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Silica Suspended Waveguide Splitter-based biosensor

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Abstract

Label-free optical sensors enable real-time monitoring of water supplies, environmental contaminants as well as the detection of fundamental biological processes without the need for a fluorescent label or a secondary antibody. This real-time detection allows us to monitor processes as they are occurring. Recently, our group developed a novel optical waveguide splitter-based biosensor which is integrated on a silicon wafer. It detects events by monitoring the change in optical power transmitted through the device. However, unlike similar waveguide sensors, the waveguide is elevated off of the silicon substrate, improving its interaction with biomolecules in solution and in a flow field. Additionally, because it is fabricated from silica, it has very low optical loss, resulting in a high signal-to-noise ratio, making it ideal for biodetection. The simple test-setup needed to test the device, along with the simple analysis of the real-time data it produces makes our waveguide splitter biosensor a strong candidate for lab-on-a-chip applications.

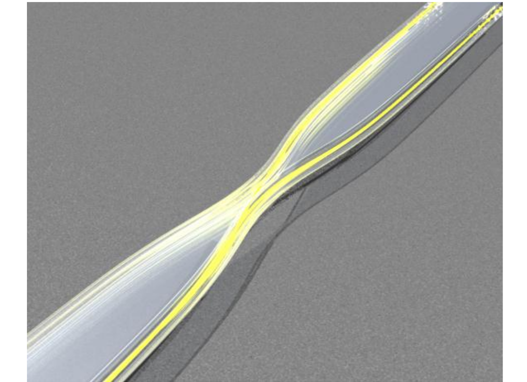
Background

Waveguide Splitters/Couplers

In any dielectric waveguide, some of the optical field will extend beyond the boundary of the waveguide as light travels down the device. This portion of the optical field is referred to as the “evanescent field.” If two waveguides are brought adjacent to each other, so that their evanescent fields overlap, light will couple from one waveguide to the other. The amount of coupling, or splitting ratio, depends on the wavelength of the light signal, the index of refraction of the waveguides, and the length of the coupling region.

Splitter Biosensing

Utilizing a surface chemistry functionalization process, we can attach probe molecules, such as antibodies, to the surface of the coupler. This allows the complimentary protein (and only the complimentary protein) to attach to these antibodies, which in turn changes refractive index of the waveguide. Because the coupling ratio of the device depends on the refractive index of the waveguide, we can monitor the binding activity of the protein by tracking the splitting ratio of the device. In this way, we can use these waveguide couplers as biosensors for the specific proteins that the devices were functionalized to detect.

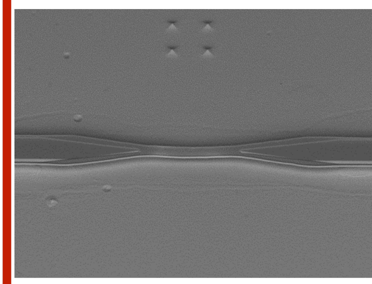


Computer rendering of waveguide splitter device, with the optical field split from one input arm to two output arms

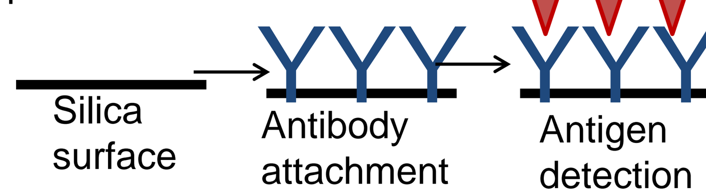
Fabrication

The devices are fabricated using a 4-step process. The steps, briefly, are as follows: 1) Double photolithography and Buffered HF etching, 2) XeF_2 etching to undercut the silica, 3) CO_2 laser reflow to create waveguide arms, 4) surface functionalization using an epoxy-silane method.

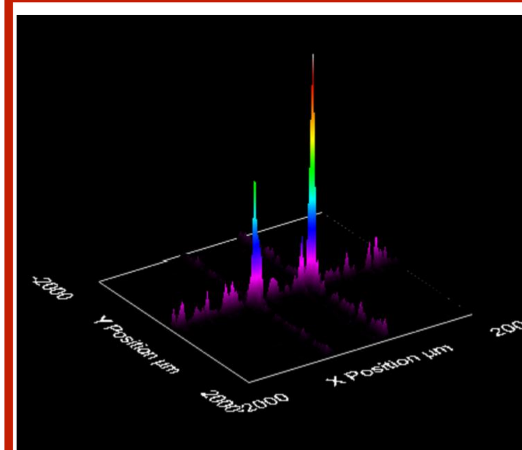
To perform detection, the surface of the splitter was chemically modified using epoxy-silane molecules with glycidyloxypropyl trimethoxysilane (GPTMS) to immobilize antibodies. The antibodies are specific to the CREB protein, which we used in our detection experiments.



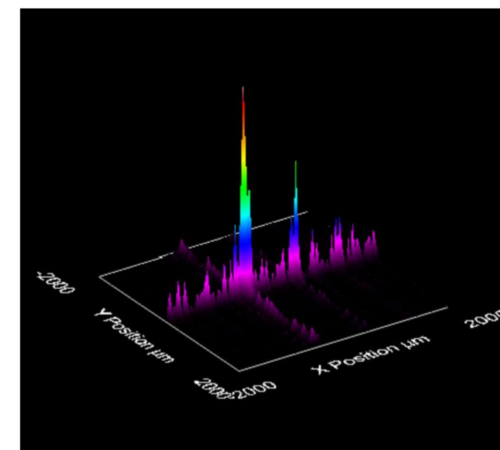
SEM image of a waveguide splitter device.



Operation



Beam profiler data of device output before the analyte has been introduced. There are two distinct peaks from which we can calculate the splitting ratio of the device.



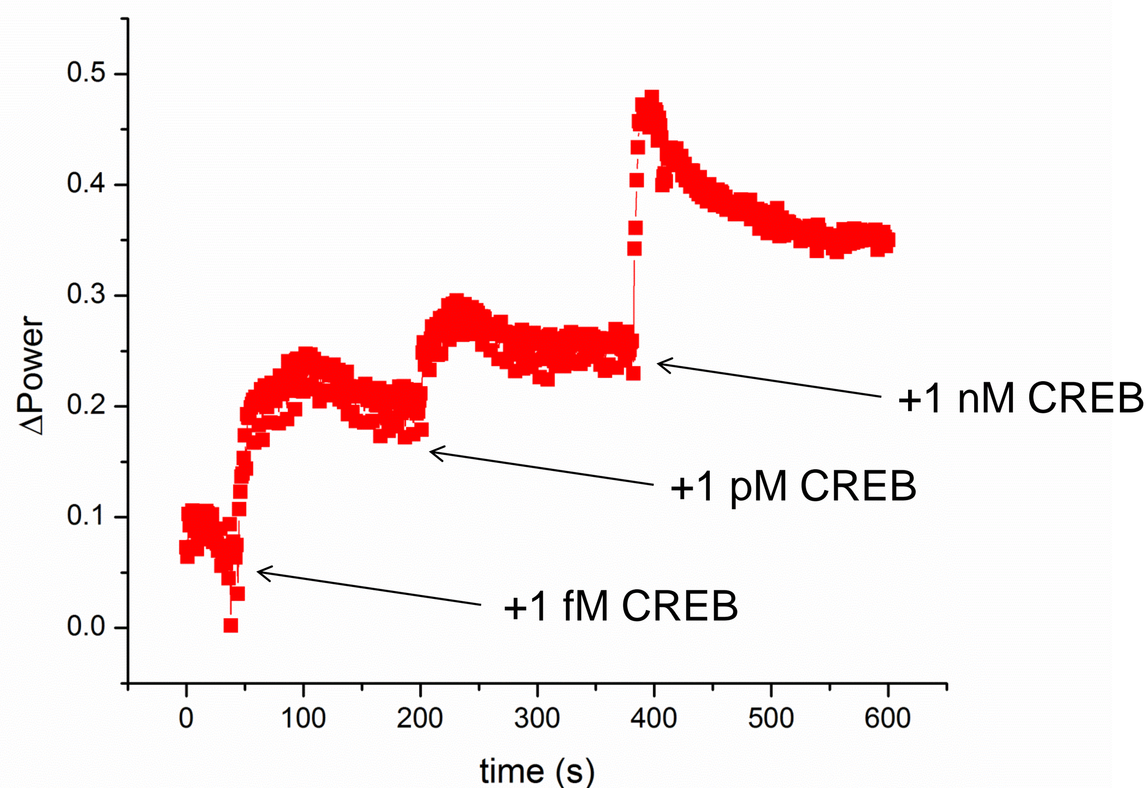
Beam profiler data of device output after the analyte has been introduced. When the analyte binds to the surface of the coupling region, it causes a shift in the splitting ratio of the device.

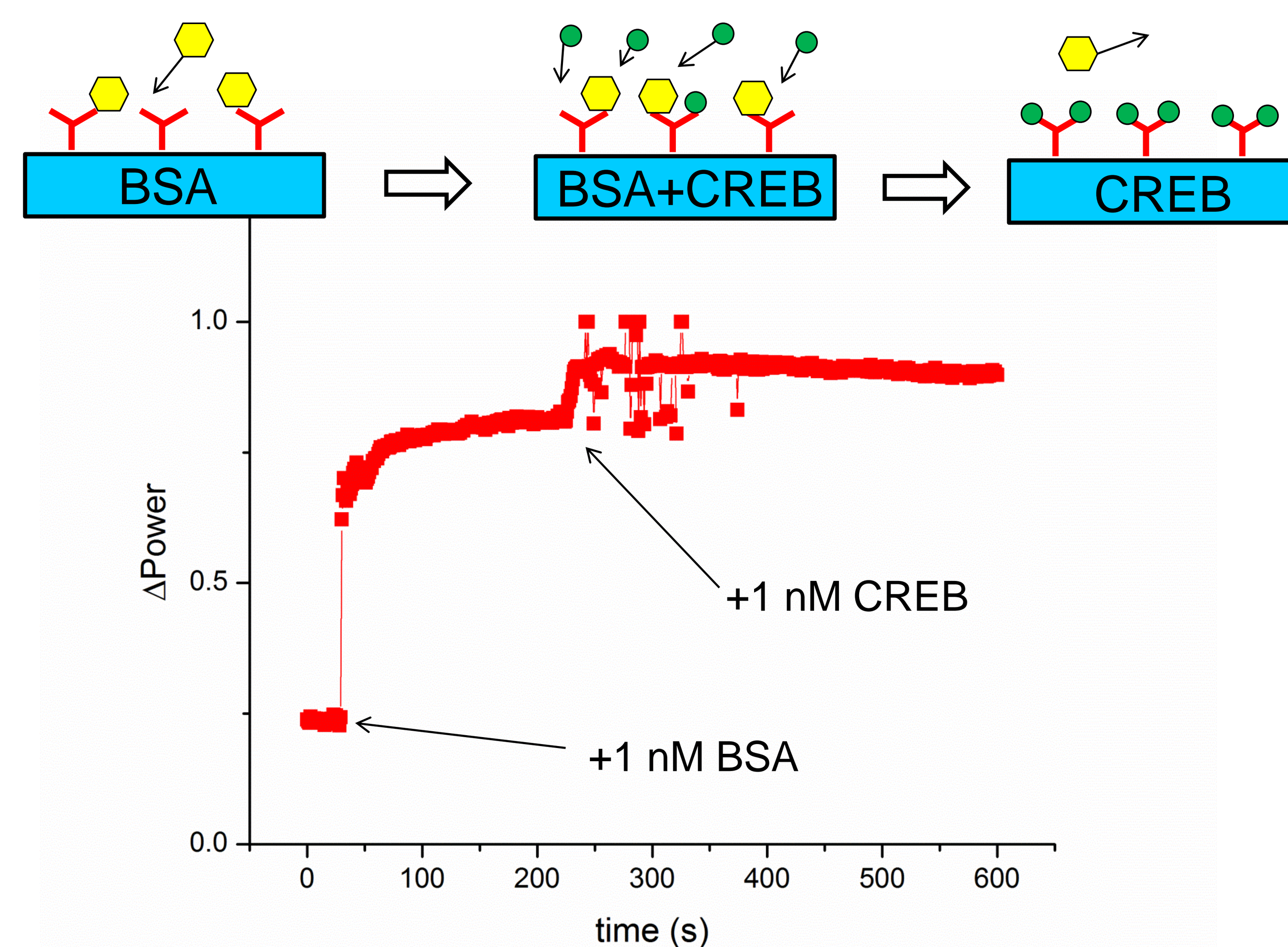
Experiments

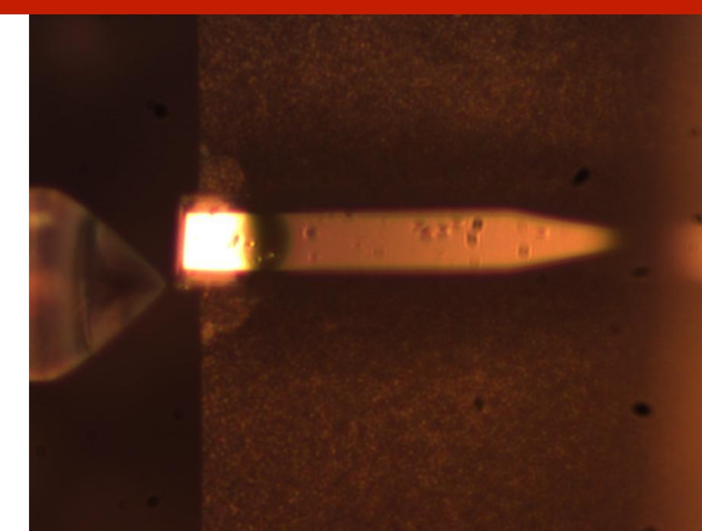
We deposit our analyte, a CREB protein solution of varying concentrations, to the coupling region of the device using a micropipette. The binding activity of the protein to its respective antibody is analyzed by monitoring the coupling ratio, which changes proportionally to the amount of bound CREB.

In all experiments, a buffer solution was added to the surface of the device first. In one experiment, we add increasing concentrations of CREB to the device. For another, as a control, BSA (Bovine Serum Albumin) was added to the existing buffer droplet, followed by a solution containing the analyte. The BSA behaved as a non-specific binder to mimic the presence of the CREB protein in a complex solution. After adding the BSA, we allowed the output of the coupler device to stabilize before adding the CREB protein.

Data and Results

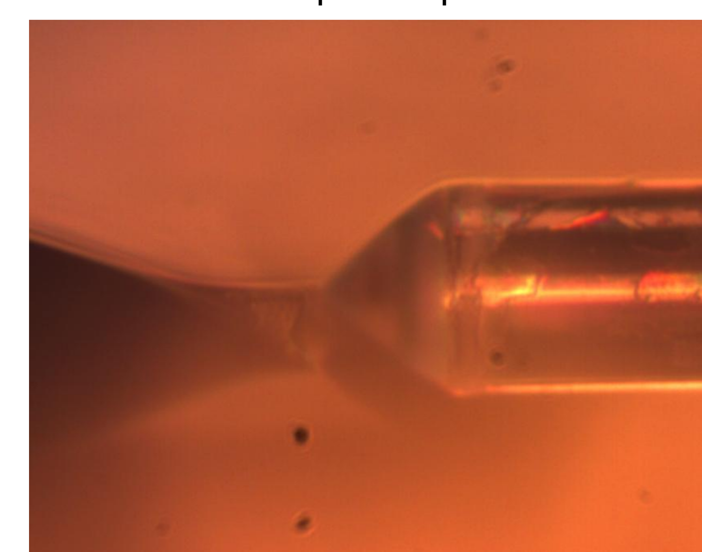






Top view of liquid droplet on device.

Side view of liquid droplet on device.



In the graphs above, you can see the results of a two important experiments, an increasing concentrations experiment on the left and a competitive binding experiment on the right. In the increasing concentrations experiment, you can see that the splitting ratio of the device shifts in varying amounts according to the concentration of protein added, and that the coupling ratio remains stable in-between droplets. In the competitive binding experiment, you can see that, although the BSA exhibits a strong response from the device, the CREB protein solution has an even stronger response, as those proteins will strongly bind to the immobilized antibodies on the device surface. It demonstrates our ability to perform detection in a complex solution.

Conclusions and Future Work

Computer rendering of waveguide splitter device integrated with a microfluidic channel.

In the results shown above, we have demonstrated real-time sensing with a very simple analysis. Furthermore, we have shown our devices have a remarkably high sensitivity, sensing down to fM concentrations. Finally, we have demonstrated the ability to perform specific detection in a complex solution. All these aspects make this waveguide splitter-based biosensor ideally suited for lab-on-a-chip applications.

We are currently working on improving the functionality of our waveguide-splitter biosensor, as well as understanding its operation more thoroughly. We plan to perform experiments using lower concentrations of analyte to determine the ultimate detection limit of the device. Another goal is to model analytically the complex relationship between the splitting ratio and the effective refractive index of the signal. Finally, we are currently working on integrating the device with microfluidics to enable flow, and improve our experiments and the device overall.

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