ADVANCED FUNCTIONAL MATERIALS

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Poly(vinyl alcohol) Rehydratable Photonic Crystal Sensor Materials**

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We developed a new photonic crystal hydrogel material based on the biocompatible polymer poly (vinyl alcohol) (PVA), which can be reversibly dehydrated and rehydrated, without the use of additional fillers, while retaining the diffraction and swelling properties of polymerized crystalline colloidal arrays (PCCA). This chemically modified PVA hydrogel photonic crystal efficiently diffracts light from the embedded crystalline colloidal array. This diffraction optically reports on volume changes occurring in the hydrogel by shifts in the wavelength of the diffracted light. We fabricated a pH sensor, which demonstrates a 350 nm wavelength shift between pH values of 3.3 and 8.5. We have also fabricated a Pb^{+2} sensor, in which pendant crown ether groups bind lead ions. Immobilization of the ions within the hydrogel increases the osmotic pressure due to the formation of a Donnan potential, swelling the hydrogel and shifting the observed diffraction in proportion to the concentration of bound ions. The sensing responses of rehydrated PVA pH and Pb^{+2} sensors were similar to that before drying. This reversibility of rehydration enables storage of these hydrogel photonic crystal sensors in the dry state, which makes them much more useful for commercial applications.

1. Introduction

Poly(vinyl alcohol) (PVA) is a polymer that is already extensively utilized in industrial and biomedical applications, owing largely to its mechanical properties and biocompatibility.[1–6] PVA hydrogels have been used or are being investigated for use in many biomedical applications, such as drug delivery,[7–9] intervertebrate discs,[10,11] contact lenses,[12,13] articular cartilage,[14,15] and wound dressing.[16,17] The properties, and thereby possible applications, of PVA hydrogels can be tailored by manipulating the type and concentration of crosslinks within the material.

PVA hydrogels can be formed utilizing using either physical or chemical crosslinking. There have been extensive studies of PVA hydrogels that contain crystalline regions, which act as physical crosslinks, which are created by repetitive freeze-thaw cycles.[4,18–26] Although these hydrogels are stable at room temperature for months, these physical crosslinks are less mechanically and thermally stable than are chemical crosslinks.

Traditionally, one of the most widely used methods for preparing chemically crosslinked PVA hydrogels utilized glutaradehyde as a crosslinker.[27–31] However, due to the cytotoxic nature of glutaradehyde[32–35] several groups have prepared chemically crosslinked PVA hydrogels utilizing other crosslinkers such as epichlorohydrin,[36] diglycidyls,[37] or by incorporation of polymerizeable functionalities[38–43] onto the PVA backbone.

We report here the fabrication of a novel and inexpensive photonic crystal hydrogel sensing material prepared from modified poly (vinyl alcohol), which is based on our previously developed photonic crystal materials.[44–51] These materials utilize a mesoscopically periodic array of colloidal particles that self-assembles into a highly-ordered crystalline colloidal array (CCA) (Figure 1A). The lattice spacing of the CCA is fabricated such that visible light is Bragg diffracted.

When the CCA is polymerized within a hydrogel (PCCA) (Figure 1B), it optically reports on volume changes experienced by the material, since the observed diffraction wavelength is directly related to the spacing between lattice planes.[47,52–64] To apply this motif to chemical sensing, the hydrogel is functionalized such that it responds to changes in the analyte concentration by altering its volume and diffraction wavelength.[52,53,55,56,65–81] Previously developed PCCA hydrogels have utilized acrylamide,[52] methylacrylate,[61] poly (ethylene glycol) acrylates,[62,64] and *N*-isopropylacrylamide.[63]

We demonstrated three primary mechanisms of PCCA photonic crystal sensing, employing changes in the hydrogel crosslink density, immobilization of ions on the hydrogel, or changes in the free energy of mixing of the hydrogel polymer with the aqueous medium. In the crosslinking archetype, the analyte molecule is bound by two molecular recognition molecules, which are tethered to the hydrogel, forming additional crosslinks within the hydrogel causing it to shrink. The consequential decrease in the particle array lattice

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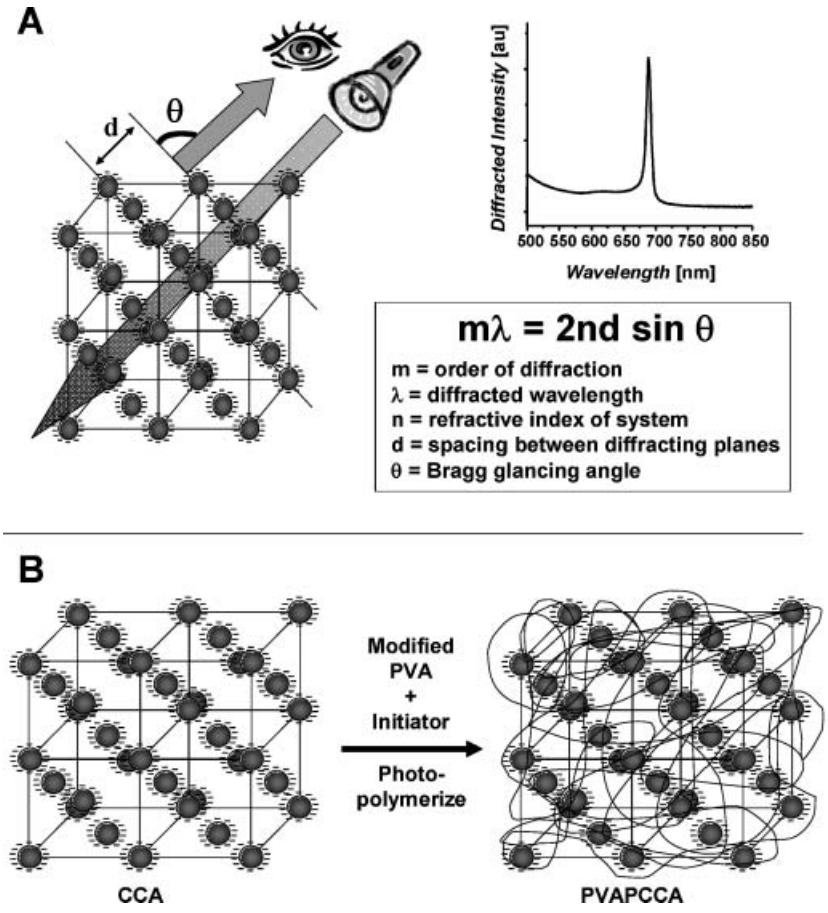

Figure 1. (A) Crystalline Colloidal Arrays (CCA) form due to the electrostatic repulsion between the highly charged, monodisperse polystyrene particles. The spacing between particles is such that they diffract visible light according to Bragg's law. (B) Polymerized Crystalline Colloidal Arrays (PCCA) are formed by polymerizing a hydrogel network around the CCA.

constant blue-shifts the wavelength of light diffracted by the PCCA as the crosslink density increases. This motif was previously demonstrated for sensing of glucose,[66,69,74] metal ions such as Cu^{+2}, [72] and ammonia.[65] The second sensing motif employs the immobilization of ions within the hydrogel, increasing the osmotic pressure and swelling the hydrogel. The resulting increase in the particle array lattice constant red-shifts the wavelength of diffracted light as the concentration of bound charges increases. This motif has been demonstrated for sensing of Pb^{+2}, [53,56,70,75,76] glucose,[53,56] pH,[55,76] and organophosphates.[67] In the third sensing motif, the balance between the free energy of mixing of the hydrogel polymer with the surrounding medium and the elastic restoring force of the hydrogel crosslinks determines the PCCA hydrogel volume. Alterations to the hydrogel polymer that result in an increase in the polymer solubility make the free energy of mixing more favorable, thereby swelling the hydrogel and red-shifting the diffraction wavelength. This motif was previously demonstrated for photochemically controlled photonic crystal materials[82–85] and utilized with the sensing of creatinine.[68]

This new PVA photonic crystal hydrogel material efficiently Bragg diffracts light and can be reversibly dried and rehydrated, without the use of fillers, while retaining the original diffraction and swelling properties. We fabricated polyvinyl alcohol PCCA (PVAPCCA) sensors for determining pH and Pb^{+2} and compared the sensor response prior to and after drying and rehydrating the material. The response of these new PVAPCCA sensors is comparable to our previously developed sensors;[53,55,56,76] however, the reversible hydration property of this new material affords for more practical storage and transport.

2. Results and Discussion

We previously fabricated acrylamide-based PCCA, which demonstrated volume-phase transitions and diffraction changes in response to variations in pH and ionic strength.[55,76] We also previously fabricated acrylamide-based PCCA lead sensors, which utilized pendant crown ether groups to bind Pb^{+2}. [49,53,56,70,75,76] The sensing capabilities of both of these hydrogel sensors relied on the formation of ionic hydrogels,[86–89] either by direct incorporation of charged groups via partial hydrolysis of amide groups by the formation of titratable carboxyls or by use of chelating agents to bind charged groups to the hydrogel. As the bound charge on the hydrogels increases, there is an immobilization of counterions within the hydrogel, which increases the osmotic pressure, thereby swelling the hydrogel against the restoring elastic constant due to the hydrogel crosslinks. This swelling red-shifts the diffracted wavelength. This red-shift continues until all carboxyl groups are deprotonated or all crown ethers are complexed to Pb^{+2}, after which further increases in pH or additional lead concentration merely increase the ionic strength such that the osmotic pressure is decreased, shrinking the hydrogel and blue-shifting the diffracted light wavelength.

Figure 2 illustrates the pH and ionic strength diffraction dependence of an ionic PVA-based pH sensing hydrogel, which was prepared by reacting a PVAPCCA with succinic anhydride in DMSO for 1.5 hours. As illustrated, the diffraction monotonically red-shifts over ~350 nm for pH values between 3.3 and 8.5 as pendant carboxyl groups are ionized, and then blue-shifts for higher pH values as the ionic strength increases. This response is similar to that observed previously by Lee et al.,[55] but differs from the recently observed hysteresis response of pH sensitive PCCA prepared

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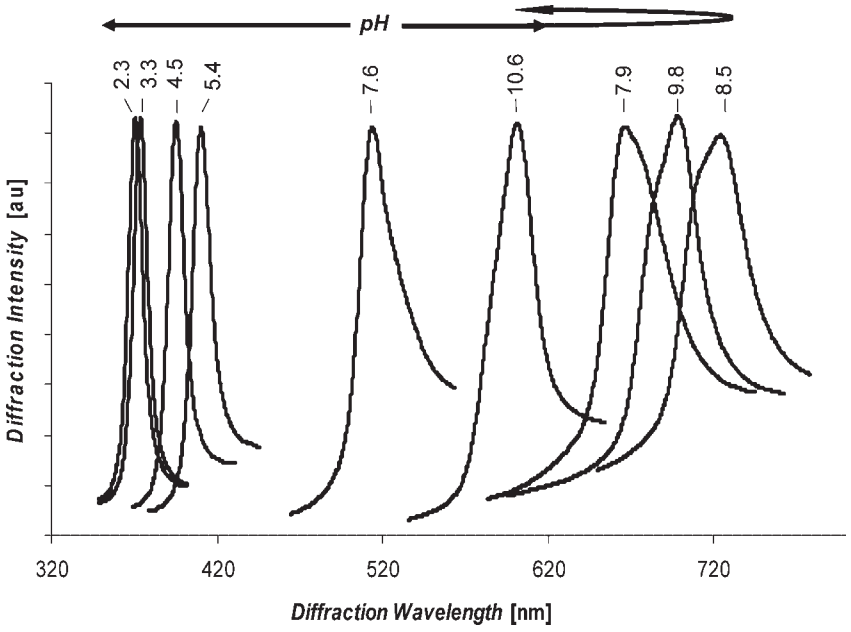

Figure 2. The diffraction dependence of an ionic PVAPCCA, prepared by coupling with succinic anhydride in DMSO for 1.5 hours, on changes in pH and ionic strength. The diffraction monotonically redshifts for pH values increasing from pH 2 to pH 9 as pendant carboxyl groups are ionized. Blue-shifts occur for higher pH values as the ionic strength increases.

by Xu et al.,[90] where the PCCA was first equilibrated at either a low or high pH and then titrated by adding either NaOH or HCl.

Although the response of this pH sensor is similar to previously developed pH sensors, a significant difference between this PVAPCCA pH sensor and previously developed PCCA pH sensors is its ability to be dehydrated and rehydrated while retaining the CCA ordering and the sensing capability of the hydrogel. Figure 3 compares the diffraction response to changes in pH experienced by the same PVAPCCA hydrogel, prior to drying and after rehydration. As can be seen in Figure 4, the swelling ability and diffraction of the material is preserved, even upon drying.

Figure 5 illustrates the diffraction dependence of a PVAPCCA, which contains pendant crown ether groups, to changes in solution Pb^{+2} concentration prior to drying in vacuum and after rehydration. As in the previously developed acrylamide-based lead sensors, when Pb^{+2} is bound by the pendant crown ether groups there is an increased osmotic pressure, which swells the hydrogel, and red-shifts the diffraction. Unlike the previously developed acrylamide-based sensor, this PVAPCCA exhibits efficient diffraction upon rehydration, as illustrated by the relatively narrow reflection peak of the rehydrated hydrogel in Figure 6. Clearly, PVA hydrogels maintain CCA order upon drying.

The variation in the observed absolute diffraction wavelength for the original and rehydrated PVCPCCA, as illustrated in Figure 6, could derive from several factors, including diffraction inhomogeneity (±5 nm) across the surface of a PCCA and the different affixation of the hydrogel to the substrate. The diffraction measurements prior to dehydration were taken from the PVAPCCA originally affixed to the quartz plate during polymerization. The diffraction measurements after rehydration were taken from the hydrogel after it was released from the quartz plate, dried, rehydrated, and reattached to a Petri dish. Release of the PVAPCCA from the quartz plate results in a diffraction blue-shift because the hydrogel is no longer constrained to swelling in only one dimension. As illustrated in Figure 5, comparison of the diffraction shift in response to changes in analyte concentration, which is an indicator of the hydrogel's mechanical properties, clearly shows that the sensing ability of the PVAPCCA remains nearly unchanged even after drying in vacuum.

Previously developed acrylamide-based PCCA disorder upon dehydration. These PCCA do not, in general, regain diffraction after rehydration due to irreversible changes in morphology and collapse of the hydrogel. However, we recently observed the reversible dehydration and rehydration of an acrylamide-based PCCA Ni^{+2} sensing material, in the case where the PCCA was covalently attached to a gel support

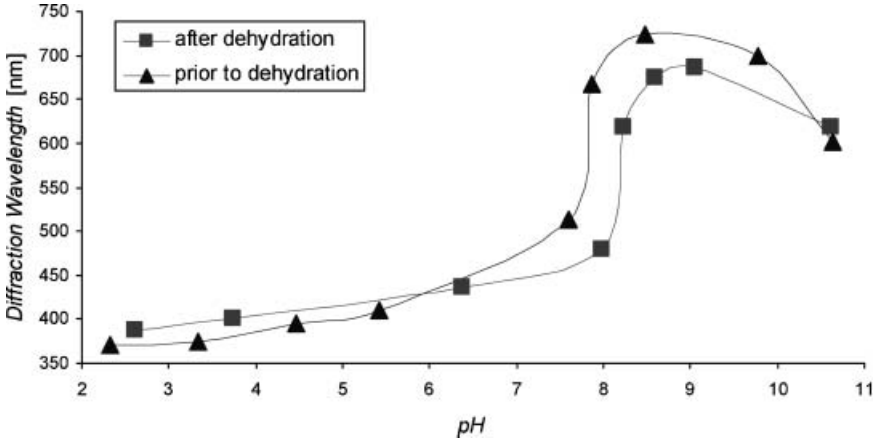

Figure 3. Comparison of diffraction response from ionic PVAPCCA to changes in pH values prior to drying (triangles) and after rehydration (squares). (Lines added to aid the eye.) Determining the reality of measured diffraction wavelength differences between the dehydrated and original sample has to take cognizance of the fact that the sample inhomogeneity across the surface is ±5 nm. The major uncertainty is the variability in the measured pH of pure water between pH = 5 to pH = 9, which shows a variability of almost ±1.5 pH units using our pH electrode. The increased ionic strength outside this range results in reliable measured pH values.

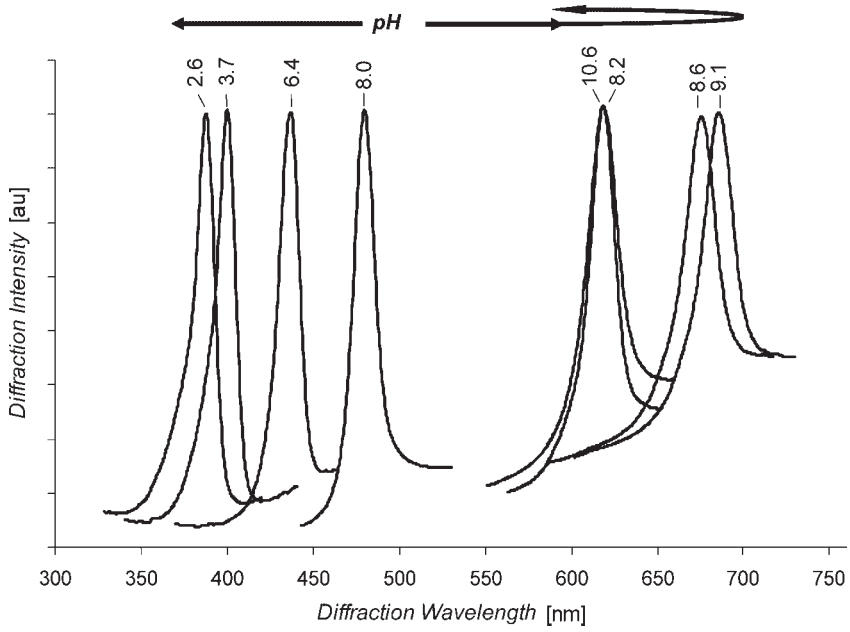

Figure 4. The diffraction dependence of an ionic PVAPCCA, after rehydration, on changes in pH and ionic strength. The material retains swelling and diffraction properties after drying.

film and dried in the presence of buffer, which served as a stabilizer as the solution concentrated upon drying.[91]

Ceylan et al. studied the deswelling in acetone and the reswelling in water of a series of ionic poly (acrylamide) hydrogels[92] and noted that acrylamide hydrogels do not regain their initial volume after collapse in acetone. Allen et al. disclosed a method to prepare rehydratable polyacrylamide hydrogels for use in electrophoresis that could be stored dry for extended periods of time at ambient temperatures and rehydrated without loss of structural or functional integrity.[93,94] These hydrogels incorporated polyols, polymeric alcohols, polyamines or high molecular weight polysaccharides such as dextran or substituted monosaccharides as stabilizers, to prevent irreversible damage to the gel matrix structure upon dehydration. Even though these hydrogels could be reswelled to 80–95% of their original volume, depending on the stabilizer used, it was preferred that they be stored in controlled humidity sealed containers since the hydrogel pore spaces could collapse if the relative humidity decreased below 70%.

PVA, on the other hand, is known to be a readily rehydratable polymer. Ricciardi et al. recently demonstrated that PVA hydrogels, lacking additives or stabilizers, exhibit physical properties upon rehydration comparable to those before dehydration.[24,25] As our PVAPCCA Bragg diffracts light from the 111 plane of the embedded CCA that is aligned parallel to the hydrogel surface and we observe the back-diffraction of incident light normal to the hydrogel surface, the back-diffracted wavelength (λ) depends on the 111 plane spacing (d) and the refractive index of the system (n): $\lambda = 2nd$.

Since changes in the PVAPCCA hydrogel volume give rise to changes in the diffracted wavelength, and given that d is proportional to the third root of the volume, the change in hydrogel volume can be easily determined:

$$\frac{\lambda}{\lambda'} = \left(\frac{V}{V'}\right)^{\frac{1}{3}} \quad (1)$$

where λ is the diffraction wavelength of the rehydrated hydrogel and λ' is the diffraction wavelength prior to dehydration.

We typically observe a 30–35 nm blue-shift in the diffraction wavelength upon removing the PCCA from its substrate. Figure 6 indicates a ~50 nm diffraction difference prior to versus after rehydration. This net 20 nm blue-shift suggests that our dehydrated crown ether PVAPCCA material reswells to ~90% of the initial volume after drying in vacuum. The recovered hydrogel maintains its sensing response, even after drying in vacuum, without the use of any filler molecules.

Successful sensor development requires the development of sensing materials with significant shelf lives at room temperature, and extended lifetimes with refrigeration or freezing. A major factor in sensor lifetime is the stability of the incorporated molecular recognition molecule, which depends on the ambient conditions inside the

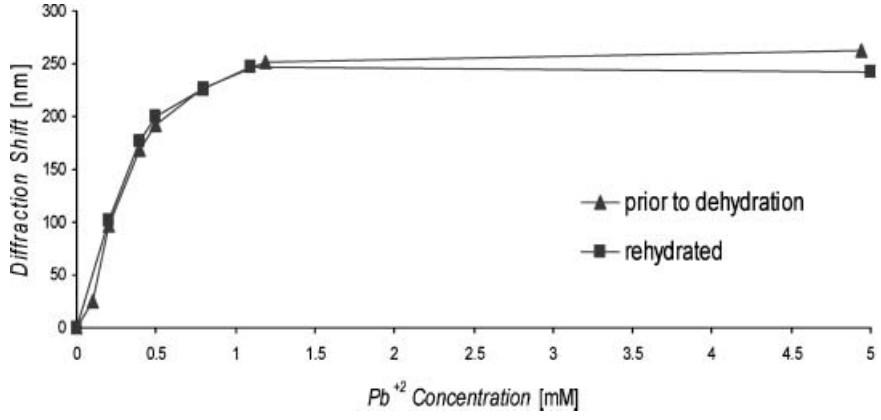

Figure 5. The diffraction dependence of a PVAPCCA containing crown ethers on Pb^{+2} concentration prior to dehydration (triangles) and after rehydration (squares). (Lines added to aid the eye.) Measured diffraction wavelength differences between the dehydrated and original sample also derive from the sample inhomogeneity across the surface (±5 nm).

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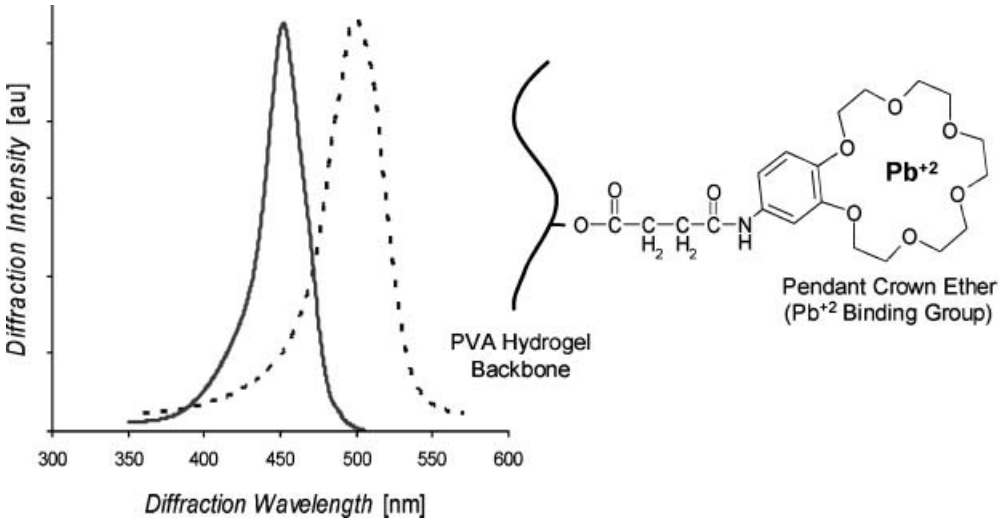

Figure 6. As Pb^{+2} is bound by the pendant crown ether groups, there is an increased osmotic pressure, swelling the hydrogel, and red-shifting the diffraction. Although the diffraction wavelength shift is nearly identical, the rehydrated sensor (solid line) shows a ~50 nm blue-shift in absolute diffraction (both peaks measured at 0.4 mM Pb^{+2}).

hydrogel, such as pH and temperature. Recently, researchers have shown that immobilization of molecular recognition elements, such as enzymes, to or within a support matrix significantly increases the enzyme activity lifetime.[95–97] The ability of our PVAPCCA hydrogel material to dehydrate and reversibly rehydrate enables the use of enzymes and increases its potential for commercial applications.

3. Conclusions

We developed a new composition of photonic crystal hydrogel materials based on chemically modified poly(vinyl alcohol). The vinyl groups attached to the PVA can be used to crosslink the polymer, eliminating the necessity of an additional crosslinker. This PVAPCCA efficiently diffracts visible light and reports on volume transitions experienced by the hydrogel by shifting the diffracted wavelength. This photonic crystal can be utilized for the determination of pH, Pb^{+2}, and, with the use of additional recognition elements, other analytes. Most notably this material can be dried and then rehydrated by immersion in water, while retaining its diffraction and mechanical properties. This reversibility of rehydration affords storage of hydrogel sensors in the dry state, facilitating their commercialization.

4. Experimental

Materials: Pyridine, $Pb(NO_3)_2$, NaOH, and KCl were purchased from Sigma. Succinic anhydride was purchased from Aldrich. Hydroquinone-monomethyl ether (HQME), glycidyl methacrylate (GMA), and 4′-Aminobenzo-18-crown-6 (18C6) were purchased from Fluka. Dimethyl sulfoxide (DMSO) and HCl were purchased from Fisher Scientific. Poly(vinyl alcohol) 88 mol% hydrolyzed, MW~25kDa (PVA) was purchased from Polysciences, Inc. Acetone was purchased from EMD Chemicals, Inc. 2,2-diethoxyacetophenone (DEAP) was purchased from Acros Organics. Ethanol (EtOH) was purchased from Pharmco Products, Inc. Phosphate Buffered Saline (0.1 M phosphate, 0.15 M NaCl, pH 7.2, PBS), and 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride (EDC) were purchased from Pierce Biotechnology. All chemicals were used as received.

Modification of Poly(vinyl alcohol) with Glycidyl Methacrylate: Partially hydrolyzed PVA was functionalized with methacrylate groups by reaction with GMA in DMSO, as reported elsewhere [42, 43] (Figure 7). In a typical synthesis HQME (0.35 g) inhibitor, DMSO (100 mL), PVA (10 g), and pure water (5 mL) were added to a jacketed round-bottom flask. The flask was sealed, and the solution was purged with N_2 (30 min) and kept under a N_2 blanket while being stirred at 300 rpm for 1.5–2 hours at 80 °C. GMA (70–90 mL) and HCl (4 mL) were added to the flask by a syringe. The temperature was lowered to 50 °C, and the reaction proceeded with constant stirring (300 rpm) under nitrogen overnight. The resulting solution was cooled to room temperature and precipitated

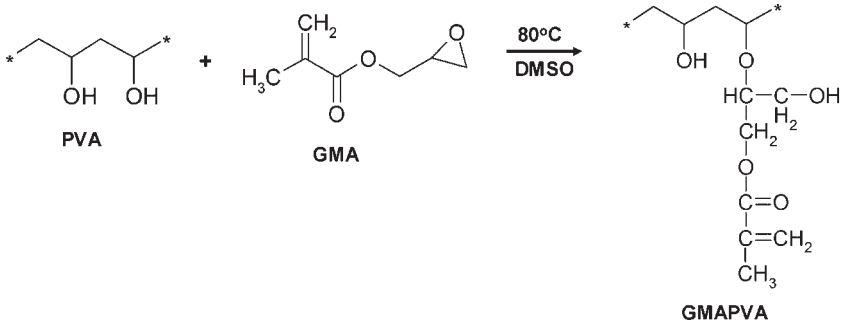

Figure 7. Poly (vinyl alcohol) (PVA) modified with a pendant methacrylate groups by reaction of a small percent of hydroxyls with glycidyl methacrylate (GMA), resulting in a readily polymerizable monomer (GMAPVA).

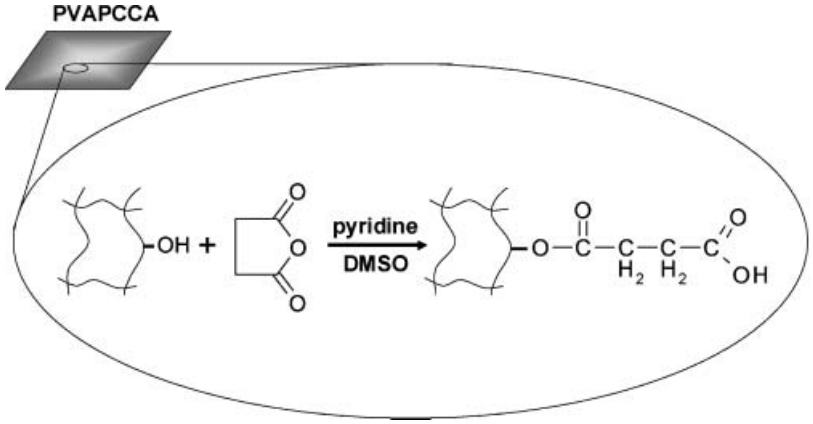

Figure 8. After polymerization of PVA, a fraction of the remaining hydroxyls were reacted with succinic anhydride to incorporate carboxyl groups onto the hydrogel backbone.

into a large volume of acetone with vigorous stirring. The precipitate was collected via filtration. The precipitate was suspended in acetone (~100 mL, changed daily) with constant shaking for 5–7 days, then collected by filtration and dried in vacuum.

CCA Preparation: Monodisperse, highly-charged colloids were prepared via emulsion polymerization as previously described [48]. We used ~15% w/w suspensions of ~100 nm polystyrene sphere CCA dispersed in pure water. The colloidal particles were cleaned via dialysis against deionized pure water and subsequently shaken with ion-exchange resin. Once sufficiently cleaned, the suspension became iridescent due to Bragg diffraction.

PVAPCCA Hydrogel Preparation: Solutions (22 wt%) of the glycidyl methacrylate modified PVA (GMAPVA) were prepared by dissolving GMAPVA in pure water via heating the solution to near-boiling and vortexing. CCA (0.8 mL) and ion exchange resin were combined with the GMAPVA solution (0.4 mL) in a vial and vortexed. DEAP (10 μL, 20% in DMSO) was added to this solution. The solution was vortexed and then centrifuged for 5 minutes. The solution was polymerized, in a cell consisting of two quartz plates separated by a 125 μm parafilm spacer and exposed to UV light from two Blak Ray (365 nm) mercury lamps. The resulting PVAPCCA was removed from the cell and rinsed with large quantities of pure water.

PVAPCCA Hydrogel Carboxylation: The PVAPCCA was carboxylated by treatment with succinic anhydride in an anhydrous solvent, such as DMSO, (Figure 8) [37]. This was accomplished by first transferring the PVAPCCA to DMSO and allowing it to equilibrate. The PVAPCCA was then placed in a solution of succinic anhydride in DMSO (0.1 g/mL), to which pyridine (0.6:1 succinic anhydride: pyridine) was added dropwise. The reaction proceeded in a 40 °C water bath for 1.5–48 hours. The hydrogel was then rinsed with DMSO and copious amounts of pure water. The level of carboxylation of the hydrogel was controlled by the succinic anhydride concentration used and/or the reaction time.

PVAPCCA Hydrogel Crown Ether Incorporation: Incorporation of the crown ether into the hydrogel backbone was accomplished through carbodiimide coupling, utilizing a solution of 18C6 (20 mM) and EDC (25 mM). The reaction proceeded for 2 hours at room temperature, after which a second coupling reaction was completed to ensure complete coupling of crown ether to carboxyl groups. The hydrogel was rinsed extensively with pure water.

Dehydrating/Rehydrating of PVAPCCA: After characterizing the response of the diffraction of the PVAPCCA to changes in pH, ionic strength, or lead concentrations, the hydrogel sensors were dehydrated as a free film. The PVAPCCA in pure water was exchanged in EtOH. The hydrogel was then air dried, while maintaining gentle mechanical constraints to prevent curling, and then dried overnight under ambient conditions. The Pb^{+2} sensitive PVAPCCA was air dried and then further dried under vacuum for 2 hours. The dehydrated PVAPCCA was rehydrated by directly immersing it in pure water and equilibrating it at room temperature.

Characterization of GMAPVA: The extent of modification of the polyvinyl alcohol was determined by using ^{1}H-NMR (300 MHz, D_2O, 25 °C). The vinyl protons were ratioed against the PVA backbone protons to calculate the percent modification. The extent of modification was varied from 0.5% to 5.5% by varying the amount of glycidyl methacrylate in the reaction mixture.

Diffraction Measurements: Diffraction measurements were conducted at a fixed 90° glancing angle utilizing an Ocean Optics USB2000-UV-VIS Spectrometer, a LS-1 Tungsten Halogen Light Source or a DT 1000 CE UV/VIS Light Source, and an R-series Fiber Optic Reflection Probe. The PVAPCCA to be characterized was affixed to a quartz plate or polystyrene petri dish, by the typical adhesion which occurs upon contact with the substrate, in order to fix the hydrogel's position throughout the diffraction measurements. Experiments were conducted in a covered petri dish, so as to avoid evaporation. Holes were drilled in the lid and were secured with parafilm, allowing access for the reflection probe and addition/removal of solutions.

To characterize the response of the PVAPCCA to changes in pH, the hydrogel was first equilibrated in pure water. Small volumes of dilute NaOH were added to the dish and the diffraction was monitored until it stabilized, at which time the pH of the water was sampled as described below and the diffraction wavelength was recorded. The titration with NaOH occurred until the diffraction red-shifting plateaued and began to blue-shift. The PVAPCCA was then rinsed with copious amounts of pure water and the process was repeated by using small increments of dilute HCl to lower the pH. HCl was added until the diffraction blue-shifting plateaued.

To characterize the response of the crown ether PVAPCCA to Pb^{+2}, the hydrogel was first equilibrated in pure water. Small increments of concentrated $Pb(NO_3)_2$ were added to the dish and the diffraction was monitored until it stabilized, at which time the diffraction wavelength was recorded. Pb^{+2} was added until the diffraction red-shifting plateaued.

pH Measurements: pH measurements were conducted by first collecting ~15 mL of water from the petri dish containing the PVAPCCA after the hydrogel had equilibrated and then replacing this sample with fresh nanopure water prior to additional adjustments in solution pH so as to maintain a constant volume. The ionic strength of the sampled water was increased by adding a small volume of concentrated KCl, resulting in a 150 mM KCl solution, thereby reducing noise and improving the accuracy and reproducibility of the measured pH.

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