# Oxygen and Carbon Dioxide Dual Responsive Nanoaggregates of Fluoro- and Amino-Containing Copolymer

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S *Supporting Information*

ABSTRACT: We report herein a novel approach for preparing CO_2- and O_2-responsive polymer nanoaggregates. The polymer, synthesized via atom transfer radical polymerization (ATRP), has one hydrophilic poly(ethylene glycol) (PEG) block, and the other hydrophobic block composed of 88 randomly distributed units of CO_2-responsive N,N-diethylaminoethyl methacrylate (DEA) and 43 units of O_2-responsive 2,2,2-trifluoroethyl methacrylate (FMA). The amphiphilic copolymer self-assembled into vesicular nanoaggregates in water. With O_2 bubbling, the vesicles expanded eight times in volume. With CO_2 bubbling, the vesicular morphology collapsed and transformed into a small spherical micelle. The dual gas-responsivity significantly expanded the scope in designing stimuli-responsive materials and processes.
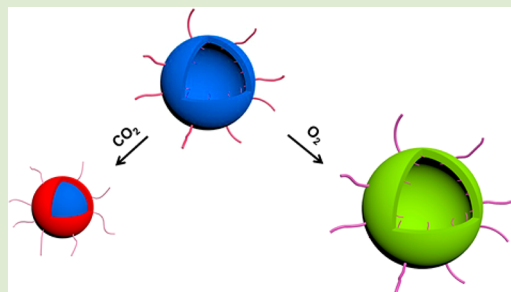
Over the past decades, developments of novel stimuli-responsive materials and systems have attracted more and more interest from researchers.[1−3] Stimuli-responsive polymeric vesicles,[4,5] as one of the examples, have been studied intensively due to its wide range of potential applications,[4,6,7] such as drug delivery, nanoseparator, and enzymatic nano-reactor.[8,9] With a proper stimulus, the vesicles could undergo different changes, including (i) disassembly into individual polymer chains;[10] (ii) expansion/shrinking caused by swelling/deswelling of vesicle wall,[11,12] or extension/collapse of corona chains;[13,14] and (iii) transformation to other morphologies, such as spherical and worm-like micelles.[15,16] Such changes are believed to benefit their applications, especially in the biological research areas.[16]

There are many stimuli/triggers reported in literature for achieving the changes of vesicles. The major types are temperature,[17,18] pH,[19−21] and light.[22−24] Each type has advantages and drawbacks. The recent advent of gas stimuli has provided a great opportunity for development of smart materials and systems. This is particularly true with CO_2.[16,25,26] As an abundant, nontoxic, and environmentally benign gas, CO_2 can reversibly react with amine,[27] amidine,[28] or carboxyl groups,[29] leading to dramatic changes in hydrophilcity and polarity. Compared to the other stimuli, CO_2 can be removed without accumulation by simple bubbling of N_2 or air, which renders CO_2-responsive polymers switchable with CO_2/N_2 treatments. In the past few years, a large number of smart materials have been crafted based on CO_2-responsive polymers.[30−34] CO_2-responsiveness has provided an alternative solution for morphologic control over polymeric vesicles. Yuan et al.[26] has developed CO_2-responsive vesicles with a biomimetic "breathing" feature. With addition and removal of CO_2, the vesicles underwent reversible expansion and shrinking in size, as well as reversible changes in the permeability of

vesicle membranes.[35] Such systems have potential applications as nanoreactors and nanoseparators.[35] Zhao and co-workers also prepared "CO_2-breathing" vesicles, with their breathing extents adjustable by the degree of dimerization of coumarin within the vesicle membrane.[36] An application of CO_2-controllable release has also been demonstrated.[36] Most recently, they showed that CO_2 is very capable of stimulating polymeric shape transformation and modulating size, shape, and morphology of polymer aggregates.[16,25] Subsequently, Feng et al. investigated CO_2-driven transformation of vesicle to micelle regulated by topology of amphiphilic polymers.[37]

The success of CO_2 as gas trigger in the development of smart materials has encouraged researchers to search for new types of gas triggers. Very recently, Jeong et al. demonstrated that pentafluorophenyl end-capped poly(ethylene glycol) was O_2-responsive.[38] Interactions between O_2 molecules and the pentafluorophenyl groups slightly improved the polymer solubility in water, resulting in 1.5 °C increase in its lower critical solution temperature (LCST) from 24.5 to 26 °C. Zhang et al. reported a new design of fluorinated polymers, which was a copolymer of commercially available 2,2,2-trifluoroethyl methacrylate (FMA) and N,N-dimethylaminoeth-yl methacrylate (DMA) synthesized by atom transfer radical polymerization (ATRP).[39] The aqueous solutions of this FMA-DMA polymer showed a good O_2/N_2-triggered transparent-turbid switchability. The copolymer had a LCST of 24.5 °C, which was increased to 50 °C after O_2 treatment.[39] The difference of about 30 °C opens a big operation window and

allows the O_2/N_2-triggered switching in a broad temperature range.

Both CO_2 and O_2 are important gases. Inspired by the above development and in this work, we aimed at design of polymers sensitive to both CO_2 and O_2. We synthesized an amphiphilic block copolymer (O_{2k}-FN) via ATRP, which consisted of a hydrophilic block of ethylene oxide (O_{2k}-FN) and a hydrophobic random copolymer block of FMA and N,N-diethylaminoethyl methacrylate (DEA). In water, O_{2k}-FN could self-assemble into vesicular architectures. Upon gas treatment, the hydrophilicity/hydrophobicity of CO_2-responsive DEA moieties and O_2-responsive FMA moieties on the polymer chains would be increased or decreased to some levels to induce the morphological transformations, as shown in Scheme 1. To the best of our knowledge, there has been no report so far on the preparation and demonstration of dual-responsive vesicles triggered by different stimulus gases.

Scheme 1. Synthesis Routes of the CO_2- and O_2-Sensitive Diblock Copolymer O_{2k}-FN, and Schematic Representation of the CO_2- and O_2-Driven Self-Assembly and Shape Transformation Behavior of the Vesicles
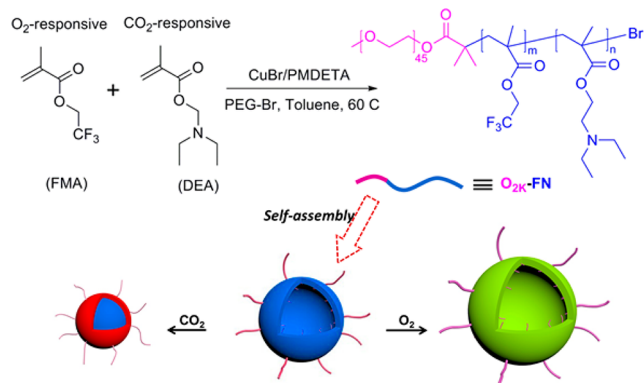
The amphiphilic copolymer O_{2k}-FN was synthesized via ATRP of DEA and FMA by using poly(ethylene glycol) methyl ether 2-bromoisobutyrate as a macroinitiator. Thus, the copolymer can be regarded as a diblock copolymer, with one hydrophilic PEG block, and the other poly(DEA-co-FMA) random copolymer block. While the PEG block is water-soluble, the poly(DEA-co-FMA) block is normally hydrophobic, with its solubility in water adjustable by CO_2 and O_2 treatment. Figure S1 shows ^{1}H NMR spectrum of the copolymer. It has 43 units of FMA and 88 units of DEA in the second block. The number-average molecular weight is 25500 g/mol, as estimated from the NMR result. The copolymer sample of 5 mg was well dissolved in 1 mL of THF. Nanoaggregate solutions were prepared by a slow injection of the THF solution into 5 mL of DI water with ultrasonication. The resulting translucent colloidal solution was then dialyzed against DI water for 2 days to remove the organic solvent.

The responsivity of the colloidal solution toward CO_2 and O_2 is of our major interest in this work. The solution had a light blue color. When treated with CO_2, the color was gradually bleached in 20 min. CO_2 bubbling continued for 1 h to ensure saturation. However, when bubbled with O_2, the phenomenon was totally different. Upon O_2 bubbling, some small white polymer aggregates precipitated out immediately. The precipitants accumulated with the time of O_2 treatment. Ultrasonication was very effective to disperse the polymer

aggregates. The container was nicely sealed to retain O_2 gas in the system when applied to ultrasonication. After O_2 saturation for 1 h, followed by ultrasonication, a translucent colloidal solution was obtained. It looked similar as the original solution before the gas treatment, but with somewhat of an increase in turbidity. This gas treatment process was recorded by a digital camera, with some photos shown in Figure 1a. The
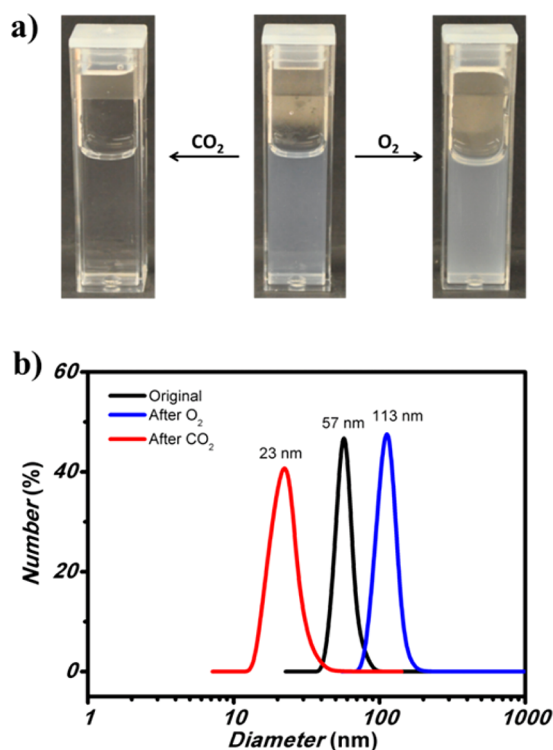

Figure 1. (a) Turbidity changes of O_{2k}-FN aggregates with different gas triggers. (b) DLS data for O_{2k}-FN aggregates before (black) and after treatment with CO_2 (red) and O_2 (blue), respectively.

change in turbidity was also measured by the solution transmittance at 500 nm. The original solution before gas treatment had a transmittance of 84%. It decreased to 34% after O_2 bubbling and increased to 98% after CO_2 bubbling, respectively.

The changes in particle size during the transition process were measured by dynamic light scattering (DLS) measurements. The results are shown in Figure 1b. The particle sizes of the original polymer aggregates in water were mostly located between 40 and 90 nm, with a peak at 57 nm. After treatment with CO_2, the peak shifted to 23 nm and the distribution was slightly broadened. On the other side, O_2 bubbling increased the peak size to around 113 nm, with little change in the size distribution. Both the turbidity tests and particle size measurements have clearly demonstrated the dual-responsiveness of the polymer nanoaggregates to the gas stimuli.

To further verify the results, transmission electron microscopy (TEM) was used to visualize morphologies of the nanoaggregates. Phosphotungstic acid (PTA) aqueous solution was used as the staining agent. A typical vesicle morphology was observed for the original aggregates prepared from the self-assembly of O_{2k}-FN copolymer. As shown in Figure 2a, there was a clear contrast between the dark rim and the hollow center. Also present were wrinkles on the sphere surface caused by wall collapse during the removal of ice by freeze-drier. Both
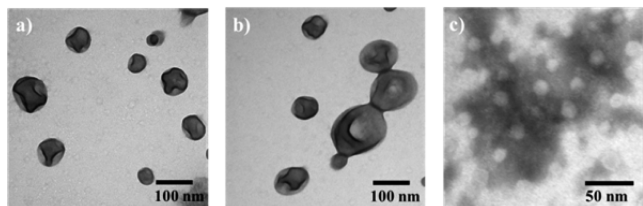
Figure 2. TEM images of (a) original O_{2k}-FN aggregates; (b) after O_2 treatment; (c) after CO_2 treatment.

suggested a morphology of spherical vesicles. While the vesicular morphology of nanoaggregates was preserved after the O_2 treatment, there was an obvious increase in their sizes (Figure 2b). In contrast, the vesicular nanoaggregates transformed into spherical particles after treatment with CO_2, as it can be seen in Figure 2c. It should be noticed that, even stained in the same way, the appearance of spherical particles was different from that of vesicles because the hydrophobic core could not be stained by the hydrophilic phosphotungstic acid. As measured from the TEM images, the average particle size of the original vesicles was approximately 49 nm. It increased to around 109 nm for the swollen vesicles after O_2 treatment. Accompanied with the morphological transition from vesicles to collapsed spherical particles, the size decreased to about 19 nm. These TEM observations were in good agreement with the DLS results. It was found that alternatively bubbling N_2 and O_2 would make the vesicles shrink and expand reversibly. It could be found in Figure 3a that DLS results showed good O_2/N_2 switchability. However, while the CO_2-saturated micelle
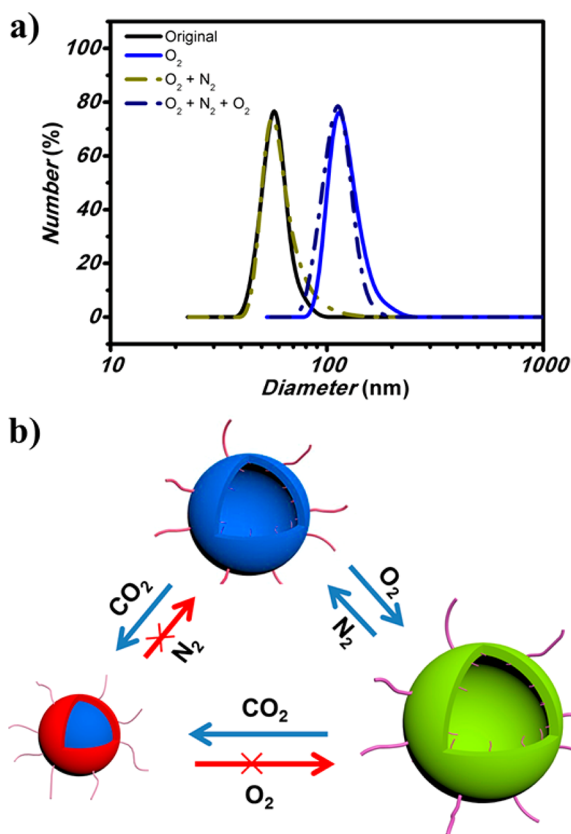

Figure 3. (a) DLS data of O_{2k}-FN aggregates for the two cycles of O_2/N_2 treatment. (b) Schematic representation of the reversible and irreversible processes of $CO_2/O_2/N_2$ treatment.

solution was treated with N_2 or O_2, the polymer precipitated out and could not be redispersed, even with ultrasound, suggesting irreversible vesicle to micelle transition. The reversible and irreversible results could be summarized in Figure 3b.

How do CO_2 and O_2 drive transformation to the different directions? CO_2 in water reacted with the tertiary amine moieties of the copolymer, generating positive charges that resided in the vesicular wall layer. The electrostatic repulsion with increase in the cationic density would increase the interfacial free energy, which provided a driving force for the vesicle−micelle transformation (Scheme 2, left direction). A

Scheme 2. Schematic Representation of CO_2 and O_2-Driven Self-Assembly Process
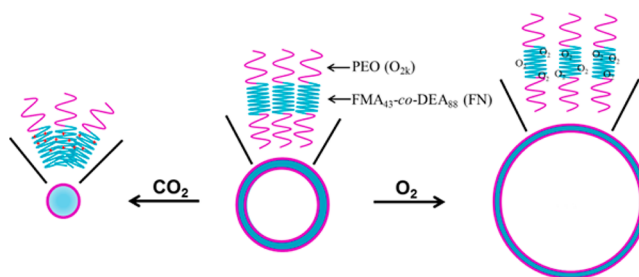
similar phenomenon of shape transformation was reported by Feng et al.,[37] in which hydrophobic styrene, instead of FMA, was used as the vesicular wall-forming component. On the other hand, O_2 could only slightly increase water solubility of the highly hydrophobic FMA without charge accumulation. As a result, the vesicular shape was preserved and the vesicle-particle transformation was prevented. The vesicle increased in size due to swelling (Scheme 2, right direction). It is worth mentioning that even though only 1/3 of the vesicular wall was composed of O_2-responsive FMA, the vesicles could be expanded 2× in diameter, that is, 8× in volume.

To conclude, we have successfully developed a novel dual gas-responsive nanoaggregate system through self-assembly of a CO_2 and O_2-responsive copolymer O_{2k}-FN. The copolymer was synthesized via atom transfer radical polymerization (ATRP). It has one hydrophilic poly(ethylene oxide) block and the other hydrophobic block containing CO_2-responsive diethylaminoethyl and O_2-responsive trifluoroethyl functional groups. In water, the amphiphilic copolymer self-assembled into vesicular nanoaggregates. When treated with CO_2, the vesicular morphology transformed into spherical micelle of smaller size, to accommodate the increased interfacial free energy. When treated with O_2, the vesicular morphology preserved but its volume expanded eight times. It was attributed to the intermolecular interaction between O_2 and FMA that slightly improved water solubility of the hydrophobic block. This dual gas-responsive polymer design significantly expands the scope of stimuli-responsive materials.

■ **ASSOCIATED CONTENT**

Ⓢ Supporting Information

Materials, polymer synthesis, sample preparation, characterization methods, and ^1H NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

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