Indetermination-free cytoarchitecture measurements in brain gray matter via a forward diffusion MRI signal separation method

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Synopsis

Non-invasive imaging at the cellular level could lead us to quantify grey matter tissue cytoarchitecture, which has so far been accessible only through histology, or by indeterminate-prone approaches.

We propose a new dMRI-based index to study modulated by the size of the somas. This index can be extracted without indeterminations from any acquisition including three b-values superior to 3 ms/μm^2. Simulations were experimentally confirmed by tests on the HCP MGH data set.

Introduction

In this work we solve the problem of estimating soma sizes in grey matter with no indetermination. To extract a soma size-modulated mesasurement, we combine approximations to a biophysical model at low b-values and its associated return-to-the-origin probability (RTOP)[1] for high b-values.
Such non-invasive measurement of cellular characteristics has the potential to quantify tissue cytoarchitecture, in a unique-solution system, which has so far been accessible only through histology.
Our contribution focuses on the human brain gray matter, which can be decomposed into three compartments, somas and processes that are modeled by spheres and 0-radius tubes, and extra-cellular water. This work shows the feasibility to extract factor that reflects the averaged diameter of the somas in the voxel with a unique solution. Our three-compartment model, under the hypothesis that there is no exchange between the three compartments[2], is as follow :

$$\frac{S(q)}{S(0)} = f_t S_{tubes}(q, D_a) + f_s S_{spheres}(q, D_s, r_s) + (1 - f_t - f_s) S_{ecs}(q, D_{ecs})$$

f_t and f_s represent the MR dendrite and soma signal fraction respectively, D_{ecs} and D_s the extra-cellular and soma diffusivities, D_a axial diffusivity and r_s the soma radius.
The tube signal is modeled by a power-law scaling[3] $\frac{1}{4\sqrt{\pi\tau D_a^{||}}} \cdot q^{-1} + \gamma$, and the sphere signal by Balinov's approximation[4] $-\log S_{spheres}(q) = C(r_s, D_s) \cdot q^2$. Here we exploit this relation to extract $C = C(r_s, D_s)$ that, at fixed D_s, **modulated by soma size** with a method that can be applied to acquisitions with just 5 b-values. Three of them must be superior to a minimum b-value defined by cell soma size, see Fig2. The spacing of these points is determined by the SNR as the signal difference between points must not be noise-dominated.
Others[5] have already propose solutions to dMRI soma measurement for high b-values, and more b-values in all, but their method leads to indeterminate systems. Our direct method is indetermination free.

Methods

By combining the expression to our biophysical model (1) for RTOP at large q (respectively b) and a Lemonade variant at low b (respectively q), we produce a method to extract the parameters of our model.
RTOP: high b. We compute a q-bounded RTOP, a direct measure of the restrictions of the diffusing fluid molecule motion that gives us information about the structure of the media[6,7]:

$$RTOP(q_{max}) = \frac{1}{(2\pi)^3} \int_0^{q_{max}} \frac{S(q)}{S(0)} dq_{max}$$

For q_{max} large enough, RTOP of the sphere signal converges towards a value that depends on C. We therefore obtain from eqs (1) and (2) assuming a large enough q_{max} :

$$RTOP(q_{max}) = \frac{(1 - f_t)}{(2\pi)^2 \cdot 8\sqrt{\pi} \cdot 4C^{3/2}} + \frac{f_t}{4(2\pi)^3\sqrt{\pi\tau D_a^{||}}} \cdot q_{max}^2 + \frac{\gamma}{3(2\pi)^3} \cdot q_{max}^3$$

By solving an ordinary least square regression we can find the coefficients a_{fit}, b_{fit} and c_{fit} of the previous polynomial and we end up with 2 equations with 3 unknowns.
Spiked LEMONADE: low b. We adapted the method proposed in [8] in adding the sphere contribution (f_s and C). Estimating the rotational invariant moment tensors $M^{(2),0}$, $M^{(2),2}$, and $M^{(4),2}$ for a b-value up to 2.5ms/μm^2 we can find 4 more equations with 6 unknowns.
Total system. We end up with a system of 6 equations for 6 unknowns that has no degeneracy.
Spiked LEMONADE, low b :

$$\begin{cases} M^{(2),0} = f_t D_a + 3 \boldsymbol{f_s C} + 3(1 - f_t - f_s) D_e \\ \frac{M^{(2),2}}{p_2} = f_t D_a \\ M^{(4),0} = f_t D_a^2 + 5 \boldsymbol{f_s C}^2 + 5(1 - f_t - f_s) D_e^2 \\ \frac{M^{(4),2}}{p_2} = f_t D_a^2 \end{cases}$$

RTOP, high b:

$$\begin{cases} a_{fit} = \frac{(1-f_t)\sqrt{\pi}}{(2\pi)^3 \cdot 4 \boldsymbol{C}^{3/2}} \\ b_{fit} = \frac{f_t \sqrt{\pi}}{2(2\pi)^4 \sqrt{\tau D_a^{\parallel}}} \end{cases}$$

Numerical simulations. To mimic neurons, we modelled the sphere and tube signals using the DMIPY simulator[7] with soma radius equal to approximately 20 and 15µm, reproducing Von Economo and pyramidal neurons.
Experimental Data. We used the HCP MGH Adult Diffusion data set to study the variation of C on the insula, precentral and postcentral parts of the Destrieux atlas. It is composed of 35 subjects, with δ/Δ=10.6/43.1ms and b=1, 3, 5, 10ms/µm2.

Results

Simulations. RTOP computation on soma simulations shows the convergence values specific to soma diameters of different neurons in the brain, obtained from Neuromorpho.org (**Fig.2a**). This value is proportional to C, and **Fig2b** shows that C is modulated by the size of the somas, and inversely proportional to it. The relative error of C with respect to the minimum b-value used for the RTOP computation is presented in **Fig2c**.
Experiments. Fig3, C value for three cortical regions on subject 1010 (right handed), preliminary evidence shows: larger soma size spread and asymmetry on the insula, agreeing with [9]. and larger somas on the left postcentral, possibly hemispheric dominance[10]. **Fig 4**. Soma-to-dendrite volume ratio showing soma predominance agreeing with literature[10]. Although further work is needed, this showcases our method's potential.

Discussion and Conclusion

The minimal b-value needed to compute the large approximation of the signal RTOP must be at least 3ms/µm^2 to get a good C approximation in the case of VEN and pyramidal neurons. The proposed method does not need a large range of b-values as in [5].

Acknowledgements

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Figures

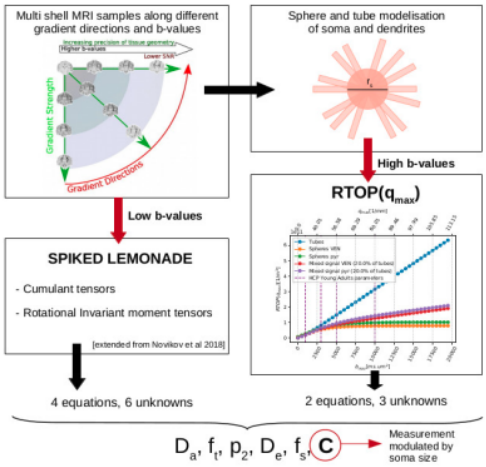


Figure 1: Visual abstract. On the top left we illustrate a multi-shell dMRI. On the one hand we are using gradient directions at low b-values to estimate rotational invariants moment tensors. On the other hand we are computing RTOP(q_{max}) for high q-values. We end up with a determinate system and get C, a measurement that is modulated by soma size.

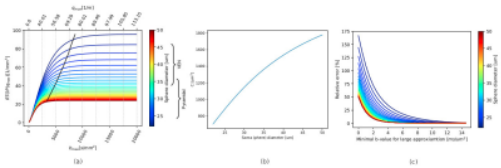


Figure 2: (a) RTOP of the soma signal depends on the sphere diameter. The minimum b-value used for the large b approximation is related to the diameter of the somas acquired. (b) C is modulated by the sphere diameter. (c) Relative error of C estimation. The bigger the soma, the lower b-values for a better realtive error. The minimum b-value used for the large b approximation is lower for VEN than pyramidal neurons.

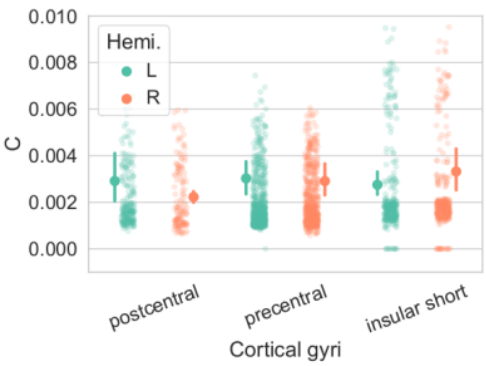
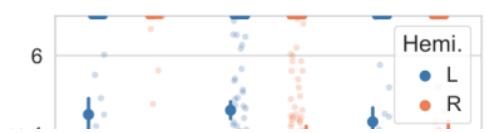


Figure 3: C value for three cortical regions on subjet 1010 (right handed), Preliminary evidence shows: larger soma size spread and asymmetry on the insula, agreeing with [9]. ; and larger somas on the left postcentral, possibly hemispheric dominance [10].



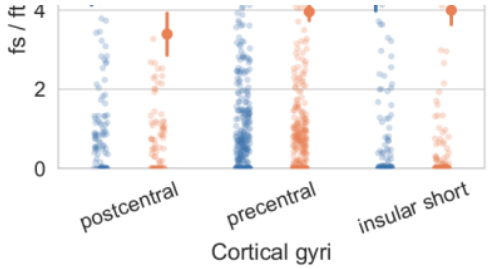


Figure 4: Soma-to-dendrite volume ratio showing soma predominance agreeing with literature [9]. Although further work is needed, this showcases our method's potential.