Novel Representation and Low level Computer Vision Techniques for Manifold Valued Diffusion Tensor MRI

by

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B.E., Visvesvaraya Technological University, 2007

A THESIS SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF

MASTER OF APPLIED SCIENCE

in

The Faculty of Graduate Studies

(Electrical Engineering)

THE UNIVERSITY OF BRITISH COLUMBIA

(Vancouver)

May 2012

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Abstract

Diffusion tensor magnetic resonance imaging (DT-MRI) is a powerful non-invasive imaging modality whose processing, analysis and visualization has become a strong focus in medical imaging research. In this modality, the direction of the water diffusion is locally modeled by a Gaussian probability density function whose covariance matrix is a second order $3 \times 3$ symmetric positive definite matrix, also called the tensor here. The manifold-valued nature of the data as well as its high dimensionality makes the computational analysis of DT images complex. Very often, the data dimensionality is reduced to a single scalar derived from the tensors. Another common approach has been to ignore the restriction to the manifold of symmetric second-order tensors and, instead, treat the data as a multi-valued image.

In this thesis, we try to address the above challenges posed by DT data using two different approaches. Our first contribution employs a geometric approach for representing DT data as low dimensional manifold embedded in higher dimensional space and then applying mathematical tools traditionally used in the study of Riemannian geometry for formulating first order and second order differential operators for DT images. Our second contribution is an algebraic one, where the key novel idea is to represent the DT data using the 8 dimensional hypercomplex algebra-biquaternions. This approach enables the processing of DT images in a holistic manner and facilitates the seamless introduction of traditional signal processing methodologies from biquaternion theory such as computing the Fourier transform, convolution, and edge detection for DT images. The preliminary results on synthetic and real DT data show great promise in both our approaches for DT image processing. In particular, we demonstrate greater detection ability of our features over scalar based approaches such as fractional anisotropy and show
novel applications of our new biquaternion tools that have not been possible before for DT images.
Preface

The work in this thesis has resulted in the following publications:


The first publication resulted from the work in chapter 2. The second publication resulted from the work in chapter 3. I was the primary author of these manuscripts and the main contributor to the design, development, and testing of the presented methods under the supervision of Dr. Rafeef Abugharbieh and Dr. Ghassan Hamarneh. I received technical help from Brian G. Booth for the work related to my first publication.
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<td>MRI</td>
<td>Magnetic Resonance Imaging</td>
</tr>
<tr>
<td>DT-MRI</td>
<td>Diffusion Tensor Magnetic Resonance Imaging</td>
</tr>
<tr>
<td>DT</td>
<td>Diffusion Tensor</td>
</tr>
<tr>
<td>CC</td>
<td>Corpus Callosum</td>
</tr>
<tr>
<td>2D</td>
<td>Two Dimensional</td>
</tr>
<tr>
<td>3D</td>
<td>Three Dimensional</td>
</tr>
<tr>
<td>FA</td>
<td>Fractional Anisotropy</td>
</tr>
<tr>
<td>DTI</td>
<td>Diffusion Tensor Imaging</td>
</tr>
<tr>
<td>LE</td>
<td>Log-Euclidean</td>
</tr>
<tr>
<td>ST</td>
<td>Structure Tensor</td>
</tr>
<tr>
<td>SPD</td>
<td>Symmetric Positive Definite</td>
</tr>
<tr>
<td>MPT</td>
<td>Moment-Preserving Thresholding</td>
</tr>
<tr>
<td>LBAM</td>
<td>Laboratory of Brain Anatomical MRI</td>
</tr>
<tr>
<td>MIDAS</td>
<td>Multimedia Digital Archiving System</td>
</tr>
<tr>
<td>CSF</td>
<td>Cerebrospinal Fluid</td>
</tr>
<tr>
<td>MD</td>
<td>Mean Diffusivity</td>
</tr>
<tr>
<td>MS</td>
<td>Multiple Sclerosis</td>
</tr>
<tr>
<td>DWI</td>
<td>Diffusion Weighted Imaging</td>
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<tr>
<td>ADC</td>
<td>Apparent Diffusion Coefficient</td>
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Acknowledgements

I would like to thank my supervisors Rafeef Abugharbieh and Ghassan Hamarneh for all of their guidance, time and dedication. I would like to thank Brian G. Booth for helping me at various times during my degree. Finally, I would like to thank my parents for their unwavering support.
Chapter 1

Introduction and Background

1.1 Motivation and Problem Description

Diffusion tensor magnetic resonance imaging (DT-MRI) is a powerful non-invasive imaging modality whose processing, analysis and visualization has become a strong focus in medical imaging research [3]. In this modality, the diffusion characteristics of water molecules in the body as a result of their random Brownian motion in concentration gradients, are recorded in vivo. These diffusion characteristics carry information about the microstructure of the underlying tissues, thus making it possible to distinguish anatomical structures. DT-MRI is becoming increasingly valuable for assessing the progression of diseases and their treatment evaluation [11–14].

In DT-MRI, the water diffusion is locally modeled by a Gaussian probability density function whose covariance matrix is a second order 3×3 symmetric positive definite matrix, also called as the diffusion tensor (DT) [3, 4]. These tensors are computed for each voxel from measurements of diffusion in several directions. Hence unlike other medical image data, DT-MRI images contain a second order tensor at each voxel of the 3D image, forming a 3-D tensor field.

DTs live on a manifold and do not constitute a vector space [15, 16]. The manifold nature of the data as well as its high dimensionality makes the computational analysis of these images complex. Hence it is not straightforward to extend low-level computer vision techniques that work on scalar and vector images to tensor images. Very often, the computations are car-
ried out by reducing the dimensionality of the data to a single scalar derived from the tensor \[^{[17, 18]}\], which has the drawback of throwing away a huge amount of useful information. Another common approach has been to carry out computations on the individual scalar channels of the tensor, not taking into account the geometrical nature of the data. The purpose of our work in this thesis is to develop novel low-level computer vision techniques for tensor images, that address the above problems.

1.2 Thesis Objectives

The aim of this thesis is develop novel low-level computer vision algorithms for DT images that make use of the full tensor (incorporating both shape and orientation information) without dimensionality reduction, while respecting the geometry of the data. Specifically,

- We take a geometric approach to develop novel first and second order spatial differential operators for DT images using the full tensor, while respecting the manifold of the tensors. Using our differential operators, we formulate geometric features in DT-MRI data like corners, tube and sheet like structures, that have not been explored before.

- We take an algebraic approach to process DT images holistically using a biquaternion representation (an 8 dimensional hypercomplex algebra), while respecting the underlying data manifold. We introduce the biquaternion Fourier transform and convolution for DT images for the first time. We also formulate a first order biquaternion differential operator and an edge detector for DT images.

All our methods are validated on synthetic as well as real DT data.
1.3 Background to Diffusion MRI

1.3.1 Biological Motivation

Diffusion is the spread of molecules in a fluid due to constant thermal motion. This phenomena was first observed in 1828 when botanist Robert Brown noticed the continuous random motion of pollen grains suspended in water [19]. This motion was later named as the Brownian motion. Einstein formalized this phenomena through the following equation

$$r^2 = 6dt,$$  \hspace{1cm} (1.1)

where $r$ is the average displacement of molecules, $d$ is the diffusion coefficient and $t$ is the observation time.

The majority of the human body is made up of water [20]. The diffusion of water molecules in the body is restricted by the presence of structures including nerves and cells [21]. Hence, the measurements of the water diffusion can reveal the micro-structural properties of the underlying tissue. For example, consider the human brain where functional regions (gray matter) are connected by a collection of neural pathways (white matter). Figure 1.1 shows synthetic examples of water diffusion in these regions. In the cerebrospinal fluid (CSF), the water diffusion is fast and isotropic as the microstructural barriers to water mobility are minimal. The brain gray matter has microstructure like the cell walls and membranes that can hinder water mobility. But since they are not organized consistently, the water diffusion is slow but isotropic. In the white matter, the neural pathways consist of bundles of myelinated axons, also known as fiber tracts. The water diffusion here is more obstructed across the tract than along the tract as the cell walls form barriers to water mobility and are consistently organized. This is also shown in figure 1.2. On average, the displacements along the fiber tract are larger than the displacements across it. Hence the water diffusion in these tissues is anisotropic [21].

This diffusion information carried by the water molecules are very useful for the analysis of brain function and structure. For example, by measuring
1.3. Background to Diffusion MRI

Figure 1.1: Synthetic examples of the diffusion seen in the brain. (a) Diffusion in the cerebrospinal fluid, (b) gray matter, and (c) white matter. The diffusion rates for various directions are shown in red. As we see, the diffusion is anisotropic in the white matter, and isotropic in CSF and gray matter, respectively. Image from [1].

Figure 1.2: Water diffusion along fiber tracts. We see that the diffusion along the tract is faster than the diffusion across the tract. Image from [2].

the water diffusion along many directions and observing that it is faster in one direction than in others, we can infer the direction of orientation of the fiber tracts at every location in the brain white matter. Another example is the average diffusion rate, which can give us significant information about the tissue’s integrity [22]. In the next section, we discuss how this diffusion is measured.
1.3. Background to Diffusion MRI

1.3.2 Diffusion Weighted Imaging

To measure diffusion, the Stejskal-Tanner imaging sequence is used [23]. We follow [3] for its description. The imaging sequence is shown in figure 1.3. In this sequence, two strong gradient pulses are applied, one before the 180° refocusing pulse and one after it. Since the spins will start to precess at different frequencies after the first gradient pulse, there will be a phase shift induced for all the spins. The second gradient pulse will invert back this phase shift. Hence for all stationary spins, the net phase shift caused by the two gradient pulses cancel out. But for spins that have moved because of Brownian motion during this time (Δ in the figure 1.3), the phase shift caused by the two gradient pulses will be different and do not cancel. Hence, these spins are not completely refocused and will result in loss of signal. Since this imaging sequence rests upon a $T_2$ weighted sequence (without the gradient pulses, the imaging sequence would result in $T_2$ weighting), the intensity of the resultant signal is basically the $T_2$ weighted signal intensity decreased by an amount related to the diffusion. This resultant signal is then visualized in what are known as diffusion weighted images. These diffusion weighted images can be obtained for various gradient directions $g$.

By using a measurement without diffusion weighting and one with diffusion weighting, Stejskal and Tanner were able to relate the diffusion coefficient to the diffusion weighted image intensities as

$$S = S_0 e^{-bd},$$  \hspace{1cm} (1.2)

where $S$ is the diffusion weighted image intensity, $S_0$ is the standard $T_2$ image intensity, $d$ is the apparent diffusion coefficient (ADC) and $b$ is the diffusion weighting factor [24]. $b$ is in turn dependent on the strength and duration of the gradient pulses as follows

$$b = \gamma^2 \delta^2 \left( \Delta - \frac{\delta}{3} \right) |g|^2,$$  \hspace{1cm} (1.3)

where $\gamma$ is the proton gyromagnetic ratio, $|g|$ is the strength of the diffusion sensitizing gradient pulses, $\delta$ is the duration of the gradient pulses, and $\Delta$...
1.3. Background to Diffusion MRI

90-pulse | \( \mathbf{g} \) | 180-pulse | \( \mathbf{g} \) | Signal

\[ \Delta \]
\[ \delta \]

Figure 1.3: The Stejskal-Tanner imaging sequence. Image from [3].

is the time between the two gradient pulses.

1.3.3 Diffusion Tensor Model

For the derivation of the tensor model, we follow [3, 25]. Let \( \hat{\mathbf{g}} \) denote the unit vector in the direction of the gradient pulse \( \mathbf{g} \). Then, we can write equation (1.2) of the previous section as

\[
S(\hat{\mathbf{g}}) = S_0 e^{-bd(\hat{\mathbf{g}})}. (1.4)
\]

If molecular diffusion is governed by the same Gaussian process everywhere within an image voxel, then the 3D displacement, \( \mathbf{x} \), of a molecule after fixed time \( t \) is drawn from a multivariate Gaussian distribution [26] with density function

\[
p_t(\mathbf{x}) = \frac{1}{\sqrt{(4\pi t)^3 |D|}} \exp \left( -\frac{\mathbf{x}^T \mathbf{D}^{-1} \mathbf{x}}{4t} \right). (1.5)
\]

\( p_t(\mathbf{x}) \) is completely defined by the covariance matrix, \( \mathbf{D} \), which is a 3X3 symmetric tensor called the diffusion tensor. Here, \( \mathbf{D} \) also relates directly to the ADC profile [26, 27] as

\[
d(\mathbf{g}) = \hat{\mathbf{g}}^T \mathbf{D} \hat{\mathbf{g}}. (1.6)
\]

Hence, (1.4) becomes

\[
S(\hat{\mathbf{g}}) = S_0 e^{-b\hat{\mathbf{g}}^T \mathbf{D} \hat{\mathbf{g}}}. (1.7)
\]

Equation (1.7) is a more general case of the Stejskal-Tanner equation.
1.3. Background to Diffusion MRI

\( D \) has 6 independent coefficients. Hence to estimate \( D \), we need at least six measurements (which can be taken using different \( g \)), in addition to \( S_0 \). Figure 1.4 shows an example of such measurements, \( (S_0, S_1, S_2, S_3, S_4, S_5 \text{ and } S_6) \) for different gradient \( g_i \). Inserting each of these measurements into (1.7) we get the following equations

\[
\begin{align*}
\ln(S_1) &= \ln(S_0) - b\hat{g}_1^T D \hat{g}_1, \\
\ln(S_2) &= \ln(S_0) - b\hat{g}_2^T D \hat{g}_2, \\
\ln(S_3) &= \ln(S_0) - b\hat{g}_3^T D \hat{g}_3, \\
\ln(S_4) &= \ln(S_0) - b\hat{g}_4^T D \hat{g}_4, \\
\ln(S_5) &= \ln(S_0) - b\hat{g}_5^T D \hat{g}_5, \\
\ln(S_6) &= \ln(S_0) - b\hat{g}_6^T D \hat{g}_6.
\end{align*}
\]

Upon expanding and rearranging terms, we can bring the above set of equations to the following linear system form

\[
s = Ad,
\]

where \( s \) is a column vector with the \( i^{th} \) element given by \( s_i = \log \left( \frac{S_i}{S_0} \right) \). The \( i^{th} \) row of the matrix \( A \) is given by \( a_i = b[g_{ix}^2, g_{ix}g_{iy}, 2g_{ix}g_{iz}, g_{iy}^2, 2g_{iy}g_{iz}, g_{iz}^2] \), where \( g_{ix}, g_{iy}, \text{ and } g_{iz} \) are the \( x, y, \text{ and } z \) components of \( \hat{g}_i \). \( d \) is a column vector consisting of the six unknown components of \( D \), given by \( d = [D_{xx}, D_{xy}, D_{xz}, D_{yy}, D_{yz}, D_{zz}]^T \). This system of linear equations can be easily solved to obtain the diffusion tensor \( D \). However, because of the noisy nature of the diffusion weighted images, a higher number of gradients (more than six) is usually used to estimate \( D \) from (1.14) using linear regression. This calculation is repeated at every voxel to compute the diffusion tensor field.

1.3.4 Diffusion Tensor Visualization and Properties

The diffusion tensor enables us to measure and visualize various diffusion properties. Let us denote a diffusion tensor by \( D \). We can obtain its eigen-
1.3. Background to Diffusion MRI

Figure 1.4: Examples of diffusion weighted images with corresponding magnetic field gradients. Image from [3].

decomposition

\[
D = \begin{bmatrix}
e_1 & e_2 & e_3
\end{bmatrix}
\begin{bmatrix}
\lambda_1 \\
\lambda_2 \\
\lambda_3
\end{bmatrix}
\begin{bmatrix}
e_1 & e_2 & e_3
\end{bmatrix}^T,
\] (1.15)

where \( \lambda_1 \geq \lambda_2 \geq \lambda_3 \geq 0 \) are the eigenvalues and \( e_1, e_2 \) and \( e_3 \) are the corresponding eigenvectors. \( \lambda_1, \lambda_2 \) and \( \lambda_3 \) encode the rates of diffusion along the three orthogonal axis \( e_1, e_2 \) and \( e_3 \). We can now visualize the diffusion tensor as an ellipsoid as shown in figure 1.5. The eigenvectors of the tensor form the axis of the ellipsoid and the corresponding eigenvalues describe the ellipsoids extent along each axis. This ellipsoid is basically the iso-probability contour of the Gaussian diffusion model described in section 1.3.3. The principal orientation of the ellipsoid is along the direction of maximum diffusion. In the case of a purely isotropic diffusion, the ellipsoid takes on a spherical shape as \( \lambda_1 = \lambda_2 = \lambda_3 \).

From the diffusion tensor, we can compute important diffusion properties such as the mean diffusivity (MD) and the fractional anisotropy (FA) [3, 4]. The MD measures the total diffusion within a voxel and is given by

\[
MD = \frac{\lambda_1 + \lambda_2 + \lambda_3}{3}.
\] (1.16)

The fractional anisotropy is a scalar measure of the degree of diffusion
1.3. Background to Diffusion MRI

Figure 1.5: Ellipsoidal representation of DT. (a) Prolate tensor. (b) Oblate tensor. Image from [4].

Anisotropy within a voxel and is given by

$$FA = \sqrt{\frac{3}{2} \frac{(\lambda_1 - MD)^2 + (\lambda_2 - MD)^2 + (\lambda_3 - MD)^2}{\lambda_1^2 + \lambda_2^2 + \lambda_3^2}}.$$  \hfill (1.17)

In figure 1.6, we see the MD and FA computed on an axial slice of a DT image. From figure 1.6(a), we see that in areas of minimal microstructure such as the ventricles, the MD has a higher value. In regions of high microstructure (white matter), the FA has a higher value as seen in figure 1.6(b). In figure 1.6(c), we see the color coded FA, where the red, green, and blue colors indicate fibers oriented along the right-left, anterior-posterior, and superior-inferior directions, respectively. Though MD and FA are the most widely used, other scalar measures from the tensor have been proposed in [3]. We can also visualize the tensors directly as ellipsoids, as seen in figure 1.7.

1.3.5 Applications

As listed in [5], diffusion MRI data has been correlated with different types of brain pathology. In most of the cases, the pathologies result in increased diffusion due to a loss of cell structure integrity. Some examples include the detection of tumours [28], vascular strokes [22, 29] and developmental abnormalities such as paraventricular leukomalacia [30] and hypoxic-ischemic
1.3. Background to Diffusion MRI

Figure 1.6: Examples of the diffusion tensor properties on an axial slice of the brain. (a) MD, (b) FA and (c) color FA. Image from [5].

Figure 1.7: Example visualization of the tensors as ellipsoids. Image generated using MedINRIA software [6] on data obtained from [7].

encephalopathy [31]. The mean diffusivity and fractional anisotropy measures from the diffusion tensor have been used to characterize the integrity of the brain’s white matter. Diseases such as Multiple Sclerosis and Parkinson’s that cause demyelination of the axons have been correlated with increase in
mean diffusivity and decrease in fractional anisotropy [22]. Developmental delays in infants have also been correlated with increased mean diffusivity and decreased fractional anisotropy [32, 33]. Chronic pain conditions have been correlated with decreased fractional anisotropy in the Cingulum [34]. DTI studies have also shown promise to improve the ability to track diseases such as Alzheimer’s, and Schizophrenia [11, 12]. Further reviews of the use of diffusion MRI in medicine can be found in [22, 29, 35].

1.4 Related Prior Work on Higher Dimensional Data

Recent years have witnessed an unprecedented increase in the dimensionality of the acquired data. Higher dimensional image data, such as vector (e.g. color, multi-spectral) and tensor (e.g. DT-MRI) data, have thus become commonplace. This development, in turn, has increased the computational complexity associated with computing differential operators and feature detectors. To date, only a few attempts have been made to develop differential operators for this kind of image data. In this section, we briefly review a representative set of these approaches.

The most successful approach for formulating first order differentials for vector valued data has been through the use of the first fundamental form [36–38]. In this approach, the change along a particular direction at a pixel in the image is formulated as a quadratic form. By optimizing the quadratic form, first order information such as the gradient vector, is extracted and used for feature detection.

Other approaches for computing first-order differentials on vector-valued image data rely on dimensionality reduction, the result of which allows for differentiation to be performed on scalar images. One such approach has been to compute differentials on each channel separately, then group the results using a p-norm [17, 18, 39, 40]. Alternatively, the authors of [41, 42] use moment-preserving thresholding (MPT) to generate a single-dimensional space onto which color images are projected. In both cases, the dimension-
1.4. Related Prior Work on Higher Dimensional Data

Dimensionality reduction does not preserve the relationship between the underlying differential information and the multi-valued data. Further, the latter projection approach is defined only for color images and not for data of higher dimensionality.

Computing spatial features for tensor image data faces the complex problem of the image differential operators having to respect the data manifold of the $3 \times 3$ positive semi-definite matrices. Most existing differentiation and feature detection approaches for tensor images have largely tried to work around this problem in two simplistic ways. One approach has been to reduce the data dimensionality to a single scalar derived from the tensors ($e.g.$, fractional anisotropy) [43–45]. The other common approach has been to ignore the restriction to the manifold of symmetric second-order tensors and, instead, to treat the data as a multi-valued image [46–48].

In [49], the authors propose to compute image differentials on a continuous tensor field estimated from the discrete DT-MRI data. Here, they represent the first-order differentials as third-order tensors. But the authors don’t show a clear mapping between these tensors and existing feature detectors.

Some progress has been made in the generation of various distance metrics that respect the manifold of symmetric second-order tensors [50–53]. Unfortunately, these metrics only provide gradient magnitude information. Feature detectors requiring further differential information are yet to be extended to manifold-valued fields.

Computing image features using second-order differentials on vector and manifold-valued data has, to date, seen even less success. In [58], spatial differentiation has been separately performed on each image channel with the weighted average of all channel derivatives used for Hessian-based blob detection. Such weighted averaging, however, amounts to dimensionality reduction and results in the same limitations mentioned earlier. In [56], a quaternion representation of color images has been used to compute Hessian-based curvature features. This approach, however, is limited as quaternions cannot represent data of more than four dimensions. In [57], the derivative of the gradient magnitude was computed in the direction orthogonal to the...
1.4. Related Prior Work on Higher Dimensional Data

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Table 1.1: Summary of existing and proposed work in differential-based feature detection for scalar, vector and manifold-valued data. The manifold of symmetric second-order positive definite tensors is represented as SPD(3). Methods listed for \( \mathbb{R}^N \) also apply to \( \mathbb{R}^3 \). Note that our contributions fit in the lower-right of the table.

gradient, but a full second-order differential was not derived.

Table 1.1 summarizes the current state-of-the-art and places our work in the context of related existing work. Our first contribution in this thesis fill in a conspicuous gap in the current methodology, as seen in the lower-right of the table.

Another set of approaches use hypercomplex algebras to process higher dimensional data. In these approaches, the data is processed as a whole in a holistic manner, while handling the coupling between the channels of the data naturally. By far, the most successful among these approaches is the quaternion approach of Sangwine and Ell [59–61]. In this approach, a color vector is represented using a pure quaternion by placing each component of the color vector into the coefficients of a quaternion. As a result of this
1.5. Thesis Organization

representation, the color vector at each pixel can be treated as a single quaternion unit. This enables to introduce conventional image processing tools from quaternion theory such as Fourier transform and convolution to process color images.

In [62], Le Bihan et al. decompose a color image using the quaternion approach. Specifically, they use quaternions to represent the color image and carry out the decomposition of the color image using the quaternion singular valued decomposition. They show applications for color image compression. Other successful applications of the quaternion approach to process vector data are that of Miron and Le Bihan et al. [63–66] for seismic and vector sensor array data processing.

Though the quaternion approaches have been successful for processing vector data, there have been no reported work so far of application of similar approaches to tensor data. As our second contribution in this thesis, we propose such an approach where, we use a biquaternion (complexified quaternion) representation to model DT data holistically, while respecting the manifold of the tensors.

1.5 Thesis Organization

This thesis is organized as follows: in chapter 2, we present novel differential operators and geometric features for DT images using our geometric approach. In chapter 3, we present our algebraic approach, where we introduce a new representation and processing tools for DT images using biquaternions. Preliminary results of applying our approaches on real and synthetic DT data are also presented in those chapters. Finally, we present the conclusions and outline future research directions for our contributions in chapter 4.
Chapter 2

New Differential Operators and Geometric Features for DT Images

2.1 Overview

In this chapter, we derive novel first and second order differential operators for DT data. Unlike existing methods, we are able to generate full first and second-order differentials without dimensionality reduction (incorporating both shape and orientation information) and while respecting the underlying manifold of the data. The key idea is to take the DTs to a vector space via the log-Euclidean (LE) transform and view the resulting LE tensors as a low dimensional manifold embedded in a higher dimensional space. Then we apply mathematical tools traditionally used in the study of Riemannian geometry, for processing DT images. We compute the first fundamental form of the embedded manifold, from which we derive first order (gradient vector, structure tensor) and second order (Hessian matrix) spatial differential operators. Using the differential operators, we further formulate feature detectors to detect geometric features in DT data like corners, tube and sheet like structures, that existing scalar based techniques cannot capture. Results using the feature detectors on DT images show the ability to highlight structure within the image that existing methods cannot.
2.2 Manifold Valued Data Mapping

DTs live on a manifold. Hence an important aspect in the formulation of the differential operators for DTs is to ensure that we respect their manifold. In this thesis, we employ the log-Euclidean transformation proposed in [50] for this purpose. The LE transformation maps the SPD(3) tensors to a vector space, where we define our differential operators. Let \( D(x) : \mathbb{R}^3 \rightarrow \text{SPD}(3) \) denote a 3D DT image indexed by spatial co-ordinates \( x = [x_1, x_2, x_3]^T \) (in general, \( x \) is given by \( x = [x_1, x_2, x_3, \ldots x_d]^T \), where \( d \) is the dimension of the space. The corresponding mapping would become \( D(x) : \mathbb{R}^d \rightarrow \text{SPD}(3) \)). Then, the LE transformation is given by

\[
L(x) = \text{logm}(D(x)),
\]  

(2.1)

where the tensor \( L(x) : \mathbb{R}^3 \rightarrow \mathbb{R}^6 \) spans the vector space of \( 3 \times 3 \) symmetric matrices also known as the log-Euclidean space [50], and \( \text{logm(\cdot)} \) is the matrix logarithm. We now proceed to derive our differential operators.

2.3 Differential Operators

2.3.1 First Order Operators

We begin our exposition by deriving the gradient vector in a DT image following [36–38]. Let \( p \) and \( q \) be two nearby points in \( \mathbb{R}^3 \). Let us consider the difference

\[
\Delta L(x) = L(p) - L(q).
\]

(2.2)

When \( p - q \) is an infinitesimal displacement \( dp = [dx_1, dx_2, dx_3]^T \), (2.2) becomes the total differential given by

\[
dL(x) = \sum_{i=1}^{3} \frac{\partial L(x)}{\partial x_i} dx_i.
\]

(2.3)
2.3. Differential Operators

The squared norm of the total differential \( dL(x) \) is given by

\[
(dL(x))^2 = \sum_{i=1}^{3} \sum_{j=1}^{3} \frac{\partial L(x)}{\partial x_i} \cdot \frac{\partial L(x)}{\partial x_j} \, dx_i dx_j.
\]  

(2.4)

Let us now define the Jacobian matrix \( J(x) \) as

\[
J_{ij} = \frac{\partial L_i}{\partial x_j}.
\]  

(2.5)

\( J(x) \) generalizes the gradient of a scalar field to the derivatives of a vector field. We further define the symmetric positive semi-definite matrix \( S(x) = (J(x))^T J(x) \). \( S(x) \) is referred to as the structure tensor and measures the directional dependence of total change. Now, we can write (2.4) in terms of \( S(x) \) as

\[
(dL(x))^2 = (dp)^T S(x) dp.
\]  

(2.6)

If we consider \( L \) as an embedded map \( L: \Sigma \rightarrow \mathbb{R}^6 \), where \( \Sigma \) is a 3D manifold, then \( (dL(x))^2 \) is basically an infinitesimal arc length on the embedded manifold. This quadratic form is called the first fundamental form. It completely describes the metric properties of the embedded manifold.

Now, for a constant displacement \( ||dp|| \), \( (dL(x))^2 \) indicates how much the DT image varies in the direction of \( dp \). Hence, for a unit vector \( n \),

\[
A(x) = n^T S(x)n
\]  

(2.7)

measures the rate of change of the DT image in the direction \( n \) and is referred to as the squared local contrast [37]. We are interested in finding the direction \( n \) that results in the maximum rate of change of the DT image. It is well known that a quadratic form like (2.7), for varying \( n \), attains a maximum when \( n \) is along the direction of the eigenvector corresponding to the largest eigenvalue of \( S(x) \). As a result, this eigenvector is taken to be the gradient direction \( \hat{g}(x) \). The gradient magnitude \( |g(x)| \) is set to the square root of the corresponding eigenvalue of \( S(x) \). The resulting gradient
vector is thus given by:

\[ g(x) = \sqrt{\lambda_1^S} \hat{e}_1^S, \]  

(2.8)

where \( \hat{e}_1^S \) is the principal eigenvector of \( S(x) \) and \( \lambda_1^S \), the corresponding eigenvalue. Here, we wish to point out that, because of the ambiguity in the sign of the eigenvector, the sign of our gradient vector is also not determined. To resolve the sign ambiguity, in our implementation, we project the gradient vectors of all the scalar log-Euclidean channels along the DT’s positive gradient direction and sum up all the projection contributions. If the sum is positive, then we adopt the positive direction for the gradient vector. If the sum is negative then we negate the gradient vector. Intuitively, the gradients of the scalar channels of the log-Euclidean tensors ‘vote’ for which sign to use.

An averaged version of \( S \) around a local neighborhood, \( \bar{S} \), allows the integration of first order information from the neighborhood and a more stable numerical derivation. We call \( \bar{S} \), the log-Euclidean structure tensor and construct it as:

\[ \bar{S}_{ik}(\sigma_I, x) = \omega_{\sigma_I}(x) \ast \sum_j \frac{\partial L_j}{\partial x_i} \frac{\partial L_j}{\partial x_k}, \]  

(2.9)

where \( \omega_{\sigma_I} \) is a Gaussian window with standard deviation \( \sigma_I \) and \( L_j \) is the \( j^{th} \) component of \( L(x) \). \( \sigma_I \) is also called the integration scale parameter.

After having derived the first order differential operators (2.8, 2.9), we now proceed to derive a second order differential operator for DT images.

### 2.3.2 Second Order Operator

The Hessian matrix is a symmetric matrix consisting of second order partial derivatives. It describes the local second order structure around each pixel in an image. We derive two forms of the Hessian matrix. The first, \( H_1 \), is based on simple weighted averaging of the Hessian matrices of each component of
2.3. Differential Operators

$L(x)$, as done for color images in [58]:

$$H_{1ik} = \sum_j W_j \frac{\partial^2 L_j}{\partial x_i \partial x_k}, \quad (2.10)$$

where $W_j$ is the weight associated with the component $L_j$ and is computed as $W_j = |L_j| / \sum_i |L_i|$. However, this formulation is suboptimal as it does not take into account the vector nature of the multivalued data and is included only for comparison purpose.

Our second formulation is based on the gradient vector we derived earlier in (2.8). Given $g(x) = [g_{x_1} \ g_{x_2} \ g_{x_3}]^T$ has been computed at every location $x$ of the DT image, the gradient vector field $g$ can be considered as a multivalued function with the mapping $g(x): \mathbb{R}^3 \rightarrow \mathbb{R}^3$. Using this context, we compute the derivative of the gradient vector field via the Jacobian matrix, $G(x)$, as

$$G_{ij} = \frac{\partial g_i}{\partial x_j}. \quad (2.11)$$

$G(x)$ encodes second order information of $L(x)$ and, for scalar images, $G(x)$ represents the Hessian matrix. However in multivalued images, $G(x)$ is generally non-symmetric. Our second formulation for the Hessian matrix $H_2$ for multivalued images is thus given by:

$$H_2(x) = \frac{G(x) + (G(x))^T}{2}, \quad (2.12)$$

which is the symmetric part of $G(x)$ and is the best $L^2$ approximation to $G(x)$ from the set of symmetric matrices [67]. Our first order (2.8, 2.9) and second order (2.12) differential operators can easily be extended to different scales, as we show in the next section.

2.3.3 Scale Space Analysis

Structures in images exist at different scales. To detect structural features at different scales, it becomes necessary to adapt a multiscale approach. Hence in this section, we discuss scaling of the DT image and extend the derived
2.3. Differential Operators

differential operators to different scales.

Let \( \omega_{\sigma_s} \) denote a Gaussian window with standard deviation \( \sigma_s \), which we use to scale the DT image. \( \sigma_s \) is also called the local scale parameter. Let \( D(\sigma_s) \) denote the DT image at scale \( \sigma_s \). (We omit the spatial index \( \mathbf{x} \) in this section for clarity.) Scaling of the DT image is carried out in the log-Euclidean space as

\[
D(\sigma_s) = \text{expm} \left( L(\sigma_s) \right),
\]

(2.13)

where \( \text{expm}(\cdot) \) is the matrix exponential function. \( L(\sigma_s) \) is the scaled log-Euclidean tensor obtained by scaling each of its components \( L_i \) as \( L_i(\sigma_s) = \omega_{\sigma_s} * L_i \), where \( * \) is the convolution operator.

Let \( S(\sigma_s) \) denote the structure tensor, \( S \), at scale \( \sigma_s \). The components of \( S(\sigma_s) \) are computed as

\[
S_{ik}(\sigma_s) = \sigma_s^2 \sum_j \frac{\partial L_j(\sigma_s)}{\partial x_i} \frac{\partial L_j(\sigma_s)}{\partial x_k},
\]

(2.14)

where \( \sigma_s^2 \) is the Lindeberg’s \( \gamma \)-normalization \([68]\). The \( \gamma \)-normalization accounts for the decrease in the magnitude of the image spatial derivatives with scale and facilitates unbiased scale selection. In this work, we set \( \gamma \) to 1.

The gradient vector at scale \( \sigma_s \), \( g(\sigma_s) \), is computed from \( S(\sigma_s) \) as before:

\[
g(\sigma_s) = \sqrt{\lambda_1 S(\sigma_s)} \hat{e}_1 S(\sigma_s),
\]

(2.15)

where \( \hat{e}_1 S(\sigma_s) \) is the principal eigenvector of \( S(\sigma_s) \) and \( \lambda_1 S(\sigma_s) \), the corresponding eigenvalue.

The multiscale log-Euclidean structure tensor, \( \bar{S}(\sigma_s, \sigma_I) \), is a function of both the local scale parameter \( \sigma_s \) and the integration scale parameter \( \sigma_I \). Its components are computed as

\[
\bar{S}_{ik}(\sigma_s, \sigma_I) = \sigma_s^2 \left[ \omega_{\sigma_I} * \sum_j \frac{\partial L_j(\sigma_s)}{\partial x_i} \frac{\partial L_j(\sigma_s)}{\partial x_k} \right].
\]

(2.16)
Here, for simplicity, we couple $\sigma_s$ and $\sigma_I$ using a constant $\nu$ as $\sigma_I = \nu \sigma_s$, where $\nu > 1$.

Finally, we compute the multiscale Hessian matrices, $H_1(\sigma_s)$ and $H_2(\sigma_s)$, as

$$H_{1ik}(\sigma_s) = \sigma_s^2 \sum_j W_j \frac{\partial^2 L_j(\sigma_s)}{\partial x_i \partial x_k},$$  

$$H_{2ij}(\sigma_s) = \frac{G_{ij}(\sigma_s) + G^T_{ij}(\sigma_s)}{2},$$

where $W_j = |L_j(\sigma_s)| / \sum_i |L_i(\sigma_s)|$ and $G_{ij}(\sigma_s) = \partial g_i(\sigma_s)/\partial x_j$.

Having extended our differential operators to different scales (2.14, 2.15, 2.16, 2.17, 2.18) in this section, we now proceed to formulate a set of highly useful geometric feature detectors for DT images in the next section.

### 2.4 Geometric Features

Our proposed differential operators fit naturally into existing feature detectors and can thus be effectively used to detect structure in DTI. Here we provide four examples from a potentially long list of feature detectors that can incorporate our differential operators. Using our first order differential in (2.16), we detect corners in DT images using the popular Harris corner detector $C_H$ [8], given by

$$C_H(\sigma_s) = \frac{\det(\bar{S}(\sigma_s))}{\tr(\bar{S}(\sigma_s))} + \epsilon,$$  

and Shi-Tomasi corner detector $C_{ST}$ [55], given by

$$C_{ST}(\sigma_s) = \min(\lambda_1 \bar{S}(\sigma_s), \lambda_2 \bar{S}(\sigma_s), \lambda_3 \bar{S}(\sigma_s)),$$

where $C_H(\sigma_s)$ and $C_{ST}(\sigma_s)$ are the Harris and Shi-Tomasi responses at scale $\sigma_s$, $\det(\bar{S}(\sigma_s))$ is the determinant of $\bar{S}(\sigma_s)$, $\tr(\bar{S}(\sigma_s))$ is the trace of $\bar{S}(\sigma_s)$ and $\lambda_1 \bar{S}(\sigma_s) \geq \lambda_2 \bar{S}(\sigma_s) \geq \lambda_3 \bar{S}(\sigma_s)$ are the eigenvalues of $\bar{S}(\sigma_s)$.

Curvature cues can also be obtained from our Hessian matrix derived in
2.4. Geometric Features

As examples, we extend the vesselness filter of [10] and the sheet-ness filter of [9] to detect tube-like and sheet-like fiber tracts in DTI. Our tubular-ness measure is given by

\[ C_{\text{tube}}(\sigma_s) = \left(1 - \exp\left(-\frac{R_A^2}{2\alpha^2}\right)\right) \left(1 - \exp\left(-\frac{S^2}{2c^2}\right)\right), \]

and our sheet-ness measure is given by

\[ C_{\text{sheet}}(\sigma_s) = \left(\exp\left(-\frac{R_A^2}{2\alpha^2}\right)\right) \left(1 - \exp\left(-\frac{R_B^2}{2\beta^2}\right)\right) \left(1 - \exp\left(-\frac{S^2}{2c^2}\right)\right), \]

where \( C_{\text{tube}}(\sigma_s) \) and \( C_{\text{sheet}}(\sigma_s) \) measure how tubular and sheet-like the structure is at scale \( \sigma_s \), \( R_A, R_B \) and \( S \) are computed from the eigenvalues of the Hessian and are used to penalize sheet-like structures, blob-like structures and noise, respectively. \( R_D \) is used to penalize tube-like and blob-like structures. Let us denote the eigenvalues of the Hessian by \( |\lambda_1^{H(\sigma_s)}| \geq |\lambda_2^{H(\sigma_s)}| \geq |\lambda_3^{H(\sigma_s)}| \). Then \( R_A, R_B, R_C, \) and \( R_D \) are given by

\[ R_A = \frac{|\lambda_2^{H(\sigma_s)}|}{|\lambda_1^{H(\sigma_s)}|}, \]
\[ R_B = \frac{|\lambda_3^{H(\sigma_s)}|}{\sqrt{|\lambda_1^{H(\sigma_s)}| \lambda_2^{H(\sigma_s)}}}, \]
\[ S = \sqrt{\left(\lambda_1^{H(\sigma_s)}\right)^2 + \left(\lambda_2^{H(\sigma_s)}\right)^2 + \left(\lambda_3^{H(\sigma_s)}\right)^2}, \]
\[ R_D = \frac{|(2|\lambda_1^{H(\sigma_s)}| - |\lambda_2^{H(\sigma_s)}| - |\lambda_3^{H(\sigma_s)}|)|}{|\lambda_1^{H(\sigma_s)}|}. \]

The constants \( \alpha, \beta, \eta \) and \( c \) control the sensitivity of \( C_{\text{tube}} \) and \( C_{\text{sheet}} \) to each term.

The response of the above features \( 2.19, 2.20, 2.21, 2.22 \) will be maximum at a scale that approximately matches the size of the structure to be...
detected. We integrate the feature responses at different scales as follows:

\[
F = \max_{\sigma_{s_{\text{min}}} \leq \sigma_s \leq \sigma_{s_{\text{max}}}} F(\sigma_s),
\]

where \(F\) is the feature response after scale selection, \(\sigma_{s_{\text{min}}}\) and \(\sigma_{s_{\text{max}}}\) are the minimum and maximum scales over which structures are expected to be found, and \(F(\sigma_s)\) is the feature response at scale \(\sigma_s\).

### 2.5 Results and Discussion

We present results of the proposed differential operators and feature detectors on synthetic and real DT data. The real DT data consisted of 24 images of normal adult brains, of which, 12 were taken from the John Hopkins LBAM [69] database and 12 from the MIDAS database [7]. The DT volumes were 128x128x63 voxels with a resolution of 2\text{mm}^3. In our experiments, the constants \(\alpha\), \(\beta\) and \(\eta\) were set to 0.5 (as suggested in [9, 10]) and \(c\) was set to 0.1. The coupling constant \(\nu\) was set to 1.1. A scale range of \(\sigma_{s_{\text{min}}} = 0.7\) to \(\sigma_{s_{\text{max}}} = 2.2\) was found to be adequate for the structures we detected in this work.

Figure 2.1 shows the proposed Harris and Shi-Tomasi corner detector results on synthetic data. The conventional scalar Harris and Shi-Tomasi features obtained from the fractional anisotropy (FA) maps are also shown for comparison. Figure 2.1(a) shows a noisy image where the tensors are pointing horizontally in the foreground (colored in red) while tensors point vertically in the background (colored in blue). Figure 2.1(b) shows an example of two fibers crossing each other. The ground truth corner points are shown in yellow. Varying levels of noise were added to these images using the method in [70]. We show in Figure 2.1(c) the drop rate of the feature response as a function of distance to the nearest ground truth corner point in the examples in Figures 2.1(a) and 2.1(b). Our results demonstrate how the response of the proposed Harris detector falls very quickly for all levels of noise when compared to the response of the scalar Harris detector on FA as we move away from the ground truth corners. We also observed consistent
2.5. Results and Discussion

Figure 2.1: Results of the proposed Harris and Shi-Tomasi corner detectors on synthetic data. (a) and (b): two synthetic slices with the ground truth corner locations shown in yellow. (c): the drop rate of the Harris feature response as a function of distance from the ground truth corners for different levels of noise (standard deviation of noise ranging from 0.01 to 0.04). Results are shown for both our method and the approach in [8] on the FA maps. Note the response of our method falls rapidly for all levels of noise, demonstrating localization accuracy.
stronger response to corners for our proposed Harris detector compared to the approach based on the FA maps. A similar behavior was also observed for the Shi-Tomasi detector. This rapid decrease in response for our method indicates its greater ability to localize the corner points under various noise conditions.

Figure 2.2 shows results of tubular-ness filter on synthetic data. The tubular-ness obtained from the corresponding FA map using the scalar version of the filter in [10] is included for comparison. Figure 2.2(a) shows a bent fiber tract and figure 2.2(c) shows linear fiber tracts oriented along different angles. Figures 2.2(b) and 2.2(d) show the corresponding tubular-ness results. We observe that tubular-ness using $H_2$ gives the highest response in both cases. In figure 2.2(e), we add noise to these images and, as before, we measure the rate of decrease of the filter’s response as a function of distance to the ground truth medial of the tube. We observe that tubular-ness using $H_2$ falls more rapidly when compared to the other filters, even when the noise is high. Again, this result illustrates our method’s greater localization ability.

To quantify the information captured by the differential operators, we compute various norms of our structure tensor, gradient vector and Hessian matrices for twelve adult brain DTI from the LBAM database. Histograms of these norms are shown in Figures 2.3 and 2.4 for the proposed methods as well as those obtained from the FA map. Note that the norms of our structure tensor and gradient vector are spread over larger values than the norms computed from the FA maps. This result stems directly from avoiding the dimensionality reduction of the tensor data to FA values and indicates that we are capturing a greater amount of first order differential information. Also note that $H_2$ captures a greater amount of second order differential information than the other two Hessian approaches as $H_2$ works with the whole tensor and not its individual channels or FA.

We applied our corner and tube detectors to 24 real adult brain DTI. Figures 2.5, 2.6 and 2.7 show representative results for the corner detectors for both our method and the conventional scalar Harris [8] and Shi-Tomasi [55] features obtained from the FA maps. First, we observe that in each case,
2.5. Results and Discussion

Figure 2.2: Tubular-ness results for synthetic 2D slices. Figures (a) and (c) show a bent fiber tract and linear fiber tracts oriented in different angles, respectively. Figures (b) and (d) show the corresponding tubular-ness responses obtained using Hessian from FA (top), $H_1$ (middle) and $H_2$ (bottom). Note that tubular-ness obtained using $H_2$ gives the strongest response in both cases. Figure (e) shows the drop rate of the filter’s response as a function of distance to the ground truth medial of the tube for different levels of noise (standard deviation of noise ranging from 0.01 to 0.04). Note that even when noise is high, tubular-ness using $H_2$ decreases more rapidly than tubular-ness using $H_1$ or FA, indicating greater localization ability.

The feature response of our approach is stronger than the feature response from the FA-based approach by three orders of magnitude. Secondly our approach generates a more distinctive response to the corners of both the Genu and the Splenium of the Corpus Callosum than the FA-based detectors. These results were consistently observed throughout the datasets.

Finally, figures 2.8, 2.9, 2.10 and 2.11 show representative tubular-ness and sheet-ness results. Figures 2.8 and 2.9 show the tubular-ness results
2.5. Results and Discussion

Figure 2.3: Histograms of the norms of the structure tensor and the gradient vector (abbreviated in the figure as ST and g, respectively) for twelve adult brain DT images from the LBAM database. Shown are the results for the proposed methods and FA-based methods. (a) logarithm of the Frobenius norm of the structure tensor. (b) logarithm of the row sum norm of the structure tensor. (c) logarithm of the $L^2$-norm of the gradient vector. Note that the norms of our proposed structure tensor and gradient are spread over larger values compared to FA-based approaches, demonstrating that we are capturing more first order differential information.

for two tubular tracts, the Cingulum and the Fornix. Note that the tubular tracts are well detected using $H_2$ and barely detected using $H_1$ and Hessian from FA. Figures 2.10 and 2.11 show the sheet-ness results for 3 sheet like tracts, the Inferior Longitudinal Fasciculus, the Corpus Callosum, and the Corticospinal tract. Note that the sheet like tracts are also better detected using $H_2$ compared to $H_1$ and FA-based features. The FA-based features fail to detect structures in most cases. These results were consistently observed throughout the datasets.
2.5. Results and Discussion

Figure 2.4: Histograms of various norms of the Hessian matrix (abbreviated in the figure as H) for twelve adult brain DT images from the LBAM database. Shown are the results for the proposed methods and FA-based methods. (a) logarithm of the Frobenius norm of the Hessian matrix. (b) logarithm of the row sum norm of the Hessian matrix. (c) logarithm of the max norm of the Hessian matrix. Note that the norms of our proposed Hessian is spread over larger values compared to FA-based approaches, demonstrating that we are capturing more differential information.
2.5. Results and Discussion

Figure 2.5: First set of representative result for the Harris and Shi-Tomasi corner detectors on an adult brain DT image. Shown are (a) the color FA map, (b) Harris features from the FA map, (c) Harris features using our method, (d) Shi-Tomasi features from the FA map, and (e) Shi-Tomasi features using our method. Note that since the responses of the FA-based detectors are extremely weak when compared to the responses of our proposed detectors, they are shown with different intensity scales. Also note the clearer response to the corners of the Genu and Splenium using our method.
2.5. Results and Discussion

Figure 2.6: Second set of representative results for the Harris and Shi-Tomasi corner detectors. Shown are (a) the color FA map, (b) Harris features from the FA map, (c) Harris features using our method, (d) Shi-Tomasi features from the FA map, and (e) Shi-Tomasi features using our method. Note that since the responses of the FA-based detectors are extremely weak when compared to the responses of our proposed detectors, they are shown with different intensity scales. Also note the clearer response to the corners of the Genu and Splenium using our method.
2.5. Results and Discussion

Figure 2.7: Third set of representative results for the Harris and Shi-Tomasi corner detectors. Shown are (a) the color FA map, (b) Harris features from the FA map, (c) Harris features using our method, (d) Shi-Tomasi features from the FA map, and (e) Shi-Tomasi features using our method. Note that since the responses of the FA-based detectors are extremely weak when compared to the responses of our proposed detectors, they are shown with different intensity scales. Also note the clearer response to the corners of the Genu and Splenium using our method.
2.5. Results and Discussion

Figure 2.8: First set of representative results for the tubular-ness on adult brain DTI data. Shown from top to bottom are: color FA image, results obtained using Hessian (abbreviated as $H$) from FA [9, 10], results obtained using $H_1$ and results obtained using $H_2$. Note the identified tubular tracts (Cingulum and Fornix) are better detected using $H_2$ than with $H_1$ and FA based method.
2.5. Results and Discussion

Figure 2.9: Second set of representative results for the tubular-ness on adult brain DTI data. Shown from top to bottom are: color FA image, results obtained using Hessian (abbreviated as $H$) from FA [9,10], results obtained using $H_1$ and results obtained using $H_2$. Note the identified tubular tracts (Cingulum and Fornix) are better detected using $H_2$ than with $H_1$ and FA based method.
2.5. Results and Discussion

Figure 2.10: First set of representative results for the sheet-ness on adult brain DTI data. Shown from top to bottom are: color FA image, results obtained using Hessian (abbreviated as $H$) from FA [9, 10], results obtained using $H_1$ and results obtained using $H_2$. Note the identified sheet-like tracts (Inferior Longitudinal Fasciculus, Corpus Callosum, and Corticospinal tract) are better detected using $H_2$ than with $H_1$ and FA based method.
2.5. Results and Discussion

Figure 2.11: Second set of representative results for the sheet-ness on adult brain DTI data. Shown from top to bottom are: color FA image, results obtained using Hessian (abbreviated as $H$) from FA [9,10], results obtained using $H_1$ and results obtained using $H_2$. Note the identified sheet-like tracts (Inferior Longitudinal Fasciculus, Corpus Callosum, and Corticospinal tract) are better detected using $H_2$ than with $H_1$ and FA based method.
Chapter 3

Novel Holistic DT Image Representation and Processing Using Biquaternions

3.1 Overview

In this chapter, we introduce a novel biquaternion formalism to represent DT-MRI data. Unlike methods that use dimensionality reduction, we are able to process the full DT in a holistic manner while respecting the underlying manifold of the data. Our approach is inspired from the quaternion approach for color image processing, which has been proven useful \cite{56,60}. The basic idea is to represent the DT at each pixel by a biquaternion via the log-Euclidean transform \cite{50}. The key innovation here is that we can now consider the DT as a whole in a holistic manner rather than as separate scalar channels or as a single scalar derived from the tensors. With this representation, we handle the coupling between the channels naturally while respecting the manifold of the symmetric second order tensors. Further, this approach enables us, for the first time, to introduce tools from biquaternion theory such as Fourier transform and convolution, which can be applied directly on the full tensor. We also present a biquaternion gradient vector and edge detector for DT images that further demonstrate the applicability of this novel representation. Our approach opens new ways for carrying out DT image processing tasks including frequency filtering, convolution,
3.2 Brief Review of Biquaternions

3.2.1 Basic Properties

In this section, we start by reviewing biquaternions and some of their basic properties. The interested reader is referred to [71] for a more comprehensive discussion.

1. Let us denote the set of complex numbers by \( \mathbb{C} \), the set of quaternions by \( \mathbb{H} \), and the set of biquaternions by \( \mathbb{H}_c \). Let the elements of \( \mathbb{C} \) be represented as \( z = \Re(z) + I\Im(z) \), where \( I = \sqrt{-1} \) is the complex imaginary unit and \( \Re(z), \Im(z) \in \mathbb{R} \). Quaternions are 4-D algebra that extend complex numbers and can be represented as \( h = h_0 + h_1i + h_2j + h_3k \), where \( h \in \mathbb{H}, h_0, h_1, h_2, h_3 \in \mathbb{R} \), and \( i, j, k \) are the quaternion imaginary units. We have the following set of standard relations between \( i, j, k \):

\[
\begin{align*}
    i^2 = j^2 = k^2 &= ijk = -1 \\
    ij &= -ji = k \\
    ki &= -ik = j \\
    jk &= -kj = i.
\end{align*}
\]  

From (3.1) we can see that quaternion multiplication is non-commutative. We can also observe that quaternions form a 4-D vector space with the basis \( \{1, i, j, k\} \) over \( \mathbb{R} \). Biquaternions are an 8-D algebra consisting
of quaternions with complex components and can be represented as

\[ q = a + bi + cj + dk, \]  

(3.2)

where \( q \in \mathbb{H}_c \), \( a, b, c, d \in \mathbb{C} \), and \( i, j, k \) are the quaternion imaginary units that satisfy 3.1. Hence, just like quaternions, biquaternion multiplication is also non-commutative. Further, we have the following relations between \( i, j, k \) and \( I \):

\[ iI = Ii; jI = Ij; kI = Ik. \]  

(3.3)

This basically means that any complex co-efficient commutes with any quaternion imaginary unit. Thus biquaternions form an 8-D vector space with the basis \( \{1, i, j, k, I, iI, jI, kI\} \) over \( \mathbb{R} \).

2. Any biquaternion can be seen as the sum of a scalar and a vector part as

\[ q = S(q) + V(q), \]  

(3.4)

where \( S(q) = a \) and \( V(q) = bi + cj + dk \). A biquaternion with zero scalar part \( (S(q) = 0) \) is called a pure biquaternion. Another way to look at a biquaternion is to consider it as the sum of a real and an imaginary part, which are themselves quaternion valued:

\[ q = \Re(q) + I\Im(q), \]  

(3.5)

where \( \Re(q), \Im(q) \in \mathbb{H} \) are given by

\[ \begin{align*} 
\Re(q) &= \Re(a) + \Re(b)i + \Re(c)j + \Re(d)k \\
\Im(q) &= \Im(a) + \Im(b)i + \Im(c)j + \Im(d)k. 
\end{align*} \]  

(3.6)

3. We can define 3 different conjugations for biquaternions. The quaternion conjugate of a biquaternion is given by

\[ q^* = a - bi - cj - dk, \]  

(3.7)
3.2 Brief Review of Biquaternions

and the complex conjugate of a biquaternion is given by

\[ q^* = a^* + b^*i + c^*j + d^*k, \]  \hspace{1cm} (3.8)

where \( a^*, b^*, c^*, \) and \( d^* \) are the complex conjugates of \( a, b, c, \) and \( d, \) respectively. We can define the total conjugate of a biquaternion by combining the quaternion and complex conjugates as

\[ \bar{q} = (q^*)^* = a^* - b^*i - c^*j - d^*k. \]  \hspace{1cm} (3.9)

4. Lastly, the norm of a biquaternion \( q \) is given by

\[ |q| = \sqrt{S(q\bar{q})} = \sqrt{|a|^2 + |b|^2 + |c|^2 + |d|^2}, \]  \hspace{1cm} (3.10)

where \( S(\cdot) \) is the scalar part. The norm of a biquaternion vector \( q \in \mathbb{H}^N_c \) (a vector whose components are biquaternions) is given by

\[ ||q|| = \sqrt{S(\sum_{n=1}^{N} q_nq_n^*)}, \]  \hspace{1cm} (3.11)

where \( q_n \) is the \( n^{th} \) component of \( q. \) It is to be noted that biquaternions do not form a normed division algebra and hence the norm of a biquaternion is not multiplicative. i.e. \( |qr| \neq |q||r|. \)

3.2.2 Biquaternion Roots of -1

To define the biquaternion based Fourier transform for DTs, we need to first define the biquaternion roots of -1, which in turn are needed to define the biquaternion exponential kernel of the transform. A biquaternion root of -1, \( \mu, \) satisfies

\[ \mu^2 = -1, \]  \hspace{1cm} (3.12)

where \( \mu \in \mathbb{H}_c. \) Let \( \mu = \Re(\mu) + I\Im(\mu). \) We can see that \( \mu = \pm I, \pm i, \pm j, \pm k \) are all trivial solutions of (3.12). Apart from these, it has been shown in [72] that the roots of the above equation are pure biquaternions that satisfy the
3.2. Brief Review of Biquaternions

following properties:

\[ |\Im(\mu)|^2 - |\Re(\mu)|^2 = -1; \quad (\Re(\mu)|\Im(\mu)) = 0, \]  

(3.13)

where \( \Re(\mu), \Im(\mu) \) are pure quaternions\(^2\), and \( (\cdot|\cdot) \) is their scalar product\(^3\). It also can be easily shown that all pure biquaternions that have a unit norm are solutions of (3.12), and satisfy the above set of properties in (3.13).

3.2.3 Biquaternion Exponential

We now define a biquaternion exponential, which is the kernel of the Fourier transform, as follows:

\[ e^q = \sum_{n \in \mathbb{N}} \frac{q^n}{n!}, \]  

(3.14)

where \( q \in \mathbb{H}_c \).

If \( q \) is a pure biquaternion (i.e. \( q = bi + cj + dk \), where \( b, c, \) and \( d \in \mathbb{C} \)), then we can define

\[ \hat{q} = \frac{bi + cj + dk}{\sqrt{b^2 + c^2 + d^2}}, \]  

(3.15)

where \( \hat{q} \) has unit norm and hence is a root of -1. Let us denote \( \sqrt{(b^2 + c^2 + d^2)} \) by \( \langle q \rangle \in \mathbb{C} \). Now let us expand \( e^q \) as

\[ e^q = e^{\langle q \rangle \hat{q}} = 1 + \frac{(\langle q \rangle \hat{q})}{1} + \frac{(\langle q \rangle \hat{q})^2}{2!} + \frac{(\langle q \rangle \hat{q})^3}{3!} + \frac{(\langle q \rangle \hat{q})^4}{4!} + \frac{(\langle q \rangle \hat{q})^5}{5!} + \frac{(\langle q \rangle \hat{q})^6}{6!} + \ldots \]  

(3.16)

Replacing \( (\hat{q})^2 \) by -1 and rearranging the terms, we get

\[ e^q = 1 + \frac{(\langle q \rangle \hat{q})}{1} + \frac{-(\langle q \rangle \hat{q})^2}{2!} + \frac{-(\langle q \rangle \hat{q})^3 \hat{q}}{3!} + \frac{(\langle q \rangle \hat{q})^4}{4!} + \frac{(\langle q \rangle \hat{q})^5 \hat{q}}{5!} + \frac{-(\langle q \rangle \hat{q})^6}{6!} + \ldots \]

\[ = \left( 1 - \frac{(\langle q \rangle)^2}{2!} + \frac{(\langle q \rangle)^4}{4!} - \frac{(\langle q \rangle)^6}{6!} + \ldots \right) + \hat{q} \left( \frac{(\langle q \rangle)^3}{3!} - \frac{(\langle q \rangle)^5}{5!} + \ldots \right) \]

\[ = \cos\langle q \rangle + \hat{q} \sin\langle q \rangle. \]  

(3.17)

\(^2\)A quaternion \( q = a + bi + cj + dk \), where \( a, b, c, d \in \mathbb{R} \) is called pure if \( a = 0 \).

\(^3\)The scalar product of two pure quaternions \( q = q_1i + q_2j + q_3k \) and \( p = p_1i + p_2j + p_3k \) is given by \( (q|p) = q_1p_1 + q_2p_2 + q_3p_3 \).
Hence, we can see that Euler’s formula generalizes to biquaternions in a straightforward way. After having discussed some properties of biquaternions, we now proceed to present the biquaternion representation for DT.

3.3 Biquaternion Representation for DT

As we have already seen in section 2.2, DTs do not form a vector space. Hence before we proceed to represent a DT by a biquaternion, we need to ensure that we respect the manifold of the DTs. For this, we again employ the log-Euclidean (LE) transformation \([50]\) to map the space of DTs into a vector space. Let us consider a 2D DT image \(D(x) : \mathbb{R}^2 \rightarrow \text{SPD}(3)\) indexed by spatial co-ordinates \(x = [x_1, x_2]^T\) (in general, \(x\) is given by \(x = [x_1, x_2, x_3, \ldots x_d]^T\), where \(d\) is the dimension of the space). The LE transformation gives us the LE tensor \(L(x) = \logm(D(x))\), which spans the vector space of \(3 \times 3\) symmetric matrices known as the LE space. Let the components of the LE tensor be denoted by \((L_0, L_1, L_2, L_3, L_4, L_5)\). The LE tensor is represented by a pure biquaternion (whose scalar part is zero) in the following way:

\[
q(x) = (L_0 + IL_1)i + (L_2 + IL_3)j + (L_4 + IL_5)k. \tag{3.18}
\]

The result of this representation is that we have now moved from the space of symmetric second order positive definite tensors to the vector space of pure biquaternions, while respecting the manifold of the tensors\(^4\). After having presented the biquaternion representation for DTs in this section, we now proceed to introduce novel tools for processing DT images in the next section.

\(^4\)Even though there are multiple ways to encode the components of \(L\) into \(q\), any one choice will result in a specific representation that can be uniquely decoded back to the LE space and the advantages/analyses that we present next still hold regardless of the choice made.
3.4 Fourier Transform, Convolution, Gradient and Edge Detector for DTs

In this section, we define four important tools for processing DT images, based on the biquaternion representation we presented in the previous section.

3.4.1 Fourier Transform for DTs

We introduce the Fourier transform for DTs based on the biquaternion Fourier transform [73]. Since biquaternion multiplication is non-commutative, we can define left and right Fourier transforms, depending on the side by which the exponential kernel is multiplied\(^5\). The left 2D DT Fourier transform and its inverse are given by:

\[
Q_L(f_1, f_2) = \frac{1}{\sqrt{MN}} \sum_{x_1=0}^{M-1} \sum_{x_2=0}^{N-1} e^{-\mu 2\pi \left( \frac{x_1 f_1}{M} + \frac{x_2 f_2}{N} \right)} q(x_1, x_2),
\]

\[
q(x_1, x_2) = \frac{1}{\sqrt{MN}} \sum_{f_1=0}^{M-1} \sum_{f_2=0}^{N-1} e^{\mu 2\pi \left( \frac{x_1 f_1}{M} + \frac{x_2 f_2}{N} \right)} Q_L(f_1, f_2),
\]

where \(q\) is the biquaternion representation of the DT image, \(f_1\) and \(f_2\) are the frequency variables, \(M\) and \(N\) are the number of pixels along \(x_1\) and \(x_2\), and \(\mu\) is a biquaternion root of -1, also called the axis of the transform. The magnitude spectrum of the Fourier transform is computed by taking the norm of \(Q_L\) using \((3.10)\). We note here that the Fourier transform depends on the choice of the transform axis \(\mu\). We can define a valid Fourier transform using every \(\mu\) which is a biquaternion root of -1.

\(^5\)Here, we only consider transforms that have a single exponential kernel on the left or the right of the signal. It is indeed possible to define a two sided Fourier transform with exponentials on both sides of the signal, whose analysis is outside the scope of this thesis.
3.4.2 Convolution for DTs

Convolution of two 2D DT images is given by

\[
(q_1 * q_2)(x_1, x_2) = \sum_{x_m=0}^{M-1} \sum_{x_n=0}^{N-1} q_1(x_m, x_n) q_2(x_1 - x_m, x_2 - x_n),
\]

(3.20)

where \(q_1\) and \(q_2\) are the biquaternion representations of the DT images.

3.4.3 Gradient Vector and Edge Detector for DTs

Finally, we introduce the biquaternion based gradient vector for 2D DT images, which is a first order differential operator, as follows:

\[
g(x_1, x_2) = \left[ \frac{\partial q(x_1, x_2)}{\partial x_1} \frac{\partial q(x_1, x_2)}{\partial x_2} \right]^T,
\]

(3.21)

where \(q\) is the biquaternion representation of the DT image and \(g\) is the biquaternion gradient vector. The differential of a biquaternion function \(q(x) = a(x) + b(x)i + c(x)j + d(x)k\) with respect to a scalar \(x\) can be computed as

\[
\frac{\partial q(x)}{\partial x} = \frac{\partial a(x)}{\partial x} + \frac{\partial b(x)}{\partial x} i + \frac{\partial c(x)}{\partial x} j + \frac{\partial d(x)}{\partial x} k,
\]

(3.22)

where \(q(x) \in \mathbb{H}_c\) and \(a(x), b(x), c(x),\) and \(d(x) \in \mathbb{C}\).

Using the biquaternion gradient vector, we further define an edge measure for 2D DT images as the norm of the gradient vector as follows:

\[
e(x_1, x_2) = ||g(x_1, x_2)||,
\]

(3.23)

where \(e\) is the edge measure. Equations (3.19 - 3.23) can be easily extended to 3D.

3.5 Results and Discussion

We present some preliminary results of the proposed biquaternion based DT image processing approach on synthetic and real DT data. The real
3.5. Results and Discussion

DT data consisted of 12 images of normal adult brains taken from the John Hopkins LBAM database [69]. The DT volumes were 128x128x63 voxels with a resolution of 2mm³. The Fourier transform axis was set to \( \mu = i + (1 + I)j + (1 - I)k \). This selection of the axis was motivated by the fact that \( \mu = i + (1 + I)j + (1 - I)k = i + j + k + I(j - k) \) doesn’t favour any of \( i, j \) or \( k \), at least in the real part. The quaternion toolbox [74] was used for the MATLAB implementations of the Fourier transform and convolution.

Figure 3.1 shows the magnitude spectra of synthetic images, where tensors are varying along the horizontal, the vertical, and the diagonal. Figures 3.1(a) and 3.1(b) show a vertical and a horizontal edge, formed by tensors varying in shape along the horizontal and the vertical, respectively. Figures 3.1(d) and 3.1(e) show a vertical and a horizontal edge, formed by tensors varying in orientation along the horizontal and the vertical, respectively. Figures 3.1(c) and 3.1(f) show tensors varying along the diagonal. As we can see, the variation is accurately reflected in their corresponding magnitude spectra, as expected.

Figure 3.2 shows more synthetic examples of tensors and their magnitude spectra. Figures 3.2(a) and 3.2(b) show DTs varying at low and high frequencies along the horizontal. We see that their magnitude spectra have high response in the expected low frequency and high frequency regions, respectively. Figure 3.2(c) shows a synthetic square image, where DTs are oriented horizontally inside the square in the centre and vertically elsewhere. As expected, the magnitude spectrum is a sinc function. These results confirm the basic working of the Fourier transform on DTs.

Figure 3.3 shows frequency filtering, convolution and edge detection on the synthetic square image in figure 3.3(a). Figure 3.3(b) shows the all-stop filtered image which has isotropic tensors everywhere\(^6\). Figure 3.3(c) shows the low-pass filtered image, where the edges are blurred. Figure 3.3(d) shows the high-pass filtered image, where the tensors are anisotropic along the edges and isotropic elsewhere. Figure 3.3(e) shows the biquaternion norms of the image convolved with itself (auto-convolution, or auto-correlation given that the image is symmetric), where we see a high response in the

\(^6\)Zero biquaternion decodes to a unit isotropic tensor in the DT domain.
3.5. Results and Discussion

centre as expected. Figure 3.3(f) shows the proposed edge computed using (3.23). Figures 3.3(g) and 3.3(h) show a noisy and the corresponding denoised image after low pass filtering, respectively. These figures illustrate sample applications of the proposed tools and show that they work as expected.

Figure 3.4 shows compression of a DT image slice of a cross section of the Corpus Callosum (CC) obtained by truncating a fraction of the low energy Fourier coefficients. Note that even when 60% of the low energy Fourier coefficients are truncated, the energy lost is minimal and the shape and orientation characteristics of the DTs are largely retained.

Figure 3.5 illustrates the rotation property of the Fourier transform on a sagittal slice of the CC. Figure 3.5(b) is a 90°-rotated version of figure 3.5(a). The corresponding frequency spectrum is also rotated by 90°, as seen in figures 3.5(c) and 3.5(d).

Figure 3.6 illustrates the application of the proposed edge detector on real DT data. Figures 3.6(a) and 3.6(b) show edge detection on a sagittal slice of the CC using the proposed biquaternion gradient and the FA based gradient, respectively. Figures 3.6(c) and 3.6(d) show a similar set of results on an axial slice of the lower part of the Corticospinal tract. In both cases, we clearly see that the biquaternion based edge captures more structure and has higher contrast than the FA based edge, demonstrating that the biquaternion gradient captures greater amount of information than the FA gradient.

Finally, figure 3.7 shows frequency domain filtering on real DT data. Figures 3.7(a), 3.7(c) and 3.7(e) show filtering on a slice containing the lateral ventricle. Figures 3.7(b), 3.7(d) and 3.7(f) show filtering on a slice containing the Genu. In both cases, we clearly see more regularized tensors after low pass filtering and highlighted edges after high pass filtering, respectively. These results show great potential for frequency domain processing of DT images.
3.5. Results and Discussion

Figure 3.1: Synthetic examples of tensors varying along different directions and their magnitude spectra. In each of the figures from (a-f), the top row is the synthetic tensor image and the bottom row is the corresponding magnitude spectrum. (a) and (b): vertical and horizontal edge formed by DTs varying in shape along the horizontal and vertical, respectively. (d) and (e): vertical and horizontal edge formed by DTs varying in orientation along the horizontal and vertical, respectively. (c) and (f): DTs varying along the diagonal.
3.5. Results and Discussion

Figure 3.2: More synthetic examples of tensors and their magnitude spectra. In each of the figures from (a-c), the top row is the synthetic tensor image and the bottom row is the corresponding magnitude spectrum. (a) and (b): DTs varying in shape along the horizontal at low and high frequencies, respectively. (c): a synthetic square image where DTs are oriented horizontally inside the square in the centre and vertically elsewhere.
3.5. Results and Discussion

Figure 3.3: Frequency filtering, convolution and edge detection on a synthetic square image (a). (b), (c) and (d) show the all-stop, low-pass and high-pass frequency filtered images, respectively. (e) shows the norms of the biquaternions after convolving the image with itself. (f) shows the edge strength computed using (3.23). (g) shows a noisy image of tensors oriented along the vertical and (h) shows the image after denoising.
3.5. Results and Discussion

Figure 3.4: DT image compression using Fourier transform. (a), (b) and (c) show reconstructed coronal slices of a cross section of the CC after a fraction of the low energy Fourier coefficients are truncated. (d) shows a plot of the energy lost for different levels of truncation. The energy lost is computed as the sum of squared magnitudes of the truncated coefficients.
3.5. Results and Discussion

Figure 3.5: Rotation property of the Fourier transform. (a) and (b) show a sagittal slice of the CC and its 90°-rotated version, respectively. (c) and (d) show their corresponding magnitude spectrum. Note that (d) is a 90°-rotated version of (c).
3.5. Results and Discussion

Figure 3.6: Edge detection using the biquaternion approach. (a) and (b) show biquaternion gradient based edge and FA gradient based edge on a sagittal slice of the CC, respectively. (c) and (d) show biquaternion gradient based edge and FA gradient based edge on an axial slice of the lower part of the Corticospinal tract, respectively. Note the higher contrast and structure captured by the biquaternion gradient based edge in both cases.
3.5. Results and Discussion

Figure 3.7: Frequency filtering on real data. (a), (c) and (e) show the left ventricle, corresponding low pass and high pass filtered images, respectively. (b), (d) and (f) show the Genu, corresponding low pass and high pass filtered images, respectively. Note that the edges are blurred after low pass filtering and highlighted after high pass filtering.
Chapter 4

Conclusions and Future Work

In this thesis, we presented novel geometric and algebraic approaches to develop low-level computer vision techniques for manifold valued DT-MRI data.

In our geometric approach, we represented DT data as low dimensional manifold embedded in higher dimensional space and then applied mathematical tools from Riemannian geometry for formulating first order and second order differential operators for DT images. Unlike existing state-of-the-art, our operators respect the manifold of symmetric second-order tensors through the use of the log-Euclidean mapping. We further showed how our differential operators can be naturally incorporated into various feature detectors in order to find structure in diffusion tensor images that, to date, has not been possible. We extend the Harris and Shi-Tomasi corner detectors to DTI and show that our approach better distinguishes corners in DT data and has better localization ability. We also extend the vesselness filter of [10] and the sheetness filter of [9] to detect tube-like and sheet-like structures. We show that our methods better detect these tube-like and sheet-like structures in DT data and have better localization ability than existing methods. We believe that our derived low-level operators and image features are very versatile and will be of great advantage to classification, registration, and segmentation of DT data.

In our algebraic approach, we proposed a biquaternion formalism to model DT-MRI data. This approach enables us to process DT images in a holistic manner. We introduced traditional signal processing methodologies
4.1 Thesis Contributions

from biquaternion theory such as the Fourier transform, convolution and edge detection for DT images. Our approach opens new ways for carrying out DT image processing tasks including frequency filtering, convolution, compression, and interpolation. We presented preliminary results of applying the Fourier transform for frequency filtering and compression, which were encouraging. Finally, we showed how our representation enables DT-MRI edge detection with favorable results over FA-derived edges. Our results demonstrate the great potential of our approach for DT image processing.

4.1 Thesis Contributions

- Derivation of first-order differentials for DT images: We derived first order differential operators, the gradient vector (2.8) and the structure tensor (2.9), for DT images. Both the differential magnitude and the direction were computed using the first fundamental form, while respecting the manifold of the data. They were further extended to different scales in (2.14), (2.15), and (2.16).

- Derivation of second-order differentials for DT images: We derived a second order differential operator, the Hessian matrix (2.12), for DT images. The Hessian was computed through an optimal projection of the derivative of the first-order differential information, thereby generating the best possible second-order differential. The multiscale version was presented in (2.18).

- Construction of corner and curvature feature detectors for DT images. Using our first order differential operators, we extended the scalar Harris [75] and Shi-Tomasi [55] corner detectors to DT images (2.19, 2.20). Using our second order differential operator, we extended the curvature features of Frangi et al. [10] and Descoteaux et al. [9] to DT images (2.21, 2.22), to detect tube-like and sheet-like fiber tracts, respectively.

- Holistic representation for DT images using biquaternions: We pre-
4.2. Future Work

We identify the following directions for future work:

- **Features for registration**: We are exploring applications of our features as similarity metrics for registering DT images.

- **Extension to other manifold valued data**: Though we focused our discussion on DT-MRI in chapter 2, our methods are applicable to all symmetric second-order positive definite tensor fields like deformation fields, stress and strain tensor fields. Further, extension of our methods to other manifold valued data [76–78] will be part of our future work.

- **Biquaternion differential operators**: Similar to our biquaternion gradient vector in chapter 3, we propose to formulate other holistic biquaternion first order (e.g. structure tensor) and second order (e.g. Hessian matrix) differential operators for DT images, which we expect to give favorable results over FA based approaches.

- **Extensive validation**: Though we have presented many results that show the potential of our approaches, a more extensive quantitative evaluation of the consistency and noise performance would further strengthen our claim regarding their effectiveness.
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