Electronic Supplementary Information

Solvent-responsive polymer nanocapsules with controlled permeability: encapsulation and release of a fluorescent dye by swelling and deswelling

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General Methods.

All the reagents and solvents employed were commercially available and used as supplied without further purification. $(Allyloxy)_{12}$cucurbit[6]uril (**1**) was synthesized according to literature.[S1] Polymer nanocapsule **3** was prepared by thiol-ene photopolymerization of $(allyloxy)_{12}$cucurbit[6]uril, dithiol **2** as described previously.[S2] The average diameter of **3** was 120 ± 40 nm as measured by dynamic light scattering experiments. Photoreaction was performed in a quartz tube by irradiating UV light at 29 ^{o}C using a Rayonet photochemical reactor (Model: RMR-600) equipped with four 254 nm lamps and four 300 nm lamps. All fluorescence measurements were performed with 10-mm quartz cells on a Shimadzu RF-5301PC spectrofluorometer. Dialysis was performed using a Spectra/Por® RC membrane (MWCO: 8,000). Dynamic light scattering experiments were performed on a DLS-7000 instrument (Otsuka Electronics) using an argon ion laser operating with vertically polarized light at λ = 488 nm. SEM images were collected using a Phillips XL30S FEG scanning electron microscope operating at 5 kV. High-resolution TEM images were recorded on a JEOL-2010F electron microscope operating at 200 kV. Cryo-TEM images were recorded on a Tecnai 12 electron microscope (Phillips, Eindhoven, Netherlands) at approximately −170 ^{o}C and with a 120 kV acceleration voltage equipped with a Multiscan 600W CCD camera (Gatan, Inc., Warrendale, PA).

Synthesis of polymer nanocapsule 4. Excess ethyl vinyl ether (505 mg, 7.0 mmol) was added to a dispersion of polymer nanocapsule **3** (20.5 mg) in methanol (10 mL). The mixture was then irradiated with UV light (254 nm and 300 nm) for 20 h after purged with N_2. The product was purified by dialysis with methanol for 2 days to obtain a colloidal solution of polymer nanocapsules **4**, which was usually used for further experiments. After removal of most of the solvent, addition of diethyl ether yielded polymer nanocapsule **4** (13.6 mg, 74 %). Anal. Calcd. for $[(C_{72}H_{96}N_{24}O_{24})(C_6H_{12}O_2S_2)_{7.4}(C_4H_9O_1)_{2.8}(CH_4O)_9(C_4H_{10}O)_3]_n$: C, 47.84; H, 7.46; N, 9.01; S, 12.72%; found: C, 47.18; H, 6.86; N, 8.44; S, 11.94%.

Swelling and deswelling of polymer nanocapsule 4. The polymer nanocapsule **4** (136 μg) dispersed in pure methanol (100 μL) was added to methanol-water mixtures (9.9 mL) to make the final composition of the solvent such as 1, 5, 10, 20, 90, 95, 99 % water/methanol and incubated for a day. The average size change of the nanocapsule in response to the change in solvent composition was monitored by DLS studies and the sizes of the nanocapsules **4** in pure methanol and 10% methanol/water were also measured by cryo-TEM. In addition, the kinetics of the swelling process of the polymer nanocapsules **4** was monitored in 5 and 10% methanol/water mixtures by DLS daily for 15 days (Fig. S1). The deswelling experiment was carried out by placing the nanocapsule **4** that had been swelled in 10% methanol/water mixture in pure methanol for 1 day, and the hydrodynamic radius was measured by DLS.

Encapsulation of carboxyfluorescein into the polymer nanocapsule 4. For swelling a dispersion of polymer nanocapsule **4 (**1.36 mg) in methanol (1 mL) was added to water (9 mL) to make the final solvent composition 10% methanol/water, and was incubated for 1 day. Subsequently, carboxyfluorescein (CF, 1.760 mg, 4.68 μmol; 10.0 equiv with respect to the amount of the CB[6] unit present in the nanocapsule) was added to the solution as a guest molecule, and the mixture was stirred for another day. The resulting dispersion was purified by dialysis against methanol for 4 days to give a colloidal solution of CF loaded polymer nanocapsule, CF@**4**. During the dialysis free (unencapsulated) CF was removed and collected. The amount of free CF was measured by fluorometry. The amount of CF loaded in nanocapsule **4** was calculated by subtracting this number from the initial amount CF, which was found to be 0.43 μg per 1.0 mg of polymer nanocapsules **4**. The average diameter of the dye-loaded nanocapsule, CF@**4**, was determined by DLS. The successful encapsulation of the guest molecules was confirmed by fluorometry (Fig. S2).

Release of carboxyfluorescein from the polymer nanocapsule loaded with carboxyfluorescein (CF@4). The above CF loaded nanocapsule (0.23 μg of CF/544 μg of **4)** in methanol (4 mL) was dialyzed against methanol/water (36/360 mL) mixture, which ensures the final composition of the solvent 10% methanol/water, for 25 days. The release of CF during the dialysis was monitored by fluorometry daily by taking a small aliquot of the solution in a given interval. The amount of released CF was measured up to the saturation point in the release profile using a calibration curve of CF in 10 % methanol/water. At the end of the dialysis (25 days), approximately 91% of encapsulated CF molecules were found to be released compared to the amount of loaded CF.

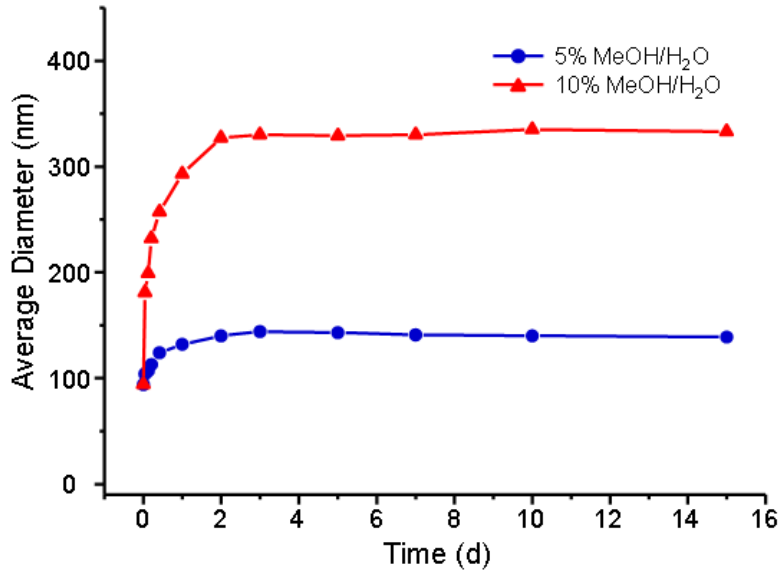

Fig. S1 Size change of polymer nanocapsule **4** in 5 % (●) and 10 % (▲) methanol/water as a function of time.

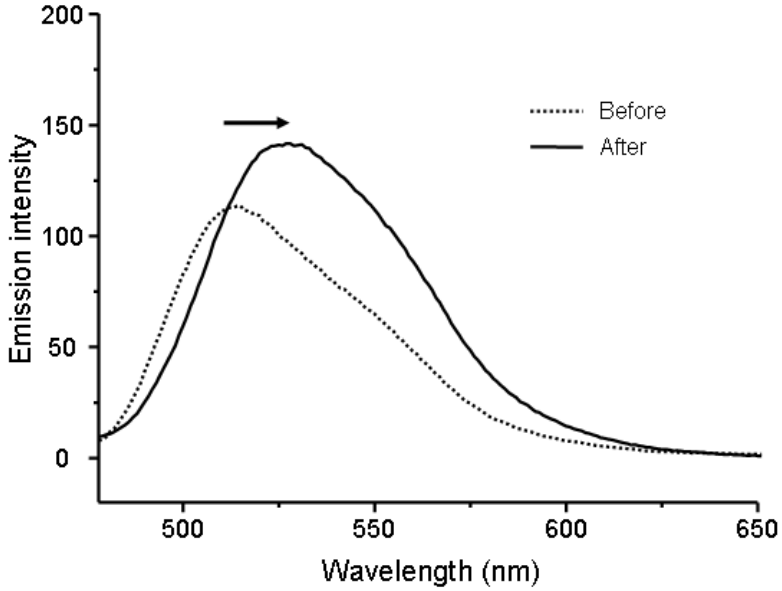

Fig. S2 Emission spectra of polymer nanocapsules CF@**4** (solid line, λ_{ex} = 458 nm, λ_{em} = 527 nm) and carboxyfluorescein before (dashed line, λ_{ex} = 458 nm, λ_{em} = 512 nm) in methanol.

Reference

[S1] S. Y. Jon, N. Selvapalam, D. H. Oh, J.-K. Kang, S.-Y. Kim, Y. J. Jeon, J. W. Lee, and K. Kim, *J. Am. Chem. Soc.,* 2003, **125**, 10186.

[S1] D. Kim, E. Kim, J. Kim, K. M. Park, K. Baek, M. Jung, Y. H. Ko, W. Sung, H. Kim, J. H. Suh, C. G. Park, O. S. Na, D.-k. Lee, K. E. Lee, S. S. Han and K. Kim, *Angew. Chem., Int. Ed.,* 2007, **46**, 3471.