Biomimetic Gels

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Autonomous Intestine-Like Motion of Tubular Self-Oscillating Gel**

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Many kinds of mechanical devices for mass transport, such as pumps and conveyers, are driven by converting electric energy into mechanical energy. On the other hand, in biological transport systems, proteins, such as actin and myosin, convert chemical energy derived from ATP hydrolysis into mechanical energy to contract a muscle. In addition to the motion of a voluntary muscle, in an involuntary muscle, autonomous and periodic contraction of the muscle is used for macroscopic transport systems, such as circulation of blood by the heart and excretion of digested foods by the intestine.

There have been many studies on stimuli-responsive polymer gels that exhibit a reversible swelling–deswelling change in response to environmental changes, such as solvent composition, temperature, and change in pH value.[1–5] In contrast, we have developed a novel "self-oscillating" polymer gel that exhibits autonomous mechanical oscillation without an external control in a completely closed solution. For the design of the gel, we focused on the Belousov–Zhabotinsky (BZ) reaction, which exhibits temporal and spatiotemporal oscillating phenomena.[6,7] We attempted to convert the chemical oscillation of the BZ reaction into a mechanical change in gels and generate an autonomous swelling–deswelling oscillation under non-oscillatory outer conditions. A copolymer gel was prepared, consisting of *N*-isopropylacrylamide (NIPAAm) and ruthenium tris(2,2′-bipyridine) ($Ru(bpy)_3$), acting as a catalyst for the BZ reaction. When the poly(NIPAAm-*co*-$Ru(bpy)_3$) gel is immersed in the catalyst-free BZ solution (containing malonic acid, sodium bromate, and nitric acid), the reaction occurs in the gel by the catalytic function of the polymerized $Ru(bpy)_3$. The redox changes of the polymerized catalyst moiety ($[Ru(bpy)_3]^{2+} \rightleftarrows [Ru(bpy)_3]^{3+}$) change the volume phase transition temperature as well as the swelling ratio of the gel, because the hydrophilicity of the polymer chains increases in the oxidized Ru^{III} state and decreases in the reduced Ru^{II} state. As a result, the gel exhibits an autonomous swelling–deswelling oscillation, with the redox oscillation in the closed solution under constant conditions. Since our self-oscillating gel was first reported in 1996,[8] we have been systematically studying the self-oscillating polymer and gel, as well as their applications to biomimetic or smart materials.[9–15]

In the gel, a train of excited pulses of the oxidized state (i.e. "chemical waves") spontaneously evolves and propagates by a reaction–diffusion mechanism when the gel size is much larger than the wavelength of the chemical wave. In the case of a two-dimensional gel sheet, concentric or spiral waves can be observed. With the propagation of chemical waves, the self-oscillating gel exhibits peristaltic motion,[10–13] that is, the locally swollen (or shrunken) region corresponding to a locally oxidized (or reduced) state propagates in the gel, similar to the locomotion of a living worm. Such macroscopic swelling–deswelling oscillations may lead to the creation of novel biomimetic actuators.[14–16]

In this study, to construct autonomous mechanical pumping systems like an intestine (Figure 1), we fabricated the self-oscillating gel in a tubular shape. Three kinds of tubular self-oscillating gels that exhibit autonomous peristaltic motion were prepared. First, a tubular poly(NIPAAm-*co*-$Ru(bpy)_3$) gel adhering to the inner wall of a glass capillary was prepared and the periodic inner diameter changes during the BZ reaction were analyzed. Second, by removing the gel from the glass capillary, a tubular gel that can swell and deswell freely without a mechanical restraint was prepared. Third, a tubular gel with an interpenetrating network structure composed of self-oscillating and non-oscillating polymers was prepared. It was shown that these tubular self-oscillating gels exhibited various behaviors of peristaltic motions. In addition, it was demonstrated that an object was autonomously transported in the gel tube by the peristaltic pumping motion, similar to an intestine.

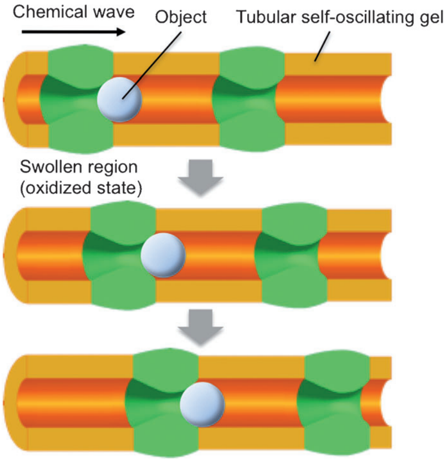

Figure 1. Schematic illustration of autonomous mass transport by peristaltic pumping of a tubular self-oscillating gel.

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A tubular poly(NIPAAm-*co*-Ru(bpy)$_3$) gel was prepared through photopolymerization by irradiating with UV light onto the pre-gel solution in a glass capillary while rotating it on its axis (see Supporting Information) and subsequent washing away of residual monomers. Figure 2 shows the peristaltic motion of the tubular self-oscillating gel, which remains adhered to the inner wall of a glass capillary. The inside of the gel tube is filled with the catalyst-free BZ solution, which is forced to flow slowly at a constant rate by using a syringe pump. The green and orange colors indicate the oxidized Ru^{III} and reduced Ru^{II} states of the gel, respectively. By way of the BZ reaction, a chemical wave propagated from right to left. The direction was the same as the direction of flow of the inner fluid. The gel layer at the oxidized region became thicker than that of the reduced region. The locally thick layer moved with the propagation of the chemical wave (see the movie in Supporting Information).

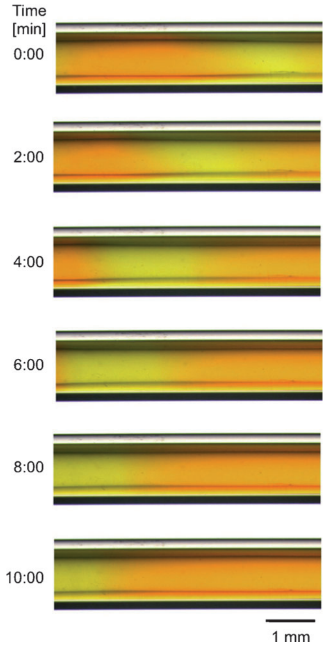

Figure 2. Time-course images of the peristaltic motion of the tubular poly(NIPAAm-*co*-Ru(bpy)$_3$) gel adhering to the inner wall of a glass capillary. Light green band moves from right to left, indicating thickening of the side walls.

To show this peristaltic behavior more clearly, a time-series image analysis was performed. Two spatiotemporal patterns were constructed by extracting one-line image along the *x* and *y* directions (Figure 3a; dashed lines) from each frame of the movie and lining it up sequentially with time (Figure 3b,c). Calculating from the slope of the stripes of the spatiotemporal pattern in Figure 3b, the wave velocity was estimated to be 0.42 mm min^{-1}. This rate is much slower than the flow rate of the catalyst-free BZ solution (4.77 mm min^{-1}). As shown in Figure 3c, the thickness of the gel layer changed only toward the inner surface because the outer side of the gel layer was fixed to the glass capillary. Figure 3d shows the oscillation profile of the signal intensity of green color along the dashed line in Figure 3c, which indicates periodic redox changes at a fixed point in the gel layer. The period of the redox changes was estimated to be 11.8 minutes. Figure 3e shows the change in the thickness of the gel layer at the fixed point, which can be obtained from Figure 3c. It is apparent that redox oscillation and swelling oscillation are synchronized, which means that the peristaltic motion of the tubular gel occurs with the propagation of the chemical wave.

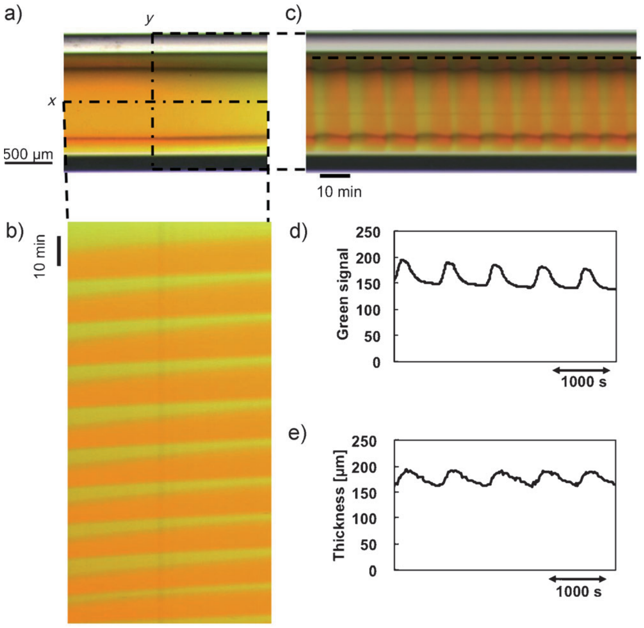

Figure 3. Time-series image analysis of the peristaltic motion of the tubular poly(NIPAAm-*co*-Ru(bpy)$_3$) gel shown in Figure 2. a) One frame image extracted from the movie. b) Spatiotemporal pattern constructed by lining up the dashed *x* line time sequentially. c) Spatiotemporal pattern constructed by lining up the dashed *y* line time sequentially. d) Redox changes at a fixed point in the gel layer, which is expressed as an intensity of the green signal along the dashed line in (c). e) Change in thickness of the gel layer at a fixed point, which is derived from (c).

Then, to obtain a free tubular gel, the glass capillary was dissolved using hydrofluoric acid. However, the tubular poly(NIPAAm-*co*-Ru(bpy)$_3$) gel obtained was fragile. To improve the mechanical strength of the gel as well as the swelling response, we added another component into the polymer network. In a previous study, we reported that it is effective to copolymerize 2-acrylamido-2′-methylpropanesulfonic acid (AMPS) with a poly(NIPAAm-*co*-Ru(bpy)$_3$) gel network to change the physical properties and generate a large-amplitude volume change during self-oscillation.[12] The poly(NIPAAm-*co*-Ru(bpy)$_3$-*co*-AMPS) gel had a micro-aggregated structure when the feed ratio of the AMPS was less than 5 mol % because of the effect of the poor solvent in the polymerization process. The micro-aggregated structure greatly improved the swelling–deswelling kinetics of the gel, and consequently, a larger swelling–deswelling amplitude was achieved, approximately ten-times larger than that of the gel with a homogeneous structure.

Based on this knowledge, we fabricated a tubular poly(NIPAAm-*co*-Ru(bpy)$_3$-*co*-AMPS) gel (Figure 4). Not only

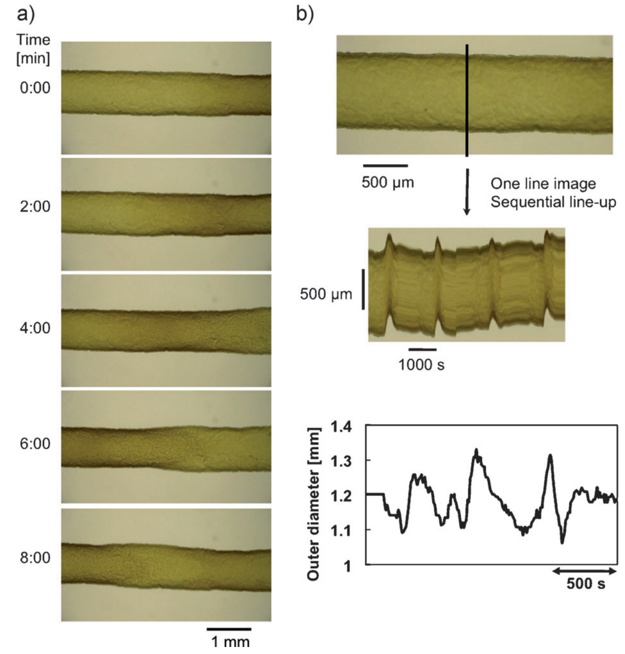

Figure 4. a) Time-course images of the peristaltic motion of the tubular poly(NIPAAm-*co*-Ru(bpy)$_3$-*co*-AMPS) gel. b) Spatiotemporal pattern and change in the outer diameter of the tubular gel at a fixed point.

was the gel opaque because of the micro-aggregated structure, but the gel tube was very thin because the UV light could not penetrate deep inside the capillary during photopolymerization. Once again the glass capillary was dissolved in hydrofluoric acid to obtain a free tubular gel. Figure 4 a shows the peristaltic motion of the tubular poly(NIPAAm-*co*-Ru(bpy)$_3$-*co*-AMPS) gel with the propagation of the chemical wave (here the wave propagates from left to right). In this case, the catalyst-free BZ solution is not forced to flow through the tube, which is different from the case of Figure 2. Instead, the gel is simply soaked in the solution. The gel exhibited peristaltic motion with a deformation of its outer side (see the movie in Supporting Information). Figure 4 b shows the spatiotemporal pattern and the change in the outer diameter of the gel. An approximately 20 % change in the outer diameter was observed. The wave velocity was 1.1 mm min^{-1} and the period was 12.4 minutes. The wave velocity increased relative to that of the two component polymer gel because the diffusivity of reaction intermediates in the gel increased because of the porous structure of the three component gel.

Changes in the outer diameter of the gel tube result from the reduced thickness of the gel layer. Therefore, the next challenge is to cause peristaltic motion only at the inner surface of the gel tube while maintaining a constant outer diameter. For this purpose, it would be desirable to make the polymer network non-oscillatory at the outer surface and oscillatory at the inner surface. To create such a structure, we introduced an interpenetrating polymer network (IPN) structure (or so-called double-network (DN) structure) into the tubular gel. That is, based on the tubular poly(NIPAAm-*co*-Ru(bpy)$_3$) gel, polyacrylamide (PAAm), a non-oscillating polymer network, was physically entangled mainly at the outer surface side. By employing the two-step photopolymerization method (see Supporting Information), the IPN gel was prepared. During photopolymerzation, the intensity of the UV light decays toward the inside of the pre-gel solution in a glass capillary. As a result, denser entanglement of the two polymer networks can be created mainly at the outer surface.

As mentioned before, the tubular poly(NIPAAm-*co*-Ru(bpy)$_3$) gel itself is fragile. By introducing the IPN structure, the mechanical properties can also be improved; it was reported by Gong et al. that DN gels have high strength and toughness.[17] The self-oscillating IPN gel we prepared was much tougher than the poly(NIPAAm-*co*-Ru(bpy)$_3$) gel. Interestingly, many cracks were observed in the gel as shown in Figure 5 a.

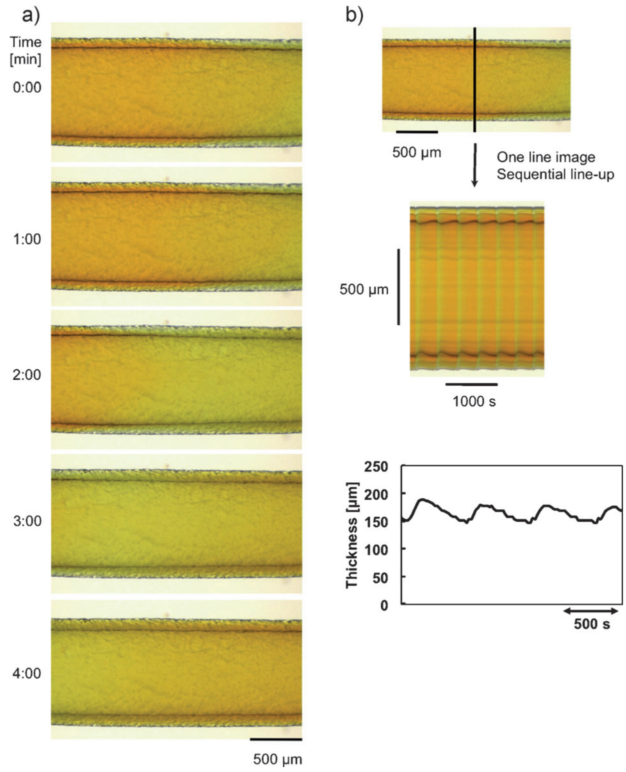

Figure 5. a) Time-course images of the peristaltic motion of the tubular IPN gel composed of poly(NIPAAm-*co*-Ru(bpy)$_3$) and PAAm networks. b) Spatiotemporal pattern and change in the thickness of the gel layer at a fixed point.

Figure 5 a shows the behavior of the peristaltic motion of the tubular IPN gel (with the chemical wave propagating from right to left). Similar to Figure 4, the catalyst-free BZ solution is not forced to flow through the tube. The gel is simply soaked in the solution. In contrast to Figure 4 a, a significant change in outer diameter was not observed (see the movie in Supporting Information). From the spatiotemporal pattern (Figure 5 b), it is clear that only the inner diameter changes while the outer diameter is kept almost constant. The wave velocity was 2.0 mm min^{-1} and the period was 7.4 minutes.

The faster wave velocity compared to the other gels may be due to the many cracks in the gel.

The BZ reaction usually generates CO_2 gas as a product while the reaction proceeds. In our experiments, the generation of a CO_2 bubble was observed inside a gel tube after a short time, and the bubble gradually grew bigger. Figure 6a shows the behavior of a CO_2 bubble which was generated in the tubular poly(NIPAAm-*co*-Ru(bpy)$_3$) gel adhering to the inner surface of a glass capillary, as in Figure 2. When the bubble became large enough to contact the inner surface of the gel layer, it started to move intermittently in the direction of chemical wave propagation with repeated deformation and restoration of the bubble (see the movie in Supporting Information). Figure 6b,c show the changes in the position and the velocity of the bubble, respectively. The velocity was calculated by determining the position with time. It is clear that a net movement of the bubble occurs by repeated backward and forward movements. In this case, the catalyst-free BZ solution is forced to flow at a constant rate by using a syringe pump, as mentioned in Figure 2. Considering the intermittent motion observed and comparing the rate of movement of the bubble with the flow rate of the solution, we conclude the bubble is transported by the peristaltic pumping of the gel, not by the convection of the flow of the inner fluid.

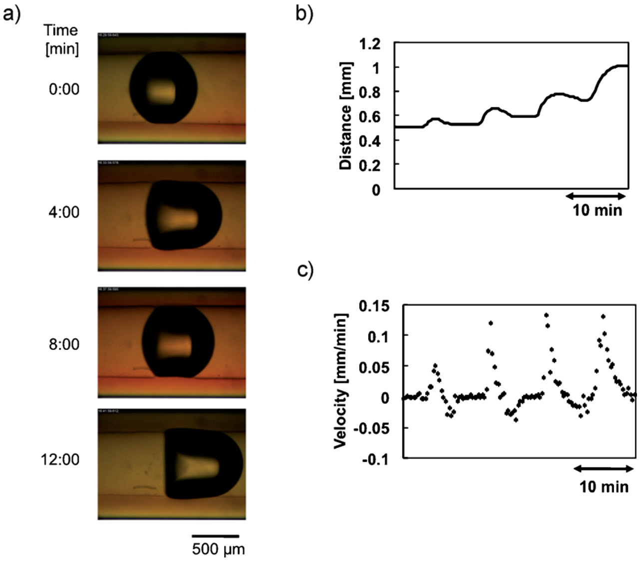

Figure 6. a) The autonomous transport of a CO_2 bubble in the gel tube by peristaltic pumping. b) Change in the position of the bubble. c) The velocity of the bubble.

When the chemical wave reaches the contact point, the bubble is squashed and deformed by the swelling of the gel layer at that point. Then the bubble is mechanically pushed forward by the peristaltic pumping mechanism. Because the catalyst-free BZ solution flows at a constant rate in the tube, an inner hydraulic pressure behind the bubble increases by a reduction of inner diameter of the tube. The increased pressure may also help to push the bubble forward. After the wave passes through, the gel layer deswells and the squashed bubble returns back to the initial round shape. Because of a decrease in pushing force and a negative pressure, the bubble moves backward slightly. After that, the movement of the bubble stops for a while, making the overall movement intermittent. By repeating this sequence of events, the bubble is transported in the gel tube.

In conclusion, tubular self-oscillating gels were fabricated by photopolymerization. Different types of peristaltic motion were demonstrated by preparing a tubular gel that adheres to an inner wall of a glass capillary, a tubular gel that can swell freely without mechanical restraint, and a tubular IPN gel consisting of self-oscillating and non-oscillating polymer networks. In the gel tube, it was observed that a gas bubble was autonomously transported. Mass transport by peristaltic pumping of the tubular self-oscillating gel was successfully demonstrated. Recently, controlled transport of small objects has become one of the hot topics in many areas of science and engineering including chemistry, physics, and biology. Small objects such as particles with self-propelled motion are beginning to be studied.[18] The autonomous transport by chemomechanical locomotion of the gel reported herein is based on a different principle from systems that have been reported to date. Potential applications including artificial intestines, and artificial digestive tracts can be envisioned. Furthermore, there is a possibility of autonomous flow of a fluid within the tube. At present only the BZ solution can be pumped, but other inner fluids could be pumped, without bubble formation, if the BZ substrates are fed from the outer surface of the gel tube. The pumping speeds could be controlled by, for example, changing reactant concentration, temperature, or improving diffusivity in the gel. We are also investigating an application of the self-oscillating tubular gels to a novel micropump for microfluidic systems.

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