

Smart Bandage - A Hydrogel Supported Optical Microcavity Sensor

L.A. DeLouise

University of Rochester Medical Center, Rochester, NY, USA, Lisa_DeLouise@urmc.rochester.edu

ABSTRACT

Porous silicon is a versatile material that is being exploited in numerous biomedical applications ranging from biosensing, drug delivery and tissue engineering. These applications exploit the exceedingly high internal surface area, the ability to tune pore morphology (porosity and pore diameter) and to tailor the silicon surface biochemical reactivity. In our laboratory we are developing a novel biosensor concept called a Smart bandage, which is comprised of an optical microcavity sensor membrane mounted in a flexible hydrogel support. Successful exploitation of porous silicon in this biosensor application hinges on our ability optimize the intrinsic microcavity sensitivity response and to fabricate sensors with pore diameters that enable facile infiltration of biomolecular reagents throughout the porous matrix. In addition, a thorough understanding of the critical parameters and trade-offs that impact detection sensitivity must be elucidated in order to achieve an optimum composite design. In this paper we introduce these trade-offs and focus on pore size optimization for which we demonstrate a high degree of fabrication control. Our success in tailoring the morphology and optical properties of porous silicon suggests that this material can be leverage in additional biomedical applications such as the design of scaffolds for tissue engineering or biofiltration and optical devices for cell grow monitoring.

Keywords: nanostructures, porous silicon, biosensor, hydrogel, optical microcavity, biomaterial

1 INTRODUCTION

Diagnostic medical technologies that can be used in the home for early detection and disease prevention are being developed at the University of Rochester Center for Future Health. This paper is concerned with developing a Smart Bandage concept which is envisioned as a therapeutic sheet containing an optical sensor element. The sensor can be designed to change color signaling an event that requires intervention such as the onset of infection or the detection of a pathogenic organism in a wound. Alternatively, the sensor can be designed to monitor the time released delivery of substances to promote wound healing.

Recently we have demonstrated a device prototype representing a significant advance toward achieving these goals. [1] The Bandage, illustrated in Figure 1, is comprised of a porous silicon optical microcavity membrane sensor (5.5 μm thick) supported in a flexible hydrogel matrix. This composite device, seeks to leverage the versatile material properties of both hydrogels and porous silicon, the latter of which is produced by electrochemical dissolution of single crystal silicon. The morphology of porous silicon is typically characterized by a pore diameter, mesoporous (2-50 nm) and macroporous (>50 nm), and a porosity ranging between 30 – 90%. Both parameters can be altered by varying the silicon wafer doping and the electrochemical etch conditions (current density and electrolyte composition).[2,3] Porous silicon optical microcavities are nanostructured multilayer interferometric devices that have predominantly been fabricated from mesoporous silicon (10-30 nm dia. pores) using p+ silicon (100) wafers. Recent research

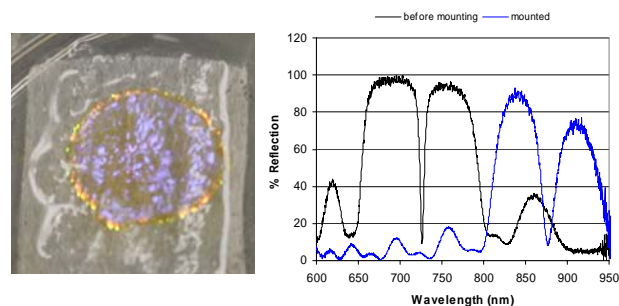


Figure 1 p+ mesoporous silicon microcavity membrane attached to a hydrogel sheet by contact lamination (left) and the microcavity reflection spectra before and after mounting in the gel support (right). [1]

has demonstrated the experimental feasibility of microcavity devices attached to the silicon wafer to function effectively as affinity based optical biosensors.[4,5] The sensing principle is based on monitoring a wavelength shift in the optical response (color change) resulting from a refractive index change that occurs within the porous matrix. For example, when a target binds to a receptor immobilized within the porous matrix the porosity decreases causing an increase in the refractive index and a red shift.

Currently, we are investigating methods to biochemically functionalize a microcavity sensor membrane detached from the silicon wafer and supported in a hydrogel matrix. Hydrogels are advantageous sensor support materials in that they are flexible and the material properties can be tailored to maintain critical environmental conditions (hydration, pH, and ionic strength) vital to sustaining activity of immobilized biomolecules. Hence, binding and recognition events can occur in a more “solution-like” environment. As such, they are being increasingly investigated as a preferred substrate for a variety of proteomic, biosensor and microarray chip applications.[6-9]

Preliminary work on gel-supported p+ mesoporous microcavity membranes discovered a remarkable long term stability of the optical response of thermally oxidized microcavities exceeding >1 yr.[1] Employing various concentration sucrose solutions the sensor dynamic range was found to remain sufficiently sensitive to small changes in index of refraction (<0.01). This and our on-going efforts to implement and demonstrate gel-supported affinity detection have revealed several significant challenges that must be met in order to bring this device concept to a successful realization. Foremost among them are questions relating to trade-offs between the porous morphology (of both the gel and the porous silicon) and how these impact biomolecular flow (diffusion and active pumping), detection sensitivity and sample analysis time. It is beyond the scope of this paper to elucidate the complex interdependencies of these parameters. Instead we will simply focus here on the importance of the porous silicon nanostructure. Because the microcavity is a volume detection device, detection sensitivity depends on a facile pore infiltration of bioreagents. Hence, pore diameter in relation to biomolecular size is a critical parameter. Recent studies by Arwin and coworkers [10,11] employing human serum albumin (HSA) found that when the size of a protein is comparable to that of the pores, loading of protein into porous matrix is limited under diffusion.[10] They observed a concentration dependence on pore penetration depth and for thicker films (> 2 μm) protein adsorbs does not penetrate to the full depth of the pores. Nonetheless, this studied showed that a relatively large size protein (~68 kDa) can penetrate porous silicon with a mean pore diameter ~11 nm. Interestingly, in our p+ mesoporous *E. coli* affinity sensor development research (unpublished), a high rate of false negatives were observed which we have attributed to pore blocking preventing target infiltration. Consequently, we have devoted a significant effort towards developing etch processes to fabricate macroporous microcavity sensors with pore diameters ranging between 50-90 nm. A key challenge

arises in fabricating macroporous microcavities in that larger pores cause of rougher morphology at the interface between multilayers which degrades the quality of the optical response. Nonetheless progress is being made. In this paper we demonstrate the ability to systematically tune the pore diameter over a wide range using n+ silicon (100) wafers and that it is possible to fabricate good quality multilayer microcavities. Our preliminary data suggests that a trade-off exists between microcavity refractive index unit (RIU) sensitivity and pore diameter which can be explained based on a decrease in porosity.

2 EXPERIMENTAL

Porous silicon (PSi) nanostructures and multilayer devices reported here were fabricated by anodic electrochemical dissolution of a n⁺-type single crystal silicon <100> wafer with a resistivity of 0.01-0.02 $\Omega\text{-cm}$ using a hydrofluoric acid (HF) containing electrolyte. Various pore diameters (10 – 500 nm) were produced

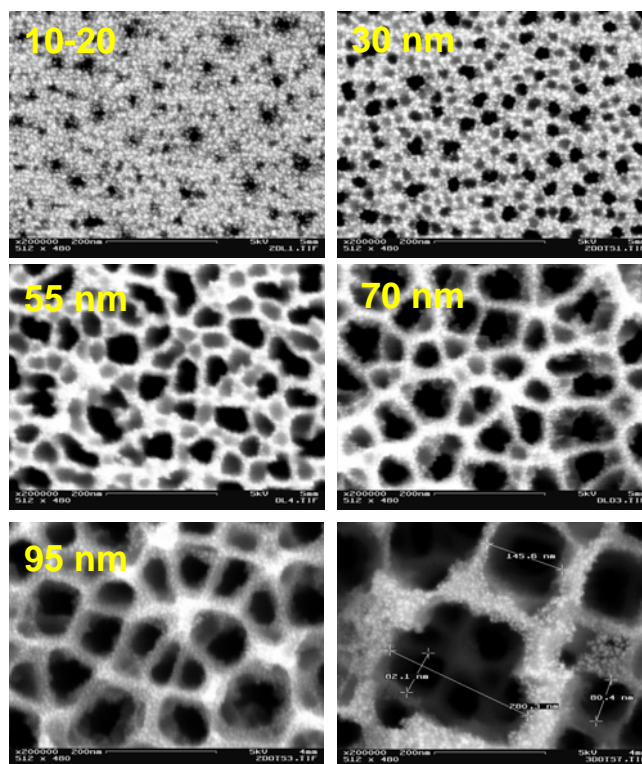


Figure 2 SEM images illustrating the wide range of pore diameters achieved in n+ silicon by varying etch parameters (electrolyte composition and current density). Lower left image illustrates a multilayer structure with the pore diameters exceeding 200 nm in the top layer through which 80 nm pore diameters in the second layer are observed. All images are at the same magnification.

by changing the electrolyte composition including the ethanol (0-50%), HF (5-20%) and surfactant (Pluronic F108 and Zonyl FSO100, 0-0.1%) concentrations and by applying various current densities (15 – 500 mA/cm²). A general trend observed is that raising the current density increases the pore diameter and that lowering HF and solvent loading enable larger pore diameters to be formed at lower current densities. Raising the HF concentration increases the etch rate and lowers porosity. Results of a comprehensive Design of Experiments (DOE) approach undertaken to explore the interdependencies are forth coming. Details of the microcavity fabrication method and a discussion of characteristic quality attributes are described elsewhere.[2,5] Briefly, sensors are fabricated by applying a constant current density for a fixed time and cycling between different current densities to produce a multilayer device with different porosity layers. Porosity is related to index of refraction through effective medium theory.[12] Interferometric interactions of white light within the multilayer structure gives rise to characteristic Fabry-Perot resonance features in the optical spectrum that are monitored to detect changes in index of refractions.

RESULTS

Various electrolyte formulations were tested by applying a constant current density (15, 40, 60 and 300 mA/cm²) for 300 sec. SEM images of pore diameter and film thickness (cross section) were measured from which the etch rate data determined. Porosity was measured using gravimetric methods.[2] Figure 2 illustrates the representative range of pore diameter and morphology readily achieved. From simple geometric considerations it is clear that a relationship exists between porosity (and internal surface area) and pore diameter. Higher porosities are common with smaller pore diameters because a higher pore density is possible. Nonetheless we observe porosities exceeding 80% with pore diameters in the 90 nm range employing a current density of 60 mA/cm² and an electrolyte containing 7.5% HF and 0.1% Pluronic F108. Because physical roughness (desired to be less than $\lambda/15$) at the interlayer interface degrades the quality of the microcavity optical response, we have concentrated our initial efforts on fabricating microcavities with pore sizes ranging between 20 – 60 nm which is on average much larger than mesoporous devices we traditionally fabricate. Utilizing an electrolyte containing 7.5% HF and 20% ethanol, the microcavity multilayer device shown in Figure 3 was fabricated. The high porosity layer (67%) contained a pore diameter ranging between 50-60 nm where as the lower porosity layer (40%) contained pore diameters ranging between 20-30 nm. The optical response from this microcavity under white

light reflection is pictured in Figure 4. The base line response with air in the pores yields a Fabry-Perot resonance dip at 729.8 nm (blue). The magnitude of the wavelength shift refractive index unit (RIU) sensitivity was determined by measuring the red shift after filling the pores 100% with water ($\eta=1.333$),

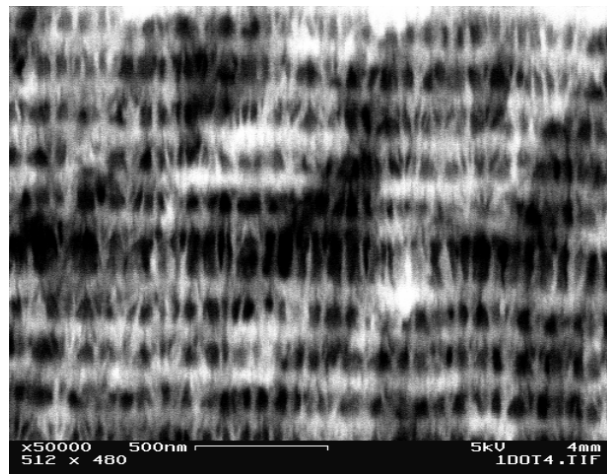


Figure 3 SEM image of a $n+\lambda/2$ microcavity comprised on 9 cycles of high (67%) and low (40%) layers per mirror (not all layers are shown).

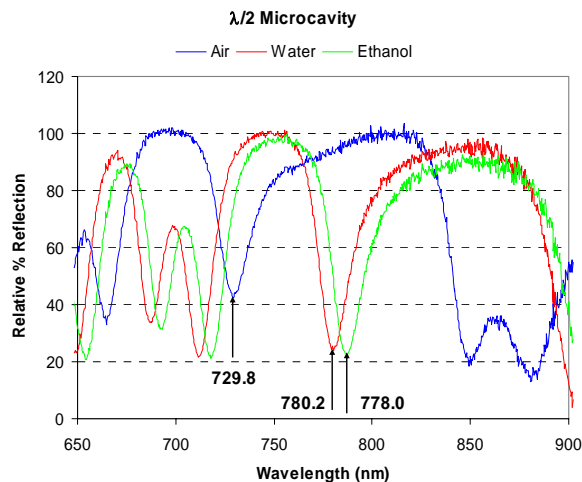


Figure 4 Optical response of the microcavity pictured in Figure 3 illustrating the Fabry-Perot resonance dips with the pore filled with air ($\eta=1.000$) and the red shift that results when the pore are filled with higher refractive index substances water ($\eta=1.333$) and ethanol ($\eta=1.3614$). Asymmetry in reflectivity about the resonance dip indicates a slight adjustment in optical thickness of one of the layers is needed..

ethanol ($\eta = 1.3614$) as illustrated in Figure 3. We also measured methanol ($\eta = 1.3284$) and dichloromethane ($\eta = 1.422$) which are not illustrated for clarity. This microcavity yielded a wavelength shift sensitivity value of 164 nm/RIU, which was determined from the slope of a linear least squared line fit to a plot of wavelength shift vs. RI. This sensitivity value is significantly lower than that observed for p+ mesoporous microcavities (74% / 89% porosity layers) tuned to operate in the visible spectrum which typically achieve 450 nm/RIU. [13] We attribute this decrease to a lower porosity. The lower void volume exists in which a refractive index change can occur.

4 CONCLUSIONS

We have demonstrated the ability to systematically tune the pore diameter of n+ porous silicon (0.01 Ω -cm) over a wide range by varying the electrochemical etch parameters (electrolyte composition and current density). The value of the wavelength shift sensitivity for a $\lambda/2$ microcavity consisting of alternating low porosity (40%, 20-30 nm dia. pores) and high porosity (67%, 50-60 nm dia. pores) layers was measured to be 164 nm/RIU. For affinity biosensor applications employing porous silicon microcavities it is advantageous to maximize the value of the wavelength shift for a given index of refraction change. Sensitivity values exceeding 2000 nm/RIU are benchmark. [14] Hence, further research is needed to identify the optimum microcavity nanostructure that embodies both large pore diameters and a maximized sensitivity response. This is especially important because preliminary studies on p+ mesoporous microcavities suggest mounting in the gel-support attenuates the sensitivity response. Designing microcavities to operate in the IR may hold promise to enhance sensitivity. [13]

REFERENCES

- [1] Lisa A. DeLouise, Philippe M. Fauchet, Benjamin L. Miller, Alice A. Pentland "Hydrogel Supported Optical Microcavity Sensors", submitted.
- [2] C. Vinegoni, M. Cazzanelli, L. Pavesi, in *Silicon based Materials and Devices Vol. 2 Properties and Devices*, (Ed: H. S. Nalwa), Academic Press **2001**, pg. 124.
- [3] Zhang, X.G., "Morphology and Formation Mechanisms of Porous Silicon", *J. Electrochem. Soc.* **2004**, *151* (1) c69-c80.
- [4] Chan, S., Horner, S. R., Miller, B. L., Fauchet, P. M. "Identification of Gram Negative Bacteria using Nanoscale Silicon Microcavities", *J. Am. Chem. Soc.*, **2001**, *123*, 11797-11798.
- [5] Chan S., Fauchet P. M., Li Y., Rothberg L. J., and Miller B. L., "Porous Silicon Microcavities for Biosensing Applications", *physica status solidi (a)*, **2000**, *182*, 541.
- [6] S. Zhang *Nature Materials* **2004** *3*, 7.
- [7] S. Kiyonaka, K. Sada, I. Yoshimura, S. Shinkai, N. Kato, I. Hamachi, *Nature Materials* **2004** *3*, 58.
- [8] P.T. Charles, E.R. Goldman, J.G. Rangasammy, C.L. Schauer, M.S. Chen, C.R. Taitt, *Biosensors and Bioelectronics*, **2004**, *20*(4) 753.
- [9] Miller, Jeremy C., Heping Zhou, Joshua Kwekel, Robert Cavallo, Jocelyn Burke, E. Brian Butler, Bin S. Teh, and Brian B. Haab "Antibody microarray profiling of human prostate cancer sera: antibody screening and identification of potential biomarkers", *Proteomics* **2003**, *3*(1): 56-63.
- [10] Karlsson LM, Tengvall P, Lundstrom I, Arwin H., "Penetration and loading of human serum albumin in porous silicon layers with different pore sizes and thicknesses.", *J Colloid Interface Sci.* **2003**, *266*(1):40-47.
- [11] H. Arwin, M. Gavutis, J. Gustafsson, M. Schultzberg, S. Zangoie, P. Tengvall, "Protein Adsorption in Thin Porous Silicon Layers", *physica status solidi (a)*, **2000**, *182*(1), 515 - 520.
- [12] Bruggeman, D.A.G. *Ann. Phys. Paris* **1935** *24*, 636 .
- [13] Lisa A. DeLouise, Peng Meng Kou, and Benjamin L. Miller, "Cross-correlation of Optical Microcavity Biosensor Response with Immobilized Enzyme Activity - Insights into Biosensor Sensitivity, In press. *Anal. Chem.*
- [14] Jung, L. S.; Nelson, K. E.; Stayton, P. S. ; Campbell, C. T. *Langmuir* **2000** *16*, 9421-9432.