

## When is a DT-MRI Sampling Scheme Truly Isotropic?

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**Synopsis:** Necessary conditions for optimal DT-MRI sampling schemes are that the gradient orientations are uniformly distributed and that the precision of the measurement of the diffusion tensor be independent of its orientation. We show that a simplifying assumption that has previously been made in the study of DT-MRI sampling schemes has important consequences in the design of rotationally invariant sampling schemes.

**Uniform distribution of gradients:** For isotropic sampling, the 3D measurement space should be sampled uniformly. Recalling that the diffusion tensor is antipodally-symmetric, a measurement along a gradient vector  $\mathbf{x}_i = (g_{x_i}, g_{y_i}, g_{z_i})$  is equivalent to a measurement along  $-\mathbf{x}_i$ . Hence, we must consider *orientational* rather than *directional* information. To determine the average orientation sampled, we compute the mean outer-product of the gradient vectors as in Eq. [1], where we have used the Einstein repeated indices notation. If the gradient orientations are uniformly distributed, then the mean outer-product should be isotropic, i.e.  $\langle \mathbf{x}^T \mathbf{x} \rangle = k\mathbf{I}$ . Note that while this condition is met by a number of schemes (e.g. dual-gradient<sup>1</sup>, tetra-orthogonal<sup>2</sup>, decahedral<sup>3</sup>, icosahedral<sup>4</sup>, electrostatic<sup>5</sup> and minimum condition number<sup>6</sup> configurations), it is not sufficient to ensure that the statistical properties of the estimated tensor are rotationally invariant.

$$\langle \mathbf{x}^T \mathbf{x} \rangle = \frac{1}{N} \sum_{i=1}^N \mathbf{x}_i^T \mathbf{x}_i = 1/N \begin{pmatrix} g_{x_i}^2 & g_{x_i} g_{y_i} & g_{x_i} g_{z_i} \\ g_{x_i} g_{y_i} & g_{y_i}^2 & g_{y_i} g_{z_i} \\ g_{x_i} g_{z_i} & g_{y_i} g_{z_i} & g_{z_i}^2 \end{pmatrix} \quad [1]$$

**Rotationally invariant precision matrix** Now we consider the precision of elements of the diffusion tensor,  $\mathbf{D} = [D_{xx}, D_{yy}, D_{zz}, D_{xy}, D_{xz}, D_{yz}]$ . The signal attenuation for measurement in a vector direction,  $\mathbf{x}_m$  is given by  $I_m = I_0 \exp(-\mathbf{B}_m \cdot \mathbf{D})$ , where  $\mathbf{B}$  is an  $N \times 6$  matrix, where the  $m^{\text{th}}$  row is given by  $\mathbf{B}_m = b [g_{x_m}^2, g_{y_m}^2, g_{z_m}^2, 2g_{x_m}g_{y_m}, 2g_{x_m}g_{z_m}, 2g_{y_m}g_{z_m}]$ . If the vector  $\mathbf{s}$  has components of  $-\log(I_m/I_0)$ , then the best estimate of the diffusion tensor is given by:  $\mathbf{D}_{est} = (\mathbf{B}^T \boldsymbol{\Sigma}^{-1} \mathbf{B})^{-1} (\mathbf{B}^T \boldsymbol{\Sigma}^{-1}) \mathbf{s}$ , where  $\boldsymbol{\Sigma}^{-1}$  is a diagonal matrix whose elements,  $f_m$ , correspond to the uncertainties in  $\mathbf{s}_m$ . The diagonal elements of the first term,  $(\mathbf{B}^T \boldsymbol{\Sigma}^{-1} \mathbf{B})^{-1}$ , represent the error variances of the estimated parameters and  $\mathbf{B}^T \boldsymbol{\Sigma}^{-1} \mathbf{B}$  therefore represents the symmetric precision matrix, (where again, we have used the Einstein repeated indices notation):

$$\mathbf{M} = \mathbf{B}^T \boldsymbol{\Sigma}^{-1} \mathbf{B} = b^2 \begin{bmatrix} f_m g_{x_m}^4 & f_m g_{x_m}^2 g_{y_m}^2 & f_m g_{x_m}^2 g_{z_m}^2 & f_m g_{x_m}^3 g_{y_m} & f_m g_{x_m}^3 g_{z_m} & f_m g_{x_m}^2 g_{y_m} g_{z_m} \\ \cdot & f_m g_{y_m}^4 & f_m g_{y_m}^2 g_{z_m}^2 & f_m g_{x_m} g_{y_m}^3 & f_m g_{x_m} g_{y_m}^2 g_{z_m} & f_m g_{y_m}^3 g_{z_m} \\ \cdot & \cdot & f_m g_{z_m}^4 & f_m g_{x_m} g_{y_m} g_{z_m}^2 & f_m g_{x_m} g_{z_m}^3 & f_m g_{y_m} g_{z_m}^3 \\ \cdot & \cdot & \cdot & f_m g_{x_m}^2 g_{y_m}^2 & f_m g_{x_m}^2 g_{y_m} g_{z_m} & f_m g_{x_m} g_{y_m}^2 g_{z_m} \\ \cdot & \cdot & \cdot & \cdot & f_m g_{x_m}^2 g_{z_m}^2 & f_m g_{x_m} g_{y_m} g_{z_m}^2 \\ \cdot & \cdot & \cdot & \cdot & \cdot & f_m g_{y_m}^2 g_{z_m}^2 \end{bmatrix} \quad [2]$$

Close inspection of Eq. [2] reveals that  $\mathbf{M}$  possesses 15 unique elements (since  $\mathbf{M}_{4,4} = 4\mathbf{M}_{1,2}$ ,  $\mathbf{M}_{5,5} = 4\mathbf{M}_{1,3}$ ,  $\mathbf{M}_{6,6} = 4\mathbf{M}_{2,3}$ ,  $\mathbf{M}_{4,5} = 2\mathbf{M}_{1,6}$ ,  $\mathbf{M}_{4,6} = 2\mathbf{M}_{2,5}$  and  $\mathbf{M}_{5,6} = 4\mathbf{M}_{1,3}$ ). It has recently been shown<sup>8</sup> that for the precision matrix to be rotationally invariant, it should take the following form.

$$\mathbf{M} = \begin{bmatrix} \Gamma & \Xi \\ \Xi & \Psi \end{bmatrix}, \text{ where } \Gamma = \begin{bmatrix} \lambda + 2\mu & \mu & \mu \\ \mu & \lambda + 2\mu & \mu \\ \mu & \mu & \lambda + 2\mu \end{bmatrix}, \Psi = \begin{bmatrix} 4\mu & 0 & 0 \\ 0 & 4\mu & 0 \\ 0 & 0 & 4\mu \end{bmatrix}, \text{ and } \Xi = \begin{bmatrix} 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix} \quad [3]$$

Since this form constrains relationships between the 15 unique elements of the precision matrix, it suggests that one only needs to find a set of gradient orientations that satisfy 15 simultaneous equations in order to obtain a rotationally invariant precision matrix. If the simplifying assumption is made that the error variances in  $\log(I_m/I_0)$  are independent of the orientation of the tensor, and equal to a constant,  $f$ , (as has been done previously<sup>6,9</sup>), then  $\boldsymbol{\Sigma}^{-1} = f\mathbf{I}$ , and the precision matrix  $\mathbf{M}$  becomes proportional to  $\mathbf{B}^T \mathbf{B}$ , which is solely dependent on the gradient orientations. Under this assumption, it is possible to find sets of gradient orientations that satisfy the 15 simultaneous equations (irrespective of the orientation of the tensor that is being estimated). Indeed, by assuming that  $\boldsymbol{\Sigma}^{-1} = f\mathbf{I}$ , it has been shown that all icosahedral sampling schemes should be equivalent to a scheme in which an infinite number of directions are sampled<sup>9</sup> (and therefore, by definition, rotationally invariant). However, there is empirical evidence<sup>6</sup> to show that an icosahedral scheme with six directions is not rotationally invariant, and that an icosahedral scheme with, say, 30 directions is more rotationally invariant.

To reconcile these disparate predictions, it should be remembered that  $\boldsymbol{\Sigma}^{-1}$  contains the reciprocal error variances of the log-transformed intensities, i.e.  $f_m = 1/\sigma_{\ln(I_m)}^2$ . To a first approximation,  $\sigma_{\ln(I_m)}^2 = \sigma_{I_m}^2 / I_m^2$  which leads to  $f_m = (I_0 / \sigma_{I_m})^2 \exp(-\mathbf{B}_m \cdot \mathbf{D})$ . When these  $f_m$  are substituted into Eq. [2], it will be seen that the diffusion tensor appears in the precision matrix, and hence  $\mathbf{M}$  is no longer solely dependent on the gradient orientations, but now also on the orientation of the tensor. (N.B. In the trivial case of isotropic tensors, the assumption that  $\boldsymbol{\Sigma}^{-1} = f\mathbf{I}$  is valid). It may be possible to find a set of gradient orientations that satisfy the 15 simultaneous equations for a particular anisotropic tensor, but this is unlikely to be the same set of orientations that solves the equations for another anisotropic tensor.

**Conclusion:** Careful analysis of the components of the precision matrix,  $\mathbf{M}$ , has shown that the design of truly rotationally-invariant DT-MRI sampling schemes is not as straightforward as was previously thought.

### References:

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