

Laplace–Beltrami Regularization for Diffusion Weighted Imaging

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Abstract

A popular method of smoothing the diffusion signal is based on a Tikhonov regularization with Laplace–Beltrami operator. In this study a systematic Monte-Carlo study of a regularization parameter selection is presented. By minimizing the difference between synthetic and reconstructed shapes the best parameter values are found. Those parameters are then tested on a real MRI image. The fibre orientation distribution functions obtained with new regularization parameters are more stable and reliable.

1 Introduction

Magnetic Resonance Imaging (MRI) is a medical imaging technique which allows for *in vivo* visualisation of internal structures in detail. It is especially sensitive to different soft tissues, producing a good contrast between them. Over the course of past decades various types of MRI applications have been introduced, some of which are linked to the measurement of water diffusion. Diffusion weighted imaging of the brain uses the displacement of water molecules in the tissue to introduce contrast to images [8]. The diffusion of water can be used to infer white matter fibre orientations and to study brain connectivity *in vivo* [10].

One of the major areas of research in diffusion imaging is the reconstruction of the distribution of water diffusion. Using the diffusion weighted imaging a single scalar diffusivity, which depends on the direction of the applied magnetic field gradient (called the diffusion sensitizing gradient), is calculated. The signal is usually approximated with a 3D function, which depending on the processing of the signal, results in a diffusion profile, diffusion orientation distribution function (ODF), or fibre orientation distribution function (FODF). Unfortunately, as the signal is heavily corrupted by noise the reconstructed signal shapes are spiky and have to be smoothed.

An elegant and straightforward way of obtaining a more regular function is to use a Tikhonov regularization during the function fitting process. One of the most successful and widely used regularizations is based on the Laplace–Beltrami operator [4]. But despite its long use, there have been almost no study regarding the selection of the regularization parameter, which relates to the strength of smoothing applied.

In the original paper [4], an L -curve analysis [7] was used to establish the optimal parameters for a very specific case ($b = 3000$ s/mm² and SNR = 35). Depending on the number of fibres within a voxel it was reported that the optimal parameter is 0.308 for one, 0.006 for two, and 0.0155 for 3 fibre crossing. 0.006 was considered a good compromise between a regularization and angular resolution, and recommended for general use. Another method, based on a generalized cross validation (GCV) used an iterative approach to automatically select the regularization parameter [9]. Later on, it was shown that both L -curve and GCV methods provide similar parameters [3], with L -curve being more stable.

The choice of the regularization parameter based on either L -curve or GCV is a compromise between preserving the data and improving the condition of the design matrix. This, due to the data being corrupted by noise, can result in an under-smoothed solution (noise spikes will be treated as a valid data). Intuitively, instead of deciding on the regularization parameter based on the goodness of fit to the noisy, measured data, one should base the decision on the unfitness to the ground truth. Additionally, depending on the objective function (best fit of diffusion profile, ODF, FODF) the regularization parameter should differ.

In this paper a thorough investigation is conducted to select regularization parameters, using such a ground truth validation. Tests are performed for a range of diffusion weighting factors, SNRs and objective functions. The findings are finally presented on a real image.

2 Methods

2.1 Synthetic Data Generation

The synthetic diffusion signal was created using the multiple tensor model [6]:

$$S_r = S_0 \sum_{k=1}^N v_k \exp(-b \vec{g}_r^T \mathbf{D}_k \vec{g}_r), \quad (1)$$

where S_r is the amplitude of the measured signal with the diffusion sensitizing gradient applied at direction r , S_0 with no diffusion sensitizing gradients applied, b a diffusion-weighting factor, \vec{g}_r the direction of the diffusion sensitizing gradient, the \mathbf{D}_k a diffusion tensor of the k th fibre, and v_k a volume fraction ($\sum_{k=1}^N v_k = 1$). Both the number of the fibre crossings and the volume fractions were selected randomly. Additionally, on average half of the simulated voxels had a partial isotropic environment present. The signal was corrupted by adding a complex Gaussian noise and taking the magnitude.

2.2 Spherical Harmonics Analysis

Spherical harmonics (SH) allow for a non-parametric analysis of the diffusion signal, and can be seen as the extension of Fourier basis functions to the sphere. The basis functions, defined as a solution to Laplace equation, are given by:

$$Y_l^m(\theta, \phi) = \sqrt{\frac{2l+1}{4\pi} \frac{(l-m)!}{(l+m)!}} P_l^m(\cos \theta) \exp(im\phi), \quad (2)$$

with P_l^m being the associated Legendre function of band (order) l and degree m , θ a colatitude, and ϕ longitude. For practical reasons a single integer $j(l, m) = (l^2 + l + 2)/2 + m$ to enumerate the spherical harmonic series (SHS) was often used.

The diffusion signal, measured using high angular resolution diffusion imaging protocol [11], can be approximated with a truncated series of SH basis functions:

$$S(\theta_i, \phi_i) = \sum_j c_j Y_j(\theta_i, \phi_i), \quad (3)$$

where c_j are SHS coefficients. Due to antipodal symmetry of diffusion, the odd order basis functions do not appear in Equation 3.

The parameters \mathbf{c} can be found using classical linear regression by minimizing the Euclidean norm:

$$\arg \min_{\mathbf{c}} \|\mathbf{Y}\mathbf{c} - \mathbf{S}\|^2, \quad \mathbf{c} = (\mathbf{Y}^T \mathbf{Y})^{-1} \mathbf{Y}^T \mathbf{S}, \quad (4)$$

where \mathbf{Y} is a spherical harmonics design matrix, and \mathbf{S} a vector with diffusion weighted measurements. To give preference to a solution with certain desirable properties (like smoothness), the regularization term is included:

$$\arg \min_{\mathbf{c}_\lambda} \|\mathbf{Y}\mathbf{c}_\lambda - \mathbf{S}\|^2 + \lambda^2 \|\Gamma \mathbf{c}_\lambda\|^2, \quad \mathbf{c}_\lambda = (\mathbf{Y}^T \mathbf{Y} + \lambda^2 \Gamma^T \Gamma)^{-1} \mathbf{Y}^T \mathbf{S}, \quad (5)$$

with Γ a chosen Tikhonov matrix and λ^2 a parameter controlling the strength of regularization. For $\lambda^2 = 0$ this reduces to the classical least squares solution. The Tikhonov regularization using Laplace–Beltrami operator, which is a natural measure of smoothness for functions defined on a sphere, is achieved by using a diagonal matrix $\Gamma^T \Gamma$ with $l_j^2 (l_j + 1)^2$ along the diagonal (l_j being the order associated with the j th coefficient).

In order to infer the fibre orientation within a voxel the diffusion signal needs to be represented as either diffusion or fibre ODF. Spherical harmonics allow for an efficient analytical computation of both, ODF using a Funk-Hecke theorem [1] and FODF using a spherical deconvolution transform [5].

2.3 Optimal Regularization Parameter

To find the optimal regularization parameter, a case by case evaluation was performed (through exhaustive search). For a set of diffusion weighting factors and SNRs (both feasible and infeasible combinations), $\lambda^2 \in [0, 0.5]$ was tested. No limits on minimal crossing angle or volume fractions was placed. The best parameter was the one minimizing (on average) the difference between synthetic and reconstructed signal:

$$\arg \min_{\lambda} \|\mathbf{W}\mathbf{A}(\mathbf{Y}^T \mathbf{Y} + \lambda^2 \Gamma^T \Gamma)^{-1} \mathbf{Y}^T \hat{\mathbf{S}} - \mathbf{W}\mathbf{A}(\mathbf{Y}^T \mathbf{Y})^{-1} \mathbf{Y}^T \mathbf{S}\|^2, \quad (6)$$

where both synthetic and reconstructed signal was approximated using 8th order SHS. It is possible to search for the optimal regularization parameters based on a different fitness measure, like correlation coefficient or angular error of estimated fibres. In those cases, the observed trends and obtained results should be similar to the ones presented here.

\mathbf{W} and \mathbf{Y} are both 8th order SH design matrices, the former is based on a dense spherical sampling (1024 diffusion encoding gradients, to evaluate the fitness), while the latter on a sparse, physically feasible measurement (60, diffusion encoding gradients, to find the SH coefficients), $\hat{\mathbf{S}}$ is a noise corrupted signal, and \mathbf{S} a ground-truth. The diagonal matrix \mathbf{A} transforms the SH expansion of the signal to either ODF or FODF. For $\mathbf{A} = \mathbf{I}$ this will in effect minimize the difference in diffusion profiles itself.

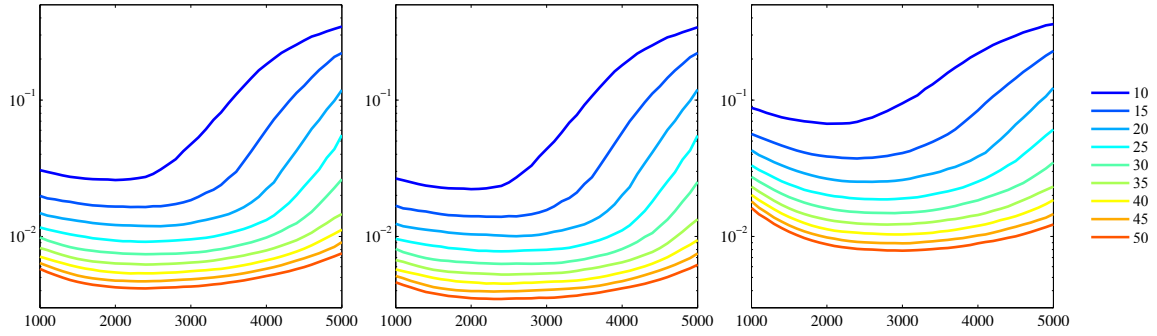


Figure 1: Regularization parameters (log-scale) as a function of diffusion weighting factor. Recommended parameter values that maximize the accuracy of (from top left) diffusion signal reconstruction, ODF, and FODF computation.

The Equation 6 can be split into two parts: reconstructed (left) and synthetic (right) signal. In both cases, the resolution of the signal is raised (using matrix \mathbf{W}) and transformed into other representation (ODF/FODF, using matrix \mathbf{A}) if necessary. The algorithm for creating the phantom signal and analysing the regularization fitness can be summarized as follows:

1. For a given diffusion weighting factor b and signal to noise ratio $1/\sigma^2$ do:
2. Select a random n (1-3) fibre crossing with random volume fractions \vec{v} .
3. Generate a synthetic signal S using a multi-tensor model.
4. Generate a noise corrupted signal $\hat{S} = \sqrt{(S + N(0, \sigma^2))^2 + N(0, \sigma^2)^2}$.
5. Investigate the fitness function for various regularization parameters λ^2 .
6. Repeat from 2 for 10000 times.

3 Results and Discussion

The optimal parameters found through this research are presented in the Figure 1, where λ^2 values for different SNR cases are plotted as a function of b -value. As expected, the parameters vary depending on both diffusion weighting that is applied and SNR.

With a low diffusion weighting applied it is possible to smooth the profile without the loss of information and accuracy. The signal becomes sharper with the increasing b -values, and the smoothing that can be applied during reconstruction decreases. This trend, however, at certain point reverses, and the recommended smoothing starts to increase. With higher diffusion weighting applied the frequency range of the signal and noise become similar, and the smoothing will remove the real signal and noise corruption indiscriminately.

With a noisier signal it is necessary to apply stronger smoothing, and prevent the resulting function from adapting to noise. At the same time, the regularization parameter should not be too large, as otherwise it will suppress the measured signal. In the simulations, a maximal parameter was set to 0.5.

The recommended parameters for reconstructing the diffusion signal and ODF are very similar (Figure 1, left and middle). At the point of interest ($b = 3000$ s/mm² and SNR = 35) both are close to 0.006 that was found analytically in [4]. In the case of FODF though, the recommended parameters are twice larger (0.012 at the point of interest).

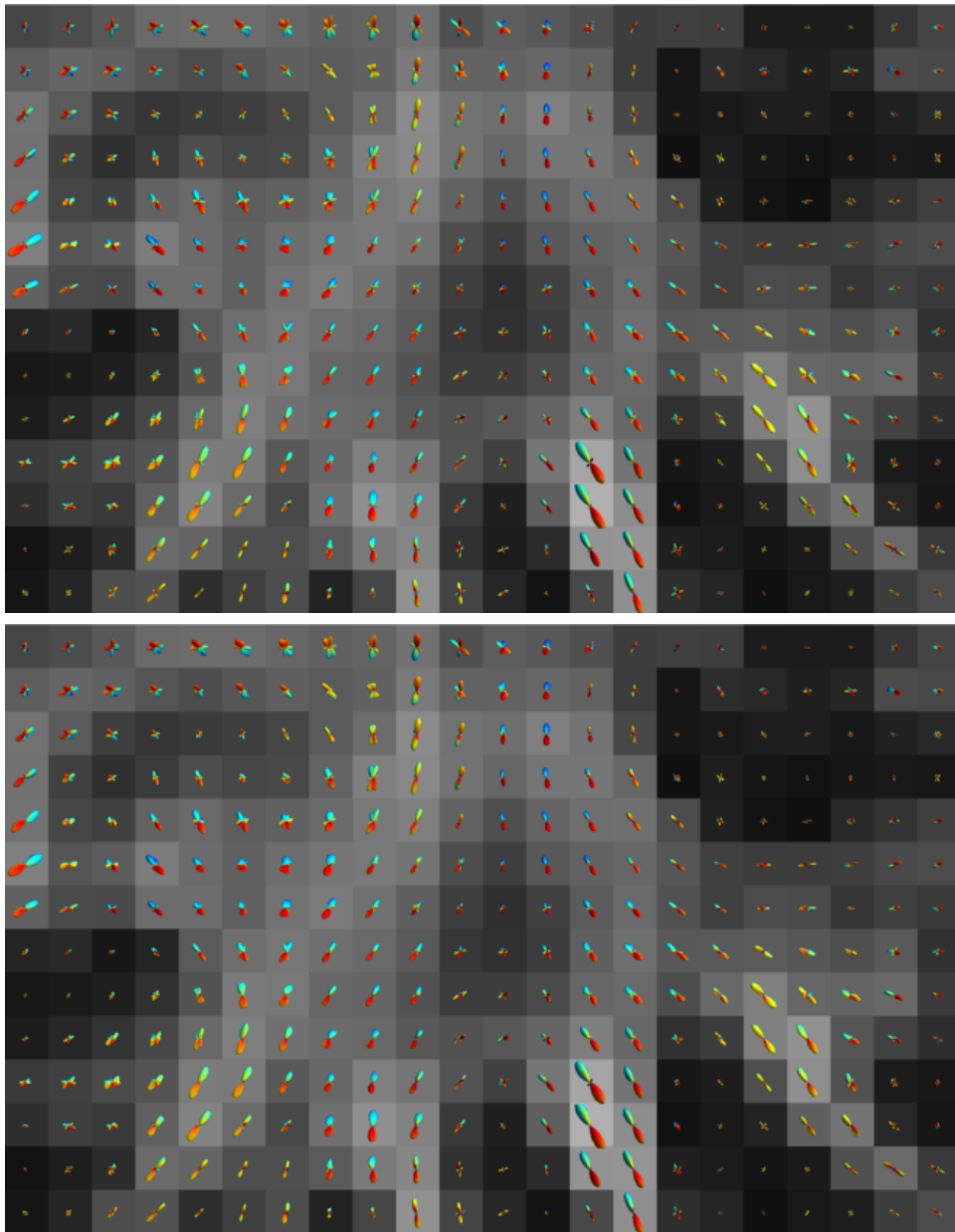


Figure 2: FODFs computed over a region of interest using two regularization parameters: $\lambda^2 = 0.006$ (top) and $\lambda^2 = 0.012$ (bottom).

The best regularization parameter were found for one, two, and three fibre crossings separately. The regularization parameter for accurate one fibre FODF estimation were approximately three times larger, and three fibre crossing were twice of the parameters presented in the Figure 1. This behaviour is similar to the one observed by Descoteaux [4], and likewise, we decided to use the two-fibre results to select the global parameter value.

Finally, a region of interest from a whole-brain scan of a healthy male subject was used to visualize the influence of a stronger regularization. The image was obtained using a single-shot, spin-echo, echo-planar, diffusion-weighted sequence in a Philips 3T Achieva clinical imaging system¹. Figure 2 shows FODFs computed over the same region regularized with two parameters – 0.006 and 0.012, our optimal FODF reconstruction parameter for $b =$

¹Acquisition matrix 112x112 with in-plane resolution 2×2 mm²; 52 slices with a thickness of 2 mm; $b = 3000$ s/mm²; $TE = 72$ ms; $TR = 15292$ ms; 61 evenly spaced diffusion weighting directions [2]; six $b = 0$ s/mm² images acquired and averaged

3000 s/mm² and SNR = 35 (Figure 1, right). The difference between the two is very subtle. The stronger regularization produced less ringing in the computed FODFs and suppressed some of the weaker false peaks. At the same time there was no significant loss of the angular resolution. The increase in FODFs stability is considered beneficial.

4 Conclusion

A systematic investigation of regularization parameter selection has been performed. Optimal parameter values for diffusion profiles, and diffusion and fibre ODFs were obtained by minimizing the difference between synthetic and reconstructed signal shapes. The findings not only corroborate previous research results but also extend them, providing a more complete picture of the parameter selection problem. While the regularization parameters for diffusion signal and ODF reconstruction are confirmed to be similar to those found in the previous research, the FODF reconstruction allows for regularisation parameters several times larger. Using the fine tuned parameter more stable and reliable FODFs were obtained.

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