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Supporting Information

The Yin and Yang of Coordinating Co-Solvents in the Size-Tuning of Fe_3O_4 Nanocrystals through Flow Synthesis

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Experimental Section

Chemicals. Ferric acetylacetonate ($Fe(acac)_3$, 517003), oleylamine (OM, O7805), oleic acid (OA, 364525), 1-octadecanol (258768), 1,2-dodecanediol (213721) were purchased from Sigma-Aldrich and used as received. Anisole (A103683) were purchased from Aladdin and used as received. Analytical grade chemicals such as acetone, ethanol, cyclohexane, and tetrahydrofuran (THF) were purchased from Sinopharm Chemical Reagent Beijing, Co., Ltd and used as received. PEG2000 bearing a catechol group (CC-PEG) was a customized product provided by Beijing Oneder Hightech Co., Ltd.

Preparation of Stock Solutions. A series of stock solutions were prepared according to the following recipe for flow synthesis of Fe_3O_4 nanocrystals. Typically, $Fe(acac)_3$ (2.0 mmol), 1-octadecanol (10.0 mmol), OM (6.0 mmol) and OA (6.0 mmol) were mixed in 20 mL anisole in a 50-mL flask. The resultant mixture was stirred at room temperature to form a homogeneous solution. After being purged with nitrogen for 10 min, the stock solution was obtained. For preparing differently sized Fe_3O_4 nanocrystals, the concentrations of OM and OA and species of alcohols were adjusted within the stock solutions.

Flow Synthesis of Fe_3O_4 nanocrystals. The stock solution was pumped into a 7.4 m hastelloy tube reactor with an inner diameter of 1.0 mm where the temperature was maintained at 250°C. The system pressure was around 30 bar controlled by a back pressure regulator. The residence time was set as 3 min. After being cooled by air to room temperature, the resultant mixture was collected via sampling vials. The resultant nanocrystals were precipitated by acetone, collected by centrifugation, washed with acetone for three cycles, and finally redispersed in cyclohexane or THF for further experiments.

Characterizations. Transmission electron microscope (TEM) images 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. Fourier transform infrared (FTIR) spectra of the nanocrystals, OM and OA were recorded on a Bruker EQUINOX55 FT-IR spectrometer at room temperature. UV–Vis absorption spectra of the iron solutions were recorded at 25°C on a Cary 50 UV–Vis absorption spectrometer. Powder X-ray diffraction (XRD) pattern of the particle sample was recorded on a Regaku D/Max-2500 diffractometer under Cu Kα_1 radiation (λ = 1.54056 Å). The viscosities of solvents were tested by an AR-2000ex rheometer (TA Instruments, USA). Dynamic light scattering (DLS) measurements were carried out at 25°C with a Nano ZS (Malvern) equipped with a solid-state He-Ne laser (λ = 633 nm) for measuring the hydrodynamic size of the resultant nanoparticles.

Ligand exchange. Approximately 10 mg of the purified nanocrystals and 100 mg of CC-PEG were dissolved in 5 mL THF. Typically, the ligand exchange reaction took place overnight at 40°C. Then, the PEGylated particles were precipitated by cyclohexane, washed with cyclohexane for three cycles, 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 3.0 T clinical MRI instrument (Philips Achieva 3.0 T TX). A series of aqueous solutions with different concentrations of CC-PEG-coated Fe_3O_4 particles were prepared and transferred into 2 mL Eppendorf tubes for longitudinal and transverse magnetic relaxivity measurements. The parameters for T_1 measurements were set as follows: echo time (TE) = 25.3 ms; repetition time (TR) = 500, 1000, 1500, 2000 ms, number of excitations (NEX) = 8. For T_2 measurements, the parameters were set as: TR = 2000 ms; and TE = 20, 40, 60, 80, 100 ms; number of excitations (NEX) = 8.

Supplementary Results

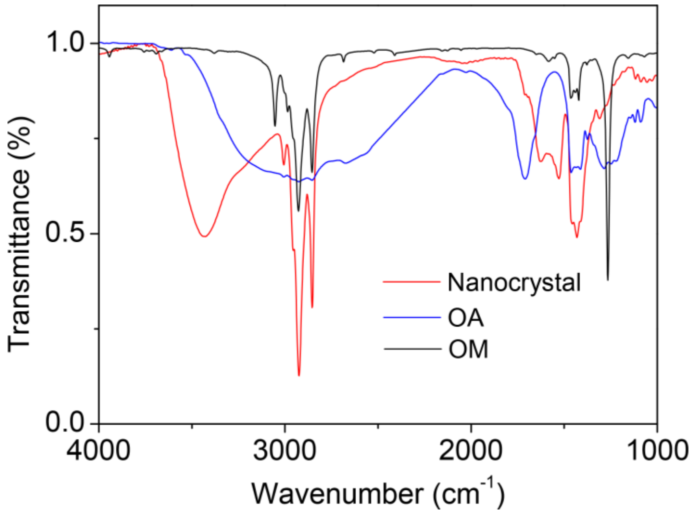

Fig. S1. FTIR spectra of the as-prepared Fe_3O_4 nanocrystals, OM and OA.

It can be found from Fig. S1 that the C=O stretch band of carboxyl group, peaking at 1712 cm^{-1} in the spectrum of OA, disappears in the spectrum of Fe_3O_4 nanocrystals, suggesting the carboxylate group of deprotonated OA in the presence of OM coordinates with the particle surface by donating its lone pair of electrons to Fe. The -NH_2 symmetric stretch vibration of OM at 1257 cm^{-1} is also greatly reduced for that of the nanocrystals, revealing the coordination between OM and the particle surface.

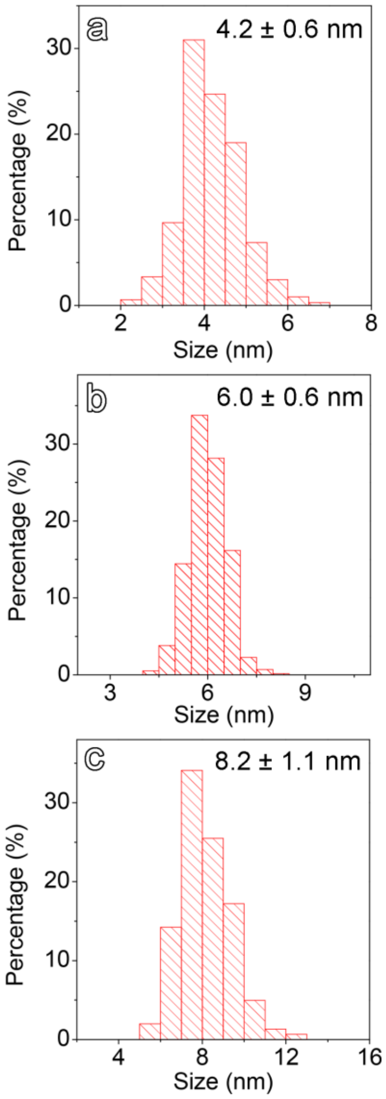

Fig. S2. Size distributions of Fe_3O_4 nanocrystals (shown in Fig. 1) prepared in the presence of different concentration of OM/OA: (a) 0.3 M, (b) 1.2 M, and (c) 0.6 M, respectively.

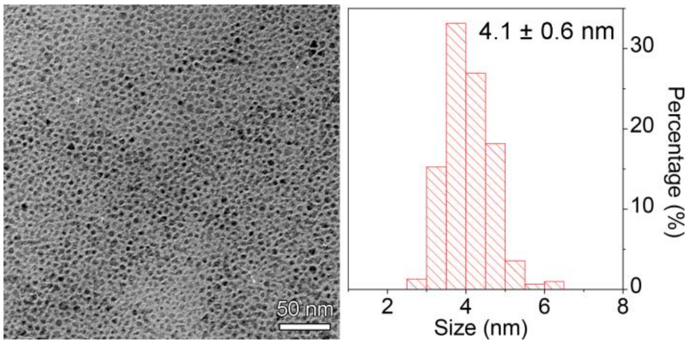

Fig. S3. TEM image and histogram of the Fe_3O_4 nanocrystals prepared by adding 11.5 mL anisole instead of OM/OA into the initial stock solution.

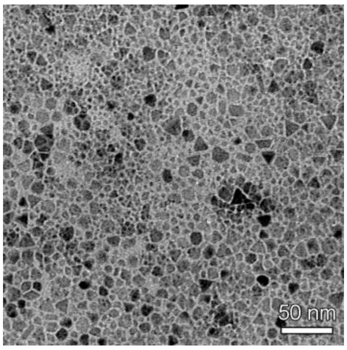

Fig. S4. TEM image of the nanocrystals prepared in the presence of 0.15 M OM/OA.

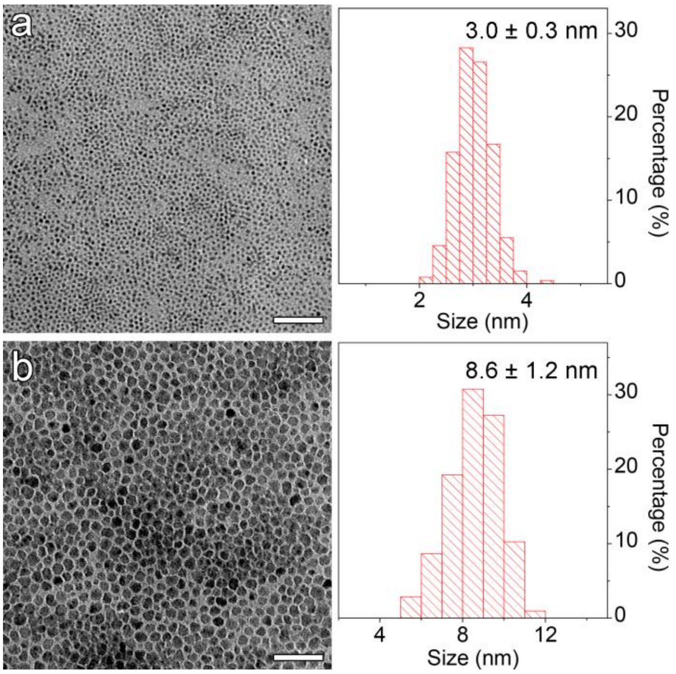

Fig. S5. TEM images of the Fe_3O_4 nanocrystals prepared in the presence of 0.6 M OM/OA, and 10.0 mmol 1,2-dodecanediol (a), no alcohol (b) (the scale bars correspond to 50 nm), and the corresponding histograms.

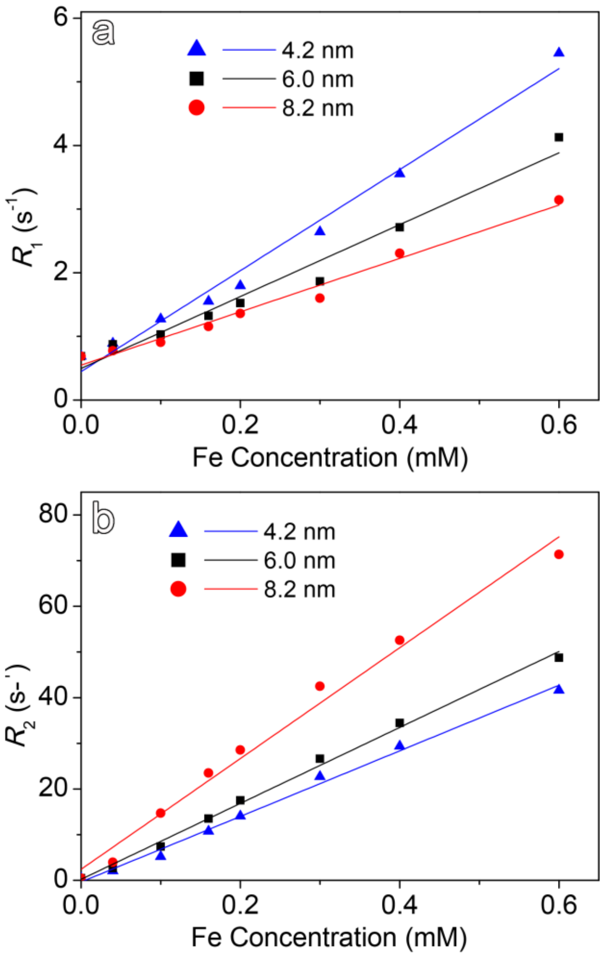

Fig. S6. Plots of R_1 (a) and R_2 (b) versus the concentration of the PEGylated Fe_3O_4 nanoparticles with different size overlaid with linear fitting curves for extracting the longitudinal and transverse relaxivities.

The diffusion coefficient *D*

D can be obtained from Einstein's formula

$$D = \frac{k_B T}{6\pi\mu r_p} \qquad S(1)$$

k_B is Boltzmann constant, T is reaction temperature, μ is the viscosity of solvent, and r_p is the average radius of the nanoparticle.

It can be seen from S(1) that D is inversely correlated with μ, therefore, due to the increased viscosity of the reaction system in the presence of 1.2 M OM/OA, the diffusion coefficient D is smaller than that of the reaction system in the presence of 0.6 M OM/OA.