# Diffusion tensors from double-PFG of the human brain

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**Introduction:** The double-pulsed field gradient (double-PFG) sequence is a recent and exciting development in diffusion MRI (dMRI) that allows for new ways to probe tissue microstructure. It uses two pairs of diffusion-sensitizing gradients instead of the current standard for diffusion MRI, which comprises a single gradient pair (single-PFG). Experimental results demonstrate that angular double-PFG analysis alleviates the demand for strong gradients for microstructure determination [Ozarslan08, Koch08, Shemesh09], and that estimation of novel features of tissue that displays a microscopic anisotropy may be possible using clinical scanners [Westin12]. We here present how diffusion tensors can be estimated from double-PFG data.

**Aims:** To explore the use of the diffusion tensor model towards the description and assessment of compartment shape anisotropy [Ozarslan08, Shemesh09] from *in vivo* double-PFG MRI of the human brain on a clinical whole-body MRI scanner. Current practice uses angular double-PFG MRI for the assessment of compartment shape anisotropy [Ozarslan09, Shemesh11, Westin12], which necessitates the selection of a 2D plane of interest in the diffusion data. Our goal is to generate tensor models that will capture interesting features in the double-PFG data, which potentially also can lead to a more general approach for describing compartment shape anisotropy, not requiring the selection of a 2D plane of interest.

**Theory and method:** Images were acquired using a stimulated-echo based double-PFG sequence at a clinical MRI scanner (Philips Achieva 3T). Imaging parameters were: $TE_1$ = 39 ms, $TE_2$ = 55 ms, TR = 2500 ms, voxel size = 3·3·3 $mm^3$. The diffusion encoding of the first and second gradient pairs were performed in the directions specified by the icosahedron (6 directions), giving a total of 6*6=36 measurements. The *b*-value of each gradient pair was 500 $s/mm^2$, yielding a total *b*-value of 1000 $s/mm^2$. The mixing time was approximately 25 ms. In order to understand what to expect from the phenomenological model, consider a voxel containing a distribution $p(\mathbf{u})$ of microscopic domains in which the diffusion is anisotropic and described by the diffusion tensor $\mathbf{D}(\mathbf{u}) = \mathbf{u}^T\mathbf{u}(AD - RD) + \mathbf{I}\,RD$, where *AD* and *RD* are the axial and radial diffusivities in the microscopic domain, and $\mathbf{u}$ is a row-vector. Under these assumptions, the expected signal from the double-PFG experiment is described

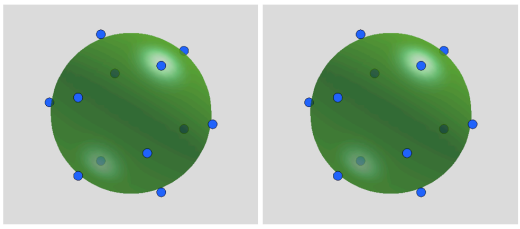


**Fig 1:** Icosahedral sampling of gradient directions $\mathbf{g}_1$ and $\mathbf{g}_2$ corresponding to the first and second diffusion block.

$$S_d(\mathbf{g}_1,\mathbf{g}_2) = \int p(\mathbf{u}) \exp(-b\mathbf{g}_1^T\mathbf{D}(\mathbf{u})\mathbf{g}_1) \cdot \exp(-b\mathbf{g}_2^T\mathbf{D}(\mathbf{u})\mathbf{g}_2)\ \mathrm{d}\mathbf{u} \quad (1)$$

$$S_d(\mathbf{g}_1,\mathbf{g}_2) = \int p(\mathbf{u}) \exp(-b(<\mathbf{D},\mathbf{g}_1\mathbf{g}_1^T> + <\mathbf{D},\mathbf{g}_2\mathbf{g}_2^T>))\ \mathrm{d}\mathbf{u} \quad (2)$$

$$S_d(\mathbf{g}_1,\mathbf{g}_2) = \int p(\mathbf{u}) \exp(-b <\mathbf{D}(\mathbf{u}), \underbrace{\mathbf{g}_1\mathbf{g}_1^T + \mathbf{g}_2\mathbf{g}_2^T}_{\text{measurement tensor}}>)\ \mathrm{d}\mathbf{u} \quad (3)$$

by Eq 3. By expressing the exponents as inner products (Eq 2), it can be seen that the two gradients $\mathbf{g}_1$ and $\mathbf{g}_2$ in the double-PFG experiment are added linearly as outer products. Eq (3) shows that with the tensor model, in double-PFG the diffusion encoding gradient vector is generalized to a planar measurement tensor. In our experiment we have acquired 36 pairs of measurements, the combinations of the two icosahedral gradient directions $\mathbf{g}_1$ and $\mathbf{g}_2$ (Fig 1). 6 of these measurements have the same directions of $\mathbf{g}_1$ and $\mathbf{g}_2$, and the remaining 30 are mixed. Due to the special geometry of the icosahedron, all gradient directions have the same "distance" between each other, and (with appropriate sign of the vectors) the angle is always 63.4 degrees, and thus give rise to the same shaped rank-2 measurements tensor (depicted in red under Eq 3). For the measurements where $\mathbf{g}_1$ and $\mathbf{g}_2$ have the same direction, the measurement tensor is of rank one, as in the cases of regular single-PFG. This means that we have two types of measurements, 1) mixed - giving planar basis functions, and 2) collinear - giving specific gradient direction. In Figure 2 we show the results from estimating the tensor model **D** from each of those two basis sets. It is known from angular double-PFG that compartment shape anisotropy can be measured with varying the angle between the gradient pairs. When there is compartment shape anisotropy, the signal will decrease (get darker) when the angle increases. As an alternative to angular double-PFG, we propose that the ratio between the tensors measured with collinear and non-collinear sets contains information about compartment shape anisotropy. A related way to estimate compartment shape anisotropy is described in [Lawrence12].

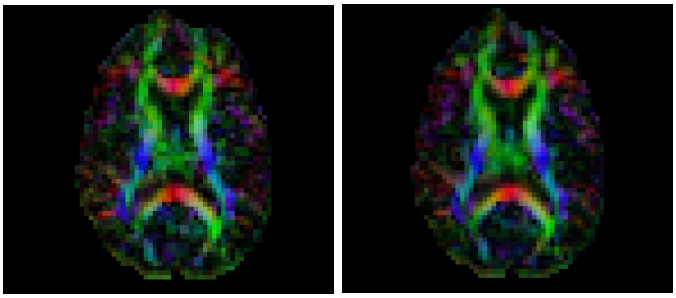

**Fig 2:** Tensors estimated from collinear basis-set (left) and tensors estimated from planar basis set (right).

**Discussion and conclusions:** The advantage of the double-PFG sequence is that it provides previously unavailable diffusion properties that can be mapped into families of new types of geometric and tissue specific parameters [Ozarslan09], and that it alleviates the requirement for high-strength gradients for microstructure determination, since the theory supports that it can be performed at the "low *b*" or "low *q*" values [Ozarslan08, Shemesh09] available on clinical scanners. The presented work shows further evidence that it is possible to perform *in vivo* double-PFG imaging of the human brain with a good SNR, indicating that the new the microstructural contrasts from double-PFG can be made available to studies of clinical populations. The tensors from collinear and non-collinear basis-sets introduced above may provide new interesting measures of microstructure.

**References:** [Ozarslan08] Özarslan E, Basser PJ. The Journal of Chemical Physics, 2008;128:154511-11. [Koch08] Koch MA and Finsterbusch J, Magn. Reson. Med. 2008, 60:90. [Shemesh09] Shemesh N, Özarslan E, Basser PJ, Cohen Y. Journal of Magnetic Resonance 2009;198:15–23. [Ozarslan09] Özarslan E. Journal of Magnetic Resonance 2009;199:56-67. [Shemesh11] Shemesh N, Sadan O, Offen D, Cohen Y. Proc Intl Soc Magn Reson Med 2011. [Westin12] Westin CF, Nilsson M, Pasternak O, Topgaard D, Knutsson H. In Proc Intl Soc Magn Reson Med 2012. [Lawrence12] Lawrence M, Finsterbusch, Magnetic Resonance in Med. 2012.