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Optimization of diffusion imaging for multiple target regions using maximum likelihood estimation

Abstract: In this work a procedure is proposed to determine an optimal distribution of b-values in diffusion MRI measurements. The optimization procedure uses a method of Maximum Likelihood Estimation which can operate on any given number of b-values, values of the diffusion coefficients (ADC) and measurement noise strengths. Optimal b-values are calculated for white and gray brain matter. An optimization for more than one ADC is demonstrated using multiple target values.

Keywords: Diffusion MRI, Maximum Likelihood analysis, MRI protocol optimization.

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1 Introduction

Diffusion MRI is a functional imaging method that is widely used in clinical stroke and tumor diagnostics. To measure the apparent diffusion coefficient (ADC), MR images with different settings of the diffusion sensitizing gradients are acquired – these settings are characterized by the b-value, which increases with gradient duration and amplitude.

Diffusion-weighted MR images at high b-values suffer from low SNR so that signal averaging is required to acquire qualitative acceptable data. Whereas averaging in MRI is typically performed on the complex data, in diffusion MRI the average of the magnitude data is used, therefore being insensitive to phase fluctuations [1]. Magnitude averaging results in a signal offset at low SNR, which needs to be accounted for in the calculation of ADC-parameter maps to provide sufficiently high image quality e.g. in automated lesion detection.

In this study a procedure to calculate optimal b-value distributions is presented which uses Maximum Likelihood Estimation (MLE) to minimize the standard deviation of the ADC values under realistic noise conditions.

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2 Methods

2.1 Maximum likelihood estimation

A mono-exponential signal decay is assumed to describe the MR signal behaviour:

$$\mathbf{S} = \boldsymbol{S_0}\, \boldsymbol{e^{-b\,D}}\,. \tag{1}$$

Note that in the following D represents the true diffusion coefficient, while the ADC is an estimator for D.

To estimate the parameters S_0, ADC, and the amplitude of the complex noise σ_s, a MLE approach can be used [2]. In MLE, the log-likelihood function $\mathcal{L}$

$$\mathcal{L}(\boldsymbol{S_m}; \boldsymbol{S_0}, \mathbf{ADC}, \boldsymbol{\sigma_s}, \boldsymbol{b}) = \sum_i \left(\log\left[\frac{S_{m,i}}{\sigma_s}\right] - \frac{S_{m,i}^2 + S_0^2 e^{-2\, b_i\, \mathrm{ADC}}}{2\,{\sigma_s}^2} + \log\left[\Im_0\left(\frac{S_{m,i}\, S_0\, e^{-b_i\, \mathrm{ADC}}}{\sigma_s^2}\right)\right]\right) \tag{2}$$

is calculated from the joint probability density function of the measured signal $\boldsymbol{S_m}$ and the Rician MR signal distribution. $\Im_0$ is the zeroth order Bessel function of first kind. Therefore, maximizing $\mathcal{L}$ yields the parameters that would most likely produce the measurement data [3-5].

The asymptotic normality property of MLE for parameter estimations states that for large sample sizes the MLE estimates will converge to a normal distribution, which allows determining the standard deviation of the ADC estimator using the Cramér-Rao Lower Bound (CRLB) of the parameter σ_{ADC}:

$$\mathbf{CRLB_{ADC}} = \boldsymbol{\sigma_{ADC}} = \frac{1}{\sqrt{-\partial^2_{ADC}\, \mathcal{L}(\boldsymbol{S_m}; \boldsymbol{S_0}, \mathbf{ADC}, \boldsymbol{\sigma_s}, \boldsymbol{b})}}. \tag{3}$$

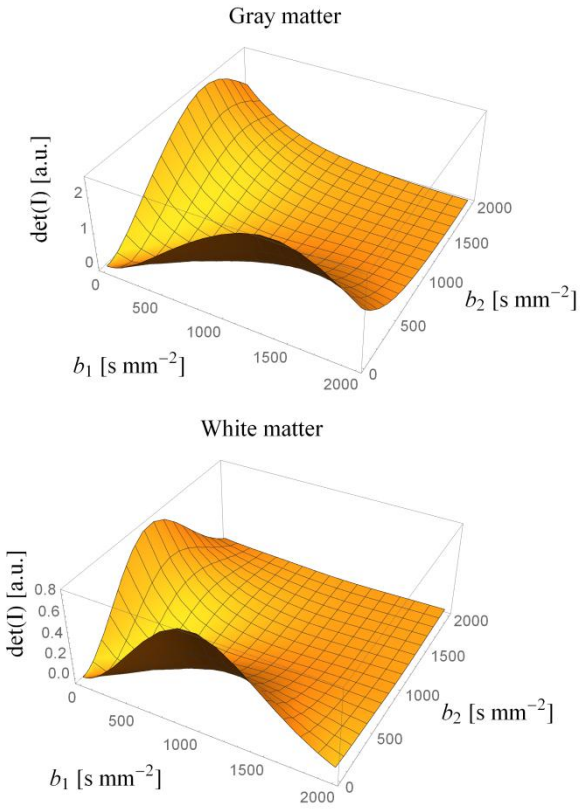

Figure 1: det(**I**) calculated for two input b-values for the example cases of gray / white brain matter. Input values were ADC= 0.643 / 0.752 10^{-3} mm^2/s, S_0 = 147 / 108 and σ=42 [a.u.], respectively.

Thus, an optimal design can be calculated for a given set of measurement parameters and expected target ADC values. As minimization of the function given in eq. (3) results in all b-values being identical, S_0, and σ_s become indeterminable. Consequently, a different optimization scheme is used based on the Fisher Information Matrix:

$$\mathbf{I}(\mathbf{b},\boldsymbol{\lambda}) = -\mathbf{E}\left[\frac{\partial^2 \mathcal{L}}{\partial \boldsymbol{\lambda}\, \partial \boldsymbol{\lambda}^T}\right], \qquad (4)$$

where $\boldsymbol{\lambda} = (S_0, \mathrm{ADC}, \sigma_s)$ is the vector of target parameters and the function E[…] denotes the expectation value. Based on eq. (4), D-optimality [6] grants minimal volume of the parameter ellipsoid (i.e., best estimation of all target parameters) by maximizing the determinant of I($\boldsymbol{b}, \boldsymbol{\lambda}$) [7-8]:

$$\mathbf{b_{opt.}} = \mathbf{arg\,max}_{\boldsymbol{b}}[\mathbf{det}(\mathbf{I}(\mathbf{b},\boldsymbol{\lambda}))]. \qquad (5)$$

Importantly, **b** is a vector of any number of b-values in this equation.

To demonstrate this optimization procedure, typical target values $\boldsymbol{\lambda}_{\mathbf{GM}}$ with S_0=147, ADC = 0.643 10^{-3} mm^2/s, σ_s= 42 and $\boldsymbol{\lambda}_{\mathbf{WM}}$ with S_0=108, ADC = 0.752 10^{-3} mm^2/s, σ_s= 42 for gray (GM) and white (WM) brain matter were chosen, and

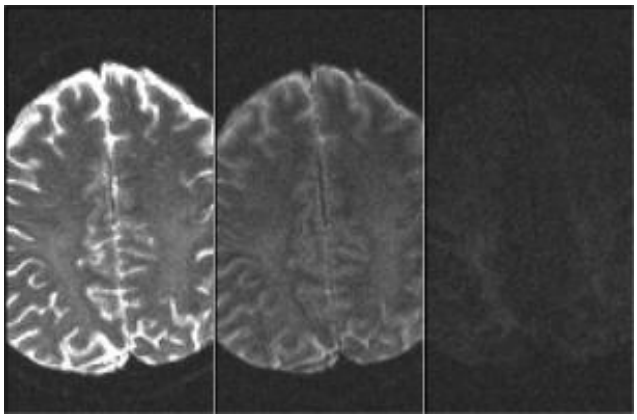

Figure 2: Diffusion weighted MR images of a volunteer at b-values of 50, 450 and 2100 s/mm^2. For comparison, all images are shown with the same window adjustments.

det (I) was plotted in fig. 1. The graph shows that the maximum of det (I) always includes the b-value of b = 0, allowing accurate estimation of S_0. As expected, the second b-value depends on the target tissue and increases with decreasing ADC. This scheme can now also be applied to multiple target ADC values by maximizing the sum of their normalized Fisher Information Matrices.

2.2 MR experiments

To demonstrate the validity of the optimization, MR diffusion measurements of the human brain were conducted at 1.5T (Siemens Symphony) using the system's 12-channel head coil. Diffusion-weighted images were acquired with a single shot Spin Echo Planar Imaging (EPI) pulse sequence with 31 different b-values ranging from 50 to 2100 s/mm^2 (cf. fig. 2). From this data, ADC values were calculated for different combinations of two b-values (b_1 = 50 s/mm^2 and b_2 > b_1), and σ_{ADC} was compared to the expected distribution given by the CRLB. For evaluation, two regions of interest in GM and WM were chosen to compare results for different target ADCs. Contrary to the result of the simulation, the lower b-value was chosen to b_1>0. The reason for this was a second high-ADC component resulting from blood flow, which is not considered in the model. This component however was assumed to be negligible at b_1 = 50 s mm^{-2}.

3 Results

Measurements at high b-values were taken close to the noise floor, as shown in figure 3 (top). With increasing b_2, the signal S_m does not converge to zero as would be expected

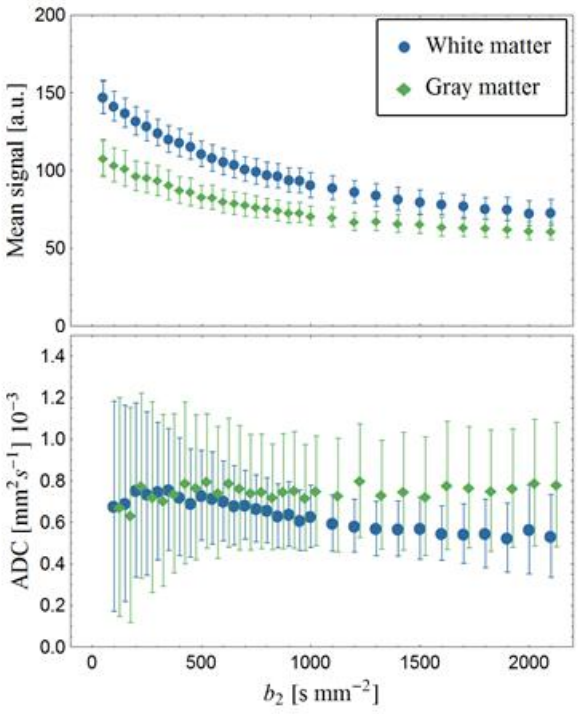

Figure 3: Mean signal intensity of WM and GM (top). Note how the signal levels off at an intensity of about 60. The bottom plot shows the mean calculated ADC values using MLE with two b-values, where b_1=50 s/mm^2. Error bars indicate standard deviations.

from eq. (1), but has a large offset which is a result of the magnitude averaging of the complex noise. Still, the MLE yields stable results on the ADC estimate (fig. 3 (bottom)), even for high b-values. Figure 4 shows the measured and predicted standard deviation of the ADC signal, where the CRLB correctly follows the general trend but underestimates the data.

Using the scheme we derived and presented above, optimal b-values were calculated to 1400 (ADC = 0.57 10^{-3} mm^2/s)) and 930 s/mm^2 (ADC = 0.75 10^{-3} mm^2/s) for WM/GM, and 1068 s/mm^2 for both simultaneously by optimizing the sum of the normalized det(I).

4 Discussion

In this work an optimization procedure for the selection of b-values in quantitative diffusion MRI is proposed. The method was evaluated both theoretically and experimentally using the example of gray and white brain matter regions.

The calculated optimal b-values are close to the minimum of the CRLB with a slight tendency to higher values, which results from the optimization procedure that does not

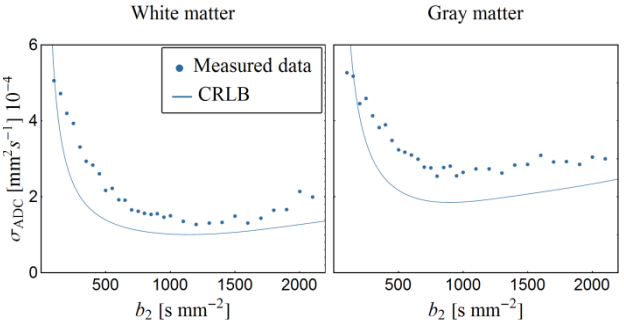

Figure 4: The measured ADC uncertainty for gray and white matter as a function of the second b-value. The solid line represents the CRLB. The underestimation of σ_{ADC} by the CRLB can be explained by additional physiological noise, which has not been incorporated in the model.

attempt to minimize the noise σ_{ADC} but to maximize det(I): The target function det(I) includes additional information about S_0 and σ_S in comparison to the $CRLB_{ADC}$. Therefore, the optimal choice of b-values, i.e. the maximum of det(I), does not coincide with the minimum of the CRLB.

The systematic underestimation of σ_{ADC} could be caused by additional noise sources not considered in the model, such as blood flow and pulsation.

The proposed optimization has been demonstrated with a combination of two b-values, but the target function operates on any number of input b-values. However, the proposed optimal design will always result in a combination of only two distinct b-values with different numbers of averages, as it consists of the summation of independent (but equal) log-likelihood functions.

Saritas et al. [9] additionally incorporate the effects of T_2-weighting on image intensity and SNR, which changes with increasing duration of the diffusion weighting gradient. T_2-weighting could also be implemented in this optimization by adjusting the signal equation (1). However, this will either depend very much on the specific implementation of the imaging sequence or introduce an additional timing parameter.

The proposed method allows to test and predict other experimental designs which make use of different combinations of b-values, resulting in adjustable relative SNR for different target ADCs.

A major drawback of MLE is the systematic underestimation of parameters that lie close to a parameter boundary, which is the case if the distribution of ADC values is close to zero. The same holds true if MLE is used to estimate the complex noise σ_S, which will almost certainly be underestimated. MLE is still a superior alternative to linear models in the optimization of a MRI diffusion experiment at high noise levels. Since the method does not make assumptions

about statistics of the data, it is preferred over least squares fitting [9], which assumes a Gaussian distribution. Finally, both parameter and error estimation show good correspondence to the expected behavior.

Further improvements in calculation times and optimization convergence can be made, improving robustness and applicability in various experimental setups.

5 Conclusion

Maximum Likelihood Estimation can be favorably used to optimize the b-values in diffusion MRI. Using an extended approach with the Fisher Information Matrix, multiple b-values can be adjusted for more than one target ADC.

Author's Statement

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