Characterizing diffusion anisotropy for molecules under the influence of a parabolic potential: A plausible alternative to DTI

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INTRODUCTION

Diffusion tensor imaging (DTI) has been widely employed to characterize anisotropy in fibrous environments such as the nervous tissue. DTI has yielded new noninvasive markers of tissue state and has provided one with the ability to map the anatomical connections between different regions of such fibrous tissues. Despite the technique's success in characterizing diffusion anisotropy in directionally homogeneous regions, the Gaussian diffusion model it employs is known to be of limited validity. The studies that have aimed to map the microstructural features of tissues have noted the deviation of the logarithm of the signal from the quadratic dependence on the wave number (*q*-value) predicted by DTI. Such dependence as well as the inability of DTI to accommodate more than one major fiber orientation can be accounted for by considering several compartments with different diffusion tensors. However, the diffusion-time dependence of the MR signal in homogeneous tissue specimens [1] as well as biophysical studies on the determinants of diffusion anisotropy [2] suggest the restricted character of diffusion.

In this study, we employ a model of diffusion-attenuated MR signal for molecules under the influence of a parabolic potential field [3]. Such potentials emerge when the molecules are subject to a Hookean force, and the resulting model can be envisioned as an approximation to the mathematically more difficult restricted diffusion problems. Quadratic *q*-dependence in the exponent prevails in this model while the diffusion-time dependence resembles that of the restricted diffusion models. The observed diffusion anisotropy is attributed to the anisotropy of a spring's stiffness tensor rather than the diffusion coefficient.

THEORY

The Bloch-Torrey equation [4] is modified to include a term similar to that in the Smoluchowski operator:

$$\frac{\partial m(\mathbf{r},t)}{\partial t} = D\nabla^2 m(\mathbf{r},t) + D\beta\nabla\cdot\mathbf{f}(\mathbf{r}\, m(\mathbf{r},t)) - i\gamma\mathbf{G}(t)\cdot\mathbf{r}\, m(\mathbf{r},t)$$

where $m(\mathbf{r},t)$ is the magnetization density, γ is the gyromagnetic ratio, $\beta=(k_B T)^{-1}$ with k_B the Boltzmann constant and T the temperature, $\mathbf{f}$ is the tensorial spring constant, D is the diffusion coefficient, and $\mathbf{G}(t)$ is the linear magnetic field gradient waveform. The second term on the right hand side of the equation is the added term due to the potential $\frac{1}{2}\,\mathbf{r}^T\mathbf{f}\mathbf{r}$. By solving this expression considering the pulsed gradient spin echo (PGSE) waveform [5] with pulse duration δ and pulse separation Δ, we obtained the expression

$$E = \exp(-\mathbf{G}^T\mathbf{A}\mathbf{G}), \text{where } A = -D\gamma^2\boldsymbol{\Omega}^{-3}\left[(1-e^{-\Omega\Delta})(1-e^{-\Omega\delta})^2 e^{\Omega\delta} - (1-e^{-2\Omega\delta})e^{\Omega\delta} + 2\boldsymbol{\Omega}\delta\right] \quad (*)$$

with $\boldsymbol{\Omega}=\beta D\mathbf{f}$. We verified that when infinitesimally narrow gradient pulses ($\delta\rightarrow 0$) are applied, the signal intensity converges to Stejskal's result [6] for the case of infinitesimal pulses.

RESULTS & DISCUSSION

To test the model on real diffusion-weighted MRI data, we used the data set "118932" made publicly available by the Human Connectome Project (see Ref. [7] for acquisition parameters). To have a meaningful comparison, we used a subset of the whole data set including only those images with a b-value of less than 1500 s/mm^2. The fitting procedure involved the following steps: (i) The diffusion tensor was estimated with positive definiteness constraint [8], and diagonalized. (ii) Using an approximate relationship between the eigenvalues of the diffusion and **A** tensors, initial values for the eigenvalues of **A** are estimated. (iii) The **A** tensor was estimated by fitting the model (*) above using the initial estimates from the previous step with positive definiteness constraint. (iv) The DTI-measures such as trace, fractional anisotropy, and direction encoded color (DEC) maps were computed for the tensor **A** as well.

In Figure 1, we illustrate the trace, FA, and DEC maps for DTI (left) and the Hookean (right) models. In general, one expects a negative image in trace(**A**) maps as regions with large diffusivity should correspond to springs with small stiffness values. Such a behavior is indeed observed in the trace maps. The most visible difference is the presence of hyperintense regions in the trace(**A**) map scattered within the white-matter areas. The FA maps contain the same information for the most part. The DEC maps are also similar when the eigenvector corresponding to the smallest eigenvalue of **A** is used. The apparently noisy and anisotropic outcome in the ventricles is fully explained by the limited sensitivity of the signal on the stiffness values when these values are small.

In Figure 2, we show the norms of the residuals. These maps are very similar indicating that when one replaces DTI with the new spring model, there is no loss in the model's ability to represent the data.

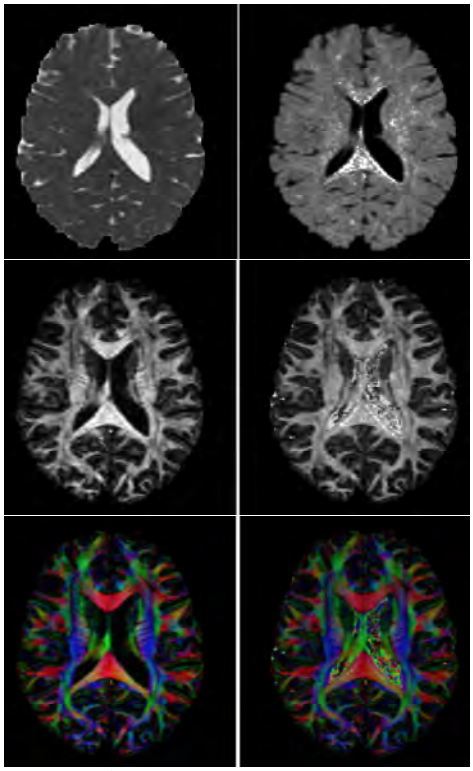

Fig. 1: Left column: DTI results. Right column: Results obtained using the new model. Top row: Trace-valued maps. Middle row: FA maps. Bottom row: Direction-encoded color (DEC) maps. For the new model, the DEC map was computed by color-coding the direction of the eigenvector of the stiffness tensor associated with its *smallest* eigenvalue.

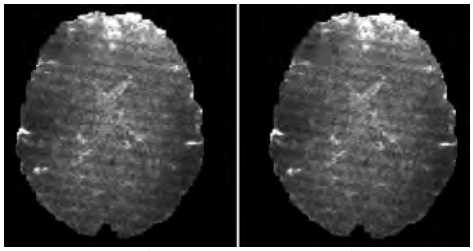

Fig. 2: Maps of the squared 2-norm of the residuals obtained from the nonlinear least-squares data-fitting for the DTI model (left) and for the new model employing anisotropic stiffness tensors (right). The images are scaled consistently. Low values indicate the agreement between the data and the models.

CONCLUSION

By studying the signal for molecules diffusing under a parabolic potential, we introduced an alternate mechanism through which diffusion anisotropy could emerge. Because the solution to this problem exhibits many features ascribed to restricted diffusion, we argue that solutions for parabolic potentials can be employed as an approximation to the solutions for the mathematically more challenging restricted diffusion problems. Our findings could also suggest an explanation for why the simple harmonic oscillator basis functions are successfully representing general diffusion-weighted MR signal profiles [9].

REFERENCES: [1] Latour et al., Proc Natl Acad Sci USA, 91:1229-1233, 1994. [2] Beaulieu and Allen, Magn Reson Med, 31:394-400, 1994. [3] Yolcu et al., submitted. [4] Torrey, Phys Rev, 104:563-565, 1956. [5] Stejskal and Tanner, J Chem Phys, 42:288-292, 1965. [6] Stejskal, J Chem Phys, 43:3597-3603, 1965. [7] Sotiropoulos et al., NeuroImage, 80:125-143, 2013. [8] Koay et al., J Magn Reson, 182:115-125, 2006. [9] Özarslan et al., NeuroImage, 78:16-32, 2013.