Smart Materials

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Optical Devices Constructed from Multiresponsive Microgels**

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Abstract: *Novel multiresponsive microgels based on poly(N-isopropylacrylamide) were synthesized to contain triphenylmethane leucohydroxide, and used to construct etalons. The optical properties of the resultant etalons were investigated, and their response to ultraviolet and visible irradiation, solution pH changes, and the presence of a mimic of the nerve agent Tabun characterized. We clearly show that the optical properties of the device depended dramatically on these stimuli. This investigation illustrates the versatility of the microgel-based etalon structure, and showcases the clear utility of such devices for remote actuation, color tunable optics, sensing, and potential remotely triggered drug delivery applications.*

Smart materials and sensors that can adapt and actuate in response to environmental or external stimuli are in great demand.[1] Specifically, polymeric materials that are able to swell, shrink, or bend in response to environmental stimuli are finding uses in fields ranging from medicine to materials science and physics.[2] Among such materials, polymeric gels have attracted particular attention, as they can exhibit discontinuous volume phase transitions.[3] The stimuli used to trigger the transitions range from temperature, to light, electric and/or magnetic fields, and applied mechanical force.[4] These materials have been exploited for biomedical applications, drug delivery, and sensor technologies.[5]

Polymeric gels can be classified into two categories, macroscopic gels, such as organogels or hydrogels, and colloidal gels. Regardless of their dimensions, the gel structure is crosslinked chemically and/or physically.[6] Colloidal gels (microgels and nanogels, depending on their diameter) have also found numerous applications in medicine, as coatings, for drug delivery, as catalysts, and for molecular recognition.[7] In order to expand the utility of the above mentioned gels, it is advantageous to develop gels that can respond to multiple stimuli. Specifically, microgels that respond to a number of stimuli (temperature, pH, light, magnetic/electric field) could yield many new applications.[8]

Previously, our group has developed responsive polymer-based devices (etalons) for applications as sensors, artificial muscles, and drug delivery motifs.[9] Poly(*N*-isopropylacrylamide) (pNIPAm)-based microgels are well known to be thermoresponsive, exhibiting a lower critical solution temperature (LCST) in water.[10] By increasing the temperature of microgels in water, their solvation state can be varied; they are hydrophilic (swollen) at $T < 32\,^{\circ}C$, whereas they collapse and transition to a more hydrophobic state at higher temperatures. In the present study, the molecule triphenylmethane leucohydroxide (TPL) was incorporated into microgels, yielding multiple responsivities, including responsivity to ultraviolet and visible light, pH, temperature, and diethylcyanophosphate (GAS), which is a derivative of the nerve agent Tabun (GA). We subsequently fabricated etalons from the microgels; the etalon structure is depicted in Figure 1. In

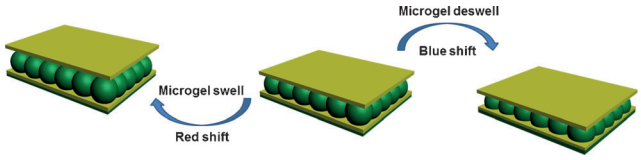

Figure 1. Etalon structure: two thin Au layers sandwiching a layer of pNIPAm-based microgels. If the microgel swells (left), the Au layers move apart, yielding a red shift in the etalons reflectance peaks. The opposite is true for microgel deswelling.

short, a concentrated microgel solution was "painted" onto a Au-coated glass substrate, followed by copious rinsing to remove microgels not directly attached to the Au. Finally, the microgel layer was dried, and a subsequent layer of Au deposited on the microgel layer. These devices show visible color and multiple peaks in their reflectance spectra. The position of the peaks in the reflectance spectra depends on the distance between the two Au layers and the refractive index of microgel.[6c,d] The position and order of the peaks can be predicted from Equation (1):

$$\lambda = 2\,n\,d\cos\theta/m \qquad (1)$$

where n is the refractive index of the dielectric layer, d is the mirror–mirror distance, θ is the angle of incident light relative to the normal, and m (an integer), is the order of the reflected peak. Therefore, the response of microgels can be observed as a shift in the position of the reflectance peaks.

As illustrated in Figure 2, TPL-containing microgels are capable of responding to the application of many stimuli. In one case, TPL is capable of absorbing red light of 630 nm. When the light is absorbed, the local temperature of the microgels increases, causing the pNIPAm-based microgels to collapse. The TPL-modified microgels are also sensitive to GAS, owing to its reaction with leucohydroxide, thus

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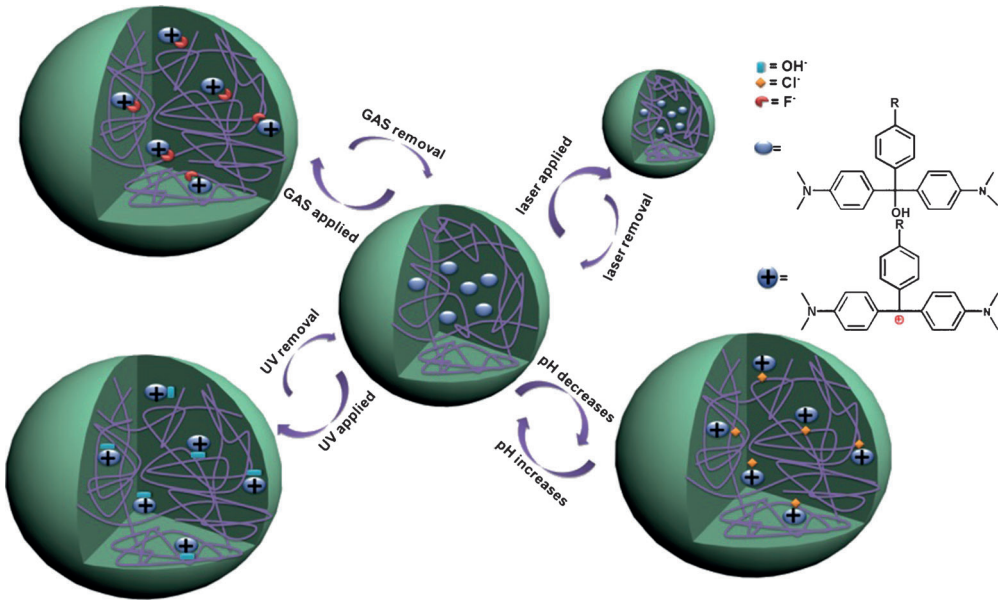

Figure 2. The various responses expected from TPL-modified microgels. The TPL structure is shown on the right.

generating the leuco cation in the microgels. The leuco cation increases the microgel's inner osmotic pressure, which results in microgel swelling. Additionally, the absorption of UV light by TPL results in the promotion of the molecule from triplet excited state to lowest energy excited singlet state. The singlet state results in the formation of leuco cation and hydroxyl anion by photoionization.[11] Finally, the weakly basic leuco-hydroxide could react with a proton, yielding the leuco cation.[12] Therefore, at high pH (pH > 10), the leuco cation and hydroxyl anion could recombine, resulting in a microgel response. Importantly, all of these responses are reversible—once the respective stimulus is removed, the microgel returns to its initial state.

To fabricate etlaons from the TPL-modified microgels, the TPL monomer was first synthesized as detailed in the Supporting Information. TPL was then incorporated into microgels by copolymerization with *N*-isopropylacrylamide and *N*,*N*′-methylenebisacrylamide (see the Supporting Information). These microgels are denoted as MG-*x* %, where *x* represents the content of TPL (either 0.75 % or 1.5 %). The transmission electron microscope (TEM) images of the resultant microgels can be seen in Figure 3, and revealed that the dried microgels had diameters of ca. 350 nm, with good monodispersity. The microgels were also characterized by dynamic light scattering (DLS), and showed hydrodynamic diameters of 1060 nm and 480 nm for MG-1.5 % in the fully swollen and collapsed state, respectively. Additionally, the MG-0.75 % microgels showed diameters of 890 nm and 360 nm in the swollen and collapsed state, respectively. Finally, a LCST of around 32.5 °C for MG-0.75 % and MG-1.5 % was determined.

After microgel characterization, etalons were constructed following the previously described protocol.[13] Initial experiments focused on etalon response to UV irradiation. Figure 4 b shows a representative reflectance spectrum for a device fabricated from MG-1.5 %, and a series of reflectance spectra after UV exposure (270–400 nm). As can be seen, UV exposure causes a red shift in the position of the reflectance peak. We propose that this red shift is a result of the TPL molecule dissociating into a cation (leuco cation) and a hydroxyl anion (Figure 4 a). This ionization increases the hydrophilicity of the microgel and generates an inner osmotic pressure, which results in microgel swelling, thus leading to an increase in the distance between the etalon's two mirrors (Figure 1) and

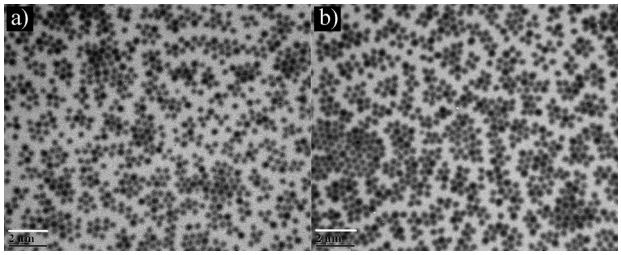

Figure 3. TEM images of a) MG-0.75 % and b) MG-1.5 %. The scale bars are 2 μm.

a concomitant red shift, as can be predicted from Equation (1). These etalons exhibited total shifts of 49 nm and 35 nm for MG-1.5 % (Figure 4 c) and MG-0.75 % (see the Supporting Information), respectively. We note that these experiments were conducted at 30 °C. We found that temperature variations could change the extent of the response, 30 °C gave us the best response, presumably owing to the favorable hydrophilic/hydrophobic interactions, combined with the microgel diameter at this temperature, thus allowing for maximal microgel size change upon TPL ionization (see the Supporting Information). Therefore, all of the experiments herein were completed at this temperature. When the etalons were stored in the dark, the leuco cation and hydroxyl anion recombine with one another, and the reflectance peak shifts back to its initial position, although the reversibility is relatively slow (14 h). The same experiments were repeated on a total of three etalons for each of the synthesized microgels. The response/reversibility for each etalon was repeated ten times with no noticeable change in its response. Furthermore, the devices were tested 15 days after the initial experiments, having been stored in water over this time, with no noticeable effect on the response. For comparison, an etalon composed of non-TPL-containing microgels showed

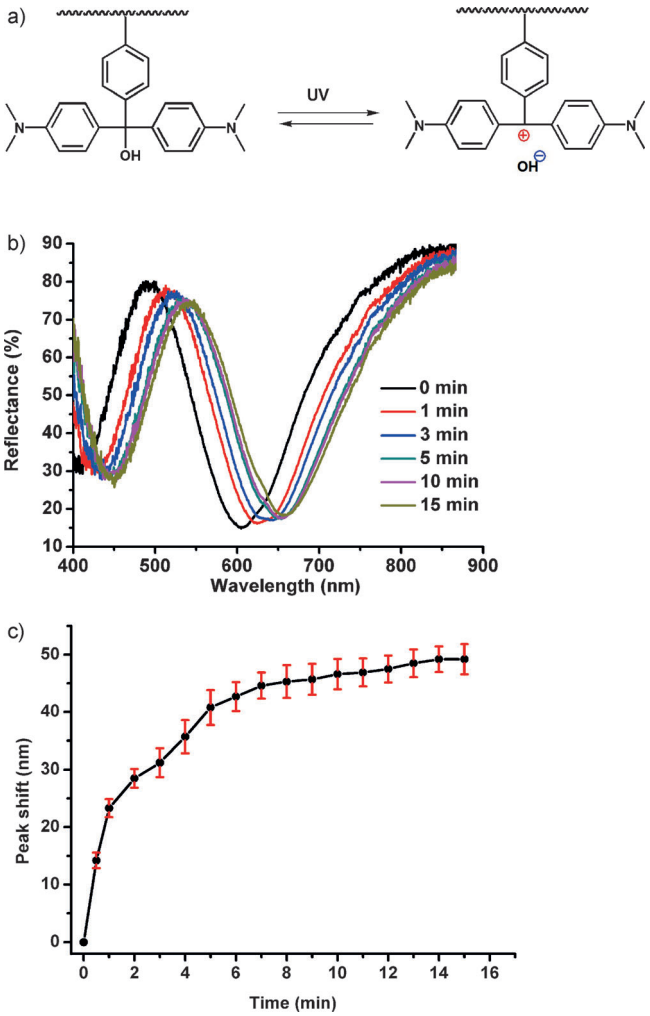

Figure 4. a) The reaction of TPL with UV light. b) Reflectance spectra for an etalon before UV exposure and after UV exposure in water for the indicated times at 30 °C. c) Peak shifts as a function of time at 30 °C for etalons composed of MG-1.5 %. Each point is an average of three repeat experiments with a single device; the error bars indicate standard deviation.

no response to UV irradiation (see the Supporting Information).

TPL also exhibits strong absorption in the visible region, with a maximum absorbance at 630 nm (see the Supporting Information). This absorbance leads to a local heating effect, which can be used to cause the pNIPAm-based microgels to change solvation state.[14] To investigate this further, we exposed the etalon to light of 633 nm (LED array). Upon exposure, the reflectance peaks of the etalon blue shifted, as can be seen in Figure 5. The total reflectance peak shift was 28 nm for MG-1.5 % (Figure 5) and 19 nm for MG-0.75 % (see the Supporting Information). The shifts are a result of microgel collapse causing the etalon's mirrors to approach one another. While this system is interesting for optical applications, it could also have implications for remotely triggered (through skin) drug delivery,[15] and is being pursued further. A total of four devices were tested, and yielded similar responses to that in Figure 5. Furthermore, the

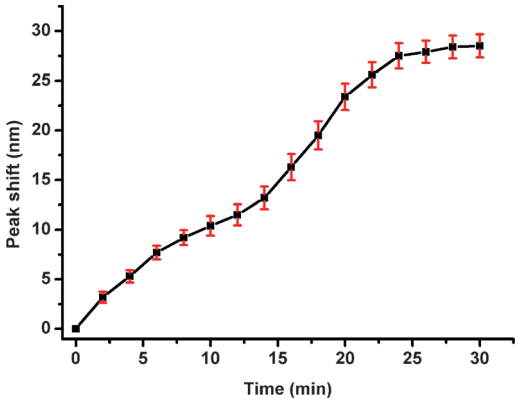

Figure 5. Spectral blue shifts observed as a function of time for etalons composed of MG-1.5 % exposed to 633 nm light in water at 30 °C. Each point is the average of three repeat experiments with a single device; the error bars indicate standard deviation.

reversibility for each device was tested three times with no noticeable change in response.

It has been reported that the hydroxide group of TPL can react with acid, generating the leuco cation, as mentioned above and illustrated in Figure 6.[16] Therefore, etalons composed of TPL-modified microgels should be pH responsive, swelling at low pH from the charge generation. When the solution pH is changed from 8 to 2, the observed reflectance peak red shifts 50 nm for MG-1.5 % (Figure 6b) and 40 nm for MG-0.75 % (see the Supporting Information). Furthermore, etalons which were then stored in 0.1 M NaOH for 14 h and reused exhibited the same responsivity. A total of four individual etalons were investigated, all exhibiting similar

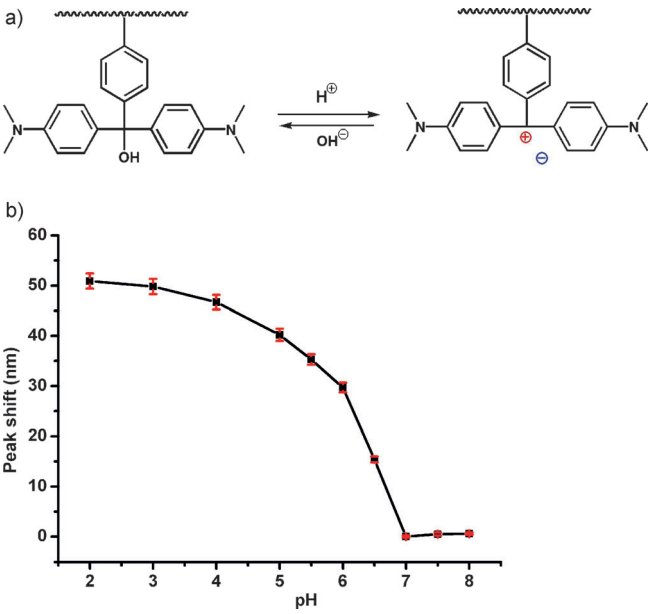

Figure 6. a) The ionization of TPL at low and high pH. b) Etalon peak shift for MG-1.5 % as a function of pH in water at 30 °C. The device took approximately 20 min to stabilize at each pH. Each point is the average of three repeat experiments with a single device; the error bars indicate standard deviation.

properties. Furthermore, the observed pK_a values for MG-1.5% (Figure 6) and MG-0.75% (see the Supporting Information) were 5.8 and 6.1, respectively. It has been reported that the photolysis of bis(4-(dimethylamino)phenyl)-(phenyl)methanol, a molecule containing the same reactive leucohydroxide as TPL, exhibits a pK_a of >6.[17] Finally, the pK_a for these microgels is in the range of interest for drug delivery to tumors.[18] Therefore, these microgels could find use in drug delivery for this application.

As indicated above, TPL-modified microgels can react with nerve agents (specifically Tabun), undergoing ionization. As is well known, nerve agents interfere with the action of the nervous system through acetylcholinesterase inhibition. This results in acetylcholine accumulation in synaptic junctions, which eventually hinders the relaxation of muscles, ultimately leading to death.[19] It is for this reason that nerve agents are considered weapons of mass destruction by the UN. Chemically, nerve agents are organophosphonates with good leaving groups. The chemical structures of some nerve agents, such as Sarin, Soman, and Tabun are shown in the Supporting Information. The nucleophilic hydroxy group in TPL provides a suitable reactive site for electrophilic phosphorous atoms in the nerve agents (Figure 7). Herein, diethylcyanophosphate (GAS) was used as a Tabun mimic. GAS has similar reactivity to Tabun, but without the potent toxicity. In the presence of GAS, phosphorylation of the TPL hydroxy group is expected, generating a leuco cation, as shown in Figure 7a. The leuco cation leads to electrostatic repulsion and increased solvation in the microgels, which results in the microgel swelling and the etalon response indicated in Figures 2 and 7. Figure 7 shows the dependence of etalon peak shifts on the GAS concentration in acetonitrile. As can be seen, the λ_{max} shifts significantly in the range of 1×10^{-5} mol L^{-1} to 6×10^{-5} mol L^{-1}, exhibiting a total shift of 53.2 and 39.2 nm for MG-1.5% and MG-0.75%, respectively (see the Supporting Information). Therefore, the device can be used for quantitative analysis of the nerve agent. For comparison, an etalon was exposed to triethyl phosphate (see the Supporting Information), and no peak shift was observed. Additionally, we investigated the response of the device to GAS in the presence of an equimolar amount of triethyl phosphate, which showed a very similar response to that in Figure 7 (see the Supporting Information). We concluded that these etalons can distinguish GAS from other related organophosphates.

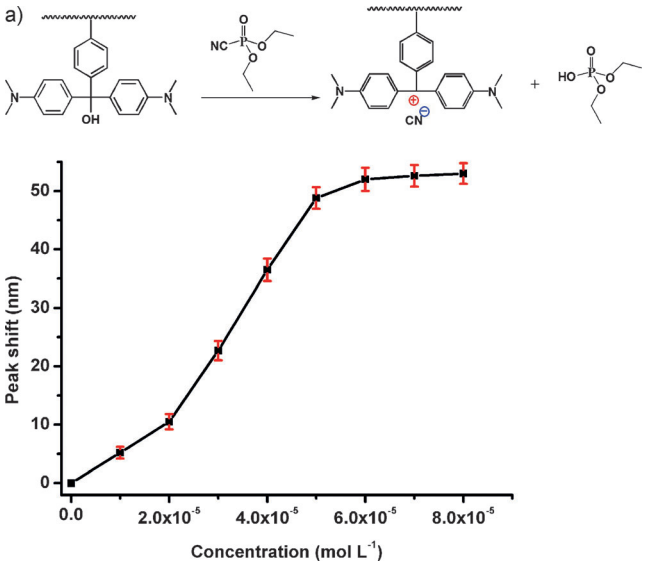

Figure 7. a) The reaction of TPL with GAS. b) Etalon peak shift for MG-1.5% as a function of GAS concentration in acetonitrile at 30°C. The device took approximately 25 min to stabilize at each concentration. Each point is the average of three repeat experiments with three different devices; the error bars indicate standard deviation.

To summarize, we reported on microgel-based etalons that are capable of changing their optical properties in response to the application of a number of different stimuli. Specifically, because of TPL modification of the microgels that make up the etalon, they are able to respond by swelling or shrinking in response to exposure to light (UV and visible), solutions of various pHs, and exposure to the nerve-agent mimic GAS. This investigation not only showcases the versatility of the etalon construct, by simple modification of the microgel chemistry, but also sheds light on the use of these and related materials for a number of applications including triggered and controlled drug delivery and sensing.

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