A variational framework for distortion correction, segmentation and cortical parcellation of diffusion MRI

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***Abstract*—In whole-brain connectivity analysis of diffusion MRI (dMRI) data, an accurate delineation of the white-matter and grey-matter interfaces is required. While high-standard segmentation is readily available for structural MRI, dMRI typically present significant cerebrospinal fluid contamination effects, mainly derived from its typical low resolution, and severe geometrical distortions. We propose a segmentation-registration variational framework that exploits the detailed anatomy extracted from structural MRI as shape-prior. We use an "active contours without edges"-like model to search for a deformation field that optimally maps the shape prior on multivariate dMRI-derived data in diffusion space, registering structural and diffusion coordinate spaces and implicitly segmenting dMRI data. The approach proven the intrinsic coupling of segmentation and distortion correction and we evaluate its results on a digital simulated phantom and real datasets. Therefore, precise and consistent cortical parcellation on dMRI is straightforward by projection from T1 space, avoiding additional registration, segmentation and/or surface matching steps.**

***Index Terms*—diffusion MRI, susceptibility distortion, segmentation, registration, parcellation, shape-prior.**

I. Introduction

DIFFUSION magnetic resonance imaging (MRI) is a widely used family of MRI techniques [1] which recently has accounted for a growing interest in its application to structural connectivity analysis of the brain. This emerging field exploits diffusion MRI (dMRI) data to derive the local axonal structure at each imaging voxel [2] and estimate a whole-brain mapping of fiber tracts represented by trajectories reconstructed from the local information. This comprehensive map of neural connections of the brain is called the *connectome* [3, 4]. The connectome analysis is a promising tool for neuroscience and clinical applications.

why? or references?

Early dMRI research focused mainly on the improvements of imaging methodologies better understanding the diffusion effect and improving image reconstruction methodologies. Currently, the connectome extraction and analysis relies on a large amount of sophisticated computational techniques [5, 6] including acquisition, reconstruction, modeling and model fitting, image processing, fibre tracking, connectivity mapping, visualization, group studies, and inference. This growing complexity has given rise to challenging issues towards reliable structural information about the neuronal tracts [7–9], and statistical analysis [10]. Here we shall address three tasks included within the image processing stage in a unified approach: brain tissue segmentation in diffusion space (subsection I-B), correction of geometrical distortions (subsection I-C), and structural image registration to diffusion coordinate space (subsection I-D). These tasks are generally solved independently, or combined in pairs. However, there exist fundamental coupling relationships that can be exploited to obtain a simultaneous solution to the three problems. This joint approach satisfactory impacts the downstream outcomes of the whole pipeline with the increase of the internal consistency.

A. dMRI data overview

VERY brief look into signal generation HERE and cite reconstruction methods.

dMRI data are usually acquired with echo-planar imaging (EPI) sequences as they allow for very fast acquisitions, but they are known to suffer from geometrical distortions and artifacts due to, mainly, three sources: the subject motion in between acquiring different sampling directions, the induced *Eddy currents* on the scanner coils, and, finally, distortions caused by the magnetic susceptibility inhomogeneity present at tissue interface. In this paper, we restrict ourselves to the last one, as it accounts for the major impact in the connectome

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analysis. *Susceptibility distortions* happen along the phase-encoding direction, and are most appreciable in the front part of the brain for the strong air/tissue interface surrounding the frontal sinuses. Two implications are associated to this artifact: the signal loss caused on highly distorted regions, and a significant added difficulty in registering with structural images (e.g. T1-weighted).

dMRI data is strongly affected by partial volume effects (PVEs) [11], which appear when several different tissues, or signal emitters, are present in the same imaging unit, producing an averaged intensity. The effect is directly related to the low resolution achievable with dMRI (typically around $2.0 \times 2.0 \times 2.0mm^3$). An additional complication specific to dMRI is the cerebrospinal fluid (CSF) *contamination* [12], that is a particular PVE in which the signal sensed inside the affected voxel is linear with respect the grey matter (GM) and white matter (WM) contributions, but non-linear with respect CSF.

Define *raw data*

Generally speaking, alongside the difficulty posed by the low resolution, dMRI processing is also challenging due to the *direction dependency* of raw data.

Introduce here what are b0, fa, md, and direction dependency problem.

These $b = 0$ volumes (also called *EPI baseline*, low-b, or just B0) are acquired without direction gradient as reference, and they present a T2-like contrast.

B. dMRI segmentation

A precise delineation of the CSF, GM and WM interfacing surfaces is required with sub-pixel resolution. The resulting segmentation is necessary to perform the majority of tractography algorithms and it is required to filter the resulting tractogram. The GM-WM interface is necessary to locate the starting and ending points of the detected fiber bundles, and CSF-WM surface is critical for pruning spurious and discontinued fiber bundles.

A number of methodologies have been proposed for dMRI segmentation, ranging from intensity thresholding to atlas-based segmentation. The first approach is performed on the fractional anisotropy (FA) [13], a well-known scalar map derived from dMRI data which depicts the isotropy of water diffusion inside the brain. Although this methodology was popular among the premier tractography studies, they were generally limited to certain regions or significant fiber tracts, and thus, it cannot be applied in whole-brain tractography. Early approaches to dMRI segmentation include level set formulations using scalar maps of direction invariants derived from the tensor model [14], directly on the diffusion raw data [15], or finding alternative diffusion representations [16]. Even though this latter case was restricted to the extraction of the corpus callosum from a real dataset, the density of the components of the diffusion tensor are approximated by multivariate Gaussians for first. Iterative clustering performed on the B0 volumes of dMRI data was proposed by [17]. Later studies investigated the application of probabilistic frameworks combining mixtures of gaussians, Markov Random Field (MRF) and labeling fusion techniques [18] using as features widely-used dMRI-derived scalar maps as FA or mean diffusivity (MD). A similar framework combining co-registered structural information (T1 weighted) with *independent orthogonal invariants* derived from the dMRI tensor model was proposed by [19]. Some proposals suggest the use of the raw diffusion data (directionally dependent) to avoid fitting a certain model [20]. In [21], graph-cuts voxel-based techniques are proposed using the most common diffusion tensor derived features. Further developments of the probabilistic approach have been proposed adding more scalar maps as features and a more detailed treatment of PVE [22].

A number of methods have been proposed using features not directly derived from dMRI data. Segmentation obtained by co-registering structural T1-weighted images will be covered in subsection I-D. Some other works delay the segmentation task after the tractogram is obtained, performing clustering on features derived on the tracts alignment [23], combined tract registration [24] or using tractography atlases [25]. However, methods based on tractography usually address the tractogram segmentation problem, to later combine the solution to answer the whole-brain segmentation problem.

None of the presented methods have claimed for definite results, mainly due to the lack of a *gold-standard* evaluation methodology. Most of them are tested only on certain regions , or do not provide sub-pixel resolution results [17–21]. Generally, results obtained with high resolution atlas co-registration (subsection I-D) are more compelling, minimizing the activity on this line which is currently being considered to be included in reconstruction algorithms [26]. *Golden-standard* evaluation frameworks have been proposed for the segmentation validation [27] on the task of lesion detection in visceral organs.

C. Correction for susceptibility distortions

One approach to correcting the susceptibility distortions was proposed with the earliest EPI sequences used in functional MRI, and relies on the acquisition of extra MRI data. Generally, a gradient echo sequence (GRE) is used to obtain a map of magnitude and phase of the actual magnetic field inside the scanner. Based on this *fieldmap* and the theory underlying the distortion, [28] proposed a correction methodology. A number of forked and improved methodologies have been developed to correct for the susceptibility distortion and received the generic name of "fieldmap correction" techniques [29, 30].

Some other retrospective methodologies do not make use of the fieldmaps, as explicitly modeling the distortion [31], registering with (anatomically correct) T2-weighted MRI [32–35] (see subsection I-D), or acquiring an extra B0 image with reversed phase encoding direction [36].

To our knowledge, there exists no study on the impact of the susceptibility distortion over the subsequent tractography and connectome analyses. However, a comparison of the diverse correction techniques is found in [37]. This study claimed that fieldmap correction methodologies are not entirely accurate and reliable, even though the method is correct in principle. This conclusion was later confirmed by [35]. Additional concerns regarding fieldmap correction are the requirement of an

extra acquisition (that is not always met or it is impractical), or the accuracy of the measured fieldmap that is sensitive to various effects (such us respiration, blood flow, etc.). All these factors have turned susceptibility distortion in EPI sequences an active field of research for the last 10 years.

D. Structural information co-registration

The last addressed task in the image processing stage of the studied connectivity analysis pipelines is the structural information co-registration. The need for this registration step is mainly raised when defining the nodes of the connectivity matrix. This definition step is named *cortical parcellation* as it imposes the regions that will be considered to cluster the fiber bundles reaching the WM-GM surface. The common procedure to accomplish this clustering is using a predefined parcellation in a high-resolution structural T1-weighted atlas. The second goal that has justified the applicability of structural images co-registration is susceptibility distortion correction as discussed in subsection I-C. In any case, susceptibility distortion hinders a rigid-registration solution to this end. Additionally, when applying non-linear intensity-based registration algorithms other difficulties have to be addressed as the significant PVE in the WM-GM layer, or the inherent inadequacy of the B0 contrast (the only *directionally independent* existing in the raw dMRI data) due to the almost null difference in intensity between WM and GM pixels. Early registration methods appeared targeting the distortion correction. They quickly standardized the choice of T2 as anatomically correct source to be registered against the B0 in dMRI. B0 images have a very similar contrast to T2 weighted due to the duality of acquisition procedure. However, parcellation is defined in T1 weighted space, adding an additional registration step missing on the literature due to the novelty of the task. Even though this registration step has a very low complexity compared to the remaining tasks of the pipeline process, it is one additional source of inconsistency and unreliability.

One of the first proposals is [32], where the deformation field is modeled with B-Splines, the cost function is least squares and optimized in a multi-resolution gradient descent strategy. Their method is evaluated in both synthetic and real 2D images. Similarly, [33] proposed a spline-based deformation but including a weighting factor proportional to the Jacobian of the transform to correct the intensity of the undistorted data. They also use the log of the signal to enhance the low-signal regions and optimize with a gradient descent algorithm the mutual information of the mapping. The basis in the procedure is still the most extended. For instance, [37] also proposed a B-Spline registration providing quantitative comparisons with fieldmap correction methods. Recent approaches take into account the signal loss due to dephasing [34], or introduce more complex variational frameworks [35].

The significant benefits of exploiting the anatomical MRI when segmenting the dMRI data have been demonstrated [38], justifying the use of the shape prior information. To our knowledge, there is no study simultaneously taking advantage from segmentation or distortion correction tasks to be applied to the co-registration problem.

E. Summary

Therefore, the problems of precise segmentation in dMRI-space and the spatial mapping between these contours and the corresponding surfaces in anatomical images bear significant redundancy. Once the spatial relationship between T1-weighted (T1) and dMRI space is established, the contours which are readily available in T1 space can simply be projected on to the dMRI data. Conversely, if a precise delineation in dMRI space was achieved, the spatial mapping with T1-space could be derived from one-to-one correspondences on the contours. However, neither segmentation nor registration can be performed flawlessly, if considered independently.

In this paper we propose a novel registration framework to simultaneously solving the segmentation, distortion and cortical parcellation challenges, by exploiting as strong shape-prior the detailed morphology extracted from high-resolution anatomically correct MRI. Indeed, hereafter we assume this segmentation problem in anatomical images is reliably and accurately solved with readily available tools. After global alignment using existing approaches, the remaining spatial mismatch between anatomical and diffusion space is due to susceptibility distortions. Finally, we need to establish precise spatial correspondence between the surfaces in both spaces, including the tangential direction for parcellation. Therefore, we can reduce the problem to finding the differences of spatial distortion in between anatomical and dMRI space. We thus reformulate the segmentation problem as an inverse problem, where we seek for an underlying deformation field (the distortion) mapping from the structural space into the diffusion space, such that the structural contours segment optimally the dMRI data. In the process, the one-to-one correspondence between the contours in both spaces is guaranteed, and projection of parcellisation to dMRI space is implicit and consistent.

(Rewrite) We test our proposed joint segmentation-registration model on two different synthetic examples. The first example is a scalar sulcus model, where the CSF-GM boundary particularly suffers from PVE and can only be segmented correctly thanks to the shape prior and its coupling with the inner, GM-WM boundary through the imposed deformation field regularity. The second case deals with more realistic dMRI data stemming from phantom simulations of a simplistic brain data. Again, we show that the proposed model successfully segments the dMRI data based on two derived scalar features, namely FA and MD, while establishing an estimate of the dense distortion field.
The rest of this paper is organized as follows. First, in section II we introduce our proposed model for joint multivariate segmentation-registration. Then we provide a more detailed description of the data and experimental setup in section III. We present results in section IV and conclude in section V.