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# Indetermination-free cytoarchitecture measurements in brain gray matter via an inverse diffusion MRI signal separation method

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**Objective:**

- Quantify grey matter cytoarchitecture using diffusion MRI
- Estimate tissue parameters with no indetermination: a unique solution is returned and there is no need to choose between several mathematical and biological possible solutions.

**1 Introduction**
**3 compartment model**

- 7 parameters to estimate:
- Compartment signal fractions:  $f_n, f_s$  and  $f_{ecs}$
  - Diffusivities:  $D_a$  and  $D_{ecs}$
  - An exiting **new parameter modulated by soma radius**:  $C_s(r_s, D_s)$
  - ODF anisotropy invariant:  $p_2$

$$\frac{S(q)}{S(0)} = f_n S_{neurites}(q) + f_s S_{soma}(q) + f_{ecs} S_{ecs}(q)$$

**Hypothesis:**

- No exchange between the 3 compartments<sup>3</sup>
- $f_t + f_s + f_{ecs} = 1$

| Intra-cellular space                                     |   |
|--|---|
| Neurites   | Soma                                    |
| 0-radius tubes <sup>1</sup>                              | Spheres with fixed radius <sup>2</sup>  |
| $S_{neurites}(q) = \frac{1}{4\sqrt{\pi}\tau D_a} q^{-1}$ | $-\log S_{soma}(q) = C_s(r_s, D_s) q^2$ |
| Extra-cellular space                                     |   |
| Ellipsoid  |   |
| $-\log S_{ecs}(q) = (2\pi q)^2 \tau D_e$                 |   |

**2 Methods**

① Estimate  $D_{ecs}$  from CSF (free diffusing fluid)

② Spiked LEMONADE

- Low b-value approximation ( $b \leq 3 \text{ ms } \mu\text{m}^{-2}$ )
- Based on cumulant decomposition of the dMRI signal<sup>4</sup>

$$\begin{cases} M^{(2),0} = f_n D_a + 3 \frac{f_s C_s}{(2\pi)^2 \tau} + 3 f_{ecs} D_e \\ M^{(2),2} = f_n D_a p_2 \\ M^{(4),0} = f_n D_a^2 + 5 f_s \left(\frac{C_s}{(2\pi)^2 \tau}\right)^2 + 5 f_{ecs} D_e^2 \\ M^{(4),2} = f_n D_a^2 p_2 \end{cases}$$

③ RTOP:<sup>5</sup>  $RTOP(q_{max}) = \frac{1}{(2\pi)^3} \int_0^{q_{max}} S(q) dq$

- High b-value approximation ( $b \geq 3 \text{ ms } \mu\text{m}^{-2}$ )
- Least square regression

$$RTOP(q_{max}) = a_{fit} + b_{fit} q_{max}^2$$

$$\begin{cases} a_{fit} = \frac{f_s \sqrt{\pi}}{(2\pi)^3 4 C_s^{3/2}} + \frac{f_{ecs}}{32 \pi^{5/2} (2\pi \sqrt{D_e} \tau)^3} \\ b_{fit} = \frac{f_n}{4 (2\pi)^4 \sqrt{D_a} \tau} \end{cases}$$

④ Solve the non-indetermination system of 7 equations and 6 unknowns using LBFSG

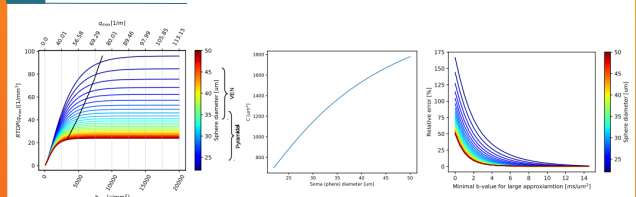
**3 Results**


Fig. 1. (a)  $C_s$  is modulated by the sphere diameter. (b) RTOP of the soma signal depends on the sphere diameter. (c) Relative error of  $C_s$  estimation. The bigger the soma, the lower b-values for a better relative error.

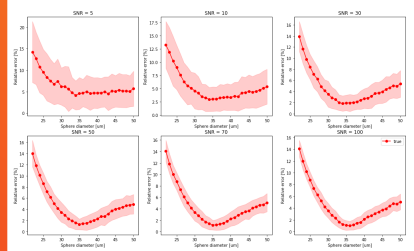


Fig. 2. Evolution of the relative error of  $C_s$  with respect to soma radius for varying SNR. Estimation is better for big soma and is robust towards noise.

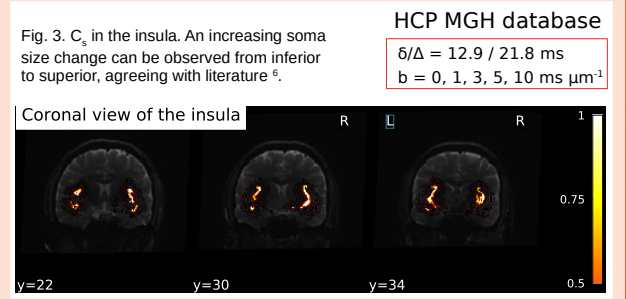


Fig. 3.  $C_s$  in the insula. An increasing soma size change can be observed from inferior to superior, agreeing with literature<sup>6</sup>.

HCP MGH database  
 $\delta/\Delta = 12.9 / 21.8 \text{ ms}$   
 $b = 0, 1, 3, 5, 10 \text{ ms } \mu\text{m}^{-1}$

**4 Discussion and Conclusion**

- $C_s$ : an exiting new parameter modulated by soma radius
- Low requirements: only 5 b-values needed, comprising 3 b-values superior or equal to  $3 \text{ ms } \mu\text{m}^{-2}$
- Unicity of the solution, unlike NODDI or SANDI<sup>3</sup>, making fitted parameters reliably interpretable
- Robust to noise
- No training on simulations required as in SANDI<sup>3</sup>

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