

Integration of A Photo-induced pH-jump Reaction into pH-responsive Hydrogels for Local Gel Shrinking

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Introduction: There have been many studies in the area of ‘smart’ polymers, which have focused on applications for a variety of medical, biological, and analytical technologies. Among many smart polymers, pH-responsive polymers have been well-known as the useful for a variety of biomedical applications. In contrast to other stimuli that can easily penetrate through materials (e.g., heat), however, changing the pH quickly and precisely at particular location in the system has been a big challenge. From these perspectives, we focused on a photoinitiated proton-releasing reaction of ‘photoacid generators’ (PAGs), the pK_a of which, in an excited state, is significantly different from that in the ground state. In this study, PAG, *o*-nitrobenzaldehyde (*o*-NBA) was integrated into the newly designed pH-responsive hydrogels (poly(*N*-isopropylacrylamide-*co*-2-carboxyisopropylacrylamide (P(NIPAAm-CIPAAm))) to induce pH-jump at particular location in the hydrogels upon UV irradiation, resulting in local shrinking of hydrogels followed by water release.

Methods: A novel carboxylate monomer CIPAAm was synthesized by a previous reported methods (Ebara, M. et. al. *Macromolecules*. 2000;33, 8312-8316.). pH-responsive P(NIPAAm-CIPAAm) hydrogels were prepared by a redox polymerization. Briefly, NIPAAm (95 mol%) and CIPAAm (5 mol%) were dissolved in water with *N,N'*-methylene-bis(acrylamide) (MBAAm) as a crosslinker, *N,N,N',N'*-tetramethylethylenediamine (TEMED), and ammonium persulfate (APS) as an initiator. The solution was kept at 4°C for one day for polymerization and spontaneous gelation in glass capillary (100 μm i.d.). The prepared hydrogels were immersed in *o*-NBA solution (1 mM) for one day. The pH change inside the gels was continuously monitored using pH-indicator (bromothymol blue). The pH-jump was also observed by measuring the swelling changes of hydrogels. Swelling ratio was defined as the ratio of gel diameter at a certain condition (d_{pH}) to the original diameter (d_0).

Results and Discussion: P(NIPAAm-CIPAAm) gels were successfully prepared and exhibited sensitive changes in swelling ratios in response to both temperature and pH changes. For example, at 40 °C, P(NIPAAm-CIPAAm) gels demonstrated a sharp volume phase transition over pH 5 which was approximately pK_a value of the gels. As seen in Fig.1, when P(NIPAAm-CIPAAm) gels were transferred to pH 3.0 condition from pH 7.0, they gradually shrank with time, forming a surface collapsing of polymer layer called ‘skin layer’ (seen in Fig.1a) (Ebara, M. et. al *J. Polym Sci. Part A*. 2001;39, 335-342.). This is because protons diffuse from outside to inside of the gel. *o*-NBA containing gels, on the other hand, shrank very rapidly without forming skin layer

upon UV irradiation because *o*-NBA released protons uniformly inside the gels (Fig.1b). Indeed, 1 mM of *o*-NBA solution changed solution pH from 7.0 to 3.0 within a few minute. Figure 2 shows the local UV irradiation on the hydrogel through a mask. The color was changed only in the photo illuminated region, duplicated the pattern on the mask although the edge of the region was not clear because the diffusion of protons were very quick.

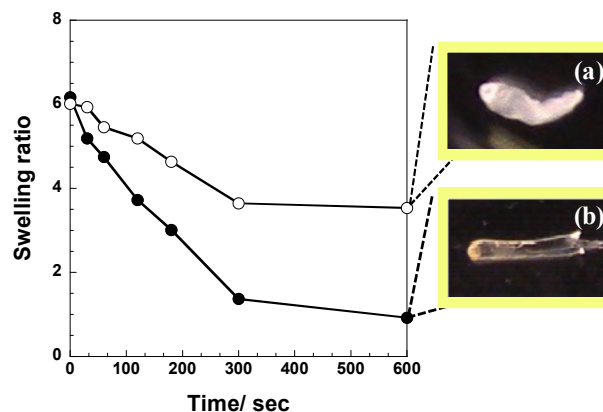


Figure 1. Shrinking kinetics for P(NIPAAm-CIPAAm) gel at 40°C at pH 7.0 (○: gels were transferred to pH 3.0 solution; ●: gels containing *o*-NBA was irradiated by UV at pH 7.0)



Figure 2. Photographs of P(NIPAAm-CIPAAm) gel containing *o*-NBA before and after UV irradiation for one minute. UV was irradiated through a mask and the color change of pH indicator in the only exposed region was observed (pH indicator, bromothymol blue; yellow below pH 6.0).

Conclusions: The rapid and local shrinking of P(NIPAAm-CIPAAm) gels containing *o*-NBA was successfully demonstrated by integrating pH-jump reaction using *o*-NBA. The unique shrinking kinetics was observed because protons were suddenly released uniformly inside the gels. A special control of pH change was also shown by irradiating UV light on a limited region of the gel through a mask. This technique enables not only prompt pH change inside the gel, but also target molecular release at a particular location by spatially controlling UV irradiation.