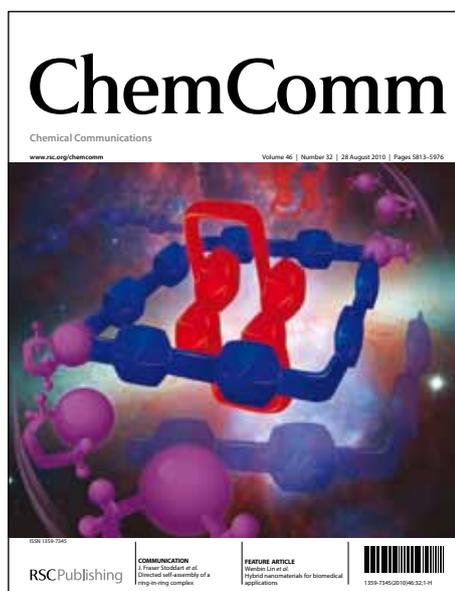


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ARTICLE TYPE

# Self-regulated Supramolecular Assembly Driven by a Chemical-Oscillating Reaction

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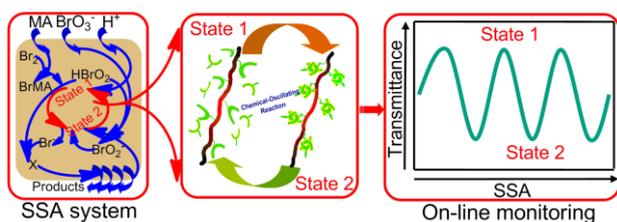
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A novel self-regulated supramolecular assembly (SSA) system driven by a chemical-oscillating reaction is constructed based on dynamic supramolecular interaction and the rhythm of such SSA process can be controlled by temperature.

How far can we push chemical self-assembly? It remains a question because supramolecular assembly has been highly attractive as an efficient and useful tool for understanding exquisitely arranged biological processes and constructing controllable assembly systems.<sup>1</sup> Various systems, especially those based on relatively strong but responsive supermolecular interactions, such as metal-ligand interaction and host-guest recognition, are extensively studied.<sup>2</sup> Despite the inherent responsive functions of these systems, “on/off” switching of external stimuli is essential to trigger a transformation of the equilibrium states,<sup>3</sup> and construction of a completely self-regulated assembly system is still a challenge.

As a pioneering attempt to develop self-regulated intelligent systems, Yoshida group achieved rhythmically pulsatile mechanical motion of a hydrogel by introducing a pH oscillating reaction in a continuous-flow stirred tank reactor.<sup>4</sup> Afterwards, this method was further developed to design a new kind of polymers and gels exhibiting similar oscillating behaviors utilizing Belousov–Zhabotinsky (BZ) reaction as a driving source.<sup>5</sup> Accordingly, it can be inferred that if the chemical-oscillating reaction is properly coupled with a respo-

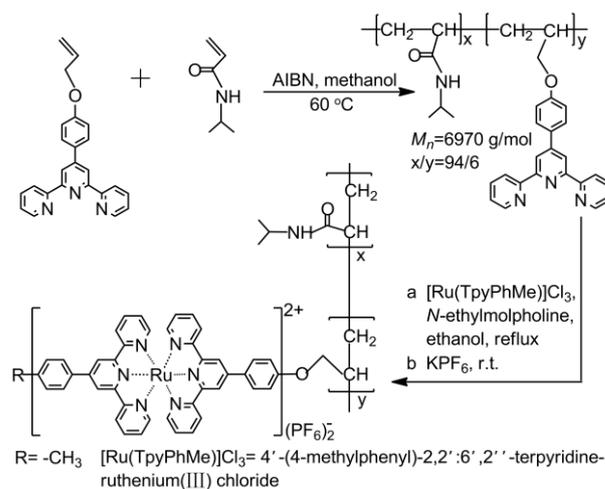


**Scheme 1.** Concept of the self-regulated supramolecular assembly. The three pictures from left to right show the SSA system, the SSA process, and on-line detection of the SSA behaviour.

nse but reversible supramolecular assembly process, a self-regulated supramolecular assembly (SSA) system should be realized (**Scheme 1**). In this way, the transformation of assembly states could be completely controlled by the system

itself without any external stimuli. Therefore, we describe herein the design and construction of such systems by utilizing BZ reaction solution as the periodical driving source and metal-ligand complexation as the supramolecular interaction.

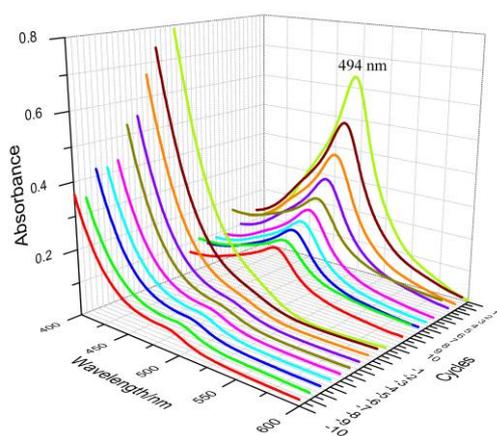
A prefabricated assembly with terpyridine-ruthenium complexes (Ru(II)(tpy)<sub>2</sub>) was first designed and prepared through a “combined protocol” of a free radical copolymerization and a following coordination process (**Scheme 1**). Reactive groups in the vacant ligands were specially designed for further functionalization or grafting modification with other linear polymers or dendrimers to obtain various topological structures.<sup>6</sup> Detailed preparation and characterization procedures can be found in **Figure S1-S9** in ESI<sup>†</sup>.



**Scheme 2** Prefabrication of the assembly.

Theoretically, the construction of the proposed SSA systems requires careful consideration of both the reversibility of the supramolecular interaction and the ability of stable assembly in the highly acidic BZ reaction environment. Therefore, the assembly/de-assembly/re-assembly behavior under separate stimulating conditions was first studied. Based on the principle that assembled bis-complex Ru(II)(tpy)<sub>2</sub> exhibits characteristic metal to ligand charge transfer (MLCT) absorption near 490 nm but de-assembled mono-complex Ru(III)(tpy) has no peak absorption at this wavelength,<sup>7</sup> a

reversibility study was first carried out by utilizing UV-vis spectrophotometry through the absorbance change at the characteristic wavelength. It was found that the Ru metal ions can be successfully oxidized by ceric sulfate ( $\text{Ce}(\text{SO}_4)_2$ ) and in reverse reduced by sodium sulfite ( $\text{Na}_2\text{SO}_3$ ) in an acidic condition, which triggers the de-assembly and re-assembly process, respectively. As revealed from **Figure 1**, in all the ten tested cycles, reversible assembly/de-assembly/re-assembly behaviours were realized and monitored by UV-vis, as can also be supported by the transformed colour (**Movie 1**), variation of average molecular weight (**Figure S10**), and the reversible sol-gel transition (**Figure S11**) simultaneously with the oxidizing and reducing process. For the state **1**, the assembly was in its branch-like assembled state with a colour of orange red, which is indicated by the MLCT absorption at 494 nm. By adding  $\text{Ce}(\text{SO}_4)_2$  solution, the system transformed to light yellow green and the characteristic absorption disappeared, demonstrating the de-assembled state **-1**. The system re-assembled again (state **2**) when the reducing agent were introduced and the further investigations of the left eight cycles also exhibited efficient reversibility. It is inevitable to have a dilution effect from accumulated addition of  $\text{Ce}(\text{SO}_4)_2/\text{Na}_2\text{SO}_3$  solutions and the possible incomplete conversion of Ru ions. That is why the absorbance at 494 nm in the ten cycles decreases with increased testing cycles.



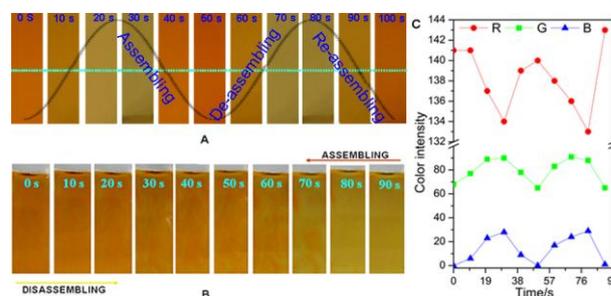
**Figure 1.** Reversible assembly/de-assembly/re-assembly behaviour under external stimuli. UV-vis spectra of the assembled states (1 to 10) and de-assembled states (-1 to -10) in water. The ordered cycles were carried out as follows, 1/-1/2/-2/.....9/-9/10/-10. Initial solution of **1** are composed of  $\text{H}_2\text{SO}_4$  ( $0.2 \text{ mol}\cdot\text{l}^{-1}$ ), [assembly]= $0.59 \text{ mg}\cdot\text{ml}^{-1}$ . From -1 to -10, a 50  $\mu\text{l}$  solution of  $\text{Ce}(\text{SO}_4)_2$  ( $0.02 \text{ mol}\cdot\text{l}^{-1}$ ) was stepwise added. From 2 to 10,  $\text{Na}_2\text{SO}_3$  solution with equal molar weight was stepwise added.

Because the possible protonation of terpyridine ligand in acidic condition may lead to a failure of re-assembly process, the assembly ability under different concentrations of  $\text{H}^+$  ( $[\text{H}^+]$ ) was then studied. This study was carried out by adding  $\text{Na}_2\text{SO}_3$  solution to an already de-assembled system to induce a re-assembly process under different  $[\text{H}^+]$  (**Figure S12**). As is revealed, the system exhibited stable re-assembly behaviours under a condition with  $[\text{H}^+]$  from  $0.4 \text{ mol}\cdot\text{l}^{-1}$  to  $2.0 \text{ mol}\cdot\text{l}^{-1}$ . When the  $[\text{H}^+]$  increased higher than  $2.0 \text{ mol}\cdot\text{l}^{-1}$ , the peak at 494 nm become asymmetric and smaller, which indicate that a protonation of terpyridine ligand occurred and the re-assembly process is to some extent restrained. Meanwhile, the system

become slightly opaque due to the known “salting-out effect”, which may also prevent the system from re-assembly. Therefore, a proper  $[\text{H}^+]$  no more than  $2.0 \text{ mol}\cdot\text{l}^{-1}$  should be chosen for the construction of SSA systems.

To gain insight into de-assembly/re-assembly process, a gradual reduction and oxidation process was carried out (**Figure S13**). By stepwise increasing the amount of stimuli, the absorption near 490 nm shows simultaneous decrease for the process of oxidation (**Figure S13-A**) and increases in the case of reduction process (**Figure S13-C**). Meanwhile, the colour of the tested systems also showed gradual change (**Figure S14**), which is similar to that observed in movie 1. This result clearly shows a continuous de-assembly and re-assembly process under separated stimulating conditions.

According to the external stimuli-regulated assembly/de-assembly/re-assembly behaviour, it can be expected that a SSA system can be constructed if ruthenium ion changes autonomously between a reduced Ru(II) state and an oxidized Ru(III) state. BZ reaction, in which the ruthenium ion works as a catalyst and periodically changes between a reduced Ru(II) state and an oxidized Ru(III) state, should be a good choice.<sup>8</sup> By dissolving proper amount of prefabricated branch-like assembly into a system of BZ reaction solution containing certain concentrations of sodium bromate ( $\text{NaBrO}_3$ ), malonic acid (MA) and sulfuric acid ( $\text{H}_2\text{SO}_4$ ), an autonomous transformation between assembled state and de-assembled state was demonstrated, as can also be vividly revealed by the periodical colour change (**Figure 2** and **Movie 2**), which is comparable to the assembly/de-assembly behaviour under external stimuli conditions. Meanwhile, the change of colour intensity of red (R), green (G) and blue (B) all exhibit an oscillating profile, further indicating the occurrence of SSA behaviour (**Figure 2-C**). What is more interesting, when SSA process was carried out in a stirred system, a homogeneous and faster transformation between assembled state to de-assembled state was observed, while a heterogeneous and slower change was observed in an unstirred system, as can be macroscopically observed in **Figure 2 A-B** and **Movie 3-4**.

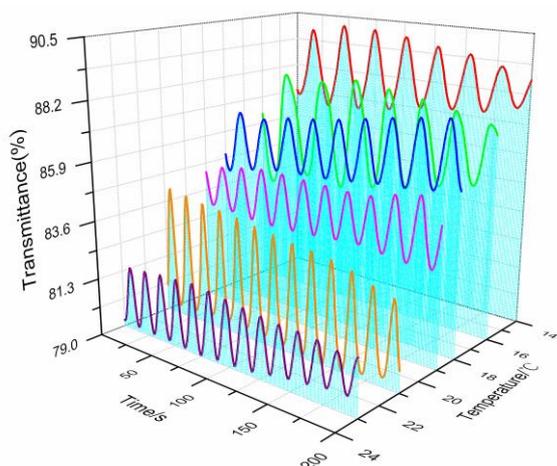


**Figure 2.** Photographs of the self-regulated supramolecular assembly systems under a stirred (A) and an unstirred (B) condition and the R/G/B value changes of the marked position in A against time (C). The initial substrate concentrations were fixed to  $[\text{MA}] = 50 \text{ mmol}\cdot\text{l}^{-1}$ ,  $[\text{NaBrO}_3] = 300 \text{ mmol}\cdot\text{l}^{-1}$ ,  $[\text{H}_2\text{SO}_4] = 1 \text{ mol}\cdot\text{l}^{-1}$ , and [assembly]= $0.5 \text{ wt}\cdot\%$ .

The different SSA behaviours are originated from the fact that a BZ reaction is controlled by both chemical reaction itself and matter diffusion process.<sup>9</sup> Under an unstirred condition, matter diffusion process was difficult to proceed and the SSA behaviour was not homogeneous and slower, while in the case

of a stirred condition, mechanical stir promoted the matter diffusion process, which led to the homogeneous and faster SSA behaviour.

Further study revealed that temperature played an important role in the SSA systems. Due to the thermosensitive poly(*N*-isopropyl acrylamide) component, a hydrophilic–hydrophobic transition occurred when the temperature was higher than the lower critical solution temperature (LCST) of the assembly and the SSA process was almost stopped. However, when the temperature was fixed below the LCST of the assembly, a SSA behavior can be successfully observed. **Figure 3** shows the SSA-induced transmittance change under different constant temperatures when the other influences factors, including the concentrations of BZ substrates and the amount of the assembly, were fixed. As is shown, in all the studied systems, the transmittance exhibits periodical change, which



**Figure 3.** Transmittance change (494 nm) of the SSA systems as a function of time under different constant temperatures. The initial substrate concentrations were fixed to  $[MA]=50 \text{ mmol}\cdot\text{l}^{-1}$ ,  $[\text{NaBrO}_3]=300 \text{ mmol}\cdot\text{l}^{-1}$ ,  $[\text{H}_2\text{SO}_4]=1 \text{ mol}\cdot\text{l}^{-1}$ , and  $[\text{assembly}]=1 \text{ wt.}\%$ .

indicates the cyclic assembly and de-assembly process. Because the assembled state has a peak absorption at the detecting wavelength but the de-assembled has slight absorption at this wavelength, the transmittance increases with the gradual de-assembly process and decreases with the re-assembly process. This is well in accordance with the result obtained under external stimuli conditions. Moreover, it can also be seen from Figure 3 that the rhythm of the SSA behavior was controlled by the temperature, as revealed by the decreased SSA periods with the increasing temperature (**Figure S15**), but the transmittance value, which reflects the extent of assembly process, decreased from ca. 90 for 14 °C to ca. 81 for 23 °C. This is because the assembly exhibited slight phase transition when the temperature was increased, although the temperature was still below the minimum LCST value of the assembly which is 33 °C. It is a pity that the average amplitude of all the studied SSA systems was much smaller than the difference of colour change or absorbance variation between assembled state and de-assembled state under external stimuli condition. This may be caused by the confined small concentration of the assembly and the incomplete conversion of Ru ions in BZ reaction. Considering

together the thermosensitivity and “salting-out effect”, a non-thermosensitive assembly system may exhibit a larger SSA amplitude by elevating the assembly concentration and further optimizing the BZ reaction system.

In conclusion, a novel kind of supramolecular assembly systems in which the transformation of assembly states was completely controlled by the system itself was presented. Control of supramolecular assembly by nonlinear chemical kinetics paves a way for studying and understanding supermolecular assembly from a new perspective. In a broader content, this system may be regarded as a template for other systems with potential self-regulated function, including amphiphilic assembly system, assembly on the surface of nanoparticle or nanosheet and hydrogel systems (in such cases, as dynamic cross-linking sites).

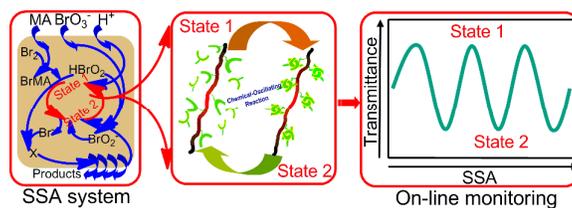
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