Dual polarisation biosensing with an SOI microring

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Optical microresonator biosensors have proven to be a valid tool for binding and affinity analysis of a biological binding event. However, when these microresonators are excited with a single optical mode they can not distinguish between a thin dense layer of biomolecules or a thick sparse layer. We succeeded in exciting a Silicon-on-Insulator (SOI) microring with both TE and TM polarisations simultaneously by using an asymmetrical directional coupler. A theoretical model is provided to solve the shifts of these modes to the thickness and refractive index of the biolayer. During a Bovine Serum Albumin (BSA) adsorption experiment, both shifts were tracked, showing the potential of the sensor for conformational analysis.

Introduction

The current crisis in the drug development industry can be hardly overlooked, with an increase in failure rate and a 50 % drop from 1996 to 2010 in number of applications to the U.S. Food and Drug Administration (FDA) as the main results. Connelly stated in a 2011 *Nature Chemistry Insight* [1] that the reason for this decline can be found in the lack of appropriate high-throughput tools to study molecular behaviour at an analytical and biophysical level of the drug candidates we produce.
To accommodate this, we propose an optical sensor system that can detect conformational changes of proteins. The preferred technology for this is based on microring resonators, designed for the Silicon-on-Insulator (SOI) platform. In a microring, specific optical modes can resonate at specific resonant wavelengths. Current microring resonators exploit this mainly by tracking the resonance wavelength of one optical mode and as such, they are able to measure the surface-bound mass as a function of time. In the past, biosensor arrays with each microring selective to a certain molecule have been reported [2]. Detection limits of this platform are ranging from 0.3 pg/mm^2 - $3pg/mm^2$, comparable to surface plasmon resonance sensors [3].
However, single-mode optical sensors can't detect a conformational change of bound proteins, since this will not induce a direct change in the amount of bound mass. By simultaneously determining the thickness(t) and the refractive index(n) (which is linked to the

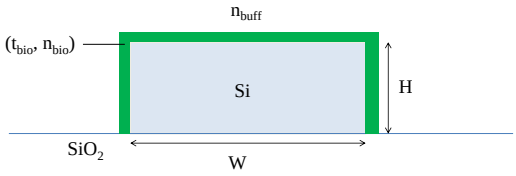

Figure 1: Cross section of the waveguide of which the microring consists.

density) of a biolayer, we can obtain information on the size and shape of biomolecules during binding with ligands. To track both t and n, we propose to excite the microring sensor with two optical modes simultaneously.

Methods & design of sensor

Working principle

The cross section of the microring consists of a 220 nm high silicon rectangle with air cladding, on top of a silicondioxide box. This vertical asymmetry causes the microring to be highly birefringent. The two optical modes that are used for the dual polarisation sensing technique are the fundamental quasi-TE and fundamental quasi-TM modes. In the remainder of this text, we shall call these modes TE and TM modes for ease of notation. The resonance wavelength of these two modes in the microring cavity is determined by:

$$\lambda_{res} = \frac{L\, n_{eff}}{m} \tag{1}$$

When biomolecules are streamed over the sensor, they can adsorb to the microring surface and form a biolayer with a certain thickness and refractive index, as illustrated in figure 1. The two optical modes interrogate the biolayer at the surface by means of their evanescent tail, that penetrates into the cladding of the waveguide. The capturing of biomolecules on the microring surface is reflected by a perturbation in n_{eff} and thus implies a shift in the resonance wavelength, which is governed by the following equation:

$$\Delta\lambda_{res}(n,t) = \frac{\Delta n_{eff}(n,t)\cdot\lambda_{res}}{n_g} \tag{2}$$

Extraction of (t,n) of the biolayer

The measurement setup tracks $\lambda_{res,TE}$ and $\lambda_{res,TM}$ during the experiment. In order to extract (t,n) of the biolayer, we propose a set of 2 equations linking the resonance wavelength shifts with (t,n). The shifts are relative to the resonance wavelength when the cladding of the microring is the buffer solution. To find these equations, simulations have been done with the eigenmode solver *Fimmwave*. For a wire waveguide as depicted on Fig. 1, with dimensions W and H, the n_{eff} and n_g of the TE and TM modes are simulated. Using equation 2, $\lambda_{res,TE}$ and $\lambda_{res,TM}$ can be calculated from these indices. We propose a model with two different constants of decay per mode, due to a non-identical effective cladding index at the top and at the side of the waveguide:

$$\Delta\lambda_{TE}(n,t) = \left(\frac{1}{1+\exp(-a_{TE}t)+\exp(-b_{TE}t)} - \frac{1}{3}\right)\left[c_{TE}(n-n_{buff}) + d_{TE}(n-n_{buff}^2)\right] \tag{3}$$

$$\Delta\lambda_{TM}(n,t) = \left(\frac{1}{1+\exp(-a_{TM}t)+\exp(-b_{TM}t)} - \frac{1}{3}\right)\left[c_{TM}(n-n_{buff}) + d_{TM}(n-n_{buff}^2)\right] \tag{4}$$

By using a nonlinear regression algorithm, we can fit the 8 parameters (with the proper constraints) of these equations using a least-square metric, obtaining a R^2 goodness-of-fit of 0.9998 over a range of 200 nm for t and of 0.2 R.I.U for Δn, confirming the validity of this model.

Sensor design

In order to excite both polarisations simultaneously we use an asymmetrical directional coupler, which can couple the TE mode to the TM mode in an adjacent waveguide by using two waveguides with different widths, such that $n_{eff,TE} \approx n_{eff,TM}$. A microring with an asymmetrical coupling section has been examined in [4], where it is shown that a TE mode in the access waveguide can successfully excite a TM mode in the ring waveguide. However, if the gap in the coupling section is sufficiently small, the TE mode in the access waveguide can also excite the TE mode in the ring waveguide even though they have a substantial phase mismatch Δn_{eff}. Due to the proximity of the waveguides, the modal overlap can be large enough as to compensate for the phase mismatch.
The waveguide of the microring was designed to have a width of 480 nm, such that with an access waveguide of 280 nm, a small phase mismatch was achieved between the TE mode of the access waveguide and the TM mode of the ring waveguide of $\Delta n = 0.0516$. On Fig. 2(a), this phase matching is illustrated. Once the sensor was fabricated by imec, fiber to fiber measurements were performed with water as air cladding. The measured spectrum is shown in Fig. 2(b), where we can clearly see two sets of polarisations with a different free spectral range (FSR).

BSA experiment

To show the potential of this sensor, the wavelength shifts of the TE and TM mode were recorded during an adsorption experiment with BSA molecules. A 2mM phosphate buffer saline (PBS) solution was prepared with pH 3 and 5, to which BSA molecules were added until a concentration of 0.1 mg/ml was attained. Some PBS with pH 3 was left as running buffer. The fluids were cycled from BSA in PBS at pH 3 to BSA in PBS at pH 5 and back to BSA in PBS at pH 3, before returning to the running buffer and eventually back to water. The recorded wavelength shifts for both TE and TM mode are shown on fig. 3. There is an increase in wavelength shift for both modes when the fluid is switched from pH 3 to pH 5. This suggests that the adsorbed mass is increased, which is confirmed in [5]. Throughout the experiment, the different behaviour of the TE mode with respect to the TM mode is clearly visible. The TM mode is less confined to the waveguide core and

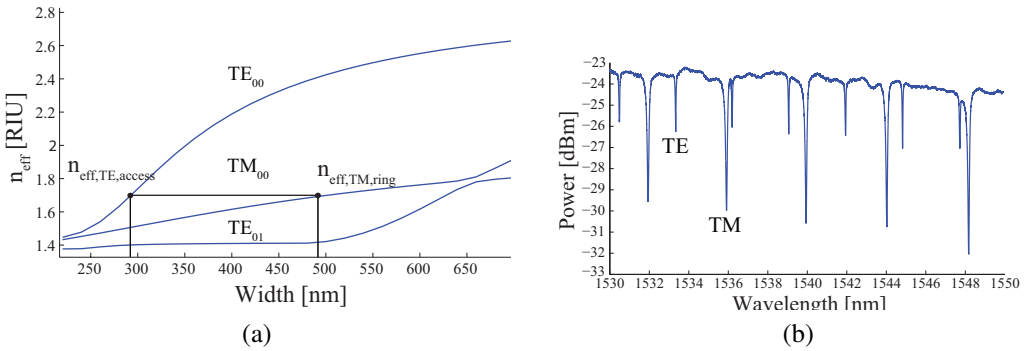

Figure 2: (a) Effective index of the first three guided modes for a rectangular waveguide with a height of 220 nm and water cladding. The black lines show how to phase match the fundamental TE mode with the TM mode. (b) Measured fiber to fiber spectrum of the microring with water cladding. Both the TE and the TM modes are visible

thus more sensitive to variations in the cladding. It is crucial that the TE mode and TM mode behave non-equally in order to make the solving to (t,n) feasible. This first test is a good indication that this biosensor can be used to measure the thickness and the refractive index of a bound biolayer.

Conclusion

We have succeeded in designing a microring which can excite both the fundamental quasi-TE mode and the fundamental quasi-TM mode simultaneously. By means of a BSA adsorption experiment we have shown that we can track the shift of both modes at the same time. A theoretical model has been presented which makes it possible to solve the obtained shifts to the the thickness and the refractive index of a bound biolayer, confirming the potential of this sensor for conformational analysis.

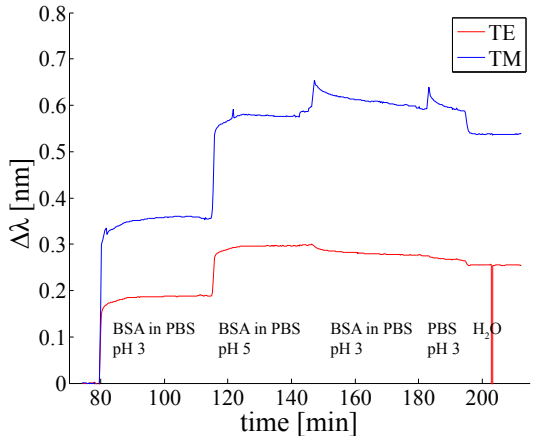

Figure 3: Resonance wavelength shift of the fundamental TE mode and the fundamental TM mode for a BSA adsorption experiment, when cycling through different pH values of the buffer .

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