Electronic Supplementary Material (ESI) for Journal of Materials Chemistry B.

ELECTRONIC SUPPLEMENTARY INFORMATION

Magnetic field responsive drug release from magnetoliposomes in biological fluids

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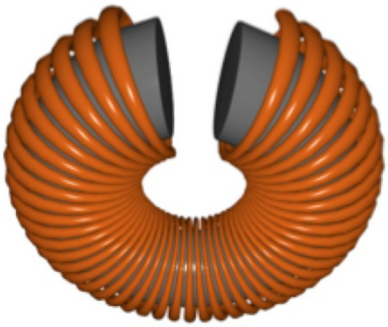
LF-AMF Setup

Fig. S1. Picture of the broken toroidal magnet used to apply the LF-AMF.

Magnetic Field at Different Positions

- **A** ≈ 270 mT
- **B** ≈ $\mathbf{B^{I}}$ ≈ 100 mT
- **C** ≈ $\mathbf{C^{II}}$ ≈ 280 mT
- **D** ≈ $\mathbf{D^{I}}$ ≈ $\mathbf{D^{II}}$ ≈ $\mathbf{D^{III}}$ ≈ 330 mT

10 V; 8 A



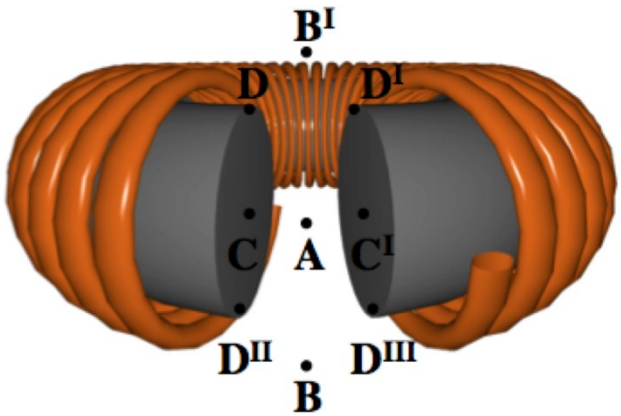


Fig. S2. Magnetic field values at different positions of the broken toroidal magnet used to apply the LF-AMF. Magnetic field values were measured by means of a GM-07 Gaussmeter (HIRST Magnetic Instruments Ltd, UK).

Size distributions of liposomes in serum

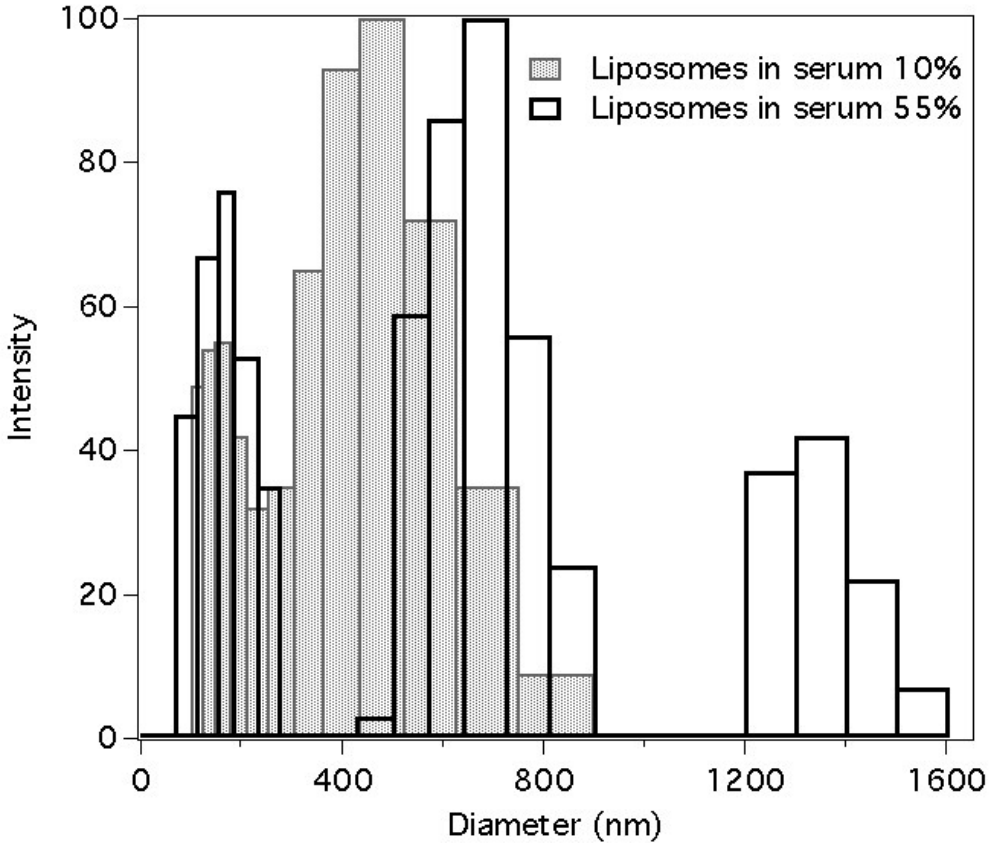
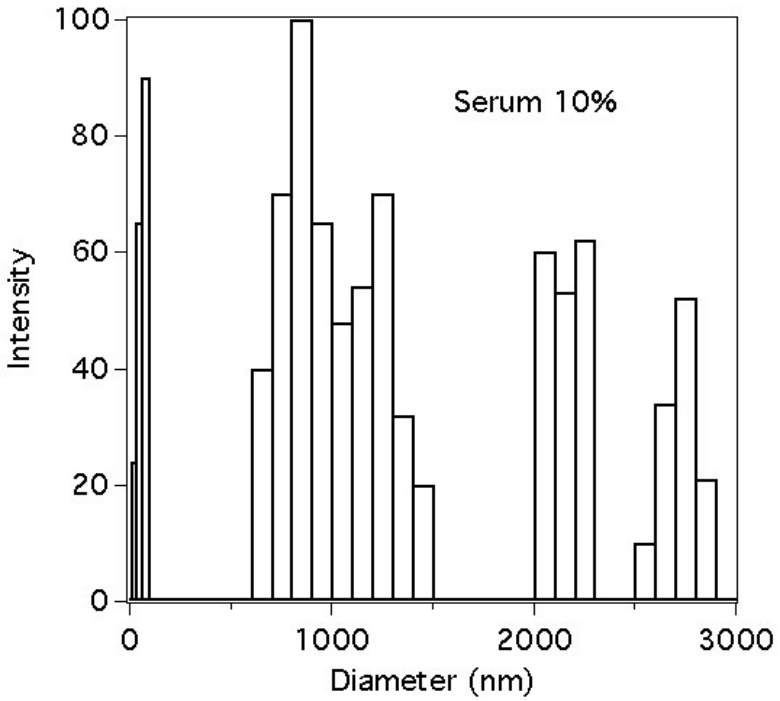
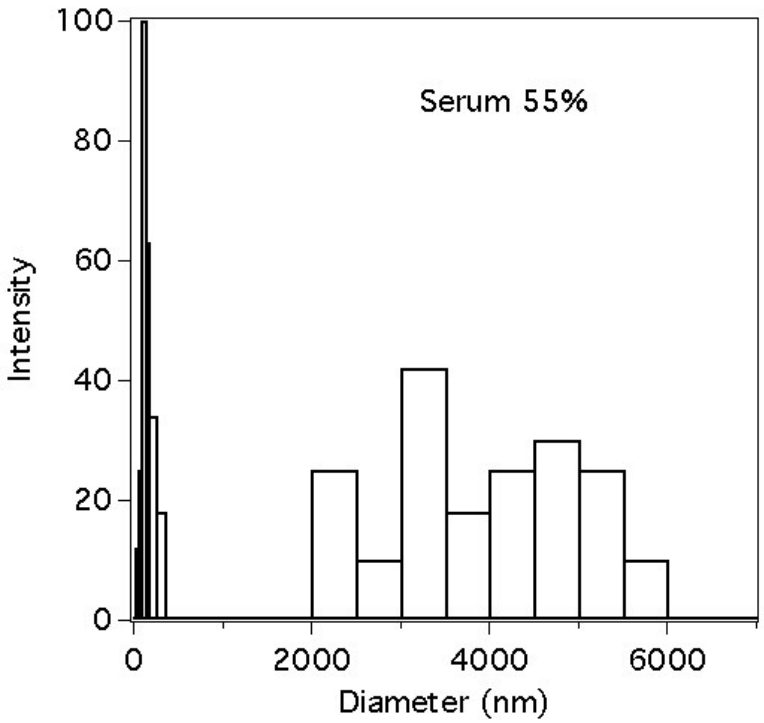


Fig. S3. Representative size distributions of liposomes in serum 10% (grey bars) and in serum 55% v/v (empty bars).

Size distributions of serum 10% and 55% v/v



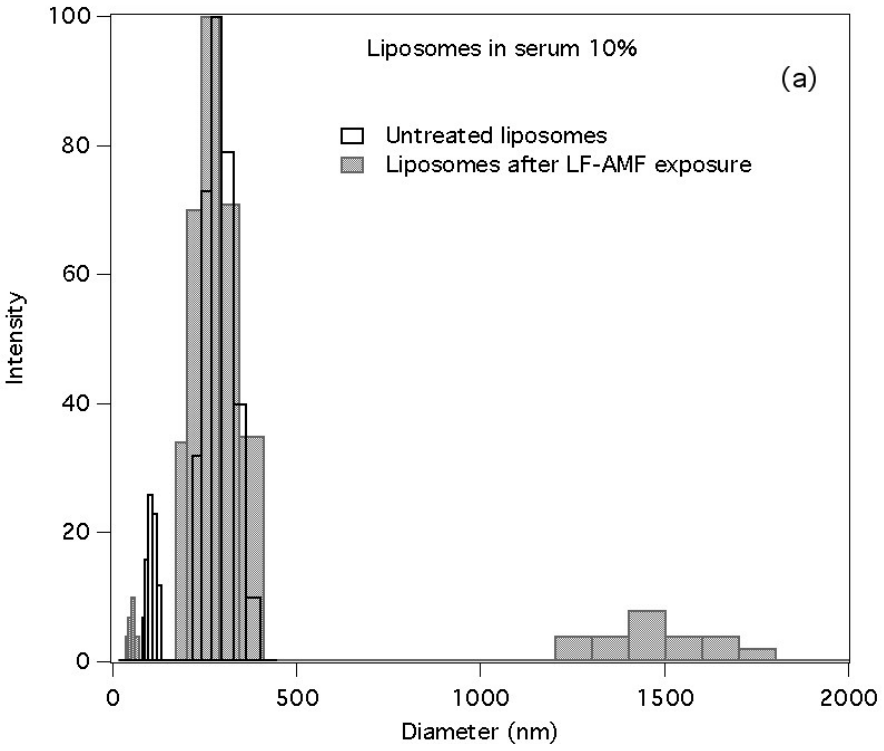
(a)

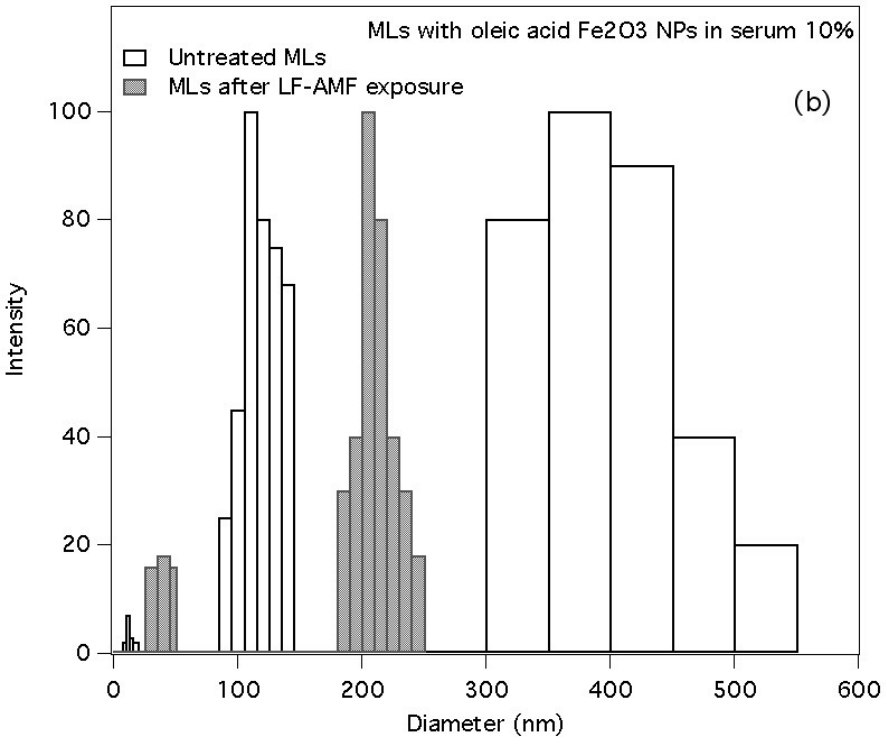


(b)

Fig. S4. Representative size distributions of (a) serum 10% v/v and (b) serum 55% v/v.

Size distribution of samples in serum before and after LF-AMF exposure





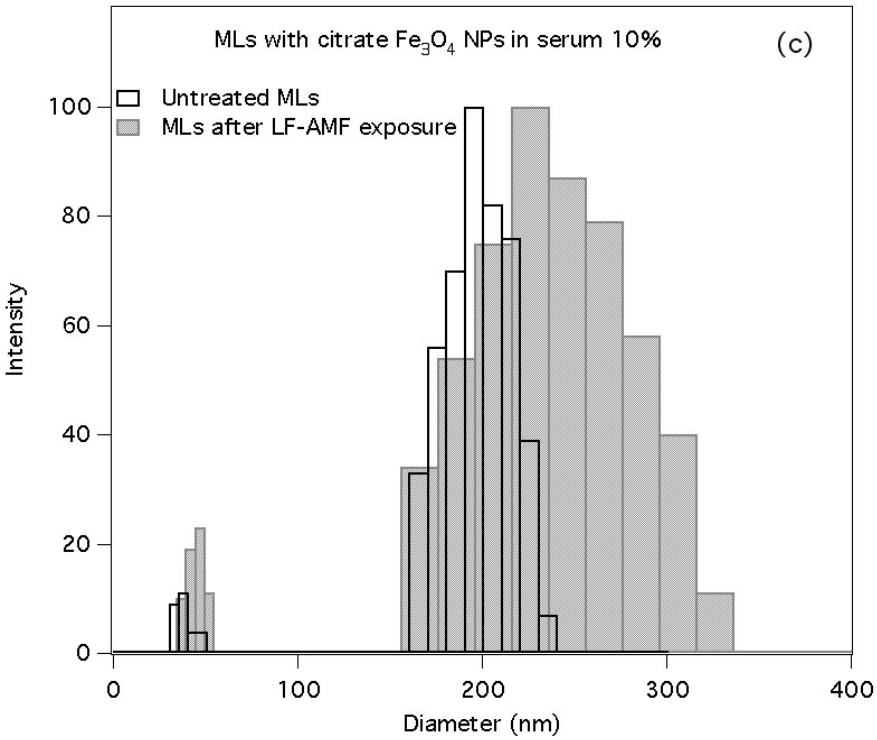


Fig. S5. Representative size distributions of (a) liposomes, (b) magnetoliposomes with oleic acid Fe_2O_3 NPs and (c) magnetoliposomes with citrate Fe_3O_4 NPs in serum 10% v/v before (empty bars) and after LF-AMF exposure (grey bars (empty black bars)

Optical microscopy images of liposomes and magnetoliposomes

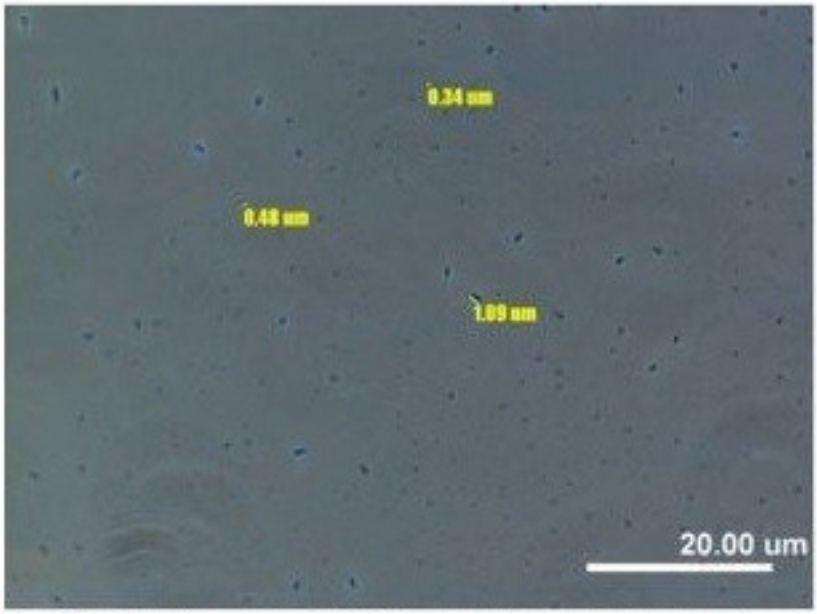


Fig. S6. Liposomes in serum 55% v/v before LF-AMF exposure

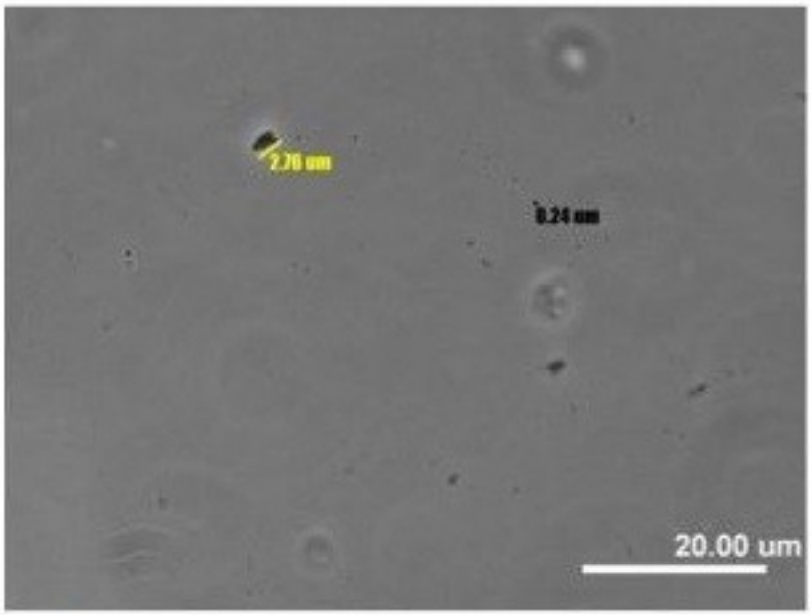


Fig.S7. Liposomes in serum 55% v/v after LF-AMF exposure

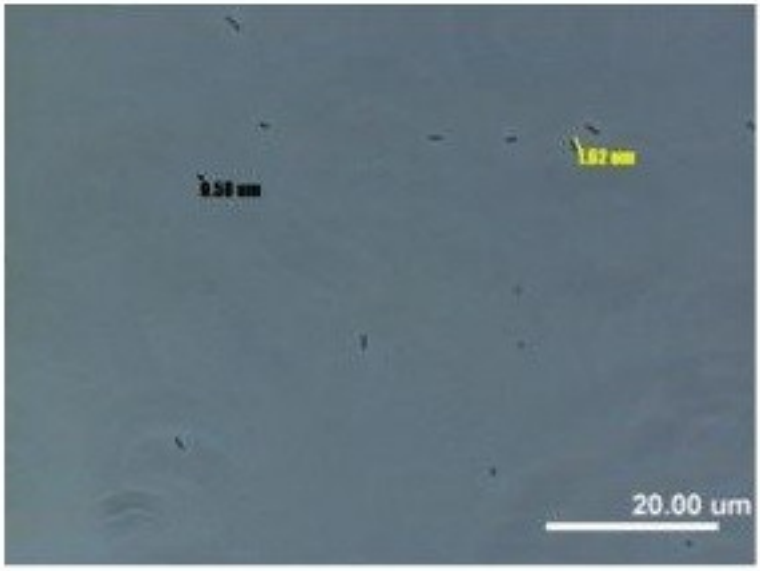


Fig. S8 Magnetoliposomes with oleic acid coated- Fe_2O_3 NPs in serum 55% v/v before LF-AMF exposure

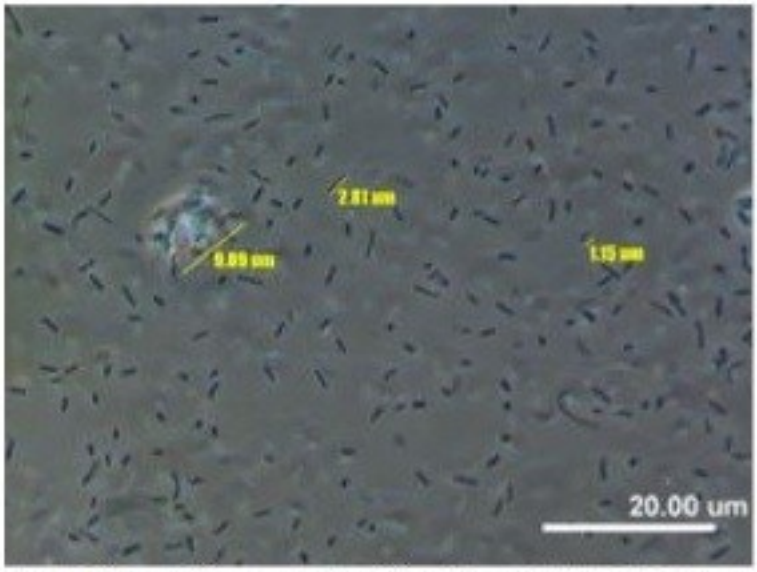


Fig. S9 Magnetoliposomes with oleic acid coated- Fe_2O_3 NPs in serum 55% v/v after LF-AMF exposure

SAXS of liposomes in serum

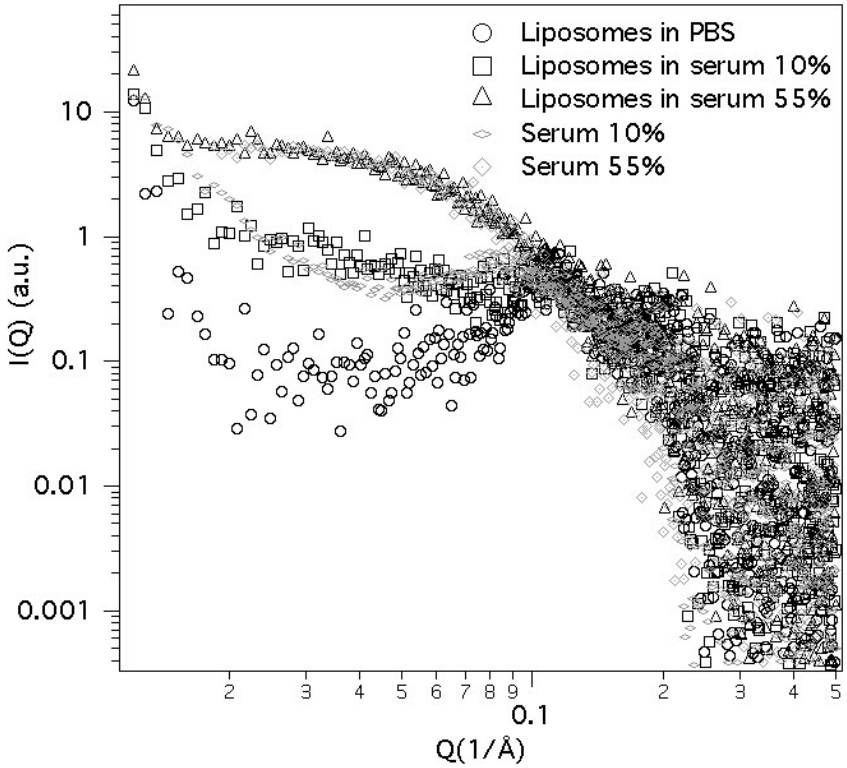


Fig. S10. SAXS spectra of liposomes in (○) PBS, (●) serum 10% (❒) and serum 55%. SAXS spectra of (🕑) serum 10% v/v and (❋) serum 55% v/v.

Release from liposomes (reference sample)

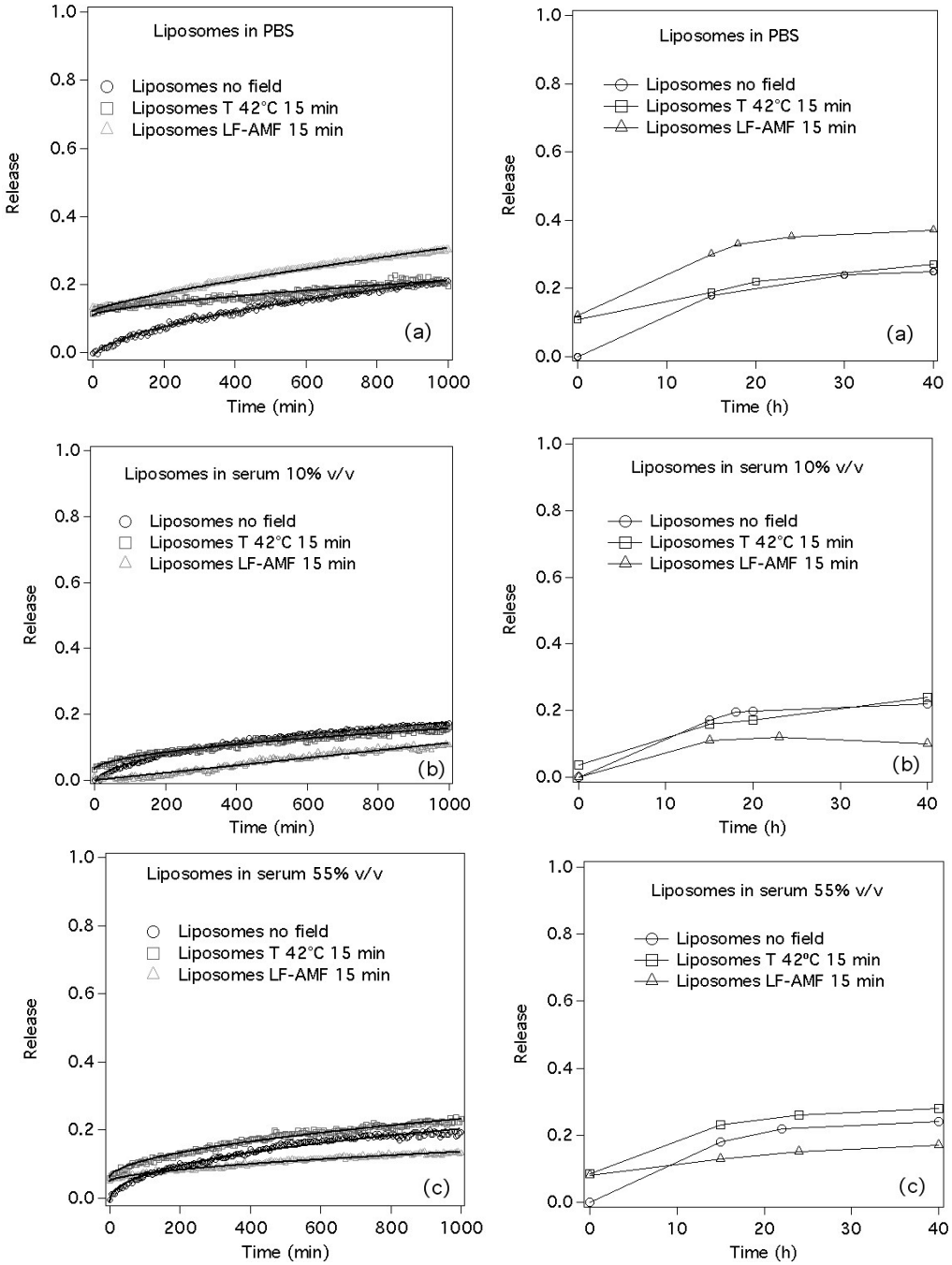


Fig. S11. CF release kinetics of liposomes dispersed in (a) PBS, (b) serum 10% and (c) serum 55% v/v.

Kinetic parameters of CF release from liposomes

	PBS	SERUM 10%	SERUM 55%
No field			
n	0.55±0.01	0.46±0.01	0.44±0.02
K	$5.01\cdot10^{-3}\pm0.48\cdot10^{-3}$	$1.17\cdot10^{-2}\pm0.12\cdot10^{-2}$	$1.57\cdot10^{-3}\pm0.01\cdot10^{-3}$
LF-AFM			
n	0.85±0.02	1.10±0.02	0.79±0.07
K	$5.09\cdot10^{-4}\pm0.36\cdot10^{-4}$	$9.89\cdot10^{-5}\pm0.44\cdot10^{-3}$	$1.57\cdot10^{-3}\pm0.01\cdot10^{-3}$

Calibration curves of Carboxyfluorescein in serum

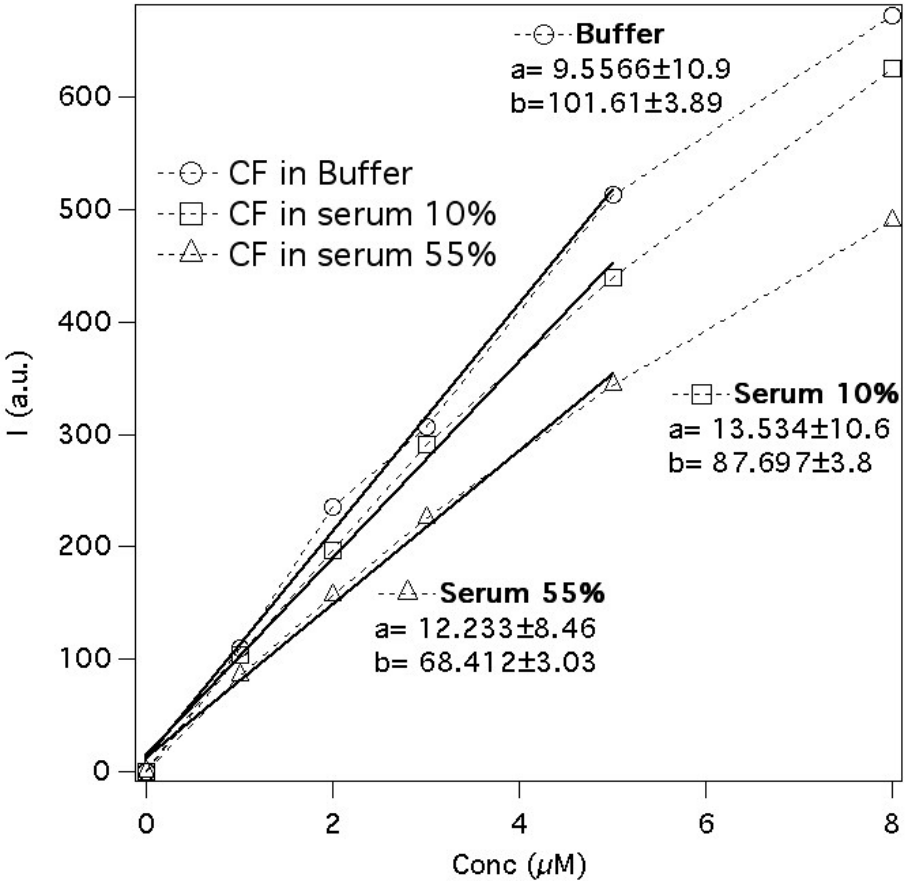


Fig. S12. Calibration curves of Carboxyfluorescein (CF) in (○) PBS, (□) serum 10% v/v and (❒) serum 55% v/v.

Models for the fitting SAXS analysis

Liposomes

The SAXS spectrum of liposome solution (control sample) has been fitted according to a model proposed by Nallet *et al*[1] for lamellar phases of amphiphilic bilayer, through the following equation:

$$I(Q) = \frac{2\pi P(Q)}{2(\delta_H + \delta_T)q^2} \qquad (1)$$

where the form factor is given by:

$$P(Q) = \frac{4}{q^2}\left\{\Delta\rho_H\left[\sin[q(\delta_H+\delta_T)] - \sin(q\delta_T)\right] + \Delta\rho_T \sin(q\delta_T)\right\}^2 \qquad (2)$$

and δ_H is the head group thickness, δ_T is the tail length, $\Delta\rho_H$ (ρ_H - ρ_{solv}) and $\Delta\rho_T$ (ρ_T - ρ_H) are the scattering length density contrast, where ρ_H , ρ_T and ρ_{solv} are the scattering length density of head group, tail and solvent, respectively. In the fitting, the scattering length densities corresponding to the theoretical atomic compositions were used. In this model no inter-lamellar structure factor S(Q) is included.

Magnetoliposomes

SAXS spectrum of magnetoliposomes has been modelled according to the following equation:

$$I(Q) = I_{liposomes} + I_{MagNPs} + I_{bkg} \quad (3)$$

where $I_{liposomes}$ is the scattering intensity from the liposomes, while I_{MagNPs} is the scattering intensity arising from magnetic nanoparticles arranged in fractal clusters and modelled according to the pearl necklace model[2]. We previously used this model to describe polydisperse spherical nanoparticles with a core-shell structure, arranged into fractal clusters[3]. The spherical particles have a constant shell thickness and a core with a Schulz distribution of radii[3,4]. The contribution to the total scattering intensity arising from these objects was calculated according to:

$$I_{MagNPs} = \phi P(Q) S(Q) \quad (4)$$

where ϕ is the particle volume fraction, P(Q) is the form factor and S(Q) is the interparticle structure factor accounting for the interparticle correlations. The form factor was modelled as:

$$P(Q) = (1/V_p)\int_0^\infty G(r_c)F^2(Qr_c)dr_c \quad (5)$$

$$F(Qr_c) = (4\pi/Q^3)(\rho_{shell} - \rho_{core})\{\rho_{scaled} j[Qr_c + (t/r_c)Qr_c] - j(Qr_c)\} \quad (6)$$

$$\rho_{scaled} = (\rho_{solv} - \rho_{shell})(\rho_{core} - \rho_{shell}) \quad (7)$$

$$j(Qr_c) = \sin(Qr_c) - (Qr_c)\cos(Qr_c) \quad (8)$$

where r_c is the core radius, t is the shell thickness, V_p is the particle volume, and ρcore, ρ_{shell} and ρ_{solv} are the scattering length densities (SLDs) of the core, shell and solvent, respectively. In the fitting, the scattering length densities corresponding to the theoretical atomic compositions were used. The function $G(r_c)$ is the normalized probability of finding a particle with a core radius between r_c and $r_c + dr_c$, and it accounts for the polydispersity of the cores according to a Schultz distribution[5,6]

$$G(rc) = \frac{r_c^{\,Z}}{\Gamma(Z+1)}\left(\frac{Z+1}{\langle r_c\rangle}\right)^{Z+1}\exp\left[-\frac{r_c}{r_{avg}}(Z+1)\right] \quad (9)$$

where $\Gamma(Z + 1)$ is the gamma function and the parameter Z is related to the polydispersity σ_c of the core radius by the expression:

$$\sigma_c = \frac{(\langle r_c^2\rangle - \langle r_c\rangle^2)^{1/2}}{\langle r_c\rangle} = \frac{1}{(Z+1)^{1/2}} \quad (10)$$

The interparticle structure factor S(Q) describes how the scattering intensity is modulated by interference effects between radiation scattered by different scattering objects. In our case, it should account for the aggregation of the magnetic nanoparticles, in analogy with the distribution of micelles along the polypeptide backbone. Therefore, we used the same expression derived by Chen and Teixeira[2]:

$$S(Q) = 1 + \frac{D\Gamma(D-1)}{(Qr)^D}\sin[(D-1)\tan^{-1}(Q\xi]\left(1+\frac{1}{Q^2\xi^2}\right)^{(1-D)/2} \quad (11)$$

where r is the mean radius of the particles as resulting from the sum of the core radius r_c and the shell thickness t, Γ is the gamma function and ξ is the correlation length, i.e. a cut-off factor related to the dimensions of the aggregates that are eventually formed by the particles. D is the fractal dimension that describes the spatial distribution of the individual scatterers and it is related to their number N(R) within a sphere of radius R through the equation:

$$N(R) = (R/r)^D \quad (12)$$

Pearl necklace nanoparticles

SAXS spectrum of γ-Fe_2O_3 NPs has been modelled in analogy to the I_{MagNPs} intensity in the case of magnetoliposomes. Owing to the low concentration of NPs in the dispersion, the interparticle structure factor *S(Q)* in Equation 4 was set equal to 1. Apart from that, the fitting procedure and model are identical.

References

(1) Nallet, F.; Laversanne, R.; Roux, D. *Journal De Physique Ii* **1993**, *3*, 487-502.
(2) Chen, S. H.; Teixeira, J. *Physical Review Letters* **1986**, *57*, 2583-2586.
(3) Bonini, M.; Fratini, E.; Baglioni, P. *Materials Science & Engineering C-Biomimetic and Supramolecular Systems* **2007**, *27*, 1377-1381.
(4) Kline, S. R. *Journal of Applied Crystallography* **2006**, *39*, 895-900.
(5) Hayter, J. B.; Penfold, J. *Mol. Phys.* **1981**, *42*, 109.
(6) Hayter, J. B. *Edited by V. DeGiorgio & M. Corti. Amsterdam: North Holland* **1983**, 59-93.