Tractography in Context: Multimodal Visualization of Probabilistic Tractograms in Anatomical Context

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Abstract

Multi-modal display of neurological data in anatomical context is a challenging issue in biomedical visualization. We present an application-driven approach, which solves the visibility issues arising from the simultaneous presentation of probabilistic tractograms and anatomical context.

The tractogram (a scalar field indicating a connectivity score between voxels) is visualized by nested surface layers, providing an overview of long-range connectivity. Unique dataset features are reflected by value-based opacity and further enhanced by depth cues. An illustrative, three-dimensional rendering of the cortex complemented with textured slices is provided as anatomical context. The presented methods are based on a detailed requirements analysis with domain experts. Two user studies were performed to evaluate our methods and the techniques were improved based on their feedback. Our methods can be applied to a wide range of data, as they can be adapted to the range and requirements of data very easily.

Categories and Subject Descriptors (according to ACM CCS): I.3.7 [Computer Graphics]: Three-Dimensional Graphics and Realism—Visible line/surface algorithms; I.3.8 [Computer Graphics]: Applications—

1. Introduction

Over the past years, human brain connectivity has become an ongoing topic in different areas of neurological research [UCL], such as brain function, neurological diseases, and developmental processes. The most informative techniques involve cross dissections combined with tracer techniques, which have high spatial resolutions [SP06]. Since they cannot be conducted with living species, they are restricted to animal and post-mortem studies. However, Magnetic Resonance Imaging (MRI), and especially diffusion-weighted MRI are promising tools for probing connectivity *in vivo*. Although MRI's precision is low compared to the axonal diameter (mm scale vs. μ m scale), advanced techniques like tractography have become an important tool for analyzing brain anatomy [JJB11].

Two-dimensional slice based techniques can give detailed information on probabilistic tracts with appropriate context, but they fail to outline long-range connectivity, i.e. the connectivity across non-adjacent slices, which is important to get an overview of the data. Furthermore, the location of tracts with respect to anatomical features is of high interest since different areas are related to different functions.

Hence, an appropriate visualization must embed information into context without occluding one with the other.

In this work, we present a multi-modal visualization approach for probabilistic tractograms in an MRI-based context. The dataset in focus is represented by nested probability-surfaces with value-dependent opacity and additional depth cues to enhance shape perception. Context consists of an illustrative cortex drawing with structure-preserving transparency to increase visibility, and selective opacity to occlude non-pertinent information. Additional anatomical information is provided as textured T_1 slices. These methods are embedded in OpenWalnut [EHWS10], an open source framework for neurological visualization.

This paper is structured as follows. First, we analyze the requirements of probabilistic tractography and context visualization in Section 2. Afterwards, we discuss a system design based on this requirements analysis, and consider related work conducted in similar fields of study. In Section 4, we evaluate expert feedback, followed by a summary of our results in Section 5. In the last section, we give an outlook on future work.

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2. Requirements Analysis

The visualization of probabilistic tractograms in anatomical context consists of two main components: a visualization technique for probabilistic tracts, and anatomical context. In this section, we discuss the requirements of both tasks.

2.1. Task Description

The visualization task was described to us in an interview with the head of a group of domain experts of neuroscience, neuroanatomy, psychology, and biology. In this interview, the medical background and its challenges were characterized and set into the context of the group's work. The experts require a visualization for three-dimensional scalar fields, which provides an overview over value distribution and relation to the cortex. This visualization should specifically target probabilistic tractograms, while remaining expediently applicable to other scalar fields. Additionally, they need anatomical context which contains the cortex and information about white matter and ventricles. To support interactive exploration of the data, and adjusting to users' needs, the methods require a sufficient performance.

Our exemplary data was acquired with a Siemens 3T Trio scanner. The T_1 -weighted MRI data has a voxel size of 1 mm, whereas DW-MRI uses 60 gradients at a voxel size of 1.72 mm. The probabilistic tracts were derived using Med-INRIA [TSF*07], and computed with a random walk method by the Lipsia toolbox [LMB*01]. They are linearly registered onto the T_1 images. The transformation matrix is determined using the fractional anisotropy image, as supplied by FSL [SJW*04].

2.2. Probabilistic Tractography Visualization

Probabilistic tractograms are scalar fields consisting of connectivity scores of voxels of the brain. While deterministic tractography creates trajectories, and thus implies certainty in data and visualization, probabilistic tractography provides a robust alternative which models uncertainty arising from partial volume effects and noise. A probabilistic tract is a 3D scalar field, which describes the probabilistic connectivity of a seed point to every other voxel in the brain. Scores tend to be highest in regions around the seed point. In analogy to mathematical morphology, we will refer to this area as the skeleton [MS86], around which the data is arranged in layers of predominantly decreasing scores. While each probabilistic tractogram describes the connectivity for one point, several tractograms can be combined into a representative tractogram (e.g. through averaging or cumulation) to account for a whole region's connectivity, producing a new scalar field. As tracts are represented volumetrically rather than by trajectories, they do not yield the misleading impression of being real fibers.

The traditional probabilistic tractogram representation

consists of slice-based display. This representation lacks information about the long-range connectivity. The number of slices that can be viewed simultaneously is already limited if they are displayed next to each other, and reduced even further if they are aligned spatially (e.g. one slice per anatomical plane). Due to this restriction, our experts collaborators requested long-range connectivity information (Req. 1). To address this issue, they suggest drawing multiple layers of isosurfaces. By examining the visualization, it should be clear to a viewer, which regions have low probabilities, and which have high probabilities. Hence, our visualization should clearly reflect data values in order to provide users with an intuitive understanding of the approximate value distribution of a probabilistic tractogram (Req. 2). Finally, we are dealing with spatial data, which is more difficult to grasp than flat images. Therefore, a good shape and depth perception should be provided (Req. 3).

To get a good impression of the data set in focus, all requirements should be met. The requirements of the focus visualization can be summarized as follows:

- (1) Depict long-range connectivity
- (2) Find intuitive value representation
- (3) Add depth cues

2.3. Anatomical Context

For anatomical context, domain experts are mainly interested in gray and white matter, and the ventricles. T_1 -weighted MRI scans are suitable for this purpose, since they provide a good contrast between gray matter and white matter [LVR*07]. As anatomical context, our collaborators suggest a "glass brain", i.e. a largely transparent rendering that retains some structure. They would like to apply it not only to probabilistic tractograms but also to other scalar field data.

From the idea of a "glass brain", we derive that the goal is a lucid cortex rendering. This means that the cortex should be visible (Req. 4) but occlusion should be avoided (Req. 5). However, these two requirements contradict each other. On the one hand, morphological structure should be preserved, since it helps neuroscientists to locate tracts in three-dimensional space, and understand the function of connected areas. On the other hand, context should not occlude the object in focus. This is a typical problem of visualizations with context, and there are prevalent solutions. Either the context is made semi-transparent, or selective parts are removed to enable users to see through. In some cases, it can also be desirable to apply occlusion as a tool to hide nonessential or distracting information. This can be necessary to enhance the focus matter (Req. 6). Finally, some additional anatomical information should be added to the glass brain. Here, domain scientists are especially interested in ventricles and the boundary between gray and white matter (Req. 7). This information is available in the data, and it should be integrated in a visually appealing and unobtrusive manner.

The requirements for the anatomical context can be summarized as follows:

- (4) Preserve cortex structure
- (5) Avoid occlusion
- (6) Enhance focus
- (7) Provide anatomical information

3. System Design

In this section, we will give an overview over related work, and discuss which methods are suited best to fulfill the requirements defined in the previous section. We then present solutions we developed based on this discussion.

3.1. Related Work

Over the past decade, DTI data has been explored as a tool to study a wide range of topics from brain development to multiple sclerosis, stroke, and mental illnesses [MyZ02].

Deterministic tractography is a widely applied method which reconstructs 3D trajectories from DTI data. There has been a lot of effort to produce visualizations that are informative and visually appealing. However, most of these techniques [MvZ02, PFK07] rely on prior knowledge about the correspondence of fibers to bundles. Everts et al. [EBR109] present a GPU-based display method that renders illustrative halos for deterministic tracts, without requiring prior knowledge. While this method is effective at bundling neighboring fibers, it does not yield a verified anatomical grouping.

As a technique based on scalar fields rather than a set of lines, probabilistic tractography requires different visualization methods. The traditional display consists of slices of a tractogram drawn on MRI slices [JBB09, JBR09, Des11]. While spatial precision within each slice is very high, such slice-based approaches have the major disadvantage that only local connectivity can be observed. This representation lacks information about long-range connectivity across slices, since a user has to inspect slices sequentially. Schultz et al. [STS07] present a topological approach. They derive critical regions for deterministic fibers from the topological features of the underlying DTI field. Brecheisen et al. [BPtHRV12] mix deterministic fibers with probabilistic tracts to illustrate uncertainty information.

There are two main approaches for the volumetric visualization of probabilistic tractograms: transfer functions and isosurfaces. Rick et al. [RvKC*11] present a transfer function-based approach for multiple probabilistic tractograms. They use transparency and color saturation to represent the probability values, and hue as encoding for different datasets, mixing colors in overlapping regions. As a result, the general probability distribution is perceivable. However, this representation lacks depth: only the maximal probability along a viewing ray can be determined. Descoteaux et al. [DDKA09] draw single isosurfaces of probabilistic tracts

in order to validate probabilistic fibers against them. This leaves the viewer with an impression of the tractogram's shape, but it lacks information about the value distribution since only one value is represented by an isosurface.

Slice-based medical imaging data is often supplied with a slice-based context. The simplest context is a textured T_1 slice. However, if neurological data is displayed in 3D, the context should provide additional information. Goldau et al. [GWG*11] present a visualization that uses DTI data and probabilistic data simultaneously by drawing DTI-based fiber stipples with varying transparency depending on the connectivity score. Context is given by transparent illustrative slices with isolines drawn along grey and white matter boundaries. The authors also sketched a solution to the problem of representing value distribution by drawing nested isosurfaces. While this surface-based approach is very basic, it inspired our method. Svetachov et al. [SEI10] present an illustrative drawing of the brain as context for deterministic fibers. They render illustrative slices with stippled gray matter regions surrounded by a hatching line rendering of the cortex in a cut-away view. This representation is suitable for deterministic tracts, but applied to probabilistic tracts, either the context or the tracts would be occluded. Born et al. [BJH*09] present a semi-transparent line rendering of the brain with colored highlights in functional MRI (fMRI) activation areas on the cortex. In addition, they provide illustrative slices in a cut-away view. However, this approach is not suitable if data is displayed inside the brain as the cortex would hardly be visible.

Beyond neuro-imaging, there have been other methods to balance focus and context. Viola et al. [VKG05] suggest volume thinning, and screen-door transparency to avoid occlusion in segmented and tagged volumetric data. Gasteiger et al. [GNKP10] present a blood vessel visualization that is more transparent towards the viewer and more opaque near the contours. Hummel et al. [HGH*10] developed an illustrative rendering for integral surfaces, which employs normal-variation-based transparency. The resulting images allow to see multiple layers of surfaces at once, since only the visual borders are opaque.

3.2. Probabilistic Tractography Visualization

According to the requirements analysis, there are three main requirements which have to be met by the visualization: long-range connectivity has to be preserved, values should be represented intuitively, and there should be depth cues to enhance shape.

3.2.1. Long-Range Connectivity

We chose a multi-surface representation for the probabilistic tractograms because they convey long-range connectivity better than slice-based representations, and thus satisfy Req. 1. Moreover, they enable a user to obtain a good 3D

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impression along the view direction, and to approximate the value distribution in between. One can expect that values decrease from skeleton to cortex.

We support displaying of up to four isosurfaces for userchosen values, which are rendered in GLSL using per-pixel shading. More surfaces can only be distinguished with difficulty, and large numbers of surfaces decrease the performance. Since the probabilistic tractogram is structured around its skeleton, it is possible to employ standard back-tofront compositing. Specular highlights are removed to avoid falsifing colors during mixing and implying non-existent value changes.

3.2.2. Intuitive Value Representation

In Req. 2, an intuitive representation of the dataset is requested. Denoting a probability, the connectivity score conveys a notion of importance of different data points. To account for this notion of importance, we introduce value-dependent opacity. Each point should be represented based on its relative value in comparison to the data range. Since values near the skeleton are higher than those further away, they have to be visible through the outer layers. Therefore, we choose *value-dependent opacity* for each voxel, where x_i is the value of point i and [a,b] is the range of values:

$$\alpha_i = \frac{x_i - a}{b - a} \in [0, 1].$$

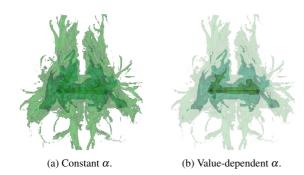


Figure 1: The values {0.2,0.4,0.6,0.8} are represented intuitively based on their importance.

Fig. 1 depicts four surfaces comparing constant opacity of $\alpha_i = 0.5$ to value-dependent opacity. While constant opacity gives little information about the data, our method enhances surfaces of high probability and provides a cue to value distribution.

3.2.3. Depth Perception

In a last step, we address Req. 3: improving spatial impression. For depth perception, emphasizing the part in focus and de-emphasizing parts that are further away helps to provide

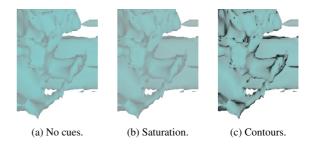


Figure 2: Comparison of different depth cues.

an estimate. There are different ways to achieve this goal, e.g. halos, contours, shadows, and atmospheric depth.

As mentioned in Section 3.1, halos have proven useful for deterministic fibers. Shadow-like halos could help smaller parts of the tractogram stick out, but occlude a lot of detail resulting in a loss of information, which our collaborators were rather sceptical of since spatial information was a key requirement (Req. 5). While not all information is needed, unnecessary visual effects at the expense of losing information should be avoided.

Instead, we developed contours which are computed based on the angle φ between the normal \vec{n} and the view vector \vec{v} , similar to the method described in Sec. 3.3.1, where $m_c \in [0,2]$ is a parameter that influences the amount of contours displayed: $\alpha' = \max(\alpha, m_c(1 - |\cos \varphi|))$.

Atmospheric depth has proven to be an effective depth cueing method [War09]. Usually, color is varied depending on the distance, and faded toward the background color. However, this technique would interfere with transparency as a major carrier of information. Troscianko et al. [TMC*91] evaluated different depth cues based on changes in hue, saturation, and luminance in a user study, finding that "a saturation gradient is particularly effective at achieving [a depth impression]". This effect is caused by atmospheric scattering, which renders distant colors less saturated than close ones. Therefore, we employ saturation modulation as a depth cue: voxels close to the viewer are fully saturated and those further away are increasingly desaturated. This is implemented as mixing a color with its intensity according to the HSI (hue, saturation, intensity) model [Smi78], where the intensity is computed as $i = \frac{r+g+b}{3}$. Depending on the relative depth d (in a dataset) and a modifiable parameter $m_s \in [0,2]$, we compute the convex combination of a color c and its intensity i:

$$c' = (1 - d^{m_s})c + d^{m_s}i$$

This *focus-dependent saturation* provides a rendering containing saturated colors in front and more subdued colors further away.

Fig. 2 demonstrates the difference between a plain render-

ing, saturation as a depth cue ($m_s = 0.7$), and contours as a depth cue ($m_c = 1.0$). The effect of saturation modulation is most perceivable in the top right corner of each image. Employing these depth cues results in a better spatial perception, but contours can also hide areas with high probability, so they should be used carefully.

3.3. Anatomical Context

In compliance with the requirements, the context should preserve cortex structure, handle occlusion, enhance focus, and provide additional anatomical information.

3.3.1. Cortex Structure

In a first step, we address Req. 4 to show the cortex and preserve its structure. We consult drawings from anatomical textbooks [Gra18, SP06]. In these, there are dark lines along sulci and silhouette, while gyri are left white.

In order to achieve such a rendering, we analyze the cortex structure obtained with a simple isosurface approach. We find that sulci and silhouettes share the property of normals pointing near-orthogonal to the view vector, whereas gyri have normals that have little deviation from the view vector. We apply one pass of binomial smoothing (kernel size $3 \times 3 \times 3$) to the T_1 data since this produces a cleaner and less bumpy rendering. To avoid distracting from the focus matter, the cortex is drawn in shades of gray rather than colors. Therefore, we determined the color in a normal-based way as $(r,g,b)' = |\cos \varphi|(i,i,i)$ for $i \in [0,1]$.

3.3.2. Occlusion

Visibility of nested objects can be improved with methods such as volume thinning, or screen-door transparency. Volume thinning produces regular gaps along the view vector, thus implying structure that does not exist in the data. However, screen-door transparency introduces a concept that can be modified to suit our application. A part of the context remains opaque, while the gaps in between offer a free view on the object in focus. In order to avoid introducing artificial borders as visual clutter, we decided to not only show lines, but also some of the shading to convey spatial relations. Since we have seen good results for conveying surface shapes by applying angle-dependent opacity [HGH*10, GNKP10], we set $\alpha = 1 - |\cos \varphi|$. Using this definition, the sulci and silhouette are very opaque, while the gyri are mostly transparent with some semi-transparent shading. With this method, we manage to preserve structure but also increase the probabilistic tractogram's visibility, as mandated by Req. 5. In Fig. 3, the differences between an opaque rendering (3a), simple semi-transparency (3b), and structure-preserving transparency (3c) can be observed.

In some cases, the given rendering may still be too obtrusive. This issue is addressed with an additional option to increase the transparency near the region in focus, i.e. close

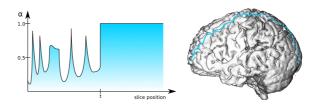


Figure 4: A sketch of opacity of the cortex along a cutting line on the surface. Left of the slice, opacity varies depending on the surface normal; on the right, it is set to 1.

to the viewer. We achieve this *selective transparency* with a similar approach as for the depth perception: $\alpha' = \alpha d^{m_t}$ Figures 3c and 3d give a comparison. It is easier to see the visualization in focus using selective transparency, however there is a clear loss of structure in the anatomical context. Users can weigh the importance of focus and context against each other using a slider for the modifier m_t .

3.3.3. Focus and Anatomical Information

The last two context-specific requirements require enhancing focus (Req. 6) and displaying anatomical information (Req. 7) such as grey and white matter boundaries. Open-Walnut offers slices for the anatomical directions: axial, coronal, and sagittal. They can be textured with the T_1 images to display the information that is requested. This increases spatial precision since users can move the slices to intersect a probabilistic tractogram if they have any doubts about the spatial position of an object. However, the slices alone look obtrusive and distract from the matter of focus. In order to integrate them with the existing cortex drawing, we introduce parameters to selectively increase the cortex opacity. This is done in a cut-away manner, as sketched in Fig. 4: for each slice, a user can choose to make the cortex on one side it opaque. We offer slices for the major anatomical directions, which have positions t_i in object space. Each of the slices has a negative (left, bottom, back) and a positive side (right, top, front), which can be selected with $v_i \in$ $\{-1,0,+1\}$. P_i denotes the current point's *i*-coordinate, and t_i is the relative slice position. For each slice, we determine which side the point lies on $(P_i - t_i)$, and whether it should be opaque $(d_i = 1)$ using $d_i = v_i \text{sign}(P_i - t_i) \in \{-1, 0, +1\}$. Finally, we compare the precomputed opacity $\alpha \in [0,1]$ with the results and choose the maximum $\max\{\alpha, d_x, d_y, d_z\}$. This method allows users to display and move slices, and to hide irrelevant parts from view by using a combination of selective opacities. Fig. 5 presents four renderings of focus and context using different combinations of selective opacity and focus-dependent transparency.

3.4. Implementation

The OpenWalnut framework has a very modular structure, in which we embedded the focus and context components of

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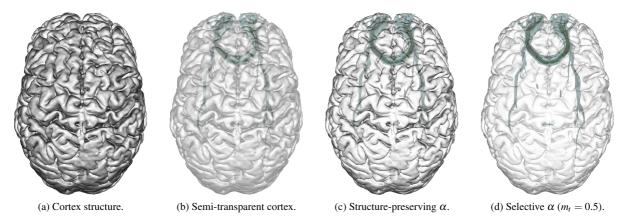


Figure 3: Preserving the cortex structure and the visibility of the probabilistic tracts.

our method as separate modules, each consisting of a basic C++ framework and GLSL shaders. Both modules employ raycasting and compute all information in real-time. First, one or more datasets are loaded, and then a user can connect any number of modules to their data, as long as a module matches the data type. This makes it very easy to apply our modules to different types of scalar field data. In order to make our methods flexible and widely applicable, we allow users to change parameters interactively using the GUI. This enables them to adapt the visualization to the specific requirements of their data.

We employ real-time raycasting with per-pixel shading, since changes of perspective or settings have no noticeable impact on performance. As expected from raycasting, the rendering window size has a significant impact on the performance, but for a moderate window size of 800x600 pixels filled entirely with the visualization, reasonable frame rates could be obtained: using a NVIDIA GeForce GTX 570 graphics card and an Intel Core i7-2600 CPU, we were able to reach a frame rate of 21.6 fps for displaying two surfaces and context. For the maximal amount of information, i.e. all four surfaces, we were still able to obtain 13.0 fps. More current models have more than three times as many cores, so we expect a massive performance increase.

4. Evaluation

In a follow-up session to the first interview, we presented the results of our work to the whole expert group and performed an informal group evaluation session, in which we presented static images of our results and asked for feedback. In addition, we requested feedback from some individual experts.

The probabilistic tract visualization was judged as suitable for exploration since long-range connectivity and value distribution were represented clearly. Due to time constraints, there were no comments about the depth perception

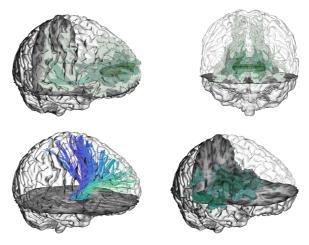


Figure 5: Two examples with probabilistic tracts, one with deterministic tracts and one with functional MRI data.

for the version presented at that point. Since there was no critique, we can only assume that the method was acceptable, but that some things could be improved. The glass brain was considered very useful for neurological visualization. According to them, the included slices are extremely helpful for orientation since one can see gray and white matter, and the ventricles. Occlusion was not seen as problematic for the context. For future work, they suggest a prior segmentation of the T_1 image to obtain a more accurate representation of the cortex.

In consequence of this lack of response about depth cues, we introduced the contours presented in Section 3. We performed an evaluation with a group of 13 visualization experts and one biology expert. Each expert was shown a series images containing different graphics (using varying ar-

rangements), and they were asked to choose a graphic based on its utilty for shape and depth perception. In addition, they were asked to comment on their choice. Comparing the probabilistic tractogram with and without contours, 7 preferred contours and 7 (including the biologist) preferred the plain version. According to the comments, contours significantly improved shape perception, but also obscured the highly probable parts of the tractogram. After adding context to the same visualizations, only 4 experts preferred the plain version, while 3 changed their mind to contours. This was a bit unexpected but the comments revealed that most users preferred a visually matching visualization. For clinical use, visibility is more important than aesthetics, so this should be validated by domain experts. Finally, we showed them an image containing nine graphics employing varying amounts of contour ($m_c \in [1.0, 2.0]$). Most users (8) preferred thin contours (1.0 - 1.1) because the dark portions were perceived to be too occlusive, some of them noting that they would prefer to use even less. Some users (5) chose moderately thick contours (1.3-1.5), and one user preferred high amounts ($m_c = 1.9$). Since most users noted that they would like to vary the contours, and some users asked for even thinner contours, we introduced a slider and set its default to very thin contours ($m_c = 0.5$). From this feedback we conclude that contours could be improved, e.g. by applying Kindlmann et al.' s approach [KWTM03] curvaturecontrolled thickness.

5. Results and Conclusions

We have presented a powerful and widely applicable tool for the visualization of probabilistic tracts in anatomical context. There is a large variety of other neurological information, which can be embedded in this anatomical context, e.g. discrimination maps (maps encoding the differences between male and female brains), or fMRI. The high flexibility allows to apply the focus visualization to any scalar field, in which intensity is connected to importance. The context visualization can supply anatomical context to any neurological data. Two examples are given in Fig. 5: a deterministic fiber bundle of the corticospinal tract and an fMRI dataset are embedded in anatomical context.

Via the GUI, users can easily adapt parameters to their datasets and displaying objective. Due to the set of interactive parameters, the tool requires a good performance. As the test results presented in Section 3.4 show, the performance with a moderate graphics card is sufficient. In the supplementary material, we included a video demonstration of our methods, in which the impact of different settings can be observed.

The tractogram display with nested surfaces gives a user an overview of long-range connectivity and spatial distribution of the values, while a single slice could only provide little spatial information. Due to the value-dependent opacity of surfaces, an intuitive clue for value distribution is provided, as the user study with visualization experts showed. In addition, it also improves the visibility of the inner surfaces as seen in Fig. 1b. To improve spatial perception, different depth cues can be added. With increasing depth, the saturation of surfaces is reduced to gray. Contours provide additional shape and depth enhancement.

The anatomical context is relatively unobtrusive yet provides a clear impression of the cortex. Users can choose to add more context using slices, and hide irrelevant regions from view using selective opacity. In cases where the context occludes too much of the focus matter, its transparency can be adjusted to reveal more information. However, this also results in a loss of cortex structure, therefore it should be carefully balanced against the focus matter.

Overall, we presented a very flexible method to embed an intuitive volumetric probabilistic tractogram in a threedimensional context, solving the particularly challenging task of avoiding mutual occlusion. Two evaluations were undertaken and most of the feedback was incorporated to improve our techniques.

6. Future Work

The work we presented improves previous efforts, as outlined in Section 3, and received positive feedback by domain experts. However, further work remains to be done.

For the probabilistic tractogram visualization, the choice of isovalues and colors for probabilistic tract surfaces can be made by users, who can change them easily using the GUI. The choice of colors has been made manually aiming to provide maximum contrast between the surfaces. While users were able to distinguish all four surfaces, the color design could be improved, e.g. by applying Wang et al.'s [WGM*08] findings. However, they could also carry additional information, e.g. to represent the brain region they belong to. While we addressed our collaborators wish for nested isosurfaces, it would now make sense to experiment with more advanced rendering techniques, such as ambient occlusion, and evaluate their effect on understandability and shape perception.

The cortex rendering with T_1 slices provides good anatomical context. However, the accuracy of the cortex rendering could be improved by employing segmentation algorithms for cortex extraction. To improve clarity, the T_1 slices could be replaced by illustrative versions. In addition to the cortex and slices, other anatomical structures such as blood vessels could be included.

Finally, before introducing our methods to clinical practice, an in-depth user study has to be carried out to evaluate aspects such as the correctness of depth perception, compare different methods, and interactively testing different parameter settings. This study should highlight the balance between flexibility and usability, and comment upon the perceived rendering performance.

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