# An Analytical Formulation for Spatial Normalization of Diffusion Tensor Images

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# Introduction

Spatial normalization of diffusion tensor images (DTI) is an essential process in multi-subject analysis for an increase of the detection sensitivity on mild alterations in white matter microarchitecture. This process is, however, not as straightforward as the normalization of scalar anatomical images as usually performed for functional MRI studies [1]. Not only the important indices such as the apparent diffusion coefficient or the fractional anisotropy should be preserved, but the principal directions should also be suitably adjusted with possible deformation of the images [2]. Current literature is in lack of a comprehensive theoretical investigation of the DTI normalization process. Therefore, in this abstract we attempt to provide an analytical formulation for DTI normalization, in order to assist practical implementation of the computational procedure for DTI normalization.

### Image transformation

The diffusion tensor is a second-rank tensor satisfying the rotational coordinate transformation relationship from coordinate S to T:

(1)

$$D_t = M D_s M^{-1}$$

where D is the diffusion tensor whose subscript stands for the coordinate system, and M is the rotation matrix from coordinate S to T. From the second-rank tensor definition, it is known that any alteration in the shape of an imaged object should satisfy the rotational property of matrix M in order to preserve the tensor.

Spatial normalization of images from source (position vector X) to target image (position vector Y) can be expressed in matrix multiplication form using an affine matrix A (which is a function of position X) plus a translational operation as:

The affine matrix *A* can be factorized as  $A = Q \cdot S \cdot U$  for rigid-body transformation (an orthogonal matrix *Q*), scaling (a diagonal matrix *S*), and shearing (an upper triangular matrix *U*), respectively. The rigid-body transformation matrix *Q* satisfies the requirements of *M* as in Eq.(1) because of the orthogonality. On the other hand however, since *U* does not satisfy Eq.(1) as a rotation matrix *M* does, spatial normalization of DTI cannot be performed using scalar image normalization procedures.

The scaling matrix *S* should be discarded in the DTI normalization process, because image scaling should not have any effects on the shape of the diffusion tensor [2]. In other words, an amplification of the image along one direction is not supposed to elongate or flatten a diffusion tensor, in order to preserve the fiber architecture. The shearing matrix *U* could be effectively replaced by another rotational matrix  $Q_{shear}$ , because the fiber connectivity in between adjacent voxels should be preserved [2]. Here the tensor orientation should not be preserved but should be appropriately adjusted according to the procedure of scalar anatomical spatial normalization. Given that the tensor orientational change due to shearing can be written as  $\frac{y}{y} = U \frac{x}{x'} |U| \frac{x}{x'}|$  from the source (position vector *X*) to the target image (position vector *Y*), for a known *U* the angular change as well as the axis of rotation can be easily found. Thus, the effect (on diffusion tensor) of "shearing

of the anatomical image" can be represented by a rotational matrix  $Q_{\text{shear}}$ . To sum up, for a spatial normalization of anatomical images using the affine matrix  $A_{\text{anat}} = Q \cdot S \cdot U$  as shown in Eq.(2), the corresponding

normalization procedure for the DTI images should be performed using  $A_{DTI} = Q \cdot Q_{shear}$ . In this manner, the rotational coordinate transformation relationship as shown in Eq.(1) can be satisfied and hence the tensor information related to the white matter architecture is preserved upon the proper DTI normalization.

#### **Image interpolation**

Interpolation of the image voxels is a necessary step in multi-subject analysis procedures such as slice reformatting. In the following, we show that the diffusion tensor can be linearly combined in a way similar to the linear interpolation of scalar anatomical images. Consider the Einstein diffusion equation given by:

$$\frac{\partial}{\partial t} p(x,t \mid x_0, t_0) = D \,\nabla^2 p(x,t \mid x_0, t_0)$$

where *p* stands for the probability density function (i.e., a scalar field) of finding a certain molecule at place *x* and at time *t*, given that its original position at time  $t_0$  is  $x_0$ . In the steady state, the equation can be written as:

$$\widetilde{J} = -D \,\nabla p(x,t \,|\, x_0, t_0)$$

where J is the flux (i.e., a vector field) of the molecules. Eq.(4) can also be viewed as an expression of the law of conservation. Note that although in reality we do not observe the water molecule flux in the human brain, a linear mixture of any two compartments yields a linear mixture of the flux with the same weights. Thus,

(4)

(6)

$$\overrightarrow{J}_{t} = k_{1} \overset{\textbf{O}}{J}_{1} + k_{2} \overset{\textbf{O}}{J}_{2} = k_{1} \overleftrightarrow{D_{1}} \nabla p_{1} + k_{2} \overleftrightarrow{D_{2}} \nabla p_{2}$$

In the white matter of human brain, we assume that the probability density function is similar in one certain type of tissue. Thus the total flux can be written as:  $\vec{L} = (k \vec{D} + k \vec{D}) \nabla p$ 

$$_{t} = (k_1 D_1 + k_2 D_2) \nabla p$$

Eq.(6) means that for linear interpolation of a scalar anatomical image, the corresponding diffusion tensor can also be linearly combined with the same weights.

#### Discussion

It is shown in this abstract that the affine matrix as used commonly for spatial normalization of scalar anatomical image does not satisfy tensor coordinate transformation due to the scaling and the shearing operations. Therefore, spatial normalization of DTI should not be performed using the scalar image normalization procedures. Nevertheless, by considering the effects of scaling and shearing on the diffusion tensor [2], appropriate modifications of the affine matrix to consist of two rotational matrices could make DTI normalization feasible under both rigid-body and elastic transformations. In addition, we have shown that with a reasonable assumption that the probability density function finding a water molecule as a function of time and space is similar in the white matter, the diffusion tensor can be linearly combined using the same weights for linear interpolation of the anatomical images. The analytical formulation stated here should be helpful in assisting future practical implementation of the computational procedures for DTI normalization.

## References

[1] Alexander DC, et al. IEEE Trans Med Imaging 2001; 20: 1131-1139. [2] Xu D, et al. MRM 2003; 50: 175-182.