On What Manifold Do Diffusion Tensors Live?

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Abstract. Diffusion tensor imaging has become an important research and clinical tool, owing to its unique ability to infer microstructural properties of living tissue. Increased use has led to a demand for statistical tools to analyze diffusion tensor data and perform, for example, confidence estimates, ROI analysis, and group comparisons. A first step towards developing a statistical framework is establishing the basic notion of distance between tensors. We investigate the properties of two previously proposed metrics that define a Riemannian manifold: the affine-invariant and Euclidean metrics. We find that the Euclidean metric is more appropriate for intra-voxel comparisons, and suggest that a context-dependent metric may be required for inter-voxel comparisons.

1 Introduction

In diffusion tensor magnetic resonance imaging (DTI), a diffusion tensor is derived in each voxel [1]. This tensor represents the intrinsic diffusion transport properties within a volume element. Diffusion tensor statistics require comparing tensors and, hence, a definition of distance between them. The general notion of distance involves a connected Riemannian manifold, containing all tensors. Over this manifold, distance is defined as the geodesic, i.e., the shortest path on the manifold. Completely describing the manifold is a metric, $G(D) = \{g_{ij}(D)\}$, which defines the infinitesimal distance: $ds^2 = dD^T G(D) dD$ [2], where D is a vector of coordinates for a chosen representation of a diffusion tensor. To define the geometric distance between tensors, a metric and a local coordinate system are chosen. Any positive-definite and symmetric metric is admissible. By selecting the metric we define the topology of the set of all tensors. Therefore, if more than one metric is admissible, selecting among them as well as determining which representation-metric combination would best characterize the distance between tensors, are challenging issues. For this we need additional information and constraints, derived, if possible, from the topology of the space, or found by other means, such as empirical observation.

The conventional approach uses the canonical tensor representation and places diffusion tensors on a Euclidean manifold, with a constant metric, resulting in $ds^2 = tr((dD)^T dD)$ [3, 4]. The geodesic between any two tensors, D_1 and D_2, with this metric, is simply a straight line, or the Euclidean distance

$$Dist_{Euc}(D_1, D_2) = ||D_1 - D_2|| \ . \tag{1}$$

The Euclidean metric is rotation invariant, and is defined for the entire space of symmetric matrices. A different approach restricts the metric to be affine-invariant, and to operate only on tensors belonging to the space of positive definite symmetric matrices, S^+ [5–9]. A Riemannian metric that satisfies these requirements has an infinitesimal distance $ds^2 = tr((D^{-1}dD)^2)$ [10]. The corresponding geodesic is found by integration [10]:

$$Dist_{Aff}(D_1, D_2) = \sqrt{tr\left(log^2(D_1^{-1}D_2)\right)} = \sqrt{\sum_{i=1}^{m} log^2(\eta_i)} \ , \qquad (2)$$

where η_i are the m eigenvalues of the matrix $D_1^{-1}D_2$. This metric is not dependent on the choice of the tensor representation.

In this paper we investigate the two constraints imposed by the use of the affine-invariant metric, and examine their relevance to the analysis of diffusion tensors. The positiveness requirement seems plausible, for we know that a negative diffusivity is not physical; negative diffusivities can generally be explained by background noise or other artifacts [11, 12]. The affine-invariance constraint originates from the use of tensors as mathematical operators (for instance deformation and rotation matrices [10, 13]). In order to investigate the physical meaning of the affine-invariant constraint let us consider the simpler case of isotropic diffusion which has many of the same properties as the 6D diffusion tensor space.

2 Isotropic Diffusion as a Special Case

The diffusion tensor provides a measure of diffusion in a 3D space. It is especially important when dealing with an anisotropic medium, when different apparent diffusion coefficients (ADCs) are associated with different orientations. The diffusion equation dictates that (for a Gaussian process) the orientational variability of the ADC be fully described by the diffusion tensor [14]. We first consider isotropic diffusion, where the diffusivity in all directions is equal and the diffusion tensor is an isotropic tensor with three equal eigenvalues: $D^{iso} = \lambda I$. The eigenvalue λ describes the entire 3D diffusion process, and is the ADC [15]. Since isotropic tensors are a specific kind of diffusion tensor, the distance measured between them has to be the same as the one applied to all tensors. Using the affine-invariant geodesic for isotropic tensors we get:

$$Dist_{Aff}(D_1^{iso}, D_2^{iso}) = \sqrt{tr\left(log^2((\lambda_1 I)^{-1}\lambda_2 I)\right)} = |log\,(\lambda_2/\lambda_1)| \ , \qquad (3)$$

where λ_1 and λ_2 are the ADCs for the isotropic tensors D_1 and D_2, respectively. This geodesic can also be derived from the infinitesimal distance function, $ds = d\lambda/\lambda$. Similarly, the Euclidean distance between isotropic tensors is simply

$$Dist_{Euc}(D_1^{iso}, D_2^{iso}) = |\lambda_2 - \lambda_1| \ , \qquad (4)$$

with the infinitesimal distance function $ds = d\lambda$. We note that for isotropic tensors, the affine-invariant metric is identical to the "Log-Euclidean" metric [16].

2.1 Jeffreys and Cartesian Quantities

We recognize that the distance functions in Eqs. (4) and (3) respectively coincide with the definition of "Cartesian" and "Jeffreys" quantities, terms coined by Tarantola [17, 18] for families of physical measurable quantities. Jeffreys quantities are always positive and sensitive to coordinate choice or scale. Tarantola suggests that being scale sensitive, a proper distance function for a Jeffreys quantity must be scale invariant. Therefore the finite distance between points X_1 and X_2 of a Jeffreys quantity is

$$Dist_{Jef}(X_1, X_2) = k\,|log(X_2/X_1)|\ . \tag{5}$$

This scale invariant metric is sensitive to the measured physical *quality* instead of the measured physical *quantity*. As such, Tarantola finds these quantities to be ubiquitous and suitable to describe a variety of physical phenomena, e.g., musical notes, heat/cold and stiffness. Moreover, he claims that most quantities used in physics are either Jeffreys quantities or simply related to them [17]. If X is a Jeffreys quantity, then $x = log(X/X_0)$,where X_0 is any fixed value of X, is a Cartesian quantity, and has the finite distance function

$$Dist_{crt}(x_1, x_2) = k|x_2 - x_1|\ . \tag{6}$$

Identifying whether a quantity is Jeffreys or Cartesian influences the statistical framework needed to compare measurements of that quantity. In particular, the Cartesian barycenter is associated with the arithmetic mean, given by

$$\mu_{crt} = \frac{1}{n}\sum_{i=1}^{n} x_n\ , \tag{7}$$

while the Jeffreys barycenter is associated with the geometric mean, given by

$$\mu_{Jef} = \left(\prod_{i=1}^{n} X_i\right)^{1/n} = exp\left(\frac{1}{n}\sum_{i=1}^{n} logX_i\right)\ . \tag{8}$$

A comparison of Eq. (3) with Eq. (5) and Eq. (4) with Eq. (6) clearly shows that the difference between the metrics stems from how the ADC quantity is interpreted: for a Jeffreys quantity, the affine-invariant metric is appropriate; for a Cartesian quantity, a Euclidean metric is appropriate.

2.2 The Diffusion Weighted Signal

Studying the properties of the diffusion weighted (DW) signal helps us determine whether the ADC is a Jeffreys or a Cartesian quantity. The DW signal is obtained by a pulse field (PFG) MR experiment, an MR protocol that makes the MR signal sensitive to the displacement of water molecules along a certain orientation [19]. The DW signal is the magnitude of a complex quantity so it is always positive, limited by the highest integer value allowed. We expect the signal to carry information regarding diffusion, but the intensity of the signal is known to be proportional to the number of molecules [20]. The exact ratio is determined by various machine and scan dependent parameters [21]. For instance, a completely homogenous object scanned with a range of voxel sizes, on different MRI scanners (with different magnetic field and gradient strengths) and different pulse timings will yield a variety of signal intensities, although the object itself, and its diffusion properties, remain the same. This means that the scale of the signal amplitude measurement is arbitrary and clearly does not imply any physical qualities of the measured object. The DW signal is therefore positive and scale sensitive, which makes it a Jeffreys quantity.

As a Jeffreys quantity, the DW signal has a related Cartesian quantity [17], which we can find: we set the non-DW signal, S_0, as the origin, and compare any other signals obtained, S_i by taking their logarithms:

$$Dist_{Jef}(S_0, S_i) = |log(S_i/S_0)| \ . \quad (9)$$

Interestingly Eq. (9) is known to be proportional to the ADC (up to the scale factor b) [19]:

$$\lambda = -b^{-1} log(S_i/S_0) \ .$$

This means that λ, the ADC, is the Cartesian quantity associated with the distance between the ratio of measured signals and, therefore, a scale invariant metric for comparing DW signals.

2.3 The ADC as a Physical Quality

Although the discussion above suggests that the ADC and the Trace of the diffusion tensor are Cartesian quantities whose metrics are given by Eq. (6), it may be worthwhile to investigate this further. Determining if the properties of the ADC satisfy the requirements of a Jeffreys quantity will help refine this argument.

The ADC as a physical quantity is non-negative. However, noise or systematic artifacts can result in ADC measurements with negative values when $S_i > S_0$. Moreover, the value of a zero ADC, while hard to achieve physically, is still admissible. It means that on average, a particle does not move from its original position during any finite diffusion time. However, ADC < 0 causes the distance (5) to be undefined, and ADC of zero causes it to diverge.

The Einstein equation establishes the fundamental defining relationship between the ADC and the mean-squared displacement [22]

$$\mathrm{E}[(x - x_0)^2] = 2\lambda t$$

Clearly, then, comparing ADCs acquired with the same diffusion time, t, is the same as comparing the corresponding mean-squared displacements. Once we determine physical units for the ADC (such as cm^2/sec), we set the units of measure for the magnitude of the distance covered by the diffusing particles (such as cm). For example, considering the application of the Einstein equation

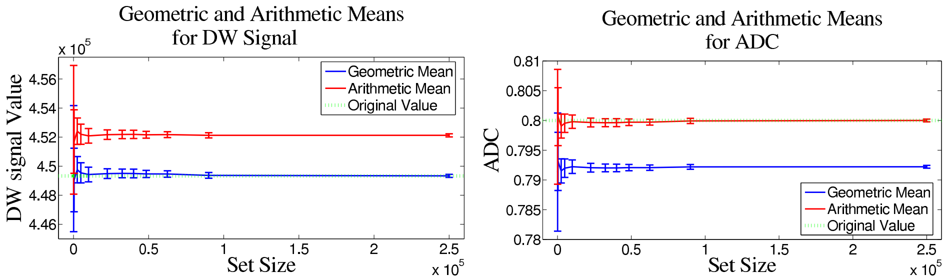

Fig. 1. Monte Carlo simulation of noisy DW signal (left) and its corresponding ADCs (right). The data is distributed around an ADC of 0.8 which yields a DW signal of 449329 (dashed lines). The **geometric** mean of DW signals converges to the original value, while the **arithnetic** mean of the ADC converges to the original value.

on three systems, in all of which diffusion is isotropic with ADC values I) $3 * 10^{-5} cm^2/sec$ (like water at body temperature), II) $3 * 10^{-10} cm^2/sec$ (like a large macromolecule) and III) $3 * 10 cm^2/sec$ (like Helium gas) shows that water will diffuse a mean-squared displacement of $10^{-2} cm$, the large molecule will diffuse on average a distance of $3.5 * 10^{-5} cm$, and Helium will diffuse $3.5 cm$. The ADC, is therefore a scale dependent quantity, since changing its units of measure changes the magnitude of the measured displacements. Therefore, a proper metric for diffusivities should depend on scale.

2.4 Intra-Voxel ADC Estimation

In diffusion imaging the accuracy of the estimation is commonly increased by performing repetitive measurements, under the assumption of a constant true diffusion coefficient over time. As a result a number of realizations of ADCs are obtained that are expected to differ from each other by the acquisition noise [4]. In MRI this is the Johnson noise, which has a Rician distribution [23], and can be synthesized using a Monte Carlo simulation [4]. We have produced a set of noisy measurements around a selected ADC value and estimated an ADC for each noisy measurement. We performed this analysis for different set sizes, and for each set size we repeated the simulation 100 times. Figure 1(left) shows the arithmetic and geometric means (obtained by Eqs (7) and (8) respectively), along with their standard deviations, for a set of ADCs generated with an original ADC of 0.8 and an SNR of 20. The values are shown as a function of the set size. Clearly, as set size increases the sample mean converges towards the value 0.8, while the geometric mean converges towards a biased value. The same analysis performed on the noisy DW signal produces the graph in Figure 1(right), where the geometric mean of the DW signals converges towards the expected value (dashed line), while the arithmetic mean converges towards a biased value. The same results are found for a range of ADC and SNR values. These findings also support the notion that the DW signal is a Jeffreys quantity, and ADC is its Cartesian quantity.

3 Metric Selection for Diffusion Tensors

A Jeffreys quantity is naturally extended to a *Jeffreys tensor*, a tensor whose eigenvalues are Jeffreys quantities [17]. The appropriate distance measure for these tensors is in Eq. (2) and associated with an affine-invariant metric. The appropriate distance for a tensor of Cartesian quantities is in Eq. (1) and associated with the Euclidean metric. The diffusion tensor is a generalization of the ADC to a higher dimensional space [24]: its eigenvalues are the ADCs along the principal axis [1]. Knowing that the DW signal is a Jeffreys quantity, we can review the connection between the signal and the Trace of the diffusion tensor [15], where it was proved that

$$\left(\prod_{i=1}^{n} S_i\right)^{1/n} = S_0 e^{-\beta Trace(D)} \tag{10}$$

for a scaler β. This equation is not restricted to isotropic tensors, and the signal intensities can be obtained using a HARDI acquisition. From Eq. (10) it is clear that the arithmetic average of the Log of the DW signal is proportional to $Trace(D)$, and as such is a linear combination of elements of the diffusion tensor [25].

Based on our conclusions regarding intra-voxel ADC estimation, since the eigenvalues of the diffusion tensor are Cartesian quantities, a scale invariant metric is not appropriate as shown above in the case of isotropic tensors. Hence, affine invariance, which encompasses scale invariance, is not a desirable property either. An appropriate metric is the one in Eq. (1), associated with a Euclidean metric.

3.1 The Swelling Effect

Along with positivity, reduction of the swelling effect was advertised as the main advantage of using the affine-invariant metric for measuring the distance between diffusion tensors [9, 16]. Swelling occurs when anisotropic tensors with different principal axes are interpolated or averaged, resulting in a more isotropic tensor with a larger determinant or volume than either tensor individually [5]. We claim that the volume preservation requirement is not consistent with the effect of background noise. Overall, shape, size, and orientation information is encoded in the tensor, and noise introduces variability in all of them. The distribution of determinants for a set of noisy realizations of the same diffusion tensor (Figure 2(left), obtained by Monte Carlo simulation as in [4]) clearly shows that the determinant is not preserved. We further analyze the variability of the tensor realizations by applying a manifold learning algorithm (Isomap) [26], and determine the dimensionality of the empirically fitted manifold. Using the graph of Log of residual variance [26] shown in Figure 2(right), we obtain a dimension of 6, indicating that Johnson noise creates variations in all tensor parameters, including the eigenvalues, and not just the eigenvectors or orientations.

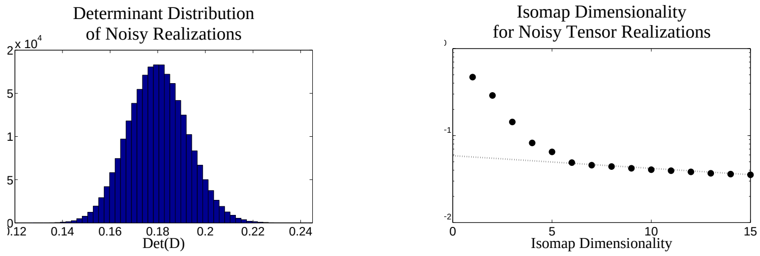

Fig. 2. Monte Carlo simulation of tensor estimations. A noisy realization of an anisotropic tensor with a determinant of 0.18. The noise does not preserve the determinant (left). The manifold dimension for the set of tensors is 6 according to the elbow at 6 in the graph of Log of residual variance vs Isomap dimensionality (right).

3.2 Context Dependent Metrics

The swelling effect leads us to the idea of context-dependent metrics. For example, if we know that two anisotropic tensors, obtained in neighboring voxels, measure diffusivities in different points along the same neuronal bundle, we are justified in expecting that interpolation will preserve the determinant. However, the same two tensors might be found in other contexts, such as in distant voxels or as different realizations of a tensor in the same voxel. Each context implies a different subset of tensors, and hence, a different underlying manifold structure. For these different applications, an appropriate tensor representation must be chosen and a context dependent metric used. Isomap, for instance, identifies an underlying manifold related to anatomical variation and finds a geodesic associated with that set of tensors [27]. Another approach [28] embeds the tensor space within the image space, to get a location dependent induced metric.

4 Conclusions and Summary

In this paper we focus on two metrics; in future work we intend to investigate other metrics that have been proposed for diffusion tensors. The main issue we address is whether a scale invariant metric is appropriate for measuring the distance between diffusion coefficients or tensors. We have shown that for intravoxel comparisons of diffusion coefficients and tensors, scale invariance is not a desirable property for a metric. For the intervoxel case, care must be taken, since the distance between tensors is context dependent. A specific context may dictate a scale invariant metric, or the use of an affine-invariant metric, but for proper use, this context has to be defined.

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