Using oscillating gradient spin-echo sequences to infer micron-sized bead and pore radii

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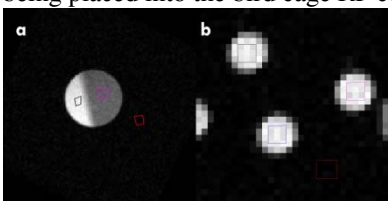
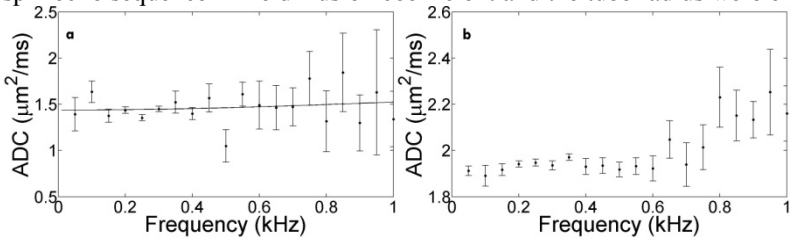
INTRODUCTION There is an increasing drive to use diffusion spectroscopy to infer the sizes of structures in samples[1-4]. Most methods use pulsed gradient spin echo sequences[2,3] which cannot provide short enough diffusion times to probe very small structures. Using oscillating gradient spin echo sequences (OGSE)[5,6] a diffusion spectrum can be obtained which probes the "short-time" or high frequency regime allowing for the size of small structures to be inferred. Here we use the apodised cosine OGSE[6] to infer the pore size between closely packed beads, and thus the bead diameter, as well as the diameter of cylindrical tubes.

METHODS MRI Each sample was imaged using a 7 T Bruker Avance III NMR system with Paravision 5.0 with a BGA6 gradient set with a maximum gradient strength of 430357 Hz/cm and a 3.5 cm diameter bird cage RF coil (Bruker Biospin). The number of sinusoidal waves in each 20 ms apodised cosine[6] gradient pulse ranged from n = 1 to 20, in steps of 1. Five gradient strengths were used for each frequency and the gradient pulses were separated by 24.52 ms. For n > 4, the gradient strengths were 0, 90, 80, 70 and 60% of maximum. Because of large signal decay, the gradient strengths for n < 5 were smaller; for n = 1, g = 0, 10, 7, 4 and 1.5 % of maximum; for n = 2, g = 0, 15, 10, 7, 4 % of maximum; for n = 3, g = 0. 30. 25. 20, 15 % of maximum; for n = 4, g = 0, 60, 50, 40, 30 % of maximum. Beads 3 µm diameter polystyrene beads (Sigma Aldrich) in water were centrifuged for 10 seconds. Excess water was removed and more bead solution was added. The solution was centrifuged again for 10 seconds, three times. A 1 mm thick $(2\text{ cm})^2$ slice was chosen to contain a region containing packed beads, and another region of only water. A 128 x 128 matrix was used for 156 µm in-plane resolution. Tubes 10 Kimble ® microcapillary pipettes (Sigma Aldrich) were used, each having a capacity of 20 µL ± 0.5%. Each tube was filled with a $CuSO_4$ solution (Bruker Biospin). Tubes were bundled together using tape, and because the tubes were open-ended, each end was secured with modeling clay. The tube bundle was then contained within a 15 mL sample tube, before being placed into the bird cage RF coil. A 3.0 mm thick $(3.2\text{ mm})^2$ slice perpendicular to the tubes was chosen. A 32 x 32 matrix was used for 100 µm in-plane resolution. Analysis ROIs were created in the water region of the bead sample, several of the water regions in the tube samples, in the bead region of the bead sample, and in the noise as shown to the left. The mean ± standard deviation of the signal in the ROIs was calculated. The log of the signal versus b-value was fitted to a straight line and the negative of the slope was used as the ADC for each measurement. The mean ± standard deviation of the ADC for each frequency was calculated and used in the fit. Bead fit The diffusion spectrum D(ω) for beads for the apodised cosine sequence data was fitted to $D(\omega) = \frac{D_0}{\alpha} + \sum_k B_k \frac{\tau_k \omega^2}{1+\tau_k^2 \omega^2}$ where the first term is the free diffusion coefficient divided by a tortuosity and the second term is a sum of terms dependent on the pore geometry, which we took to be a sphere[1]. D_0 was held fixed to the ADC value obtained for water. Both α and the pore radius were extracted from the fit. We assumed that the beads were tightly packed in an FCC lattice. In a tightly packed FCC lattice of spheres, there are two types of interstitial holes (pores), one with radius 0.414 times the diameter of the spheres, and one 0.225 times the diameter of the spheres[7]. These relations were used to relate the pore size to the bead size. Tube fit The tube ADC data were fitted to the diffusion spectrum for a cylinder due to a cosine spin echo sequence[8]. The diffusion coefficient and the tube radius were extracted from the fit.





RESULTS ADC vs frequency is plotted on the left for the beads (a) and tubes (b). The fit is shown with the solid line. The pore radius between the beads was found to be 0.6 ± 0.5 µm containing water diffusing at 1.4 ± 0.1 μm^2/ms. This corresponds to bead diameters ranging from 3 ± 2 µm to 5 ± 4 µm. The tube diameter could not be calculated because the D(ω) of the tube data was the same as the free diffusion coefficient. We believe the frequencies were too high, corresponding to diffusion times that were too short, so that the water in the ~780 um tubes was experiencing unrestricted diffusion during the diffusion measurements.

DISCUSSION AND CONCLUSIONS This work provides experimental evidence for using apodised cosine OGSE to infer the size of very small structures. Structures of radius 0.6 ± 0.5 µm were inferred using this method which is 2-10 times smaller than structures measured with AxCaliber[2] and more accurate than previous measurements[1]. This work lays the foundation for inferring the size of submicron structures, such as axon diameters in samples using MRI.

REFERENCES 1. Parsons MRM 55:75-84 2006. 2. Assaf MRM 59:1347-1354 2008. 3. Alexander Neuroimage 52:1374-89 2010. 4. Martin MRInsights 6:59-64 2013. 5. Schachter JMR 147(2):233-237 2000. 6. Does MRM 49:206–215 2003. 7. Smart LE, Moore EA Solid State Chemistry: An Introduction, Third edition. 8.Xu JMR 200:189-197 2009. Funding NSERC, MHRC, CFI, and MRIF.