

Methods to array photonic crystal microcavities for high throughput high sensitivity biosensing on a silicon-chip based platform

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ABSTRACT

A platform for multiplexed detection of several biomolecular events, simultaneously at the same instant of time, is highly desirable in biomolecular diagnostics. Silicon Photonics is ideally suited for the above requirement. Our biosensor comprises a PC microcavity coupled to a PC waveguide. High sensitivities were achieved by slow light engineering which reduced the radiation loss and increased the stored energy in the photonic crystal microcavity resonance mode. Resonances with high quality factor $Q \sim 26,760$ coupled with larger optical mode volumes allowed enhanced interaction with the analyte biomolecules which resulted in sensitivities down to 3.35pg/ml. We have multiplexed up to 64 PC microcavities in series and parallel for high throughput multiplexing using silicon integrated photonic components such as multimode interference power splitters combined with advanced group index engineering.

Keywords: photonic crystal slot waveguide, biosensing, integrated photonics, photonic crystal microarray, group index engineering, multimode interference.

1. INTRODUCTION

Chip-integrated label-free optical biosensing microarrays are extremely attractive in several applications ranging from detection of cancers and allergens, for drug discovery and biomarker discovery in medicine and life sciences, to food science and biodefense. A label-free platform further eliminates steric hindrance and simplifies the biochemistry. Till date, photonic crystal (PC) microcavity based biosensors have demonstrated highest sensitivities among all chip based optical technologies [1-8]. Concentrations down to 50fM (3pg/ml) have been experimentally demonstrated [9]. While there is obviously significant merit in detecting small and smaller concentrations from the perspective of early diagnosis of cancers, very often patient samples are not available in abundance. Consequently, a platform for multiplexed detection of several biomolecular events, simultaneously at the same instant of time, is highly desirable.

We propose a photonic crystal (PC) open sensor chip-integrated platform using silicon integrated photonics for high throughput low cost optical sensing with high sensitivity and selectivity with projected applications in environmental sensing, biomedical sensing, as well as explosives detection for national security. Silicon based devices provide a generic platform for the development of these devices due to its mature processing technology which makes it amenable for cost-effective high volume production.

2. PHOTONIC CRYSTAL BIOSENSORS

Label-free biosensors are particularly attractive since they avoid complex chemistries caused by steric hindrance of the labels. All the different methods of detection transduce the specific binding of the biomolecule of interest to its specific conjugate biomolecule receptor bound to the device substrate, into an electrical, mechanical or optical signal. Optical detection techniques provide freedom from electromagnetic interference. While several platforms based on ring resonators [10], wire waveguides [11] and surface plasmon resonance (SPR) [12] have been investigated, photonic crystal (PC) microcavities, in general, are more compact (of the order of a few square microns in surface area) and have higher sensitivity than other devices due to slow light effect and the larger optical mode overlap with the analyte within compact optical mode volume.

Photonic crystal (PC) microcavities coupled to photonic crystal waveguides (PCWs) have been studied extensively in the literature by us [1-9] and other research groups. In this section, we provide a short summary of the design philosophy in our sensors. Our sensors comprise the familiar L_n type PC microcavity coupled to a $W1$ PCW where n denotes that n air holes have been removed in a row along the Γ -K direction in a triangular lattice PC. $W1$ denotes that the width of the PCW is $\sqrt{3}a$ where a denotes the lattice constant. Various research groups have attempted different design principles to increase the sensitivity of PC biosensors. These have included optimization of the optical mode overlap with the analyte and the resonance quality factor. Increase of the optical mode volume requires that the analyte have an increased overlap with the optical mode. The requirement of large analyte mode overlap with the optical mode resulted in a decrease in the resonance quality (Q) factor. Since the resonance Q -factor determines the length of time the resonant mode is trapped in the optical microcavity, a reduced Q implies a reduced interaction time between light and the analyte and thus a reduced sensitivity.

The total quality factor Q_T of the resonance mode of a PC microcavity, which is related to the photon lifetime τ_p , at frequency ω by $Q_T = \omega\tau_p$ is given by

$$\frac{1}{Q_T} = \frac{1}{Q_R} + \frac{1}{Q_i} \dots \dots \dots (1)$$

where $Q_R = \omega\tau_R$ and $Q_i = \omega\tau_i$, τ_R and τ_i represent the radiation loss and intrinsic cavity loss respectively. τ_R is given by:

$$\frac{1}{\tau_R} = \frac{P_R}{W_E} \dots \dots \dots (2)$$

where P_R denotes the total power radiated by the cavity and W_E denotes the stored energy in the cavity which is proportional to the cavity mode volume. Hence a method that reduces P_R and increases W_E will decrease the radiation loss from the cavity and hence increase the effective Q . A high Q implies that the light is trapped for a longer period of time in the cavity and hence interacts longer with any analyte in the vicinity of the photonic crystal microcavity. In addition, since W_E is proportional to the optical mode volume, a higher W_E leads to potential for larger optical mode overlap with the analyte which also contributes to higher sensitivity.

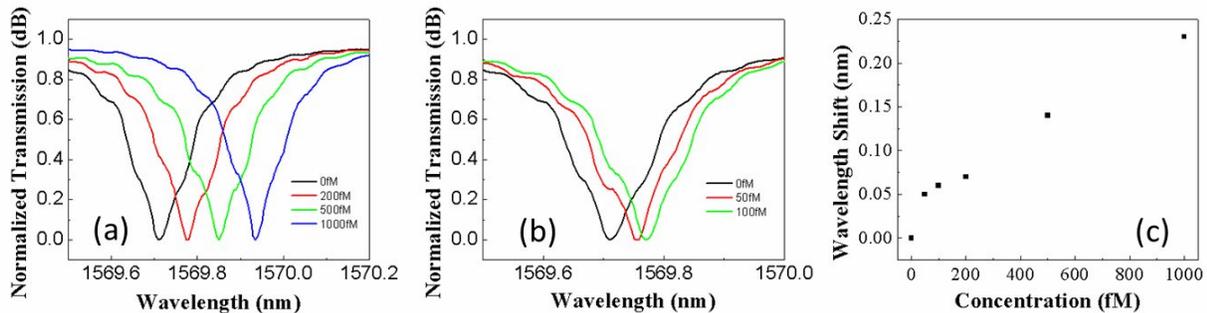


Fig. 1. Experimental drop resonance spectra for the binding between Avidin to Biotin ($K_d \sim 10^{-15}M$) on L55PC microcavity device (a) between 0fM to 1000fM and (b) at the lower concentration range between 0fM and 100fM. (c) Experimental spectral shift for various concentrations of avidin binding to biotin in L55 PC microcavities [9].

We further showed that in biosensing microarrays, where multiple sensor spots must be coated with unique immobilized antibodies, the method of dispensing the antibodies to be immobilized such as via ink-jet printing or by using microfluidic channels, determines the density of integration. The diameter of the dispensed spot in ink-jet printing is 35 μm in our system with a 50 μm center-to-center spacing between individual dispensed spots [1]. The diameter of 35 μm thus determines the upper limit of miniaturization in biosensing microarrays. We therefore employ the benefit of the bio-patterning engineering limitation to increase the size of the photonic crystal microcavity sensor to achieve higher sensitivities.

Photonic crystal microcavities of longer lengths such as L13 (13 missing holes), L21 (21 missing holes) and L55 (55 missing holes) satisfy the above requirement. The details have been presented elsewhere and are not repeated here [9]. We detected the binding of biotin to avidin down to a concentration of 50fM (3.35pg/ml) with L55 PC microcavities [9]. Fig. 1 shows the experimental data. In Fig. 1(a), we show the binding of avidin to binding and the corresponding

resonance wavelength shifts at higher concentrations. In Fig. 1(b), we show the binding of avidin to binding and the corresponding resonance wavelength shifts at lower concentrations showing the minimum experimentally detected resonance wavelength shift at 50fM concentration. In Fig. 1(c), we show the different resonance wavelength shifts as a function of increasing concentration of binding of biotin to avidin.

3. ARRAYING PC MICROCAVITIES IN PARALLEL

The literature in silicon photonic crystal biosensor has primarily focused on a single sensor. However, in the context of a microarray, one must consider methods to interrogate several sensors from a single optical measurement. This requirement is particularly critical in the context of portable platforms, where one does not have the flexibility of benchtop systems.

PC microcavities can be arrayed in parallel using multimode interference (MMI) power splitters. Fig. 2 shows the schematic of the test system on chip.

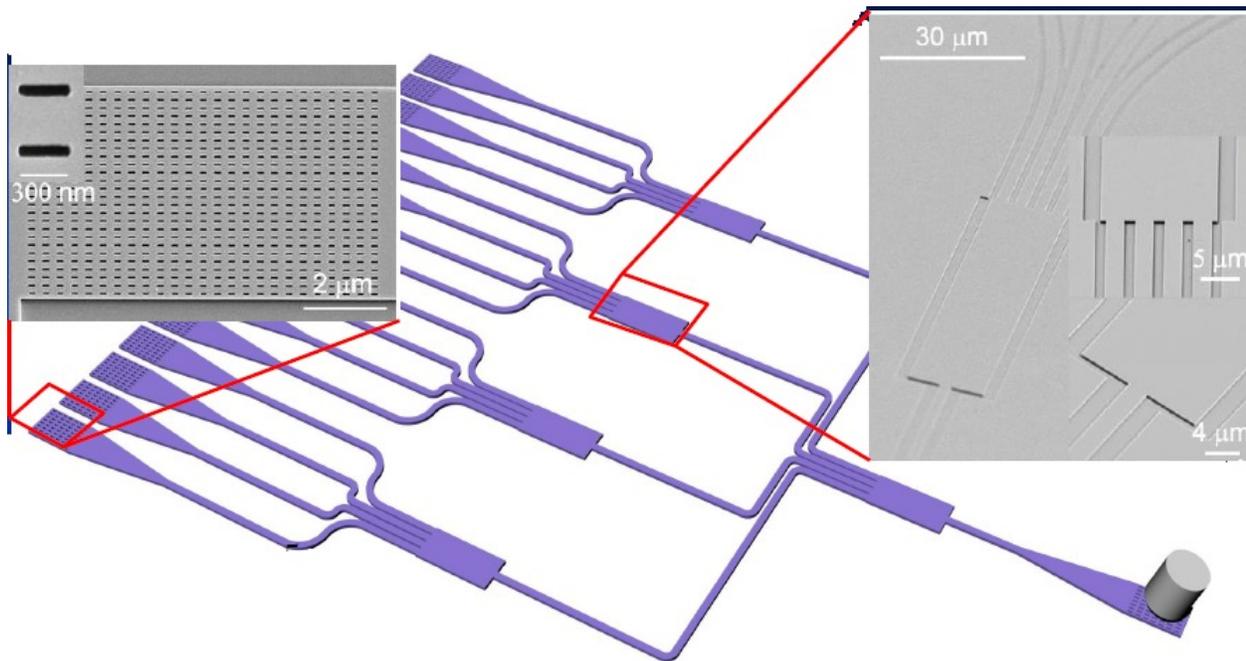


Fig. 2: Generalized schematic of the test system on chip with integrated cascaded 1x4 MMI. Light is coupled into and out of the waveguides using integrated sub-wavelength grating couplers.

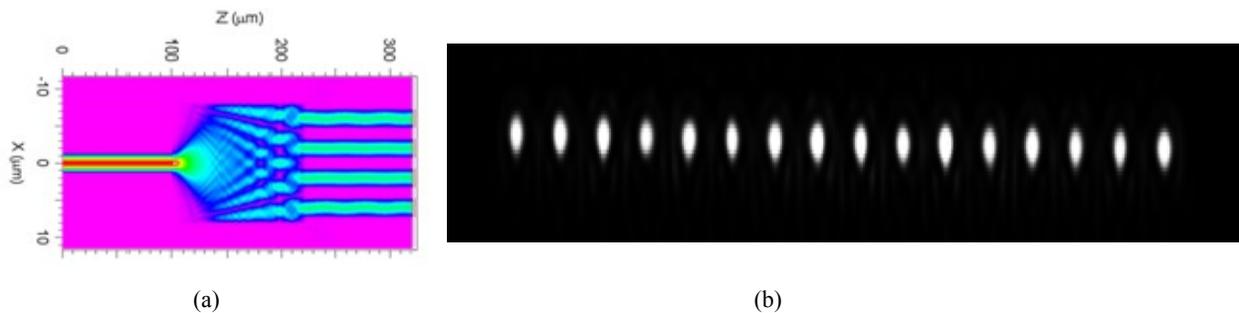


Fig. 3: (a) Beamprop simulation of light propagation and splitting in a 1x4 MMI. Experimentally observed light output from the 16 output channels in Fig. 2.

Fig. 2 shows light being input and output from the integrated device using sub-wavelength grating (SWG) couplers. Magnified scanning electron micrograph (SEM) images of the SWG couplers are also shown. Input light is split into 4 channels using a 1×4 MMI. The light in each output channel of the first stage MMI is further split into 4 channels using a second stage of 1×4 MMIs. As a result, 16 output channels are obtained in parallel.

The MMI was simulated by two-dimensional beam propagation method using RSoft's BeamProp software. The simulation result is shown in Fig. 3(a). The length and width of the MMI were designed as $123\mu\text{m}$ and $16\mu\text{m}$ respectively. Each of the input and output waveguide arms after the 1×4 MMI is $2.5\mu\text{m}$ wide and the output waveguides are separated by $1.5\mu\text{m}$. The light output from the 16 arms is shown in Fig. 3(b).

On each of the 16 arms, PC microcavities can be arrayed in series or in parallel. Unique probe biomarkers are immobilized on each of the PC microcavities. Preliminary measurements were done for the detection of lung cancer cell line lysates. A reduced set comprising a single stage 1×4 MMI was taken and the individual PC microcavities in each arm were functionalized by probe biomarkers as shown in Fig. 4(a). L13 PC microcavities (with 13 missing holes were considered for this experiment).

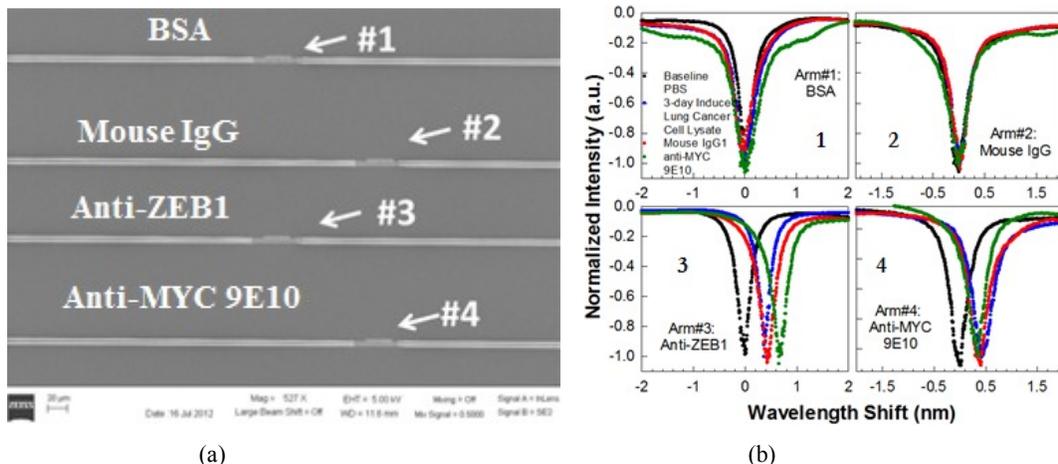


Fig. 4: (a) SEM image of PC microcavities on the 4 arms of a 1×4 MMI. The individual probe biomarkers that are immobilized on top of each PC microcavity by ink-jet printing are indicated. (b) Resonance wavelength changes are monitored for each PC microcavity in (a) simultaneously and the specificity of detection was confirmed via multiplexed detection [13].

As shown in Fig. 4(b), baseline spectra were measured in PBS (phosphate buffered saline) for each of the 4 PC microcavities (spectra in black). Resonance wavelength positions shown in red, blue, green respectively indicate spectra on sequential addition of 3-day induced (1:10) lung cancer cell lysates, mouse IgG1 and anti-MYC 9E10, respectively. The measurements validated the principle of multiplexed detection from the photonics perspective, as well as the specificity of detection from the biochemistry perspective. Details are provided in ref. [13].

4. ARRAYING PC MICROCAVITIES IN SERIES

Multiplexing of two and five H0 (one missing or modified hole) PC microcavities in series were demonstrated previously in 2D [14] and 1D [15] PCs respectively. While the 1D PC couples to a ridge waveguide at group index $n_g \sim 3.7$, the 2D H0 PC microcavity couples to the 2D PCW at $n_g \sim 4.2$. 2D PC microcavities of the L3, L13 or L55 types which have demonstrated experimentally higher sensitivities [9] than devices in ref. [14, 15], however couple to the photonic crystal waveguides at $n_g > 12$ [16]. Group index engineering must therefore be performed when connecting several PC microcavities in series [17].

Fig. 5 shows the experimental spectra when 2, 3 and 4 PC microcavities of the L3 type are connected in series. Figs. 5(a), (c) and (e) show experimental results when group index engineering is employed. Sharp resonance peaks are clearly observed, one resonance arising from each individual PC microcavity. Instead of several PC microcavities in series on the same PCW, we instead have several PC sections connected by ridge waveguides, each PC section comprising a single PC microcavity coupled to a single PCW. In the absence of group index engineering, spectra in Figs. 5(b), (d) and (f) are observed from which it is extremely difficult to distinguish the individual resonances, although the PCW transmission band edges are clearly discernible. The large mismatch in group index between the ridge waveguide

and the individual PCWs results in large Fresnel reflection losses at the PCW-ridge waveguide interface and also gives rise to Fabry-Perot oscillations resulting from the high index cavity formed in between the two strip waveguides.

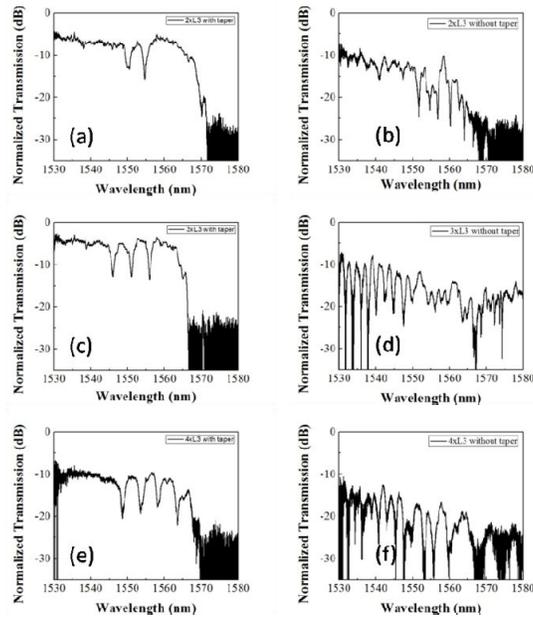


Fig.5. Normalized transmission spectral of W1 PCW with coupled series-connected L3 PC microcavities, a) 2 cavities, c) 3 cavities, e) 4 cavities with index taper; b) 2 cavities, d) 3 cavities, f) 4 cavities without index taper. All spectra are measured in water ambient.

5. ARRAYING PC MICROCAVITIES IN SERIES AND PARALLEL

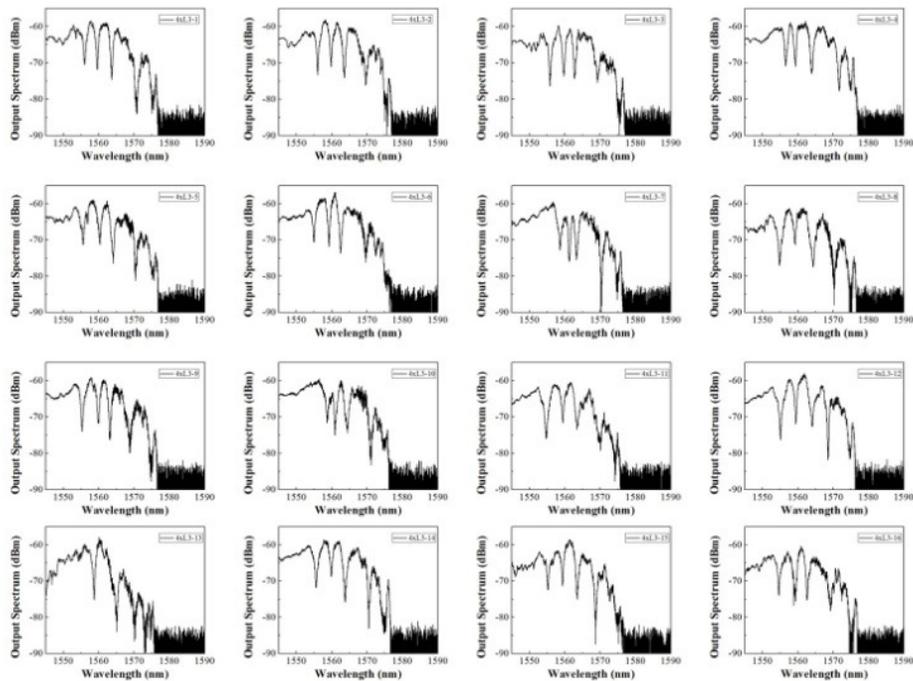


Fig. 6. Output spectral of high density microarray with 16 arms and 4 series-connected L3 microcavity side coupled to PCW on each arm. All spectra are measured in water. The 16 arms are realized by a two stage cascaded 1×4 MMI in Fig. 2

The series cascaded L3 PC microcavities are next combined with two-stage cascaded 1×4 MMIs in Fig. 2. 4 L3 PC microcavities are connected in series on each arm. Thus, in total, 64 PC microcavities are integrated in one device. The output transmission spectrum in all 16 arms is shown in Fig.6. All 16 arms have similar spectra; 4 distinct resonant peaks and sharp band edges can be seen from each spectrum. The Q-factor in all microcavities in water varies between 2000-4000, which is a typical range of Q's that have been observed in oxide clad single L3 PC microcavities in silicon.

6. SUMMARY

In summary, we demonstrated methods to connect PC microcavities in series and parallel in silicon photonic integrated circuits for application in biosensing microarrays. 64 PC microcavities were simultaneously measured at the same instant of time. Baseline spectra were collected from all devices, showing not only multiplexing, but also reproducibility of resonance peaks, which is significant from the perspective of device yield.

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