

General Comments

This is a very interesting manuscript and goes towards furthering the amount of information that will ultimately be available from clinical MRIs in the future.

Although the theory looks correct to me, I think that a more detailed discussion/elaboration of the mathematical derivations would make this work much more usable to the MRI audience and likely to increase its uptake and the likelihood of it filtering through to clinical usage. The MR literature is replete with examples of excellent theoretical developments being lost in the literature because the explanation of the theoretical developments in the papers were too brief – some of the works by Stepišnik come to mind. Following on from the comments of Tom Barbara, a more complete description, say as Supplementary Information, would really assist and avoid a “paper chase”. And now, given the possibility of having large electronic Supplementary Information documents there is no reason not to.

Specific Comments

Lines 9-10 The sentence “Higher specificity to restriction ... to the property not being of direct interest” is not easy to understand, at least on the first pass. The authors might like to rewrite this sentence.

Around lines 19, many of the intended readership would benefit from a clear explanation of what is meant by the frequency ω and how it relates to the pulse sequence parameters.

Eqs. (14) and (15), it might be advisable to use a letter different than A since in Eq. (17) A is used in D_A to signify axial.

Some of the Figures or parts of Figures are too small. (e.g., the lower two graphs in Figure 1, in Fig. 3c perhaps just plot a subset of the data).

Line 160. What was T_1 reduced to?

Line 164. What was actually done in allowing for the cell sedimentation? Was the supernatant removed?

Line 173. Did the 5 s recycle delay include the acquisition time?

The Proof of Principle experiments were conducted on high field very high gradient MRI equipment. It would be useful to see more discussion/outlook about the available parameter space (e.g., ω_{ent}) and implications for running on clinical MRI equipment (e.g., lower gradient strengths) – assuming that SNR wasn't a limiting factor.

Line 206. Why didn't the extracellular compartments exhibit restricted (ω -dependent) diffusion. Was it because the restrictions were not characterised by a reasonably homogeneous characteristic distance?

Technical Corrections

Line 77. axial and radial eigenvalues.

Line 88. Following previous works.

Line 99. Eq. (2) that is, include a space before the “(“/