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Accounts

Self-Oscillating Polymer and Gels as Novel Biomimetic Materials

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Stimuli-responsive polymers and their application to biomaterials have been widely studied. On the other hand, as a novel biomimetic polymer, we have been studying a polymer with an autonomous self-oscillating function by utilizing oscillating chemical reactions. So far, we have succeeded in developing a novel self-oscillating polymer and gels by utilizing the Belousov–Zhabotinsky (BZ) reaction. The self-oscillating polymer is composed of poly(*N*-isopropylacrylamide) (PNIPAAm), in which $\mathrm{Ru(bpy)_3}^{2+}$ is incorporated as a catalyst for the BZ reaction. Under the coexistence of the reactants (malonic acid, sodium bromate, and nitric acid), the polymer undergoes spontaneous cyclic soluble–insoluble changes or swelling–deswelling changes (in the case of gel) without any on–off switching of external stimuli. In this paper, our recent studies on the self-oscillating polymer and the design of functional material systems using the polymer are summarized.

1. Introduction

Polymer gels is a research field of polymer science which has seen rapid progress during the past 20–30 years. Gel can be widely defined as a crosslinked polymer network which is swollen by absorbing large amounts of solvent such as water. Theoretical study of the characteristics of gel had already proceeded in the 1940's, and the principle of swelling by water absorption based on thermodynamics had been clarified by Flory.[1] As an application of gel research, soft contact lenses were developed in the 1960's, and subsequently gels have been widely used in medical and pharmaceutical fields. Since a polymer which can absorb about 1000 times as much water as its own weight was developed in the US in the 1970's, gels have been applied as super absorbent polymers in several industrial fields, mainly application to sanitary items, disposable diapers, etc. Further, in 1978, it was discovered by Tanaka[2] that gels change volume reversibly and discontinuously in response to environmental changes such as solvent composition, temperature, pH change, etc. (called "volume-phase transition" phenomena). With this discovery as a turning point, research to use gels as functional materials for artificial muscle, robot hands (actuator), stimuli-responsive drug delivery systems (DDS), separation or purification, cell culture, biosensors, shape memory materials, etc. was activated.[3–8]

Until now, fundamental and applied research which include many different fields such as elucidation of gelation mechanisms, analysis of physical properties and structure, functional control by molecular design, etc. have been done. Especially, from the early 1990's, new functional gels which include the following three functions in themselves; sensing an external signal (sensor function), judging it (processor function), and taking action (actuator function), have been developed by many researchers as "intelligent gels" or "smart gels."

Further, in recent years, the usefulness of gels has also been shown in the field of micromachines and nanotechnology. In addition to new synthetic methods to give unique functions by molecular design in nano-order scale including supramolecular design, the design and construction of micro or nano material systems with the biomimetic functions of motion, mass transport, transformation and transmission of information, molecular recognition, etc. have been attempted.

So far, many researchers have developed stimuli-responsive polymer gels that change volume abruptly in response to a change in their surroundings such as solvent composition, temperature, pH, supply of electric field, etc. Their ability to swell and deswell according to conditions makes them an interesting proposition for use in new intelligent materials. In particular, applications for biomedical fields are extensively studied. One of the strategies of these applications is to develop biomimetic material systems with stimuli-responding function; i.e., systems in which the materials sense environmental changes by themselves and go into action. For these systems, the on–off switching of external stimuli is essential to instigate the action of the gel. Upon switching, the gels provide only one unique action, either swelling or deswelling.

This stimuli-responding behavior is temporary action toward an equilibrium state. In contrast, there are many physiological phenomena in our body that continue their own native cyclic changes. These phenomena exist over a wide range from cell to body level, as represented by the cell cycle, cyclic reaction in glycolysis, pulsatile secretion of hormones, pulsatile

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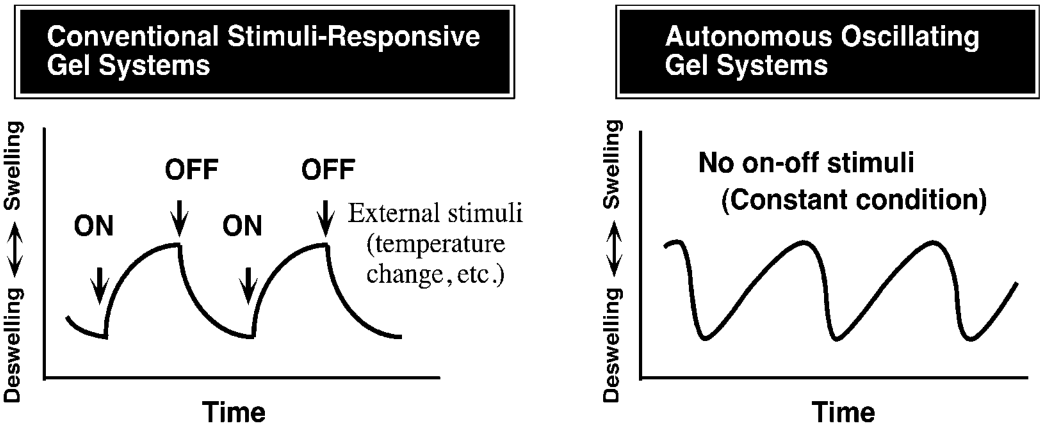

Figure 1. Stimuli-responsive systems and autonomous oscillating systems.

potential of nerve cells, brain waves, heartbeat, peristaltic motion in the digestive tract, human biorhythms, etc. If such self-oscillation could be achieved for gels, possibilities would emerge for new biomimetic intelligent materials that exhibit autonomous rhythmical motion.

In this paper, a new design concept for polymer gels which exhibit spontaneous and autonomous periodic swelling–deswelling changes under constant conditions without on–off switching of external stimuli will be introduced (Figure 1). In the materials design, nonlinear dynamics of chemical reactions and characteristics of gels as open systems play an important role.

2. Design of Self-Oscillating Gel

2.1 Oscillating Chemical Reaction: The Belousov–Zhabotinsky Reaction. The mechanical oscillation of the gel is produced via an oscillating chemical reaction, called the Belousov–Zhabotinsky (BZ) reaction.[9–11] The BZ reaction has a cyclic reaction network similar to the TCA cycle which is a metabolic reaction in living systems. The BZ reaction is well known for exhibiting temporal and spatial oscillating phenomena with periodic redox changes of the catalysts in a closed solution. The overall process is the oxidation of an organic substrate such as citric or malonic acid (MA) by an oxidizing agent (bromate) in the presence of a metal catalyst under acidic conditiona. Metal ions or metal complexes with high redox potentials (1.0–1.4 V/SHE), such as cerium ion, ferroin, or ruthenium tris(2,2′-bipyridine) ($Ru(bpy)_3^{2+}$) are widely used as catalysts. In the course of the reaction, the catalyst ion periodically changes its charge number to oscillate between the oxidized and reduced states for several hours as long as the substrate exists. When the solution is homogeneously stirred, the color of the solution periodically changes, like a neon sign, based on the redox changes of the metal catalyst. When the solution is placed as a thin film in stationary conditions, concentric or spiral wave patterns develop in the solution. The wave of oxidized state propagating in the medium at a constant speed is called a "chemical wave." The significance of the BZ reaction has been recognized as a chemical model for understanding some aspects of biological phenomena, such as glycolytic oscillations or biorhythms,[12] cardiac fibrillation,[13] self-organization of amoeba cells,[14] pattern formation on animal skin,[15–17] visual pattern processing on retina,[18] etc.

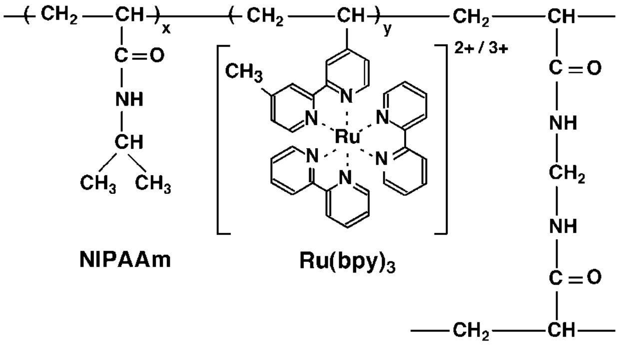

Figure 2. Chemical structure of poly(NIPAAm-*co*-Ru-$(bpy)_3^{2+}$) gel.

2.2 Preparation of Poly(NIPAAm-*co*-$Ru(bpy)_3^{2+}$) Gel Undergoing Redox Changes. We attempted to convert the chemical oscillation of the BZ reaction to the mechanical changes of gels and generate an autonomic swelling–deswelling oscillation under nonoscillatory outer conditions. A copolymer gel which consists of *N*-isopropylacrylamide (NIPAAm) and $Ru(bpy)_3^{2+}$ was prepared. $Ru(bpy)_3^{2+}$, acting as a catalyst for the BZ reaction, is pendent to the polymer chains of NIPAAm (Figure 2). It is well known that homopolymer gels of NIPAAm have thermosensitivity and undergo an abrupt volume-collapse (phase transition) when heated at around 32 °C. The poly(NIPAAm-*co*-$Ru(bpy)_3^{2+}$) gel has a phase-transition temperature because of themosensitive constituent NIPAAm. The oxidation of the $Ru(bpy)_3^{2+}$ moiety caused not only an increase in the swelling degree of the gel, but also a rise in the transition temperature (Figure 3). These characteristics may be interpreted by considering an increase in hydrophilicity of the polymer chains due to the oxidation of Ru^{II} to Ru^{III} in the $Ru(bpy)_3$ moiety. As a result, it is expected that the gel undergoes a cyclic swelling–deswelling alteration when the $Ru(bpy)_3$ moiety is periodically oxidized and reduced under constant temperature. When the gel is immersed in an aqueous solution containing the substrate of the BZ reaction except for the catalyst, the substrates penetrates into the polymer network and the BZ reaction occurs in the gel. Consequently, periodical redox changes induced by the BZ reaction produce periodical swelling–deswelling changes of the gel (Figure 4).[19–21] The gel has the cyclic reaction network in itself to generate periodic mechanical energy from the chemical energy of the BZ reaction.

3. Swelling–Deswelling Oscillation of the Gel with Periodic Redox Changes

3.1 Self-Oscillation of the Miniature Bulk Gel. The miniature cubic poly(NIPAAm-*co*-Ru(bpy)$_3{}^{2+}$) gel (each length of about 0.5 mm) was immersed into an aqueous solution containing MA, sodium $NaBrO_3$, and HNO_3 at constant temperature (20 °C). This outer solution comprised the reactants of the BZ reaction, with the exception of the catalyst. Therefore, the redox oscillation does not take place in this solution. However, as it penetrates into the gel, the BZ reaction is induced within the gel by the Ru(bpy)$_3{}^{2+}$ copolymerized as a catalyst on the polymer chains. Under the reaction, the Ru(bpy)$_3{}^{2+}$ in the gel network periodically changes between reduced and oxidized states. In miniature gels sufficiently smaller than the wavelength of the chemical wave (typically several mm), the redox change of ruthenium catalyst can be regarded to occur homogeneously without pattern formation.[22] Figure 5 shows the observed oscillating behavior under a microscope. Color changes of the gel accompanied by redox oscillations (orange: reduced state, light green: the oxidized state) were converted to 8-bit grayscale changes (dark: reduced, light: oxidized) by image processing. Due to the redox oscillation of the immobilized Ru(bpy)$_3{}^{2+}$, mechanical swelling–deswelling oscillation of the gel autonomously occurs with the same period as for the redox oscillation. The volume change is isotropic and the gel beats as a whole, like a heart muscle cell. The chemical and mechanical oscillations are synchronized without a phase difference (i.e., the gel exhibits swelling during the oxidized state and deswelling during the reduced state).

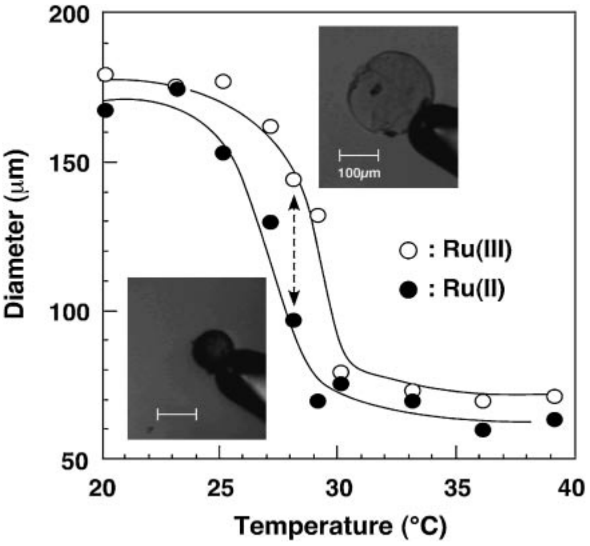

Figure 3. Temperature dependence of diameter for poly(NIPAAm-*co*-Ru(bpy)$_3{}^{2+}$) gel particles under different conditions of reduced Ru^{II} state (in Ce^{III} solution) and oxidized Ru^{III} state (in Ce^{IV} solution).

3.2 Control of Oscillation Period and Amplitude. In order to enhance the amplitude of swelling–deswelling oscillations of the gel, control of the period and amplitude of the re-

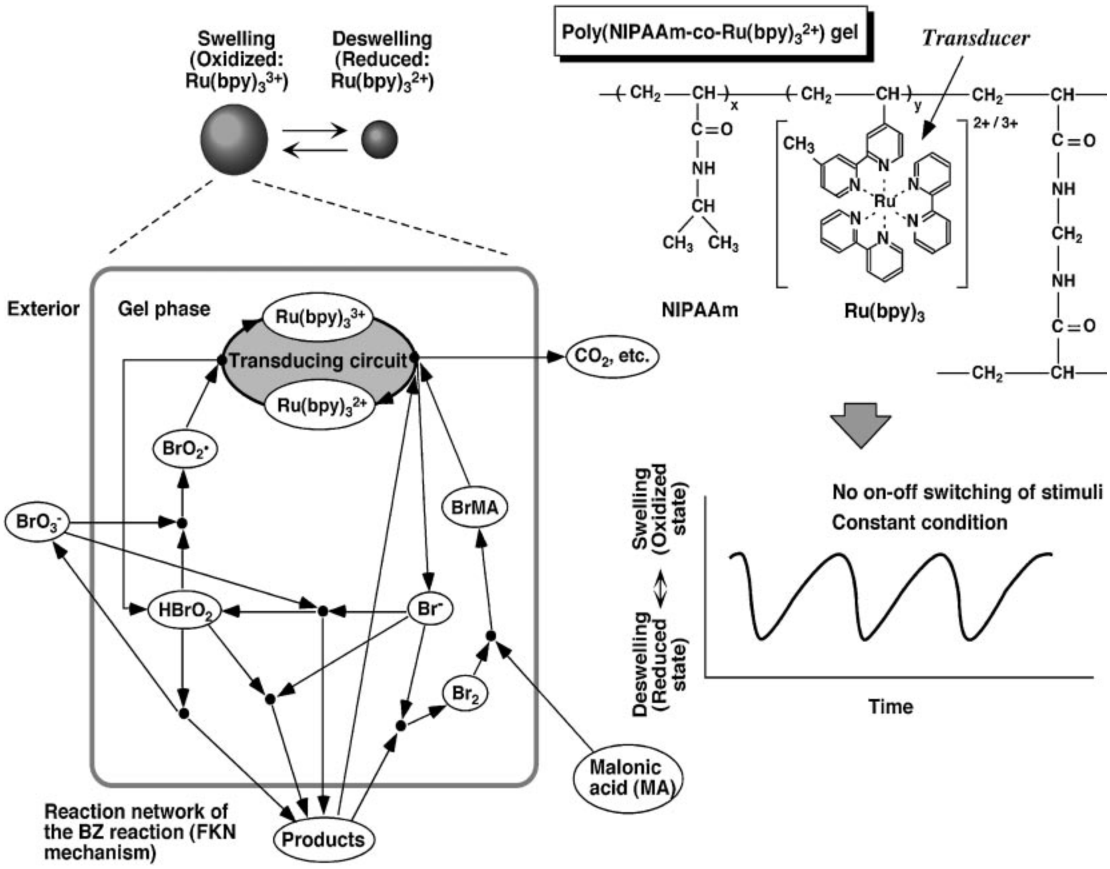

Figure 4. Mechanism of self-oscillation for poly(NIPAAm-*co*-Ru(bpy)$_3{}^{2+}$) gel coupled with the Belousov–Zhabotinsky reaction.

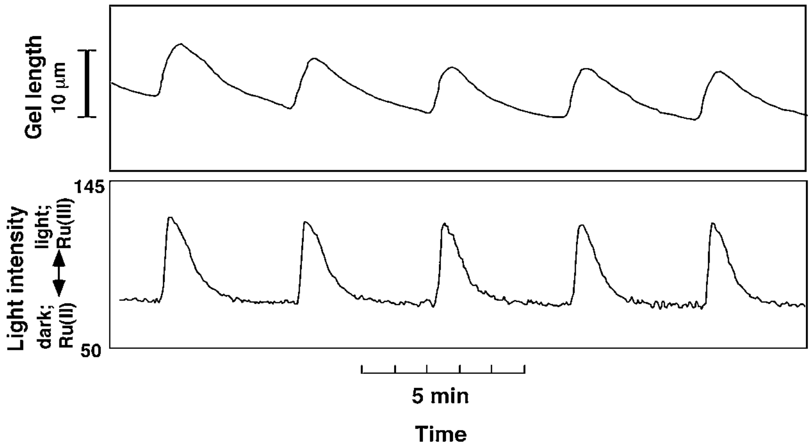

Figure 5. Periodic redox changes of the miniature cubic poly(NIPAAm-*co*-Ru(bpy)$_3{}^{2+}$) gel (lower) and the swelling–deswelling oscillation (upper) at 20 °C. Transmitted light intensity is expressed as an 8-bit grayscale value. Outer solution: [MA] = 62.5 mM; [NaBrO$_3$] = 84 mM; and [HNO$_3$] = 0.6 M.

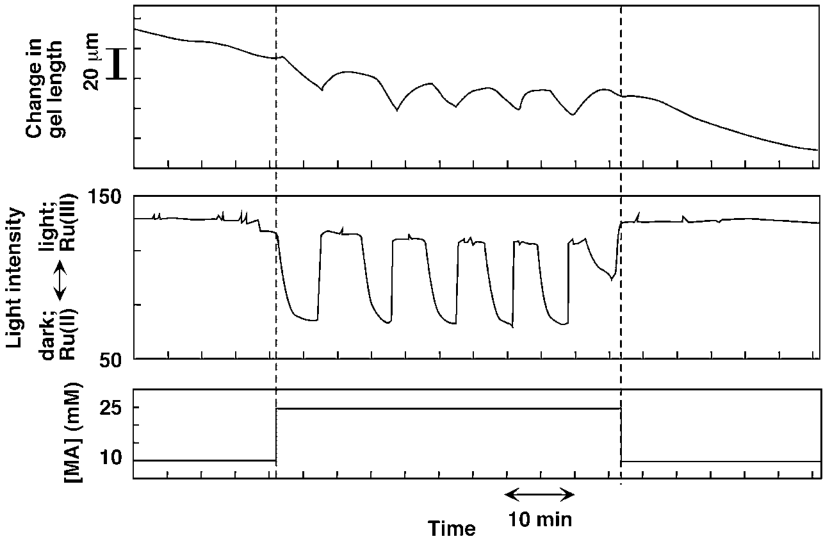

Figure 6. Change in oscillating behavior of the gel in response to the stepwise concentration changes of MA between 10 and 25 mM (others: [NaBrO$_3$] = 84 mM and [HNO$_3$] = 0.3 M, 20 °C).

dox oscillation was attempted by varying the initial concentration of substrates. It is a general tendency that the oscillation period increases with a decrease in concentration of substrates. The variation in chemical oscillation leads to a change in the swelling–deswelling oscillation: i.e., the swelling–deswelling amplitude (the change in gel length, Δd) increases with an increase in the period and amplitude of the redox changes. Empirically, the relation between Δd [μm] and the substrate concentrations was expressed as:

$$\Delta d = 2.38[\mathrm{MA}]^{0.392}[\mathrm{NaBrO_3}]^{0.059}[\mathrm{HNO_3}]^{0.764} \qquad (1)$$

As a result, it is apparent that the swelling–deswelling amplitude of the gel is controllable by changing the initial concentration of substrates. So far, a swelling–deswelling amplitude with ca. 20% of the initial gel size has been obtained as a maximum value. When the amplitude of swelling–deswelling oscillation increased, the waveform of redox changes deformed to a rectangular shape with a plateau period.[22] From this result, it is supposed that not only energy transformation from chemical to mechanical change, but also a feedback mechanism from mechanical to chemical change acts in the synchronization process.

3.3 On–Off Regulation of Self-Beating Motion. As an inherent behavior of the BZ reaction, the abrupt transition from steady state (non-oscillating state) to oscillating state occurs with a change in controlling parameter such as chemical composition, etc. This change is termed "bifurcation." Considering this characteristic, it is expected that the rhythmical motion of the gel can be controlled by changing substrate concentration during the oscillation. For example, if the [MA] is switched between the concentration regions of steady state and oscillating state, on–off control of the beating would be possible.[23] Figure 6 shows the oscillating behavior of the gel when a stepwise change in [MA] was repeated between lower concentration (10 mM) in steady state and higher concentration (25 mM) in oscillating state. At [MA] = 10 mM, the redox oscillation does not occur and consequently the gel exhibited no swelling–deswellng changes. Then, the concentration was

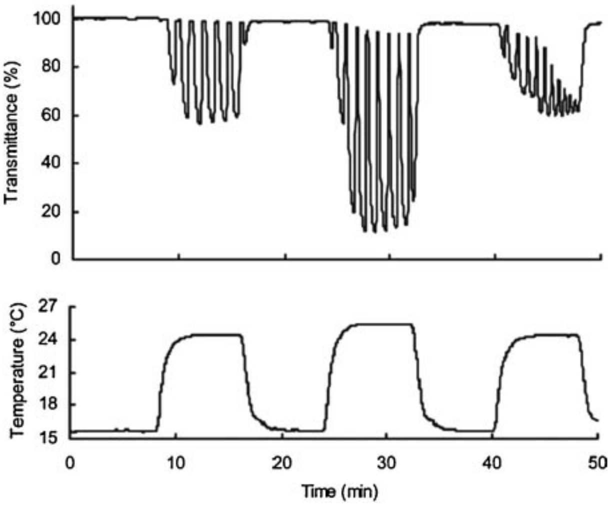

Figure 7. Oscillating profiles of optical transmittance for poly(NIPAAm-*co*-Ru(bpy)$_3$-*co*-AAc) solution ([MA] = 0.1 M, [NaBrO$_3$] = 0.2 M, and [HNO$_3$] = 0.3 M) under the condition that temperature was changed stepwise.

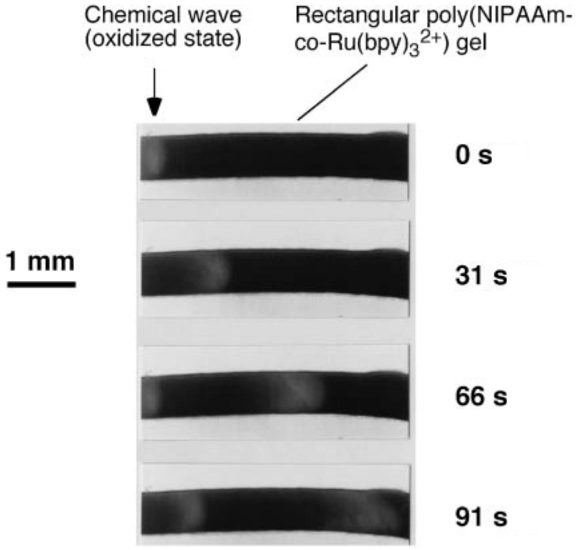

Figure 8. Propagation of chemical wave in rectangular poly(NIPAAm-*co*-Ru(bpy)$_3$$^{2+}$) gel.

quickly increased to 25 mM. Immediately after increasing concentration, the gel started self-beating. The beating stopped again as soon as the concentration was decreased back to the initial value. In these ways, reversible on–off regulation of self-beating triggered by MA was successfully achieved. Since there are some organic acids which can be the substrate for the BZ reaction (e.g., citric acid), the same regulation of beating is possible by using those organic acids instead of MA. And also, as the gel has thermosensitivity due to the NIPAAm component, the beating rhythm can be also controlled by temperature (Figure 7).[24]

4. Self-Oscillating Behaviors with the Propagation of Chemical Wave

4.1 Peristaltic Motion of Rectangular Gels. Figure 8 shows a rectangular piece of gel (ca. 1 mm × 1 mm × 20 mm) which is immersed in an aqueous solution containing the three reactants of the BZ reaction. The chemical waves propagate in the gel at a constant speed in the direction of the gel length.[25–28] Considering the dark (Ru$^{\mathrm{II}}$) and light (Ru$^{\mathrm{III}}$) zones represent simply the shrunken and swollen parts respectively, the locally swollen and shrunken parts move with the chemical wave, like the peristaltic motion of living worms. The propagation of the chemical wave makes the free end of the gel move back and forth at a rate corresponding to the wave propagation speed. As a result, the total length of the gel periodically changes. It was demonstrated by mathematical model simulations that the change in the overall gel length is equivalent to that in the remainder of gel length devided by the wavelength, because the swelling and the deswelling cancel each other per one period of oscillations under steady oscillating conditions.[29,30]

We succeeded in measuring the oscillating force of cylindrical poly(NIPAAm-*co*-Ru(bpy)$_3$$^{2+}$) gel accompanied by the BZ reaction.[31,32] The measurements were made for three gels with different diameters, 0.65, 1.17, and 1.88 mm, at 15 °C. It was found that the amplitude of oscillatory tensile stress of the reacting cylindrical gel with a diameter of 0.65 mm is much higher than the stress theoretically expected from the Donnan osmotic pressure. The amplitude is explained by an oscillatory change of the interaction parameter, χ, which might be induced by the hydration and dehydration of the chain due to the oscillatory charge density on the polymer chain. The oscillation behavior of the BZ reaction is found to be strongly dependent on the diameter of the gel. The staying period in the oxidative state and the period of the oscillation increase with a decrease in the diameter of the cylindrical gel.

And also, it was reported that the structural color behavior of a periodic ordered mesoporous gel synchronized with the BZ reaction.[33] We prepared a periodically ordered mesoporous gel which reveals "structural color" depending on its swelling ratio. To obtain the gel, we used as a template the closest-packing colloidal crystal composed of silica sphere particles 210 nm in diameter. The structural colored concentric rings which were spatiotemporally spread out on the porous gel were observed during the BZ reaction. The color tone of the structural color, which is determined by the swelling ratio of the gel, periodically changed. This is the first evidence that a self-sustaining peristaltic motion occurs on the surface of a gel.

4.2 Control of Chemical Wavelength by Laser Irradiation to Pacemaker Site. It is well known that the period of oscillation is affected by light illumination for the Ru(bpy)$_3$$^{2+}$-catalysed BZ reaction. The excited state of the catalyst (Ru(bpy)$_3$$^{2+*}$) causes a new reaction process: production of activator (reaction (R1)), or production of inhibitor (reaction (R2)), which depends on the solute compositions.[34]

$$\begin{aligned}&\mathrm{Ru(bpy)_3}^{2+*} + \mathrm{Ru(bpy)_3}^{2+} + \mathrm{BrO_3}^{-} + 3\mathrm{H}^{+}\\&\qquad \rightarrow \mathrm{HBrO_2} + 2\mathrm{Ru(bpy)_3}^{3+} + \mathrm{H_2O} \quad (\mathrm{R1})\\&\mathrm{Ru(bpy)_3}^{2+*} + \mathrm{BrMA} + \mathrm{H}^{+}\\&\qquad \rightarrow \mathrm{Br}^{-} + \mathrm{Ru(bpy)_3}^{3+} + \text{products} \quad (\mathrm{R2})\end{aligned} \tag{2}$$

Therefore, (i) we can intentionally make a pacemaker with a desired period (or wavelength) by local illumination by laser beam of the gel, or (ii) we can change the period (or wave-

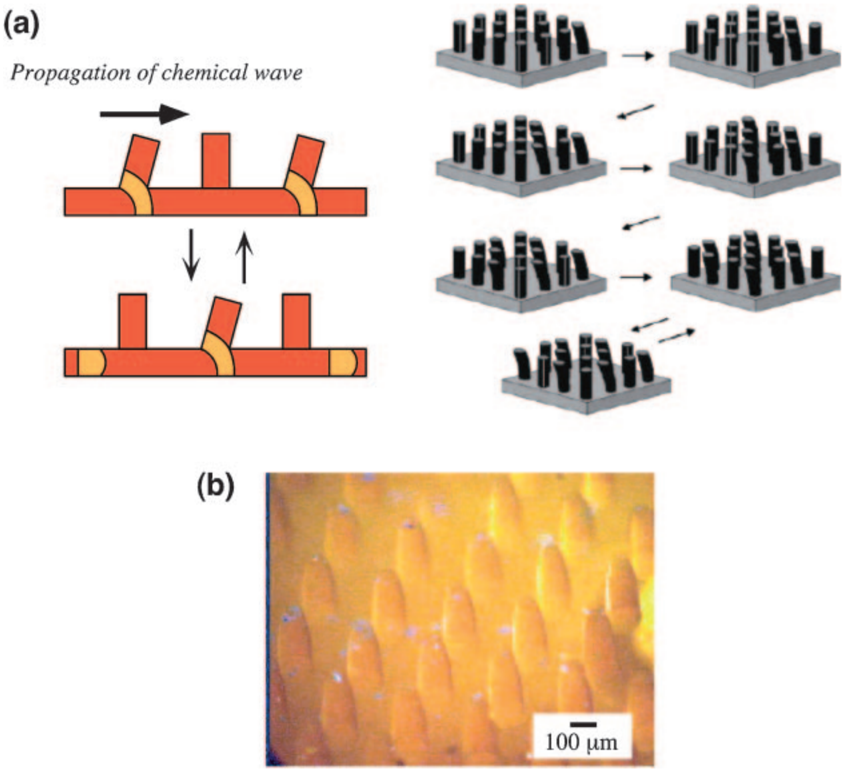

Figure 9. (a) Concept of ciliary motion actuator using self-oscillating gel and (b) the micro projection structure array on the gel surface fabricated by X-ray lithography.

length) by local illumination of a pacemaker which already exists in the gel.

In a rectangular gel, the corner often becomes a pacemaker from which chemical waves start to propagate. Therefore, the self-oscillating behaviors of the gel can be controlled by irradiating laser light locally to the pacemaker site of gels. The effect of laser irradiation on the pacemaker was investigated under the condition that photo-illumination produces activator.[35] The pacemaker size was altered by changing the diameter of irradiated region on the gel through a pinhole on the light path. It was found that the wavelength of traveling waves in the gel decreased as the size of the pacemaker increased. The results were in good agreement with a theoretical model simulation.[36] This result means that we can control the macroscopic swelling–deswelling behavior of the gel by local perturbation, i.e., a small signal can be amplified to macroscopic change.

5. Design of Biomimetic Microactuator Using Self-Oscillating Gel

5.1 Microfabrication of the Gel by Photolithography. Recently, microfabrication technologies such as photolithography have also been attempted for preparation of microgels. Since any shape of gel can be created by these methods, application as a new manufacturing method for soft microactuators, microgel valves, gel displays, etc. is a possibility. Microfabrication of self-oscillating gel has also been attempted by photolithography for application to such micro-devices.[37,38]

5.2 Ciliary Motion Actuator Using Self-Oscillating Gel. One of the promising fields of the MEMS is micro actuator array or distributed actuator systems. The actuators, which have a very simple actuation motion such as up and down motion, are arranged in an array form. If their motions are random, no work is extracted from this array. However, by controlling them to operate in a certain order, they can generate work as a system. A typical example of this kind of actuation array is a ciliary motion micro actuator array. There have been many reports of this. Although various actuation principles have been proposed, all the previous work is based on the concept that the motion of actuators is controlled by external signals. If a self-oscillating gel plate with a micro projection structure array on top were realized, it would be expected that the chemical wave propagation would create dynamic rhythmic motion of the structure array (Figure 9a). This proposed structure could exhibit spontaneous dynamic propagating oscillation producing a ciliary motion array.

A gel plate with micro projection array was fabricated by molding.[39,40] First, moving mask deep-X-ray lithography was utilized to fabricate a PMMA plate with a truncated conical shape microstructure array. This step was followed by evaporation of a Au seed layer and subsequent electroplating of nickel to form the metal mold structure. Then, a PDMS mold structure was duplicated from the Ni structure and utilized for gel molding. The formation of gel was carried out by vacuum injection molding. A structure with a height of 300 μm and bottom diameter of 100 μm was successfully fabricated by the described process (Figure 9b). The propagation of chemical reaction wave and dynamic rhythmic motion of the micro projection array were confirmed by chemical wave observation and displacement measurements. Figure 10 shows the measured lateral and vertical movements and the motion trajectory of the projection top. Motion of the top with 5 μm range in both lateral and vertical directions, and elliptical motion of the projection top were observed.

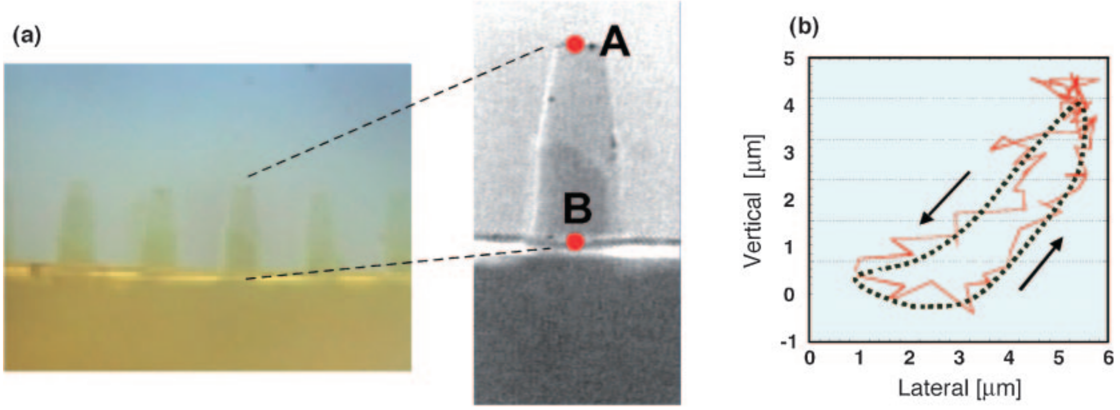

Figure 10. (a) Cross-sectional view of the micro projection and (b) measured motion of the projection top.

The feasibility of the new concept of the ciliary motion actuator made of self-oscillating polymer gel was successfully confirmed. The actuator may serve as a micro-conveyer to transport micro- or nano-particles on the surface. And we are trying to develop a chemical robot, which is unlike a conventional electrically powered robot, by coupling with a PDMS membrane.[41]

5.3 Self-Walking Gel. Further, we successfully developed a novel biomimetic walking-gel actuator made of self-oscillating gel.[42,43] To produce directional movement of gel, asymmetrical swelling–deswelling is desired. For these purposes, as a third component, hydrophilic 2-acrylamido-2-methylpropanesulfonic acid (AMPS) was copolymerized into the polymer to lubricate the gel and to cause anisotropic contraction. During polymerization, the monomer solution faces two different surfaces of plates; a hydrophilic glass surface and a hydrophobic Teflon surface. Since $Ru(bpy)_3^{2+}$ monomer is hydrophobic, it easily migrates to the Teflon surface side. As a result, a non-uniform distribution along the height is formed by the components, and the resulting gel has gradient distribution for the content of each component in the polymer network. At the surface side where the content of hydrophilic AMPS is higher, the swelling ratio of the gel membrane in water becomes larger than that at the opposite side in the same gel where the content of hydrophobic $Ru(bpy)_3^{2+}$ is higher. Consequently, in water, the gel strip always bends in the direction of the surface which was facing the Teflon plate during polymerization.

In order to convert the bending and stretching changes to one-directional motion, we employed a ratchet mechanism. A ratchet base with an asymmetrical surface structure was fabricated from an acrylic sheet. On the ratchet base, the gel repeatedly bends and stretches autonomously resulting in the forward motion of the gel, while sliding backwards is prevented by the teeth of the ratchet. Figure 11 shows successive profiles of the "self-walking" motion of the gel like a looper in the BZ substrate solution under constant temperature. The period of chemical oscillation was approximately 112 s, and the walking velocity of the gel actuator was approximately 170 µm min^{-1}. Since the oscillating period and the propagating velocity of chemical wave change with concentration of substrates in the outer solution, the walking velocity of the gel can be controlled.

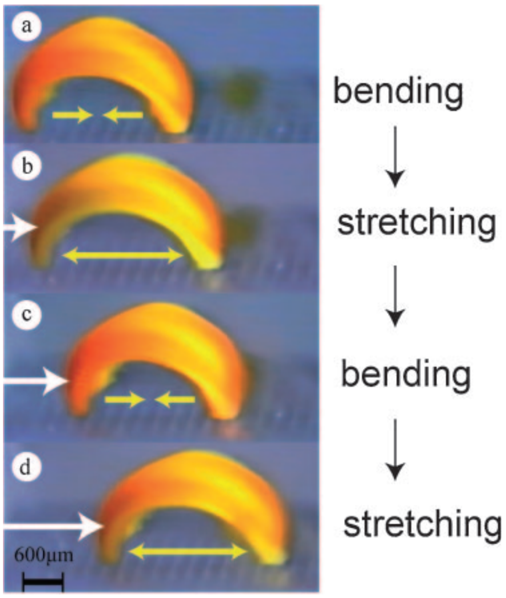

Figure 11. Time course of self-walking motion of the gel actuator. During stretching, the front edge can slide forward on the base, but the rear edge is prevented from sliding backwards. Oppositely, during bending, the front edge is prevented from sliding backwards while the rear edge can slide forward. This action is repeated, and as a result, the gel walks forward (the walking velocity: 170 µm min^{-1}). Outer solution: $[MA] = 62.5$ mM, $[NaBrO_3] = 84$ mM, and $[HNO_3] = 0.894$ M, 18 °C.

6. Self-Oscillating Polymer Chains and Gel Particles as "Nano-Oscillator"

6.1 Self-Oscillation of Polymer Chains with Rhythmical Soluble–Insoluble Changes. In self-oscillating gel, redox changes of $Ru(bpy)_3^{2+}$ catalyst are converted to conformational changes of polymer chain by polymerization. The conformational changes are amplified to macroscopic swelling–deswelling changes of the polymer network by crosslinking. Further, when the gel size is larger than chemical wavelength, the chemical wave propagates in the gel by coupling with diffusion. Then, peristaltic motion of the gel is created. In this manner, a hierarchical synchronization process exists in the self-

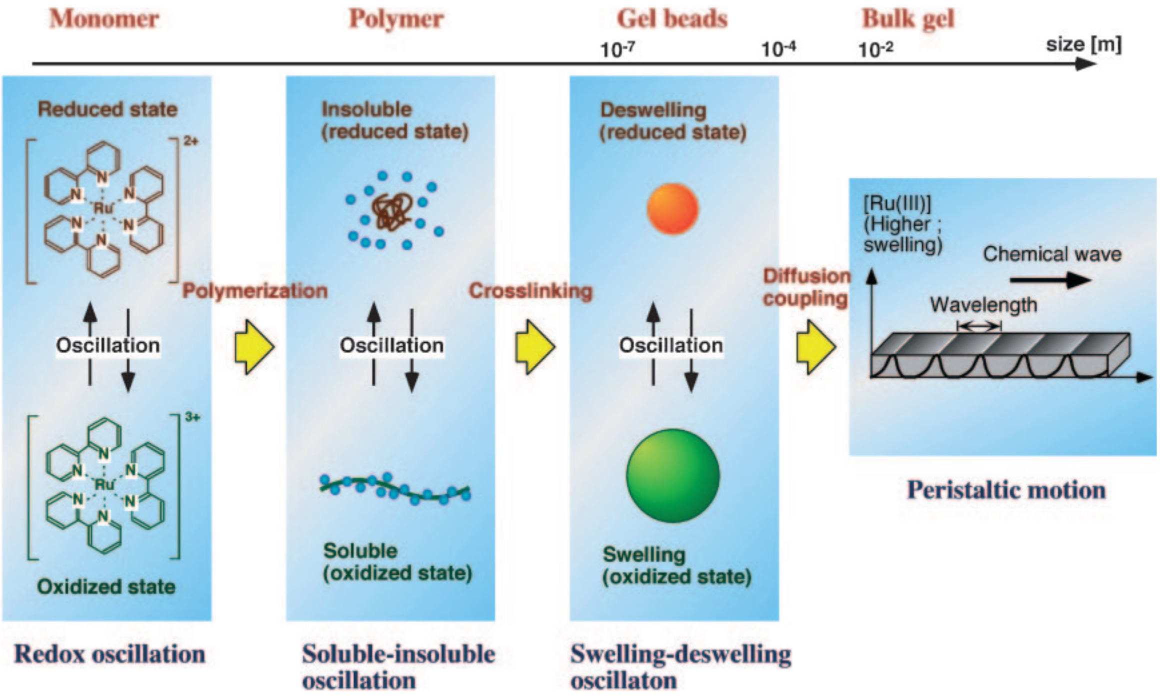

Figure 12. Hierarchical synchronization in self-oscillating gel.

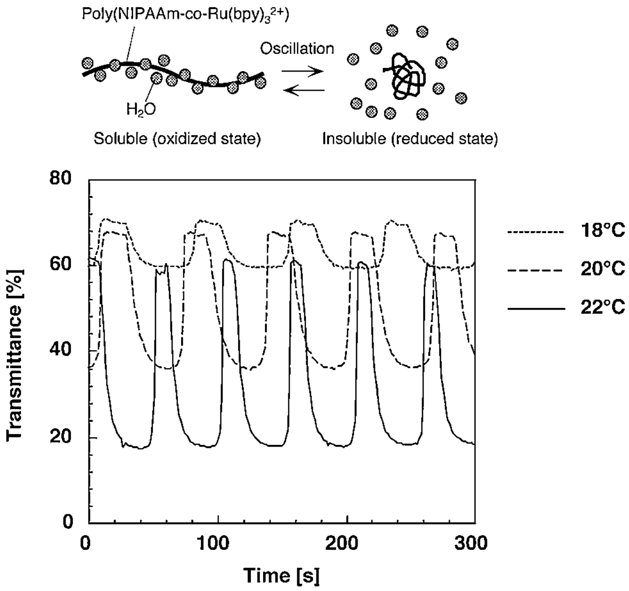

Figure 13. Oscillating profiles of optical transmittance for poly(NIPAAm-*co*-Ru(bpy)$_3^{2+}$) (Ru(bpy)$_3^{2+}$ = 5 wt %) solution at constant temperatures.

oscillating gel (Figure 12).

These periodic changes of linear and uncrosslinked polymer chains can be easily observed as cyclic transparent and opaque changes for the polymer solution with color changes due to the redox oscillation of the catalyst.[44] Figure 13 shows the oscillation profiles of transmittance for a polymer solution which consists of linear poly(NIPAAm-*co*-Ru(bpy)$_3^{2+}$), MA, NaBrO$_3$, and HNO$_3$ at constant temperatures. The wavelength (570 nm) at the isosbestic point of reduced and oxidized states was used to detect the optical transmittance changes based on soluble–insoluble changes of the polymer, not on the redox changes of the Ru(bpy)$_3$ moiety. Synchronized with the periodical changes between Ru$^{\mathrm{II}}$ and Ru$^{\mathrm{III}}$ states of the Ru(bpy)$_3^{2+}$ site, the polymer becomes hydrophobic and hydrophilic, and exhibits cyclic soluble–insoluble changes.

6.2 Self-Flocculating/Dispersing Oscillation of Microgels. We then prepared submicron-sized poly(NIPAAm-*co*-Ru(bpy)$_3^{2+}$) gel beads by surfactant-free aqueous precipitation polymerization, and analyzed the oscillating behaviors.[45–47] In both cases of the reduced Ru$^{\mathrm{II}}$ and the oxidized Ru$^{\mathrm{III}}$ states, the microgels were also flocculated when they were heated above the volume-phase transition temperature (VPTT) because the interparticle electrostatic repulsion is extremely low at a high salt concentration ($\approx$0.3 M) (Figure 14). The microgels in the oxidized Ru$^{\mathrm{III}}$ state became flocculated at slightly higher temperature (34 °C) than those in the reduced Ru$^{\mathrm{II}}$ state (32 °C). This temperature shift is due to an increase in hydrophilicity of the polymer by the increased charge density on the copolymer chains. As a result, microgels in the oxidized Ru$^{\mathrm{III}}$ state show larger hydrodynamic diameters at each temperature because PNIPAAm-based microgels show continuous change of diameter below the VPTT. These deviations of the hydrodynamic diameters and differences of the colloidal stabilities at the same temperature should lead to self-oscillation of the microgels.

Figure 15 shows the oscillation profiles of transmittance for the microgel dispersions. First, temperature dependence of the oscillation was checked (Figure 15a). At low temperatures (20–26.5 °C), on raising the temperature, the amplitude of the oscillation became bigger. The increase in the amplitude is due to the increased deviation of the hydrodynamic diameters between the Ru$^{\mathrm{II}}$ and Ru$^{\mathrm{III}}$ states as shown in Figure 14. Furthermore, a remarkable change in the waveforms was observed between 26.5 and 27 °C. Then, the amplitude of the

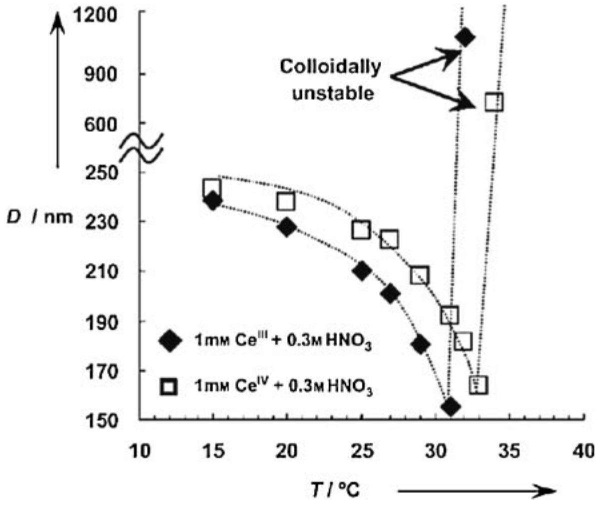

Figure 14. Deswelling curves for microgels under different conditions as measured by dynamic light scattering: the reduced Ru^{II} state in 1 mM Ce^{III} and 0.3 M HNO_3 solution (solid diamond), and the oxidized Ru^{III} state in 1 mM Ce^{IV} and 0.3 M HNO_3 solution (open square). Note that each dispersion concentration was 0.005 wt %.

oscillation dramatically decreased at higher temperature (27.5 °C), and finally periodical transmittance change could not be observed at 28 °C. Taking the results obtained in Figure 14 into consideration, the sudden change in the oscillation's waveforms should be related to the colloidal stability change between the Ru^{II} and Ru^{III} states. Here, the microgels should be flocculated due to lack of electrostatic repulsion at a high salt concentration when the microgels were deswollen. The temperature at which the colloidal stability change in Figure 14 is different from that of the remarkable change in the waveforms was observed, because colloidal stability is sensitive to ionic strength and dispersion concentration (being easier at higher concentrations and ionic strengths). In this system, because precise adjustment of ionic strength is very difficult, we checked a dependence of dispersion concentrations on oscillation at 27 °C where the remarkable change in the waveform was observed in Figure 15a. As can be seen clearly from Figure 15b, the waveforms of the oscillation are related to the dispersion concentrations: remarkable change in the waveforms was only observed at higher dispersion concentrations (>0.225 wt %). The self-oscillating property makes microgels attractive for future development as microgel assemblies, drug/gene controlled release, and optical and rheological applications.

7. Design of Nano-Actuating Systems

7.1 AFM Observation of Immobilized Self-Oscillating Polymer. Further, by grafting the polymers or arraying the gel beads on the surface of substrates, we have attempted to design self-oscillating surfaces as nano-conveyers to transport cells, etc. with the spontaneous propagation of chemical waves (Figure 16).

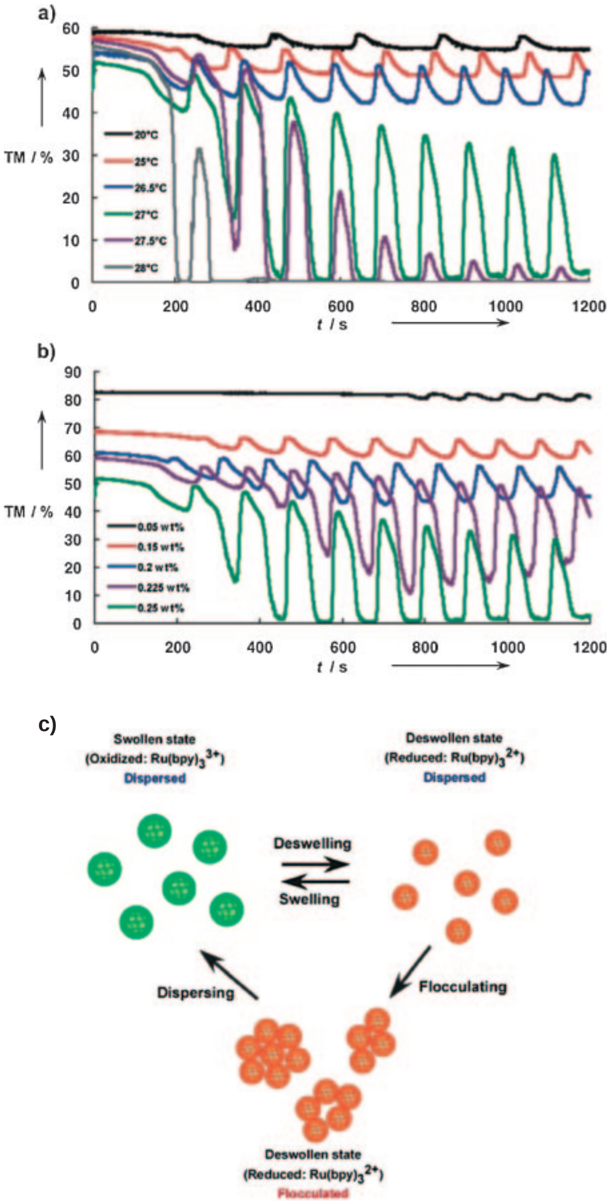

Figure 15. Self-oscillating profiles of optical transmittance for microgel dispersions. The microgels were dispersed in aqueous solutions containing MA (62.5 mM), $NaBrO_3$ (84 mM), and HNO_3 (0.3 M). Microgel concentration was 0.25 wt %. (a) Profiles measured at different temperatures. (b) Profiles measured at different microgel dispersion concentrations at 27 °C. (c) Self-oscillation of microgels around the phase-transition temperature.

The polymer was covalently immobilized on a surface and self-oscillation was directly observed at a molecular level by scanning probe microscopy.[48] A self-oscillating polymer was synthesized using $Ru(bpy)_3$ monomer, NIPAAm and an *N*-succinimidyl group (NAS, a component for linking to the substrate). The synthesized copolymer was immobilized on an aminosilane-coupled glass plate. The immobilized copolymer was measured by SPM operating in tapping mode. While no oscillation was observed in pure water, nano-scale oscillation was observed in an aqueous solution of the BZ reaction which consisted of malonic acid, $NaBrO_3$, and HNO_3 (Figure 17). The amplitude was about 10–15 nm and the period was about 70 s, although some irregular behavior was observed. Although no stirring could lead to the observed irregularity, the oscillation was reproducibly observed.

The amplitude of oscillation of the immobilized polymer (about 10–15 nm) was less than that in solution, as observed by DLS (23.9 and 59.6 nm). This smaller amplitude may be because the structure of the immobilized polymer was a loop-train-tail: the moving regions were shorter than that of the soluble polymer, as illustrated in Figure 17. In addition, the oscillation amplitude may have been suppressed due to the force applied by the weight of the cantilever, although the effect was not quantitatively evaluated. The amplitude and frequency were controlled by the concentration of reactant, as observed in the solution. Here, nano-scale molecular self-oscillation was observed for the first time. The oscillation polymer chain may be used as a component of a nano-clock or nano-machine.

7.2 Fabrication of Microgel Beads Monolayer. As discussed in the previous section, we have been interested in the construction of nano-conveyers by functionalizing surfaces with self-oscillating gels or polymer beads. For this purpose, a fabrication method for organized monolayers of microgel beads was investigated.[49] A 2D close-packed array of thermosensitive microgel beads was prepared by double template polymerization. First, a 2D colloidal crystal of silica beads with 10 μm diameter was obtained by solvent evaporation. This monolayer of colloidal crystal can serve as the first template for preparation of macroporous polystyrene. The macroporous polystyrene trapping the crystalline order can be used as a negative template for fabricating a gel bead array (Figure 18). Functional surfaces using thermosensitive PNIPAAm gel beads were fabricated by the double template polymerization. It was observed that topography of the surface changed with temperature. The fabrication method demonstrated here was so versatile that any kind of gel beads could be obtained. This method may be a key technology to create new functional surface.

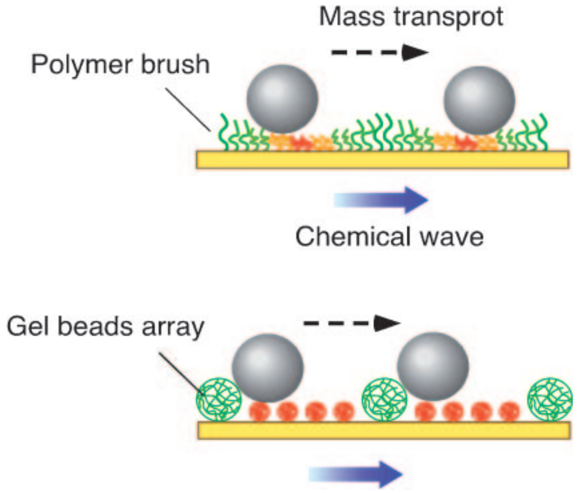

Figure 16. Concept of functional surface (nano-conveyer) using self-oscillating polymer and gel beads.

8. Attempts toward Self-Oscillation under Biological Conditions

8.1 Self-Oscillation of Polymer Chains under Acid-Free Conditions. So far, we had succeeded in developing a novel self-oscillating polymer (or gel) by utilizing the BZ reaction. However, the operating conditions for the self-oscillation are limited to conditions under which the BZ reaction occurs. For practical applications as functional bio- or biomimetic materials, it is necessary to design a self-oscillating polymer which acts under biological environments.

To cause self-oscillation of polymer systems under physiological conditions, BZ substrates other than organic ones, such as malonic acid and citric acid, must be built into the polymer system itself. Therefore, we took the next step, namely, to design novel self-oscillating polymer chains with incorporated pH-control sites, that is, novel polymer chains which exhibit rhythmic oscillations in aqueous solutions containing only the two BZ substrates, without using acid as an added agent.

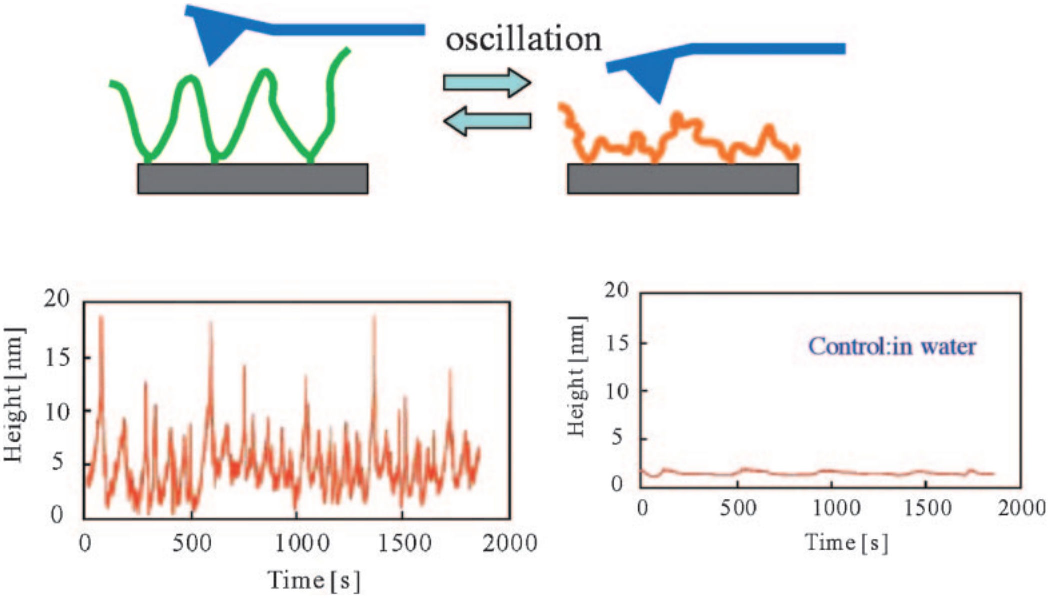

Figure 17. Self-oscillating behavior of immobilized polymer in BZ substrate solution ([MA] = 0.1 M, [$NaBrO_3$] = 0.3 M, and [HNO_3] = 0.3 M) measured by AFM.

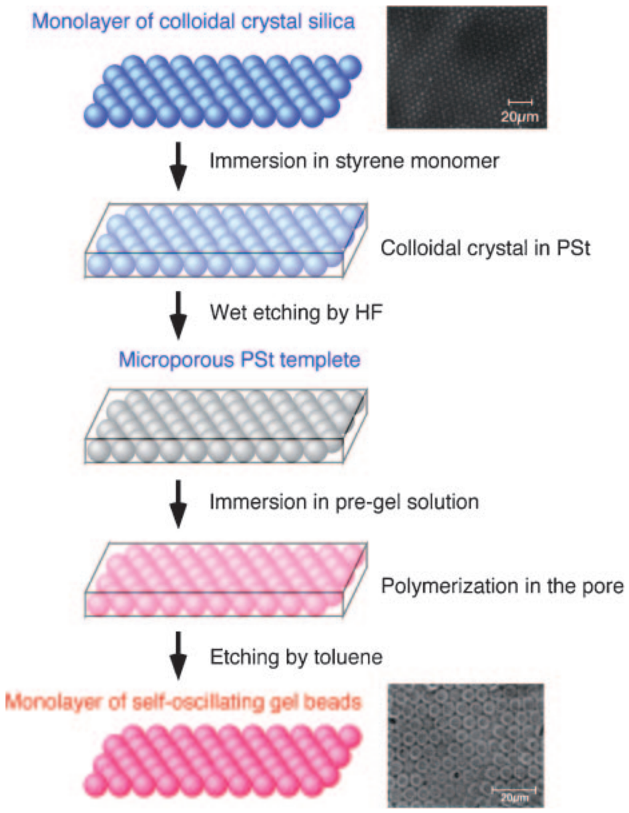

Figure 18. Preparation of self-oscillating gel bead monolayer by two-step template polymerization.

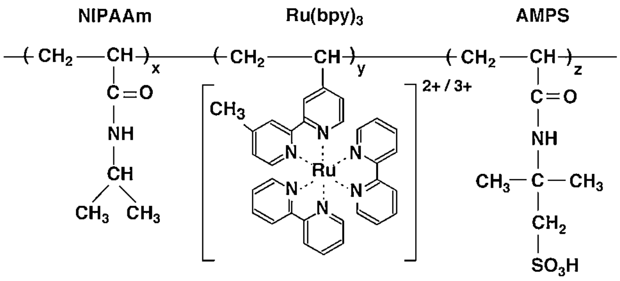

Figure 19. Chemical structure of poly(NIPAAm-*co*-$Ru(bpy)_3^{2+}$-*co*-AMPS).

For this purpose, 2-acrylamido-2-methylpropanesulfonic acid (AMPS) was incorporated into the poly(NIPAAm-*co*-$Ru(bpy)_3^{2+}$) chain as the pH-control site (Figure 19).[50,51]

Figure 20 shows the self-oscillating transmittance change for the solutions of poly(NIPAAm-*co*-$Ru(bpy)_3^{2+}$-*co*-AMPS) (20:10:70 wt % in feed) at three constant temperatures (18, 21, and 24 °C). Under acid-free conditions and in the presence of only two BZ substrates (malonic acid and sodium bromate), we succeeded in causing soluble–insoluble self-oscillation of a polymer solution. Oscillating behaviors were remarkably influenced by the temperature, polymer concentration, and composition.

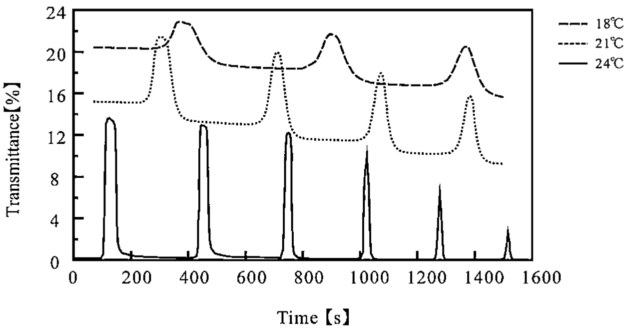

Figure 20. Oscillating profiles of optical transmittance for poly(NIPAAm-*co*-$Ru(bpy)_3^{2+}$-*co*-AMPS) solutions (polymer concentration = 2.0 wt %) at several constant temperatures.

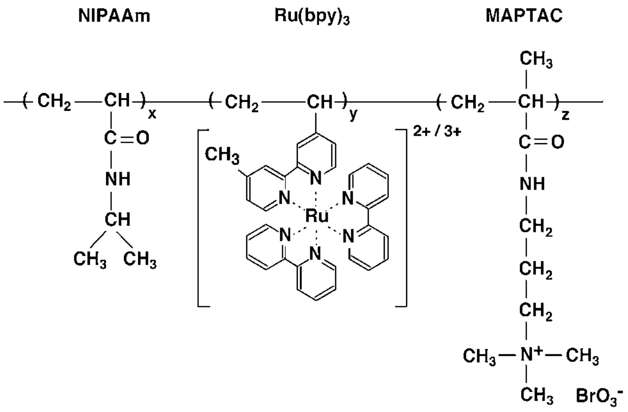

Figure 21. Chemical structure of poly(NIPAAm-*co*-$Ru(bpy)_3^{2+}$-*co*-MAPTAC).

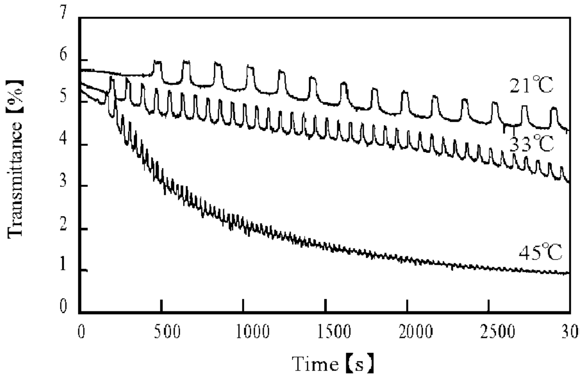

Figure 22. Oscillating profiles of optical transmittance for poly(NIPAAm-*co*-$Ru(bpy)_3^{2+}$-*co*-MAPTAC) solutions (5.0 wt %) at several constant temperatures ([MA] = 0.1 M and [H_2SO_4] = 0.3 M).

8.2 Self-Oscillation under Oxidant-Free Conditions. As the next step, we attempted to introduce the oxidizing agent into the polymer. Methacrylamidopropyltrimethylammonium chloride (MAPTAC), with a positively charged group, was incorporated into the poly(NIPAAm-*co*-$Ru(bpy)_3^{2+}$) as a capture site for an anionic oxidizing agent (bromate ion) (Figure 21).[52] The bromate ion was introduced into the MAPTAC-containing polymer through ion exchange. Under the conditions in which only two BZ substrates (malonic acid and sulfuric acid) were present, soluble–insoluble self-oscillation of the polymer was observed (Figure 22).

In the self-oscillating polymer solution system induced by the BZ reaction, self-oscillation was achieved without addition of oxidizing agent by utilizing the MAPTAC-containing polymer which included sodium bromate as a counter ion. The self-oscillating behavior was controllable by temperature. The polymer has two advantages because of the higher LCST; one is self-oscillation around body temperature, and the other is oscillation for a longer time without intermolecular aggregation among the polymer chains in the reduced state. A step toward practical use of self-oscillating polymers under biological conditions as novel smart materials has been established. Further, we have synthesized a quarternary copolymer which includes both pH-control and oxidant-supplying sites in the poly(NIPAAm-*co*-Ru(bpy)$_3$$^{2+}$) chain at the same time. By using the polymer, self-oscillation under biological condition where only the organic acid (malonic acid) exists has been actually achieved (unpublished data).

9. Conclusion

As a material, gels have many unique characteristics which differ from other materials. Gels are not only soft materials which are wet and flexible like living body tissue, but also open materials which can exchange energy and substance with the external environment. Especially the latter characteristic is important, and it enables the design of intelligent gels with the combined functions of sensor, processor, and actuator. The dynamic behavior of gel is governed by cooperative motion of the polymer network. For this reason, the mechanism amplifying a minute external signal to macroscopic change through cooperation and synchronization of molecular interaction can be built into gels. The design concept of functional materials based on such a molecular synchronization has just started in the field of materials science and engineering, and polymer gels will become more important as a material which realizes the new concept. In that case, a living body serves as the best model, and it will be more important to design the materials from the standpoint of biomimetics and to clarify the molecular mechanism of the function.

As mentioned in this paper, novel functional gels have been constructed by designing biomimetic gels with self-oscillating function. The self-oscillating gel may be useful in a number of important applications such as pulse generators or chemical pacemakers, self-walking (auto-mobile) actuators or micropumps with autonomous beating or peristaltic motion, devices for signal transmission utilizing propagation of chemical waves, oscillatory drug release synchronized with cell cycles or human biorhythms, etc. Further studies on the control of oscillating behavior as well as practical applications are expected.

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