Why is the trace of the Diffusion Tensor constant across brain?

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INTRODUCTION - Despite widespread observation that the trace of the diffusion tensor is constant across brain tissue, there has been no sufficient theoretical explanation for why this is the case [6]. It has been proposed [1] that the constancy of the trace follows from the tightness of the Hashin-Shtrikman

(HS) bounds [2-5] which were originally derived for the effective transport properties of composite materials. Here, we sought to determine whether the HS bounds could explain the observed trance conservation in brain tissue. We derived bounds on the trace of the diffusion from the generalized HS variational principles. These bounds are *universal*, in the sense that they are independent of the geometry and distribution of the components within the composite. This is highly significant as we can obtain information about the overall transport properties of the material, without any information about the shape, distribution or geometry of the constituent components. Here we justify that these bounds are narrow within the brain, across different tissue types implying approximate trace conservation.



Fig 1. The upper bound and the lower bound on the diffusion tensor trace, for various values of mixing fraction θ and ratio of diffusitivities δ .

METHODS - To formally test the hypothesis that the trace is constant across the brain we tested the model $\lambda_1 = -\lambda_2 - \lambda_3 + constant$ in 4 normal subjects using multiple

linear regression and the bootstrap method [1]. The DTI data were acquired on a Siemens 3T Allegra MR scanner with b=700s/mm². To derive the HS bounds on the diffusion tensor trace, we modeled brain tissue as a two phase composite, consisting of extracellular space and intracellular space. White matter and gray matter differ in this model, primarily in the volume fraction of the extracellular space to the intracellular space which we denote by the variable θ . The diffusivities of the two components taken separately are assumed to be isotropic and are denoted by α and β , with $0 < \alpha \le \beta$. The ratio of the diffusivities

is defined as $\delta = \alpha / \beta$, where $0 < \delta \le 1$. If the upper and lower bounds are denoted by HS^+ and HS^- , with $\overline{\mathbf{D}}$ being the diffusion tensor, then one can show [5] that



Fig. 2. Contours of HS⁺-HS⁻. For a large range of values of parameters θ and δ , the bounds are relatively narrow and lie within a few percent.

 $HS^{-} \leq (1/3\beta) Trace(\overline{\mathbf{D}}) \leq HS^{+}, \text{ where}$ $HS^{-} = (3\delta - 2\theta\delta(1-\delta))/(3\delta + \theta(1-\delta))$ $HS^{+} = (2+\delta - 2\theta(1-\delta))/(2+\delta + \theta(1-\delta))$

RESULTS - For the DTI data, we found that the trace conservation model could account for 55% (R^2 =0.55) of the variation in λ_1 given λ_2 and λ_3 . To exclude the possibility that the correlation was a confound due to eigenvalue sorting bias we randomly permuted the eigenvalues for each subject across the voxels and and resorted the eigenvalues. We found that for the permuted data the regression model could only account for 8% (R^2 =0.08) of the variation in λ_1 , which excludes the possibility that eigenvalue sorting bias contributed substantially to the observed correlation.

The HS bounds on the diffusion tensor trace were found to be tight over a range of physiological parameters. From the inequality above and the plots, it can be seen that the bounds are comparatively tight (within a few percent) for a large range of values for mixing fraction θ and the ratio of diffusivities δ (Figs. 1 and 2).

CONCLUSIONS - Using the HS effective medium bounds, we have derived bounds on the trace of the diffusion tensor in neural tissue. The tightness of the bounds can account for the observed conservation of trace across the brain. In general, effective medium theory provides a powerful framework for understanding diffusion in brain tissue without need for a model of the tissue microgeometry.

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