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Design and Development of Optical Biosensor for Medical Applications

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Abstract: Currently, cancer detection is a difficult, long and invasive process. Cancer is a common condition and where the body cell began too grows and reproduces in an uncontrollable manner. Cancer ranks 2nd after heart disease in causing death. Many times the symptoms are unclear or tumors are detected far into the stages of cancer, especially in the case of breast cancer detection below the age of 40 years. Clinical diagnostics aim to recognize abnormal characteristics as efficiently and quickly as possible. Already, mammography, sonography, ultrasound techniques are available for breast cancer detector but they can give ambiguous report because of higher order granular. Therefore, for solving this problem, in this work optical ring resonator (single and double) and waveguide biosensor have been developed. The optical biosensor is a faster, cheaper alternative for cancer cell detection. With this new machine for cancer screening integrated into the clinic, a more comprehensive healthcare tool would be more widely available to health care professionals. This project addresses optical biosensors. A lens (Virtual blood cell) is placed in the ring resonator which acts as a virtual blood cell, and then light is passed in side ring resonator through waveguide for detection of cancerous cell. Cancerous blood cell and healthy blood cell have been developed by changing the refractive index of cell, while the refractive index of normal cells is 1.30-1.32µm and that of cancerous cell is 1.37-1.40µm.

Keywords: OFRR, Optical Biosensor, Optical Ring Resonator, Optical Wave Guide.

I. INTRODUCTION

Cancer is a group of diseases involving abnormal cell growth with the potential to invade or spread to other parts of the body. Cancer is a class of diseases characterized by out-of-control cell growth. Cancer harms the body when damaged cells divide uncontrollably to form lumps or masses of tissue called tumors (except in the case of leukemia where cancer prohibits normal blood function by abnormal cell division in the blood stream). Tumors can grow and interfere with the digestive, nervous, and circulatory systems and they can release hormones that alter body function. Tumors that stay in one spot and demonstrate limited growth are generally considered to be benign.
More dangerous, or malignant, tumors form when two things occur [1].

- A cancerous cell manages to move throughout the body using the blood or lymph systems, destroying healthy tissue in a process called invasion.
- That cell manages to divide and grow, making new blood vessels to feed itself in a process called angiogenesis.

When a tumor successfully spreads to other parts of the body and grows, invading and destroying other healthy tissues, it is said to have metastasized. This process itself is called metastasis, and the result is a serious condition that is very difficult to treat.

A. How is Cancer Classified?

There are five broad groups that are used to classify cancer:

- Carcinomas are characterized by cells that cover internal and external parts of the body such as lung, breast, and colon cancer.
- Sarcomas are characterized by cells that are located in bone, cartilage, fat, connective tissue, muscle, and other supportive tissues.
- Lymphomas are cancers that begin in the lymph nodes and immune system tissues.
- Leukemia's are cancers that begin in the bone marrow and often accumulate in the bloodstream.
- Adenomas are cancers that arise in the thyroid, the pituitary gland, the adrenal gland, and other glandular tissues. Biopsy as the definitive diagnostic and primary treatment method [2].

B. Cancer Cells and Cell Biology

It's important to have some basic knowledge on the related topics of cancer cells and cell biology. Furthermore, an analogy is used to explain the process behind the project.

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There are many different cells and origins of cells in the human body. One type of cell that is used in the lab is leukocytes or white blood cells. These cells primarily fight off foreign materials and infections within the body. There are many subtypes of cells found within the white blood cells such as monocytes, neutrophils, and lymphocytes [3].

II. BIOSENSOR

Biosensors are devices that are designed to detect a specific biological analyte by essentially converting a biological entity (i.e. protein, DNA, RNA) into an electrical signal that can be detected and analyzed. A biosensor is a device used to detect a biological analyte, be it environmental or biological in origin (i.e. within the human body). Information such as whether or not the analyte is present and at what level is transduced into an electrical signal that can be amplified, displayed, and analyzed [4]. Examples of analytes include proteins (antigen, antibody, and enzyme), nucleic acid, or other biological or metabolic component (i.e. glucose).

In terms of cancer, the analyte being detected by the biosensor is a tumor biomarker. Thus, by measuring levels of certain proteins expressed and/or secreted by tumor cell biosensors can detect whether a tumor is present, whether it is benign or cancerous, and whether treatment has been effective in reducing or eliminating cancerous cells. Biosensors that can detect multiple analytes may prove particularly useful in cancer diagnosis and monitoring, since most types of cancer involve multiple biomarkers. The ability of a biosensor to test for multiple markers at once not only helps with diagnosis, but also saves time and financial resources [5].

A. Advantages

- They can measure nonpolar molecules that do not respond to most measurement devices.
- Biosensors are specific due to the immobilized system used in them.
- Rapid and continuous control is possible with biosensors.
- Response time is short (typically less than a minute).

B. Disadvantages

- Heat sterilization is not possible because of denaturalization of biological material.
- Stability of biological material (such as enzyme, cell, antibody, tissue, etc.), depends on the natural properties of the molecule that can be denaturalized under environmental conditions (pH, temperature or ions).

III. OPTICAL RING RESONATOR

Optical ring resonators have recently been under intensive investigation as a promising label free bio sensing technology. This sensor realizes on light analyte interaction to convert to presence of biological1 analyte into quantitatively measurable optical signal. Here, an analyte means a substance or chemical constituent that is of interest in an analytical procedure. The OFRR, which is a glass capillary based cavity, integrates micro fluidics with photonics. The ring resonator includes a ring, a waveguide and a gap separating the ring and waveguide. In a ring resonator Whispering Gallery modes(WGM's) form due to the total internal reflection of light along the curve boundary surface. The WGM has an evanescent field outside the ring resonator with a characteristic length [6].

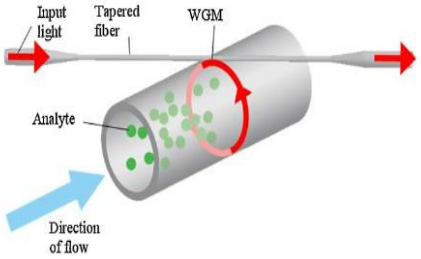

Figure 1. OFRR Sensor.

The thin wall of a silica micro capillary forms a ring resonator able to support whispering gallery modes (WGMs) and, at the same time, has the function of a micro fluidic core for fluid flowing. The WGM is a surface mode which evanescently couples with liquid sample flowing through the capillary or with the analyte on the interior surface wall. Capillaries that have very smooth sidewalls can be used, thus allowing high Q factors of the order of 10^6 . The sensing

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capability to bulk RI changes in the Core has been successfully demonstrated and a bulk detection limit of approximately 10^{-7} RIU has been proved [7].

A. Optical Single Ring Resonator Principle

The basic optical phenomenon that allows ring resonators to function is the circular resonant mode, which relies on total internal reflection to circulate light at resonant wavelengths. In a ring resonator, there exist two types of these modes that can be utilized for various applications, the whispering gallery mode (WGM), the circulating waveguide mode. The difference between the WGM and the circulating waveguide mode is that the WGM is guided by the total internal reflection at the outer boundary of the ring resonator, whereas the circulating waveguide mode is confined by the total internal reflection at both the outer and inner boundary. The former case occurs in a microsphere, micro droplet, micro disk, and thick-walled capillary ring resonator, whereas the latter one is represented by a ring-shaped waveguide and thin-walled capillary ring resonators [8].

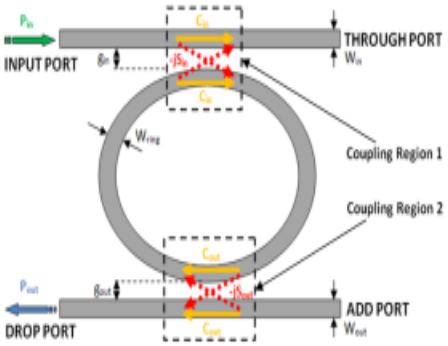

Figure 2. Principle of OFRR.

B. Optical Double Ring Resonator

A Double ring resonator with rings of varying radii in series showing the relative intensities of light passing through on the first cycle. Note that the light passing through a double ring resonator would more often travel in multiple loops around each ring rather than as pictured [9].

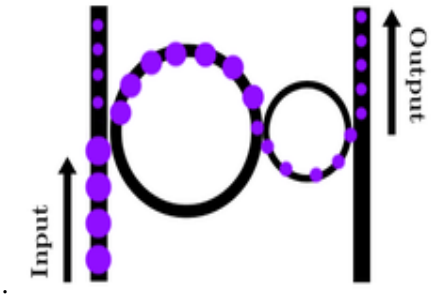

Figure 3. Double Ring Resonator.

In a Double Ring Resonator, two ring waveguides are used instead of one. They may be arranged in series (as shown on the right) or in parallel. When using two ring waveguides in series, the output of the double ring resonator will be in the same direction as the input. When the input light meets the resonance condition of the first ring, it will couple into the ring and travel around inside of it.

As subsequent loops around the first ring bring the light to the resonance condition of the second ring, the two rings will be coupled together and the light will be passed into the second ring. By the same method, the light will then eventually be transferred into the bus output waveguide. Therefore, in order to transmit light through a double ring resonator system, we will need to satisfy the resonant condition for both rings as follows:

$$2\pi n1R1 = m1\lambda1 \quad (1)$$

$$2\pi n2R2 = m2\lambda2 \quad (2)$$

Where, m1 and m2 are the mode numbers of the first and second ring respectively and they must remain as positive integer numbers.

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For the light to exit the ring resonator to the output bus waveguide, the wavelength of the light in each ring must be same. That is,

$$\lambda 1 = \lambda 2 \qquad (3)$$

For resonance to occur. As such, we get the following equation governing resonance:

$$\frac{n1R1}{m1} = \frac{n2R2}{m2} \qquad (4)$$

Note that both m1 and m2 need to remain integers.

C. Advantages

- The OFRR has achieved a sensitivity of 10^{-7} refractive index unit (RIU), which corresponds, to a mass detection limit of subpicograms per square millimeter, competitive with or even better than other commercialized label-free sensors such as surface Plasmon resonance (SPR) sensors [10].
- In addition, as compared to other label-free sensors, the OFRR sensor is more suitable as a cheap and disposable device due to its low fabrication cost.
- Small physical size.
- Easy operation principle.
- Multiplexing capability.
- Small sample consumption volume.

IV. SIMULATIONS RESULTS

A. Waveguide

Figure4 represents the simple straight waveguide in which a cell is placed at the centre shown by green colour. This cell is under observation to detect whether the cell is Normal or Cancerous.

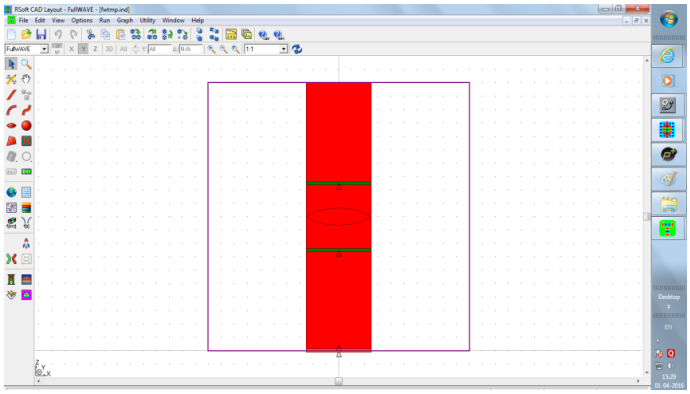

Figure 4. Optical Waveguide Structure for cancer detection.

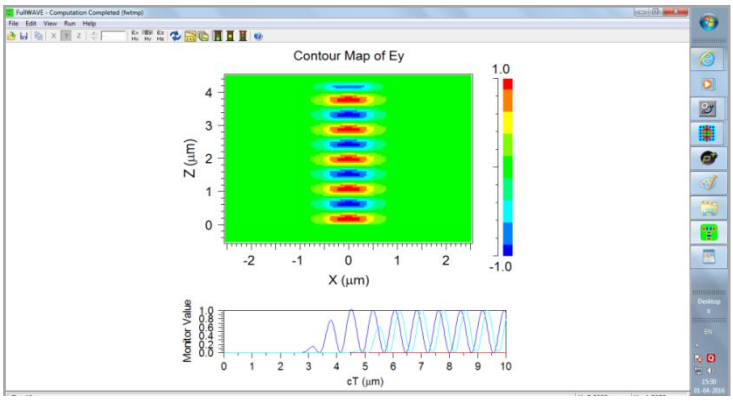

Figure 5. Plot of Optical Waveguide for Time vs. Amplitude.

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The graphical analysis of a waveguide can be seen in Figure5 When a beam of light is passed through this waveguide, the cell absorbed some amount of light. When the output beam of light is compared with the input beam of light, the obtained result does not clear whether the cell is Normal or Cancerous.

B. Optical Ring Resonator

The FDTD has been commonly used for numerical studies f4or optical fibre system. A simulation domain is of 140µm*140µm rectangular area. A ring resonator is centrally located and two waveguides are positioned on both sides of resonator. Separation distance between the resonator and waveguide is called Gap.

The waveguide length is the same as the width of the simulation domain. The outer diameter and the thickness of the ring resonator are 3.6µm and 0.3µm respectively and the width of the waveguide is 0.2µm. Gap widths between the resonator and waveguide is 0.2 µm. The wavelength incident laser is between 1.55µm 1.5906µm. The simulation is examined under 1st resonance and off resonance.

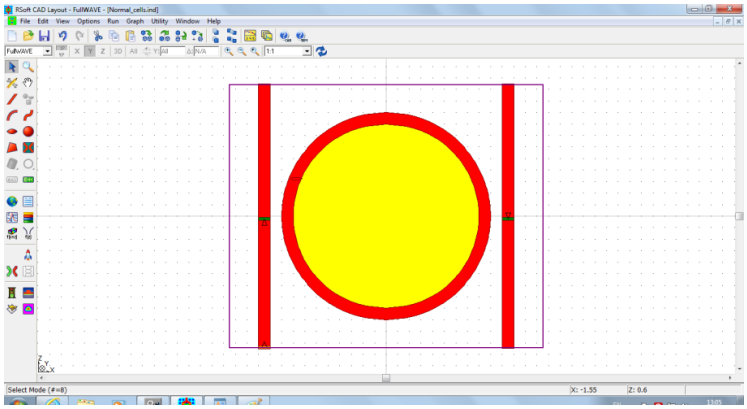

Figure 6. Optical Single Ring Resonator

- Normal cell

Figure7 shows Graphical analysis of Single ring resonator for normal cell. We can observe that the input beam and output beam of light are nearly same which indicate that the placed cell is normal as discussed earlier.

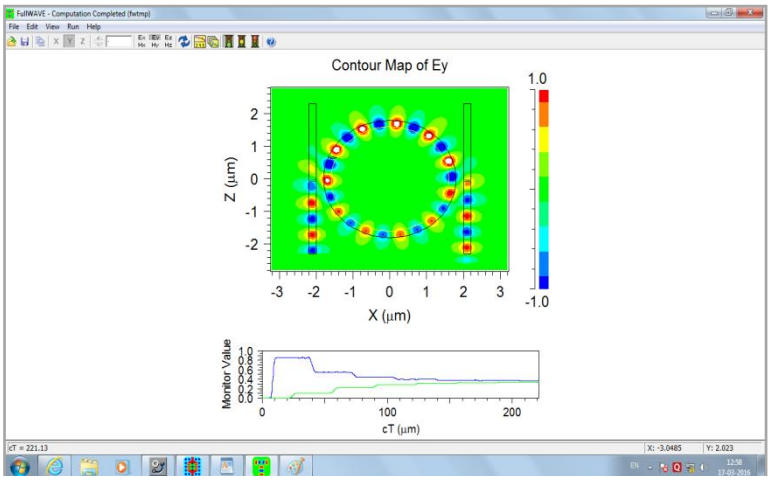

Figure7. Plot of Optical Single Ring resonator for Time vs. Amplitude for Normal cell.

- Cancerous cell

Figure8 shows Graphical analysis of Single Ring Resonator for Cancerous cell. We can observe that the input beam and output beam of light are far from each other which indicate that the placed cell is Cancerous as discussed earlier.

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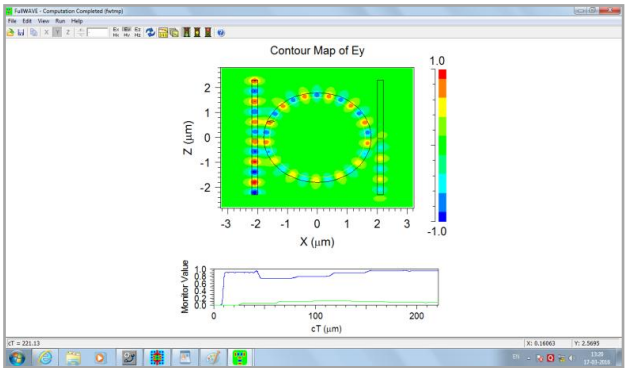

Figure 8. Plot of Optical Single Ring resonator for Time vs. Amplitude for Cancerous cell.

C. Optical Double Ring Resonator

A simulation domain is of 140µm*240µm rectangular area. A Double Ring Resonator is centrally located and two waveguides are positioned on both sides of resonator. Separation distance between the resonator and waveguide is called Gap. The waveguide length is the same as the width of the simulation domain. The outer diameter and the thickness of the ring resonator are 3.6µm, 2.4µm and 0.2µm respectively and the width of the waveguide is 0.2µm. Gap widths between the resonator and waveguide is 0.2µm. The wavelength incident laser is between 1.55µm 1.5906µm. The simulation is examined under 1st resonance and 2ndresonance.

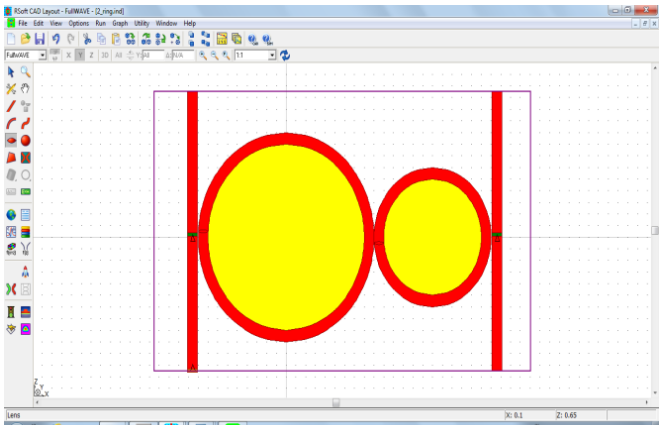

Figure 9. Optical Double Ring Resonator.

- Normal cell

Figure10 shows Graphical analysis of double ring resonator for normal cell. We can observe that the input beam and output beam of light are nearly same which indicate that the placed cell is Normal as discussed earlier. The Double Ring Resonator gives more accurate result because the light rotates in a ring again and again which make it possible to get the average value of the results.

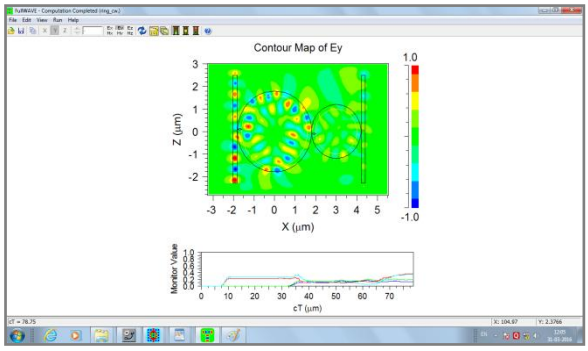

Figure 10. Plot of Optical Double Ring Resonator for Time vs. Amplitude for Normal cell.

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- Cancerous cell

Figure11 shows Graphical analysis of double ring resonator for Cancerous cell. We can observe that the input beam and output beam of light are far away from each other which indicate that the placed cell is cancerous as discussed earlier. The Double Ring Resonator gives more accurate result because the light rotates in a ring again and again which make it possible to get the average value of the results.

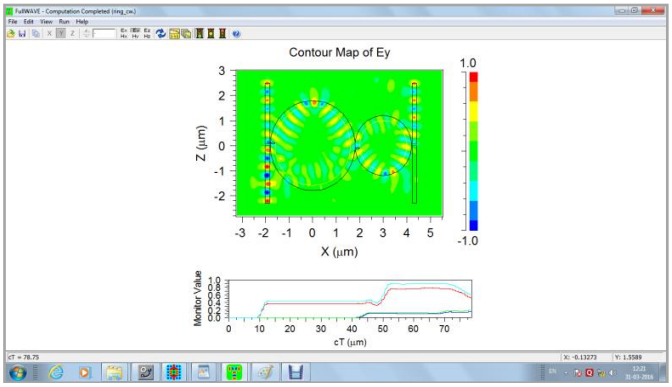

Figure 11. Plot of Optical Double Ring Resonator for Time vs. Amplitude for Cancerous cell.

VI. CONCLUSION

Ring resonator is still a relatively young research that will be more progressed in coming future. In this work a critical review of biosensor and biomarker have been carried out and it has been observed that single and double optical ring resonator are more suitable in early stage breast cancer detection. Furthermore, a waveguide, single and double ring resonator have been developed and simulated by using R-soft Cad and simulator. From the result it has been observed that double ring resonator is more suitable as compared to single optical ring resonator and optical waveguide. The result of double ring resonator reveals that breast cancer can be detected in early stage.
Our work will lead to a device that can increase the accuracy and can monitor treatment effectiveness at low cost and rapid response, which improves the breast cancer diagnosis and prognosis efficiently.

REFERENCES

[1] Onur Tigli, Louis Bivonaetall "Fabrication and Characterization of a Surface-Acoustic-Wave Biosensor in CMOS Technology for Cancer Biomarker Detection" IEEE Transction on Biomedical Circuits and System, Vol. 4. No. 1, Feb 2010.
[2] NumaCouniot, Student Member, David Boletall "A Capacitance-to-Frequency Converter with On-Chip Passivated Microelectrodes for Bacteria Detection in Saline Buffers Up to 575 MHz" IEEE Transactions on circuits and sytem-II: express briefs, Vol. 62, No. 2, Feb 2015.
[3] M. Tariqus Salam, Jose Luis Perez Velazquez; Roman Genov, etall "Seizure Suppression Efficacy of Closed-loop Versus Open-loop Deep Brain Stimulation in a Rodent Model of Epilepsy" This article has been accepted for publication in a future issue of this journal, but has not been fully edited. Content may change prior to final publication. Citation information: DOI 10.1109/TNSRE.2015.
[4] Zheng Zhang, Nuri William Emanetoglu, GauravSarafetall "DNA Immobilization and SAW Response in ZnONanotips Grown on LiNbO3 Substrates" IEEE transactions on ultrasonics, ferroelectrics, and frequency control, vol. 53, no. 4, APR 2006.
[5] Drew A. Hall, RichardS. Gaster, Kofi A. A. Makinwaetall "A 256 Pixel Magnetoresistive Biosensor Microarray in 0.18 µm CMOs" IEEE Journal of solid state circuits, Vol. 48, NO. 5, MAY 2013.
[6] C. S. Premachandran, Ahmad Khairyanto, Kelvin Chen Wei Sheng, Janak Singh etall "Design, Fabrication, and Assembly of an Optical Biosensor Probe Package for OCT (Optical Coherence Tomography) Application" IEEE Transactions on advanced Packaging, Vol. 32, No. 2, MAY 2009.
[7] Gerard L. Cote Ryszard M. Lec, and Michael V. Pishkoetall "Emerging Biomedical Sensing Technologies and Their Applications IEEE sensor journal, Vol. 3, No. 3, JUN 2003.
[8] Luca De Stefano, Luigi Moretti, Annalisa Lamberti, Olimpia Longo etall "Optical Sensors for Vapors, Liquids, and Biological Molecules Based on Porous Silicon Technology" IEEE Transactions on Nanotechnology, Vol. 3, No. 1, MAR 2004.
[9] Andrea Bandiziol, PierpaoloPalestri, Federico Pittino, David Esseni, and Luca Selmietall "A TCAD-Based Methodology to Model the Site-Binding Charge at ISFET/Electrolyte Interfaces" IEEE Transactions on electron devices, Vol. 62, No. 10, OCT 2015.
[10] Charles J. Choi, Ian D. Block, Brian Bole, David Dralle, and Brian T. Cunninghametall "Label-Free Photonic Crystal Biosensor Integrated Microfluidic Chip for Determination of Kinetic Reaction Rate Constants" IEEE sensor journal, Vol. 9, No. 12, DEC 2009.