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Review

Self-oscillating gel as novel biomimetic materials

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ABSTRACT

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 the polymer with an autonomous self-oscillating function by utilizing oscillating chemical reactions. So far, we succeeded in developing a novel self-oscillating polymer and gels by utilizing the oscillating reaction, called the Belousov–Zhabotinsky (BZ) reaction, which is recognized as a chemical model for understanding several autonomous phenomena in biological systems. The self-oscillating polymer is composed of poly(N-isopropylacrylamide) (PNIPAAm) network in which the catalyst for the BZ reaction is covalently immobilized. Under the coexistence of the reactants, 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 gels and the design of functional material systems using the polymer are summarized.

Contents

1. Introduction

Over about the last two or three decades, many kinds of stimuli-responsive polymer gels in response to the change in their surroundings such as temperature, pH, and supply of electric field, etc., have been developed. They have attracted much attention as intelligent (or smart, biomimetic) materials, and several biomedical applications to actuator (artificial muscle), biosensor, purification or separation systems, tissue engineering, etc. are extensively studied [1–3]. Applications to drug delivery systems have also been attempted by many researchers [4–10]. By loading drug into stimuli-responsive gels, intelligent DDS with auto-feedback mechanism to release drug only

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when drug is required and stop the release when back to normal state, are expected. Typical examples are the system to release antipyretics only when body temperature rises, the system to sense an increase in glucose concentration in blood and release insulin automatically, etc. Actually, on–off control of drug release in response to minute temperature changes around body temperature was realized by using temperature-responsive poly(N-isopropylacrylamide) (PNIPAAm) copolymer gels [4,5]. Glucose-responsive gel which had phenylboronic acid group was prepared by Kataoka et al. [6]. On–off regulation of insulin release in response to external glucose concentration was achieved by utilizing reversible complex formation between glucose and the phenylboronic acid group. The glucose-responsive gels which operate at physiological pH condition are also prepared by bearing phenylborate derivatives as a glucose-sensing moiety [7]. Other than these systems, many kinds of self-regulated DDS in response to specific molecules, pH change, an electric field, a magnetic field, etc. are designed [8–10].

As one of characteristic behaviors in living systems, autonomous oscillation, that is, spontaneous changes with temporal periodicity (called "temporal structure") such as heartbeat, brain waves, pulsatile secretion of hormone, cell cycle, biorhythm, and so forth, can be exemplified. From the standpoint of biomimetics, several stimuli-responsive polymer systems have been studied extensively as mentioned above, but the polymer systems undergoing self-oscillation under constant condition without any on–off switching of external stimuli are still undeveloped. If such autonomous polymer systems like a living organism can be realized by using completely synthetic polymers, then unprecedented biomimetic materials will be created.

Recently, by utilizing oscillating chemical reaction [11,12], we succeeded in developing such a novel self-oscillating polymer and gels [13–43]. These self-oscillating polymer gels may be useful in a number of important applications to intelligent biomaterials such as pulse generator or chemical pacemaker, beating micropumps, auto-mobile actuators with peristaltic motion, etc. Actually, by using microfabrication technique, a ciliary motion actuator and self-walking gel have been demonstrated. Further, in order to realize nano-actuator exhibiting autonomous oscillation (nano-oscillator), the linear polymer chain and the submicrometer-sized gel beads were prepared. By grafting the polymers or arraying the gel beads on the surface of substrates, we have attempted to design self-oscillating surface as nano-conveyer to transport cells, etc. with the spontaneous propagation of chemical waves. For practical application to biomaterials, the self-oscillation under biological condition without using non-biorelated BZ substrates was attempted by introducing pH-control and oxidant-supplying sites into the polymer. Self-oscillation only in the existence of biorelated organic acid was actually achieved, and several kinds of biomedical applications including DDS can be expected in the future. In this paper, these recent studies on the self-oscillating polymer and gels and the design of functional material systems are summarized.

2. Design of self-oscillating gel

In order to realize the autonomous polymer system by tailormade molecular design, we focused on the Belousov–Zhabotinsky (BZ) reaction [11,12], which is well-known for exhibiting temporal and spatiotemporal oscillating phenomena. The BZ reaction is often analogically compared with the TCA cycle (Krebs cycle), which is a key metabolic process taking place in the living body. The overall process of the BZ reaction is the oxidation of an organic substrate, such as malonic acid (MA) or citric acid, by an oxidizing agent (bromate ion) in the presence of a strong acid and a metal catalyst. In the course of the reaction, the catalyst undergoes spontaneous redox oscillation. When the solution is homogeneously stirred, the color of the solution periodically changes, like a neon sign, based on the redox changes of

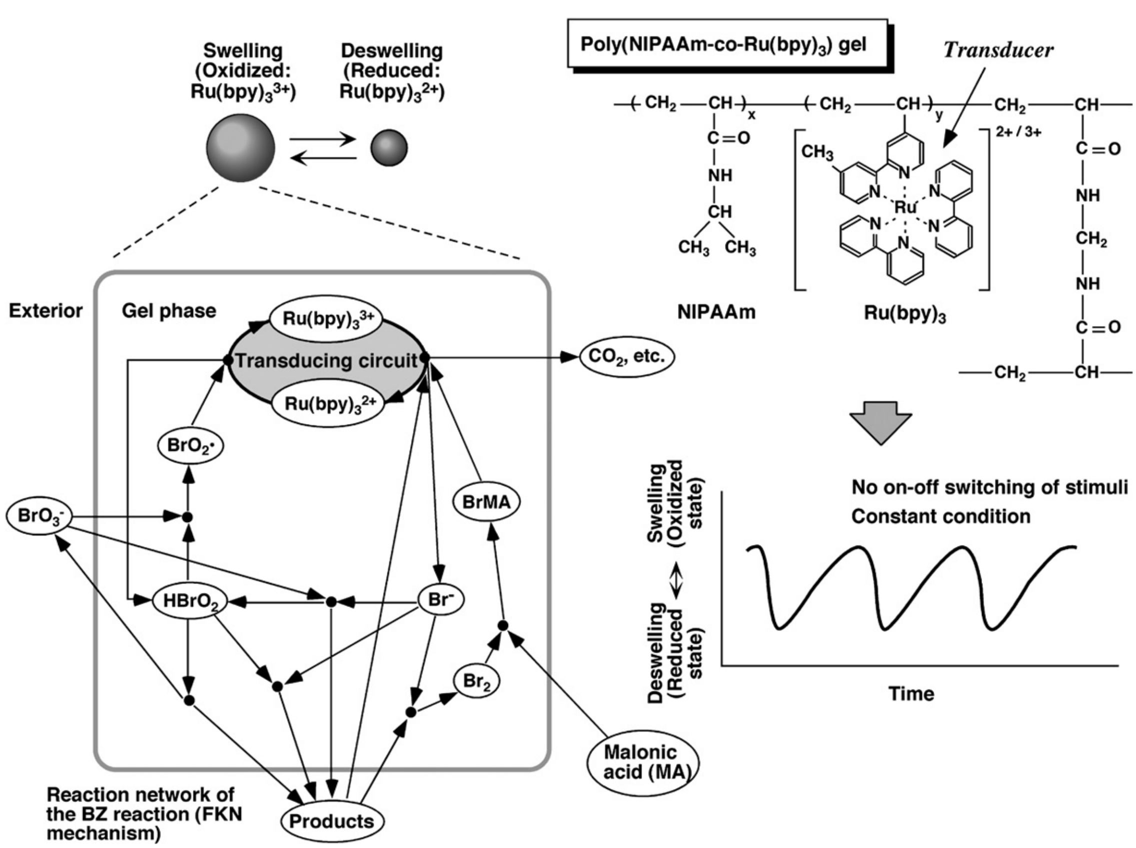

Fig. 1. Mechanism of self-oscillation for poly(NIPAAm-co-Ru(bpy)$_3^{2+}$) gel coupled with the Belousov–Zhabotinsky reaction.