SILICON SUBSTRTATES WITH BURIED DISTRIBUTED BRAGG REFLECTORS FOR BIOSENSING

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High quality silicon substrates with buried Bragg reflectors previously developed within our group for improved photodetectors, have enabled a new biosensing modality. The goal of this technique is to detect the presence of biomolecules binding to a surface coated with different localized capturing agents. Such ability yields information about the affinity of the biomolecules under test for the molecules on the capturing surface. Capturing surfaces such as microarrays featuring thousands of different binding locations with different fixed capturing agents offer the greatest amount of information and hence benefit. Information about the affinity between molecules of interest such as particular proteins or DNA strands, yields great benefit to a number of applications in biological research and may soon become applicable in medical diagnostics as well.

Microarrays are a technology that accomplishes just this [1]. Thousands or hundreds of thousands of different capturing agents are fixed in localized spots or features on the microarray surface, typically glass. Molecules under test are first affixed with a fluorescent label and then introduced to the microarray surface. A fluorescent scanner then scans the surface with a laser and records the fluorescent signal with a PMT to determine the amount of binding at each location.

But microarray technology has its limitations despite its wide spread success. Namely, the need to fluorescently label the molecules of interest can preclude microarrays from many applications where affixing a label to the test molecules may not be practical or possible. In addition, proteins in particular may suffer from altered binding properties once the label is affixed. For these reasons, a label-free sensing technology, such as described here, would be preferable.

Optical detection of low level molecular binding is achieved using an interferometric technique that benefits from a resonant cavity enhancement. The resonant cavity is formed between two facing planar Bragg reflectors bearing the following qualities: high reflectivity, low loss, exceptional smoothness, and cost effectiveness. Light enters the cavity through the back of the first Bragg reflector. The wavelength is swept in time using a wavelength tunable laser source. When the wavelength satisfies the resonant condition of the cavity for a particular location, the cavity builds up local energy that couples through and is recorded by a camera pixel corresponding to that location, or alternatively a photodiode in a photodiode array. The high finesse of the cavity afforded by the high reflectivity of the reflectors causes the resonance to be highly sensitive to slight changes within the cavity. Biological agents binding to the capturing agents at different locations within the cavity modulate the local resonant condition within the cavity. As the wavelength is swept in time and images recorded on the camera, resonant wavelength-transmission curves are recorded for each cavity locations. Shifts in these curves indicate binding. This measurement can be made simultaneously at thousands of locations, in minutes.

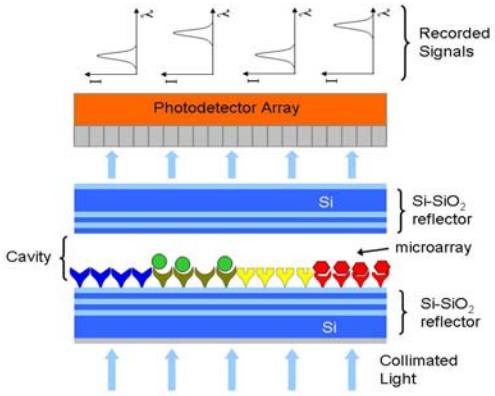

Fig. 1 The wavelength of the excitation light swept and wavelength vs. transmission curves are recorded by a camera positioned beyond the cavity. The microarray is fabricated on one of the reflector surfaces. Binding to the surface is indicated by a local shift in the resonant response of the cavity.

The reflectors are a key component that enables this technology. In order to detect minute changes of material on a reflector surface, the surface must be smooth and the cavity finesse high. Furthermore, since the microarray is covalently bound to the surface, and since microarrays are gerenally one-time-use only, inexpensive reflectors are preferable.

Reflectors that meet this requirement have been developed previously by our goup for applications in resonant cavity enhanced photodetection [2]. The substrates consist of two layers of buried SiO_2 oxide within a Si substrate. The key advantage of the Si- SiO_2 material choice is the large index contrast compared to that of other materials (60% vs 17% with GaAs-AlAs for instance). It has long been of great interest to the semiconductor industry to develop Si wafers with an SiO_2 layer buried just beneath a top Si layer. Such Silicon-On-Insulator (SOI) substrates offer reduced capacitance and improved performance.

There a few different techniques for creating SOI wafers. We have chosen to use ion-cut technology which relies on blistering. Blistering is induced when a high-dosage implantation of hydrogen ions is heated. The gas

pressure in the material causes microcavities, which are formed close to the implant range depth, to propagate and form fractures that cause the surface to blister and peel. The present technique starts with an Si wafer with a thermally grown top oxide layer about 250 nm thick. Hydrogen ions are then implanted in the Si to a depth of around 300nm below the oxide layer with a dispersion of less than 8 nm. The top surface of the wafer is then pressed against a new Si wafer and heated to form a hydrophilic bond. Further heating causes the hydrogen layer to blister and leave the new Si wafer with an 300 nm Si top surface and 250 nm buried oxide layer. The Si top surface is then chemomechanically polished to a smoothness of better than 1 nm RMS measured on AFM. This process is then repeated a second time, except that the additional Si wafer is replaced with the SOI wafer from the first iteration. In this way, multiple layers can be constructed. With only two iterations of this process (2 buried layers), substrates can be produced with better than 90% reflectivity. The reflector on which the microarray is fabricated is given a final 270 nm SiO_2 layer that is sputtered on the top Si surface. This final SiO_2 layer optimizes sensitivity by placing the biosensing layer in a feild maximum within the cavity. What constitutes these reflectors as an enabling technology of the biosensor is cost effectiveness as a disposable element, high reflectivity, low loss (negligible at 1500 nm), and remarkable smoothness.

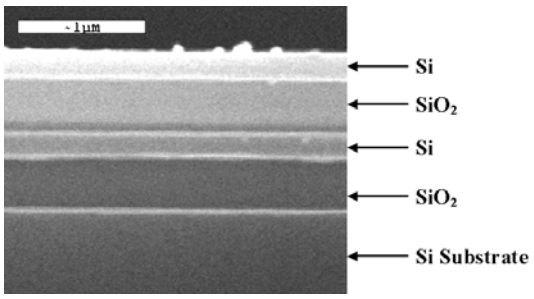

Fig. 3: Cross-sectional SEM of reflecting (double SOI) substrate

The biosensor optical cavity is formed between two of these reflectors. The top reflector is glued to a stage that can translate in the vertical direction to control the cavity thickness, generally set at around 100 µm. The bottom reflector has the capturing agents patterned on its surface and rests on a stage that can angle with 0.06 arc sec resolution to maintain parallel reflectors. A 40-mm focal length lens images the transmission from the cavity onto an infrared camera featuring an InGaAs photodetector array with high sensitivity in the 1550-nm range. All the lenses and optical components are anti-reflection coated for 1550 nm to avoid resonant behavior from the optical components themselves.

Artificial structures were used to demonstrate the biosensor operation. The structures were 4 boxes etched out of the SiO_2 surface that were 50 µm x 50 µm x 5 nm in size. The boxes were etched with hydrofluoric acid into the top SiO_2 surface of one of the reflectors using standard photolithography. The wavelength shift in the resonant curve was correlated to a height difference on the reflector surface. The four box structures can be clearly seen in the 2D image (Fig. 2). The deviation from the actual hieghts was found to be 0.7 nm RMS, corresponding to an accuracy of 1pg of protein in the 50 µm x 50 µm feature. Future work to improve these results includes identifying sources of vibrations and reducing their effect, cancelling out laser intensity noise, and improving the signal processing algorithms.

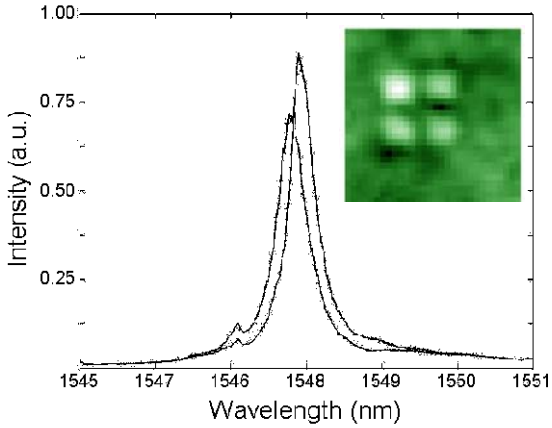

Fig. 2: Recorded resonant curves for two pixels. Shift indicates a 5-nm difference in height. (Insert) A 2-D image where brightness indicates the surface height at every location. Four box features can be seen. Measured boxes deviate from actual dimensions by 0.7 nm RMS.

We have demonstrated the use of novel buried SOI Bragg reflectors as an enabling technology of a novel resonant cavity biosensor. Bragg reflectors consisting of two buried oxide layers prove a cost effective platform for creating disposable cavities with high finesse. Artificial microarray features 5 nm in height have been detected with sensitivity sufficient for some biosensor applications. Improved sensitivity is expected with system improvements.

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References

[1] M. Schena, Microarray Biochip Technology, Natick, MA: Eaton Publishing, 2000.

[2] M. K. Emsley, O. Dosunmu, and M. S. Ünlü, "Silicon substrates with buried distributed Bragg reflectors for resonant cavity-enhanced optoelectronics," *IEEE Journal of Selected Topics in Quantum Electronics*, Vol. 8, No. 4, pp. 948-955, July/August 2002.