

**Supporting information for:**

**Simultaneous Spectroscopic Measurements of  
the Interior Temperature and Induced Cargo  
Release from Pore-restricted Mesoporous Silica  
Nanoparticles**

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## **Experimental Section**

### **Material**

Yttrium(III) chloride (99.99 %, Aldrich), ytterbium(III) chloride hexahydrate (99.9 %, Aldrich), erbium(III) chloride hexahydrate (99.9 %, Aldrich), oleic acid (90%, Sigma-Aldrich), 1-octadecene (95.0 % Aldrich), ammonium fluoride (98.0 %, Sigma-Aldrich), sodium hydroxide (97.0 %, Fisher), 4-phenylazophenol (98 %, Sigma-Aldrich), 3-(triethoxysilyl)propyl isocyanate (95 % Aldrich), cetyltrimethylammonium bromide (CTAB) (95 %, Sigma-Aldrich), tetraethyl orthosilicate (TEOS) (98 %, Aldrich), ammonium nitrate (98 %, Sigma-Aldrich), cascade blue hydrazide, trisodium salt(Life Technologies), hexane (98.5 %, Fisher), toluene

(99.5 %, Sigma-Aldrich), methanol (99.9 %, Fisher), chloroform (99.8 %, Fisher) and ethanol (99.5 %, Fisher) were used. All chemicals are reagent grade and used without further purification or modification.

## Characterization

Transmission electron microscopy (TEM) was carried out on a JEM1200-EX (JEOL) instrument. High resolution transmission electron microscopy (HRTEM) was performed using a Titan S/TEM (FEI, 300kV) instrument. An Instrument SA HR 320 spectrograph/monochromator together with a PI-MAX intensified CCD camera from Princeton Instruments was used to record the luminescence spectra. Coherent CUBE 448 nm laser (20 mW) was used to excite the released fluorophore. A TechnicaLaser MLL-III-980-2w laser emitting 2 W at 980 nm was utilized as the exciting source for nanocrystals. A 950 nm cut-on filter(10SWF-950-B) and a 475 nm longpass glass filter from Newport were employed to filter out the exciting light at the detector window. The UV-vis absorption spectra were collected by a Cary 5000 UV-vis-NIR spectrophotometer.

## Synthesis of $\text{NaYF}_4:\text{Yb}^{3+}, \text{Er}^{3+}$ nanocrystals (ErNCs)

The lanthanide upconversion nanocrystals were synthesized by a modified thermolysis method using lanthanide chlorides as the precursors.<sup>S1,S2</sup> More detailedly,  $\text{YCl}_3$  (156 mg),  $\text{YbCl}_3 \cdot 6\text{H}_2\text{O}$  (70 mg) and  $\text{ErCl}_3 \cdot 6\text{H}_2\text{O}$  (8 mg) were mixed in a solution composed of 15 mL 1-octadecene and 12 mL oleic acid. The solution was heated to and kept at 120 °C for half an hour to remove the water, and slowly cooled down. In a separate container, 100 mg NaOH and 149 mg  $\text{NH}_4\text{F}$  were dissolved in 10 mL of methanol. After the lanthanide mixture was cooled to 50 °C, the basic  $\text{NH}_4\text{F}$  methanol solution was added into it and together, heated to 80 °C to evaporate the methanol. This reaction solution was then purged with argon gas and reacted at 300 °C for an hour. The solution was let to slowly cool down to room temperature. An excess amount of ethanol was added into the reacted dark solution

to precipitate the nanocrystals. They were further washed by hexane and ethanol, and suspended in chloroform at a concentration of 20 mg/mL.

The hydrophobic surface capping agent of the nanocrystals was exchanged to hydrophilic chains with the help of a surfactant, cetyltrimethylammonium bromide (CTAB). About 40 mg of ErNCs in the chloroform solution was added into an aqueous solution (20 mL) with 400 mg of CTAB. The mixture was thoroughly sonicated and slowly heated to 65 °C to evaporate the chloroform. The nanocrystal concentration in the resulted aqueous solution is about 2 mg/mL.

## **Synthesis of nanothermometer embedded functional MSNs**

Core-shell nanoparticles with 4-(phenyldiazenyl)phenyl propylcarbamate (PDAPPC) modifications were synthesized by adding the ErNCs into the previously reported co-condensation procedure.<sup>S3-S5</sup> The surfactant molecule, CTAB, serves both as the surface capping molecule for nanocrystals and as the templating agent for forming the particle porous structure. The procedure started with the synthesis of the PDAPPC linker molecule: 0.565 mmol of 4-hydroxyazobenzene was reacted with 141  $\mu\text{L}$  3-(triethoxysilyl)propyl isocyanate in 5 mL of anhydrous acetone under nitrogen gas for 4 h at room temperature. In a different container, 13.5 mL of  $\text{H}_2\text{O}$  was mixed with 1.5 mL of ErNC aqueous solution and the catalysis, 2 M NaOH (110  $\mu\text{L}$ ). The reaction solution was heated to 80 °C before 320  $\mu\text{L}$  of the as-prepared PDAPPC linker solution and 150  $\mu\text{L}$  of TEOS were added slowly. The reaction was continued at 80 °C for 2 h. The synthesized particles were separated by centrifuge and washed with water and methanol repeatedly. In order to remove the surfactant from the pores,  $\sim$  50 mg of particles were suspended in 60 mL of methanol together with 60 mL of water, into which 0.4 g of  $\text{NH}_4\text{NO}_3$  was added. The reaction was carried out at 60 °C for 30 min before the particles were centrifuged and washed by water and methanol.

## Temperature detection working curve

The working curve that correlates the nanoparticle internal temperature and the upconversion emission intensities of the lanthanide nanocrystals was generated by collecting the luminescence spectra at different temperatures. The ErNC embedded MSNs were submerged in water in a cuvette at a concentration of 1 mg/mL. The solution was heated slowly by a hot stir plate. When a desired temperature was reached, the 980 nm laser was switched on briefly for 10 s to collect the emission spectrum of ErNCs. The procedure was performed at various temperatures from 25 °C to 65 °C . For all the collected spectra, a background baseline was subtracted, and the 520 nm and 540 nm emission peak intensities were calculated. The natural logs of the intensity ratios were plotted against the inverse of absolute temperature to generate the linear correlation.

## MSN cargo loading and release

Blue fluorescent dye molecule cascade blue was loaded into the functionalized nanoparticles by suspending 10 mg of particles in 1 mL of 1 mM dye solution. The suspension was stirred for 24 h and washed with pure water to remove any surface absorbed dyes. Particles were then dried in air before use. To examine their release performance in according to the temperature change, 2 - 4 mg of the prepared particles were weighted and placed carefully in the corner of the cuvette. Water was added slowly to submerge the particles. A small stir bar was stirring the solution in the cuvette during the experiment without perturbing the particles. A 448 nm laser was directed to illuminate the supernatant aqueous solution and the fluorescence intensity of this solution was recorded by a CCD detector continuously as an indication of the released cargo amount. A 475 nm cut-off filter was placed in front of the detector. After collecting a baseline without activating the release system, the excitation beam at 980 nm was turn on to irradiate the particle pile in the corner of cuvette. Upon the finish of the experiment, the UV-vis absorption spectrum of the supernatant solution was scanned, in order to calculate the cargo release amount by using the Beer's law.

# Spectrum deconvolution

The luminescence spectra collected after turning on the 980 nm laser all have two components: the upconversion emission from ErNCs and the fluorescent signal from the released dye molecules. Since the two signals are partially overlapped, a simple mathematical processing was carried out to resolve the peaks following the equation below.

$$I'(j) = I(j) - k \cdot C(j), \text{ where } k = \frac{\int_{464}^{487} I(j) dj}{\int_{464}^{487} C(j) dj} \quad (1)$$

where  $I(j)$  stands for the raw intensity value of the collected spectrum at a certain wavelength  $j$ ;  $C(j)$  is the intensity value of the standard cascade blue solution at the wavelength  $j$ ;  $I'(j)$  is the lanthanide nanocrystal emission at the wavelength  $j$ , and  $k$  is the scale factor to normalize the cascade blue standard emission. For both of the raw spectrum and the standard cascade blue spectrum, the intensity was integrated from 464 nm to 487 nm to calculate the relative ratio  $k$ . In this range, cascade blue emission is the only component in the spectrum. In the overlapped part, the contribution of cascade blue emission is derived by normalizing the standard solution emission intensity ( $C(j)$ ) with the factor  $k$ . After subtracting the cascade blue band in the overlapped range, we could resolve the lanthanide emission intensity ( $I'(j)$ ) at a certain wavelength  $j$ . Figure 3 in the main manuscript illustrates this processing method. The black trace shows the original raw spectrum; the red trace is the calculated cascade blue contribution in the raw spectrum (the inset is the cascade blue standard solution emission); and the blue trace is the resolved upconversion emission. The intensity ratio of the 520 nm and 540 nm peaks in the blue spectrum is thus calculated and used to extract the temperature information by plugging into the working curve. The same baseline was subtracted from all of the spectra before this processing.

In an effort to evaluate the accuracy of the temperature measurement in this dual-detection mode, a control experiment was carried out where the same core-shell nanoparticles were not loaded and their internal temperature change under 980 nm irradiation was

recorded. In the absence of fluorescence signals from the dyes, the lanthanide emission intensity ratios could be collected and processed directly to retrieve the nanoparticle temperature, without the interference of dye emissions or the mathematic step to resolve the overlapped peaks. The unloaded particles were placed in the corner of cuvette and irradiated under the same experimental condition. The calculated nanoparticle temperatures are plotted as a function of irradiation time in Figure S1. The results (red solid squares) match with that of the loaded particles (blue empty circles) in the dual-detection release experiment, verifying that our method for nanoparticle temperature measurement in the dual-detection mode is valid and accurate.

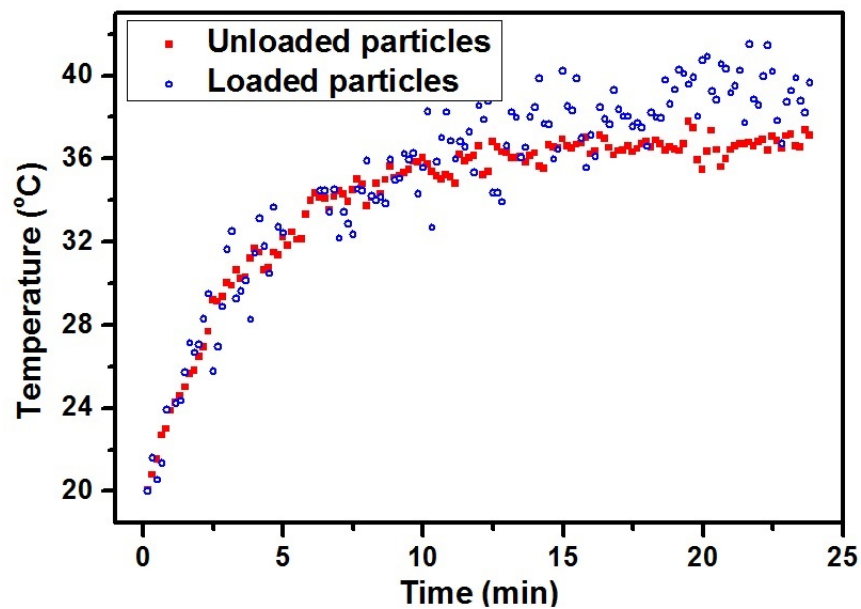


Figure S1: The nanoparticle local temperature measured simultaneously with the release behavior (blue empty circles) is compared with the that of it when only the particle temperature is examined (red solid squares). Our method proves to be valid in measuring the local temperature together with the cargo release performance.

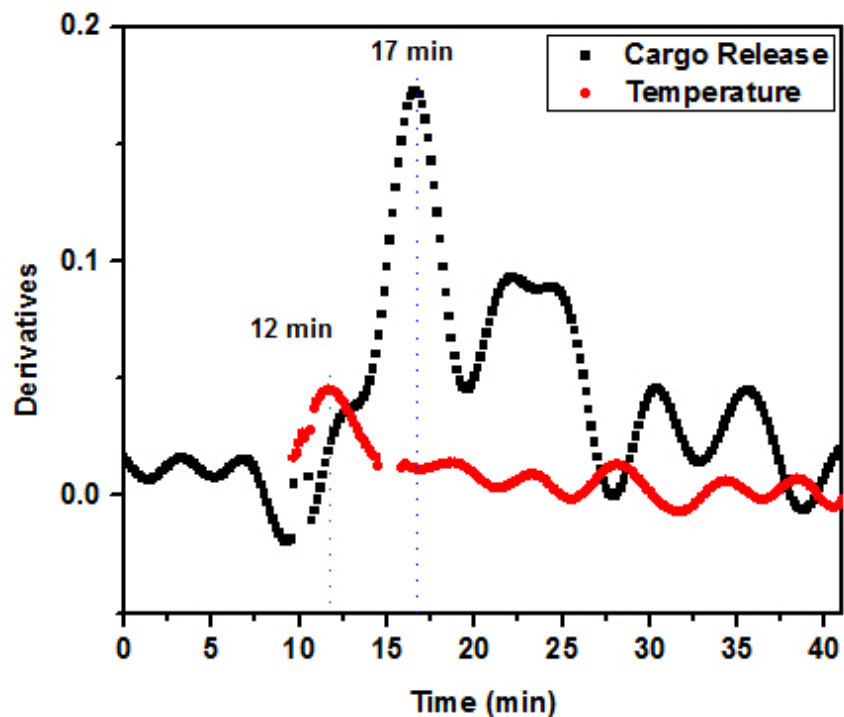


Figure S2: Derivative curves of the temperature change inside the nanoparticles and the cargo release amount as a function of the time. The maximum local temperature increase of nanoparticles occurred almost immediately after switching on the activation laser, suggesting the fast photothermal response. The cargo concentration change, on the other hand, accelerated about five minute after the heating started. It also experienced more fluctuation after reaching the maximum value than that of the temperature derivative. The lagging of the release event compared to the temperature acceleration suggests that the cargo release is motivated by the accumulation of their kinetic energy as the temperature increases and would need the extra energy absorption to be achieved. A SavitzkyGolay filter was applied to smooth both sets of results before the derivatives were calculated.



## References

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