

## Dependence of Molecular Recognition for a Specific Cation on the Change of the Oxidation State of the Metal Catalyst Component in the Hydrogel Network

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Molecular recognition for a specific cation depending on the change of the oxidation state of the metal catalyst component contained in the hydrogel network has been studied in a self-oscillating hydrogel. The self-oscillating hydrogels are synthesized by the copolymerization of *N*-isopropylacrylamide (NIPAAm), lead methacrylic acid (Pb(MAA)<sub>2</sub>), and Ru(bpy)<sub>3</sub><sup>2+</sup> monomer as a metal catalyst component. The recognition for a specific cation (in this study, Ca<sup>2+</sup> has been used) is characterized by the adsorbed amount of Ca<sup>2+</sup> into the gel. The recognition of the gels for Ca<sup>2+</sup> is higher at the temperature below the LCST, and also higher at the oxidized state than at reduced state of the metal catalyst component which corresponds to a more swollen state. Moreover, a propagating wave induced by a periodic change of the oxidation state with the diffusion phenomena in the oscillating hydrogel shows a possibility for temporal and site-specific molecular recognition due to the local swelling of the gel.

**Key Words** : Molecular recognition, Oxidation state, Oscillating-hydrogel, Chemical waves, BZ reaction

### Introduction

Hydrogels are insoluble, cross-linked network polymer structures composed of hydrophilic homo- or hetero-copolymers, which have the ability to absorb significant amounts of water,<sup>1-3</sup> and are also triggered by a variety of external stimuli such as pH,<sup>4</sup> temperature,<sup>5,6</sup> solvent composition,<sup>7</sup> ionic strength,<sup>8</sup> external electric or magnetic fields,<sup>9</sup> and current and light irradiation.<sup>10</sup> Therefore, these excellent characteristics of hydrogel guarantee their numerous applications in various fields. Examples of which are their use in drug carrier systems exemplified by materials releasing drugs in a controlled manner, catalysis, and mimetics of various organic systems.<sup>11</sup>

The design of precise macromolecular chemical architecture, in which a target molecule can be recognized from an ensemble of closely related molecules, has been extensively studied.<sup>12</sup> The technique involves forming a pre-polymerization complex between the template molecule and the functional monomers with specific chemical structures designed to interact with the template either by covalent bond,<sup>13</sup> non-covalent bond,<sup>14,15</sup> or both systems.<sup>16,17</sup> The pre-polymerization reaction occurred with the presence of a cross-linking monomer and an appropriate template molecule that controls the overall morphology and macro-porous structure of the hydrogel network for the recognition of specific species by imprinting. The application of the research in this field has included separation processes such as chromatography,<sup>18</sup> immunoassays and antibody mimics,<sup>19</sup> dispensing recognition elements,<sup>20</sup> and catalysis and artificial enzymes.<sup>21</sup> In addition, a wide range of cross-linked imprinted hydrogels has been proven to be useful as drug

delivery platforms.<sup>22</sup>

Recently, Tanaka *et al.*<sup>23-25</sup> have described a stimuli-sensitive recognizing hydrogel using the intelligent character of stimuli-sensitive hydrogel, which is very similar to the recognition in proteins by combining the two functions of sensitivity and molecular recognition in a gel. Their design includes a stimuli-sensitive monomer, such as a temperature-sensitive monomer, for the polymerization of molecular recognition hydrogel in the presence of the target molecule. With this result, the recognition sites were destroyed upon hydrogel swelling and were reformed upon reverse deswelling. This suggested an ideal biomimetic material similar to proteins that recognize a specific target material responding to the environmental conditions with self-organizing active adsorption sites. However, these conventional stimulus-responsive hydrogel systems provide only one unique action to the response of the stimuli.

On the contrary, the self-oscillating hydrogel systems introduced by Yoshida *et al.* undergo autonomous oscillations of swelling and deswelling in a closed container without external stimuli.<sup>26,27</sup> The hydrogel systems are composed of *N*-isopropylacrylamide (NIPAAm) and ruthenium(4-vinyl-4'-methyl-2,2'-bipyridine)bis(2,2'-bipyridine)bis(hexafluorophosphate) (abbreviated as Ru(bpy)<sub>3</sub><sup>2+</sup> monomer hereafter). The Ru(bpy)<sub>3</sub><sup>2+</sup> monomer ion acts as a metal catalyst for the Belousov-Zhabotinsky (BZ) reaction.<sup>28-30</sup> Thus, the mechanical oscillation of the gel is induced by the BZ reaction that generates the rhythmical redox changes of the catalyst covalently bound to the polymer chain. When the hydrogel is immersed in an aqueous BZ solution without a catalyst, the substrates penetrate the polymer network, and an oscillation reaction will occur in the polymer chain. The

redox change of the catalyst moiety can lead to a change in the hydrophilicity of the polymer chain, and the oscillation of the swelling state of the gel can be obtained by the oscillation of the polymer chain's hydrophilicity. Thus, the self-oscillation of the redox state in the hydrogel can be used as a periodic controller in the molecular recognition of the gel by reversing the swelling state. This means that the hydrogel swells with the oxidation of the ruthenium catalyst, and the recognition of specific species will be decreased as compared to the reduced state of the catalyst.

In this paper, we have designed a self-oscillating hydrogel in which the molecular recognition for specific species is influenced by the environmental physical and chemical condition. The oxidation state of the metal catalyst component in the hydrogel network, and the solution temperature has been changed for the variation of the recognition. The oscillating hydrogel was synthesized by free radical polymerization using lead methacrylic acid as the functional monomer for calcium ions,  $\text{Ru}(\text{bpy})_3^{2+}$  monomer for the variation of the oxidation state in the hydrogel network, and NIPAAm as the backbone monomer. The hydrogels swell below their lower critical solution temperature (LCST) at around 35 °C and shrink above the LCST. The LCST was slightly dependent on the used monomer composition during the copolymerization process. Molecular recognition was compared between the oxidized and reduced states of the metal catalyst in the gel chain. The recognition of the hydrogel in the oxidized state of the metal catalyst was slightly lower than that in the reduced state of the metal catalyst at the same temperature.

In addition, a propagating chemical wave has also been studied in the cylindrical oscillating hydrogel by immersing it into the BZ solution. It shows a spatio-temporal change of oxidation state in the gel, which suggests a possibility for temporal and site-specific molecular recognition by the periodic variation of oxidation state in the gel.

## Experimental

**Synthesis of the Oscillating Hydrogels.** The oscillating hydrogels were prepared using three monomers of *N*-isopropylacrylamide (NIPAAm) (Aldrich, 97%), lead methacrylic acid ( $\text{Pb}(\text{MAA})_2$ ), and  $\text{Ru}(\text{bpy})_3^{2+}$  monomer.  $\text{Pb}(\text{MAA})_2$  and  $\text{Ru}(\text{bpy})_3^{2+}$  monomers were purchased from Monomer-Polymer and Dajac Laboratories, Inc. (Feasterville, PA) and Fuji Molecular Ltd. (99.8% Japan), respectively. For the preparation of the hydrogels with free radical polymerization, *N,N'*-Methylenebisacrylamide (BIS) (Aldrich, 99.8%) as a cross-linker and 2,2-azobis(isobutyronitrile) (AIBN) (Aldrich, 99.8%) as an initiator were used. The mixed solutions of NIPAAm (6 M),  $\text{Pb}(\text{MAA})_2$  (20 mM),  $\text{Ru}(\text{bpy})_3^{2+}$  [2.5-3.0% (w/w) of NIPAAm] with BIS (50-120 mM) as a cross-linker in dioxane were immediately transferred into the glass capillaries with an inner diameter of 1 to 2 mm after the addition of AIBN to the solutions. The capillaries were degassed under nitrogen gas for about 15 minutes, and the polymerization was carried out at 60 °C for

24 hours. After gelation was completed, the hydrogels were taken out of the capillaries and were washed consecutively with deionized water, HCl, and NaOH in order to remove unreacted molecules and lead ions. The hydrogels were immersed and maintained in a 1 mM NaCl solution throughout all subsequent experiments to ensure the complete dissociation of methacrylic acid.

In order to compare the molecular recognition between the oscillating hydrogel which can recognize  $\text{Ca}^{2+}$  and a simple oscillating hydrogel which does not have a function for the recognition of  $\text{Ca}^{2+}$ , a polymer using methacrylic acid (MAA) instead of functional monomer,  $\text{Pb}(\text{MAA})_2$ , was also synthesized with the same procedure by mixing NIPAAm (6 M), MAA (40 mM), and  $\text{Ru}(\text{bpy})_3^{2+}$  [2.5% (w/w) of NIPAAm]. In addition, to determine the influence of ruthenium monomer in the hydrogel network for the molecular recognition, a non-oscillating hydrogel without ruthenium monomer was also prepared using NIPAAm (6 M) and  $\text{Pb}(\text{MAA})_2$  (20 mM) alone.

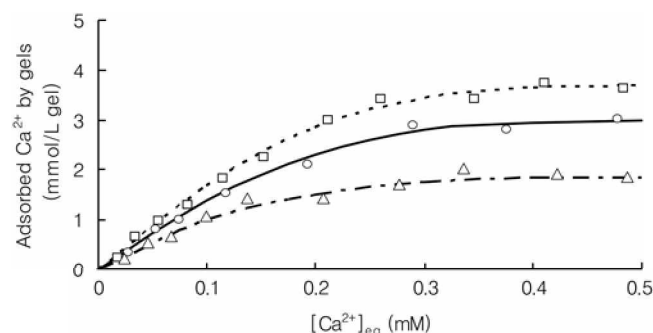
**Adsorption Experiments for the Recognition of Calcium Ions in the Hydrogels.** Before the adsorption experiment, all the cylindrical hydrogels were dried completely in vacuum oven for four days at room temperature. For the calcium ion adsorption, pieces of the cylindrical gels having a dry weight of 50 to 80 mg were cut into small pieces ( $\leq 2$  mm) and were put into the  $\text{CaCl}_2$  solution (10 mL), varying the concentration of  $\text{CaCl}_2$  from 0.01 mM to 0.8 mM. The solution also contained 1 mM NaCl to provide monovalent sodium ions. It is due to replace calcium ions. Equilibrium calcium concentration in the medium was measured using a calcium ion selective electrode (Cole-Parmer, 27502-09). The adsorbed amount was obtained by the calculation of the difference of the initial calcium concentration in the solution  $C_i$ , and the final equilibrium calcium concentration in the solution  $C_{\text{eq}}$ . The electrode was used after calibration by the solution which has a known concentration of calcium ion.

**Oscillation Experiments and Monitoring of Chemical Waves in the Hydrogels.** The working solutions for self-oscillation of the hydrogel in the BZ reaction system were prepared from the stock solutions of 0.3 M malonic acid (Aldrich, 99.8%), 0.6 M  $\text{NaBrO}_3$  (Aldrich, 99.9%), and 1 M  $\text{HNO}_3$  (Aldrich, 98%). All chemicals were used in their commercial grade without further purification. The 80 to 100 mg of the hydrogel cut within 2 mm was used for the oscillations of calcium ion adsorption to the hydrogel in 15 mL of BZ solution composed of malonic acid, sodium bromate, and nitric acid without metal catalyst. For the wave formation in the gel by the BZ reaction, the hydrogels with a length of 8 to 12 mm and a diameter of 1.6 to 1.8 mm were used. Before obtaining the waves in the gels by using the BZ solution, the recognizing oscillating hydrogels were kept in a buffer solution of NaCl (1 mM solution), stirring it slowly for 24 hours. All experiments for propagating the chemical waves were monitored with a CCD camera (Sony, SSC-370) equipped with a microscope (Leica, model Mz75). The CCD camera was connected to a personal computer running a frame grabber (Flash Point, Optimum 6.1).

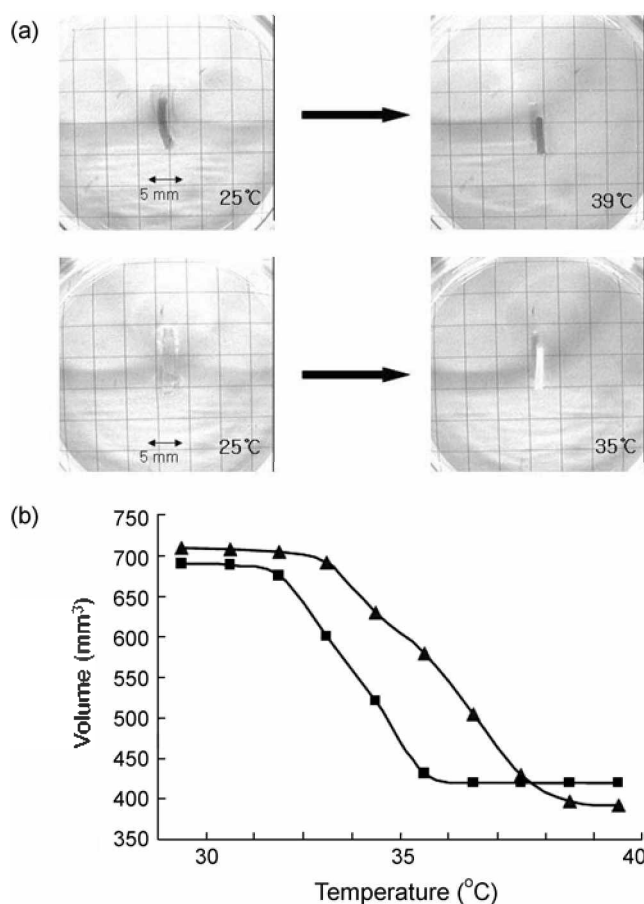
## Results and Discussion

**Adsorption in the Oscillating Hydrogels and Non-Oscillating Hydrogels.** Figure 1 shows comparison of the adsorption of calcium ions in three types of hydrogels. The adsorption pattern follows the famous Langmuir's isotherm expressed as,  $A = bC_{eq}/(1 + aC_{eq})$ .<sup>31</sup> For the gels which were prepared using 95 mM of BIS as the cross-linker, the recognition (adsorption) for calcium ions in the oscillating hydrogel composed of NIPAAm/Pb(MAA)<sub>2</sub>/Ru(bpy)<sub>3</sub><sup>2+</sup> was higher than that of the oscillating hydrogel composed of NIPAAm/MAA/Ru(bpy)<sub>3</sub><sup>2+</sup> at all concentration ranges of the calcium ion. This means that the functional monomer in the gel network has a role for molecular recognition toward Ca<sup>2+</sup>. However, the adsorption of the oscillating hydrogel toward calcium ions was much lower than that of the non-oscillating hydrogel composed only of NIPAAm/Pb(MAA)<sub>2</sub> with the same concentration of BIS. The lower adsorption of the oscillating hydrogel as compared to that of the non-oscillating hydrogel can be due to several reasons. We can suppose that it is originated by the loose network of the functional monomer with templates due to the addition the ruthenium metal catalyst component in the gel networks.<sup>23</sup> It can be induced by polymerization kinetics and the nature of the chains formed by the polymerization process, which influence the network morphology on a molecular level. Secondly, the addition of another monomer to the functional monomer networks could result in a significant decrease of adsorption sites in the gel structure.<sup>12,23</sup> Moreover, the Donnan effect can inhibit the free diffusion of the permeable calcium ion into the gel membrane through unequal equilibrium distribution by the macromolecular electrolyte of the ruthenium monomer on the gel network.<sup>32</sup>

**LCST of the Oscillating Hydrogels and Temperature Dependence of the Adsorption in the Oscillating Hydrogels.** Before studying the dependence of molecular recognition on the oxidation state of the metal catalyst in the self-oscillating hydrogel which corresponds to a chemical environmental stimulus, we have studied at first studied temperature dependence of the hydrogels. For the purpose, the LCST



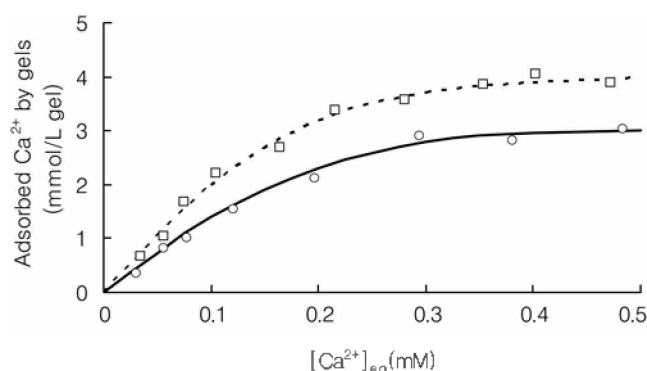
**Figure 1.** Comparison of adsorption for calcium ions in three kinds of gels using the same concentration of BIS (95 mM) at 25 °C. A non-oscillating gel composed of NIPAAm/Pb(MAA)<sub>2</sub> is represented by (○), an oscillating gel composed of NIPAAm/Pb(MAA)<sub>2</sub>/Ru(bpy)<sub>3</sub><sup>2+</sup> is represented by (□), and an oscillating gel composed of NIPAAm/MAA/Ru(bpy)<sub>3</sub><sup>2+</sup> is represented by (△).



**Figure 2.** Temperature dependence of the hydrogels. (a) Visual change of the swelling state in the oscillating hydrogel composed by NIPAAm/Pb(MAA)<sub>2</sub>/Ru(bpy)<sub>3</sub><sup>2+</sup> (orange color), and the non-oscillating hydrogel composed by NIPAAm/Pb(MAA)<sub>2</sub> (white color). (b) the comparison of LCST between an oscillating hydrogel (▲) and a non-oscillating hydrogel (■) obtained from the volume change of the gels by measuring the length using the computer program connected to the CCD camera.

(Lower Critical Solution Temperature) of the hydrogels composed of NIPAAm/Pb(MAA)<sub>2</sub>/Ru(bpy)<sub>3</sub><sup>2+</sup> and NIPAAm/Pb(MAA)<sub>2</sub> was obtained by measuring the approximate length and diameter of the cylindrical gels using the CCD camera. Due to the thermosensitive NIPAAm component, the temperature dependence of the swelling state is easily visualized as shown in Figure 2(a), and the hydrogels swell below LCST at around 35 °C and shrink above the LCST as shown in Figure 2(b). Between the two hydrogels of the oscillating and non-oscillating, the LCST is a little higher in the oscillating hydrogel composed by NIPAAm/Pb(MAA)<sub>2</sub>/Ru(bpy)<sub>3</sub><sup>2+</sup> than that of the non-oscillating hydrogel composed only by NIPAAm/Pb(MAA)<sub>2</sub>. This can be interpreted by the effect of charged ruthenium ion in the polymer chains, which increases the hydrophilicity of the polymer chain.

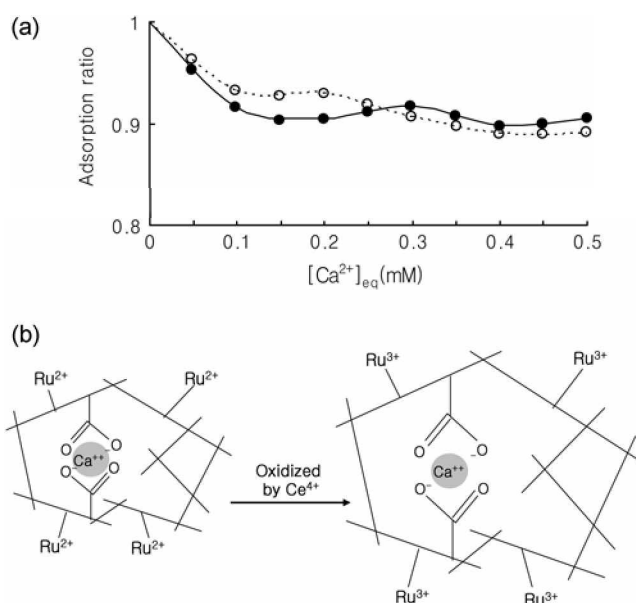
Due to the LCST in the oscillating hydrogel, the adsorption in the oscillating hydrogel is affected by the environmental solution temperature as shown in Figure 3. It shows higher adsorption towards calcium ions at 60 ± 1 °C than that at 25 ± 1 °C. For the experiments, the samples were



**Figure 3.** Adsorption of the oscillating hydrogel depending on the temperature. The result for the adsorption at the temperature above the LCST at  $60 \pm 1$  °C is represented as (□) and the result obtained at  $25 \pm 1$  °C is given as (○).

allowed to equilibrate at  $25 \pm 1$  °C for the swollen state and at  $60 \pm 1$  °C for the shrunken state for 48 hours. The equilibrium calcium concentration in the outer solution was measured using the same method as introduced in Figure 1. The obtained result for the temperature effect on the adsorption in the oscillating hydrogel composed of NIPAAm/Pb(MAA)<sub>2</sub>/Ru(bpy)<sub>3</sub><sup>2+</sup> is similar with the result obtained by Tanaka *et al.* using a non-oscillating hydrogel composed of NIPAAm/Pb(MAA)<sub>2</sub>.<sup>23,24</sup> Decreasing the environmental temperature could increase the distance between the nearest MAA by swelling of the hydrogels, and decrease the probability for pair formation. Therefore, the sites for the formation of Ca<sup>2+</sup> assemblies are decreased by the swelling of the gel. The change means that the adsorption and release of calcium ions are reversible, and the closeness of the adsorbing groups is controlled by the reversible phase transition of the hydrogel that consequently controls the adsorption process. Also, the temperature dependence of the oscillating hydrogel in Ca<sup>2+</sup> adsorption indicates that the oscillating hydrogels can respond reversibly to a change in other environmental or internal stimuli, which brings out the swelling state of the gel.

**Dependence of Adsorption on the Oxidation State of the Metal Catalyst Component in the Hydrogel Network.** Figure 4(a) shows the dependence of molecular recognition on the chemical environmental condition in the oscillating hydrogels, where the ratio of adsorption amount between the oxidized state and the reduced state in the oscillating hydrogel using 2.5% (w/w) of ruthenium monomer and 3.0% of ruthenium monomer is shown. In order to oxidize the metal catalyst of Ru<sup>2+</sup> in the gel network to Ru<sup>3+</sup> state, the oscillating hydrogels were immersed in a 1 M ceric ammonium nitrate solution with a buffer solution of NaCl (1 mM), stirring it slowly for 48 hours. For the adsorption experiment of the oxidized gel, it was used after cleaning the gel with a buffer solution of NaCl (1 mM) for two hours twice. After each experiment varying the calcium concentration, the gel sample was discarded, and a new gel was used by considering a minute difference of adsorption between the oxidized and the reduced states of the gel. The

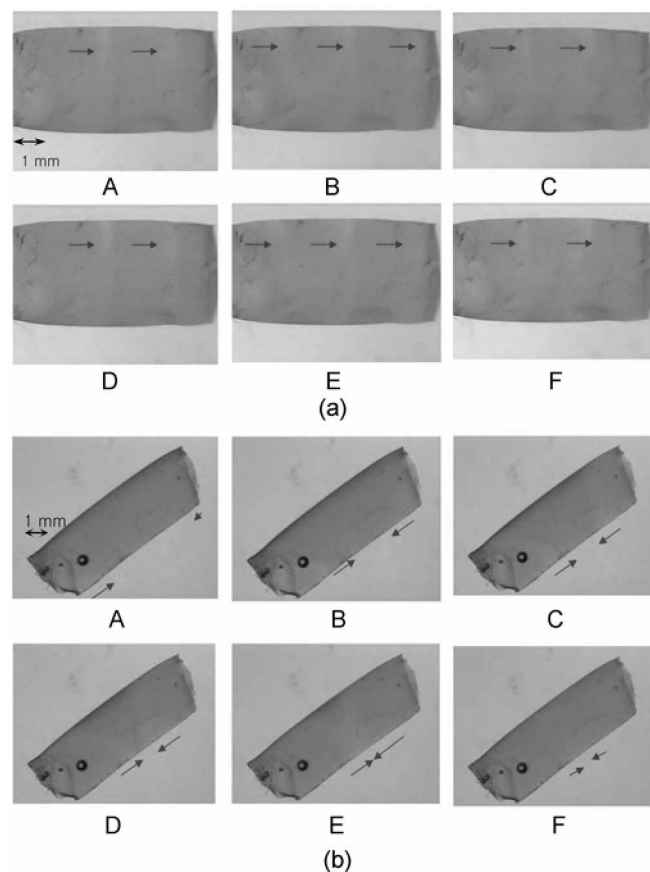


**Figure 4.** Adsorption of the oscillating hydrogel depending on the oxidation state of the metal catalyst in the gel network. (a) Typical ratio of adsorption amount between the oxidized state and the reduced state in the oscillating hydrogel using Ru(bpy)<sub>3</sub><sup>2+</sup> = 2.5% (w/w) of NIPAAm (○) and 3.0% of NIPAAm (●). (b) A model explaining the decrease of the adsorption by oxidation of the metal catalyst. It explains the mechanism in which the active sites for the adsorption are loosened by the oxidation of the gel at the more swollen state.

result of lower adsorption in the oxidized gel means that the adsorption is affected by the heterogeneous redox reaction between the gel network and the solution state. We assumed that the difference of adsorption amount can be described by a model of network diagram as shown in Figure 4(b), which is similar with the temperature effect. By the redox reaction between the Ru(bpy)<sub>3</sub><sup>2+</sup> component in the gel and the Ce<sup>4+</sup> ion in the solution, the oxidation state of the metal catalyst changes from Ru(bpy)<sub>3</sub><sup>2+</sup> to Ru(bpy)<sub>3</sub><sup>3+</sup>, which induces the oscillating hydrogels as a swollen state by increasing the hydrophilicity. Then the assemblies of the Ca<sup>2+</sup> templates in the gel cavity are destroyed by hydrogel swelling; therefore, the amounts adsorbed by the oxidized state of the gel could be lower than that adsorbed by the reduced state of the gel. However, we cannot conclude that the difference is deducted by the cavity effect alone since the repulsion force between calcium cations and ruthenium ion in the network also exists. Then the repulsion between calcium ion in the solution and oxidized ruthenium in the gel is higher than that in the reduced state, which causes smaller adsorption in the oxidized state. Therefore, we repeated the same experiment for the purpose of checking the effect of ruthenium cation on the absorption of calcium in the gel by increasing the composition of the ruthenium monomer from 2.5% to 3.0% of NIPAAm during the synthesizing process. In the gel including high percentage of ruthenium ion, the adsorption amount was decreased a little in both reduced and oxidized states, which proves some repulsion effect of the ruthenium ion. However, the adsorption was also decreased by the

oxidation of the gel with the same trend as shown in Figure 4(a).

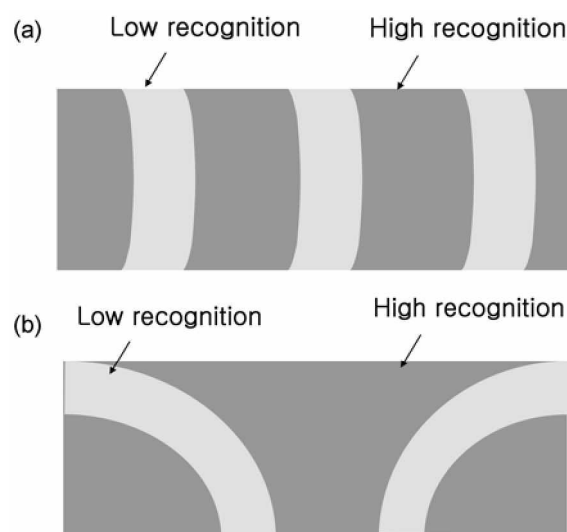
The dependence of molecular recognition for  $\text{Ca}^{2+}$  on the oxidation state of the metal catalyst included in the hydrogel network as shown in Figure 4(a) suggests a possibility for the oscillation of the adsorption of  $\text{Ca}^{2+}$  in the BZ reaction system. For the oscillation experiments, 60 mg of dried hydrogel was added in a 15 mL BZ solution without metal catalyst. In order to protect the formation of wave propagation along the length of a cylindrical hydrogel, the gel cut within 2 mm at swollen state was used. However, temporal oscillations for the concentration of  $\text{Ca}^{2+}$  in the BZ solution were not detected directly in our experimental system using the calcium ion selective electrode, though the redox oscillation of metal catalyst component was detected by a Pt-electrode in the same solution. We came up with several reasons for the experimental result of no-oscillations of calcium ion adsorption in the self-oscillation hydrogel in spite of redox oscillations. First, we can suppose that it was



**Figure 5.** (a) Snapshots of typical propagating waves obtained in the oscillating hydrogel with the BZ reaction solution, which was taken at 450, 465, 480, 495, 510, and 525 seconds after soaking into the BZ solution. The initial composition of the solution was as follows: [malonic acid] = 0.1 M,  $[\text{BrO}_3^-]$  = 0.2 M,  $[\text{H}^+]$  = 0.3 M,  $[\text{Ru}^{2+}]$  =  $5.0 \times 10^{-4}$ . (b) Another type of wave propagation obtained by using a lower cross-linked hydrogel, in which the catalyst monomer was increased to  $\text{Ru}(\text{bpy})_3^{2+}$  = 3.0% (w/w) of NIPAAm. The initial composition of the BZ solution is the same with (a), and the images were taken at, 315, 330, 345, 360, 375, and 390 seconds after soaking the hydrogel into the solution.

due to an insignificant variation of calcium ion amount because the dynamic redox change with a short oscillation period in the metal catalyst cannot induce a great change of the adsorption amount. Second, the response time of the gel to an environmental stimulus could be slower as compared to the period of the reversible change of environmental stimuli, which corresponds to the period of the chemical oscillations of the metal catalyst's oxidation state. A longer time needed for the change of swelling state by temperature or oxidizing agent well supports the assumption. Lastly, the concentration change of calcium ion in the solution by oscillating hydrogel can be insignificant for our experimental system which adopts a calcium ion selective electrode. The detectable limit of the electrode for calcium ion was only about  $2 \times 10^{-5}$  M in our experimental system.

**Propagating Chemical Waves in the Self-Oscillating Hydrogel.** Figure 5 shows propagating chemical waves in the oscillating hydrogel produced *via* an oscillating chemical reaction called the BZ reaction. For developing the wave pattern in the oscillating hydrogels, a one-dimensional cylindrical piece (out diameter = 1.5-2 mm) of poly NIPAAm/ $\text{Pb}(\text{MAA})_2/\text{Ru}(\text{bpy})_3^{2+}$  monomer hydrogel was immersed in the aqueous BZ reaction system containing MA,  $\text{NaBrO}_3$ , and  $\text{HNO}_3$  in a 6 mL cylindrical reactor at room temperature. By coupling the chemical oscillation reaction with the diffusion of a reaction intermediate of  $\text{HBrO}_2$  through the hydrogel phase, a periodical redox pattern change is obtained along the length of the cylindrical hydrogel. A typical pattern of propagating wave is introduced in Figure 5(a), in which red is the reduced state and green is the oxidized state of the metal catalyst component in the hydrogel network. The wave initiates from one side of the oscillating hydrogel, and then moves to another side with an alternate color change from red to green. Figure 5(b) shows another type of wave pattern obtained by using a lower cross-linked hydro-



**Figure 6.** A model for spatio-temporal nonhomogeneous recognition induced by a propagating wave formed by the self-oscillating hydrogel in the BZ system. It shows a possibility for a site-dependent molecular recognition by the gel system.

gel, in which the used catalyst monomer for the preparation of the gel was increased to  $\text{Ru}(\text{bpy})_3^{2+} = 3.0\%$ (w/w) of NIPAAm. In this case, a wave tends to appear at both corners of the gel and propagates into the center direction differently from that shown in Figure 5(a), in which the wave propagates into one direction only. Figure 6 shows a model of the periodic change of oxidation state in which the oxidized and reduced states change alternatively by band I and band II, respectively. Then the molecular recognition of the gel for a specific target material will change site specifically, since the reduced state represented by the red color of the shrunken state can adsorb the target material more easily than the region of the swollen state which is green in color, as explained in Figure 4(a).

### Conclusion

We have studied a self-oscillating hydrogel which recognizes a specific cation depending on the physico-chemical environmental condition. Solution temperature and oxidation state of the metal catalyst component included in the gel network were changed for the change of the swollen state of the gel. Molecular recognition depending on the environmental stimuli was explained by the mechanism in which the assemblies of  $\text{Ca}^{2+}$  templates in the gel cavity are destroyed by the swelling of hydrogel, and therefore the amounts adsorbed by the oscillating hydrogel might be lower in the swollen state. This means that molecular recognition for a specific cation is higher at a lower temperature than at a higher temperature, and is also higher at a reduced state of the metal catalyst in the gel network than at an oxidized state of the gel because of hydrophilicity inducing more swollen condition. However, the effect of ion-repulsion force between ruthenium ion in the network and calcium ion in the solution on molecular recognition was not considered seriously in this report. It will be studied continuously by varying the condition for hydrogel synthesizing more detail, such as the ratio of the cross-linking agent and the composition of the monomer. In addition, the oscillating hydrogel offers a new possibility of biomimetic material, which recognizes a specific target material depending on the environmental condition with spatio-temporal pattern, that is, site-specific recognition similar with protein.

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