

Optical Biosensor based on Silicon-on-Insulator Microring Resonators for Specific Protein Binding Detection

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Optical label-free biosensors to detect biomolecular interaction attempt to overcome the drawbacks of commercialized systems relying on the detection of labeled biomolecules. We propose an integrated Silicon-on-Insulator optical biosensor, fabricated with Deep UV-lithography, based on resonant microring cavities. The shift of resonance wavelength that occurs when the dielectric surroundings of a cavity is changed, can be used for sensing. An SOI optical microring resonator with a radius of 5 micron is capable of detecting bulk refractive index changes of 10^{-4} . We use the avidin/biotin high affinity couple to demonstrate good repeatability and the detection of avidin concentrations down to 50 ng/ml.

Introduction

Sensing of biomolecules is gaining interest due to its applications in many areas such as bacterial and virus detection, medical diagnostics, drug development, food and environmental control. Most commercialized biosensors rely on detection of labeled molecules. The intermediate labeling step however complicates the detection process and decreases reliability so there is a growing need for label-free detection methods, enabling the monitoring of the dynamics of molecular reactions and quantitative concentration measurements. Different approaches for integrated optical biosensors based on Surface Plasmon Resonances (SPR) [1], interferometers [2] and resonant cavities [3][4] are previously reported. Often these components still require relatively large amounts of analyte and are not suited for cheap high throughput fabrication. The integrated Silicon-on-Insulator (SOI) optical biosensor we propose combines fast sample preparation, real time and quantitative measurements and reduced analyte quantities with a high throughput fabrication method using standard microelectronics processing, in particular deep UV lithography. SOI offers a high refractive index contrast suitable for the fabrication of optical cavities of very high quality. The shift of resonance wavelength that occurs when the surroundings of such a cavity is changed, can be used for sensing. Integrated in a microfluidic setup thousands of cavities can be lined up in arrays for multiparameter sensing within a few square millimeters.

Direct sensing of proteins is based on affinity between protein couples; a protein (ligand) fixed to the sensor's surface forms a complex with a complementary protein (analyte). In this work we used the avidin/biotin protein couple which gives a very specific and stable interaction. Anchoring biotin to the sensor requires a chemical modification of the semiconductor surface which has to be chemically and morphologically homogeneous, and has to prevent from non-specific protein adsorption.

1 Silicon-on-Insulator microrings for sensing purposes: design and fabrication

When light with a wavelength $\lambda = \frac{n_{eff}L}{m}$, $m = 1, 2, \dots$ and L being the circumference, couples to a microring resonator whispering gallery modes occur. This results in a sharp dip in the transmission. A change in the refractive index of the ring's environment shifts the resonance spectrum, which can be monitored by scanning the wavelength and by measuring the intensity profile at one well chosen wavelength. For both techniques the sensitivity increases with increasing quality factors Q of the resonator. The Q -factor expresses the peak's width: $Q = \frac{\lambda_{resonance}}{\delta\lambda_{3dB}}$. Q -factors over 20,000 are easily achievable with our fabrication process and optimized design. The pass and drop spectra of a $5\mu\text{m}$ racetrack resonator are shown in Fig. 1. We observe a 3dB peak width of 7.5pm.

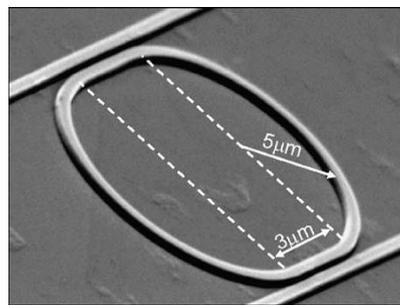
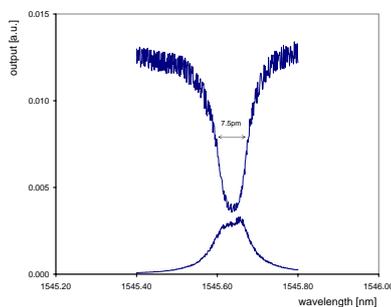


Figure 1: Measured pass and drop spectrum.

Figure 2: SEM picture of the device.

Deep ultraviolet (UV) lithography, the technology used for advanced complementary metal-oxide-semiconductor (CMOS) fabrication offers both the required resolution and the throughput needed for commercial applications. This was previously reported in [5]. A SEM picture of the device is shown in Fig. 2.

2 Surface functionalization

Silanization of the surface is used to provide a suitable biointerface between the transducer element and the biological medium. In the present work we used the avidin/biotin system which has a high affinity constant ($K_a = 10^{15} \text{M}^{-1}$) and therefore has a stable and specific interaction, as a model of biomolecular interaction. Biotin was immobilized on the aminofunctionalized silicon surface and the biotinylated surface was exposed to an avidin solution to allow the complex formation. X-ray Photoelectron Spectroscopy (XPS) confirmed the success of both the aminosilanization and the biotin anchoring step. Contact angle and ellipsometry suggested the formation of multilayers where the amino functional groups might be partially buried. However, the modification was effective to provide a biotinylated surface which was used in binding experiments with avidin.

3 Measurements

A schematic drawing of the proof-of-principle measurement setup is given in Fig.3. Optical

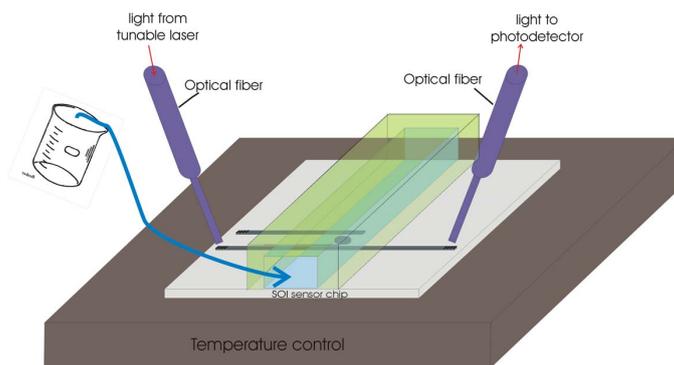


Figure 3: Measurement setup.

fibers are vertically coupled to the in- and output integrated waveguides through grating couplers [5]. This allows for easy coupling with high alignment tolerances.

3.1 Bulk refractive index sensing

Liquids with varying refractive indices (aqueous solutions of NaCl) are flown across the ring resonator in order to characterize the sensor for bulk refractive index sensitivity. Fig.4a shows a linear shift of the resonance wavelength with increasing refractive index units (RIU) of 70nm/RIU. A minimal detectable wavelength shift of 7.5pm, one tenth of the peak broadness, corresponds to a minimal detectable refractive index shift of $1 \times 10^{-4} \text{RIU}$.

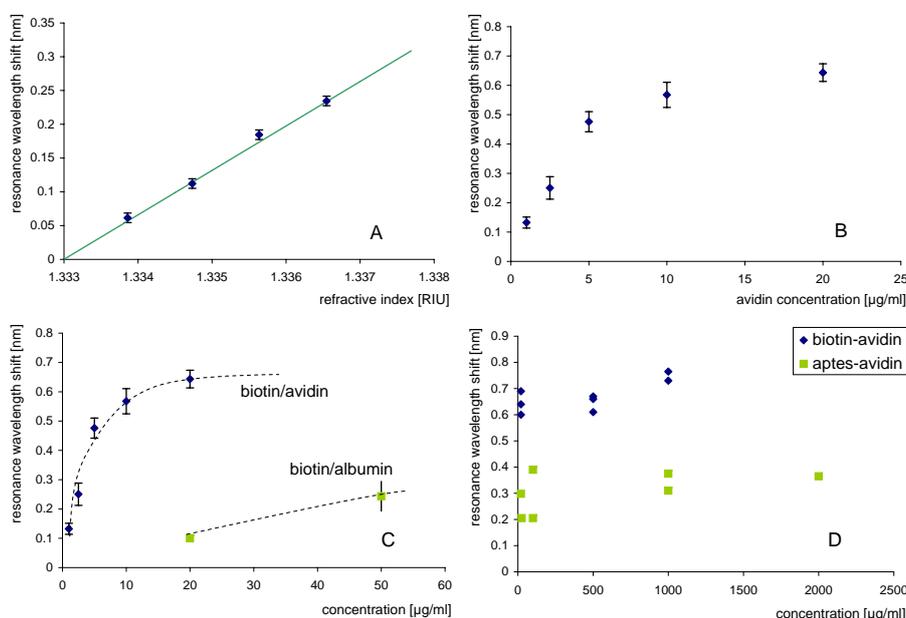


Figure 4: a) Resonance wavelength shift versus bulk refractive index change. b) Quantitative avidin/biotin detection with an SOI microring cavity. c) Nonspecific binding test biotin/albumin. d) Nonspecific binding test aptes/avidin.

3.2 Surface sensing of biotin/avidin coupling

We compare the resonance wavelength of the cavity immersed in Phosphate Buffer Solution (PBS), before and after being in contact with avidin solution. The evolution of the wavelength shift for different avidin concentrations is shown in Fig.4b. For high avidin concentrations all binding sites are occupied and the curve saturates. For low avidin concentrations the wavelength shift corresponds to the concentration. The estimated lowest detectable concentration, for a minimal detectable wavelength shift of 7.5pm, is 50ng/ml. Furthermore two nonspecific binding tests are accomplished (Fig.4c and d). Firstly Bovine Serum Albumin (BSA), a protein with similar molecular weight to avidin but with low affinity to biotin, is brought into contact with the biotin layer. Secondly avidin is brought into contact with the aminosilanized surface without biotin. Both measurements resulted in a smaller wavelength shift due to a decreased molecular interaction, proving the specificity of the sensor.

4 Conclusions and Perspectives

We have demonstrated a highly miniaturized optical label-free biosensor based on a Silicon-on-Insulator microring cavity with high Q-factors and fabricated with Deep UV lithography, a high-throughput fabrication method. Measurements reveal proper operation of the device, being able to detect in a specific way avidin concentrations down to 50ng/ml, which compares favorably with commercial biosensors. Further improvements will be made to increase the sensitivity, by increasing the cavity's Q-factor and reduce its size. The microrings are suitable for lining up in arrays to perform multiarray molecular detection.

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