

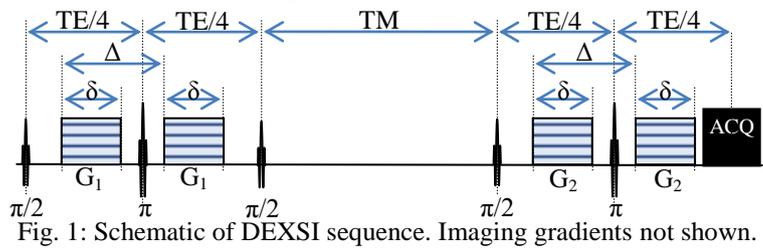
# Diffusion-diffusion Exchange Spectroscopic Imaging (DEXSI) MRI in a rat corpus callosum

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**Introduction:** The permeability of membranes within tissue microstructure is abnormal in a number of pathologies, for example in cancer<sup>1</sup> and stroke<sup>2</sup>. We adapt the Diffusion-diffusion Exchange Spectroscopy (DEXSY)<sup>3,4</sup> NMR technique for MRI biological samples to quantify permeability. Previous studies that estimate permeability have adapted the Karger framework<sup>5</sup> using biophysical models of tissue. An alternative, phenomenological approach, Filter Exchange Imaging (FEXI) has been used to quantify permeability in the human brain<sup>5</sup>. The FEXI study assumed a two site system and that the rate of exchange between sites was mono-exponential. A recent study suggests white matter can be better described by at least three compartments<sup>6</sup>. Diffusion-diffusion exchange techniques are inherently able to detect multiple diffusivities and thus the exchange of water between them. We demonstrate the first use of diffusion-diffusion exchange spectroscopy in an imaging application and, furthermore, the first use with biological tissue.

**Methods:** The DEXSI pulse sequence is shown in Fig 1. For this study, a single spin-echo readout was used and implemented on a 9.4T Agilent small bore scanner equipped with 1T/m gradients and 26mm r.f. volume coil. Diffusion gradients were aligned



perpendicular to axonal fibres in the mid-sagittal slice of the corpus callosum. 16x16 steps of G1 and G2 were taken (256 measurements in total). Parameters were:  $\delta=5\text{ms}$ ,  $\Delta=10\text{ms}$ ,  $G_1=0$  to 0.7 T/m,  $G_2=0$  to 0.7 T/m,  $TM = 200\text{ms}$ , TE was minimized, 12x24mm FoV, 128x128 matrix. A rat brain was perfused fixed and immersion fixed for 1 week in 4% aqueous formaldehyde from paraformaldehyde, then immersed in phosphate buffer solution for 1 week. The sample was immersed in perfluorosolv PFS-1 (Solvay Solexis) prior to scanning. Temperature was maintained at 18°C throughout the experiment. 2D diffusion spectra were generated using 2D inverse Laplace transform software<sup>7</sup>.

**Results:** An unweighted image of the mid-sagittal slice and 2D diffusion spectra of the corpus callosum are shown in Fig. 2&3 respectively. Peaks in the 2D diffusion spectrum are seen at  $(D_1, D_2) \sim (3, 3)$  and  $(2.5, 0.4) \times 10^{-10} \text{m}^2/\text{s}$ . There are also corresponding peaks with very low diffusion constants.

**Discussion:** For the first time we have applied diffusion-diffusion exchange spectroscopy in an imaging application in biological tissue. Diffusion constants are consistent with fixed tissue at room temperature<sup>8</sup>. Future work will decrease total acquisition time by fast imaging and optimising the diffusion protocol<sup>9</sup>.

**References:** 1. Lätt J et al. NMR Biomed 22: 619–628 2. Nilsson M et al. Magn Reson Med, 69: 1572–1580 3. Qiao Y et al. J Chem Phys 122:214912 4. Hubbard PL et al. J Phys Chem B 110, 20781–20788. 5. Kärger J, Adv Coll Interf Sci 23, 129–148 6. Panagiotaki E et al. Neuroimage 59(3), 2241–2254 7. Godefroy S, Ryland B and Callaghan PT, Victoria University of Wellington, Wellington, New Zealand. Provided courtesy of Petrik Galvosas. 8. Alexander DC et al. NeuroImage 52, 1374–1389. 9. Alexander DC, Magn Reson Med 60, 439–448.

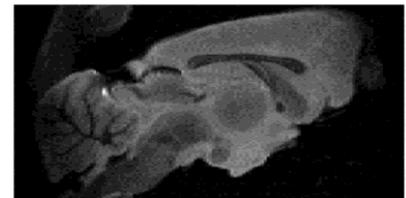


Fig. 2: Unweighted image of mid-sagittal slice

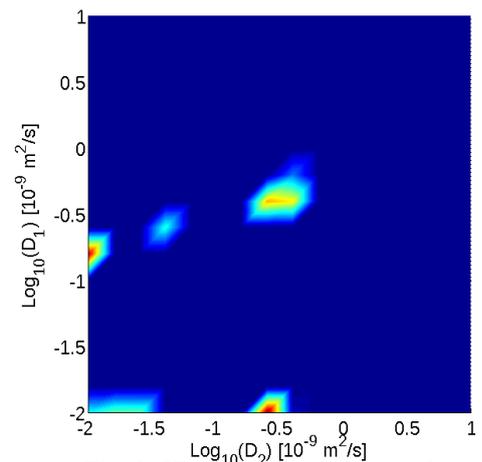


Fig. 3: 2D diffusion spectrum of rat corpus callosum