Application of phase shift ring down spectroscopy to microcavities for biosensing

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ABSTRACT

Phase shift ring down measurement approach (PS-CRDS) is used to develop a real time biosensor which can simultaneously track the quality factor Q and the resonant wavelength λ_r of microcavities as a function of the biodetection event. We have developed a mathematical model to predict the binding event with high accuracy by utilizing the information from these two physical parameters (Q and λ_r). Experiments are also conducted to validate the model. Hence, PS-CRDS biosensor in conjunction with the estimation model, will pave the way for highly sensitive measurements of biological entities/processes ranging from micron to nano scale.

Keywords: Cavity ring down spectroscopy, microcavity, estimation, biosensing

1. INTRODUCTION

Microcavities are widely used for sensing applications. In these applications, binding events induce changes to the effective refractive indices of the cavity modes, which are then detected primarily by tracking the change in the resonant wavelength (λ_r) of microcavities.[1] Such a measurement suffer from variety of noise mechanisms e.g. laser intensity noise and laser wavelength instability. A binding event will also impact the quality factor (Q) of microcavities. We have recently demonstrated the first application of the phase shift ring down measurement approach to microcavities for biosensing.[2] In this sensor it has been shown that both λ_r and Q of a toroidal microcavity can be tracked at the same time as a function of biodetection event. In such a sensor many noise mechanisms such as laser intensity noise and laser wavelength instability which impact the measurement of λ_r are minimized in Q measurement.[2]

Both of these parameters (λ_r and Q) carry information about the biodetection event and can be combined to provide more accurate estimate of the event. By using statistical estimation approaches, we have obtained a mathematical relationship that combines the two measurements (λ_r and Q) and provide a better estimate of a sensing result. The mathematical model is verified by performing the sensing of bulk refractive index change with a microtoroidal cavity immersed in liquid. Hence, phase shift cavity ring down (PS-CRDS) biosensor along with the application of estimation model, has potential of providing more sensitive and accurate results for wide range of biodetection events.

This paper begins with the theoretical background on whispering gallery modes and the cavity ring down spectroscopy in section 2. The estimation model is provided in section 3. The experimental setup and results are shown in section 4 and finally conclusions are outlined in section 5.

2. THEORETICAL BACKGROUND

In this section, concepts of whispering gallery modes and phase shift cavity ring down measurement approach are briefly presented.

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2.1 Whispering Gallery Mode Microcavities

An optical cavity traps light depending on its geometry, material and incident wavelength. In axisymmetric microcavities light circulates in the form of whispering gallery modes (WGM). The portion of WGM lying outside the microcavity interacts with a biological event and as a result its properties (wavelength λ_r and quality factor Q) change. In a wavelength shift based WGM sensor, a biodetection event is tracked as a function of the change in the resonant wavelength of the microcavity. In such a sensor, light can be coupled to the microcavity by using a tapered optical fiber and tunable laser. An occurrence of a binding event at the microcavity surface induces a change in both λ_r and Q of the cavity (fig. 1). The quality factor is related to the

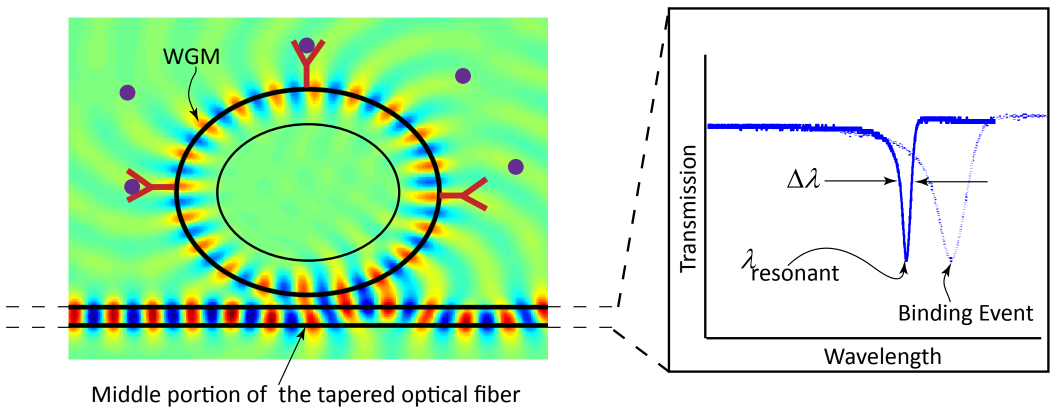


Figure 1. A tapered fiber in conjunction with tunable laser source couples light in a microcavity. A biodetection event induces change in both λ_r and Q of the cavity.

lifetime of photons in the cavity. The Q can be influenced by various loss mechanisms and is given by

$$Q_{total} = \frac{1}{Q_{wgm}^{-1} + Q_{surroundings}^{-1} + Q_{material}^{-1} + Q_{scattering}^{-1} + Q_{contaminants}^{-1} + Q_{external}^{-1}} \tag{1}$$

The wavelength based sensing approach is affected by intensity fluctuations and wavelength instability of the tunable laser which will add noise to the λ_r measurement and thus limit the sensitivity of the sensor. In the wavelength measurement scheme, real time tracking of the quality factor Q as a function of a biodetection event is difficult (requiring a non-linear fitting algorithm which will be slow) and also carries noise from more sources. The limitations for Q measurements can be eliminated by using cavity ring down spectroscopy.

2.2 Cavity Ring Down Spectroscopy (CRDS)

Cavity ring down spectroscopy (CRDS) was first demonstrated in 1984 for measuring reflectivity of cavity mirrors.[3] By measuring the absorption of molecular oxygen, CRDS was transformed into a sensing method in 1988.[4] Many variants of the original design have been proposed and CRDS in conjunction with free space cavities is now a well established technique[5] for sensing absorption of gasses.

In CRDS, a laser pulse is injected into a cavity and its decay rate is measured which can be correlated to the absorption of the cavity medium(figure 2). The decay rate is then extracted by using numerical fitting procedures. The ring down time τ and quality factor Q of a microcavity are related by

$$\frac{1}{\tau} = \frac{2\pi c}{\lambda_r Q_{total}} \tag{2}$$

where τ is the total decay time(ring down time), Q_{total} is defined in 1.

The CRDS is advantageous as it is insensitive to intensity fluctuation. However, it is not appropriate for real time biosensing applications due to difficulty of applying of fitting algorithms in real time for extraction of the ring down time. This disadvantage is overcome by employing phase-shift cavity ring down spectroscopy (PS-CRDS).

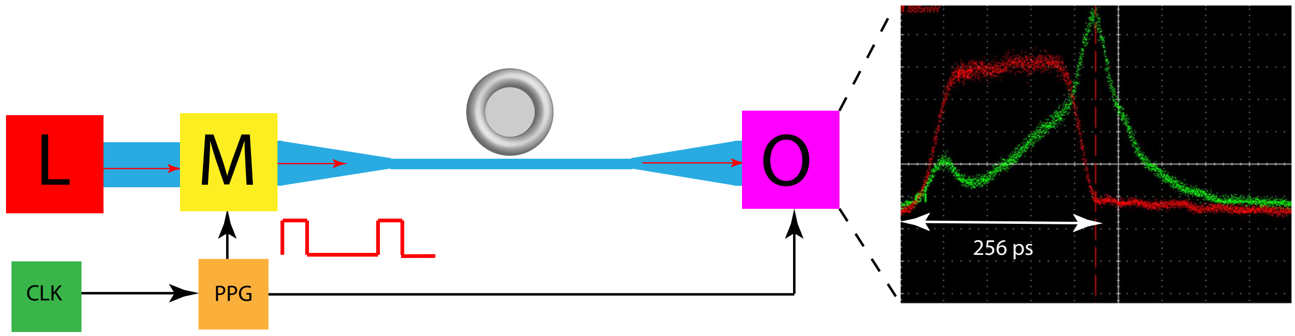


Figure 2. Ring down measurement of a microtoroidal cavity in air. Square waveform (red) is at non resonant wavelength. While green waveform is at the resonant wavelength. L-Laser, M-Electrooptic Modulator, CLK-Clock, PPG-Pulse pattern generator, O-Optical oscilloscope

2.3 Phase Shift-Cavity Ring Down Spectroscopy

PS-CRDS was first demonstrated in 1980 for measuring reflectance of free space cavity mirrors.[6] It was successfully applied to investigate the absorption of vibration states of molecular oxygen in 1996.[7] In PS-CRDS, an intensity modulated laser light is coupled to the cavity:

$$I = I_o(1 + \alpha_{input} \sin \omega t) \tag{3}$$

where α is the modulation depth and ω is the modulation frequency.

A phase shift will be induced in the output light[7] (fig. 3). The phase shift and cavity decay time are related according to the equation 4:

$$\tan \phi = -\omega\tau \tag{4}$$

PS-CRDS is highly suitable for sensing applications as the phase shift can be measured in real time by using phase sensitive detection techniques. By employing a lock in amplifier (phase sensitive detection) for measuring ϕ, PS-CRDS also becomes insensitive to intensity fluctuations of the laser source.

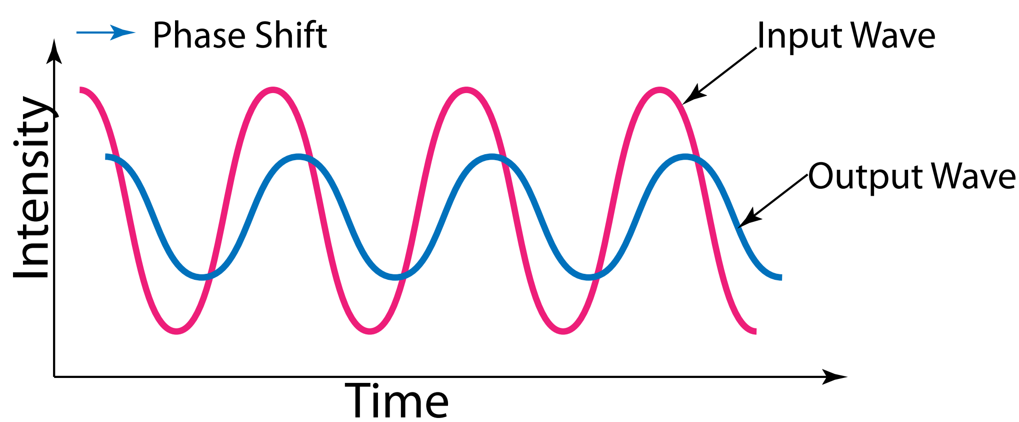


Figure 3. PS-CRDS Principle

3. ESTIMATION

From our recently demonstrated PS-CRDS biosensor,[2] we can obtain formation about a biodetection event (X) from two experimentally measured parameters i.e. change in resonant wavelength ($\Delta\lambda$), and quality factor

(ΔQ)as a function of the biodetection event. Both of these experiential parameters represent entirely different physical processes, yet carry information about the same event. Figure 4 represents an intuitive picture of the estimation process. i.e. Mathematically we can write:

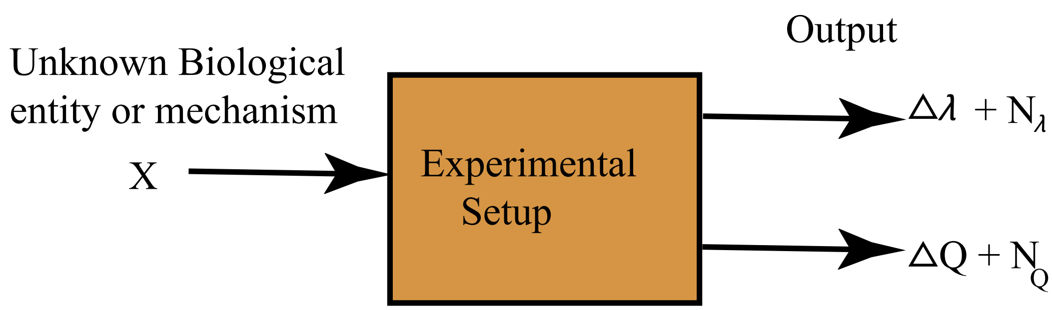


Figure 4. Estimator Concept

$$\Delta\lambda = f(\Delta X) + N_\lambda \tag{5}$$

$$\Delta Q = f(\Delta X) + N_Q \tag{6}$$

where N_λ and N_Q are noises in each measurement.

Depending upon the experimental setup, both N_λ and N_Q can be correlated or uncorrelated. By applying statistical estimation techniques,[8] and with the assumptions that the sensor response is linear and there is no absorption due to biodetection event, following relationship can be derived:

$$\hat{\Delta X} = \frac{\left(\frac{\sigma_Q}{m_Q}\right)^2 \left(\frac{\Delta\lambda + \mu_\lambda}{m_\lambda}\right) + \left(\frac{\sigma_\lambda}{m_\lambda}\right)^2 \left(\frac{\Delta Q + \mu_Q}{m_Q}\right)}{\left(\frac{\sigma_\lambda}{m_\lambda}\right)^2 + \left(\frac{\sigma_Q}{m_Q}\right)^2} \tag{7}$$

where σ and μ are standard deviation and mean of the noises. m_λ and m_Q are slopes of linear curves(i.e. the sensitivities) for change in λ_r and Q as a function of the biodetection event respectively. In deriving the above relationship it is also assumed that the noises have normal distribution and are uncorrelated. Both of these assumptions are valid for our experiments.

4. EXPERIMENTAL SETUP AND RESULTS

The experimental setup is shown in figure 5. A tapered fiber[9] is used to couple the light to a microtoroidal cavity.[10] The two function generators, FG_1(100mHz, 6V peak-to-peak, triangular wave) , and FG_2 (40MHz, 200mV peak-to-peak, sinusoid) are simultaneously modulating the wavelength and intensity of the tunable laser (Yenista, Tunics T100, 1550nm tunable laser) respectively. The shift in phase between the reference sinusoid and the sinusoid at the fiber output is continuously recorded by phase sensitive detection technique which is implemented by using a 50Mhz Lock in amplifier. The resonant wavelength is also tracked simultaneously on an oscilloscope.

The toroidal microcavity is immersed in a heavy water (D_2O) microacquarium. The heavy water is used to reduce the absorption losses at $1550nm$.[11] The change in refractive index (δn) in micoracquarium is introduced by injecting a D_2O salt solution. Both the quality factor and the resonant wavelength are tracked as a function of this injected refractive index change (RI). The results are shown in figure 6. The results show that both the λ_r and Q change linearly as a function of the introduced RI change in the microacquarium. The estimator (Eqn. 7) is then applied to the experimental points in figure 6 and results obtained are consistent with the injected RI changes.

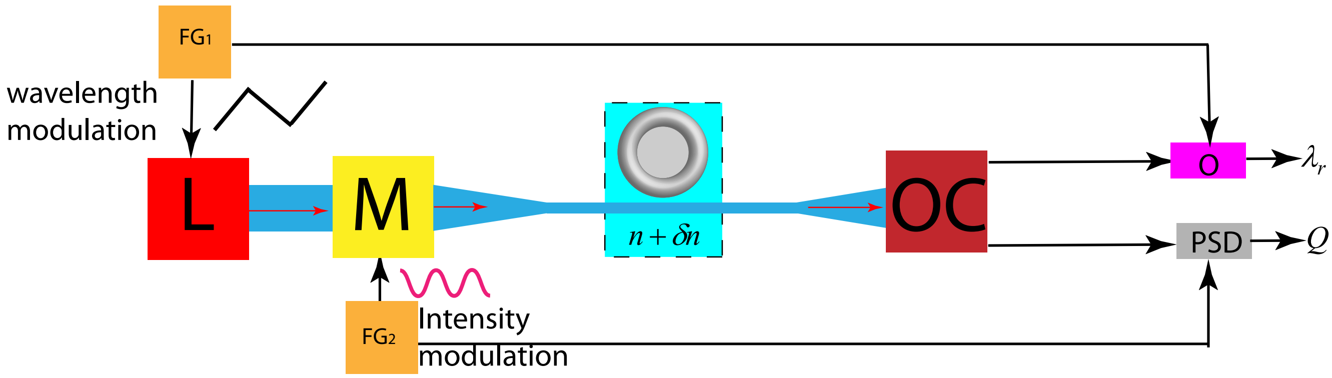
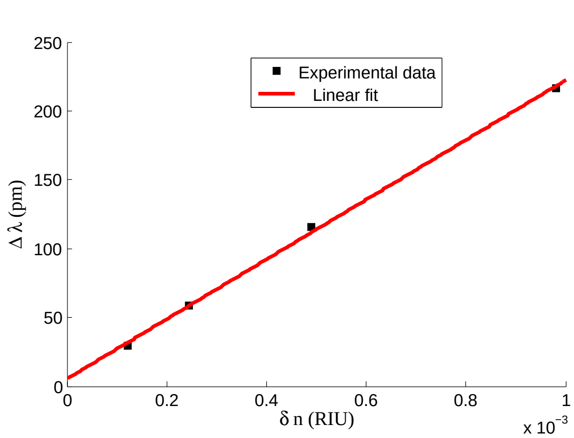
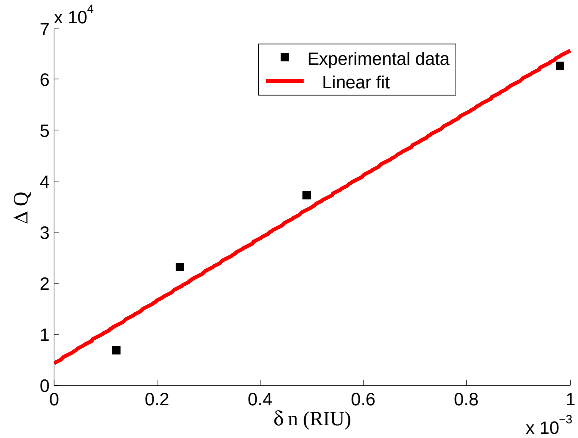


Figure 5. Experimental Setup, FG - Function Generator, L-Tunable laser, M- Electrooptic Modulator, OC- 50/50 optical coupler, O-Oscilloscope, PSD-Phase sensitive detection technique using Lock in amplifier



(a) Wavelength



(b) Quality factor

Figure 6. Experimental results

5. CONCLUSIONS

This work shows that the PS-CRDS sensor in conjunction with estimation model can utilize both the experimental measurements (λ_r, and Q) for predicting the biodetetction event. The current work will find applications in a wide range of sensing schemes.

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