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# Theoretical and Experimental Analysis of Imaging Gradients in DTI

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***Abstract*—A comprehensive, analytical framework for MR–DTI is constructed in a linear algebra setup. The expressions describing the effects of imaging gradients show formulation ambiguities. Center–symmetric gradient schemes use no cross terms (NoCroT) in the calculations resulting, at least in theory, in the alleviation of the issue. When three estimation methods, *all gradients*, NoCroT and *diffusion gradients only* are compared based on experimental results it is observed that the full inclusion of imaging gradients can be detrimental and there is slight improvement with NoCroT over *diffusion gradients only*. It is concluded that design of new diffusion gradient schemes via optimization is necessary to decouple to the maximum extent the effects of imaging gradients.**

## I. INTRODUCTION

The mathematical setup provided in the literature [1], [2] that describes the effects of all gradients for Diffusion Tensor Imaging (DTI) experiments is not adequate for the formulation of optimization problems with improvement objectives of the diffusion gradient scheme performance. The effects are relevant when a small field of view, thus large imaging gradients, is used. A concise framework is provided in this manuscript that yields interesting conclusions about the DTI model after the analysis of the experimental results.

The solution of the modified Bloch equation in [3] models the effects of diffusion in pulsed gradient spin echo (PGSE) experiment. The generalization to DTI experiments is expressed by [1], [2]

$$S(G,t) = S_0\, exp\left(-\gamma^2 \int_0^t h(G(\zeta))\, D\, [h(G(\zeta))]^T\, d\zeta\right). \tag{1}$$

Here $G(\cdot) = [\, G_x(\cdot) \quad G_y(\cdot) \quad G_z(\cdot)\,]$ denotes the time course of the magnetic field gradient vector, $\gamma$ is the gyromagnetic ratio of the proton, $S$ denotes the signal intensity at each pixel and $S_0$ comes from the reference image obtained without diffusion gradients. The time $t$ is chosen to be $T_E$, the echo time. The vector valued function $h(\cdot)$ is given by

$$h(G,\zeta) = \int_0^\zeta G(\xi)d\xi - 2u(\zeta-\tau)\int_0^\tau G(\xi)d\xi \tag{2}$$

where $\tau$ is the time of the $\pi$ pulse and $u(\cdot)$ denotes the unit step function. It is important to note that calculation of $h$ involves the time course of all gradients [1], [4], [5] not only the diffusion sensitizing ones.

The diffusion tensor in (1) is of rank two and both of the arguments it operates on are always equal, thus it is a quadratic form and is represented by $3\times3$ symmetric matrix. By treating the set of symmetric matrices as a six dimensional vector (sub)space, (1) can be written as a set of linear equations between the $m$ diffusion weighted measurements and the representation of $D$, $d \in \mathbb{R}^6$, with the choice of basis vectors corresponding to the map

$$d = [d_1, d_2, d_3, d_4, d_5, d_6]^T \longmapsto D = \begin{bmatrix} d_1 & d_4 & d_6 \\ d_4 & d_2 & d_5 \\ d_6 & d_5 & d_3 \end{bmatrix}. \tag{3}$$

By defining $h_i(\cdot) = h(G^i(\cdot))$ with $G^i(\cdot)$ denoting the time course of the gradients at the $i^th$ acquisition and $p = [\,\ln(S_0) - \ln(S_1), \quad \ldots \quad \ln(S_0) - \ln(S_m)]^T$ the equation is written as

$$\gamma^2\, V\, d = p \tag{4}$$

where $V$ is

$$\int_0^t \begin{bmatrix} h_{1x}^2 & h_{1y}^2 & h_{1z}^2 & 2h_{1x}h_{1y} & 2h_{1y}h_{1z} & 2h_{1x}h_{1z} \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\ h_{mx}^2 & h_{my}^2 & h_{mz}^2 & 2h_{mx}h_{my} & 2h_{my}h_{mz} & 2h_{mx}h_{mz} \end{bmatrix} d\zeta. \tag{5}$$

## II. COMPONENTS OF $V$

The matrix $V$ defined in (5) is a nonlinear function of gradients. In order to distinguish the effects of diffusion and imaging gradients in $V$, $G$ can be written as a sum of its diffusion and imaging parts $G = G_D + G_I$ since their (time axis) support does not intersect. The definition of $h$ given in (2) implies that $h(G_D+G_I) = h(G_D)+h(G_I)$. Based on this observation, $V$ can be separated into three parts by expanding (5), $V = V_D + V_I + V_C$ (see the top of the next page for the definition).

Here, $V_D$ represents the effect of diffusion gradients, $V_I$ is for imaging gradients and $V_C$ describes the cross terms between the two types of gradients.

In the ideal case where the imaging and diffusion gradients have rectangular shapes (rather than trapezoids) one can separate both imaging and diffusion gradients as a product of a scalar function of time and a vector (not necessarily of unit norm):

$$G_*(\xi) = \beta_*(\xi)\, g_* = \beta_*(\xi)\, [\, g_{*x} \quad g_{*y} \quad g_{*z}\,] \tag{6}$$

where the asterisk can be any of $ro, pe, ss$ (read out, phase encode, slice select) for imaging or $D$ for diffusion gradients. Define

$$\mu_*(\zeta) = \int_0^\zeta \beta_*(\xi)d\xi - 2u(\zeta-\tau)\int_0^\tau \beta_*(\xi)d\xi. \tag{7}$$

to obtain from (2)

$$h(G_*,\zeta) = \mu_*(\zeta)\, g_* = \mu_*(\zeta)\, [\, g_{*x} \quad g_{*y} \quad g_{*z}\,]. \tag{8}$$

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$$
\begin{aligned}
V &= \int_0^t \begin{bmatrix} h_x^2(G_{1D}) & \cdots & 2h_x(G_{1D})\,h_z(G_{1D}) \\ \vdots & & \vdots \\ h_x^2(G_{mD}) & \cdots & 2h_x(G_{mD})\,h_z(G_{mD}) \end{bmatrix} d\zeta + \int_0^t \begin{bmatrix} h_x^2(G_I) & \cdots & 2h_x(G_I)\,h_z(G_I) \\ \vdots & & \vdots \\ h_x^2(G_I) & \cdots & 2h_x(G_I)\,h_z(G_I) \end{bmatrix} d\zeta \\
&\quad + 2\int_0^t \begin{bmatrix} h_x(G_{1D})\,h_x(G_I) & \cdots & h_x(G_{1D})\,h_z(G_I) + h_x(G_I)\,h_z(G_{1D}) \\ \vdots & & \vdots \\ h_x(G_{mD})\,h_x(G_I) & \cdots & h_x(G_{mD})\,h_z(G_I) + h_x(G_I)\,h_z(G_{mD}) \end{bmatrix} d\zeta \\
&= V_D + V_I + V_C \qquad (9)
\end{aligned}
$$

$$
V_C = 2\int_0^t \mu_D \begin{bmatrix} \mu_{ro}\,g_{1x} & \mu_{pe}\,g_{1y} & \mu_{ss}\,g_{1z} & (\mu_{pe}\,g_{1x} + \mu_{ro}\,g_{1y}) & (\mu_{ss}\,g_{1y} + \mu_{ss}\,g_{1z}) & (\mu_{ss}\,g_{1x} + \mu_{ro}\,g_{1z}) \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\ \mu_{ro}\,g_{mx} & \mu_{pe}\,g_{my} & \mu_{ss}\,g_{mz} & (\mu_{pe}\,g_{mx} + \mu_{ro}\,g_{my}) & (\mu_{ss}\,g_{my} + \mu_{ss}\,g_{mz}) & (\mu_{ss}\,g_{mx} + \mu_{ro}\,g_{mz}) \end{bmatrix} d\zeta. \qquad (10)
$$

### A. Calculation of $V_D$

For ease of notation, denote $g_{iD}$ by $g_i$, then $G_{iD}(\xi) = \beta_D(\xi)\,g_i$. Using (7) and (8), $V_D$ in (9) can also be factored into a scalar time function and a matrix which is a function of the diffusion gradient vectors. Define the vector $g_i = [\,g_{ix} \quad g_{iy} \quad g_{iz}\,]$, let $g = (g_1, \ldots, g_m)$ denote the ordered set of the diffusion gradient vectors then the expression for $V_D$ in (9) and the definition (2) give

$$
V_D = b\,V_g \qquad (11)
$$

where $V_{(\cdot)}$ on the right hand side is the nonlinear map that takes $g$ to $m \times 6$ matrix $V_g$:

$$
\begin{bmatrix} g_{1x}^2 & g_{1y}^2 & g_{1z}^2 & 2g_{1x}g_{1y} & 2g_{1y}g_{1z} & 2g_{1x}g_{1z} \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\ g_{mx}^2 & g_{my}^2 & g_{mz}^2 & 2g_{mx}g_{my} & 2g_{my}g_{mz} & 2g_{mx}g_{mz} \end{bmatrix} \qquad (12)
$$

and $b$ is calculated using (7) and (8):

$$
\begin{aligned}
b &= \int_0^t \left( \int_0^\zeta \beta_D(\xi)\,d\xi - 2u(\zeta - \tau) \int_0^\tau \beta_D(\xi) d\xi \right)^2 d\zeta \\
&= \int_0^t \mu_D^2(\zeta) d\zeta. \qquad (13)
\end{aligned}
$$

For example, the scalar factor for the case of rectangular diffusion gradient pulses is $b = \delta^2(\Delta - \frac{1}{3}\delta)$ and for trapezoidal pulses $\delta^2(\Delta - \frac{1}{3}\delta) - \frac{1}{6}\delta\,t_{rise}^2 + \frac{1}{30}t_{rise}^3$ where $\delta$ is the length of the pulses, $\Delta$ is the time between them, and $t_{rise}$ is the time for the gradients to reach a specified value.

### B. Calculation of $V_I$

During an experiment once the slice and image orientations are selected, they do not change. This implies that the imaging part of $V$, $V_I$, has all its rows equal to each other in (9). The time dependent imaging gradient vector $G_I$ can be written as a linear combination of three unit vectors corresponding to read out, phase encode and slice select directions. The coefficients are scalar functions of time:

$$
G_I(\xi) = \beta_{ro}(\xi)\,g_{ro} + \beta_{pe}(\xi)\,g_{pe} + \beta_{ss}(\xi)\,g_{ss} \qquad (14)
$$

By the linearity of $h$, (7), (8) and (14) one obtains:

$$
h(G_I, \zeta) = \mu_{ro}(\zeta)\,g_{ro} + \mu_{pe}(\zeta)\,g_{pe} + \mu_{ss}(\zeta)\,g_{ss} \qquad (15)
$$

The calculation of $V_I$, which only necessitates one row, is accomplished by:

$$
\int_0^t [\,\mu_{ro}^2 \quad \mu_{pe}^2 \quad \mu_{ss}^2 \quad 2\,\mu_{ro}\,\mu_{pe} \quad 2\,\mu_{pe}\,\mu_{ss} \quad 2\,\mu_{ro}\,\mu_{ss}\,]\,d\zeta. \qquad (16)
$$

### C. Calculation of $V_C$

$V_C$ can be computed in a straightforward manner using the functions given in previous sections, especially (15). It consists purely of the cross terms of the imaging and diffusion parts of $h$. The calculations result in $V_{C(g)}$, shown in (10), as a nonlinear function of diffusion gradients.

Note that there is no clear choice for the value of the phase encoding gradient in the calculation of $V_I$ and $V_C$.

## III. Center Symmetric Diffusion Gradients: NoCroT and CroTO

The appearance of the cross terms can be eliminated by using the properties of the components of $V$ and a specific organization of gradients. Equations (12) and (10) show that when the sign of the diffusion gradients is changed, $V_D$ remains the same, because $V_g = V_{(-g)}$, as opposed to the cross terms matrix which changes sign, $V_{C(-g)} = -V_{C(g)}$. Experiments performed with center–symmetric diffusion gradients, i.e. with the gradient set $(g, -g) = (g_1, \ldots, g_{\frac{m}{2}}, -g_1, \ldots, -g_{\frac{m}{2}})$ will result in:

$$
\gamma^2 \begin{bmatrix} (b\,V_g + V_{C(g)} + V_I) \\ (b\,V_{(-g)} + V_{C(-g)} + V_I) \end{bmatrix} d = \begin{bmatrix} p_1 \\ p_2 \end{bmatrix}. \qquad (17)
$$

The sum and the difference of Eqs. 17 yield

$$
\begin{aligned}
2\,\gamma^2\,(b\,V_g + V_I)\,d &= p_1 + p_2 \qquad \text{(NoCroT)} \quad (18) \\
2\,\gamma^2\,V_{C(g)}\,d &= p_1 - p_2 \qquad \text{(CroTO).} \quad (19)
\end{aligned}
$$

In this manner $V_C$ does not appear in (18), hence the name 'No Cross Terms': NoCroT; in contrast to (19) which consists of 'Cross Terms Only': CroTO. Since the center–symmetric gradient pairs point to the same direction, the first

necessary condition given in [6] for $V$ to have full rank is violated. The correct way to choose the center–symmetric diffusion gradients is to first select 6 vectors that will ensure the full rank condition on $V_g$ [6] and then add in their center–symmetric counterparts. This implies that the minimum number of NoCroT diffusion gradients is 12. In that case NoCroT, (18), is solved by matrix inversion and therefore $d$ is perfectly fitted to $(p_1 + p_2)/2$. In other words, the fit is to the average of the two sets of measurements rather than to the measurements themselves, which is equivalent to solving the following inconsistent set of equations

$$\gamma^2 \begin{bmatrix} V_D + V_I \\ V_D + V_I \end{bmatrix} d = \begin{bmatrix} p_1 \\ p_2 \end{bmatrix} \tag{20}$$

by least squares estimation. Therefore, the true residual error is calculated based on (20) in the sequel.

Note that NoCroT is more robust than CroTO since $p_1 \simeq p_2$ implies that the propagated error will perturb highly the right hand side of (19). Analysis of the data using CroTO verifies this observation, there is an overwhelming number of negative eigenvalues in the water phantom described in Section IV. One limitation is that for the method to work properly, hardware, specifically the gradient system, must be able to revert the diffusion gradients exactly.

## IV. Experimental Results

First and foremost, the estimation procedures must work properly for the simplest case for diffusion with known characteristics, an isotropic sample. To test this case, a polypropylene centrifuge tube by FisherBrand (Cat. No. 05–539–6) filled with tap water at room temperature, with an inner diameter at the slice of 2.7 cm was chosen. In this manuscript, a combination of three different types of coefficient matrices, $V = V_D + V_I + V_C$, NoCroT ($V_D + V_I$) and $V_D$, with several diffusion gradient schemes are presented.

The experiments were carried out on a 4.7 Tesla MR scanner (Varian NMR Systems, Palo Alto, CA) with a gradient system of bore size of 15 cm, maximum gradient strength of 45 gauss/cm and rise time of 0.2 ms using a quadrature birdcage coil (Varian NMR Systems, Palo Alto, CA) with 108/63 mm outer/inner diameter sizes. DTI data were obtained using the standard spin echo multi slice sequence with in house modifications that store all the relevant parameters, including the timing and amplitudes of all the crusher gradients. The images were $128 \times 128$ pixels with a field of view $64 \times 64\,\text{mm}^2$ and 1 mm slice thickness. The repetition time $TR = 1$ s, echo time $TE = 35$ ms, $\Delta = 18$ ms, $\delta = 6$ ms. All the experiments were carried out consecutively after leaving the sample in the scanner for approximately 12 hours to reach a stable temperature.

Center–symmetric diffusion gradient schemes with 12 diffusion gradient vectors were used to obtain data. The gradient schemes were constructed by appending to the gradient schemes with 6 vectors cited in [7] their central symmetric part: Tetrahedral, Cond6, Jones noniso (without the last vector) renamed as Cond* because it yields to a $V_g$ with a good condition number, Jones ($N = 6$), Muthupallai, Downhill Simplex Minimization (DSM), Dual Gradient and in addition Icosahedron (ICOSA6) scheme from [8]. A maximum diffusion gradient strength of $g_{diff} = 12$ gauss/cm was used. With boxcar approximation at maximum diffusion gradient, the value of the coefficient is $\gamma^2\, b\, g_{diff}^2 = 593.6115\,\text{s/mm}^2$.

In house Mathematica® (Wolfram Research, Champaign, IL USA) code was used to compute components of $V$ as described in Section II using the parameter values written to the hard disk by the pulse sequence. Integrals were computed using trapezoidal shapes rather than rectangular ones. The calculations included all the crusher gradients. In house written Matlab® (Mathworks, Natick, MA USA) programs were used for the estimation of $d$ at each pixel and graphical representation and maps of related results. Standard Matlab®Image Processing Toolbox® routines, Sobel edge detection and morphological reconstruction were used to detect the signal region of the phantom in non-diffusion weighted images for each gradient scheme. The edges were removed to obtain region free of susceptibility artifacts and the intersection of all regions was taken to obtain the circular area with 2022 pixels.

The estimation was done with non–weighted least squares because of its speed and simplicity. In the computation of $V_C$ and $V_I$ the phase encoding gradient value of 0 was selected based on the observation that the eigenvectors show a bias towards the orientation of the phase encoding gradient. It should be clear that this choice does not bring a resolution to the existing ambiguity.

Table I presents analysis results as mean±standard deviation. The analysis was done by three different coefficient matrices: $V$, NoCroT ($V_D + V_I$) and $V_D$ which are shown in respective rows. Exclamation points indicate the existence of negative eigenvalues. Although mathematically there is no restriction on the definiteness of $D$, negative eigenvalues have no physical meaning. Cond6 and Tetrahedral schemes exhibit negative eigenvalues with $V$, indicating high sensitivity to perturbations of the coefficient matrices. The ratios of the number of pixels with negative eigenvalues to the total number of pixels are 0.00791 and 0.998 for Cond6 and Tetrahedral respectively ($n_{roi} = 2022$).

$\overline{FA}$ is the mean of the pixel fractional anisotropy index [9] which should be close to zero because the sample is uniform and isotropic. It is the lowest when all of the imaging gradients are neglected from the calculations (row 3). The standard deviation of fractional anisotropy does not change drastically between the three methods but the values from $V_D$ and NoCroT are much closer than the ones between $V$ and NoCroT. In brief, completely neglecting imaging gradients provides the best precision for the fractional anisotropy.

$\bar{\lambda}_i$'s ($10^{-5}\text{cm}^2/\text{s}$) are the mean eigenvalues and their precision is consistently the best for NoCroT and the worst for $V$. $V_D$ estimates larger eigenvalues (except $\bar{\lambda}_1$–icosahedron); moreover, $\bar{\lambda}_3$ increases with decreasing number of components of $V$ ($V_D + V_I + V_C$, $V_D + V_I$, $V_D$). In that regard, NoCroT is a better choice for the precision of the eigenvalues.

TABLE I
SUMMARY OF ANALYSIS RESULTS

| | | cond6 | cond* | dsm | dualgr | icosa | jones6 | muthup | tetra |
|---|---|---|---|---|---|---|---|---|---|
| $\overline{FA}$ | $V$ | !–! | 0.109±0.0271 | 0.0884±0.0195 | 0.161±0.0243 | 0.606±0.0431 | 0.107±0.0203 | 0.107±0.0206 | !–! |
| | NoCroT | 0.178±0.114 | 0.0669±0.0228 | 0.053±0.0175 | 0.0526±0.0183 | 0.101±0.0578 | 0.05±0.0165 | 0.0506±0.0167 | 0.103±0.0535 |
| | $V_D$ | 0.171± 0.11 | 0.0639±0.0218 | 0.0506±0.0167 | 0.0502±0.0175 | 0.0964±0.0552 | 0.0477±0.0158 | 0.0483±0.016 | 0.0986±0.0511 |
| $\bar{\lambda}_1$ | $V$ | !2.94±0.277! | 2.01±0.0778 | 1.91±0.0486 | 1.98±0.0543 | 3.84±0.254 | 1.9±0.0454 | 1.89±0.0486 | !3.1±0.104! |
| | NoCroT | 2.18±0.231 | 1.95±0.061 | 1.91±0.0481 | 1.9±0.0523 | 1.97±0.125 | 1.88±0.0455 | 1.87±0.0466 | 1.96±0.102 |
| | $V_D$ | 2.27±0.229 | 2.04±0.062 | 1.99±0.0492 | 1.98±0.0537 | 2.05±0.126 | 1.96±0.0467 | 1.95±0.0478 | 2.04±0.102 |
| $\bar{\lambda}_2$ | $V$ | !1.62 ±0.0653! | 1.83±0.0614 | 1.8±0.0447 | 1.87±0.0553 | 1.55±0.0551 | 1.8±0.0451 | 1.79±0.0463 | !2.92 ±0.105! |
| | NoCroT | 1.88±0.0714 | 1.83±0.0507 | 1.81±0.0402 | 1.8±0.0443 | 1.79±0.0471 | 1.79±0.0387 | 1.78±0.0393 | 1.78±0.0798 |
| | $V_D$ | 1.97±0.0774 | 1.92±0.0519 | 1.9±0.0414 | 1.89±0.0458 | 1.88±0.0479 | 1.88± 0.04 | 1.86±0.0405 | 1.86±0.0811 |
| $\bar{\lambda}_3$ | $V$ | !0.852 ±0.33! | 1.62±0.0516 | 1.6±0.0498 | 1.44±0.0616 | 1.02±0.0772 | 1.54±0.051 | 1.53±0.0494 | !-0.373±0.123! |
| | NoCroT | 1.51±0.243 | 1.71±0.0572 | 1.72±0.0441 | 1.71±0.0501 | 1.62± 0.14 | 1.7±0.0419 | 1.69±0.0427 | 1.6±0.0999 |
| | $V_D$ | 1.6±0.241 | 1.8±0.0581 | 1.81±0.0449 | 1.8±0.051 | 1.7±0.141 | 1.79±0.0426 | 1.78±0.0434 | 1.69±0.0999 |
| $\bar{\chi}$ | $V$ | 1148±81.17 | 1102±64.12 | 1060±66.92 | 1042±63.21 | 975.1±66.1 | 1074±68.68 | 1070±64.76 | 852.3±62.1 |
| | NoCroT | 635.3±63.11 | 595.1±53.39 | 564.6±54.83 | 571.3±51.98 | 577.7±55.07 | 572.5±54.1 | 573.9±52.26 | 651.8±56.28 |
| | $V_D$ | 635.3±63.11 | 595.1±53.39 | 564.6±54.83 | 571.3±51.98 | 577.7±55.07 | 572.5±54.1 | 573.9±52.26 | 651.8±56.28 |

$\bar{\chi}$ is the mean of the pixel residual error:

$$\|\chi\|_2^2 = \frac{1}{m}\sum_{i=1}^{m}(\hat{S}_i - S(v_i\, d))^2 \tag{21}$$

where $v_i$ denotes the $i^{th}$ row of the coefficient matrix. It depicts that there is an increase in the model matching error when the imaging gradients are *not* dropped from the calculations. The last two rows of the table are identical because the calculations for $V_D$ are equivalent to solving NoCroT (20) with $V_I = 0$. Since all the rows of $V_I$ are equal and the measurements are the same for both methods, the residuals defined in (21) do not change.

In conclusion, while the inclusion of all imaging and cross terms creates great disturbances and gives poor results for the estimation process, the performance indices favor NoCroT.

## V. CONCLUSION

In the translation of diffusion NMR experiments to MR–DTI, analytical expressions for the effects of imaging gradients exhibit ambiguities about the choice of the phase encoding gradient values to use in the computations. Center–symmetric gradient schemes, at least in theory, make it possible to use no cross terms (NoCroT) in the calculations, thus eliminating the impact of imaging gradients.

When three estimation methods, *all gradients* ($V$), NoCroT ($V_D + V_I$) and *diffusion gradients only* ($V_D$) are compared on the same experimental data obtained from a uniform isotropic phantom, it is observed that the full inclusion of imaging gradients to the calculations can be detrimental. Moreover, there is only slight improvement with NoCroT over *diffusion gradients only*. This is unexpected since more comprehensive models including all the gradients should give better results.

It is inconceivable that these drastic changes are due only to the uncertainty in phase encoding gradients. Such sensitivity would make MR–DTI unrealizable. Despite the unavoidable factors such as noise, gradient reversal mismatch and inhomogeneities that are difficult to measure and model, every possible theoretical incentive is incorporated into the process: exact analytic expressions of the coefficient matrices and the special gradient selection that suppresses the cross terms. Therefore the next attainable goal is to design new diffusion gradient schemes that will improve the robustness by decoupling to the maximum extent the effects of imaging gradients. This is the subject of the companion paper [10].

## REFERENCES


[1] P. J. Basser, J. Matiello, and D. LeBihan, "Estimation of the effective self-diffusion tensor from the NMR spin echo," *Journal of Magnetic Resonance Series B*, vol. 103, pp. 247–254, 1994.

[2] J. Matiello, P. J. Basser, and D. LeBihan, "Analytical expressions for the B matrix in NMR diffusion imaging and spectroscopy," *Journal of Magnetic Resonance Series A*, vol. 108, pp. 131–141, 1994.

[3] E. O. Stejskal, "Use of spin echoes in a pulsed magnetic-field gradient to study anisotropic restricted diffusion and flow," *The Journal of Chemical Physics*, vol. 43, no. 10, pp. 3597–3603, Nov. 1965.

[4] T. E. Conturo, R. C. McKinstry, J. A. Aronovitz, and J. J. Neil, "Diffusion MRI: Precision, accuracy and flow effects," *NMR in Biomedicine*, vol. 8, pp. 307–332, 1995.

[5] P. J. Basser and C. Pierpaoli, "A simplified method to measure the diffusion tensor from seven MR images," *Magnetic Resonance in Medicine*, vol. 39, pp. 928–934, 1998.

[6] A. Özcan, "(Mathematical) necessary conditions for the selection of gradient vectors in DTI," *Journal of Magnetic Resonance*, vol. 172, no. 2, pp. 238–241, Feb. 2005.

[7] S. Skare, M. Hedehus, M. E. Moseley, and T.-Q. Li, "Condition number as a measure of noise performance of diffusion tensor data acquisition schemes with MRI," *Journal of Magnetic Resonance*, vol. 147, pp. 340–352, 2000.

[8] K. M. Hasan, D. L. Parker, and A. L. Alexander, "Comparison of gradient encoding schemes for diffusion-tensor MRI," *Journal of Magnetic Resonance Imaging*, vol. 13, pp. 769–780, 2001.

[9] P. J. Basser and C. Pierpaoli, "Microstructral and physiological features of tissues elucidated by quantitative-diffusion-tensor MRI," *Journal of Magnetic Resonance Series B*, vol. 111, pp. 209–219, 1996.

[10] A. Özcan, "Decoupling of imaging and diffusion gradients in DTI," in *Proceedings of the 31st Annual International Conference of the IEEE EMB Society*, 2009.