

Towards on-chip, integrated chalcogenide glass based biochemical sensors

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Abstract: This paper reviews ongoing progress in the development of novel on-chip planar molecular sensors in infrared-transparent chalcogenide glasses. We demonstrate on-chip cavity-enhanced refractometry and infrared absorption spectroscopy for sensitive detection of proteins and small molecules.

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OCIS codes: (230.5750) Resonators; (160.2750) Glass and other amorphous materials.

1. Introduction

Chalcogenide glasses, namely the amorphous compounds of sulfur, selenium and/or tellurium, have emerged as a promising material candidate for biochemical sensing. They feature wide infrared transparency windows stretching from visible to far-infrared (wavelength $> 20 \mu\text{m}$) with an intrinsic optical loss $< \text{dB/m}$, which covers most of the technically important wave bands for infrared spectroscopy [1]. In addition, chalcogenide glasses possess good chemical stability and almost unlimited capacity for compositional alloying and property tailoring, useful characteristics for photonic applications. Further, their amorphous nature also facilitates monolithic integration on silicon, as well as a low-temperature thermal reflow process for removing sidewall roughness scattering loss [2].

On the device front, conventional chalcogenide glass based optical sensors employ an optical fiber platform which is not amenable to large-scale planar integration and cost reduction. In this paper, we report the design, fabrication and testing of novel planar chalcogenide glass photonic devices for biochemical sensing applications. Center to these efforts is the development of microfluidic-integrated high-Q chalcogenide glass optical resonators, which serves as a versatile device platform for different cavity-enhanced spectroscopic techniques, including refractometry for protein detection and infrared absorption spectroscopy for chemical molecule sensing.

2. Device fabrication

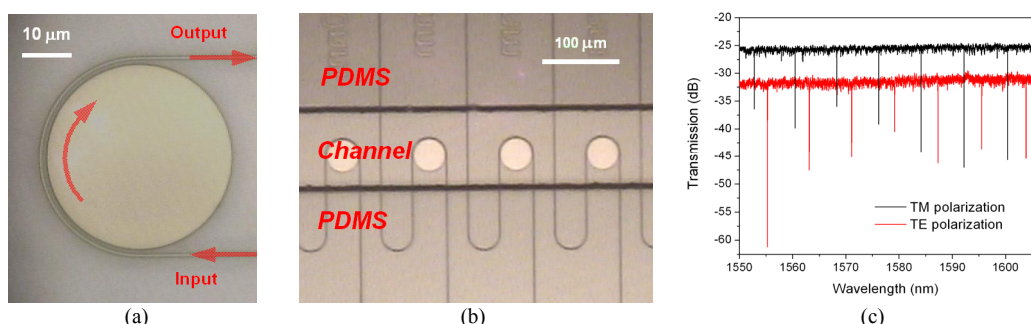


Fig. 1. (a) Top-view of a pulley-type chalcogenide glass microdisk resonator; (b) Top view micrograph of a PDMS microfluidic channel overlaid with a linear array of Ge-Sb-S microdisks; (c) Measured transmission spectra of a microdisk resonator; the cavity Q-factors measure up to 5×10^5 .

While the majority of chalcogenide glass fiber sensor work is based on As-based glasses, we select and develop chalcogenide glass compositions in the Ge-Sb-S family for our on-chip spectroscopic sensing applications given their superior chemical stability, low cytotoxicity and excellent thermal-mechanical robustness over their As-based counterparts [3]. In addition, Ge-Sb-S glasses exhibit a glass transition temperature $> 300 \text{ }^\circ\text{C}$, and thus possess good long-term structure and property stability critical to field applications.

In the fabrication process, high quality Ge-Sb-S chalcogenide glass bulk is prepared using a melt-quenching technique [3]. Thin glass films are then formed with high uniformity over large substrate area ($> 6''$) through baffled thermal evaporation and then patterned using a CMOS-backend compatible lift-off technique we developed [4].

These devices are entirely fabricated using a 500 nm CMOS line. Their CMOS-backend compatibility allows the process to be scaled up for mass production. Replica-molded PDMS microfluidic channels are subsequently bonded onto the device for analyte transport. Figure 1(a) shows the top view of a 20 μm radius microdisk resonator fabricated using lift-off and Figure 1(b) shows a PDMS microfluidic channel overlaid with a linear array of Ge-Sb-S microdisks. Metal electrodes are deposited and patterned in the microfluidic inlet and outlet reservoirs to allow electro-osmotic pumping of aqueous solutions into the channel. Non-aqueous solutions are injected into the channels through a syringe pump. Compared to the commonly used pressure driven flow scheme, such an electro-osmotic approach enables accurate control of flow rate by tuning the applied voltage and excellent reproducibility.

Transmission spectra of the fabricated device are measured on a Newport AutoAlign workstation in conjunction with a LUNA tunable laser. Lens-tipped fibers are used to couple light from the laser into and out of the devices. Reproducible coupling is achieved via an automatic alignment system. The sample is mounted on a thermostat stage and kept at 25 $^{\circ}\text{C}$ for all measurements. Figure 1(b) shows the measured transmission spectra of a pulley-type microdisk resonator. Clear resonant notches with high extinction ratio are observed for both TE and TM polarizations, indicating near critical-coupling operation of the device. For sensing applications, we choose to use the TM polarization given its large evanescent field and high-Q factor. The loaded cavity Q-factor measures up to 5×10^5 ($\pm 10\%$) for TM polarization, representing the highest Q reported in planar chalcogenide resonators.

3. Cavity-enhanced infrared absorption spectroscopy testing

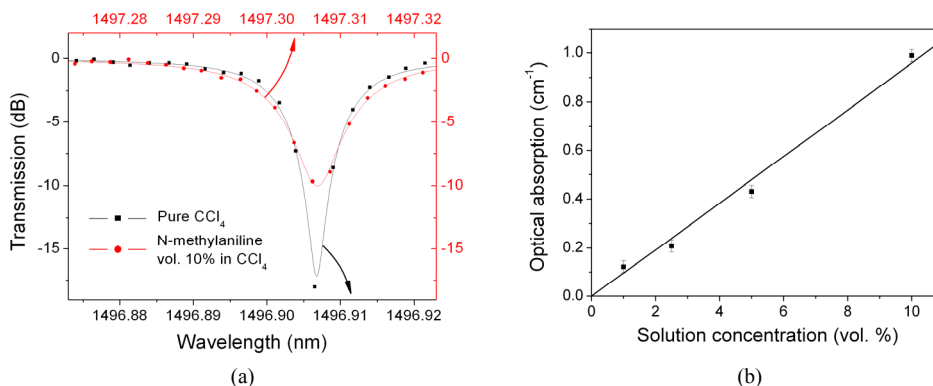


Fig. 2. (a) Microdisk transmission spectra around a resonant peak before and after N-methylaniline solution injection: the dots are experimentally measured data points and the lines are theoretical fitting results based on the generalized coupling matrix formalism; (b) Measured optical absorption of N-methylaniline solutions in CCl₄ as a function of N-methylaniline concentration near the wavelength of 1500 nm.

In order to resolve the trade-off between improving sensitivity and reducing device size (optical path length), we employ a device configuration based on cavity-enhanced absorption [5, 6]. This design leverages optical resonance enhancement to achieve multiple sampling of the analyte and hence improved sensitivity while still maintaining a small device footprint, and therefore it is highly appropriate for future generations of on-chip spectrophotometers.

Cavity-enhanced absorption sensor performance is tested by monitoring the resonant peak extinction ratio variation while injecting a solution of N-methylaniline into the micro-fluidic channel through a syringe pump. The N-H bond in N-methylaniline is known to exhibit an absorption peak near 1500 nm, which is used as the characteristic fingerprint for species identification in our test. The absorption induced by N-methylaniline is derived using the generalized coupling matrix formalism. Figure 2(a) shows the transmission spectra around a resonant peak, both before and after injection of N-methylaniline solution into the microfluidic channel. The resonator works in an under-coupling regime; therefore the additional optical loss due to N-methylaniline absorption results in a decrease of the extinction ratio along with broadening of the resonant peak. The peak absorption at 1496 nm is measured for different N-methylaniline concentrations and the result is shown in Figure 2(b). The excellent linear fit suggests that the sensor exhibits linear response when varying analyte concentrations in the range investigated.

The detection limit in our tests is measured to be 0.02 cm^{-1} based on experimentally determined noise floor. This is attained with a total integration time of 0.6 s. The 0.02 cm^{-1} detection limit is in good agreement with the theoretically simulated value of 0.016 cm^{-1} , using a Monte-Carlo method. The experimentally measured detection limit features an order of magnitude improvement over on-chip infrared spectroscopy using silicon resonators [6]. The result also represents a three-fold improvement compared to our previous result attained with a microfluidic waveguide sensor [7], while the physical device length is decreased by 40-fold. Such comparison clearly

demonstrates the competitive advantage of using micro-resonators for “sensor-on-a-chip” infrared spectroscopy.

4. Protein detection using cavity refractometry

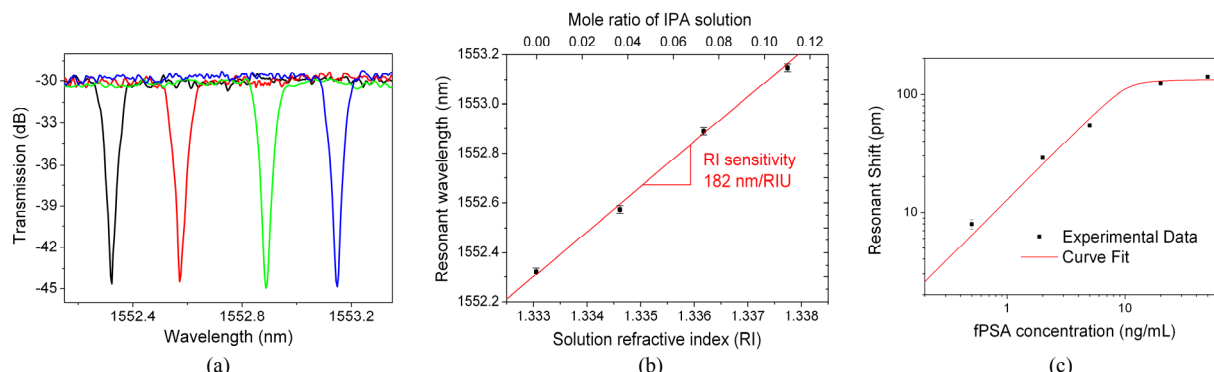


Fig. 3. (a) TM polarization transmission spectra of a Ge-Sb-S microdisk in IPA solutions with four different concentrations; (b) Measured resonant peak wavelength shift as a function of IPA solution mole ratio concentration and corresponding solution refractive index; (c) Resonant wavelength shift due to surface binding of PSA molecules in PSA solutions with different concentrations.

In addition to infrared absorption spectroscopy, optical resonator can be utilized as a highly sensitive tool to detect refractive index changes arising from surface binding of molecules such as proteins. The high-Q optical resonance leads to strong interaction between photons and the molecules to be detected and hence very high sensitivity. We foresee that resonator refractometry offer a promising solution to sensitive, quantitative, and miniaturized biosensors.

The resonator devices used in the test are designed with appropriate dimensions so that the positive thermo-optic (TO) coefficient of glass is cancelled out by the negative TO response of aqueous water, resulting in negligible thermally-induced noise. Bulk refractive index sensitivity is measured via injecting liquids with different refractive indices into the microfluidic channel and measuring the corresponding resonant wavelength shift [8]. TM polarization transmission spectra of a Ge-Sb-S resonator in IPA solutions of various concentrations are shown in Figure 3(a). The resonance shift as a function of IPA concentration and corresponding solution refractive index is plotted in Figure 3(b), and a refractive index sensitivity of (182 ± 5) nm/RIU is inferred from the fitted curve slope.

We selected prostate specific antigen (PSA) as the target species for our biological in-vitro test. PSA has been clinically verified as a biomarker for prostate cancer, and PSA tests using Enzyme-Linked ImmunoSorbent Assay (ELISA) have become a widely accepted early screening technique for prostate cancer. In our experiments, we use an aldehyde chemistry to functionalize the surface of resonators with PSA antibodies. Serial dilutions in phosphate buffer (pH = 7.4) of PSA protein are tested by the resonator sensor. Figure 3(c) shows the resonance shift (after buffer solution wash) resulting from molecular binding in PSA solutions with different concentrations. The experimental data are fitted to a theoretical curve derived based on a molecular binding model we derive and the antibody binding affinity. The excellent agreement between theory and experiment thus validates our molecular binding model. Based on the noise floor measured in the tests (~ 0.8 pm), we can extract a detection limit down to 0.05 ng/mL, which compares favorably with the detection limit of ELISA tests (~ 0.2 ng/mL). Cross-reactivity is tested by performing the same test with human serum albumin (HSA) solution at concentrations up to 50 μ g/mL. No significant resonance shift is observed after buffer wash, suggesting good specificity of the surface functionalization.

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