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

H. Ahmadi [a], H. Heidarzadeh [a], A. Taghipour [a], A. Rostami [a,b,*], H. Baghban [b], M. Dolatyari [b], G. Rostami [b]

[a] Photonics and Nanocrystal Research Lab (PNRL), University of Tabriz, Tabriz 5166614761, Iran
[b] School of Engineering-Emerging Technologies, University of Tabriz, Tabriz 5166614761, Iran

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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

* Corresponding author at: Photonics and Nanocrystal Research Lab (PNRL), University of Tabriz, Tabriz 5166614761, Iran. Tel.: +98 411 3294626; fax: +98 411 3294626.
E-mail address: Rostami@tabrizu.ac.ir (A. Rostami).

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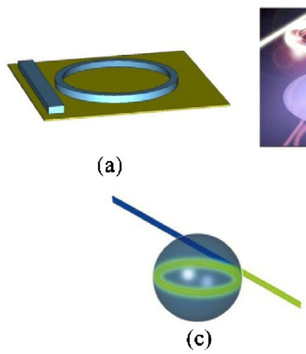

Fig. 1. Different types of optical microcavities, (a) Micro-ring resonator, (b) Micro-toroid resonator, (c) Micro-Sphere resonator.

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]:

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

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 $\beta_l = (l^2+1)^{1/2}/R_s$.

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].

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.

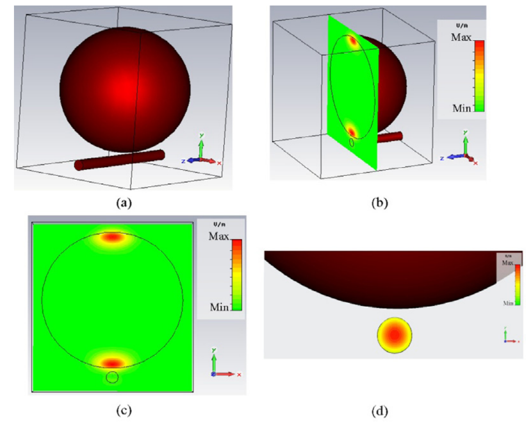

Fig. 2. (a) Perspective of microsphere and optical fiber system. (b) Perspective of fundamental mode of microsphere in x–y plane. (c) Fundamental mode of microsphere. (d) Fundamental mode of optical fiber.

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