurement, as photographed by a scanning electron microscope (SEM). The wall thickness is not perfectly uniform because of the flame-pulling process currently used. According to the figure, the thickness is in the range of 3–6 μm. We have developed a theoretical model based on Mie theory to analyze the sensitivity versus the wall thickness. The radial distribution of the WGM of an LCORR can be described by [48]

$$E_{m,l}(r) = \begin{cases} AJ_m\left(k_0^{(l)} n_1 r\right) & (r \le r_1) \\ BJ_m\left(k_0^{(l)} n_2 r\right) + CH_m^{(1)}(k_0^{(l)} n_2 r) & (r_1 \le r \le r_2), \\ DH_m^{(1)}\left(k_0^{(l)} n_3 r\right) & (r \ge r_2) \end{cases} \quad (2)$$

where J_m and $H_m^{(1)}$ are the mth Bessel function and the mth Hankel function of the first kind, respectively. The refractive

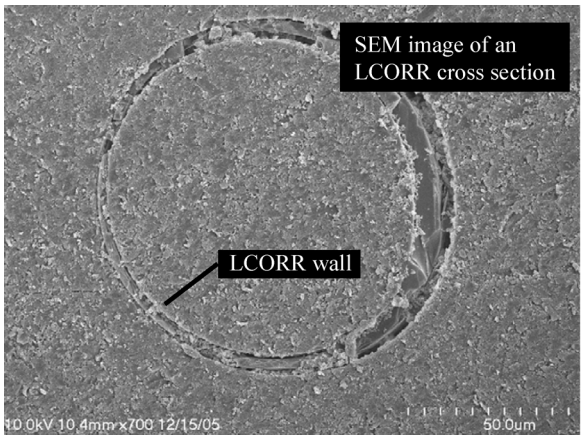

Fig. 10. SEM image of the cross-section of the LCORR. To obtain this image, the LCORR was broken at the sensing region, then covered in a UV-curable glue, and then polished at the cross-section.

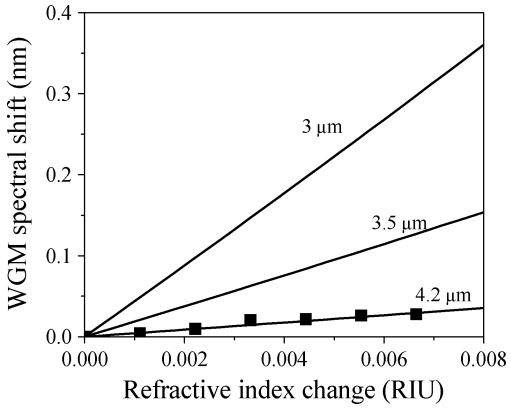

Fig. 11. Calculation of the sensitivity for LCORR wall thicknesses of 3 μm, 3.5 μm, and 4.2 μm. The second radial TM mode is used. Experimental data (■) is shown for comparison with the calculation using a 4.2-μm wall thickness.

indices of the core, wall, and the surrounding medium are described by n_1, n_2, and n_3. The terms r_1 and r_2 represent the inner and outer radius of the LCORR, respectively, and $k_0^{(l)}$ is the amplitude of the wave vector in a vacuum for the lth-order radial WGM.

Fig. 11 shows the calculated WGM spectral shift versus refractive index change using this model for wall thicknesses of 4.2 μm, 3.5 μm, and 3 μm, where the outer diameter is 100 μm, and the excitation wavelength is $\sim$1550 nm. The experimental data is also plotted and shows that the effective wall thickness of the LCORR demonstrated here is 4.2 μm for 1550 nm. This graph illustrates the significant impact that a small change in wall thickness can have. As compared to the 4.2-μm wall LCORR used for ethanol sensing, which has a sensitivity of 4.5 nm/RIU, the LCORR with a 3.5-μm wall exhibits a sensitivity of 19.6 nm/RIU, and the 3-μm wall LCORR demonstrates 45.8 nm/RIU.

The sensitivity can also be tuned by varying the diameter of the LCORR. Fig. 12(a) shows the sensitivity dependence upon outer diameter, as calculated by our tool. In the simulations, the diameter is varied, but the thickness of the wall is held constant at 4 μm. As the graph shows, the sensitivity increases for larger diameter. This phenomenon is explained by Fig. 12(b), which shows the evanescent intensity at the inner surface of the LCORR for diameters of 60 μm and 100 μm. The LCORR with the larger diameter has a stronger evanescent field at the inner surface, thus increasing the light-matter interaction and raising the sensitivity. Note that this radial dependence is opposite from that of a microsphere, which has an increased sensitivity for smaller radius, as shown in [49] and [50]. This contrast may be expected, as microspheres utilize the evanescent field at the outer surface, while LOCRRs rely on the evanescent field at the inner surface. As a practical point, there are bounds on the scalability of the diameter of the LCORR. First, a higher aspect ratio (diameter/wall thickness) may result in mechanical instability. In addition, smaller fluidic channels are desirable in order to minimize the total size and sample consumption of the lab-on-a-chip system.

The experimental demonstrations and the simulations show the potential for the LCORRs to be excellent label-free sensors. However, it must be noted that the LCORRs also suffer from some of the typical handicaps of label-free sensors. One drawback that must be countered is the temperature dependence of the resulting signal. Small temperature fluctuations result in small fluctuations of the WGM spectral position, which produces noise in the sensor signal. Temperature control is one option to combat this issue. Additionally, we have demonstrated the use of a reference channel for temperature noise subtraction.

We use the configuration presented in Fig. 5, except that a second fiber taper is placed in contact with the LCORR about 1.5 mm away from the other fiber taper. The output of this second taper is used as a reference signal. The signals at both fiber taper outputs are recorded and plotted in Fig. 13. The signals show common noise features that are produced by temperature fluctuations in the sensor environment. The bottom trace in Fig. 13 shows that the relatively large noise swings can easily be subtracted out using the reference channel. The resulting WGM variation after subtraction of the reference is on the order of 0.1 pm.

V. Discussion and Conclusion

The experimental results presented here show the excellent capability of a microsphere resonator to measure the refractive index of liquids. The microsphere can achieve similar or even better results than typical waveguide-based sensors while only consuming picoliter sample volume because of the resonating nature of the cavity. The high sensitivity and low sample consumption are excellent characteristics for lab-on-a-chip systems. However, some design concepts are in need of improvement. First, the microsphere in the experiment presented here is 100 μm in diameter. Although this is small compared to waveguide sensors, it is still larger than the typical desired range for advanced microfluidic systems. Second, perfect alignment of the microsphere to the light delivery system (waveguide, prism) is nontrivial, and maintaining that alignment during fluid flow is also an issue that must be addressed.

The LCORR appears to offer both high performance and stable operation, as well as an economical multiplexed operational configuration. In addition, because it is capillary based, it can integrate well with microfluidic systems. The sensitivity reported in this experiment is slightly lower than the microsphere

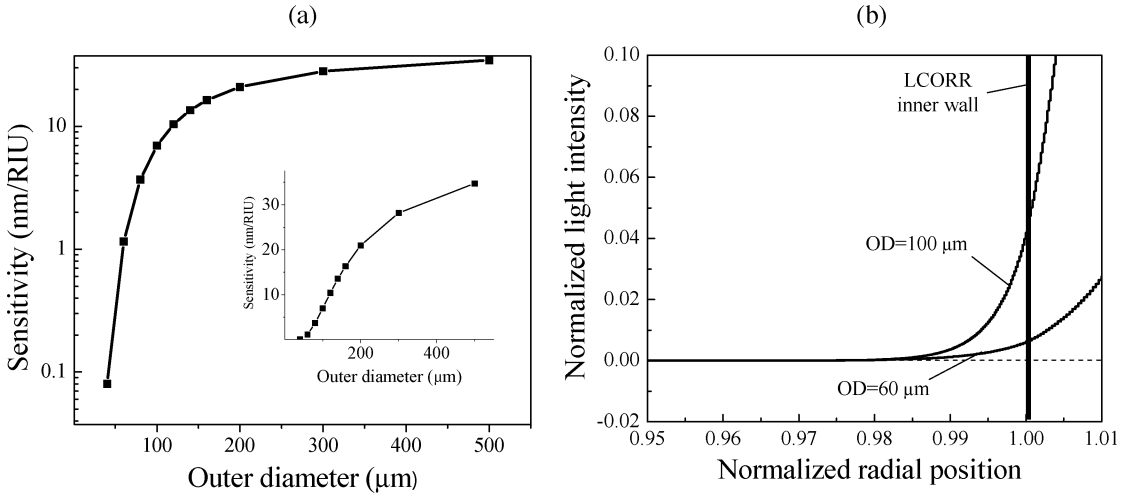

Fig. 12. (a) Calculated LCORR sensitivity dependence on the diameter; the wall thickness is held constant at 4 μm. The second radial TM mode is used. (b) Comparison of the evanescent intensities at the interior surface for LCORRs with diameters of 60 μm and 100 μm.

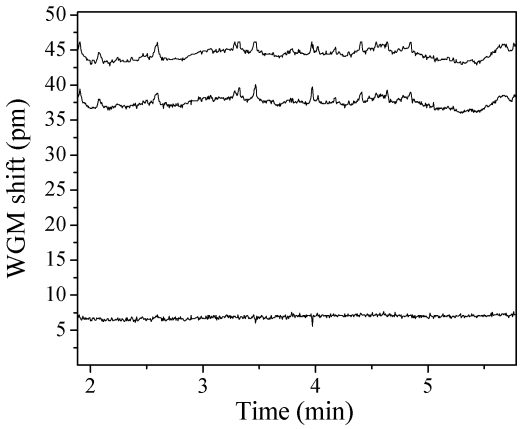

Fig. 13. Subtracting the signal produced by the reference channel from that produced by the sensing channel results in a very low noise signal.

(30 nm/RIU versus 16.1 nm/RIU), but, as shown, a slightly thinner wall can significantly raise the LCORR sensitivity. Also, improvements to the LCORR fabrication process can significantly boost the Q-factor, which will lead to an improved detection limit.

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