

Supporting Information

Hybrid Polymeric Nanostructures Stabilized by Zirconium and Gadolinium ions for Use as Magnetic Resonance Imaging Contrast Agents

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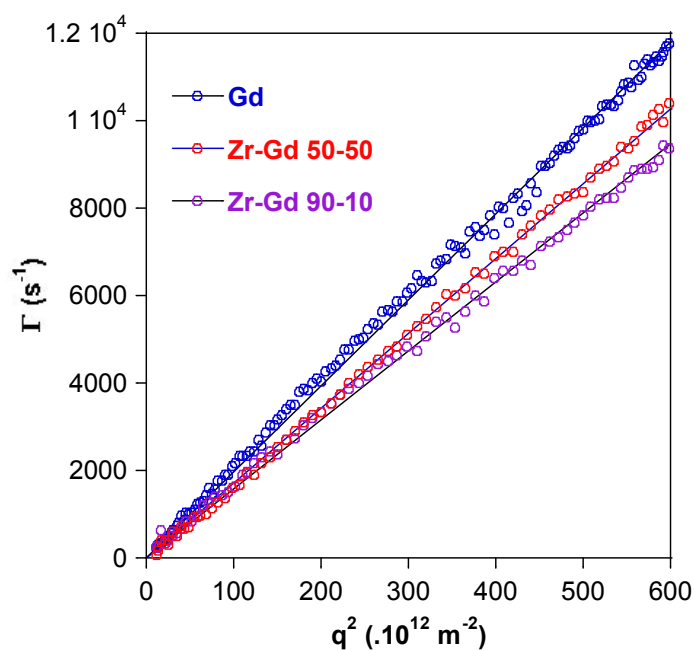
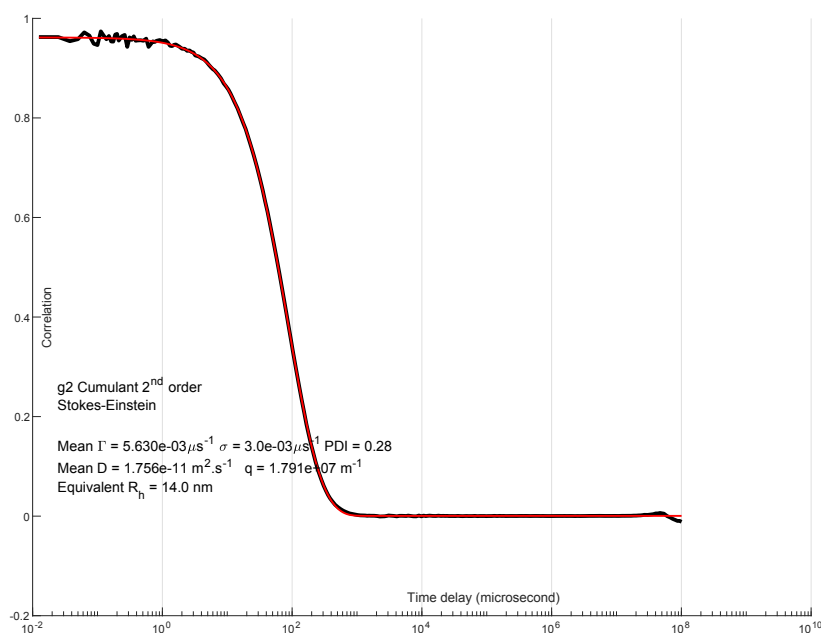


Figure S1. Top : typical correlogram (black solid line) obtained for (90% Zr- 10% Gd) HPIC solution at a scattering angle of 90°. In red, best fit using the cumulant method (second order) with the M-STORMS software.

Bottom: Analysis of the multi-angle DLS data for various HPIC solutions. The decay rate Γ , estimated using the cumulant method, was calculated for various angles and therefore scattering vector q . Blue circles: HPIC with pure Gd ($\rho_{\text{Gd}} = 100\%$). Red circles: HPIC with 50% Gd – 50 % Zr ($\rho_{\text{Gd}} = 50\%$). Purple circles: HPIC with 10% Gd – 90 % Zr ($\rho_{\text{Gd}} = 10\%$).

The linear dependency of $\Gamma=1/T_1$ versus q^2 is expected for nano-objects undergoing Brownian motion. The decreasing slope of Γ versus q^2 with the increasing Zr content suggests a slight increase of the HPIC radius when zirconium is added (see Table 1).

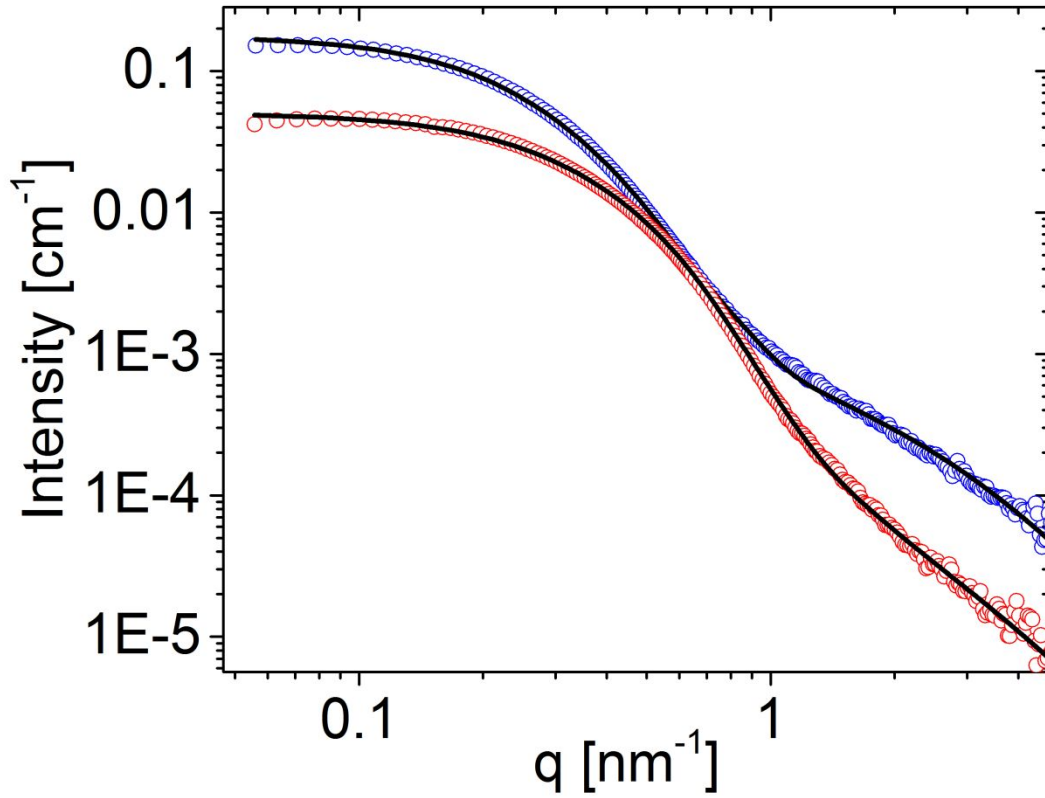


Figure S2. SAXS: Scattering curve (symbols) and relative fit (line) of HPIC Gd 100% (red circles) and Gd-Zr 50 % (blue circles) at pH 6.2 in aqueous solution at 25°C.

The low- q region of the data was used to evaluate the radius of gyration, R_g , using the Guinier analysis according to eq. (1) (see A. Guinier, G. Fournet, Small-Angle Scattering of X-Rays, John Wiley & Sons, New York (1955)):

$$I(q) = I_o \exp \left(-\frac{R_g^2}{3} q^2 \right) \quad (1)$$

The value of the R_g for the HPICs (see Table S1) was found around 5-7 nm and is increasing with the Zr content.

| | R_g (nm) | R_c (nm) | R_s (nm) |
|---------------------|------------|---------------|------------|
| $\rho_{Gd} = 100\%$ | 4.6 | 2.8 ± 0.8 | 3.3 |
| $\rho_{Gd} = 50\%$ | 6.7 | 3.3 ± 0.9 | 4.8 |

Table S1. Characteristic size as obtained by the fitting using as a model for the nano-objects a spherical polydisperse core-shell particle plus the Ornstein-Zernike term as described in the main text.

The SAXS background-subtracted scattered intensity $I(q)$ for non-interacting nano objects ($S(q) \approx 1$) can then be expressed as:

$$I(q) = NV^2 \Delta \rho^2 P(q) \quad (2)$$

where N is the number of particles per unit volume V , $\Delta \rho$ is the difference in the scattering length densities (SLD) between the nano-objects and the medium, $P(q)$ and $S(q)$ are the form and the structure factor, describing the shape and interaction between particles, respectively.

Here the data were analysed by using the form factor of polydisperse spherical core-shell particles $P(q)_{CS}$.

$$P(q)_{cs} = \left[V_c(\rho_c - \rho_s) \frac{\sin(qR_c) - qR_c \cos(qR_c)}{(qR_c)^3} + V_s(\rho_s - \rho_m) \frac{\sin(qR_e) - qR_e \cos(qR_e)}{(qR_e)^3} \right]^2 \quad (3)$$

V_c and V_s indicate the volumes of core and shell, R_c the radius of the core, R_e is the external radius, and ρ_c, ρ_s, ρ_m are the SLD of the core (PAA and inorganic ions), shell (PEO) and solvent. The spatial fluctuations of the polymer chains in the shell were also added to model the high- q behaviour of the scattering data (Ornstein-Zernike term). Therefore, the total intensity $I(q)$ is described as:

$$I(q) = V^2 \Delta \rho^2 P(q)_{cs} + I(q)_{OZ} \quad (4)$$

$$\text{where } I(q)_{OZ} = \frac{I_0}{(1 + \xi^2 q^2)^d}$$

Where d was fixed to 1.6 as expected for swollen polymer chains in good solvent.

The SLD of the core was calculated considering the presence of Gd^{3+} , ZrO_2^{2+} and acrylic acid units according to their stoichiometry and used as fixed parameter for the fitting: 0.001197 nm^{-2} . The measured scattering was found to mainly originate from the core of the nano-objects, since the PEO chains of the corona show low X-ray contrast (SLD of the PEO shell 0.00097 nm^{-2}). From the fitting procedure, a radius of the core R_c around 3 nm and a radius of the shell, R_s , around 3-5 nm were obtained. The calculated sizes of the nano-objects are smaller than the one estimated from DLS. This is expected: hydrated PEO layer should be poorly characterized by SAXS and DLS leads to hydrodynamical sizes larger than the geometrical dimension. The ratio $(R_g/R)^2$ found around 0.6 – 0.7 is very similar to the one expected for a solid sphere (i.e. 3/5), thus indicating the compactness of the core of the nano-objects.

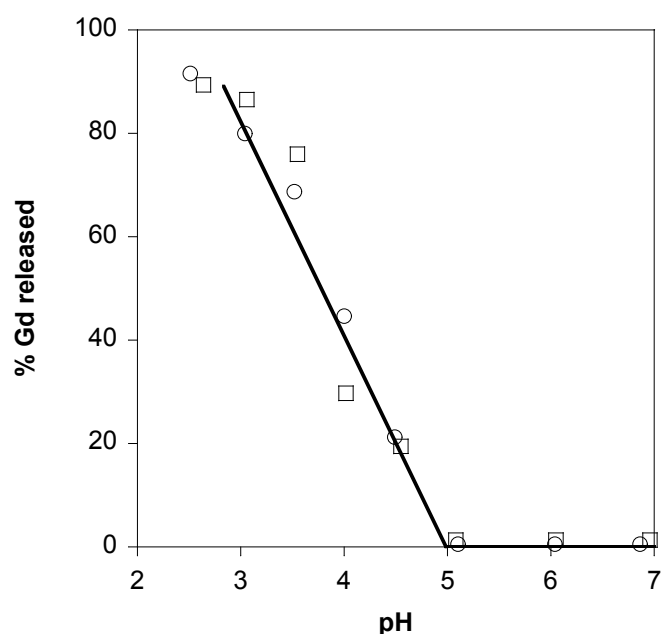


Figure S3. Percentage of gadolinium released from the HPICs versus the pH. This percentage is determined by titration using inductively coupled plasma atomic emission spectrometry (ICP-AES) of the HPIC solutions (open circles 25% Gd – Zr 75% HPICs and open square 10% Gd – 90% Zr HPICs) filtered with centrifugal filters. Results demonstrate that virtually no gadolinium is released from the polymeric assemblies for pH above 5 and that no effect on the composition was detected.