frontiers in PHYSICS

GENERAL COMMENTARY
published: 13 May 2014
doi: 10.3389/fphy.2014.00028

Commentary on "Microanisotropy imaging: quantification of microscopic diffusion anisotropy and orientation of order parameter by diffusion MRI with magic-angle spinning of the q-vector"

Sune N. Jespersen[1,2]*, Henrik Lundell[3], Casper K. Sønderby[3] and Tim B. Dyrby[3]

[1] *CFIN/MINDLab, Department of Clinical Medicine, Aarhus University, Aarhus, Denmark*
[2] *Department of Physics and Astronomy, Aarhus University, Aarhus, Denmark*
[3] *Danish Research Centre for Magnetic Resonance, Copenhagen University Hospital, Hvidovre, Denmark*
**Correspondence: sunenj@gmail.com*

Edited by:
Mario Nicodemi, Universita' di Napoli "Federico II", Italy

Reviewed by:
Indika Rajapakse, University of Michigan, USA

Keywords: microscopic diffusion anisotropy, fractional anisotropy, microscopic fractional anisotropy, orientation dispersion, d-PFG, MRI

A commentary on

Microanisotropy imaging: quantification of microscopic diffusion anisotropy and orientation of order parameter by diffusion MRI with magic-angle spinning of the q-vector
by Lasič, S., Szczepankiewicz, F., Eriksson, S., Nilsson, M., and Topgaard, D. (2014). Front. Phys. 2:11. doi: 10.3389/fphy.2014.00011

In their recent paper, Lasič et al. describe a parameter termed μFA (*microscopic fractional anisotropy*) that quantifies microscopic anisotropy independently of macroscopic anisotropy [1]. Specifically such a microstructural parameter makes it possible to detect and characterize anisotropic domains even if they are organized in a macroscopically (i.e., at the level of the voxel) isotropic way—essentially decoupling macroscopic and microscopic anisotropy. Their method is based on the combination of two types of diffusion measurements, a powder average experiment and magic angle spinning of the q vector: The powder average experiment uses a traditional single pulsed field gradient or PGSE acquisition, where the signal along a large number of diffusion directions is averaged, thus emulating an isotropic preparation of the sample. The magic angle spinning of the q vector, the so-called q-MAS, is an approach for isotropic diffusion weighting recently introduced by the same group [2].

A similar parameter of microscopic anisotropy, termed fractional eccentricity (FE), but relying on double pulsed field gradient (dPFG) diffusion experiments was introduced by us recently in Jespersen et al. [3]. In it we extended previous work on indices of microscopic anisotropy in the long diffusion time limit proposed by Lawrenz et al. [4]. The FE terminology was motivated by the existing nomenclature in the dPFG field. However, a simple argument shows that the two metrics μFA and FE are in fact identical in systems consisting of identical pores. First, when all domains are coherently aligned along one direction, it was shown in Jespersen et al. [3] that FE=FA, and similarly in Lasič et al. [1] that μFA=FA: thus FE=μFA in such a system. Secondly, both metrics are independent of the pore orientation distribution function, so both FE and μFA are unaffected when reorganizing the domains to match any anisotropic distribution. Hence the identity FE=μFA is conserved. Nevertheless, a number of observations concerning differences and similarities must be made.

Clearly, both approaches presuppose the existence of compartments (pores), in which the bulk of the spins will remain during the relevant time of observation. For the q-MAS approach, this is the duration of the q-MAS modulation, 40 ms in Lasič et al. [1]. For the dPFG approach, the relevant time is the sum of diffusion and exchange times from the onset of the first field pulse to the end of the last field pulse, which was 43 ms in Jespersen et al. [3]. These (comparable) numbers put constraints on the exchange time/permeability of the compartments. Moreover, both approaches involve non-conventional diffusion sequences, requiring programming of gradient modulation waveforms. The q-MAS approach requires the combination of two different types of diffusion experiments, and both approaches use data acquired along several diffusion directions. The dPFG experiment can be used to extract also the diffusion tensor.

The q-MAS approach assumes that diffusion in the individual pores is Gaussian. This can be a good approximation for example when diffusion weighting is not too strong and diffusion times are large. However, another requirement of the q-MAS analysis approach is that the diffusion coefficients in the individual pores are time independent, a condition which may be challenging to balance against the necessity for the spins to experience the pore boundaries, the very source of the μFA. On the other hand, this is presumably a good approximation for the extracellular space in the long diffusion time limit, still assuming no exchange between the intra- and extracellular space. The Gaussian approximation can be accurate also when diffusion times are very small, but in this regime μFA will be vanishing as the effect of the confinement is negligible.

The dPFG approach to microscopic anisotropy requires long mixing times,

more specifically it should be long enough that spin displacements separated by the mixing time are statistically independent. This can happen not only for Gaussian diffusion, but also when the diffusion length over the mixing time is comparable to the pore size (or the disorder length scale). Another condition of the dPFG approach is that terms beyond b^2 in the cumulant expansion of the signal must be negligible. This can be difficult to establish in practice, and would require the dPFG experiment to be repeated for a number of different *b*-values for verification.

Finally, a disadvantage of the μFA/FE parameter is that it is not additive over pore populations, a property that complicates interpretation. However, this could be circumvented by adopting instead the parameters $\Delta\tilde{\mu}_2$ [1] or ε [3], which are both additive, but unnormalized. In fact, these two parameters are likewise identical in multi-Gaussian systems, and their estimations are characterized by the same constraints and assumptions described above for μFA and FE.

In conclusion, we argued that the indices μFA and FE are in fact the same parameter of microscopic diffusion anisotropy. The name μFA is arguably a better name, as it more directly reflects the connection to FA of individual pores and emphasizes its microstructural nature. The two indices were estimated from two different acquisition strategies, q-MAS [1] and dPFG [3] with each of their advantages and disadvantages, and detailed considerations of pros and cons should be made on a case-by-case level when choosing one or the other. To better inform such decision-making, it would be very interesting to see a detailed comparison of the two approaches on the same system, perhaps a well-characterized model system.

ACKNOWLEDGMENTS

We acknowledge financial support from: Danish Ministry of Science, Technology and Innovation's University InvestmentGrant (MINDLab); FET-Open grant No 238292("CONNECT"); Lundbeck Fonden on the Control of Action (grant No R59 A5399); Lundbeck Fonden grant No R83-A7548.

REFERENCES

1. Lasič S, Szczepankiewicz F, Eriksson S, Nilsson M, Topgaard D. Microanisotropy imaging: quantification of microscopic diffusion anisotropy and orientational order parameter by diffusion MRI with magic-angle spinning of the q-vector. *Front Phys.* (2014) **2**:11. doi: 10.3389/fphy.2014.00011
2. Eriksson S, Lasič S, Topgaard D. Isotropic diffusion weighting in PGSE NMR by magic-angle spinning of the q-vector. *J Magn Reson.* (2013) **226**:13–18. doi: 10.1016/j.jmr.2012.10.015
3. Jespersen SN, Lundell H, Sønderby CK, Dyrby TB. Orientationally invariant metrics of apparent compartment eccentricity from double pulsed field gradient diffusion experiments. *NMR Biomed.* (2013) **26**:1647–1662. doi: 10.1002/nbm.2999
4. Lawrenz M, Koch MA, Finsterbusch J. A tensor model and measures of microscopic anisotropy for double-wave-vector diffusion-weighting experiments with long mixing times. *J Magn Reson.* (2010) **202**:43–56. doi: 10.1016/j.jmr.2009.09.015

Conflict of Interest Statement: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Received: 04 April 2014; accepted: 23 April 2014; published online: 13 May 2014.
*Citation: Jespersen SN, Lundell H, Sønderby CK and Dyrby TB (2014) Commentary on "Microanisotropy imaging: quantification of microscopic diffusion anisotropy and orientation of order parameter by diffusion MRI with magic-angle spinning of the q-vector". Front. Physics **2**:28. doi: 10.3389/fphy.2014.00028*
This article was submitted to Biophysics, a section of the journal Frontiers in Physics.