Experimental design for the estimation of Rician-distributed intensity fields in MRI

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Abstract In diffusion magnetic resonance imaging the measured intensity signal allows to estimate the Apparent Diffusion Coefficient (ADC), which helps detecting the presence of tumors and necrotic areas. This signal is Rician-distributed, so assuming an approximate Gaussian model can lead to serious bias when the signal-to-noise ratio is low. In this work we consider a maximum likelihood estimator of the ADC, also estimating the noise dispersion parameter from the same data, and we propose different experimental design solutions for increasing the accuracy of estimates with few observations, based on the optimization of a functional of the Fisher Information Matrix. The proposed methods, implemented in R, are then validated using real measurements performed on a dummy.

Key words: Experimental design, Magnetic resonance imaging, Rician distribution.

1 Introduction

Diffusion Magnetic Resonance (MR) is a clinical imaging technique that allows to detect some important properties of biological tissues. In particular, when the tissue region of interest can be considered as isotropic, the *Apparent Diffusion Coefficient* (ADC) can be used as an index of water diffusivity in the tissues. Its reduced value in lesions with respect to the surrounding physiological tissues allows to identify

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regional necrosis, making it a useful quantity for the diagnosis of some types of tumors, like breast and prostate cancer (see for example [8] and [6]). This parameter can be estimated pixel-by-pixel by analyzing the dependence between the MR magnitude signal and a function of the MR acquisition parameters, the so-called *b-value*. For an overview on magnetic resonance, see for example [3].

In many practical situations it may not be possible to collect more than few measures at different *b*-values, so a reduction in the total number of measurements necessary to achieve a certain accuracy in ADC estimation is convenient in term of costs and patient involvement time. The purpose of this work is to increase the accuracy of ADC estimates by using maximum likelihood (ML) methods and by formulating an efficient design of the experiment.

2 Rician distribution and estimation problem

The considered magnitude data derive from the complex signal $w = w_r + iw_i$ measured in diffusion MR. It is usual to assume that both w_r and w_i are affected by a Gaussian noise with equal, constant variance, i.e. $w_r \sim \mathcal{N}(\nu\cos(\vartheta),\sigma^2)$ and $w_i \sim \mathcal{N}(\nu\sin(\vartheta),\sigma^2)$, with $\nu \in \mathbb{R}^+$ and $\vartheta \in [0,2\pi)$. The measured magnitude $M = \sqrt{w_r^2 + w_i^2}$ then follows a Rician distribution, with probability density given by

$$f_M(m) = \frac{m}{\sigma^2} e^{-\frac{m^2+\nu^2}{2\sigma^2}} I_0\left(\frac{m\nu}{\sigma^2}\right) \mathbb{1}_{(0,+\infty)}(m),$$

where I_0 is the zeroth-order modified Bessel function of the first kind. In the limiting case $\sigma^2 = 0$ (no noise), the parameter ν would be the "true" signal of interest.

A widely accepted model for the dependence of the signal ν on the b-value b is the *Stejskal-Tanner equation*, here specified in the case of an isotropic tissue,

$$\nu = \nu_0 \exp(-\alpha b), \tag{1}$$

where α is the ADC, i.e. the parameter of interest.

Least squares fitting is commonly used to estimate the parameters $(\nu_0, \alpha, \sigma^2)$ of this model, thus approximating the problem to a non linear regression with gaussian additive noise. This approximation loses accuracy when the *Signal-to-Noise Ratio* (SNR) ν/σ is low (see [7] for a discussion on this topic), while ML estimation for the Rician model leads to more accurate estimates of the parameters. In this work we assume the magnitude signal on each pixel of an MR image as Rician-distributed, with a local ν parameter that depends on the *b*-value following equation (1).

Let us consider a sample of observations of a magnitude signal $\mathbf{m} = m_1, \ldots, m_n$ obtained as responses to the b-values $\mathbf{b} = b_1, ..., b_n$ on a single pixel of a MR image. The likelihood function for the considered model is

$$L(\nu_0,\alpha,\sigma^2|\mathbf{m},\mathbf{b}) = \prod_{i=1}^{n} \frac{m_i}{\sigma^2} e^{-\frac{m_i^2+\nu_0^2 e^{-2\alpha b_i}}{2\sigma^2}} I_0\left(\frac{m_i \nu_0 e^{-\alpha b_i}}{\sigma^2}\right) \mathbb{1}_{(0,+\infty)}(m_i). \qquad (2)$$

The optimal values of ν_0 and α for equation (2) cannot be obtained explicitly, so a numerical optimization method is required to obtain estimates $\hat{\nu}_0$ and $\hat{\alpha}$. In this work we use the *L-BFGS* method (see [4]) with interval constraints, implemented in the `R` function `optim` [5].

The parameter σ^2 is commonly estimated separately before the estimation of other parameters, considering areas of tissue where the measured signal is believed to be almost pure noise. Considering a joint likelihood for the whole MR image, σ^2 can also be estimated using an alternated maximization approach: fixing the vectors ν_0 and α of parameter values on different pixels, σ^2 is estimated by ML, then σ^2 is fixed to its updated estimate and $\hat{\nu}_0$ and $\hat{\alpha}$ are obtained separately on each pixel. This method has good empirical convergence properties.

3 Experimental design

We propose an experimental design performed by choosing a convenient b-value for a new measurement, basing on estimates obtained in previous measurements. Since the inverse of the Fisher Information Matrix (briefly FIM) $\mathscr{I}^{-1}(\theta|\sigma^2,\mathbf{b})$ for large samples approaches the covariance matrix of a vector of ML estimators $\hat{\theta} = (\hat{\theta}_1,\ldots,\hat{\theta}_k)$, we iteratively optimize a convenient functional of the FIM with respect to $\mathbf{b} = (b_1,\ldots,b_n)$ for a fixed sample size n. The FIM depends on the values of the unknown parameters ν_0 and α in a non trivial way, so we perform the optimization fixing their values and assuming that they are near to the real ones. We propose an adaptive greedy optimization, that can alternates the following steps:

1. Compute estimates $\hat{\nu}_0^{(h)}$ and $\hat{\alpha}^{(h)}$ of ν_0 and α using measurements performed on $b_1^*,\ldots,b_h^*$.
2. Fixing $(b_1,\ldots,b_h) = (b_1^*,\ldots,b_h^*)$ and $(\nu,\alpha) = (\hat{\nu}_0^{(h)},\hat{\alpha}^{(h)})$, find

$$b_{h+1}^* = \arg\min_b F\left[\mathscr{I}(\hat{\nu}^{(h)},\hat{\alpha}^{(h)}|\sigma^2,b_1^*,\ldots,b_h^*,b)\right],$$

being F a suitable functional of the FIM, then perform a new measurement m_{h+1} at point b_{h+1}^* and increment h by 1.

In our implementation we consider $F\left[\mathscr{I}(\hat{\nu}_0,\hat{\alpha}|\sigma^2,b_1^*,\ldots,b_n^*)\right] = \mathscr{I}_{22}^{-1}$, the asymptotic variance of the ML estimator $\hat{\alpha}$; other solutions are possible, like the determinant or the trace of $\mathscr{I}^{-1}$.

The method described above refers to a single pixel of a MR image, but in applications it is necessary to improve some index of global precision on the whole image. This can be achieved, for example, by minimizing the sum of variances of ADC estimators on all pixels of the image.

The experimental design can be validated using measures performed on a dummy with known diffusion properties, collected on a fine grid of b-values. A subset of the available b-values and related measures can be used as fixed design observations, while the adaptive design can be approximated choosing adaptively the available b-value nearest to the computed optimum. Estimates obtained in both cases can then be compared with the known physical values, at different sample sizes. Preliminary simulation studies have underlined the potential efficacy of the adaptive approach based on the sum of asymptotic variances with respect to a fixed design (see [1]).

4 Conclusions

The proposed method is a promising strategy for achieving higher accuracy in the estimation of an ADC field, when compared to fixed design estimation. The application of our approach to the considered statistical model is new and innovative in the field of diffusion MR, and could lead to an improvement of diagnoses without having to increase the size of information available. In the future both the estimation methods, here based on maximum likelihood, and various experimental designs will be extensively compared to alternative approaches (see [2] for a simulation comparison of frequentist and Bayesian methods for the single-pixel case).

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