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

• $A \approx 270 \text{ mT}$
• $B \approx B_1 \approx 100 \text{ mT}$
• $C \approx C_\Pi \approx 280 \text{ mT}$
• $D \approx D_1 \approx D_\Pi \approx D_\III \approx 330 \text{ mT}$

$10 \text{ V; 8 A}$

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

**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

(a) Liposomes in serum 10%  
- Untreated liposomes
- Liposomes after LF-AMF exposure

(b) MLs with oleic acid Fe2O3 NPs in serum 10%  
- Untreated MLs
- MLs after LF-AMF exposure
Fig. S5. Representative size distributions of (a) liposomes, (b) magnetoliposomes with oleic acid Fe$_3$O$_4$ NPs and (c) magnetoliposomes with citrate Fe$_3$O$_4$ 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$_3$O$_4$ NPs in serum 55% v/v before LF-AMF exposure

**Fig. S9** Magnetoliposomes with oleic acid coated- Fe$_3$O$_4$ 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

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<th>PBS</th>
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<th>SERUM 55%</th>
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<tr>
<td>n</td>
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<td>1.57·10^{-3}±0.01·10^{-3}</td>
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<tr>
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<td>1.10±0.02</td>
<td>0.79±0.07</td>
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<td>K</td>
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<td>9.89·10^{-3}±0.44·10^{-3}</td>
<td>1.57·10^{-3}±0.01·10^{-3}</td>
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Calibration curves of Carboxyfluorescein in serum

\[ I(Q) = \frac{2\pi P(Q)}{2(\delta_H + \delta_T)q^2} \]  

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

where the form factor is given by:

and \( \delta_H \) is the head group thickness, \( \delta_T \) is the tail length, \( \Delta \rho_H (\rho_H - \rho_{solv}) \) and \( \Delta \rho_T (\rho_T - \rho_H) \) are the scattering length density contrast, where \( \rho_H \), \( \rho_T \) and \( \rho_{solv} \) 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.

**Liposomes**

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

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

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

$$ I(Q) = I_{\text{liposomes}} + I_{\text{MagNPs}} + I_{\text{bg}} $$

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

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

where $\phi$ 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:

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

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

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

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

where $r_c$ is the core radius, $t$ is the shell thickness, $V_p$ is the particle volume, and $\rho_{\text{core}}$, $\rho_{\text{shell}}$ and $\rho_{\text{solv}}$ 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:

$$ G(r_c) = \frac{r_c^Z}{\Gamma(Z+1)} \left( \frac{Z+1}{r_c} \right)^{Z+1} \exp \left[ -\frac{r_c}{r_{\text{avg}}}(Z+1) \right] $$

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

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

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.
\[ S(Q) = 1 + \frac{D\Gamma(D-1)}{(Qr)^D} \sin[(D-1)\tan^{-1}(Q\xi)(1 + \frac{1}{Q^2\xi^2})^{(1-D)/2}] \]  

where \( r \) is the mean radius of the particles as resulting from the sum of the core radius \( r_c \) and the shell thickness \( t \), \( \Gamma \) is the gamma function and \( \xi \) 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:

\[ N(R) = (R/r)^D \]  

**Pearl necklace nanoparticles**

SAXS spectrum of \( \gamma \)-Fe\(_2\)O\(_3\) 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**