Characterization of commercial iron oxide clusters as potential Magnetic Resonance Imaging contrast agent

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BIOPHYS

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Commercial clusters of iron oxide particles, originally used for magnetofection, could constitute excellent MRI contrast agents

1. NMR relaxation induced by clusters of iron oxide particles

- The efficiency of a contrast agent is given by its longitudinal and transverse relaxivities r_i

$$r_i = \left(\frac{1}{T_i} - \frac{1}{T_i^{dia}}\right) \Big/ [Fe] \quad \text{with } i = 1,2$$

where
- [Fe] is the iron concentration,
- $1/T_i$ is the relaxation rate of the solution,
- $1/T_i^{dia}$ is the relaxation rate of pure water,

- For magnetite particles with magnetization M_v = 350 000 A/m, the maximum r_2 is :

$r_2^{max} \simeq 750 s^{-1} mM^{-1}$ that can be reached with
- -large single crystals,
- -large clusters of smaller iron oxide cores[1],

- For clusters of cores of given M_v, two parameters influence the relaxation regime:

(1) the radius R of the cluster and (2) the fraction ϕ_{intra} of the cluster volume occupied by cores

- r_2^{max} is reached in the static dephasing regime (SDR) when $5 < \Delta\omega_{cluster}\tau_D^{cluster} < 20$

with $\Delta\omega_{cluster} = \phi_{intra}\dfrac{\mu_0 \gamma M_V}{3}$ and $\tau_D^{cluster} = \dfrac{R^2}{D}$ [D = 3 10^{-9} m²/s = water diffusion coefficient, γ=2,68 10^8 Hz/T, $\mu_0 = 4\pi\ 10^{-7}$ Tm/A]

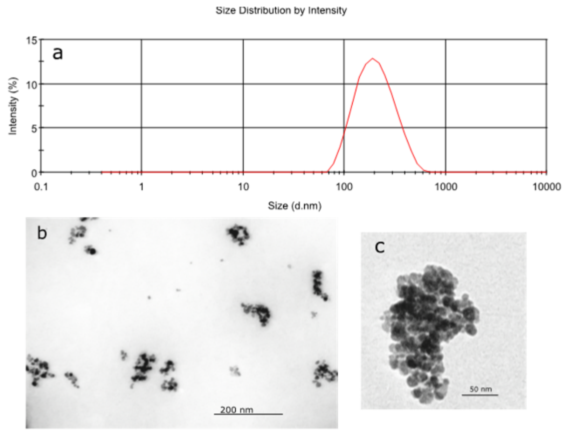

Figure 1: a) Hydrodynamic size distribution of the clusters obtained by DLS, b) TEM picture of several clusters, c) High magnification TEM image of a single cluster.

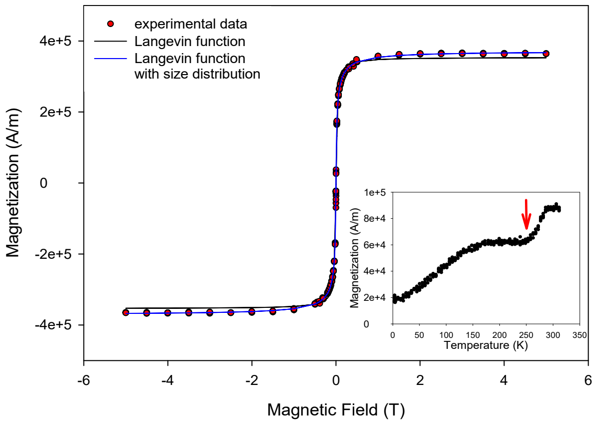

Figure 2: Effect of the field on the magnetization of the Polymag ™ clusters. The inset shows the ZFC curve of the clusters.

3. Characterization of the Polymag™ iron oxide clusters

- Sample = Polymag™ clusters from Chemicell designed for magnetofection[2],
- Hydrodynamic size of the clusters estimated by Dynamic Light Scattering (DLS):

⇒ Z-average diameter = 180 nm (PDI = 0.15) - (fig.1a),
- Images of the clusters obtained thanks to Transmission Electron Microscopy (TEM):

⇒ Dense clusters with cores of size comprised between 5 and 15 nm - (fig.1b and c),
- Size distribution (assumed log-normal) of the cores obtained by magnetometry:

⇒ $d_{0,c}$ = 4.9 ± 0.13 nm and σ = 0.53 ± 0.01 - (fig.2),
- Zero field Cooling Curve (ZFC) with high blocking temperature and discontinuity at 273 K

=> typical of aqueous solutions of magnetic clusters (inset of fig.2),

2. NMR relaxation properties of the Polymag™ iron oxide clusters

- Evolution with time of the transverse relaxation time T_2 when placed in the magnetic field,

⇒ reversible additional clustering in the field (disappears after removal from field and vortexing),
- The evolution of $1/T_2$ with [Fe] is shown in figure 4 for two magnetic fields (0.68 and 1.41 T),
- r_2 ~ 470 $s^{-1}mM^{-1}$ is among the largest reported in literature, logical since $\Delta\omega_{cluster}\tau_D^{cluster} \sim 55$

⇒ The clusters are close to the SDR, without effect of temperature and interecho time on T_2

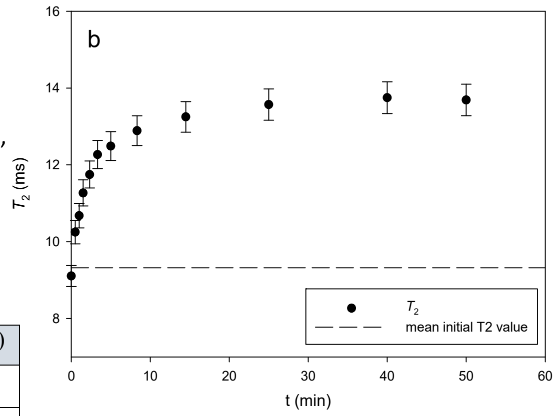

Figure 3: Evolution of T_2 with time after vortexing and insertion in the magnetic field at 0.68 T and 25°C.

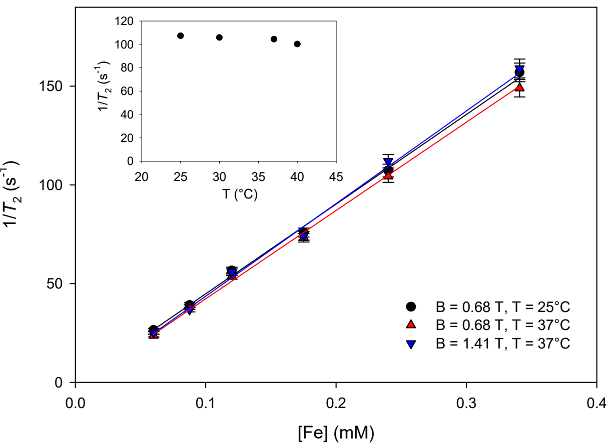

Figure 4: Evolution of $1/T_2$ with iron concentration of the Polymag ™ aqueous solutions.

Table 1: relaxivities of the Polymag ™ clusters.

	r_1 ($s^{-1}mM^{-1}$)	r_2 ($s^{-1}mM^{-1}$)
0.68 T, 25°C	20.5 ± 0.6	454 ± 12
0.68 T, 37°C	20.9 ± 0.7	447 ± 13
1.41 T, 37°C	9 ± 0.9	469 ± 17

5. Conclusions and perspectives

- The ready-to-use Polymag™ clusters present excellent transverse relaxivity[3] at 1.41 T,
- The reversible clustering observed in the field could be a disadvantage,
- Magnetofection could be used to load cells with the iron oxide clusters,
- The relaxation properties of such loaded cells still has to be evaluated in vitro and in vivo

References

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