Saturn: A software application of tensor utilities for research in neuroimaging

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A B S T R A C T

We present an advanced software tool designed for visualization and quantitative analysis of Diffusion Tensor Imaging (DTI) called Saturn. The software is specially developed to help clinicians and researchers in neuroimaging, and includes a complete set of visualization capabilities to browse and analyze efficiently DTI data, making this application a powerful tool also for diagnosis purposes. The software includes a robust quantification method for DTI data, using an atlas-based method to automatically obtain equivalent anatomical fiber bundles and regions of interest among different DTI data sets. Consequently, a set of measurements is also implemented to perform robust group studies among subjects affected by neurological disorders and control groups in order to look for significant differences. Finally, a comparison study with five similar DTI applications is presented, showing the advantages offered by this tool.

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1. Introduction

Diffusion Tensor Magnetic Resonance Imaging (DTMRI) or Diffusion Tensor Imaging (DTI) has become an important medical image modality in the diagnosis of many neurological diseases due to its capabilities to explore the structure of the brain white matter. This image modality allows to measure the diffusion of water molecules in tissues, at a macroscopic level. In the case of nerve fibers, due to the myelin covering of the axons, the diffusion is constrained mainly in the direction parallel to the fiber, and therefore their structure can be analyzed by DTI. This technique computes a tensor at each voxel, called diffusion tensor (DT), that is commonly a second order tensor, that can be represented as a $3 \times 3$ positive definite matrix.

Due to the importance gained by this image modality in the last years, many research studies in the medical imaging field have been developed to deal with this type of data, and many are under development as shown by the recent advances in research on neurological diseases using DTI. For example, studies about multiple sclerosis [1,2], epilepsy [3,4] and brain tumors [5] are taking advantage of this technique to better explain the damages caused by these diseases. For this reason, there exist an increasing need for visualization and analysis of this kind of data.

In general, a software application developed for medical research purposes has to fulfill a series of requirements in order to be useful and valuable for the research community. Among these requirements, the main ones are robustness, efficiency, usability and documentation support. Other additional and desirable features for a tool of this kind are multi-platform availability, modularity, online help, and ease of installation.

In this paper we present a tool called Saturn, that implements a solution for the visualization and processing of DTI data, that meets the general features listed above. Our tool

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presents several important features, where one of the more relevant ones is a robust method for quantitative analysis to find statistical differences between control and patient DTI data groups, using standard and advanced measures over regions of interest (ROIs), and over fiber bundles. The differences between the application here presented and five similar applications freely available are highlighted, and the improvements offered by this tool are also shown, demonstrating that it is an interesting and powerful tool for researchers and clinicians in the DTI area.

The paper is structured as follows. In the following section we present the state of the art in DTI software applications. Then in Section 3 the main DTI processing techniques implemented in the proposed tool are described. We will focus on the following aspects: scalar derived magnitudes (Section 3.2) tractography (Section 3.3), automatic selection of fiber tracts (Section 3.4) and DTI quantitative analysis (Section 3.5). After that, implementation details are outlined in Section 4, corresponding to data manipulation (Section 4.1), visualization (Section 4.2), fiber tracts editing (Section 4.3) and graphic user interface (Section 4.4). Then, a comparison with other applications is presented in Section 5, a short case study is shown in Section 6 to show the usefulness of this tool, and finally the conclusions and future lines are outlined in Section 7.

2. Background and state of the art

2.1. Background of DTI

As mentioned previously, DTI is an image modality where the information contained at each voxel is a tensor, called the diffusion tensor (DT), instead of a scalar value. This tensor represents the amount of diffusion of the tissue involved in the volume element considered. More specifically, the DT is the contribution of the movement of the water molecules, considering a volume element that typically ranges from 1 mm$^3$ to 5 mm$^3$. The resulting tensor contains information of the tissue structure, because for instance, the water molecules can be constrained to move in a predominant direction, as occurs in the axons covering. This information can be contained in a 3 $\times$ 3 positive definite matrix. In order to obtain the DT, a set of images called diffusion weighted images (DWIs) are needed. They are magnetic resonance images that measure the amount of diffusion in a particular direction, by using a spin echo sequence in which two gradient pulses are positioned around a 180 refocusing pulse for diffusion weighting. The DT can be obtained from the DWIs using the Stejskal–Tanner [6] equation:

$$S_i = S_0 e^{bD_jt^7},$$

where each $S_i$ is the DWI in the direction given by the unitary vector $j_i$, $S_0$ is a reference image (usually a T2 weighted image), $D$ is the diffusion tensor to be determined, and $b$ is the diffusion weighting factor, that is a parameter that controls the amount of diffusion applied [7]. At least six DWIs should be acquired in different non-co-linear directions in order to solve this equation.

Several scalar magnitudes can be derived from the tensor $D$, as described in the literature [8,9]. The most frequently used scalar magnitudes are:

- **Tensor eigenvalues.** We refer to the eigenvalues of the DT in decreasing order as $(\lambda_i, i = 1, 2, 3)$.
- **Fractional anisotropy (FA).** It provides an anisotropy measure of the diffusion at each voxel and is computed from the tensor eigenvalues as:

$$FA = \sqrt{\frac{3}{2} \left( \frac{(\lambda_1 - \lambda_0)^2 + (\lambda_2 - \lambda_0)^2 + (\lambda_3 - \lambda_0)^2}{\lambda_1^2 + \lambda_2^2 + \lambda_3^2} \right)},$$

where $\lambda_0$ is the average eigenvalue. This magnitude is limited between 0 and 1.
- **Relative anisotropy (RA).** This is another way to measure anisotropy as a function of the eigenvalues, also ranging between 0 and 1, and is given by:

$$RA = \sqrt{\frac{3}{2} \left( \frac{(\lambda_1 - \lambda_0)^2 + (\lambda_2 - \lambda_0)^2 + (\lambda_3 - \lambda_0)^2}{\lambda_1 + \lambda_2 + \lambda_3} \right)},$$

- **Mean diffusivity (MD).** It is also related to the diffusion magnitude, and it is computed as the average tensor trace, or average eigenvalue:

$$MD = \lambda = \frac{1}{3} \sum_{i=1}^{3} \lambda_i$$

- **Geometric coefficients.** Proposed by Westin et al. [8], they are the linear ($C_l$), planar ($C_p$) and spherical ($C_s$) coefficients, that describe the shape of the DT, that is, if the diffusion is produced in a predominant direction, in a plane or in all directions respectively. They sum up to one, and are computed from the eigenvalues as:

$$C_l = \frac{\lambda_1 - \lambda_2}{\lambda_1}; \quad C_p = \frac{\lambda_2 - \lambda_3}{\lambda_1}; \quad C_s = \frac{\lambda_3}{\lambda_1}.$$  

One of the most useful processing techniques in DTI is tractography or fiber tracking, which consists in the estimation and visualization of the trajectories or the fiber paths existing in the white matter. This technique is performed by following the principal direction given by the major eigenvector of the DT at each voxel. Generally, a set of seeds or regions of interest (ROIs) have to be defined to select the zone from which the algorithm starts to compute the fiber trajectories, and also a stopping criterion is usually defined to avoid non-realistic fiber estimations. The most commonly used tractography approaches use only the information provided by the major eigenvector, for instance the Runge–Kutta integration methods [10], that solve the equation:

$$\frac{d\vec{r}(t)}{dt} = \vec{v}_i(t),$$

where $\vec{r}(t)$ is the fiber trajectory parameterized by the arc length $t$, and $\vec{v}_i(t)$ is the unit tangent vector to $\vec{r}(t)$ at $t$, that is usually chosen as the major eigenvector, because it lies par-
allel to the fiber pathway within an acceptable experimental error [11]. The main advantage of these methods is their high efficiency. There are several issues affecting the accuracy and reliability of fiber tracking methods. One of the most important is the limited resolution of the data sets. This issue hinders the reliability of the estimated trajectories, especially when there are fiber crossings at the same voxel. This situation is difficult to solve, but it can be alleviated using a more sophisticated method, such as High Angular Resolution Diffusion Imaging (HARDI) [12], Q-Ball Imaging (QBI) [13] or Q-Space Imaging (QSI) [14].

Other advanced related techniques are the probabilistic tractography methods, where instead of computing deterministic trajectories from a seed, a probability of connection between the voxels and the seed region is obtained. In this sense there exist, for instance, Fast-Marching approaches that evolves a surface from the seeds and then a probability of connection between the seeds and the points reached by the surface are assigned [15].

2.2. State of the art

There exist several software applications developed to deal with DTI data. Commercial applications such as Analyze [16] (Mayo Clinic) or FuncTool FiberTrak (GE Healthcare), offer intuitive and user-friendly graphical user interfaces (GUIs) from the clinical point of view, but they are not freely available for researchers and their main advantages are their robustness and their visualization capabilities for diagnosis in clinical environments. Among non-commercial applications developed for researchers in the DTI field, we can highlight several applications. For instance, DiSTudio [17] is a versatile software application with an easy to use GUI, which is commonly used in DTI research analysis. Another DTI application is included in MedINRIA [18], which is a set of applications for medical image analysis that also includes two modules for fiber tracking and tensor visualization. These modules are easy to use and are freely available. One important application is the widely used 3D Slicer [19], used for medical research and diagnosis, which among its numerous modules, includes one for DTI analysis. Another interesting tool is Camino [20], a free package for analysis and reconstruction of DTI data that also allows tractography and connectivity mapping. Another application, Volume-One, contains a useful package for the visualization of fiber tracts, called diffusion Tensor Visualizer (dTV). A specific tool for DTI data manipulation is teem [21], a powerful command line set of utilities that does not include a GUI, but implements routines to deal with DTI data using the ‘nrrd’ [22] file format. Another set of tools commonly used for medical image processing is the FMRIB Software Library (FSL) [23], which also includes an utility for quantitative analysis, called Tract Based Spatial Statistics (TBSS) [24], and another utility for probabilistic tractography FMRIB’s Diffusion Toolbox (FDT). All these non-commercial applications accomplish many of the requirements mentioned above for medical applications, and most of them provide standard visualization and processing techniques of DTI data, such as tensor estimation, mask computation, tractography, ROIs editing, and computation and visualization of scalar magnitudes derived from DTI. A detailed list of features of some of these applications will be presented in Section 5.

Although some of the aforementioned applications can perform measures over DTI data, only a few ones allow quantitative analysis. For instance, DiSTudio and MedINRIA include some measures over the ROIs defined by the fiber tracts, but none of them implements robust methods to compare specific measures among a set of subjects. One of the few applications that implements a robust quantitative analysis of DTI data is TBSS, included in FSL. This tool avoids the use of fiber tracking, but the method reduces the fiber structure of the brain to a projection onto the skeleton of the FA.

3. Theory and methods

This section describes the underlying processing techniques implemented in Saturn to deal with DTI data. Due to the complexity of the data used, first we will describe the inputs required for this application as well as how the tensor computation is performed by this tool. Then, the operations made over tensor data implemented in the application are presented.

3.1. Input data and tensor computing

Saturn supports two types of input data: DWIs and Diffusion Tensor Images (DTIs). In the former case, the tensor at each voxel is not available and must be estimated. In our tool, Eq. (1) is solved using the least squares method described in [25]. If the input is DTI, the tensor data is directly obtained.

Some processing techniques are implemented at this step to improve the quality of the data that will be used next. For instance, before tensor estimation, the DWIs can be filtered to increase the SNR, and to obtain smoother solutions. For that purpose we have developed a LMMSE method described in [26], in order to remove noise preserving structures of interest. Another useful available technique is the mask computation, that is implemented using the Otsu [27] threshold method. This method obtains a threshold value from the DWIs, that is used to obtain robustly a mask or a binary volume, where the background voxels are set to zero and the foreground voxels are set to one. Multiplying the mask to the DWIs, the background is removed, as well as non-brain structures, such as the skull. This operation is specially useful for subsequent operations, that will take place only in the foreground points of the mask, or those that are different from zero, saving computational time. An example of a reconstructed FA image obtained from the tensor data is shown in Fig. 1, without DWI filtering, with DWI filtering, and with the mask applied in addition to DWI filtering. Once the tensor is estimated at each voxel of the volume, several processing techniques can be applied to the data. These techniques are described next.

3.2. Scalar derived magnitudes

All the scalar magnitudes described in Section 2.1 can be computed and displayed in Saturn as grayscale images, or alternatively as color images as shown in Fig. 2. Additionally,
there exists an enhanced feature called color by orientation map, where each of the components of the eigenvector associated with the major eigenvalue, hereafter the major eigenvector, is assigned with a primary color and weighted by the FA to better visualize the diffusion information of the data. By convention the colors used are red for the L–R coordinate, green for the A–P coordinate and blue for the I–S coordinate. The resulting RGB image (shown in the bottom left of Fig. 2) can be displayed in a 2D viewer gathering a high amount of structure information which is extremely useful to analyze the data at a glance.

3.3. Tractography

In Saturn the tractography method implemented is the widely used fourth order Runge–Kutta method, because of its high efficiency and stability. The method can be performed in different ways. The most simple procedure is to perform the tractography from a set of seeds, which computes the fibers that start from the voxels of the ROIs drawn by the user. There exists however, the possibility to perform a brute force approach as performed also in other software applications [17]. In this case, the fiber trajectories are computed using as starting seeds all the voxels above a given FA threshold. The result of this operation is a large set of fiber paths covering the region above the FA threshold. Each obtained fiber is marked with an unique index, and they are stored by defining at each voxel a vector of indexes corresponding to the fibers that pass through it. Using this structure, it is easy to select and show only the fibers that pass through a set of voxels, because managing all the fibers at the same time is not practical. The brute force approach provides more fibers because the
sources used to grow them are more extensive, and more reliable because bifurcations of paths from the ROI are taken into account.

Finally, logical operations can be used to refine the fibers obtained. Three logical operations are permitted: OR, AND and NOT, and can only be performed within the brute force mode. The OR operation is used by default. If several ROIs are drawn, the fibers obtained are those passing through all the voxels contained in that ROIs. The AND operation must be specified for two regions. When the AND operation is active, the resulting fibers are those passing through the two ROIs selected. Finally, the NOT operation requires the selection of an additional ROI. If this operation is active the fiber tracking removes those fibers that pass through the ROI selected in the NOT operation. The NOT operation is compatible with the other two logical operations. Fig. 3 illustrates the effect of these logical operations in the inferior fronto-occipital tract in a healthy subject with three different ROIs. An axial slice with the ROIs used is also shown in Fig. 4. Fig. 3a shows the result of applying a NOT operation with the green ROIs and Fig. 3d is the result of applying the AND and the NOT operations at the same time.

3.4. **Automatic fiber clustering**

The automatic fiber tract clustering technique implemented in the application is an atlas-based method. We have constructed first a DTI model of the brain, or atlas, using 30 control healthy subjects. The data sets used have been acquired in a GE Signa 1.5 T MR scanner using 15 gradient directions, $b = 1000 \text{s/mm}^2$, $1.015 \text{mm} \times 1.015 \text{mm} \times 3 \text{mm}$ of voxel size, $\text{TR} = 9999.9 \text{ms}$, $\text{TE} = 80.90 \text{ms}$, $\text{NEX} = 8$, and spanning the entire brain. For the model construction, a template matching registration algorithm is performed over the DTI data, as detailed in [28]. The transformation obtained with the DTI registration step is then applied to the DWIs to normalize them to the same reference system. These normalized images are averaged, to finally estimate the tensor from them.

Based on the anatomical DTI atlas by Mori [29] we have selected ROIs of the main fiber bundles present in the white matter. Namely, we have delineated in the model the ROIs corresponding to the following tract bundles: pyramidal or...
corticospinal tract (cst), cingulum (cg), uncinate fasciculus (unc), medial lemniscus (ml), superior cerebellar peduncle (scp), inferior cerebellar peduncle (icp), tapetum (tap), superior fronto-occipital fasciculus (sfo), inferior fronto-occipital fasciculus (ifo), superior longitudinal fasciculus (slf), inferior longitudinal fasciculus (ilf), fornix (fx), corpus callosum (cc) and medial cerebellar peduncle (mcp). These ROIs are separated between left and right, except fx, cc and mcp. In Fig. 5a some ROIs are shown (cc, fx, cg, and unc), overlapped with the FA of the model, and the same ROIs warped to fit with the corresponding regions in a control subject, are also shown in Fig. 5b.

To automatically obtain the tracts of a given subject, the ROIs obtained for the model are deformed to fit the subject data. This deformation is a non-linear transformation, obtained by means of a registration between the model FA and the subject FA volumes, using a multi resolution template matching algorithm [30]. In this case, the FA volumes are used instead of the DTI data in order to speed up the registration procedure. An example of some warped ROIs are used instead of the DTI data in order to speed up the registration procedure. An example of some warped ROIs are used instead of the DTI data in order to speed up the registration procedure.

Several kinds of conditions may be additionally imposed to obtain the desired tract. In some cases, it would be enough to use a ROI that is crossed by the tract, but in other cases, the definition of two ROIs are required and the tract is defined as the fibers that crosses both ROIs using the AND operation. Also, it would be possible to define ROIs that the tract should not cross, to avoid mistakes in the definition of tracts that follow close paths as is the case of the cg and the cc.

Note that this methodology of fiber tract identification does not warp the fibers in the subject. This allows to perform robust measures over the original fibers computed from each subject, and not over warped fibers (as in [31]), or over a set of voxels in the skeleton (as in [24]). Notice that comparison with other clustering methods is not the objective of this work, and there is no experimental evidence to state if our method is better for comparison in group studies. However our method is built to perform measures directly over the fiber bundles of the subjects under study, which is its main advantage. Of course, our methodology is not error free, and is affected by the accuracy of the tractography and the registration. However, the experiments carried out with our application show a good performance of the method, which can be further improved using more sophisticated registration and tractography algorithms. In Fig. 6 we show the same fiber tracts obtained in the model (top row), in a healthy subject using the described clustering method (middle row) and in the same subject using manually defined ROIs (bottom row).

3.5. DTI quantitative analysis

One of the main features of the tool presented here is the quantitative analysis of DTI, whose goal is to discriminate between normal and abnormal fiber bundles, using the automatic fiber tracts clustering described above. It is important to highlight that the so computed fibers are not warped, and due to the automatic method to extract them the user variability is removed from the process. Measurements along the fiber tracts obtained at this point can be performed, such as the FA, MD, eigenvalues, geometric coefficients, etc., computed along the fiber bundles and over the regions covered by the fiber tracts (voxel based measures). We explain next the measures implemented in Saturn for both modes: ROIs and fiber bundles.

3.5.1. Region based measures

The regions associated with the fiber bundles, i.e. the voxels involved in the fiber paths, are used to compute measures in specific anatomical areas of interest. Additionally other ROIs selected by the user could be employed to perform these measures. The values computed are: FA, RA, MD, eigenvalues (λ1, λ2 and λ3), tensor components (Dxx, Dxy, Dxz, Dyy, Dyz, Dzz) and geometric coefficients (C1, C2, C3). All the values obtained can be shown in a window (as shown in Fig. 7a) or stored in an output text file to process them with any other application.

3.5.2. Fiber tracts measures

Saturn also includes a set of measures computed in the fiber bundles, or along them. The measures available for a given fiber bundle are summarized below:

- Number of fibers in a bundle Nf.
- Average L, maximum Lmax and minimum Lmin fiber length in a fiber bundle.
- Total amount of measure in the fiber bundle Xtot, average measure in the total fiber bundle Xtot, maximum of the fiber measure averages X̄max and minimum of the fiber measure averages X̄min. If N is the total number of fiber points, and each fiber point is denoted as xi, these quantities can be expressed as follows:

\[ X_{\text{tot}} = \sum_{i=1}^{N} X(x_i), \]
\[ \bar{X}_{\text{tot}} = \frac{1}{N} \sum_{i=1}^{N} X(x_i), \]
\[ \bar{X}_{\max} = \max(X_j), \quad j = 1, \ldots, N_f, \]
\[ \bar{X}_{\min} = \min(X_j), \quad j = 1, \ldots, N_f, \]

where X̄j is the average measure at fiber j:

\[ \bar{X}_j = \frac{1}{M_j} \sum_{i=1}^{M_j} X(x_i). \]

\[ 1 \] this registration takes for a volume data set of 256 × 256 × 41 voxels, in a MacBook with a 2.16 GHz Intel Core 2 Duo processor, around 55 s and it is one of the more time consuming tasks implemented in Saturn.

\[ 2 \] Here point coordinates x̂j differ from voxel coordinates, vi, and the values at x̂j are obtained by linear interpolation.
Fig. 5 – Axial slice of the model FA (a) and control FA (b) with some ROIs overlaid: light blue for cc, light green for fx, red for right cg, dark blue for left cg, light green for fx, violet for right unc and dark green for left unc. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

Fig. 6 – Fiber tracts extracted from the model data (top row), from a healthy subject using our method (middle row) and from the same subject using manually defined ROIs (bottom row) in axial, coronal, and sagittal view.

Fig. 7 – Measure panels, for ROIs (a) and for fiber tracts (b).
Fig. 8 – Average FA profiles in the right pyramidal tract of a control (a) and a patient with a tumor in the right hemisphere (b).

The measures computed can be shown in a separate window (see Fig. 7b) and also saved into a file for further processing. Saturn can also save the FA values of each fiber point in a text file, saving the values of each fiber in a separate line. This is specially useful to analyze the FA profiles of a fiber bundle, as shown in Fig. 8. These profiles correspond to the average FA profiles of the right pyramidal tracts of a healthy subject, Fig. 8a, and of a patient with a tumor in the right hemisphere, Fig. 8b. Notice the different behavior presented by these two profiles. In addition, there exist a procedure to ensure that the points stored in the file are ordered correctly, in order to obtain profiles that correspond with the real trajectory of the fiber paths.

In addition to the measures mentioned here, we introduce another measure computed also along the fiber paths that reflects better the state of integrity of a given set of fibers, and is computed longitudinally. We call this measure tract integrity measure and it is defined as the total amount of diffusion contained in a tract divided by the number of fibers in it:

\[ I = \frac{\text{FA}_{\text{tot}}}{N_f} \]  

The measure is based on FA because it is directly related to the number of axons aligned in a predominant direction, and therefore it is a good descriptor of integrity. Notice that short fibers contribute with low values to this measure, which is good for comparison of fiber bundles, and therefore it takes into account length discrepancy between tracts. For this reason this measure is better than the average FA. It is also better than \( \text{FA}_{\text{tot}} \) to discriminate between fiber tracts, because equivalent tracts with small differences in \( N_f \) give larger differences in \( \text{FA}_{\text{tot}} \) than in the integrity measure. Integrity ranges from 0 to \( N_a \) where \( N_a \) is the average number of fiber points.

4. Implementation

Saturn is built using the Insight Toolkit (ITK) [32] image processing libraries, the Visualization Toolkit (VTK) [33] libraries for 3D visualization and the Fast Light Toolkit (FLTK) libraries [34] for the graphical user interface objects. All these libraries...
are open source and written in C++. The methods and algorithms for image processing and visualization are included in separate classes, also included as library modules in C++ language. As those libraries can be compiled in multiple operating systems, Saturn is also a multi-platform application, and is available for Linux, MacOS and Windows here [35].

4.1. Data manipulation

In this section the management of the data types used by Saturn are described. As mentioned in Section 3, DWI and DTI are supported as input data types, but standard scalar data and model data are also supported. Model data is used to manage 3D objects, such as fiber tracts (composed by point data), and 3D surfaces (composed by polygonal data) as for example, the surface reconstruction of the gray matter of the brain. The supported formats for DWI data are ‘DICOM series’ and ‘nrrd’ [22], and for DTI data the input supported formats are ‘vtk tensor’ and ‘nrrd’, and the output supported format is ‘vtk tensor’. With respect to the standard scalar data the input/output supported formats are ‘DICOM series’, ‘nifti’, ‘mhd’ and ‘raw data’. Additionally ‘Kretz’ format is supported for scalar data only for reading. The supported input/output format for model data is ‘vtk’.

There are four data types managed internally by this tool: DWI data, DTI or tensor data, scalar data and model data. All these data types can be visualized, processed, renamed and removed from the workspace in the data panels, shown in Fig. 9, placed in the upper left part of the GUI. This organization provides the user with an easy way to manipulate the different data types. With this philosophy each procedure is made over the data selected in the panel, and therefore each data panel has different processing features. For instance, the data selected in the scalar data panel can be visualized in a 2D viewer with the ‘view’ button and the properties of the model data selected (color, opacity, specular power, etc.) can be edited with the ‘prop’ button.

4.2. Visualization

Our application has four main visualization modes. The first mode, called $4 \times 2D$ is formed by four independent 2D viewers to visualize slices of volumetric data, for instance, to show at the same time the FA, the T2, the $C_l$ coefficient in color mode and the color by orientation volumes of the same subject, as shown in Fig. 10a. Each 2D viewer can be expanded to the maximum size of the visualization panel, showing the $1 \times 2D$ mode, like in Fig. 10b. In the third mode, $3 + 1$ the fourth 2D viewer is changed by a 3D viewer as shown in Fig. 10c. The last one is the 3D mode, where a 3D viewer is shown in the whole visualization panel as shown in Fig. 10d showing a surface rendering of the model data and orthogonal 2D planes.

Each 2D viewer supports the following functions: zoom, orthogonal views (axial, sagittal and coronal), flip, transpose, ROI draw and display, image details view, anatomical tags view, pixel value and location of cursor display, change intensity window and level, switch between grayscale visualization modes, switch between several color modes, and change the range of the color map. The user can also use an auxiliary viewer in a separate window with the same visualization features as the main viewers (see Fig. 11a).
The 3D viewer supports visualization of 3D models and 2D orthogonal planes of scalar data. The planes can be viewed in two modes, grayscale and color. Each of them supports several features such as intensity level and intensity window change, switching between the slices in the volume, and repositioning of the plane in any oblique direction, all these features are available by means of mouse actions. The oblique plane is an advance feature not available in many applications, one example of this is shown in Fig. 11b. The opacity of the planes can be also changed from the slider at the top right of the panel. The whole scene shown in this viewer can be adjusted (angle of view and zoom) using the mouse or using the specific controls at the top of this panel. There exist six predefined angles of view, as well as a center button that resets the default viewer values.

4.3. Fiber tracts edition and visualization

The fiber tract procedure implemented in this tool (Runge-Kutta integration approach), has been proved to provide good correspondence between the fiber tracts computed and the real anatomical fiber bundles, with random and systematic errors typically below the voxel dimension [36]. However, obtaining anatomical fiber bundles appropriately,
is sometimes a challenging issue, even imposing logical conditions. This goal is specially difficult when the anatomy is affected by a tumor, or if we want to obtain small fiber bundles that are close to other major tracts, such as the ml or the fx. In those cases it is more efficient and convenient to perform manual edition.

For this reason, Saturn includes several edition procedures over fiber tracts. There are two semiautomatic operations to
edit fiber tracts: fibers resizing and large fibers removal. The former operation removes the fiber points located at a distance greater than a given threshold with respect to the nearest voxels of the ROI that corresponds to this tract. This operation reduces the size of the fibers that are very large, removing the points that are too distant from the ROI associated with that fiber bundle. The latter operation removes entirely those fibers greater than a given threshold. In both operations the mean size of the fibers in the tract is computed in order to use a threshold dependent on the percentage of the mean size.

Some manual editing procedures are also available. A fiber bundle can be also cut in any orthogonal plane (axial, sagittal or coronal), by adjusting the orthogonal slices in the 3D window and then using the corresponding cut buttons. An example of fiber edition is shown in Fig. 12, where the three main operations described are illustrated.

Regarding the fiber tracts visualization, Saturn provides several features to show the fibers in different ways. For instance, the radius of the fibers drawn can be set at execution time, and once the fibers are computed, the color, opacity, and other parameters can be changed. Three color modes are available to visualize the fibers: color map based on FA, color map based on fibers size and user defined colors, as shown in Fig. 13.

### 4.4. GUI

With respect to the GUI, Saturn is equipped with several panels to manage the different operations allowed for DTI data. Fig. 14 shows the panels used for DTI processing and visualization. The first panel is used to perform the tractography and is divided into four groups: ‘ROIs’, ‘parameters’, ‘color’ and ‘execution’ as shown in Fig. 14a. The ‘ROIs editing’ allows to draw ROIs to start the fibers computation or to select the fibers after a computation is performed. Different labels can be used for different regions, using different colors for them. By left clicking in any 2D viewer the ROI is drawn with and adjustable radius.

The parameters section is used to change the stopping criterion used by the tractography algorithm (minimum FA threshold, or maximum curvature angle), the time step used in the Runge–Kutta integration, and the radius of the fibers rendered in the 3D window. In the color editing section it is possible to assign different color maps to the fiber tracts extracted using the FA, MD or size of the fibers as the scalar values used in the color map. Alternatively the fibers can be rendered with a user defined color.

In the ‘execution’ section of this panel, the tractography can be performed in the two ways mentioned in Section 3.3: using the ‘tractography’ button, the fibers that start from the voxels of the ROIs drawn by the user are computed and using the ‘brute force’ button, the fibers in all the voxels above the given FA threshold are computed. In this latter case, the ‘select fibers’ button is used to select and visualize the fibers passing through the ROIs drawn by the user, and then they can be used for statistical studies. Finally, logical AND and NOT operations can be used with the ‘Tract. Logic’ button, using the labels defined in the ‘ROI1’, ‘ROI2’ and ‘Ex’ entries.

The second panel, Fig. 14b, is used to perform the automatic fiber clustering. In this panel, a list of fiber bundles is presented, and the user have to select those to be computed with the automatic method. First, the warped ROIs are obtained,

---

### Table 1 – Available features in six different DTI applications, including Saturn.

<table>
<thead>
<tr>
<th>Features</th>
<th>DtiStudio</th>
<th>FSL</th>
<th>MedINRIA</th>
<th>3D Slicer</th>
<th>Teem</th>
<th>Saturn</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scalar magnitudes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>C1, C2, C3</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<td>Color by orientation</td>
<td>Yes</td>
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<td>Yes</td>
<td>Yes</td>
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<td>Tractography</td>
<td>Yes</td>
<td>No</td>
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<td>Stochastic tract.</td>
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<td>Yes</td>
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<td>Brute force tract.</td>
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<td>No</td>
<td>(*)</td>
<td>No</td>
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<td>Auto fiber clustering</td>
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<td>No</td>
<td>No</td>
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<td>No</td>
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<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Fibers cut</td>
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<td>No</td>
<td>Yes</td>
<td>Yes</td>
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<td>Fibers resize</td>
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<td>Fibers profile</td>
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<td>No</td>
<td>No</td>
<td>Yes</td>
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<tr>
<td>AND, NOT op.</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>(*)</td>
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<tr>
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<td>(*)</td>
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<td>No</td>
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<td>DCM(1)</td>
<td>nii</td>
<td>DCM, vtk(2)</td>
<td>DCM, vtk, nrrd</td>
<td>nrrd</td>
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<td>Mac, Lin, Win</td>
<td>Mac, Lin, Win</td>
<td>Mac, Lin, Win</td>
</tr>
</tbody>
</table>

(1) Support for DICOM series from multiple vendors. (2) Own file format also supported. Marked with (*) if partially supported.
using the ‘Warp ROIs’ button. Alternatively, a file with the precomputed warped ROIs can be loaded with the ‘load ROI’ button. Once the ROIs are loaded, the fiber tracts can be computed with the ‘auto-select’ or ‘select-tract’ buttons, depending on whether the user wants to apply predefined logical operations or not.

The third panel, Fig. 14c, is used to compute the measures available in this tool, the fourth panel, Fig. 14d, shown is used to compute and visualize the scalar magnitudes associated with the tensor data, and the last panel shown, Fig. 14e, allows the fiber editing procedures described in Section 4.3.

5. Comparisons with other applications

In this section Saturn is compared with five DTI applications commonly used by researchers in the medical imaging field, freely available and with similar features than our tool. As mentioned in Section 2, these applications are: DtiStudio [17], MedINRIA [18], 3D Slicer [19], teem [21] and FSL [23]. In Table 1 a set of basic and advanced features specific for DTI applications, are shown along with the features offered by Saturn, for the sake of comparison. These tools differ in the features offered, that make them desirable for different goals. The most similar tool to the one proposed in this work is DtiStudio, which contains visualization and processing capabilities for DTI data, but with noticeable differences, especially DtiStudio does not include any automatic fiber clustering, it has no fibers editing procedures, the measures obtained are limited, and it is only available for windows platforms, whereas Saturn has no quality image inspection and distortion correction features, and the support for DICOM input files from different vendors is reduced. 3D Slicer is used for many other medical applications and has shown to be especially useful for researchers in medical imaging, but although its DTI module has many capabilities, it requires some experience to use it properly. For instance, to perform a single tractography once the tensor data is loaded, 3D Slicer requires a higher number of actions to perform. Namely, a ROI choice item plus two more items are required to select the seeds with the mouse and the keyboard. After that, another four choice items are required to perform the fiber track and visualize the fibers. In Saturn the left mouse button can be directly used in the 2D viewer to select the seeds, and two buttons to do the fiber track and show the fibers respectively. Although some user tests need to be done to evaluate the usability of both tools, the differences in their use is evident in this simple task. MedINRIA has a quite useful module to visualize DTI data, but although it is quite easy to use, it is not especially efficient. For instance computation times obtained in MedINRIA for tensor loading (from nrrd file format) and FA computation are 95 s and 10 s respectively, measured in a MacBook with a 2.16 GHz Intel Core 2 Duo processor, whereas the same tasks performed in Saturn in the same machine takes about 3 s and less than 1 s respectively. Teem is an efficient and complete tool for processing tensor data designed to be used with scripts or command line, and therefore it does not provide a friendly GUI. This is also the case of FSL which provides a tool called TBSS for DTI quantification and a tool for performing probabilistic tractography, but it does not provide simple tractography and there is not a user friendly GUI to deal with DTI data.

From the features shown in Table 1, it is clear that Saturn is a powerful and valuable DTI application, comparable with other tools currently used by the scientific community. It also improves some features offered by those tools. In particular the software here presented has several features not supported in general by other similar applications: the automatic fibers clustering method, the robust measurement over ROIs and fiber bundles, the fiber editing module (cut, resize and coloring), the fibers profile computation, and the oblique plane visualization.

6. Case study

To illustrate the utility of Saturn, a study has been made in two patients affected with a tumor in only one hemisphere.
Fig. 16 – Differences between the pyramidal tract in two hemispheres. Left: control subject; right: tumor patient.

(P1 with a tumor in the left hemisphere and P2 with a tumor in the right hemisphere). The study has been focused on the pyramidal tracts, that are obtained using the automatic fiber clustering method implemented in Saturn. The integrity measure described in Section 3.5.2 and the average FA values are used to compare the pyramidal tracts in the two hemispheres of the same patient, and also to compare the patients with a set of 16 control subjects. The values are shown in Fig. 15, including the mean and standard deviation (std) values for the controls in thicker bars for both hemispheres. Notice that the values for the left pyramidal tract are in general higher than the right, possibly because the controls are right handed. In that figure it is also clear that the patients affected with a tumor have integrity values that differ noticeably between the healthy and the pathological hemispheres, and the affected pyramidal tract presents low values compared with the controls (below 18). The average FA also provides low values for the pathological cases, but are less discriminant, as shown in the P2 case, where both hemispheres present similar values. We have also observed that there is a good correlation between the obtained values and the state of the patients, although clinical tests need to be done to validate results like this. For more detailed studies carried out using Saturn, see the work in [37].

In order to show the fiber tract structure, Saturn allows fiber visualization with several color codes as mentioned in Section 4.3. This is specially useful in this case study, as shown in Fig. 16, where the pyramidal tracts of a control and one of the patients (P2) are shown using a color map based on the FA. The color range is set between 0.2 and 0.7, using red for the low values (near or under 0.2), blue for the high values (near or over 0.7) and green for the intermediate values (around 0.45). In this figure it is clear that although the fiber structure is similar in both cases, the FA is highly reduced in the right pyramidal tract of the patient due to the tumor, as shown by the red color of the fibers passing near the tumor.

7. Conclusions and future works

In this paper we have presented a new powerful and versatile tool for DTI visualization and processing, freely available for research purposes in three different platforms [35]. The presented tool implements the basic DTI processing techniques, such as DTI estimation, mask computation and derived scalar magnitudes computation and visualization, and improves important routines such as filtering of DWI data. Additionally, Saturn is to the best of our knowledge, the first DTI tool that provides an automatic fiber clustering method, designed for robust quantitative analysis among different subjects. We have also presented and included in this tool a new measure for the quantification of fiber bundles, that along with the standard tensor measures and the automatic fiber tracts clustering method, provides an efficient method to find out significant differences between groups of subjects in anatomical fiber bundles. This issue has been shown in the case study presented here, proving that our tool and the methods included in it are of paramount relevance for the analysis of DTI data, that is of particular importance in the research of neurological disorders.

Saturn is also extremely helpful for the visualization and exploration of fiber tracts, due to its efficient computation routines as well as for its user friendly GUI. The advanced visualization features implemented, such as the versatile visualization of 2D planes in the 3D window, able to be located in any oblique direction, the fibers color options, using FA or size color maps, and the fiber editing module to remove and resize non-relevant fibers, allows to explore DTI data easily, and makes this tool quite useful also for clinical use, for instance for surgical planning.

We have also shown that the features included in this tool are comparable and even enhance the features included in other similar DTI applications currently used by researchers of this area, as shown in Section 5, but more effort has to be done in order to improve this tool to make it more efficient and robust. In particular, more complex tractography techniques, such as Fast-Marching [15] or stochastic techniques [38], are needed in order to obtain connectivity maps, or more sophisticated diffusion models ([12–14]) can be used to obtain more reliable fiber tracts, or for instance, better filtering techniques can be used to reduce more efficiently the noise in the input DWI data. Also advanced visualization techniques can be added, such as volume rendering and glyphs visualization for tensor data.
Conflict of interest

None declared.

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REFERENCES

[16] None declared.
