Photo-induced Control of Smart Polymer Systems via pH Jump Reaction

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1. Introduction

Polymers that respond dramatically to very slight changes in their environments are called ‘stimuli-responsive’ or ‘smart’ polymers. Such materials have already opened new frontiers in biomedical technologies, such as diagnostics [1, 2], therapies [3, 4], analytical technologies [5, 6], and actuators [7, 8]. The uniqueness of smart polymers lies not only in the rapid macroscopic changes occurring in their structure but also in the reversible nature of these transitions. The affected factors include shape [9], surface characteristics [10], solubility [11], molecular affinity [12], and sol–gel transition [13], etc., whereas the external triggers can be temperature, pH, ionic strength, certain chemicals, electric fields, magnetic fields, or light. Among them, photo-responsive polymers have several promising applications because the stimuli can be applied or removed instantaneously, avoiding the delay associated with the diffusion of the stimulus in many other cases [14, 15].

Although physical stimuli are advantageous because they allow local and remote control, chemical stimuli such as concentration gradients of protons, ions, and oxidizing/ reducing agents are also important characteristics observed in living systems. The human body, for example, exhibits variations of pH along the gastrointestinal tract, tumoral areas, inflamed or infected tissues, and the endosomal lumen. In contrast to other stimuli that can easily penetrate through materials, however, changing the pH quickly and precisely at a particular location in the system has been a big challenge.

From this regard, we propose a new system that utilizes a photoacid generator (PAG) to reduce the local pH of solution via photo irradiation (Fig.1).

PAGs are chemicals that release protons via a photoinitiated reaction because the pKa of PAG in an excited state is significantly lower than the ground state [16]. In this study, we have integrated the photo-induced pH jump reaction into smart polymer systems and demonstrated the spatio-temporal control of their properties upon photo irradiation.

![Photochemistry mechanism of PAG, o-nitrobenzaldehyde (NBA).](image)

Fig.1. Photochemistry mechanism of PAG, o-nitrobenzaldehyde (NBA).

2. Method

2.1 Hydrogels

The pH-responsive poly(N-isopropylacrylamide-co-2-carboxyisopropylacrylamide) (P(NIPAAm-co-CIPAAm)) hydrogels were prepared by a redox polymerization [17]. The prepared gels were swollen in a solution containing various concentrations of o-nitrobenzaldehyde (NBA) as a PAG for two days.

2.2 Microfluidic devices

NBA was integrated into polydimethylsiloxane (PDMS) microchannels by presorbing NBA within the PDMS channel surface regions [18]. NBA was dissolved in acetone and flowed into the channel for less than one minute. The NBA-coated channel was shown to capture the pH-sensitive poly(NIPAAm-co-propylacrylic acid (PAAc)) -grafted nanobeads onto the channel walls where P(NIPAAm-co-PAAc) was also grafted. Spatial control of bead traps in the channel was achieved by irradiating UV light to a limited region of the
channel through a mask.

2.3 Nanoassemblies

Block copolymers having dual-temperature and pH responsive properties of P(NIPAAm-co-N-(isobutoxymethyl)acrylamide (BMAAm))-b-P(NIPAAm-co-CIPAAm) were prepared by reversible addition-fragmentation chain transfer (RAFT) polymerization. To achieve a remote-controlled assembly/aggregation behavior of the micelle, NBA was capsulated into the micelle.

![Fig.2. Spatial control of pH jump reaction in the gels at 37°C. Slab gels were swollen in pH 7.0 solution containing NBA and bromocresol gree (yellow: pH < 3.8). The gels were the exposed to UV light through photomask [17].](image)

3. Results

3.1 A photo-induced gel shrinking

The spatial control of pH jump in the gel was demonstrated by irradiating the mask-covered gel with UV light. UV was irradiated for 3 min.

Fig. 2 shows the time-dependent color change of the gels after UV irradiation at 37°C. After UV irradiation, the color started to change instantaneously from blue to yellow (yellow: pH < 3.8) only in the photo illuminated region, which was duplicated in a circle pattern from the mask onto the surface of the hydrogels [16]. The border of the yellow circle region gradually moved in an outward direction with time and the color of the entire gel changed to yellow within 30 min. The result indicates that protons were efficiently released from the NBA, decreasing the pH inside the gel at least below pH 3.8 which is lower than pKa of P(NIPAAm-co-CIPAAm). The NBA-integrated gel was also successfully employed for the controlled release of entrapped dextran, where dextran was successfully entrapped into the gel and then released into water in a controlled manner under 365 nm UV illumination. This system shows significant promise as a smart platform for triggered and programmed delivery of drugs [19].

![Fig.3. Spatial control of bead trap inside the channel. The channels were modified with P(NIPAAm-co-PAAc) followed by coating with NBA. The suspension of beads in PBS (pH 7.4) was injected into the channel and incubated at 37°C, and then exposed to UV lamp through a mask for one minute [18].](image)

3.2 A photo-induced nanoparticle separation

A photoinitiated proton-releasing reaction of NBA was also integrated into microfluidic devices for surface traps of pH-sensitive nanoparticles. NBA-coated microchannel walls demonstrated quick proton release upon UV irradiation, allowing the pH of a buffer solution within the microchannel to decrease from 7.4 to 4.5 in one minute. The NBA-coated channel was shown to capture the pH-sensitive nanobeads onto the channel walls where pH-sensitive polymer was also grafted. Spatial control of bead traps in the channel was achieved by irradiating UV light to a limited region of the channel through a mask (Fig.3) [18].

By
controlling UV irradiation, this technique enables not only prompt pH changes within the channel, but also the capture of target molecules at specific locations within the channel.

3.3 A photo-induced nanoassembly

To achieve a remote-controlled assembly/aggregation behavior of the micelle, NBA was also capsulated into the micelle (Fig.4). First, block copolymers of P(NIPAAm-co-BMAAm)-b-P(NIPAAm-co-CIPAAm)s with dual-temperature and pH responsive properties were successfully prepared by RAFT polymerization. By UV irradiation, the P(NIPAAm-co-CIPAAm) shell were dehydrated and led the aggregation for the acidic condition caused by protons generated from the NBA. This assemble system will be applied in a remote-controlled drug release system.

4. Conclusions

We have developed photo-induced pH-responsive systems using NBA that release protons via a photoinitiated reaction. The photo-induced pH jump reaction was integrated into various materials such as pH-responsive hydrogels, microfluidic devices, and nanoparticles. The spatio-temporal control of their properties upon photo irradiation has been successfully demonstrated. This technique can potentially be utilized to create smart platforms such as remote and programmed delivery of drugs or effective target molecule separation in the microfluidic channels.

References