# It is *Not* Possible to Design a Rotationally Invariant Sampling Scheme for DT-MRI

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**INTRODUCTION:** The choice of gradient sampling orientations for DT-MRI experiments has exercised many groups in the field. Of particular interest is the design of sampling schemes that will ensure that the error / variance in tensor estimates is independent of the relative orientation of the tensor to the reference frame established by the sampling vectors, which others have termed 'statistical rotational invariance' or '*SRI*'[1,2]. Previous work has identified a relationship between the condition number of the quadratic encoding matrix, formed from the gradient sampling orientations, and the variance in the estimated diffusion tensor[3]. Batchelor *et al.*[4] showed that certain sampling schemes (e.g., the dual-gradient scheme) had rotationally *variant* condition numbers while, those derived from the vertices of an icosahedron had rotationally *invariant* condition numbers. Thus, schemes based on vectors pointing to the vertices of an icosahedron (or tessellated icosahedrons) cause initial excitement. However, Jones[2] showed that, in discord with this theory, not all icosahedral schemes are the same – and that rotationally invariant condition number is a necessary but insufficient requirement for rotational invariance. A more general framework has been proposed[1,5] – which provides a template for sampling schemes in terms of the fourth order precision matrix. Previous theoretical considerations suggested that, under the *linear* framework, a statistically rotationally invariant sampling scheme could not be designed, except for the trivial case of isotropic tensors[5]. Here, we address an important and long outstanding question in the DT-MRI literature, i.e. In the limit of an infinite number of sampling orientations, can one design a sampling scheme which is statistically rotationally invariant?

**THEORY:** By combining results from previous works[1,5,6], we can show how the precision matrix, **M'**, in estimation of the diffusion tensor, **D**, can be expressed in terms of the elements of the $m$ unit sampling vectors, $\mathbf{g}$ , the $b$-values, $b_m$ and resultant **B** matrices, $\mathbf{B}_m$ (where $\mathbf{B}_m = b_m \mathbf{g}_m{}^{\mathbf{T}} \mathbf{g}_m$), via Eq. [1] , where $\alpha = 0$ and 1 for non-linear and linear regression, respectively:

$$\mathbf{M'}=\begin{bmatrix}
\sum_m \frac{b_m^2 g_{X_m}^4}{\alpha+\exp(2Tr(\mathbf{B}_m\mathbf{D})} & \sum_m \frac{b_m^2 g_{X_m}^2 g_{Y_m}^2}{\alpha+\exp(2Tr(\mathbf{B}_m\mathbf{D})} & \sum_m \frac{b_m^2 g_{X_m}^2 g_{Z_m}^2}{\alpha+\exp(2Tr(\mathbf{B}_m\mathbf{D})} & 2\sum_m \frac{b_m^2 g_{X_m}^3 g_{Y_m}}{\alpha+\exp(2Tr(\mathbf{B}_m\mathbf{D})} & 2\sum_m \frac{b_m^2 g_{X_m}^3 g_{Z_m}}{\alpha+\exp(2Tr(\mathbf{B}_m\mathbf{D})} & 2\sum_m \frac{b_m^2 g_{X_m}^2 g_{Y_m} g_{Z_m}}{\alpha+\exp(2Tr(\mathbf{B}_m\mathbf{D})} \\
. & \sum_m \frac{b_m^2 g_{Y_m}^4}{\alpha+\exp(2Tr(\mathbf{B}_m\mathbf{D})} & \sum_m \frac{b_m^2 g_{Y_m}^2 g_{Z_m}^2}{\alpha+\exp(2Tr(\mathbf{B}_m\mathbf{D})} & 2\sum_m \frac{b_m^2 g_{X_m} g_{Y_m}^3}{\alpha+\exp(2Tr(\mathbf{B}_m\mathbf{D})} & 2\sum_m \frac{b_m^2 g_{X_m} g_{Y_m}^2 g_{Z_m}}{\alpha+\exp(2Tr(\mathbf{B}_m\mathbf{D})} & 2\sum_m \frac{b_m^2 g_{Y_m}^3 g_{Z_m}}{\alpha+\exp(2Tr(\mathbf{B}_m\mathbf{D})} \\
. & . & \sum_m \frac{b_m^2 g_{Z_m}^4}{\alpha+\exp(2Tr(\mathbf{B}_m\mathbf{D})} & 2\sum_m \frac{b_m^2 g_{X_m} g_{Y_m} g_{Z_m}^2}{\alpha+\exp(2Tr(\mathbf{B}_m\mathbf{D})} & 2\sum_m \frac{b_m^2 g_{X_m} g_{Z_m}^3}{\alpha+\exp(2Tr(\mathbf{B}_m\mathbf{D})} & 2\sum_m \frac{b_m^2 g_{Y_m} g_{Z_m}^3}{\alpha+\exp(2Tr(\mathbf{B}_m\mathbf{D})} \\
. & . & . & 4\sum_m \frac{b_m^2 g_{X_m}^2 g_{Y_m}^2}{\alpha+\exp(2Tr(\mathbf{B}_m\mathbf{D})} & 4\sum_m \frac{b_m^2 g_{X_m}^2 g_{Y_m} g_{Z_m}}{\alpha+\exp(2Tr(\mathbf{B}_m\mathbf{D})} & 4\sum_m \frac{b_m^2 g_{X_m} g_{Y_m}^2 g_{Z_m}}{\alpha+\exp(2Tr(\mathbf{B}_m\mathbf{D})} \\
. & . & . & . & 4\sum_m \frac{b_m^2 g_{X_m}^2 g_{Z_m}^2}{\alpha+\exp(2Tr(\mathbf{B}_m\mathbf{D})} & 4\sum_m \frac{b_m^2 g_{X_m} g_{Y_m} g_{Z_m}^2}{\alpha+\exp(2Tr(\mathbf{B}_m\mathbf{D})} \\
. & . & . & . & . & 4\sum_m \frac{b_m^2 g_{Y_m}^2 g_{Z_m}^2}{\alpha+\exp(2Tr(\mathbf{B}_m\mathbf{D})}
\end{bmatrix} \quad [1]$$

It has been shown that for the precision matrix to be statistically rotationally invariant, it should take the following general form[1,7]:

$$\mathbf{M}_{\text{iso}}=\begin{bmatrix}
\lambda+2\mu & \lambda & \lambda & 0 & 0 & 0 \\
\lambda & \lambda+2\mu & \lambda & 0 & 0 & 0 \\
\lambda & \lambda & \lambda+2\mu & 0 & 0 & 0 \\
0 & 0 & 0 & 4\mu & 0 & 0 \\
0 & 0 & 0 & 0 & 4\mu & 0 \\
0 & 0 & 0 & 0 & 0 & 4\mu
\end{bmatrix} \quad [2]$$

In Eq. [1], $\mathbf{M'}_{4,4} = 4\mathbf{M'}_{1,2}$ , $\mathbf{M'}_{5,5} = 4\mathbf{M'}_{1,3}$ and $\mathbf{M'}_{6,6} = 4\mathbf{M'}_{2,3}$, which on comparison with Eq. [2] means that $\lambda$ must be equal to $\mu$.. To conform to the prescription in Eq. [2], *all* elements of M' should conform for *all* possible tensors. Therefore, if we can find just one example of non-conformance, we have shown that the design is not *SRI*. To make progress, we examine just the non-zero elements of M', which contain only even powers of the elements of sampling vector **g**. Thus, we define an even function of these elements, as: $\kappa(\mathbf{g}_p) = (g_{X_p})^{2l}(g_{Y_p})^{2m}(g_{Z_p})^{2n}$ . Summing over an *infinite* number of directions, is the same as integrating over all angles – so we re-parameterize **g** in spherical co-ordinates, $\mathbf{g} = [\sin\theta\cos\phi, \sin\theta\sin\phi, \cos\phi]$, thus the form for the infinite sums in Eq. [1] becomes

$$< f >= \frac{b^2}{4\pi}\int_{\phi=0}^{2\pi}\int_{\theta=0}^{\pi} \exp(-2Tr(\mathbf{BD}))\kappa(\mathbf{g})\sin(\theta)d\theta d\phi \quad [3]$$

If we assume **D** is aligned with principal lab frame, (i.e., $\mathbf{D}_{ij}=\delta_{ij}\lambda_i$, where $\delta_{ij}$ is the Dirac delta function, and $\lambda_i$ are eigenvalues), then

$$< f >= \frac{b^2}{4\pi}\int_{\phi=0}^{2\pi}\int_{\theta=0}^{\pi} (g_X)^{2l}(g_Y)^{2m}(g_Z)^{2n}\exp(-(s_1 g_X^2 + s_2 g_Y^2 + s_3 g_Z^2))\sin(\theta)d\theta d\phi \quad [4]$$

where $s_i = 2b\lambda_i$, for $i$=1,2,3.

First, we consider the trivial case of isotropic tensors, i.e., $\lambda_i = \lambda$. The exponent in Eq.[4] can be factored out as a scalar multiplier, and the result is the sum of an infinite number of sampling orientations which Batchelor et al.[4] have previously shown takes the form in Eq. [2]. For a more general case, however, the evaluation of Eq.[4] becomes more complex. Space prohibits detailed working, (utilizing Mathematica), but the end result is:

$$\langle f(l,m,n,s_1,s_2,s_3)\rangle = \frac{b^2}{2\sqrt{\pi}}e^{-s_3}\frac{\Gamma(1+l+m)\Gamma(\frac{1}{2}+n)}{\Gamma(\frac{3}{2}+l+m+n)}\sum_{k=0}^{\infty}\left(\frac{(1+l+m)_k}{k!\,(\frac{3}{2}+l+m+n)_k}\sum_{q=0}^{k}\left(\binom{k}{q}(s_3-s_1)^{k-q}(s_1-s_2)^q\frac{\Gamma(\frac{1}{2}+m+q)}{\Gamma(1+m+q)}{}_2F_1(-2l;\tfrac{1}{2}+m+q;1+2m+2q;2)\right)\right) \quad [5]$$

where ${}_1\tilde{F}_1(a;b;z) = {}_1F_1(a;b;z)/\Gamma(b)$ is the regularized confluent hypergeometric function, ${}_1F_1(a;b;z) = \sum_{k=0}^{\infty}\left((a)_k z^k/(b)_k k!\right)$ is the Kummer hypergeometric function, and $(a)_n = a(a+1)(a+2)\cdots(a+(n-1))$ is the Pochhammer function. We now assume a general tensor such that $(s_1, s_2, s_3)=(2b\lambda_1, 2b\lambda_2, 2b\lambda_3)=(0.1, 0.01, 0.001)$ and evaluate the leading three diagonal elements of M', ($M_{1,1}$, $M_{2,2}$ and $M_{3,3}$) using Eq. [5]. The results are $f(2,0,0, 0.1, 0.01, 0.001) = 0.195056\ldots$; $f(0,2,0,0.1,0.01,0.001) = 0.195754\ldots$ and $f(0,0,2,0.1,0.01,0.001) = 0.190843\ldots$. This indicates that the leading terms are not equal and therefore the prescription given in Eq. [2] is violated.

**CONCLUSION:** In the limit of an infinite number of sampling vectors, the precision matrix is rotationally invariant *only* for the trivial case of isotropic tensors – a result previously outlined elsewhere[5]. Even in this infinite limit, however, for a given anisotropic tensor, the leading 3 diagonal terms of M' are unequal and hence the condition laid out in Eq. [2] is violated. As discussed earlier, just one example of non-conformance to Eq. [2] is sufficient to conclude that, despite claims by some groups to the contrary, it is indeed <u>NOT</u> possible to design a statistically rotationally invariant sampling scheme.

**REFERENCES:** **1.** Basser et al. *TMI* 2003 ; 22 :785- ; **2.** Jones *MRM* 2004; 51:807-; **3.** Skare et al. *J Magn Reson* 2000; 147: 340- ; **4.** Batchelor et al. *MRM* 2003; 49:1143-; **5.** Jones *Proc ISMRM* 2003, p. 2118. **6.** Koay et al. *J Magn Reson* 2006; 182:115-; **7.** Hext *Biometrika* 1963; 50:353-;