Evaluation of single virus detection through optical biosensor based on microsphere resonator

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Evaluation of single virus detection through optical biosensor based on microsphere resonator

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ABSTRACT

Shift of resonance frequency in microsphere optical resonator due to attachment of a desirable particle is obtained. Our 3-D finite element numerical method (FEM) simulations' results show the path of light through microsphere and its variation due to attachment of particle. It is apparent that after attachment of particle to microsphere's surface, light is inclined to pass through the particle. Subsequently, the path of light becomes longer than previous. Because of this phenomenon, the resonance wavelength shifts to longer wavelengths. It is shown that microsphere optical resonator is a prominent biosensor for single virus detection since we applied characteristics of virus for particle in our simulations. Response of this biosensor depends on the characteristics of particle like its radius as we show in this article. Transmission spectrum of fiber which reveals a selected resonance frequency, have been studied in the frequency range of 106.3 to 107 THz under three different sizes of particles. The results show that the amount of frequency shift rises by enhancement of particle's size.

1. Introduction

Virus particles are a major cause for human diseases, and their early detection is of added urgency since modern day travel has enabled these diseases agents to be spread through population across the globe [1]. Early detection of viruses which are critical issue in diagnosis of viral diseases can be hastened by biosensors. There are many types of biosensors with diverse physical basics such as electrochemical biosensors [2], mass-based biosensors [3], optical biosensors [4], etc. Among these different types of biosensors, optical biosensors provide more efficiency because of their exclusive features which stem from light-based detection. These types of biosensors have high sensitivity, immunity to electromagnetic interferences, and fast detection procedure [5]. One kind of optical biosensors is Whispering Gallery Mode (WGM)-based optical biosensors [6] which provide label free detection. The development of label free detection method of biosensing would bring significant benefits, specially for portable or hand-held diagnostic devices. There are many potential advantages to label free approaches, most noteworthy is that they can provide direct monitoring of analyte binding to target molecules without modifying the molecules of interest with labels or by using reporter systems. Labels can structurally and functionally interfere with an assay, may not be specific and may be difficult to conjugate. The WGM resonance phenomenon has recently received increasing attention due to their high potential for the realization of micro-lasers [7], narrow filters [8], optical switching [9], miniature biosensors [10], high resolution spectroscopy [11], etc. Detection of viruses is one of the high potential applications of WGM-based biosensors. For instance, the research group of F. Vollmer et al. probed the single virus detection by microsphere resonator, practically [12]. WGM phenomenon is occurred in optical microcavities (optical micro resonators) [13]. Optical microcavities confine light in a circular path and make resonance phenomenon in specific wavelengths [14,15]. So, the resonance wavelengths emerge as depths in transmission spectrum. There are various types of optical microcavities according to their shapes. Three major types of optical microcavities can be seen in Fig. 1.

Despite easy fabrication process, the ring resonator has a small quality factor (Q) rather than micro toroid and microsphere [13,14]. Specifically, microspheres are three-dimensional WGM resonators, a few hundred micrometers in diameter, often fabricated by simply

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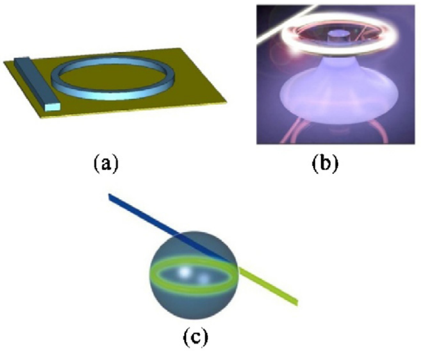

(a) (b) (c)

Fig. 1. Different types of optical microcavities, (a) Micro-ring resonator, (b) Micro-toroid resonator, (c) Micro-Sphere resonator.

melting the tip of an optical fiber. The total optical loss experienced by a WGM in such resonators can be extremely low (Q as high as 10^8 are routinely demonstrated) [16]. These extraordinary Q-values translate directly to high energy density, narrow resonant-wavelength lines and a lengthy cavity ring down. Because of this advantages, they are prone structure for being competent optical biosensors.

Microsphere resonators are used for biosensing applications on the basis of shift of resonant frequency due to attachment of desirable particles to the surface of microspheres. There are many cases which microspheres are used as a high sensitive biosensor for detection of particles based on shift of resonance frequency [17,18]. Simulation and evaluation of its results for microsphere resonator-based biosensor is essential to develop this type of biosensor. Quan and Guo evaluated microsphere resonator-based biosensors by 2-D simulation [19]. They supposed microsphere as a ring resonator and attachment of particles to surface of microsphere like increase of efficient radius of sphere. As this is not a comprehensive and adequate evaluation for microsphere resonator-based biosensors, we evaluated this type of biosenosr by comprehensive three-dimensional simulation with finite element numerical method (FEM). The shifts of resonance frequencies and the quality factor (Q) were obtained through simulation results. Also, evaluation of obtained electromagnetic fields' propagation to show the origin of shift of resonance frequency in this type of biosensor is carried out in this paper. Finally the effect of particle's radius in the amount of resonance frequency shift is probed.

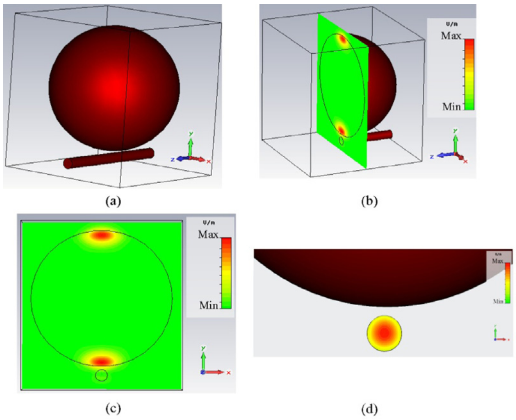
2. Mathematical formulation and model analysis

In order to determine of a microsphere resonant modes, Maxwell's equations in spherical coordinate must be solved which results in characteristic equation. For solving of this equation for obtaining of microsphere modes, we use Finite Element numerical method. Solving of Maxwell's equation for light in spherical coordinate leads to following characteristic equation [20]:

$$\left(\eta_s\alpha_s + \frac{1}{R_s}\right) \times j_l(kn_sR_s) = kn_s \times j_{l+1}(kn_sR_s) \qquad (1)$$

where η_s is 1 for TE and ${n_s}^2/{n_0}^2$ for TM. n_s and n_0 is refractive indices of sphere and surrounding medium, respectively. Also, R_s is the radius of microsphere, l is a number obtained from solving Helmholtz equation with separation of variable method, and k is the wave number. j_l and j_{l+1} are spherical Bessel functions. In (1), $\alpha_s = ({\beta_l}^2 - k^2{n_0}^2)^{1/2}$ where $\beta_l = (l^2+l)^{1/2}/R_s$.

Pattern of modes in a microsphere are characterized by three following numbers: l, m, and n. The fundamental mode of a microsphere is obtained when $l = m$ and $n = l$ [14]. An initial guess for l is $l = kn_sR$. It is derived from the approximation that β_l is nearly equal to l/R, and that being a projection of k, β_l will be of only slightly smaller magnitude than the k vector, especially in the limits of a fundamental mode and a large sphere size compared to the wavelength [20].



(a) (b) (c) (d)

Fig. 2. (a) Perspective of microsphere and optical fiber system. (b) Perspective of fundamental mode of microsphere in x–y plane. (c) Fundamental mode of microsphere. (d) Fundamental mode of optical fiber.

Because of acquiring maximum coupling between optical fiber and microsphere, the mode of microsphere must be chosen as it has same pattern like mode of fiber. Fig. 2(a) shows the structure of microsphere-based biosensor in our simulations. The analyzed modes of microsphere and optical fiber through simulations are shown in Fig. 2(b)–(d). As it is apparent in Fig. 2(b) and (c), the mode of light in the microsphere is fundamental mode. Giving the fact that optical fiber is single mode that its fundamental mode is depicted in Fig. 2(d), the patterns of operation modes in microsphere and optical fiber are similar. This selection of operation wavelength which leads to emerge similar fundamental modes in coupling optical fiber and microsphere resonator, results in high coupling strength and quality factor.

3. Microsphere-based biosensor principles and simulation results

The basis of this type of biosensors is WGM phenomenon. An optical WGM may be represented by a light wave that circumnavigates near the surface of a glass sphere. Attachment of a particle to the surface of microsphere causes shift in resonance frequency of transmission spectrum due to perturbation in path of light [18,21]. Consequence of this variation in traveling path of light is satisfaction of condition of WGM in the other frequency which advents as shift of resonance frequency.

We simulated a microsphere with 24 μm diameter by Finite Element numerical method. Given the fact that microsphere and optical fiber typically are fabricated from silica, we considered 1.45 which is the Refractive Index (RI) of silica for microsphere and optical fiber. Fig. 3 shows the WGM phenomenon in our 3D simulation of this structure. It is obvious from Fig. 3 that in resonance frequency, the light passing in the fiber will be trapped in microsphere, so this frequency will be omitted from transmission spectrum of optical fiber.

The next step is attachment of a particle to the surface of microsphere which can be seen in Fig. 4. It is assumed that spherical-shape particle has 0.15 μm radius and RI near the RI of common viruses. We placed the particle in y–z symmetry plane of microsphere which results in maximum shift because in this plane the particle is in maximum reach of propagation field of light [21]. By this way we can evaluate this biosensor in single detection scale. Giving the fact that molecular size of antibody for virus

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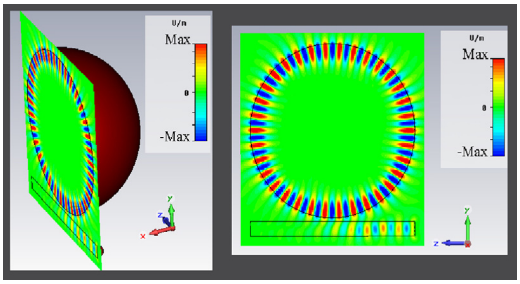

Fig. 3. WGM phenomenon in microsphere.

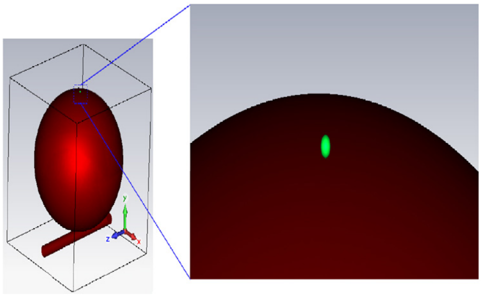

Fig. 4. Attachment of a particle to the surface of microsphere.

trapping is between 12 and 15 nm [22], we ignore this layer on the microsphere's surface and place particle tangent to the surface of microsphere. Transmission spectrum of microsphere resonator without particle attachment is shown in Fig. 5. The obtained Q for this microsphere resonator is calculated as 8.8×10^4. This amount of Q is far small from ultimate Q for microsphere which is almost 10^9 [23]. This smallness of Q for simulated microsphere is because of its small diameter.

The increase of microsphere's size results in higher Q, but it decreases capability of small-size single particle detection. Fig. 6 shows the result of attachment a particle with 150 nm size to the surface of the microsphere. It causes a shift of resonance notch in the transmission spectrum. Δf is the amount of the frequency shift due to attachment of this particle to the surface of the microsphere. The simulation results reveal that this amount of Δf is almost 152.59 MHz. In Fig. 6, Δf is depicted exaggeratedly to clarify the shift of the resonance frequency. This amount of frequency shift is sensible by specific optical methods like wavelength-phase conversion, easily [24]. The shift of light from the microsphere to the particle which make the path of light longer, is shown in Fig. 7. It shows the magnitude of electromagnetic field in the shown cross line. It also depicts the fundamental mode of light in microsphere and the fact about capture of light by particle. The transfer of energy of light from the microsphere to the particle can be inferred from this simulation's result.

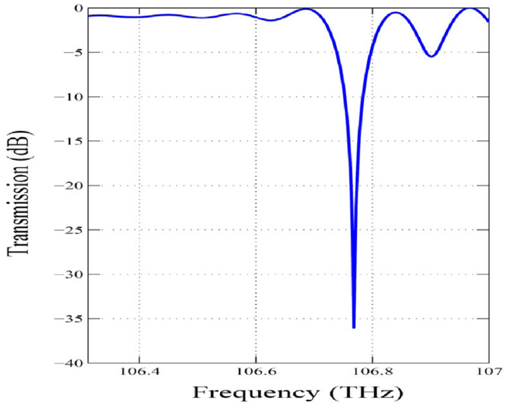

Fig. 5. Transmission spectrum of microsphere biosensor without particle attachment.

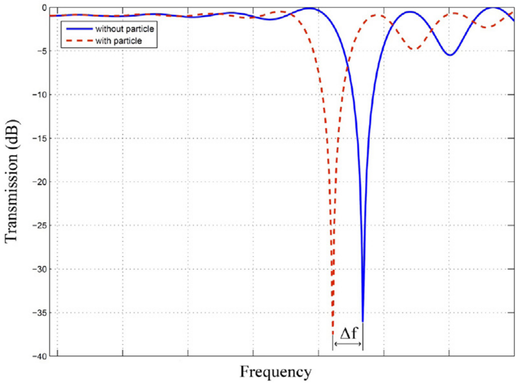

Fig. 6. Shift of the resonance frequency due to attachment of particle.

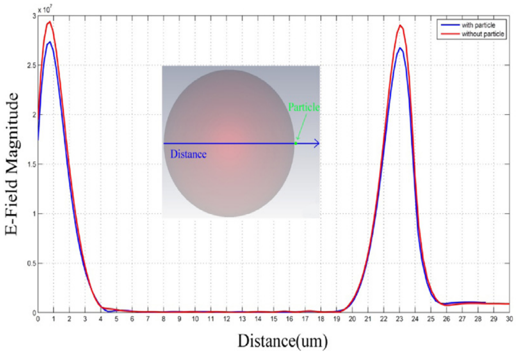

Fig. 7. Intensity of propagating electromagnetic field in the shown cross line.

There is an analytical formula for relationship between the amount of shift of resonance frequency and particle's characteristics when particle attaches to the equator of microsphere [12]. We found the resonance frequency shift for three radiuses of particle, 100, 150, and 200 nm. We compared our results of simulations with this formula as it can be seen in Fig. 8. There is good agreement between our simulation results and reported formula. The amount of resonance frequency shift increase by enhancement of particle's

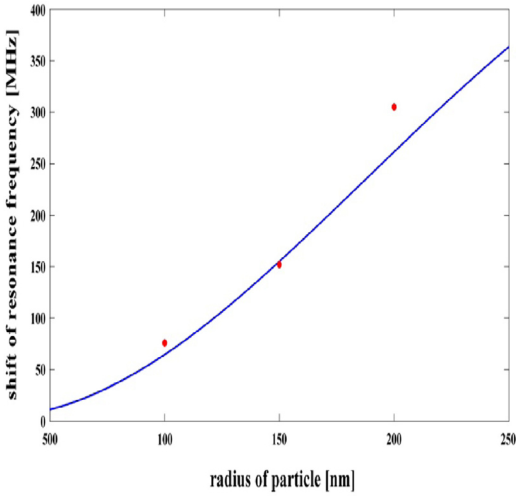

Fig. 8. Shift of resonance frequency versus radius of particles.

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radius. This fact is reasonable because the path of light through particle increases further when the radius of particle is enhanced. It is noteworthy to mention that the size, shape and refractive index of particles for simulation are selected regarding the characteristics of viruses. Majority of viruses are spherical shape and their size range in 20–400 nm in diameter [25].

4. Conclusion

The variation in the path of light which results in the shift of resonance frequency in microsphere resonator due to attachment of particle to its surface was evaluated by 3-D numerical simulations. This amount of shift depends on the radius of particle as we demonstrated it by simulation. We considered three particles with size and optical characteristics for majority of viruses. The amount of frequency shifts for these three particles with radius of 100, 150 and 200 nm, are 76, 152 and 305 MHz, respectively. In conclusion, Microsphere is an appropriate biosensor that can detect the existence of single desirable virus in environment.

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