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# New Invariant "Lattice" Index Achieves Significant Noise Reduction in Measuring Diffusion Anisotropy

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## INTRODUCTION

The development of a quantitative, noise-immune MRI measure of diffusion anisotropy could have important biological and diagnostic applications, helping clinicians infer both the normal physiologic state of anisotropic tissues, and pathological changes in their microstructure. On theoretical grounds, indices of diffusion anisotropy derived from two or three apparent diffusion coefficients (ADCs) are not quantitative. Specifically, they exhibit a significant orientational artifact. Although rotationally invariant anisotropy indices derived from the diffusion tensor,  $\mathbf{D}$ , such as  $\lambda_1/\lambda_2 = D_{\parallel}/D_{\perp}$  do not exhibit this orientational artifact (1), they are predicted to be susceptible to contamination by noise. Our goals here are a) to understand the effect of background noise (inherent in all diffusion-weighted images (DWIs) on rotationally invariant anisotropy measures, and b) to propose a new rotationally invariant anisotropy measure that is noise-immune.

## METHODS

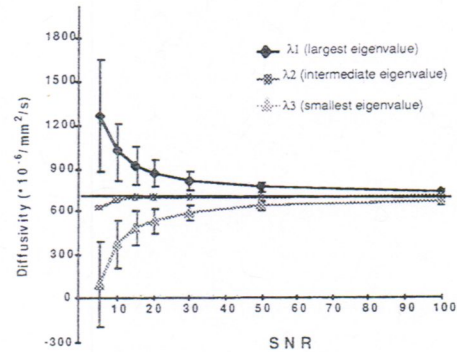
Using Monte Carlo methods, we synthesize DWIs using diffusion tensors that are representative of those we measure in different regions of living monkey brain, and the b-matrix calculated for each DWI. To each DWI, we add Gaussian noise. From this set of noisy DWIs, we estimate a diffusion tensor in each voxel, from which we calculate various diffusion anisotropy measures and characterize their statistical distributions. These include the anisotropy ratio,  $\lambda_1/\lambda_3$ , the same ratio calculated assuming cylindrical symmetry of diffusion,  $2\lambda_1/(\lambda_2+\lambda_3)$ , as well as several other rotationally invariant anisotropy measures whose value does not depend upon the manner in which of the eigenvalues of  $\mathbf{D}$  are ordered or sorted (1,2). Imaging parameters in these simulations are identical to those used in brain imaging experiments with six monkeys (2).

**"Lattice" anisotropy indices.** The invariant anisotropy indices proposed to date use only the eigenvalues of  $\mathbf{D}$  within a voxel to characterize anisotropy. The approach we propose here is to improve our estimate of diffusion anisotropy within a reference voxel by incorporating correlations between it and those in neighboring voxels. Equivalently, we use the correlations between the *shape* and *orientation* of the diffusion tensor in a reference voxel with those of its neighbors. If the measured anisotropy in a voxel results purely from random noise then we would expect the orientation of the diffusion ellipsoid in one voxel to be uncorrelated with that of its neighbors. However, if the anisotropy is a characteristic of the tissue, the diffusion ellipsoid in a particular voxel will have a preferential direction. If the tissue is locally homogeneous, there will also be a strong correlation with the orientation of the ellipsoids in adjacent voxels. The new "lattice" anisotropy index that we propose here reduces noise not by averaging the diffusion tensors over a region of interest, but by averaging the tensor dot product (a measure of the similarity) of the anisotropic parts of diffusion tensors in adjacent voxels (1).

## RESULTS AND DISCUSSION

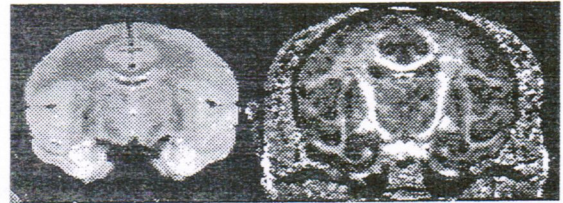
Figure 1 shows the sorted principal diffusivities,  $\lambda_1$ ,  $\lambda_2$ , and  $\lambda_3$ , each as a function of SNR, for a voxel containing an isotropic tissue (comparable to gray matter). Expected values of  $\lambda_1$ ,  $\lambda_2$  and  $\lambda_3$  are also shown. A systematic sorting bias exists, such that for any non-zero noise level,  $\lambda_1$  is larger and  $\lambda_3$  is smaller than their expected values. The sorting bias in  $\lambda_2$  is much smaller at all SNRs. As

SNR increases, an isotropic medium appears increasingly anisotropic.



This systematic "sorting" bias causes  $\lambda_1/\lambda_3$  to be consistently larger than its expected value, both in isotropic and in anisotropic media. This bias can be mitigated, in part, by using  $2\lambda_1/(\lambda_2+\lambda_3)$ , however, this measure explicitly assumes that diffusion is cylindrically symmetric without experimental evidence. The scalar invariant anisotropy indices, such as the Volume Ratio (2), and the Relative and Fractional Anisotropies (1) are all insensitive to this sorting bias because they are insensitive to the order in which the principal diffusivities are assigned. Still, our simulations show that these measures are sensitive to noise contamination. The new "lattice" anisotropy index is virtually bias-free at all noise levels and has error variances significantly smaller than those of all the other indices at noise levels typical of clinical DW-MR studies.

Figure 2 shows multislice images of a) the T2-weighted amplitude,  $A(b=0)$ ; and b) the new "lattice" anisotropy index. The lattice anisotropy image shows the white matter regions clearly, and suppresses signal from the gray matter and CSF filled compartments. Significant noise reduction is achieved without compromising structural details.



## CONCLUSIONS

We show that background noise in the DWIs significantly affects the distribution of anisotropy measures estimated from the diffusion tensor. Monte Carlo simulations of Diffusion Tensor Imaging experiments explain the origin of the statistical bias in some measures. Anisotropy measures that do not depend upon the order in which the principal diffusivities are sorted help eliminate this bias, but not the sensitivity to background noise. New "lattice" anisotropy indices are rotationally invariant, are free of bias, and show significant noise reduction at noise levels typical of clinical DW-MRI studies.

## REFERENCES

- 1) Basser, P., Pierpaoli C., 1995, SMR/ESMRMB, v2, p. 900.
- 2) Pierpaoli C., et al., 1994, SMR, vol. 2 pp 1038.