Supporting Information

Differently Sized Magnetic/Upconversion Luminescent NaGdF4:Yb,Er Nanocrystals: Flow Synthesis and Solvent Effects

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Experimental Section

Chemicals. GdCl₃·6H₂O (450855), YbCl₃·6H₂O (337927), ErCl₃·6H₂O (259256), oleic acid (OA, 364525), 1-octadecene (ODE, O806), ammonium fluoride (NH₄F, 216011) were purchased from Sigma-Aldrich and used as received. Analytical grade chemicals such as NaOH, ethanol, cyclohexane, and tetrahydrofuran (THF) were purchased from Sinopharm Chemical Reagent Beijing, Co., Ltd and used as received. PEG2000 bearing a maleimide group at one end and two phosphate groups at the other end (mal-PEG-dp) was a customized product provided by Beijing Oneder Hightech Co., Ltd.

Preparation of Stock Solutions. A series of stock solutions was prepared according to the following recipe for flow synthesis of NaGdF4:Yb,Er nanocrystals. Typically, GdCl₃·6H₂O (0.80 mmol), YbCl₃·6H₂O (0.18 mmol), and ErCl₃·6H₂O (0.02 mmol) were mixed with 14 mL OA and 16 mL ODE in a 100-mL flask. The resultant mixture was then heated to 150°C to form a homogeneous solution under vacuum. After the solution was cooled down to room temperature, 10 mL of methanol solution containing NaOH (2.5 mmol) and NH₄F (4 mmol) was slowly introduced, and the mixture was then kept under stirring at room temperature overnight. Subsequently, methanol in the system was removed by keeping the reaction system at 100°C for 10 min under vacuum, and the stock solutions were obtained.

Flow Synthesis of NaGdF4:Yb,Er nanocrystals. After adding low boiling point

solvent (10 mL cyclohexane, 5 mL or 10 mL methanol) into the stock solution, the reaction mixture was pumped into a 7.4 m hastelloy tube reactor with an inner diameter of 1.0 mm where the temperature was maintained at 260°C. The system pressure was around 30 bars controlled by a back pressure regulator. The residence time was set to 30 min. After being cooled by air to room temperature, the resultant mixture was collected via sampling vials. The resultant nanocrystals were precipitated by ethanol, collected by centrifugation, washed with ethanol several times, and finally redispersed in cyclohexane or THF for further experiments.

Characterizations. Transmission electron microscope (TEM) images and electron diffraction patterns of the nanocrystals were taken on a JEM-100CXII electron microscope at an acceleration voltage of 100 kV. The particle size was determined by averaging at least 300 particles per sample. The upconversion luminescence spectra were recorded on a Cary Eclipse fluorescence spectrophotometer equipped with a 980 nm CW laser diode (2 W) serving as the excitation source. The concentrations of the rare earth elements in different systems were determined by using inductively coupled plasma atomic emission spectrometer (ICP-AES) produced by Jiangsu Skyray instrument Co., Ltd after the particles were eroded with concentrated nitric acid. The viscosities of solvents were tested by an AR-2000ex rheometer (TA Instruments, USA). Dynamic light scattering (DLS) measurements were carried out at 298.0 K with a Nano ZS (Malvern) equipped with a solid-state He-Ne laser ($\lambda = 633$ nm) for measuring the hydrodynamic size of the resultant nanoparticles.

Ligand exchange. Approximately 10 mg of the purified nanocrystals and 100 mg of mal-PEG-dp were dissolved in 5 mL THF. Typically, the ligand exchange reaction took place overnight at room temperature. Then, the PEGylated particles were precipitated by cyclohexane, washed with cyclohexane for three times, and dried under vacuum at room temperature. The particle powders obtained were found to be readily dissolved in water, supporting that the PEG coating was effectively realized. To remove excess PEG ligand, the resultant aqueous solutions containing the PEGylated particles were purified by ultrafiltration for 4 cycles using 10 kDa MWCO centrifugal filter

(Millipore YM-10).

Relaxivity Measurements. The relaxivity measurements were carried out on a 3 T clinical MRI instrument (Philips Achieva 3.0 T TX). A series of aqueous solutions with different concentrations of (mal-PEG-dp)-coated NaGdF4:Yb,Er particles were prepared and transferred into 2 mL Eppendorf tubes for longitudinal magnetic relaxivity measurements. The parameters were set as follows: echo time (TE) = 15.3 ms; repetition time (TR) = 500, 1000, 1500, 2000 ms; number of excitations (NEX) = 8.

Supplementary Results



Fig. S1. Size distributions of NaGdF4:Yb,Er nanocrystals (shown in Fig. 1) prepared in the absence of any low boiling point solvent (a), in the presence of 10 mL cyclohexane (b), 5 mL methanol (c), or 10 mL methanol (d).



Fig. S2. TEM image (a) and histogram (b) of NaGdF4:Yb,Er nanocrystals prepared by adding 10 mL ODE into the stock solution.



Fig. S3. Plots of R_1 versus the concentration of the PEGylated NaGdF₄:Yb,Er nanoparticles overlaid with linear fitting curves for extracting the longitudinal relaxivities.

The diffusion coefficient **D**

D can be obtained from Einstein's formula

$$D = \frac{k_{\rm B}T}{6\pi\mu r_{\rm p}}$$
 S(1)

 $k_{\rm B}$ is Boltzmann constant, *T* is reaction temperature, μ is the viscosity of solvent, and $r_{\rm p}$ is the average radius of the nanoparticle.

It can be seen from S(1) that D is inversely correlated with μ , so the reaction system

in the presence of cyclohexane or methanol has more increased D than that in absence of low boiling point solvent.