#### The effect of linear and micro-circular shear flow on diffusion MR measurements

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#### **Objectives**

Diffusion weighted MRI measures molecular displacements by tagging spins phase according to their position, consequently, incoherent displacements cause dephasing, which results in a measurable signal attenuation. Usually, in clinical and biological applications, this incoherent motion is attributed to molecular diffusion (i.e., Brownian motion) within hindered and restricted domains. However, any incoherent displacements (however, non-random), such as shear flow or shearing motion, may affect dephasing and attenuation of the DW-MRI signal. These could originate from pressure, thermal or electrical gradients within the tissue, cell streaming, molecular transport, ionic currents, etc. In this work we study, analytically and experimentally, the effect of shear flow on conventional diffusion MRI measurements. We calculate the contribution of the shear to signal attenuation and demonstrate how non-Brownian displacements can be erroneously interpreted as arising from molecular diffusion.

## Theory - linear and circular shear flow in DW-MRI

We use the q-space and propagator formalisms to address two classes of shear flows: linear shear flow and microcircular flow, which will serve as 'building blocks' to describe more complicated flow patterns.

**Linear shear flow** - Consider a 3-dimensional space in which fluid flows with a linear shear  $\beta$  (Fig. 1a) in x-axis. We assume that the stochastic nature of the displacement is fully described by the diffusion and by dispersion along the xdirection caused by the shear flow (Taylor dispersion [1]). We can thus describe the average propagator as composed of three contributions: (a) diffusion, (b) modified diffusion parallel to the direction of the flow (Taylor-dispersion), and (c)  $\overline{P_s}(\mathbf{R},t) = \left(\overline{P_{x,flow}}(x,t) \otimes \overline{P_{x,Taylor-diff}}(x,t)\right) \cdot \overline{P_{y,diff}}(y,t) \quad \overline{P_{z,diff}}(z,t)$ 

The attenuation in a PGSE experiment over a square voxel of area  $a^2$ , with diffusion time, t, over such a sample will be:

$$E(\mathbf{q},t) = E_{flow}(q_x,t) \cdot E_{diff}(\overline{q},t)$$

where  $E_{flow}(q_x,t) = e^{-2\pi i q_x v_{ext}t} \cdot sinc(\pi q_x \beta at)$  and  $E_{diff}(\overline{q},t) = e^{-(q_x^2 \cdot (1+f_{Toplar})+q_y^2+q_z^2) \cdot D \cdot t}$  Taylor dispersion enhances the apparent diffusion coefficient along x by a factor  $f_{Taylor}$ , relative to the actual diffusion coefficient (in the absence of flow) D.

Microcirculation - In the case of a cylindrical micro-circular motion (Fig. 1b), an accurate analytic separation of the contributions of diffusion and shear is complicated. We will thus limit our derivation to the case where displacement due to shear dominates (i.e. high viscosity or high shear rate). Consider an infinitesimally thin ring of fluid with radius r that rotates at an angular velocity ω(r). Since each element of that ring is displaced along r, its change of phase due to flow (given a diffusion gradient applied along x) is:

$$\Delta \phi = 2\pi q_x r \left(\cos(\theta + \omega \cdot \Delta) - r \cos\theta\right)$$

Assuming a constant density, the attenuator for that ring is obtained by integrating over the circle:

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$$E_{ring}(\omega, \Delta) = \frac{1}{2\pi} \int_{0}^{2\pi} e^{2\pi i q_{x} r (\cos(\theta + \omega \cdot \Delta) - r \cos \theta)} d\theta = \frac{1}{2\pi} \int_{0}^{2\pi} e^{i\kappa \cdot r \sin \alpha} d\alpha = J_{0}(\kappa) \quad \text{where} \quad \kappa(r) = 4\pi q_{x} r \sin \frac{\omega(r) \cdot t}{2}$$
and  $J_{0}$  is the zeroth order Bessel function of the first kind

and Jo is the zeroth order Bessel attenuation of a circulating band of by integrating over all rings from

$$E_{beand}\left(\omega(r),t\right) = \frac{1}{A} \int_{r_{ent}}^{r_{ext}} J_0\left(\kappa(\omega(r))\right) \cdot r dr$$

It is important to note that pure circular shear results in diffusion-like signal decay.

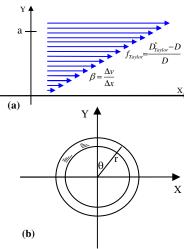


Fig. 1: Linear (a) and circular (b) shear flow

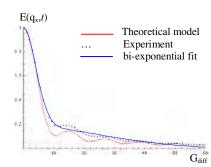


Fig. 2: Theoretical and experimental attenuation curves for a rotating Couette cell.

### Methods

To mimic a micro-circular flow inside a voxel we performed a DW-NMR measurement using a rotating Couette cell, with the RheoNMR system [2], inside a 7-T vertical scanner (Bruker). The inner cylinder of the Couette cell (1.7cm ID, 1.9cm OD) is rotated by a stepper motor at a frequency of 0.96 rpm, creating a shear flow in the fluid within the cell (PDMS, 1000cst). PGSE experiments were performed with TR/TE= 6000/300 msec,  $\Delta/\delta = 200/12$  msec,  $G_d = 0.60$  mT/m (65 values). Dataanalysis and simulations were performed using Matlab<sup>TM</sup> and Mathematica<sup>TM</sup>.

# Results and Discussion

The diffusion coefficient of PDMS in the absence of flow was found to be 3.75x10<sup>-6</sup> mm<sup>2</sup>/sec. Figure 2 shows the measured DW attenuation in an experiment with a rotating Couette cell. Experimental data fits the expectations of our analytical model. Disparities are probably due to inhomogeneities in the magnetic field and the field gradients (our sample which is much larger than the focal center of our scanner). The oscillating pattern of the Bessel function is apparent in the data. In addition, the attenuation versus gradient strength is characterized by a sharp drop followed by a moderate slope. Such an attenuation profile could be modeled by a bi-exponential curve. In this case, we obtained  $D_{fast} = 0.0148$  and  $D_{slow} = 0.00037$  mm<sup>2</sup>/sec. However, this bi-exponential model would inappropriately assume that the attenuation profile is composed of a "fast" and "slow" component. Note that in biological tissues, the velocity profiles will not be symmetric as in the Couette cell. Consequently, the oscillations in the attenuation curve will not appear in DWI data, and the simplest model describing the attenuation curve will likely be a multi-exponential one.

This work predicts the effect of simple shear flow profiles on the signal attenuation in a DW-NMR experiment. Mechanisms of shear flow may induce attenuation patterns similar to those usually observed in DW-MRI of biological tissues (pseudo multi-exponential behavior). Such displacement mechanisms may explain some of the observed discrepancies between experiment and theory in biological DW-MRI [3]. We analyzed and performed experiments on a macroscopic flow phantom, and yet the suggested mechanism of shear induced signal loss is applicable to the cellular level, and could improve our understanding of the origins of the DW-MR signal.

[1] Brenner H. & Edwards D.A. Macrotransport processes, Butterworth-Heinmann 1993. References

[2] Britton M.M. et al. Applies Magnetic Resonance, 1998. [3] Assaf Y. & Cohen Y., NMR Biomed. 2002.