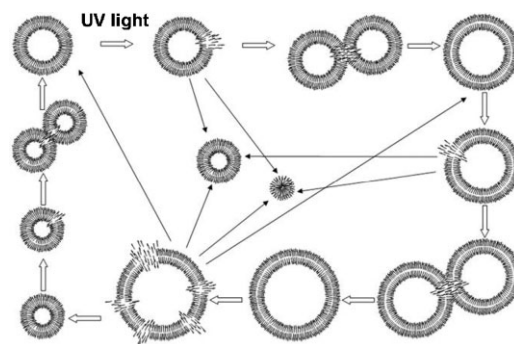


# UV-Responsive Behavior of Azopyridine-Containing Diblock Copolymeric Vesicles: Photoinduced Fusion, Disintegration and Rearrangement<sup>a</sup>

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A novel amphiphilic diblock copolymer composed of a hydrophilic poly(ethylene oxide) and a hydrophobic polymethacrylate with photochromic azopyridine moieties in the side groups was synthesized by atom transfer radical polymerization. The copolymeric vesicles showed photoinduced circular process including fusion, damage and defect formation, disruption, disintegration and rearrangement in H<sub>2</sub>O/THF during the irradiation of UV light. The process of photoresponsive cycle can be inhibited at any moment by visible light.



## Introduction

Polymer vesicles formed from amphiphilic block copolymers have been well investigated. Among them, the vesicles that can respond to internal or external stimuli like temperature, pH, solvent composition, ionic strength, electric field and light attract much attention.<sup>[1]</sup> These stimuli-responsive vesicles can implement controllable release of encapsulated or entrapped reagents. Hitherto, an overwhelming majority of studies focused on temperature and pH-responsive polymer vesicles. In recent years, light-

responsive polymer vesicles have received more and more interest.

Generally, in order to obtain light-responsive ability, it is necessary for polymers to be equipped with photosensitive chromophores. Much research has been conducted on copolymers containing azobenzene units, which can undergo *trans-cis* photoisomerization in response to UV and visible light. Zhao et al. observed that micelles of azo copolymers underwent disruption and reformation under alternating UV and visible light irradiation.<sup>[2]</sup> Wang et al. reported that colloidal particles of a random azo copolymer disaggregated in a water/tetrahydrofuran (H<sub>2</sub>O/THF) solution upon the irradiation of UV light.<sup>[3]</sup> Liu and Jiang reported that a hydrogen bonded azo polymer exhibited reversible photoinduced micellization and micelle-hollow-sphere transition.<sup>[4]</sup> Zhang's group found that copolymeric micro-vesicles generated a fusion into giant vesicles in H<sub>2</sub>O/THF solution induced by UV light.<sup>[5]</sup> Recently, they reported that micro-vesicles of an azopyridine-containing diblock copolymer exhibited reversible photocontrolled swelling-shrinking behavior.<sup>[6]</sup> The above-mentioned aggregates can

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implement reversible or irreversible photoresponsive behavior; however, there is still no research concerning photoresponsive aggregates that can show versatile, continuous or circular transitions.

In our previous work, we prepared a series of crosslinked LC polymers containing azobenzene mesogens and found they showed interesting photoinduced deformation, attributed primarily to photoisomerization of azobenzene mesogens.<sup>[7]</sup> The investigations of these azobenzene-containing polymers are all based on the solid state. However, those systems concerning the solution state have not yet been fully studied. Herein, we report a novel kind of light-responsive polymer vesicles formed from the self-assembly of a copolymer in solution, which consists of hydrophilic poly(ethylene oxide)(PEO) and hydrophobic azopyridine-containing polymethacrylate (PAP). Interestingly, the vesicles show a photoinduced cycle of fusion, disintegration and rearrangement in H<sub>2</sub>O/THF with the irradiation of UV light. This cycle stops when UV light is switched off or the incident light is changed to visible light. To the best of our knowledge, this is the first report that self-assembled vesicles can generate this kind of photoinduced cycle. It would be helpful to realize continuous, steady and slow release of encapsulated reagents using light control.

## Experimental Part

### Synthesis of an Amphiphilic Diblock Copolymer Containing Azopyridine Moieties

PEO-*b*-PAP was synthesized by atom transfer radical polymerization (ATRP) using a bromo-substituted poly(ethylene oxide) macro-initiator in combination with copper (I) bromide. The experimental details are given in the Supporting Information.

### Preparation of PEO-*b*-PAP Vesicles

PEO-*b*-PAP was dissolved in THF to obtain a solution with an initial concentration of 4.0 mg · mL<sup>-1</sup>. The solution was stirred overnight at room temperature. The self-assembly process was performed by adding the required amount of deionized water into the THF solution at a rate of 5 μL · s<sup>-1</sup> with a durative stirring.

### Measurements

The self-assembly morphology and photoresponsive behavior of the copolymeric vesicles in solution were observed with an optical microscope (OLYMPUS BH-2) and the images were taken with a digital camera (OLYMPUS C-5050ZOOM). To investigate the photoresponsive process of the vesicles, the vesicle solution (ca. 2 mL) was placed in a quartz cuvette with a stopper and irradiated with a UV-LED irradiator (OMRON ZUV-C30H) with a wavelength of

365 nm under the stirring. Once the UV light was turned off, the vesicle solution was immediately transferred into a glass cell (17 mm × 6 mm × 200 μm) for the optical microscopic observations. All the photoresponsive experiments were performed at 25 °C.

## Results and Discussion

### Self-Assembly of PEO-*b*-PAP

The preparation method for self-assembled vesicles was similar to that of “crew-cut” aggregates from block copolymers used by Eisenberg et al.<sup>[8]</sup> The copolymer was firstly dissolved in a common good solvent (THF) for both hydrophobic and hydrophilic blocks. Subsequently, deionized water was slowly added to the solution to drive an aggregation of the PAP blocks because of hydrophobic interactions. When the water content reached a critical value (about 45 vol.%), the PAP blocks with photochromic azopyridine moieties in the side chains start to form vesicular bilayers and the remaining hydrophilic PEO chains dangle in the surrounding solution simultaneously. When the water added was more than the critical water content (CWC), the obtained vesicles became much larger. Because the size of vesicles is thermodynamically controlled by solvent composition, the enlargement of size is correlated with the increase in the interfacial energy of the system.<sup>[9]</sup>

Figure 1 shows a typical morphology of the PEO-*b*-PAP vesicles, which were formed in a 55 vol.% H<sub>2</sub>O/THF solution with the initial concentration of 4.0 mg · mL<sup>-1</sup>. The size distribution of the vesicles covers from 0.2 μm to 0.7 μm. The mean diameter is 0.42 μm with a polydispersity index of 0.266.

### Photoresponsive Behavior of the Copolymeric Vesicles

To study the morphological change in the vesicles upon the irradiation of UV light, it is essential to choose an appropriate vesicle system. As mentioned above, when the water

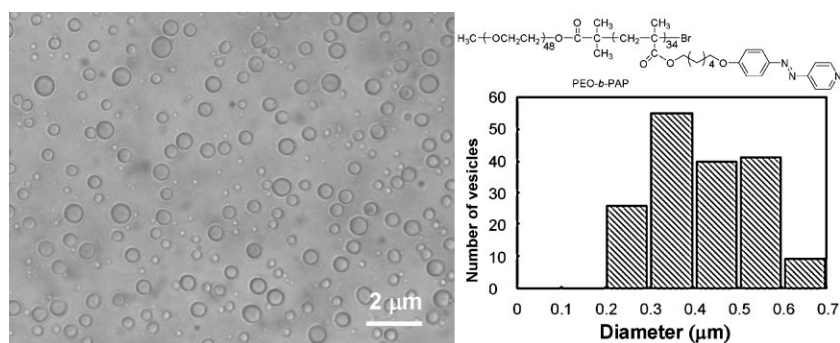


Figure 1. Optical micrograph (left), chemical structure and size distribution (right) of the PEO-*b*-PAP vesicles in 55 vol.% H<sub>2</sub>O/THF solution.

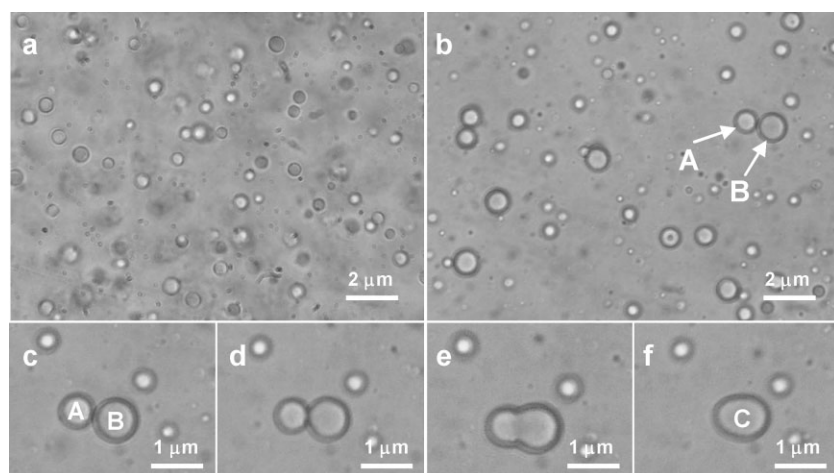
content was close to CWC (about 45 vol.%), the vesicles began to form and were relatively unstable; however, a higher water content (such as 65 vol.-%) led to the freezing of polymer chains, because water is a non-solvent for the PAP blocks. The increase in water content would compel the polymer chains to generate collapse and entanglement, and moreover, the glass transition temperature ( $T_g$ ) of bulk PAP is higher than room temperature.<sup>[10]</sup> A similar frozen effect was also reported in other systems consisting of amphiphilic copolymers.<sup>[8a,11]</sup> Although the vesicles formed at a water content of 65 vol.-% were more stable than those formed at about 45 vol.-%, the azopyridine groups do not have enough free volume to undergo photoisomerization in vesicle solution. Herein, we chose the vesicle solution with an initial concentration of  $4 \text{ mg} \cdot \text{mL}^{-1}$  and a water content of 55 vol.-% to investigate the morphological change in the vesicles upon the irradiation of UV light.

Figure 2(a) shows the initial vesicles with an average diameter of about  $0.4 \mu\text{m}$  randomly suspended in solution before irradiation. The size and the size distribution of the vesicles were stable without any change with prolonged time. After the irradiation with UV light ( $365 \text{ nm}$ ,  $36 \text{ mWcm}^{-2}$ ) for 10 min, as shown in Figure 2(b), many vesicles with a size of  $1 \mu\text{m}$  were observed. The increase in vesicles size is caused by the occurrence of photoinduced fusion, which is illustrated well by the two vesicles A and B marked in Figure 2(b). Figure 2(c) to 2(f) display that these two adjacent vesicles underwent close contact and mergence to become the bigger vesicle C denoted in Figure 2(f). Hereby, the fusion of the vesicles could be triggered exclusively by UV light.

As shown in Figure 3, when the irradiation time of UV light was prolonged from 10 min to 60 min, it was interesting to find a series of photoresponsive behavior for the

vesicles. Figure 3(a) shows that several vesicles were damaged in solution after 20 min and other vesicles became bigger than those exhibited in Figure 2(b). The extent of membrane disruption and size increase was raised after 30 min as shown in Figure 3(b). After irradiation for 40 min, the disruption almost existed in all the vesicular membranes (Figure 3(c)). Moreover, when increasing the irradiation time to 50 min, the vesicles continued to fuse with each other to form larger vesicles with sizes greater than  $2 \mu\text{m}$ , and at the same time the disruption still appeared in these vesicular membranes, as indicated in Figure 3(d). After the sample was irradiated for 60 min, those larger vesicles with damages and defects severely ruptured until almost complete disintegration occurred, and then rearranged to form a large number of very small vesicles (Figure 3(e)). In addition, the UV-vis spectra of the PEO-*b*-PAP vesicle solution upon the irradiation of UV and visible light were measured (see Supporting Information). It was found that after irradiation with UV light for 10 min to 50 min, the amount of *cis* isomers increased gradually from 39% to 49% and lastly reached a stable value (ca. 50%) when the irradiation time was 60 min.

Figure 3(f1) to 3(f3) show three kinds of photoinduced changes simultaneously occurring in the system after the irradiation of UV light for more than 60 min, including fusion (Figure 3(f1)), damage and defect formation in membrane (Figure 3(f2)), and disintegration and rearrangement (Figure 3(f3)). When the vesicle solution was exposed to UV light again, those reassembled small vesicles also underwent the above mentioned photoinduced behavior. However, when the solution was exposed to visible light at  $>540 \text{ nm}$ , this cycle was inhibited and a new relatively stable state appeared in the system, in which many vesicles with bigger sizes had few defects and little damage (Figure 3(g)).

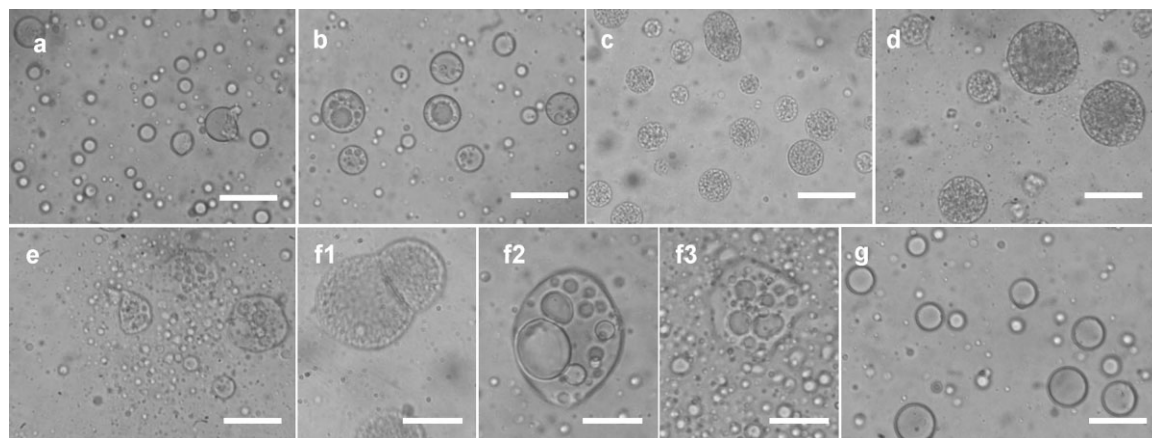


**Figure 2.** Optical micrographs of the PEO-*b*-PAP vesicles in 55 vol.-%  $\text{H}_2\text{O}/\text{THF}$  solution before (a) and after irradiation of UV light ( $365 \text{ nm}$ ,  $36 \text{ mW} \cdot \text{cm}^{-2}$ ) for 10 min (b), and optical micrographs of two vesicles (denoted as A and B) (c) undergoing the fusion process after 2 s (d), 4 s (e), and 6 s (f).

### The Mechanism of Photoinduced Circular Process in the Vesicle Solution

Figure 4 schematically represents such photoresponsive behavior as fusion, damage and defect formation, disintegration and rearrangement of the self-assembled vesicles, formed by the amphiphilic copolymer containing azopyridine groups. The photochromic and hydrophobic azopyridine groups generate compact packing in the bilayer membranes of the vesicles due to a strong non-covalent aromatic-aromatic interaction and tend to form H-aggregation at relatively high water content. Under the irradiation of UV light, the *trans*-azopyridine groups with



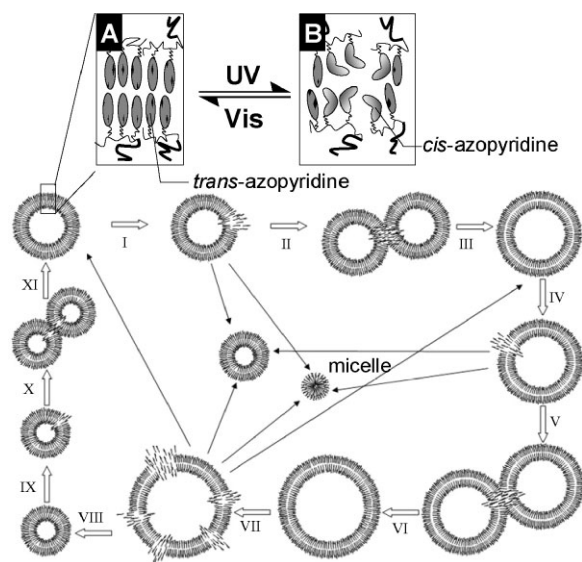


**Figure 3.** Optical micrographs of photoresponsive process of the PEO-*b*-PAP vesicles in 55 vol.-% H<sub>2</sub>O/THF solution after the irradiation of UV light (365 nm, 36 mW · cm<sup>-2</sup>) for 20 min (a), 30 min (b), 40 min (c), 50 min (d), 60 min (e), and more than 60 min (f1-f3), and subsequently after exposed to visible light at >540 nm (g). The scale bars represent 2 μm for all images.

a rod-like shape are converted to the bent *cis* form, which could disrupt the original relatively tight packing and bring a loose stacking formation in the vesicular membrane. When this disruption induced by photoisomerization happens, it is expected to cause instability of the bilayers due to the configurational change in the azopyridine groups and the transition from tight to loose packing in membrane regions. Accordingly, the irradiation of UV light initially brings about damage and defects in membrane regions, leading to a decrease of their mechanical stability. In addition, the expansion of the surface area appears in these vesicles as a result of the transition from tight to loose packing, leading to an increase in instantaneous surface

free energy. Therefore, fusion is the most likely pathway for the vesicles to become stable and reduce their surface free energy.<sup>[12]</sup> Irrespective of its trigger condition, it has been proposed that fusion involves the formation of a highly bent stalk intermediate between the interacting membranes.<sup>[13]</sup> The formation of the stalk structure requires overcoming the free energy. As a matter of fact, the change from tight to loose packing can increase the entropy without adversely affecting the enthalpy and as a result lowers the free energy barriers, which benefits the fusion process.<sup>[14]</sup> In other words, the defects in the loose packing state with more structural flexibility and plasticity may facilitate the restructuring of the PAP bilayer in the fusion process. Moreover, the stalk may also appear in these defect sites.<sup>[15]</sup>

The fusion process cannot be inhibited until the irradiation of UV light is switched off. During the irradiation, the regions of incipient damages or defects are not large enough to cause the individual vesicle to rupture, because the rupture must overcome the entanglement of polymer chains and the increase of surface free energy. The disruption extent of membranes gradually increases with continuous irradiation. The following decrease in mechanical stability of vesicles eventually results in the rupture of vesicular membrane under stirring. When the vesicles with large disruption areas appear, two kinds of photoresponsive behavior take place, namely the fusion of the damaged vesicles with one another and the disintegration of the vesicles due to the severe disruption. Subsequently, the disintegrated fragments rearrange to a majority of small vesicles and micelle aggregates by virtue of the hydrophobic interaction. It is worth mentioning that the photoinduced disintegration can be observed in those vesicles with bigger sizes, because the vesicles possess little mechanical stability and easily deformable property; moreover, stirring may play a role in the process because it provides a shear force to help break the vesicles.<sup>[2]</sup>



**Figure 4.** Schematic illustration of the photoresponsive process of the PEO-*b*-PAP vesicles in solution upon the irradiation of UV light. Inset A and B illustrate the molecular packing models in the vesicle bilayer membrane before and after the irradiation of UV light.

Under irradiation with visible light, since the *cis*-azopyridine groups turn into the thermodynamically stable *trans* form, those vesicles with defects return to their undamaged shape. Certainly the original morphology shown in Figure 2(a) cannot be reached because of the occurrence of the fusion. In fact, the *cis*-to-*trans* photoisomerization caused by visible light would inhibit the UV-light-induced cycle from fusion to rearrangement of the vesicles and make the system reach a relatively new equilibrium state.

## Conclusion

In summary, we firstly reported the synthesis of the azopyridine-containing amphiphilic diblock copolymer by ATRP and the photoinduced circular process of the copolymeric vesicles including fusion, damage and defect formation, disruption, disintegration and rearrangement. The defects are expected to increase the permeability of vesicular bilayer membranes. Moreover, the disruption of vesicular membrane is possible to promote the exchange between the outer and inner substance of vesicles. Therefore it would be easy to achieve a controlled release and delivery of encapsulated chemical species by adjusting the extent of photoinduced change in the morphology of vesicles. The release process can also be inhibited at any moment by visible light. Based on the pH sensitiveness of the azopyridine groups, we are planning to study the pH-responsive behavior of vesicles as a way to explore and achieve multi-control of the vesicles.

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