1. NMR relaxation induced by clusters of iron oxide particles

- The efficiency of a contrast agent is given by its longitudinal and transverse relaxivities \( r_i \), with \( i = 1,2 \)

- For magnetite particles with magnetization \( M_i = 350 \, 000 \, A/m \), the maximum \( r_i \) is:

  \[
  r_i^{\text{max}} \approx 750 \, s^{-1} \, mM^{-1} \quad \text{that can be reached with}
  \]

  - single large crystals,
  - large clusters of smaller iron oxide cores \(^1\),

- For clusters of cores of given \( M_i \), two parameters influence the relaxation regime:

  1. The radius \( R \) of the cluster and (2) the fraction \( \phi_{\text{core}} \) of the cluster volume occupied by cores

  \[
  r_i^{\text{cluster}} \text{ is reached in the static dephasing regime (SDR) when} \quad 5 < \Delta \omega_{\text{cluster}} \, r_i^{\text{cluster}} < 20
  \]

  with \( \Delta \omega_{\text{cluster}} = \phi_{\text{core}} \frac{\mu_0 M_i}{3} \) and \( r_i^{\text{cluster}} = \frac{R^2}{D} \) \( [D = 3 \times 10^{-9} \, m^2/s = \text{water diffusion coefficient}, \gamma = 2.68 \times 10^8 \, Hz/T, \mu_0 = 4\pi \times 10^{-7} \, Tm/A] \)

2. NMR relaxation properties 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):

  \( \Rightarrow \) Z-average diameter \( = 180 \, nm \) (PDI = 0.15) \( \cdot \) (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 \( \cdot \) (fig.1b and c),

  - Size distribution (assumed log-normal) of the cores obtained by magnetometry:

    \( \Rightarrow d_{0,c} = 4.9 \pm 0.13 \, nm \) and \( \sigma = 0.53 \pm 0.01 \) \( \cdot \) (fig.2),

  - Zero field Cooling Curve (ZFC) with high blocking temperature and discontinuity at 273 K

  \( \Rightarrow \) typical of aqueous solutions of magnetic clusters (inset of fig.2),

3. Characterization of the Polymag™ iron oxide clusters

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

  \( \Rightarrow \) reversible additional clustering in the field (disappears after removal from field and vortexing),

- The evolution of \( T_2 \) with [Fe] is shown in figure 4 for two magnetic fields (0.68 and 1.41 T),

  \( r_2 \approx 470 \, s^{-1} \, mM^{-1} \) is among the largest reported in literature, logical since \( \Delta \omega_{\text{cluster}} \, r_i^{\text{cluster}} \approx 55 \)

  \( \Rightarrow \) The clusters are close to the SDR, without effect of temperature and interecho time on \( T_2 \)

4. Evolution of \( 1/T_2 \) with iron concentration of the Polymag™ aqueous solutions.

Table 1: Relaxivities of the Polymag™ Clusters.

<table>
<thead>
<tr>
<th>[Fe] (mM)</th>
<th>( r_1 ) (s(^{-1})mM(^{-1}))</th>
<th>( r_2 ) (s(^{-1})mM(^{-1}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.68 T, 25°C</td>
<td>20.5 ± 0.6</td>
<td>454 ± 12</td>
</tr>
<tr>
<td>0.68 T, 37°C</td>
<td>20.9 ± 0.7</td>
<td>447 ± 13</td>
</tr>
<tr>
<td>1.41 T, 37°C</td>
<td>9 ± 0.9</td>
<td>469 ± 17</td>
</tr>
</tbody>
</table>

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

