Nanocharacterization of Polymer-Modified Microring Resonators for Performance in Complex Media

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Introduction:

Silicon photonic microring resonators are label-free biosensors that are able to detect very small changes in bound mass on the surface of a nanophotonic waveguide in real-time, while requiring only a few microliters of sample. However, to realize the full potential of this biosensing technology, it's necessary to address the challenge of surface fouling and biocompatibility when performing diagnostic assays in complex biological matrices (e.g. blood, plasma, serum). Due to high interfacial energy at the surface, proteins irreversibly adsorb to the microrings upon contact. This non-specific fouling of the sensor surface leads to false positives and reduces the device's ability to detect specific binding interactions.

One strategy used to reduce non-specific adsorption is to grow a thin zwitterionic polymer layer from the silicon substrate of the sensor, producing a hydrophilic, non-fouling coating. In this study, carboxybetaine acrylamide (CBAA) was polymerized from microring resonators using atom transfer radical polymerization (ATRP). Sensors were then exposed to undiluted human blood plasma to determine the extent of fouling. The polymer film was characterized using atomic force microscopy (AFM) and scanning electron microscopy (SEM).

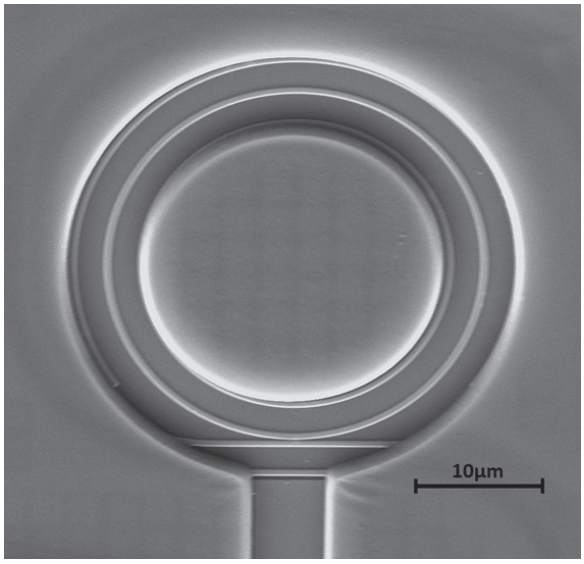

Figure 1: An SEM image of a microring resonator. Light is directed down a waveguide that runs adjacent to each microring (bottom). Resonance wavelengths are coupled into the microring, causing a decrease in output power.

AFM, SEM, and plasma fouling data were used to refine the ATRP process in order to establish a polymerization procedure that enables a microring resonator biosensor to be used in real-world diagnostic applications.

Methods:

Polymerization. First, trichlorosilane initiators were covalently bound to a surface by soaking in a toluene solution or by vapor deposition. Next, a CBAA polymer layer was grown via ATRP using a monomer/catalyst solution. After the reaction completed, the polymerized surface was tested for non-fouling properties. The initiator deposition procedure (liquid and vapor) and the reaction time (17- and 24-hour) were varied in order to determine optimal ATRP conditions.

Non-Fouling Test on Silicon Microring Resonators. Each silicon microring resonator biosensor chip contained 272 microring resonators (see Figure 1). An increase in resonance wavelength of a microring indicated an increase in mass density of the regions surrounding the ring.

Polymer-coated chips were tested for non-fouling properties by flowing undiluted human blood plasma over the chips for 15 minutes at a rate of 20 μL/minute. Prior to and after being exposed to plasma, the chips were washed with phosphate buffered saline (PBS) at the same flow rate for 20 minutes.

Results and Conclusions:

The first attribute of ATRP optimized in this study was the method of initiator deposition (liquid or vapor). For chips using liquid initiator deposition, high variance in signal attenuation indicated that the polymer growth was non-uniform (see Figures 2 and 3). The "liquid deposited" chip showed a fouling level of 92 ± 123 ng/cm^2. Although this chip achieved a lower fouling level than many others, the high standard deviation indicated non-uniform polymer growth.

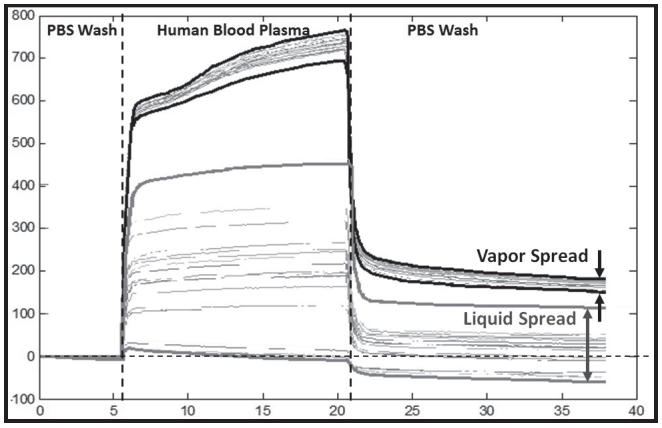

Figure 2: Microring resonator sensorgrams for vapor deposited (black) and liquid deposited (gray) chips. The liquid deposited chip is less uniform (as is apparent by examining the spread in each chip). The standard deviations are 13 ng/cm² and 123 ng/cm² respectively.

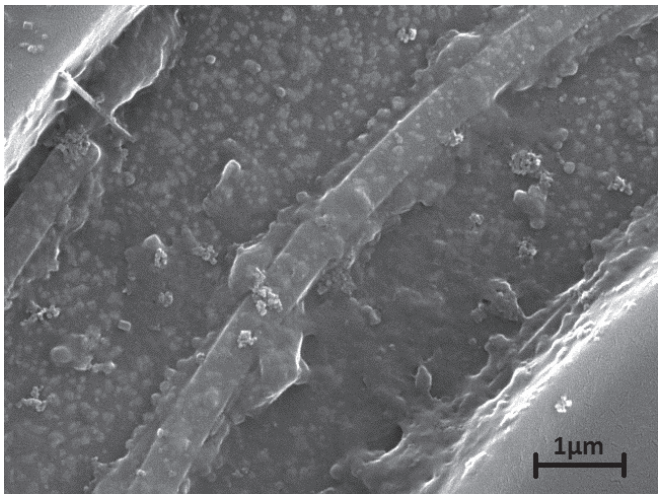

Figure 3: An SEM image of a microring resonator polymerized using liquid initiator deposition. Non-uniform polymer growth was confirmed using this (and other) SEM images.

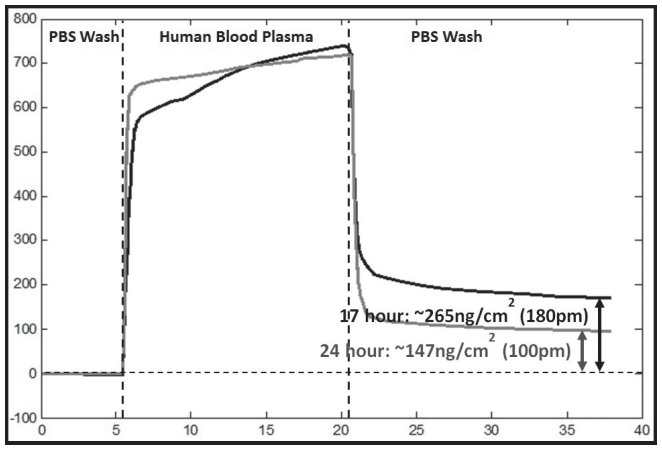

Figure 4: Microring resonator sensorgrams for 17-hour (black) and 24-hour (gray) ATRP reacted chips. These data showed fouling levels of 265 and 147 ng/cm² respectively.

The "vapor deposited" chip showed a fouling level of 265 ± 13ng/cm². Although this is much higher than the ultra-low fouling goal of 5 ng/cm2 [2], the small standard deviation showed that vapor deposition created a much more uniform polymer layer and a more robust biosensor.

The ATRP reaction time was also optimized in this study. Average fouling levels were compared for 17- and 24-hour vapor deposited chips. The 17- and 24-hour chips showed fouling levels of approximately 265 ng/cm² and 147 ng/cm² respectively (see Figure 4). Lower fouling levels on the 24-hour chips indicated that longer reaction time produced a denser polymer film, yielding a lower fouling surface.

Although the "ultra-low fouling" levels described previously [2] have not yet been reached, the results of this study support using a 24-hour ATRP reaction using vapor deposition of initiators. The 24-hour fouling levels were consistently lower than 17-hour levels. Liquid deposition of initiators showed greatly varied levels of polymerization, indicating varied thicknesses on sensor arrays. SEM and AFM images confirmed that polymer coatings had varied thicknesses among microring arrays and that each ring layer was non-uniform.

These data suggest that initiators should be bound using vapor deposition and that a 24-hour ATRP reaction should be used in future experiments.

Future Work:

Literature suggests that higher methanol percentage creates a denser film and a lower-fouling surface [1]. More manipulation of the solvent ratio could be experimented with to further decrease protein fouling levels. In addition, functionalization procedures (binding a capture element to the surface) will be tested for the non-fouling surface to enable specific analyte detection.

Acknowledgments:

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