Paper C

Generating a Synthetic Diffusion Tensor Dataset

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An error from the original paper has been corrected in the version reproduced here. In particular; the three last lines in section 2.2 have been rewritten and some notation has been changed to clarify the distinction between the quantities there defined.

Generating a Synthetic Diffusion Tensor Dataset

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Abstract

During the last years, many techniques for de-noising, segmentation and fiber-tracking have been applied to diffusion tensor MR image data (DTI) from human and animal brains. However, evaluating such methods may be difficult on these data since there is no gold standard regarding the true geometry of the brain anatomy or fiber bundles reconstructed in each particular case. In order to study, validate and compare various de-noising and fiber-tracking methods, there is a need for a (mathematical) phantom consisting of semi-realistic images with well-known properties. In this work we generate such a phantom and provide a description of the calculation process all the way up to voxel-wise diffusion tensor visualization.

1 Background

A modern MR scanner is able to measure apparent water diffusion in each voxel of a given subject's brain. For each voxel the scanner can measure water self-diffusion in K preconfigured directions (where typical values for K are 6, 25 or 55). These diffusion-sensitizing directions are commonly referred to as *gradient directions* in MR-literature. From these K measurements (plus a measurement of the MR-signal without diffusion-sensitizing gradients), one can calculate a measure known as the diffusion tensor (DT) [4]. The diffusion tensor will in this context refer to a symmetric 3×3 matrix for each voxel.

Many interesting quantities, related to local tissue micro-architecture, can be computed directly from the diffusion tensor. Two clinically useful measures are *fractional anisotropy* and *relative anisotropy* [4]. These are both directly related to the eigenvalues of the diffusion tensor and describe whether the amount of diffusion is equal in all directions (known as *isotropic diffusion*) or not (*anisotropic diffusion*).

For collecting DT imaging (DTI) data on a MR scanner, the Stejskal-Tanner sequence [1, 2, 3, 4] is typically used. Since we are dealing with water (uncharged molecules), the diffusion tensor is symmetric positive semidefinite – at least in the absence of noise. Therefore we know that the eigenvectors of the diffusion tensor form an orthogonal basis for the diffusion in each voxel and that the eigenvalues are positive. The diffusion is dominant in the direction corresponding to the largest eigenvalue (*principal diffusion direction*). One common way of visualizing both the eigenvectors and the eigenvalues in $\mathbb{R}^3$ is to let the eigenvectors be the basis of an ellipsoid where the distance from the center to the surface in each basis-direction is equal to the eigenvalue of that eigenvector.

1.1 Problem description

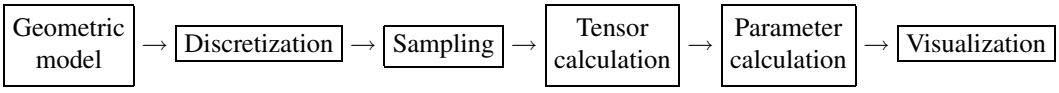
Considering the increasing number of reports on DTI post-processing research we observe that most of them apply their methods only to real data, acquired from human or animal test-subjects [4, 5]. This approach

is hampered with the following problems: (i) the true anatomy of each imaged subject is not known in detail, (ii) there is little control of the noise introduced by the scanning-process, (iii) cost of scanner time is usually high, (iv) it is difficult to compare methods and results from different studies since the test-data has been acquired on different MR scanner hardware, often using different imaging protocols, and finally, (v) the test-data is collected from different subjects, each having unique characteristics in gross anatomy and tissue micro-architecture.

In order to reduce these problems we have developed a synthetic DTI dataset with known geometric and signal properties from the ground up. Other related work include [1, 2]. [2] uses a parameterized helix as an example, but does not generate a full DTI dataset. Similarly, [1] defines a general model in terms of convolution for direct use in *fiber-tracking* [5]. Our process supports both of these models (we also examine a helix model), as well as describe a sampling procedure (where realistic noise can be added) and the diffusion tensor calculation.

2 The process described

In this work we specify two 3D geometric models characterized by anisotropic Gaussian diffusion. We sample these models and generate output similar to those obtained from MR scanners. Both our procedure and the MR scanner gives, by simple calculations, apparent diffusion coefficients along each gradient direction as output. From this output we calculate the diffusion tensor efficiently and use the diffusion tensors to generate several common measures and visualizations describing Gaussian water diffusion.



A model must describes how water diffuse in the synthetic dataset. For simplicity we have in this work considered only two very basic models. However, more complex models are easily accommodated in the same framework.

2.1 The geometric models

A model must for each voxel provide an orthogonal set of directions of water diffusion as well as a measure of the amount of diffusion in each of these directions. We will in this work consider two separate models with different geometric properties. In the rest of this work we let subindices such as i in a_i denote element i in the vector a.

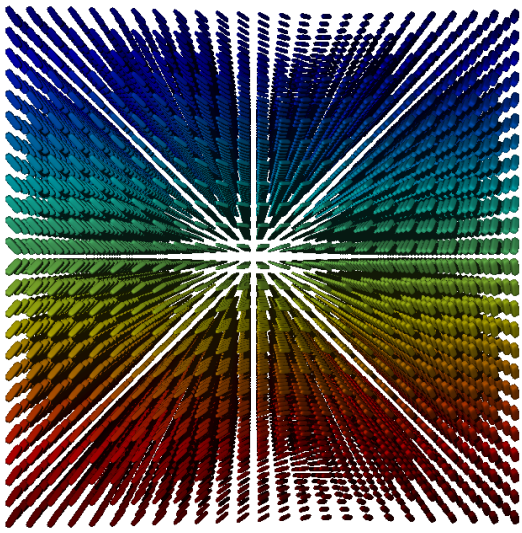
2.1.1 The double arch

The double arch model demonstrates a known phenomenon that can be observed in real applications. If two fibers (or fiber-bundles), which may originate from different parts of the brain, approach each other and run alongside tangentially, we say that they are "kissing". Kissing fibers is a pathological case in fiber tracking, because small amounts of noise introduced into the datasets may cause fiber tracking-algorithms to believe that the fibers are crossing and thus reconstruct wrong fiber trajectories for any or both of the fiber-bundles in question.

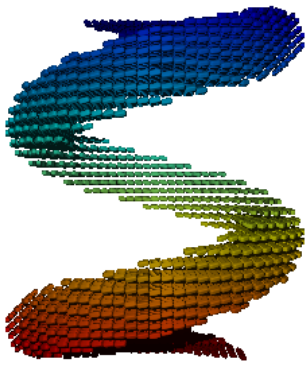
In this model we let the orientation of the diffusion basis be as follows: if p is a voxel (and $p_i \in [-1, 1]$ for $i \in \{x, y, z\}$), then we let the model return the direction $m(p) = [1,\ \ 1,\ \ \mathrm{sign}(p_z)2p_x]$. This model gives a single direction at each voxel, corresponding to the direction of principal diffusion.

We now expand this direction into an orthogonal basis by setting $q^{(1)} = m(p)$, selecting $q^{(2)}$ to be orthogonal to $q^{(1)}$ and be in the xy-plane and finally letting $q^{(3)}$ be the cross-product between $q^{(1)}$ and $q^{(2)}$. Let Q be the 3×3 matrix where column i is $q^{(i)}$. Then, in the basis Q we now have the orientation of the diffusion ellipsoid for each voxel. Since we in this model are concerned only with the *direction* of the diffusion and wish to allow processing of all parts of the volume, we let the diffusion in direction $q^{(1)}$ be $\alpha_1 = 2$, and let $\alpha_2 = \alpha_3 = 1$. This model then displays constant anisotropy throughout the volume.

The diffusion ellipsoid is now uniquely defined for each voxel.



(a) The double arch model discretized at a resolution of $25 \times 25 \times 25$ voxels



(b) The helix model discretized at $40 \times 40 \times 40$ voxels

Figure 1. Boxes showing orientation of the diffusion basis per voxel

(a) Horizontal slice of phantom showing principal eigenvalues of the helix model

(b) Noise added to the samples before computing tensor and showing principal eigenvalues

Figure 2. The eigenvalues of the helix model

2.1.2 The helix

We now consider the model described by a parameterized helix. This model was chosen because it allows experimentation with various degrees of curvature by simple adjustment of the radius of the helix. This is desirable when for instance the model is used to explore fiber-tracking algorithms.

The center-curve of the helix is defined as the vector-valued function $c(t) = [\sin(vt),\ \cos(vt),\ t]$ for $t \in [0, 1]$. As t varies, this function defines points that will comprise a path "in the center of the helix". Let p denote the voxel (defined on the same range as in the previous model) at which we want to sample the model, and let $t_0 = \arg\min_t \|p - c(t)\|_2$. Then the model will return the vector $m(p) = w(p)\frac{\nabla c(t_0)}{\|\nabla c(t_0)\|_2}$ where $w(p) = \exp\{\frac{\|p-c(t_0)\|_2}{-c}\}$.

This model can be easily modified by changing the thickness of the helix (represented by the constant $c > 0$) or by adjusting the number of revolutions the helix makes (controlled by the constant v). The radius of the helix can be changed by scaling the trigonometric functions in $c(t)$ with a constant. In our example $v = 2\pi$ and $c = 0.07$.

Again we expand this direction into an orthonormal basis for the diffusion ellipsoid by setting $q^{(1)} = m(p)$ and $q^{(2)} = p - m(p)$. Next we let $q^{(3)}$ be the cross-product between $q^{(1)}$ and $q^{(2)}$ and normalize the results. Let Q be the 3×3 matrix where column i is $q^{(i)}$. Next we choose the scaling of the ellipsoid along each of these basis directions. We let the scaling of axis $q^{(1)}$ be $\alpha_1 = 1$ and set the scaling of the other two axes to $\alpha_2 = \alpha_3 = 1 - w(p)$. This allows the model to display isotropic diffusion outside the helix and anisotropic inside it.

2.2 Sampling the model

In the following we let Q and α be as defined in either one of the previous two sections. In order to measure the amount of diffusion along each of the K gradient directions $r^{(1)}, \ldots, r^{(K)} \in \mathbb{R}^3$, we first calculate a curve $f(x) = \frac{1}{2}x^T Ax = 1$ which interpolates $\alpha_1 q^{(1)}, \alpha_2 q^{(2)}$ and $\alpha_3 q^{(3)}$. We write $A = QDQ^T$ where $D = \mathrm{diag}(\lambda_1, \lambda_2, \lambda_3)$. Thus we have defined A in terms of an orthogonal eigenvalue decomposition. Carrying out the multiplication we obtain the eigenvalues of A as $\lambda_i = \frac{2}{\alpha_i^2}, i \in \{1, 2, 3\}$. Having done so we can sample the model in an arbitrary direction $r^{(k)}$ by calculating the intersection between the curve f and the line $z_k r^{(k)}$ where z_k is a scalar. Thus the voxelwise diffusion estimates become $z_k = \sqrt{\frac{2}{r^{(k)^T} A r^{(k)}}}$.

The output produced by an MR scanner equipped with a diffusion tensor pulse sequence on the other hand is $s_k = \exp\{-r^{(k)^T} Q\,\mathrm{diag}(\alpha) Q^T r^{(k)}\}$. Next, we describe the diffusion tensor calculation.

2.3 Computing the diffusion tensors

The general form of the Stejskal-Tanner equations [4] describes, for each voxel, anisotropic diffusion of water molecules as: $S_k = S_0 \exp\{-b_k\, r^{(k)^T} X r^{(k)}\}$. This set of K equations defines the relationship between (i) the observed diffusion-weighted signal intensity, S_k ($1 \leq k \leq K$) in direction $r^{(k)}$ obtained from the DTI image acquisitions (or, from the synthetic sampling procedure presented above), (ii) the observed signal intensity, S_0 acquired without diffusion-weighting, (iii) the predefined diffusion-sensitizing directions, $r^{(k)}$, (iv) the so-called b-values, b_k defined by the pulse sequence (usually, b_k is a fixed value, say 1000 [s/mm^2]), and (v) the diffusion tensor, X. Since X is a symmetric 3×3 matrix, we only have six unknowns in this equation. However, K is generally larger than six, and we therefore solve the set of equations by least-squares minimization. Taking the logarithm on both sides and setting $d_k = \frac{\ln(S_0) - \ln(S_k)}{b_k}$, we obtain the least-squares minimization problem $\min_X \sum_{k=1}^{K} (r^{(k)^T} X r^{(k)} - d_k)^2$.

Next we observe that if we set $R^{(k)} = \begin{bmatrix} r_1^{(k)^2} & 2r_1^{(k)}r_2^{(k)} & 2r_1^{(k)}r_3^{(k)} & r_2^{(k)^2} & 2r_2^{(k)}r_3^{(k)} & r_3^{(k)^2} \end{bmatrix}$ and let the vector $x = \begin{bmatrix} x_{11} & x_{12} & x_{13} & x_{22} & x_{23} & x_{33} \end{bmatrix}^T$ then the k'th element in the sum can be rewritten as $(R^{(k)}x - d_k)^2$. Finally letting R be the $K \times 6$ matrix whose row number k is $R^{(k)}$ we obtain the well-known linear least-squares problem $\min_x \|Rx - d\|_2^2$. We solve this problem using a standard QR algorithm.

Unfortunately, there is no guaranty that the diffusion tensor X computed by this process is positive definite in the presence of noise introduced into the samples. The possible lack of this property is often disregarded in literature. One possible way to ensure positive definiteness is to write $X = LL^T$, and then solve a minimization problem with regards to L [3].

3 Conclusion

We have designed a simple numerical procedure for creating synthetic 3D diffusion tensor MRI datasets. This allows the user to specify a wide range of geometric models that can be used to generate outputs similar to those produced from MR scanners with conventional DTI measuring techniques. This approach will facilitate quantitative comparisons between various methods used for processing DTI data, as opposed to qualitative visual inspection of the resulting images.

Future work will include quantitative studies of how noise introduced at various stages of the process will affect the final output such as scalar invariants of the diffusion tensor and fiber tracking, as well as ways to ensure positive definiteness of the diffusion tensor.

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