Published in final edited form as:

Adv Funct Mater. 2010 January 19; 20(4): 573–578. doi:10.1002/adfm.200901694.

Integration of a Chemical-Responsive Hydrogel into a Porous Silicon Photonic Sensor for Visual Colorimetric Readout

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Abstract

The incorporation of a chemo-responsive hydrogel into a 1D photonic porous silicon (PSi) transducer is demonstrated. A versatile hydrogel backbone is designed via the synthesis of an amine-functionalized polyacrylamide copolymer where further amine-specific biochemical reactions can enable control of cross-links between copolymer chains based on complementary target–probe systems. As an initial demonstration, the incorporation of disulfide chemistry to control cross-linking of this hydrogel system within a PSi Bragg mirror sensor is reported. Direct optical monitoring of a characteristic peak in the white light reflectivity spectrum of the incorporated PSi Bragg mirror facilitates real-time detection of the hydrogel dissolution in response to the target analyte (reducing agent) over a timescale of minutes. The hybrid sensor response characteristics are shown to systematically depend on hydrogel cross-linking density and applied target analyte concentration. Additionally, effects due to responsive hydrogel confinement in a porous template are shown to depend on pore size and architecture of the PSi transducer substrate. Sufficient copolymer and water is removed from the PSi transducer upon dissolution and drying of the hydrogel to induce color changes that can be detected by the unaided eye. This highlights the potential for future development for point-of-care diagnostic biosensing.

1. Introduction

Clinical and point-of-care (POC) diagnostic devices require the specific detection of biological and/or chemical targets at low concentration, in an inexpensive, convenient, reliable, and rapid manner. Many innovative approaches have been reported to address this complex problem yet a need still exists for practical technology solutions. Responsive hydrogels that undergo morphological changes resulting from external stimuli have displayed great promise in chemical sensing^[1] and medical diagnostics,^[2–4] as well as drug delivery,^[5] tissue engineering,^[6,7] and microfluidic applications.^[8] Variation of polymer composition, structure, and incorporation of specific functional groups have been exploited to develop hydrogels that respond to an array of biochemical targets including antigen,^[8] DNA,^[9] toxins,^[10] drugs,^[11] and enzymes.^[12] Integration of these smart polymers into specifically engineered sensing systems constitutes an active area of research.

Miniaturization of hydrogel dimensions facilitates reduced response times relative to bulk gel kinetics as required particularly for POC diagnostic testing.^[13] Notable success in development of smart hydrogel microlenses into multiplexed stimuli-sensor arrays has been achieved with response time of seconds.^[14,15] However, reliance on optical instrumentation

to monitor the responses from these microscale devices (change in refractive index or lens radius of curvature) is a drawback for POC applications.

A more attractive approach for POC applications is to integrate smart hydrogels with colloidal crystal arrays^[1,2] or photonic bandgap materials.^[16] These composite materials potentially enable direct optical detection of hydrogel morphological changes with rapid steady state response times of seconds to minutes. Porous silicon (PSi) is a photonic material that is ideally suited for this application due to its inexpensive fabrication, robust optical transduction, and ease in translation for high-throughput analysis.^[17–20] The unique optical properties of PSi can be exploited to sensitively detect small changes in the effective refractive index (η) that occurs within the porous matrix. Chemical and biological sensors have been developed to specifically capture target molecules onto the porous surface area to analyze complex samples in high-throughput and multiplexed assays.^[17–20] In addition, visual color readout has been achieved in the detection of protease activity.^[21,22] Protease digestion of a protein layer coated on top of a PSi photonic crystal caused cleavage products to infiltrate the pores producing a large η change that was observed by eye as a color change. These studies highlight the potential for developing PSi photonic sensors for POC diagnostic applications. The capability to easily tune the optical spectrum of the PSi-based 1D photonic crystal during fabrication facilitates a more deterministic color change combination for portable POC sensing applications. For example, design of a green-to-red color change may be more readily interpreted than a sensor that results in a red-to-deeper-red or blue-to-green color change.

Hydrogel-supported PSi sensors have also been investigated.^[16,23–25] Results show that the sensor maintains the capability to detect small changes in η (10^{-3} – 10^{-4}) that result from diffusion of small analytes.^[23] Composite hydrogel–PSi sensors are also able to detect gel structural changes induced in response to stimuli (temperature and pH)^[16] or that result from changes in gel composition.^[24,25] However, incorporation of a bio- or chemoresponsive hydrogel into a photonic PSi sensor with a tunable target response remains to be demonstrated and is the focus of our research.

Our hydrogel synthesis strategy is based on amine functionalization of the otherwise chemically inert polyacrylamide. The amine groups allow incorporation of versatile reaction chemistries enabling the control of cross-links between copolymer chains based on complementary target–probe systems. Here we demonstrate for the first time, incorporation of a model chemical-responsive hydrogel into a photonic PSi sensor to achieve tunable direct optical detection. Changes in η of a disulfide cross-linked hydrogel (S-S-coPAAm) incorporated into a PSi Bragg mirror are monitored upon exposure to a target reducing agent analyte, tris(2-carboxyethyl) phosphine (TCEP). Fabrication of a PSi Bragg mirror involves anodic electrochemical etching of a p-type, boron-doped Si wafer.^[26] Control of the applied current is used to create alternating layers of high and low porosity to dictate the frequency of a distinct peak in the white-light reflectivity spectrum. TCEP-induced dissolution of the S-S-coPAAm hydrogel results in decreasing η . Large η changes result in visual color responses that can be observed by the unaided eye. The dissolution characteristics of the S-S-coPAAm hydrogel are shown to depend on hydrogel cross-linking density, applied concentration of TCEP, and pore size and architecture of the PSi template structure. This hybrid design exhibits characteristics optimal for POC chemical and/or biological sensing due to its inexpensive fabrication, straightforward optical detection, and capability for visual color readout without any secondary label amplification.

2. Results and Discussion

2.1. Synthesis of Disulfide Cross-Linked Hydrogels (S-S-coPAAm)

Chemical formation of S-S-coPAAm is shown in Figure 1. Free radical polymerization of acrylamide (AAm) and *N*-(3-aminopropyl)-methacrylamide (NAPMAAm) monomers formed copolymer chains with a controlled concentration of nucleophilic amine moieties (Fig. 1a,b).^[24,25,27] Reaction with *N*-succinimidyl-*S*-acetylthiopropionate (SATP) adds protected sulfhydryl groups to the copolymer chains. The NHS-ester present in the SATP molecule reacts with primary amines to form stable amide bonds (Fig. 1c). The sulfhydryl groups were subsequently deprotected by hydroxylamine (Fig. 1d,e) and cross-links between copolymer chains result upon formation of disulfide bonds (Fig. 1f) producing a hydrogel network. Addition of TCEP reducing agent cleaves the cross-links inducing hydrogel dissolution.

Characterization by ¹H NMR spectroscopy proved that increasing the molar ratio of NAPMAAm to AAm in the prepolymer solution resulted in sequentially more amine moieties in the copolymer chains (Table S1, Supporting Information (SI)).^[25] The reaction chemistry for cross-linking is specific to the amine moieties. Therefore, varying the molar percentage of NAPMAAm in the copolymer backbone controls the cross-linking ability of the copolymer chains. As cross-linking density increases swelling is restricted, and the η of the resulting hydrogel increases. Visual increases in rigidity of the formed hydrogels were also observed as the molar percentage of NAPMAAm was increased (4.14, 17.82, and 37.27%, Fig. S1 (SI)). The negative control (0 mol% NAPMAAm copolymer) did not form a hydrogel, but remained in solution phase as expected.

2.2. Optical Characterization of Hybrid S-S-coPAAm-PSi Sensors

A bench-top Abbe refractometer (Bausch and Lomb) was used to measure the η of each bulk hydrogel sample produced. Samples were first incubated in deionized water for 2 days on a shaker plate to allow for equilibrium swelling and non-cross-linked copolymer chains to diffuse out. A direct linear relationship between the molar percentage of NAPMAAm and η values was observed (Fig. 2a). The optical response of the PSi Bragg mirror was used to analyze hydrogel infiltration into the porous matrix. Sulfhydryl functional copolymers in solution (10 wt%) were added to PSi Bragg mirrors that were functionalized with 3-(mercaptopropyl)-trimethoxysilane (mercaptosilane) as described in detail in the Experimental. The mercaptosilane coating enables the copolymer chains to cross-link via disulfide bonds to the PSi substrate. Chemically tethering the hydrogel to the PSi is essential for producing reproducible optical responses that vary systematically with hydrogel composition.^[25] Changes in η of the PSi sensor resulting from addition of mercaptosilane and hydrogel (after soaked in water for 2 days) can be seen as wavelength shifts in the spectral peak in Figure 2b. The wavelength shift for water ($\eta = 1.333$) filling the pores is also shown as a reference spectrum to illustrate the additional shift attributed to cross-linked polymer fibers of the hydrogel.

The magnitude of wavelength shifts resulting for S-S-coPAAm hydrogels with varying molar percentages of NAPMAAm cross-linked in the PSi Bragg mirror are shown in Figure 2c. As the molar percentage of NAPMAAm is increased, a red-shift is observed which is consistent with an increase in η of the resulting hydrogel confined in the PSi. As expected, a 0 mol% NAPMAAm negative control polymer solution (100% AAm, 10 wt%, $\eta = 1.3455$) produced no detectable wavelength shift beyond that observed for water (107.1 nm) filling the pores. Here, polymer chains lack reactive amine moieties for sulfhydryl conversion and thus uncross-linked chains washed away during the 2 day soak period.

The wavelength shift for each hydrogel filling the PSi sensor was theoretically predicted using Bruggeman effective-medium approximation.^[26] Pores were simulated to be filled 100% with materials of η equal to what was measured on the bulk hydrogels (4.14, 17.82, 37.27 mol% NAPMAAm) using a bench-top Abbe refractometer, and $\eta_{\text{water}} = 1.333$ was used for the 0 mol % NAPMAAm control (Fig. 2c). Simulation parameter values of thickness and open porosity of the PSi layers (Table S2 (SI)) were determined by scanning electron microscopy (SEM, thickness only), gravimetry, and optical measurements as previously described by Segal et al.^[16] Simulation and experimental results correlate within 1 standard deviation for each polymer tested (Fig. 2c). These optical measurement data prove that the cross-linked hydrogel fills the 3D PSi matrix. Stability of the fully hydrated hybrid sensors (in 1 mL water) was optically monitored for 48 h. No observable wavelength shift was detected for any of the samples (0, 4.14, 17.82, 37.27 mol% NAPMAAm) indicating that the state of the composite hydrogel–PSi material is stable over this period (data not shown). Initial testing indicates that dry storage (1 month) of the hybrid hydrogel–PSi devices and rehydration before use facilitated reproducible results. This is consistent with previous work of hydrogel-supported PSi sensors.^[23]

2.3. Investigation of System Factors that Govern Sensor Temporal Response

Alternate forms of disulfide cross-linked hydrogels have previously been used as a proof-of-concept for integrating chemical-responsive hydrogels into microfluidic sensor systems.^[28, 29] In each case, a disulfide-containing cross-linker (cystaminebisacrylamide, BAC) was used to form polyacrylamide hydrogels inside microchannels (diameter, d , is on the order of hundreds of nanometers). Addition of reducing agents under flow conditions caused gel dissolution. Three important design parameters were highlighted: 1) outside concentration of target molecule, 2) original volume of the hydrogel, and 3) cross-linking density of the hydrogel.^[29] Important differences in our design include different hydrogel structure (disulfide cross-linking of preformed copolymer chains), confinement of hydrogel into smaller PSi pores (d : tens of nanometers) that have one inlet/outlet, and static (no flow) conditions. The aforementioned design parameters were investigated individually as they pertain to our sensor system (Fig. 3).

After TCEP analyte diffuses into the hydrogel-filled PSi matrix a small positive wavelength shift can be observed correlating to the increased η of the TCEP solution (Table S3 (SI)). Within seconds the hydrogel begins to dissolve causing a blue-shift in the wavelength as the non-cross-linked copolymer chains diffuse out of the PSi matrix. All wavelength shift data in Figure 3 are displayed in reference (0 on x -axis) to the reflectance peak position with water filling the PSi matrix.

2.3.1. Effect of Hydrogel Structure on Observed Dissolution Response—Cross-linking density is shown to greatly affect hydrogel dissolution in Figure 3a. Measurements were taken in a 1 mL bath of 50 mM TCEP for all cases. The negative control (0 mol% NAPMAAm) displays a red-shift in the wavelength of 0.98 nm. This value correlates well with simulation for the increase in η of the TCEP solution ($\eta = 1.3368$) entering the pores compared to water ($\eta_{\text{water}} = 1.333$). No additional shift due to the polymer is observed because no amine moieties exist in the polymer backbone to allow sulfhydryl attachment or subsequent cross-linking. Moreover, no temporal response shows that the PSi sensor is stable in the TCEP solution over the test interval.

Samples that formed hydrogel networks (4.14–37.27 mol% NAPMAAm, Fig. 3a) displayed an increased rate of blue-shift response to TCEP with lowering cross-linking density. This suggests that less cross-linked hydrogels break apart and diffuse out of the PSi matrix more quickly. With higher cross-linking density, more entanglement of copolymer chains is probable, and more disulfide bonds must break to free the chains. For the highest cross-linked

sample (37.27 mol% NAPMAAm) only a small decrease in wavelength shift was observed, even after 4 h incubation in >100 mol excess of TCEP (5×10^{-5} mol). Quantification of sulfhydryl groups on the pre-copolymer chains (5.49×10^{-8} mol) was performed with an Ellman Assay (Table S4 (SI)).^[30] This result is consistent with literature, which reports that similarly high concentrations of reducing agents (0.1–1 M) were needed to dissolve disulfide cross-linked hydrogels (0.273–0.682 mol% BAC cross-linker) over similar time periods.^[28, 29] One key difference observed with our sensor system is that the wavelength shift never returns to zero (water filling the pores) even after overnight soaking in 0.1 M TCEP and subsequent rinsing with water (data not shown). This suggests that residual polymer remains in the PSi, which we discuss further below.

2.3.2. Dependence of Dissolution Response on the Concentration of Applied Target Analyte

—The sensor system response was shown to also depend greatly on the concentration of TCEP (Fig. 3b). Measurements were taken on 4.14 mol% NAPMAAm hydrogels cross-linked into PSi Bragg mirrors mounted inside a 500 μ L bath with varying TCEP concentrations (0–100 mM). The negative control (water only) showed no response whereas a wavelength blue-shift is observed for all concentrations of TCEP tested (1–100 mM). The magnitude and rate of the response increase with the TCEP bath concentration for 1–50 mM solutions. Both 50 and 100 mM TCEP solutions result in similar response, suggesting that dissolution of the hydrogel is the limiting factor. As TCEP is noted for its fast diffusion and reactivity, chain disentanglement has previously been highlighted as the rate-limiting step for disulfide cross-linked hydrogel dissolution.^[29] These initial experiments were performed in static solutions, and future work may investigate how mixing improves dissolution kinetics.

2.3.3. Effects of PSi Transducer Architecture on Confined Hydrogel Dissolution

—In this work we were particularly interested in investigating how confinement of the hydrogel inside the PSi volume affected dissolution. Recent results by Segal et al. showed that pore size and porosity strongly influenced the extent and rate of the optical response reporting the phase transition behavior of a thermoresponsive hydrogel (poly(*N*-isopropylacrylamide)) confined within a single layer porous SiO₂ template.^[16] Therefore, we chose to investigate effects of pore diameter (d) and porosity (P) in single-layer PSi films as well as Bragg mirror architectures comprising alternating high and low porosity (large and small pore diameter) layers (Fig. 3c).^[26] TCEP concentration (500 μ L, 50 mM) and hydrogel cross-linking (4.14 mol% NAPMAAm) were kept constant. Data in Figure 3c,d are normalized to the initial wavelength shift value attained with hydrogel filling the pores for each sensor investigated. This allowed for easier comparison between different PSi architectures as they display different wavelength shift sensitivity to changes in η (Table S2 (SI)).^[26]

The influence of PSi sensor architecture on the incorporated hydrogel dissolution is evident in Figure 3c. Dissolution includes three sequential phases: disentanglement of copolymer, dissolution of copolymer chains, and convective mass transport out of the PSi matrix.^[29] The overall dissolution rate is determined by the slowest phase. The rate and saturating magnitude of the optical response decreases as pore diameter (d) was decreased in the single layers. This suggests that smaller pores restrict dissolution. In both cases, mirrors created from alternating porous layers ($d = 19/43$ and $73/106$ nm) display slower rates and smaller magnitudes of response than single layers of the same pore sizes. We hypothesize that irregular geometries existing at the interface between layers contributes to hindered disentanglement and/or diffusion. Porosity does not seem to have as large of an effect on dissolution as pore size displays. This is evident by the fact that similar porosity single layers with different pore sizes exhibit different behavior (Fig. 3c). A single time point at 4 h of incubation in TCEP is displayed for each of the investigated PSi architectures (Fig. 3d). A strong inverse linear dependence between average pore diameter and dissolution in single-layer PSi sensors is shown. Again, it

can also be seen that mirrors illustrate slightly higher amounts of polymer remaining (residual wavelength shift) in the PSi matrix than single layers with similar average pore diameter.

2.4. Colorimetric Detection of Target Analyte in Solution

Visual detection of TCEP by the unaided eye was achieved with the model hydrogel–PSi sensor system by color readout (Fig. 4). Pictures of bulk S-S-coPAAm hydrogel (4.14 mol% NAPMAAm) are contrasted to pictures of the same S-S-coPAAm cross-linked into a PSi Bragg mirror ($d = 19/43$ nm) prior and after exposure to TCEP (Fig. 4a). A visual color change from red to green in the PSi sensor is evident after a 15 min soak in TCEP (500 μ L, 50 mM) on a shaker plate, subsequent rinse with water, and 5 min air-drying on the bench-top. In contrast to the wet measurements shown in Figure 3, the dry measurements taken here resulted in a large wavelength blue-shift (>100 nm) of the peak reflected light. This corresponds to sufficient dissolution of hydrogel from the PSi matrix to prevent retention of water inside the internal pore volume resulting in the loss of water from the PSi matrix in addition to copolymer. A dilution series of TCEP concentration (0–100 mM) shows that the initiation of color change is dependant on applied TCEP concentration (Fig. 4b). For exposure to TCEP > 10 mM a complete visual color change from red to green is evident.

3. Conclusions

The disulfide-linked hydrogel system described here serves as an initial proof-of-concept for integrating chemical-responsive hydrogels into nanostructured PSi sensors. The main advantage of this sensing system is the capability for direct visual color readout (15 min soak time and 5 min drying time) in addition to the capability for more precise temporal monitoring with reflectance spectrometry. While this study specifically reports on optical detection of the dissolution response of a disulfide cross-linked hydrogel in response to TCEP, which is well known; the disulfide crosslinking of this copolymer system is unique and the optical detection of dissolution based on refractive index changes of the nanoscale-confined responsive hydrogel is demonstrated for the first time in the work. In addition, effects of nanoscale confinement of hydrogel dissolution properties are demonstrated. These results are important milestones for achieving our future goal of incorporating bioresponsive gels into our PSi sensor system. This hybrid material system remains low-cost and proves to be easily translatable for POC sensing. Future work will be directed at incorporating biologically relevant probe–target interactions onto the amine-functionalized copolymer backbone synthesized here to create crosslinked hydrogel networks and investigating how precise the onset of dissolution and color change can be controlled upon exposure to target. Work to incorporate array-based sensing will also aim to reduce the sample volume needed for testing.

4. Experimental

Copolymer Synthesis

Procedures to copolymerize AAm with NAPMAAm were adopted from Seiffert and Oppermann [27] and details are reported elsewhere [25]. In brief, AAm (MP Biomedical, molecular weight (MW) = 71.08 g mol^{−1}), NAPMAAm (Polysciences Inc., MW = 178.7 g mol^{−1}), and sodium formate (HCOONa, Alfa Aesar, MW = 68.01 g mol^{−1}) were added to deionized water (30 °C, 15 min) and stirred under nitrogen. The total monomer concentration was fixed (4.6 mM in 10 mL water), and the exact monomer formulations are listed in Table S1 (SI). Chain transfer agent, HCOONa, was added to control linear polymer chain length [31]. Free radical polymerization was initiated with *N,N,N',N'*-tetramethylethylenediamine (0.25 mol%, 1.7 μ L, Sigma, MW = 116.2 g mol^{−1}) and ammonium persulfate (0.1 mol%, 70 μ L of a 2 wt% aqueous solution, Sigma). Precipitation in methanol (2 wt% hydrochloric acid) resulted in crude product that was filtered, washed in methanol, resolubilized in deionized

water, and dialyzed against water (2 days at 4 °C) with stirring (Spectra/Por, molecular weight cut-off (MWCO) = 3500 g mol⁻¹). Remaining solvent was removed via rotary evaporation and high vacuum for 24 h. Characterization of the various copolymer products was completed by ¹H NMR spectroscopy and size-exclusion chromatography (SEC) as described previously [25].

Sulfhydryl Functionalization of Copolymer

Copolymer was dissolved in phosphate-buffered saline buffer (PBS, pH 7.4, 10 wt%). SATP (Thermo Scientific, 2 μL of 1.533 M, MW = 245.25 g mol⁻¹) diluted in dimethylformamide was added to 50 μL of copolymer solution (2 h at room temperature, RT). Unbound SATP was removed with dialysis (Harvard Apparatus, Dispo Equilibrium Dialyzer, MWCO = 5000 g mol⁻¹) overnight at RT against a 1000 excess volume of PBS. Hydroxylamine-HCl in PBS (5 μL of 1 M, pH 7.1) was added to 50 μL SATP bound copolymer solution (mix 1 h at RT) to deprotect the acetylated sulfhydryl (SH) groups. Ellman's Assay [30] was performed to quantify SH attachment to copolymer chains with varying mol% NAPMAAm (Table S4 (SI)). Dimethylsulfoxide (DMSO) was added as an oxidizing agent (2 μL) to sulfhydryl functionalized copolymer solutions (50 μL of 10 wt%) to promote disulfide bond formation.

PSi Sensor Preparation

The methods employed to produce PSi films have been described in detail elsewhere [26]. Briefly, mesoporous PSi Bragg mirrors were fabricated from p+ ⟨100⟩ silicon wafers (B doped, 0.006–0.009 Ω cm) using an electrochemical etch process at RT. Etching was completed in electrolyte containing ethanol (70%) and hydrofluoric acid (HF, 15%). The Bragg mirror consisted of 16 alternating layers of porosity (79 and 87%, *d* = 19 and 43 nm) with a total thickness (~3.2 μm) measured by SEM. The wavelength shift sensitivity (WSS = 308.6 nm/RIU) was determined using infiltration of liquids with known *n* values. The other PSi architectures studied in Figure 3 were fabricated using similar electrochemical etching techniques and resulting pore characteristics are listed in Table S2 (SI). Macroporous PSi (*d* > 50 μm) was etched into n+ ⟨100⟩ silicon wafers (Sb doped, 0.01–0.08 Ω cm) in electrolyte containing Pluronic L31 (0.1%) and HF (5%). After thermal oxidation (900 °C, 3 min) all PSi sensors were silanized with (mercaptopropyl)trimethoxysilane (2 wt%, Gelest) in ethanol (50%) for 15 min, rinsed with ethanol and water, dried with nitrogen gas, and kept at 100 °C for 20 min to cross-link the silane and evaporate any remaining solvent.

Preparation of S-S-coPAAm-PSi Hybrid Sensor

The sulfhydryl-functionalized copolymer solutions prepared above were immediately applied to the mercaptosilane-treated PSi sensors in a custom glass fixture within a humidified chamber to minimize thickness of polymer on top of the PSi sensor (700 μm). Disulfide bond formation (cross-linking of the hydrogel) was allowed to continue at RT in the humidified chamber for 6 days as Ellman's Assay [30] results indicated complete disulfide formation occurs within 5 days (Fig. S2 (SI)). The resulting hybrid S-S-coPAAm-PSi sensors were soaked in deionized water (10 mL) for 2 days on a shaker plate (water replaced after 1 day) to allow equilibrium swelling and release of non-cross-linked copolymer chains.

Optical Detection of Reflectance Spectra

The hybrid S-S-coPAAm-PSi sensors were held within a custom fixture and exposed to a normal incident beam of white light (spot size ~1.3 mm²). Reflectance spectra normal to the surface were measured using an Advantes 3648-USB2 spectrophotometer (optical resolution of 0.06 nm pixel⁻¹). The custom fixture holds the PSi sensor in a well, containing various solutions, and is covered by glass to diminish solution evaporation. All error bars in plots

represent the standard deviation of each data point taken with a minimum of $n = 2$ for interday experiment trials and 3 measurement locations per sensor.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

The authors graciously acknowledge the NIH/NIAID (5K25AI060884) and NIH/NIDA (T32DA007232, F31DA025398) for financial support of this research, Benjamin Miller for insightful chemistry discussions, and Lisa Slater and Thomas Mourey at Eastman Kodak Company for SEC analysis and helpful polymer chemistry discussions. Supporting Information is available online from WileyInterscience or from the authors.

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Figure 1.

Schematic of chemical procedure to synthesize the disulfide cross-linked hydrogel. a) Various molar ratios of AAm and NAPMAAm monomers are diluted in water. APS and TEMED represent ammonium persulfate and tetramethylethylenediamine, respectively. b) Free radical polymerization of monomers form copolymer chains with reactive primary amine groups. c) Reaction with SATP chemical and d) deprotection with hydroxylamine yields e) sulfhydryl functional copolymer chains in solution. f) Formation of disulfide bonds results in the cross-linked hydrogel (S-S-coPAAm).

Figure 2.

Optical characterization of hydrogel and infiltration into PSi sensor template. a) Refractive indices of bulk S-S-coPAAm hydrogels with varying molar percentages of NAPMAAm measured on a bench-top Abbe refractometer. Negative control, 0 mol% NAPMAAm, did not form hydrogel, but bulk refractive index of polymer solution was measured. b) Raw reflectance spectra measured using an Avantes spectrometer show wavelength shifts associated with addition of mercaptosilane (MPTS), filling the PSi pores with water, and swollen S-S-coPAAm hydrogel after a 2 day soak in water. c) Comparison of optical wavelength shift response experimentally determined by PSi sensors and simulation results when S-S-coPAAm hydrogels with refractive indices of bulk gels with varying molar percentages of NAPMAAm fill pore volume.

Figure 3.

Temporal optical detection of TCEP-responsive S-S-coPAAm hydrogel dissolution by wet PSi sensor reflectance spectrometry measurements taken while varying three important design parameters: a) S-S-coPAAm hydrogel cross-linking density varied by adjusting the molar percentage of NAPMAAm (0–37.27 mol%); b) outside concentration of TCEP varied (500 μ L of 0–100 mM); c) PSi pore diameter and architecture is varied (single layer pores with $d = 19$ –106 nm, each with a constant thickness of 1.68 μ m; Bragg mirrors with alternating $d = 19/43$ nm and $d = 73/106$ nm with thicknesses of 3.2 and 2.8 μ m, respectively). d) A single time point at 4 h displays dissolution dependence on average pore diameter of PSi substrate.

Figure 4.

Visual color readout of hybrid hydrogel-PSi sensor upon drying. a) Side views of 10 mol% NAPMAAm S-S-coPAAm hydrogels bulk and cross-linked into a PSi sensor before and after exposure to 1 mL of 50 mM TCEP for 15 min, rinsing with water, and air-drying for 5 min. b) Color shift from red to green is evident in top-down views of 4.14 mol% NAPMAAm S-S-coPAAm hydrogels cross-linked into PSi Bragg mirrors after incubation in 1 mL of varying concentrations of TCEP solution on shaker 15 min, subsequent rinse with water, and air-dry for 5 min.