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DeepTract: A Probabilistic Deep Learning Framework for White Matter Fiber Tractography

Itay Benou and Tammy Riklin Raviv[1,2]

[1] Department of Electrical and Computer Engineering,
Ben-Gurion University of the Negev, Beer-Sheva, Israel
[2] The Zlotowski Center for Neuroscience,
Ben-Gurion University of the Negev, Beer-Sheva, Israel

Abstract. We present DeepTract, a deep-learning framework for estimation of white matter fibers orientation and streamline tractography. We adopt a data-driven approach for fiber reconstruction from diffusion-weighted images (DWI), which does not assume a specific diffusion model. We use a recurrent neural network for mapping sequences of DWI values into probabilistic fiber orientation distributions. Based on these estimations, our model facilitates both deterministic and probabilistic streamline tractography. We quantitatively evaluate our method using the Tractometer tool, demonstrating comparable performance to state-of-the-art classical and machine learning based tractography algorithms. We further present qualitative results of bundle-specific probabilistic tractography obtained using our method.

1 Introduction

Diffusion MRI (dMRI) and tractography are useful tools in the study of white matter (WM) structures in the brain. Thanks to the ability of dMRI-based tractography to visualize complex neural tracts, it has become a key component in a variety of applications such as brain connectivity studies [6] and investigation of neurological disorders [4,8].

Standard tractography pipelines usually consist of a diffusion modeling stage, in which local fiber orientations are estimated from diffusion weighted images (DWI), followed by a tracking stage in which these orientations are translated into WM streamlines. At the heart of the modeling stage lays the inverse problem of finding the configuration of local WM fibers that gave rise to the measured DWI signal. Given the fact that a single brain voxel can contain tens of thousands of differently oriented fibers, accurate reconstruction of fiber orientations is a very challenging task.

Over the last two decades, various tractography algorithms have been proposed. While some of these methods are deterministic, i.e., provide a single streamline orientation in each voxel [2,16], others perform probabilistic tracking [5] or take a global tractography approach [11]. Nevertheless, all of these methods are model-based, in the sense that they rely on specific, pre-defined,

mathematical models for mapping dMRI signals into fiber orientation estimates. Among others, these models include the diffusion tensor model [3], Q-ball imaging [10] and spherical deconvolution [22]. Despite remarkable progress made, current model-based methods are not without limitations [13]. Each such model makes specific assumptions regarding WM tissue properties and the dMRI signal, which may vary substantially depending on the subject and the data acquisition process [19]. Furthermore, some models impose specific requirements on the data quality and acquisition protocol, e.g., a large number of gradient directions. Therefore, from the user's point of view, choosing a suitable model may prove to be a non-trivial task that requires a high level of expertise.

Machine learning (ML) and deep learning (DL) techniques have demonstrated remarkable abilities in tackling complex problems in a data-driven manner, rather than model-based, for a wide variety of domains. Recently, such approaches have been applied to the task of WM tractography, aiming to directly learn the mapping between input DWI scans and output WM tractography streamlines. By not assuming a specific diffusion model, data-driven algorithms can reduce the dependence on data acquisition schemes and require less user intervention. Neher et al. [20] pioneered this line of work, proposing a supervised ML tractography algorithm based on random forest (RF) classifier. The RF classifier was trained to predict a local fiber orientation from a discrete set of possible directions, based on the surrounding dMRI values. More recently, [21] suggested a DL model for fiber tractography, examining a fully-connected (FC) and a recurrent neural network (RNN) architectures. In contrast to [20], streamline tractography was treated as a regression problem by training a neural network to predict continuous tracking directions based on sequences of dMRI values. A similar regression-based approach was presented in [23] using a multi-layer perceptron (MLP) network. We note that all of these methods perform deterministic tractography, outputting a single streamline direction in each tracking step. Other DL-based works have focused strictly on fiber orientation estimation. For example [15] presented a deep convolutional neural network (CNN) for estimating discrete fiber orientation distribution functions (fODFs) from dMRI scans. A variation of this idea was presented in [14], using a CNN to predict the spherical harmonics (SH) coefficients from which continuous fODFs are reconstructed. These works, however, do not perform fiber tractography.

In this work we present a novel DL-based tractography framework, addressing *both* fiber orientation estimation and streamline tractography from raw DWI scans. To exploit the sequential nature of tractography data, we treat the problem as a sequential classification task by training an RNN model to predict local fiber orientations (i.e., classes) along tractography streamlines. Unlike other DL-based tractography algorithms, our model does not output a single (deterministic) fiber orientation in each tracking step. Instead, it provides a probabilistic estimation of the local fiber orientation distribution in the form of a discrete probability density function. In addition to deterministic streamline tracking, this enables the proposed method to perform probabilistic tractography by sampling random directions from the estimated distributions.

We quantitatively evaluate the proposed method using the Tractometer tool [9], demonstrating comparable results to state-of-the-art classical and DL-based tractography algorithms. We further present qualitative results of high-quality probabilistic tractograms generated by our method.

2 Methods

In the following sections we describe the proposed DeepTract framework: (1) the input model, (2) how the network learns to predict fiber orientations from DWI data, (3) how new tractograms are generated from unseen data, and (4) the implementation details of the neural network's architecture.

2.1 Input Model

The training data consists of two sets: a DWI set $\mathcal{D}$ and its corresponding whole-brain tractography $\mathbf{T} = \{S_i\}_{i=1}^{N}$ with N streamlines. Each streamline is represented by a sequence of equi-distant 3D coordinates, i.e., $S_i = \{p_j\}_{j=1}^{n_i}$.

Pre-Processing: To handle datasets acquired with different gradient schemes, we first resample the DWI set into K pre-defined gradient directions evenly distributed on the unit hemisphere, using spherical harmonics (we use K=100). Each DWI volume is then centred according to its mean and normalized by the b_0 (non-diffusion weighted) volume.

Sequential Input Model: To make our model invariant to spatial transformations, we feed it with sequences of DWI values instead of directly using the 3D coordinates of the streamlines, as suggested in [21]. Formally, given a DWI dataset $\mathcal{D}$ and a streamline segment $\{p_0, ..., p_k\}$, the input to our model is the series of DWI values measured along this segment, i.e. $\{\mathcal{D}(p_0), ..., \mathcal{D}(p_k)\}$. Notice that every input entry $\mathcal{D}(p)$ is a vector containing K DWI values, such that a single streamline segment of length n corresponds to an input tensor of size nxK.

2.2 Fiber Orientation Estimation

Aiming to facilitate both deterministic and probabilistic tractography, we require our model to provide a probabilistic estimation of local fiber orientations prior to tracking. For this purpose, a discrete representation of an fODF is obtained by sampling the unit sphere at M evenly-distributed points $\mathbf{d} = \{d_i\}_{i=1}^{M}$, each representing a possible fiber orientation. We therefore treat the problem as a classification task, where each orientation is treated as a separate "class". An additional "end-of-fiber" (EoF) class is used for labeling streamline termination points. Given an input streamline, our model predicts a probability density function $P(\mathbf{d})$ with M+1 class probabilities at each point. We note that this formulation poses a tradeoff between higher angular resolution, achieved by increasing the number of classes, and the complexity of the classification problem. We used M=724, which provides an angular quantization error of ∼3.5 degrees.

Fig. 1. Architecture of the proposed model (the graph is unrolled in time). (a) Training: Sequences of DWI values are fed into the network to produce CfODF estimations, which are compared to the true streamline direction. (b) Tracking: Once the model is trained, a new streamline is generated iteratively starting from a given seed point.

Conditional fODFs: Standard fODFs represent the *total* orientation distribution function at a voxel location p, independent of other voxels, i.e. fODF(p) = $P(\mathbf{d})$. Being sequence-based, our model has the advantage of utilizing the "history" of DWI values along an input streamline $S = \{p_0, ..., p_k\}$. Accordingly, this yields a *conditional* estimation of the local fiber orientation distribution function $CfODF(p_k \mid S) = P\left(\mathbf{d} \mid \mathcal{D}\left(p_k\right), ..., \mathcal{D}\left(p_1\right)\right)$.

Let $prob\left(S_j\right)$ denote the probability of reaching the point p via path S_j, out of all streamlines passing through p. Using the total probability theorem, a direct relation between CfODFs and total fODFs can be obtained as follows:

$$fODF\left(p\right) = \mathbb{E}_S\left[CfODF(p \mid S)\right] = \sum_j prob\left(S_j\right) CfODF(p \mid S_j) \tag{1}$$

2.3 Streamline Tractography

During training, the predicted CfODF at location p_k is compared to the "true" orientation defined by $d_{label} = (p_{k+1} - p_k)/\left\|p_{k+1} - p_k\right\|$ (see Fig. 1(a)). The corresponding class label y_{label} is the orientation in $\mathbf{d}$ which is closest to d_{label}, represent by a "1-hot" vector. Once the model is fully trained, streamline tractography can be performed on unseen DWI scans in an iterative process as illustrated in Fig. 1(b). Provided with an initial seed point p_0, the corresponding DWI values $\mathcal{D}(p_0)$ are measured and fed into the network. The network in turn provides an estimated CfODF(p_0) as output. *Deterministic* tracking is performed by stepping in the most likely fiber orientation, i.e. $\hat{d}_0 = \arg\max_d CfODF(p_0)$. Alternatively, *probabilistic* tracking can be performed by randomly sampling a direction from the CfODF. Either way, the streamline is propagated iteratively

as in standard tractography algorithms according to $\hat{p}_{k+1} = \hat{p}_k + \alpha \hat{d}_k$, where α is the step size. The process is repeated until the EoF class is predicted by the model.

2.4 Network Architecture and Loss Function

We implement our model using an RNN, specifically a gated recurrent unit (GRU) [7]. The proposed network consists of five stacked GRU layers, each containing 1000 units. We use ReLU activations for all layers but the last one, which is a fully-connected (FC) layer with a softmax activation. The loss function is the mean cross-entropy between the predicted CfODFs and the true labels.

Label Smoothing: Unlike traditional classification tasks, here the classes are geometrically structured with a well-defined angular metric. This implies that different classifications errors should be weighted according to this metric, thus a 1-hot label (i.e., a delta function) in not suitable. To account for the spatial structure of the classes, we propose to smooth the true label by convolving it with a Gaussian kernel G of width τ on the unit sphere:

$$y_{smooth}\left(d\right) = \delta\left(d - d_{label}\right) * G\left(d\right) = \frac{1}{Z} \exp\left(-\frac{\measuredangle\left(d, d_{label}\right)}{\tau}\right) \tag{2}$$

where $\measuredangle\left(d, d_{label}\right)$ is the angle between a direction d and the ground truth direction d_{label}, and Z is a normalization constant (see Fig. 2).

Entropy-Based Tracking Termination: During generative process of RNNs at test time, accumulated error may divert predictions from the training data distribution [12], towards "unfamiliar" input values. This may result in an increased uncertainty of our model's predictions, manifesting as more isotropic CfODF estimations and erroneous tracking steps. To alleviate this problem, we introduce an entropy-based tracking termination criterion, in addition to the EoF class. Specifically, we terminate the tracking process whenever the entropy of a predicted CfODF exceeds the following dynamic threshold $E_{th}\left(t\right) = a \exp\left(-t/b\right) + c$, where t is the sequence time step, and a,b and c are hyperparameters.

3 Experiments and Results

To test the performance of the proposed method we conducted the following experiments based on the ISMRM tractography challenge DWI phantom dataset

Fig. 2. Label smoothing. The original sparse label (left) is smoothed using a Gaussian kernel on the unit sphere, transferring probability mass to neighboring classes (right).

[17]: 1) Quantitative evaluation of whole brain tractography using the Tractometer tool. 2) Qualitative (visual) demonstration of bundle-specific probabilistic tractography performed by our model.

Pre-Processing: DWI scans were denoised [18] and corrected for eddy currents and head motion. For supervision, whole brain tractography was performed using Q-ball reconstruction [1] followed by probabilistic streamline tracking using the MITK diffusion tool. The resulting streamlines were randomly divided into training and validation sets using a 90%-10% split. Data augmentation was performed by reversing the orientation of all streamlines in the training set.

Training Procedure: Training was performed using the Adam optimizer with a batch size of 32 streamlines. Dropout was used with deletion probability of 0.3 to avoid overfitting, as well as gradient clipping to avoid exploding gradients.

3.1 1st Experiment - Tractometer Analysis

In this experiment we evaluate our method using Tractometer - a publicly available online tool for assessment of whole brain tractography algorithms.

Tractography: We used our trained model to perform whole brain streamline tractography. Tracking was initialized by randomly placing 200K seed points within the DWI volume. The step-size was set to $\alpha = 0.5$ (in voxels), and the entropy-based stopping parameters to a=3, b=10 and c=4.5. Tracking was also terminated for high-curvature steps (over 60 degrees), and output streamlines longer than 200mm and shorter than 20mm were discarded.

Evaluation: Tractometer evaluates a whole brain tractogram with respect to 25 gold standard streamline bundles, outputting several scores: the number of valid and invalid bundles identified (VB and IB); the percentage of valid, invalid and non-connections (VC, IC and NC); and the overlap (OL), overreach (OR) and F_1 scores of the output tractography. Please refer to [9] for full details.

Results: The whole brain tractography generated by our method is shown in Fig. 3, alongside the MITK tractography used for supervision, and the gold standard tractography of the ISMRM challenge. The Tractometer scores of our method are summarized in table 1, as well as the performance of the MITK's tractography (supervisor), the average ISMRM challenge performance, and two other DL-based methods tractography [21,23]. We also present the results obtained when training our model on the gold-standard tractography, to show the high-limit performance of our method. From the results we see that our model was able to properly generalize to the test set, performing better than the average ISMRM submission in most parameters. Moreover, while only moderately outperformed by its MITK supervisor in terms of valid connections, we note that our model achieved the best false-positive rates (OR and IB) out of all examined methods. This is most likely due to our entropy-based termination criterion, which prevents streamlines from straying off coherent bundle structures.

3.2 2nd Experiment - Probabilistic Tracking

We further performed probabilistic tracking on the phantom DWI dataset of the ISMRM challenge, by seeding from ground truth bundle-specific endpoints

Fig. 3. Whole brain tractography results - visual comparison.

Model	Connections (%)			Bundles		Avg. coverage (%)		
	VC	**IC**	**NC**	**VB**	**IB**	**OL**	**OR**	**F1**
ISMRM mean results	53.6	19.7	25.2	21.4	281	31.0	23.0	44.2
Poulin et al. [21]	41.6	45.6	12.8	23	130	64.4	35.4	64.5
Wegmayr et al. [23]	**72**	-	-	23	57	16.0	28.0	-
MITK (supervisor)	59.1	27.8	13.1	24	69	47.2	31.2	52.5
Proposed (GT supervision)	70.6	**19.5**	**9.9**	**25**	56	**69.3**	22.7	**70.1**
Proposed (MITK supervision)	40.5	32.6	22.9	23	**51**	34.4	**17.3**	44.2

Table 1. Quantitative evaluation results using Tractometer.

available on the ISMRM challenge website. Streamlines were generated in a probabilistic manner by sampling from the CfODFs, and the process was repeated several times to create a probabilistic map counting the number of "visits" in each voxel. Results for the Frontopontine tract (FPT) and Unicate Fasciculus (UF) are shown in Fig. 4, alongside the ground-truth bundles. Visual evaluation shows that the resulting bundles are in-line with the ground truth tractograms. Also in-line with probabilistic tractography, note that higher probabilities were assigned to the bundles' core, gradually decreasing towards their endpoints.

4 Summary and Discussion

We presented the first deep learning framework which is capable of performing **both deterministic and probabilistic** streamline tractography directly from raw DWI data. We showed that by combining an RNN-based sequential processing approach with a discrete classification framework, our model provides reliable probabilistic fiber orientation estimations, i.e., CfODFs. In a quantitative evaluation, the proposed method demonstrated comparable performance to state-of-the-art classical and DL-based tractography algorithms. While larger dMRI and tractography training datasets are needed to further progress this area of research, the results obtained demonstrate the potential of DL methods for WM tractography applications.

Fig. 4. Bundle-specific probabilistic tractography results of the proposed method.

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