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# Magic Sandwich to Stimulated Echo Relative change to identify sign and intensity of dipolar interaction in anisotropic tissue

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#### Synopsis (100 words):

Among the MR techniques playing on dipolar interaction (Hd), the magic sandwich echo sequence (MSE) is very seldom used in biological application. So far, the magic echo has been compared to the spin echo. However, MSE is closer to a stimulated echo thus a Magic Sandwich to Stimulated echo relative change (MaSteR) is of interest to study. The MaSteR evolution with spin-lock intensity increase was studied for thawed tendon for different orientations within B0 to modulate the dipolar interaction.

We show that MaSteR is correlated to dipolar interaction, sample composition and its evolution with orientation is sensitive to Hd sign.

#### Summary (250 characters):

A marker of macromolecular dipolar interactions (Hd) is introduced as the Magic Sandwich to Stimulated Echo relative change (MaSteR). Different B1 spin lock intensities are used to modulate Hd. MaSteR is sensitive to Hd sign and fiber orientation.

#### Abstract (850 words):

Introduction:

Among the sequences (1–3) giving access to dipolar interaction (Hd) in tissue and providing quantitative parameters related to the sample macromolecular contents, the magic sandwich echo (MSE) (4-7) is underused on biological tissue. This sequence contains a spin-lock, which modulates Hd in the double rotary frame according to Redfield's theory (4). MSE has been compared to spin echo (5, 6) to measure an enhancement of SNR associated to dipolar interaction cancellation. Nevertheless, the sequence architecture of MSE without spin-lock RF pulse (fig.1) is closer to the stimulated echo sequence (STE) proposed by Frahm *et al.* (7). We introduce here the Magic sandwich to Stimulated echo signal Relative change MaSteR to provide quantitative information about the dipolar interaction in tissue. In addition, we highlight, using a non-localized spectroscopic magic sandwich echo sequence, that the behavior of this ratio as a function of the spin-lock intensity is sensitive to Hd sign.

#### Methods:

Samples consisted of two frozen beef tendons from butcher and thawed in water at room temperature during at least 2 hours. Acquisitions were performed on a 4.7 T Bruker system with a non-localized spectroscopic MSE (fig.1) with  $6\tau = 35$  ms. To modify the Hd effect, samples were rotated with respect to B<sub>0</sub>, resulting in nine positions starting with fibers aligned with B<sub>0</sub>. The spin-lock RF pulse shape was a binomial 1 (11), with a constant amplitude and a phase inversion. Ten different spin-lock RF pulse intensity values (B<sub>1sl</sub>) were taken between 0 and 162  $\mu$ T (corresponding to the coil power limitation) for each sample orientation. The angles were retrospectively evaluated from measures on gradient echo image. The results on both samples are close, such that only one is presented.

The STE amplitudes (B<sub>1sl</sub> = 0) plotted as a function of angle are first fitted by an expression containing only the dipolar interaction, where Hd is considered as a little perturbation responsible of signal decrease, and then the contribution of susceptibility is added in a second step. Susceptibility is modelled as a square function centered on 90° derived from home numerical simulations in accordance with cylindrical model described by Haacke *et al.(8)*. The signal analysis consisted in following the MaSteR given by:  $MaSteR = \frac{I_{MSE}-I_{STE}}{I_{STE}}$ , according to B<sub>1sl</sub> and fiber orientation, where I<sub>STE</sub> was the maximum intensity of stimulated echo (when B<sub>1sl</sub> = 0). The averaged on the five higher values of B<sub>1sl</sub> of the MaSteR is monitored to discriminate different Hd intensity according to the angle. Finally, a transition point defined experimentally can be identified when the MaSteR reaches its minimum and its behavior can be viewed for different orientation.

#### **Results and Discussion:**

#### STE is principally modulated by dipolar interaction in our protocol:

From fig.2 it is shown that the rotation of the sample with respect to B0 modulates the stimulated echo amplitude up to 25 %. The results of the fit using an empirical parametric model described on legend table (fig.3) shows that dipolar interaction accounts for most of signal modulation compared to susceptibility. Measures of  $I_{STE}$  for different orientations enables to distinguish different groups related to both Hd conditions: the strong Hd around  $0 \pm 5^{\circ}$  and  $89 \pm 5^{\circ}$ , the weak Hd for  $44 \pm 5^{\circ}$  and  $119 \pm 5^{\circ}$ .

#### Averaged value of 5 MasteR as function of B<sub>1sl</sub> to discriminate different Hd:

The strong and weak dipolar interaction (A and B on fig.4) can easily be distinguished just by averaging the last 5 MaSteR values (above 22  $\mu$ T). The average value provides information on Hd intensity. When the modulus of the average is low the Hd is weak, and inversely with strong Hd.

#### MaSteR behavior of the transition point to discriminate Hd sign with respect to BO:

When the dipolar interaction effect is low, close to the magic angle (54°) (diamond on fig.5), the B<sub>1sl</sub> of the transition point is around 1.26  $\mu$ T. In accordance with the dipolar interaction expression ( $\frac{(1-3cos^2(\theta))}{2r^3}$ ), we observed differences between the negative Hd (triangle on fig.5) and the positive Hd (circle). When Hd is negative, the transition point appears for a higher value of B<sub>1sl</sub> (23.03  $\mu$ T) than the one for positive dipolar interaction (7.10  $\mu$ T). Consequently, the MaSteR acquired with only few adequate values of B<sub>1sl</sub> dependent on material (0, 5, 10, 22, 50, 100, 162 $\mu$ T for example on thawed tendon) can provide valuable information on Hd intensity (see paragraph above) and Hd sign and by inference on the fiber averaged orientations. With a short echo time, this method provides a coarser result than diffusion tensor imaging (9) but invoking different physical phenomenon and do not need T<sub>2</sub> measures like in DAFI technics (10). The future would be to develop an imaging version of this sequence for biomedical application.

#### **Conclusion:**

Measures with the MSE sequence and using the MaSteR for the analysis can provide additional information on the sample architecture with respect to other imaging technics. The MaSteR variations with increasing  $B_{1sl}$  gives new perspectives for MSE-based imaging sequence and their usefulness in the diagnosis of pathologies resulting in fiber disorders, like arthritis and neurodegenerative diseases.

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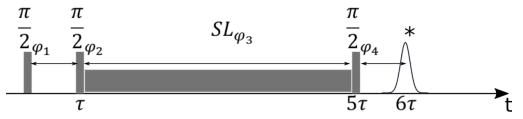
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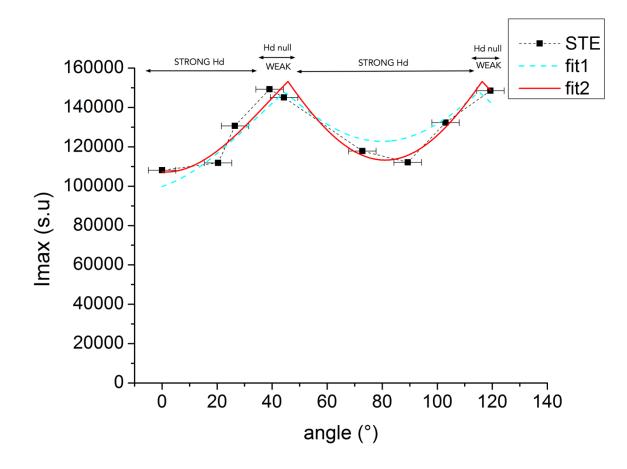
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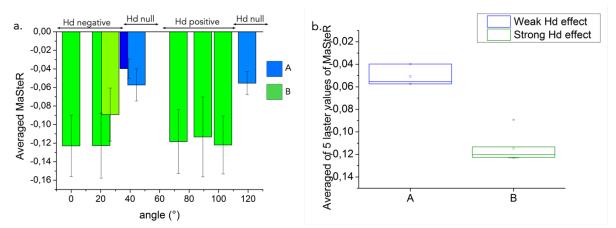
**Fig.1: Magic sandwich echo sequence.** The three  $\frac{\pi}{2}$  RF pulses are gaussians (0.1ms), SL RF is binomial 1 (11). The phases of different pulses are taken such that  $\varphi_1 = x$ ,  $\varphi_2 = x$ ,  $\varphi_3 = y$ ,  $\varphi_4 = x$ . The  $6\tau$  for the following study on tendon is taken equal to 35 ms.



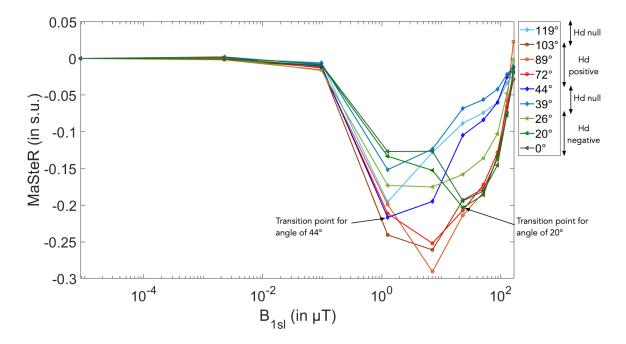
**Fig.2: Stimulated echo amplitude behavior for different orientations for**  $6\tau$  **= 35 ms.** The data is acquired with B<sub>1sl</sub> = 0 µT on thawed tendon and the angles were evaluated on gradient echo image. The angles were measured (precision of 5°) with respect to an initial position where fibers were aligned with B0.

	fit1 $\mathcal{Y}_{fit1}$ = $B * \left( 1 - \left  \frac{(1-3\cos^2((\theta - A)))}{2} \right  \right) + C$	$\begin{aligned} & \qquad $
A (°)	-10.17 ± 3.44	-8.97 ± 1.89
В	50412 ± 10376	69899 ± 9528
С	97529 ± 7308	78309 ± 8049
D	-	13198 ± 4386
Reduced Chi <sup>2</sup>	7.43.10 <sup>7</sup>	3.23.10 <sup>7</sup>
Coefficient of Determination	0.80	0.93

**Fig.3: Fitted parameters and model used on fig.2.** Fit1 is chosen to take into account only the dipolar interaction effect. Fit2 integrates additional susceptibility  $D((\theta - A) - 90)^2$  effects, in accordance with home numerical simulation using a cylindrical model.



**Fig.4: Averaged MaSteR over the five higher B**<sub>1sl</sub>**.** a. Averaged values of MaSteR as a function of angle. Blue bars represent cases of weak Hd (A) and the green is associated to the higher Hd (B). b. Distribution of the averaged value inside the both groups A and B.



**Fig.5: MaSteR as a function of the B**<sub>1sl</sub> **for the different relative orientations.** The diamonds indicate the angle corresponding to low Hd ( $|Hd| \approx 0$ ). The circles materialize the positive Hd. The triangles correspond to negative Hd. Both examples of transition point are pointed on the graph for an angle of 44° and an angle of 20°. This one appears later for Hd negative than Hd positive or null.

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