Development of Novel Nano-photonics Based Biosensors for Biomedical Applications

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Abstract

Advancements in Nanotechnology have significantly influenced developments in medical diagnostics and biotechnology. The nano-structures with photonic band gap due to their unique optical properties of guiding specific wavelength inside the crystal have found significant applications in various fields such as This idea has been applied to many optical transistors, waveguides, chemical and biochemical sensors. The highly ordered 3-D structures possessing periodic refractive index and dielectric constant prove to be promising material for photonic crystals based biosensing. Present paper deals with a novel approach of photonic crystal based bio sensing using Gold nanoparticles. Study of Surface Plasmon Resonance (SPR) phenomenon occurring in Gold nanoparticles is done and prospects for for the development of Biosensors are studied herewith. Noble nanoparticles have got the inherent ability to tansduce dielectric charges at the molecular level by SPR whose plasmonic response for various application depend upon nature, size and shape of metal nanostructures , nature of the capping agent and nature of the medium during the synthesis. The gold nanoparticle-based photonic crystals have specific reflection wavelength and Surface Plasmon Resonance (SPR) characteristics. Gold nanostructures that hold the possibility to manipulate light on a bio chip can be of much importance to be used in fabrication of efficient photonics based sensors with very low response time and high sensitivity and selectivity. Localization of light below the sub diffraction limits and field enhancement increases the light –molecule interaction and binding between the two takes place efficiently. The refractive index of metallic photonic crystal can be changed easily from the defects, resulting in the change in color for detection. In addition, the immobilization of enzymes makes the biosensors highly sensitive and selective. Gold nanoparticles prepared by Sol Gel Reduction Method are characterized by X Ray Diffractometer (XRD), Transmission Electron Microscope (TEM) and High Resolution TEM (HRTEM). SPR in the gold nanoparticles occurs due to collective electron density oscillations that are resonantly driven by incident electromagnetic radiation at different wavelengths. High degree of tunability allows real time detection of biomolecular bindings. An array of gold nano particles fabricated with lithography can be used in the biosensor. Gold nanoparticles are coupled to the surface via biomolecules. When light hits a dielectric metal interface under certain conditions surface plasmon is created. This optical signal is then detected by the detector. Changes in the optical signal are demonstrated with the change in the distance. This makes it suitable to be used in Biosensors to detect the presence of target molecule. Biosensors formed using this novel approach are found to be highly selective, sensitive with a less response time as compared to their counterparts.

Keywords - BioSensing, Transduce, Dielectric, Surface Plasmon Resonance, Biomolecular, Plasmon.

Introduction

Significant research and advancements in nanotechnology have rendered various promising developments in biotechnology and medicine. The interdisciplinary field of biology and nanotechnology has resulted in the development of new generation nano devices for analysis and characterization of chemical, mechanical, and other molecular properties, as well as in discovering novel phenomena occurring at the cellular level. These advances provide science with a wide range of tools for biomedical applications for therapeutic and diagnostic purposes. This research has resulted in recent advances in instrumentation and development of various methods for designing efficient nanobiosensors with various analytical techniques for the detection and monitoring of specific bio molecules. Portable and cost-effective devices for medical diagnostics can be designed that work on the basis of photonic nanostructures. Light-based measurement principles that have been already applied to develop a variety of indispensable analytical instruments, is used for designing novel biosensors based upon this concept. Such novel integrated photonic biosensors, are found to have enormous potential due to their high sensitivity, small size and high efficiency with comparable costs.

Photonic Nanostructures as Optical Waveguides

Photonic crystals (PC) are artificially synthesised materials with optical properties arising due to band gap in the material periodic modulation of the refractive index. Photonic crystal structures offer a better environment than traditional optical waveguides that can be used for sensing applications. Particularly fast and effective optical biosensors can be developed with high sensitivity, high selectivity, compactness, low price, and easy fabrication and integration with other optical or electrical components. The finite element method (FEM) can be applied to waveguides in general and PCFs in particular to investigate propagation characteristics of modes. In the case of PCFs, the fibre cross section is divided into homogeneous subspaces where Maxwell's equations are solved by accounting for the adjacent subspaces. These subspaces are triangles which give good approximation of circular structures (Saitoh & Koshiba, 2002). In order to allow the study of fibres with arbitrary air filling fraction and refractive index contrast, a full vector formulation is required. A full vector FEM formulation based on anisotropic perfectly matched layers (PMLs) is able to calculate as many modes as desired in a single run without setting any iterative procedure. Generally compatible SOI-wafer (silicon-on-insulator) along with other electronic and optical devices is used for bio sensing. By using this SOI, photonic crystal waveguide can be made very compact and the sample volume can also be reduced considerably compared to many other biosensors presented in the literature. It is realized in a SOI-wafer comprising a SiO2 layer with a thickness of 2μm and refractive index 1.44, and a 320nm thick silicon slab with refractive index 3.48. Also, bending on birefringence, confinement losses and chromatic dispersion of PCFs have been thoroughly validated using the full vectorial finite element method FEM (Ademgil *et al*., 2009). By selecting appropriate structural and material parameters, the sensor can be configured to operate as either multi analyte or self referencing sensor.The multi analyte configuration will be suitable for applications where simultaneous detection of analytes is desired (Akowuah *et al*., 2010).The properties of crystal waveguides are highly influenced by changes in refractive index at the silicon surface, which accounts for the property of the device utilized. Bio-sensing typically involves detection of specific biological molecules at the sensor surface. Transmission edge of the lowest band-gap defect-mode of the photonic crystal waveguide is used as the sensing probe. Sudden drop in transmission spectrum vs. wavelength and can be used for sensor probe as the wavelength position of this transmission drop increases/decreases with an increase/decrease in refractive index of the cover medium. The finite element method with perfectly matched absorbing layers boundary condition is used to investigate the guiding properties. Using the FEM, the PCF cross-section, with the finite number of air holes is divided into homogeneous subspaces where Maxwell's equations are solved by accounting for the adjacent subspaces (Bukas, 2001).

Biosensing Using Gold Nanoparticles

Gold nanoparticles, are one of the most widely investigated nanoparticles (NP) owing to their significant optical and electrical properties. Additionally excellent Surface Plasmon Resonance in the case of Gold NP makes it extremely suitable for various applications, the most important being the use of biosensors. There is a growing interest in the development of SPR sensor platforms capable of discriminating specific sensor response (resulting from capture of analyte molecules by bio molecular recognition) from non – specific response, which is mainly due to temperature fluctuation, analyte composition variation and adsorption of non – target molecules on the sensor surface SPR biosensing is prominently used for the detection of a multitude of biomolecules as it offers label-free detection in real time (Hoa *et al*., 2007). Incorporation of AuNPs, either within the sensing surface itself or as signal enhancive in tagging molecules makes it possible to be used for the study of proteins, nucleic acids, and other bio molecules. The importance of AuNP and detecting agent spacing is described and techniques using macromolecular spacing aids are highlighted. Recent methods to enhance SPR detection capabilities using gold nanoparticles are reviewed, as well as device fabrication and the results of incorporation. SPR detection is a highly versatile method for the detection of biomolecules and, with the incorporation of AuNPs, shows promise in extending it to a number of new applications. Different sensing systems using gold nanoparticles are established which are lateral flow immunoassay (LFIA), surface plasmon resonance (SPR), and surface-enhanced Raman scattering (SERS).

Surface Plasmon Resonance in au NP Photonic Biosensor

Gold NPs absorbs light on their surface, of a resonant wavelength that causes the electron cloud to vibrate, and therefore dissipation of the energy. This process is known as SPR as it results from the formation of plasmons, which refers to the oscillations of electron cloud which results from certain wavelengths for metal where photons are not reflected, but instead are absorbed and converted into surface plasmon resonance (electron cloud vibrations). Peak wavelength of light scattered by an individual plasmonic nanoparticle to the number of bound analyte molecules provides an analytical formulation that predicts relevant figures-of-merit of the sensor such as the molecular detection limit (MDL) and dynamic range as a function of nanoparticle geometry and detection system parameters (Nusz *et al*., 2009).Biosensors employed for biosensing may be of different types depending upon the biomolecules employed in the sensor development such as immunocompounds, DNA/RNA and functional DNA/RNAe, enzymes and Heme proteins. Gold nanoparticles based immunosensors have a wide range of applications in food, environmental, pharmaceutical, chemistry and clinical diagnostics. The nanoparticles are employed to improve the analytical signal or the immunocompounds immobilization. For example, biosensors based on DNA using gold nanostructures as labels and label-free functional DNA biosensors associated to gold nanostructures as transducers were systematically reported for rapid identification of pathogens, species of environmental interest and clinical diagnostics, respectively. Use of gold nanoparticles in the sensor enhances the electron transfer between the transducer and biomolecules leading to improved analytical devices when redox enzymes and heme proteins are used.

Applications of Gold NP Based Biosensor

Au based Nano Bio Sensor is used for varied applications , the most commonly being used for human pregnancy .Gold nanoparticle aggregation is used to create a colormetric response in which nanoparticles (< 50 nm) are bound to antibodies complementary to a hormone produced during pregnancy (Figure 6).

Gold nanorods with an aspect ratio of 4.4 can also be prepared using a silver nitrate assisted, seed mediated growth method (Nikoobakht & El-Sayed, 2003). Latex microspheres are also bound to antibodies for the hormone. When the stick is submerged in urine flow, if the hormone is present it will bind to the microspheres (~ 500 μm) and nanoparticles causing aggregates to form. The solution then passes through a paper filter. If the pregnancy hormone is present, the aggregates will be trapped by the filter producing a colour product. If the pregnancy hormone is not detected, the nanoparticles will pass through the filter because of their small size. Although this test does not rely explicitly on plasmon resonance to create the signal, the deep red colour of the nanoparticles employed results directly from this feature. Secondly it can also be used for DNA detection. For example, one kind of DNA test looks for certain bases. In this test, nanoparticles start out as large aggregates that are blue. If the complementary DNA base is present, the nanoparticles will bind to that base instead of each other and the aggregates will dissolve producing a deep red colour. This can be followed using an instrument called a spectrophotometer that measures transmission edge of the band-gap for sensor applications and allow sensitivity beyond that for present-day optical sensors based on cavities. The limit of detection of the sensor is 0.005 microg/mL (94 pM) in PBS and 1 microg/mL (19 nM) in serum, and the dynamic range spans 94 pM to 0.19 microM (Marinakos *et al*., 2007).

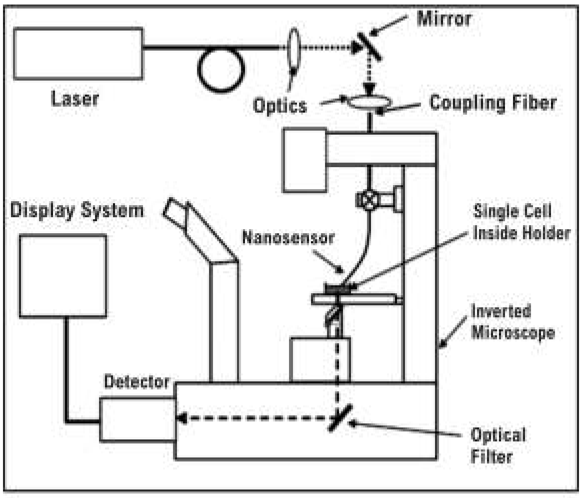

Figure 1: Fabrication of the set up of Photonic Biosensor.

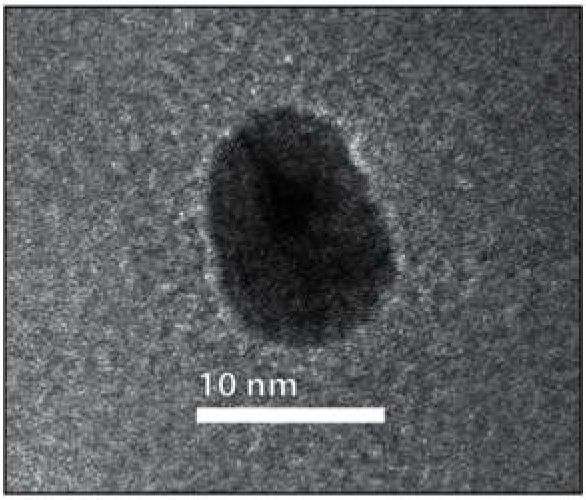

Figure 2: TEM image of Au NP.

Future Scope

Future studies aim at increasing sensitivity that can be enhanced by nearly 200 times. For practical applications it is easy to integrate the necessary polarizer on the same chip, so no external polarization tuning will be needed. Further improvements in sensitivity and selectivity are possible by using two or more waveguides with different antibodies in balanced bridge configurations. The narrow feature shifts approximately the same amount in wavelength as the edge, but since it is several hundred times narrower, the sensitivity is greatly enhanced.

Reliable modeling, characterization and optimization of the physical and chemical properties is yet another challenge.

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