Robust and efficient linear registration of white-matter fascicles in the space of streamlines

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ABSTRACT

The neuroscientific community today is very much interested in analyzing specific white matter bundles like the arcuate fasciculus, the corticospinal tract, or the recently discovered Aslant tract to study sex differences, lateralization and many other connectivity applications. For this reason, experts spend time manually segmenting these fascicles and bundles using streamlines obtained from diffusion MRI tractography. However, to date, there are very few computational tools available to register these fascicles directly so that they can be analyzed and their differences quantified across populations. In this paper, we introduce a novel, robust and efficient framework to align bundles of streamlines directly in the space of streamlines. We call this framework Streamline-based Linear Registration. We first show that this method can be used successfully to align individual bundles as well as whole brain streamlines. Additionally, if used as a piecewise linear registration across many bundles, we show that our novel method systematically provides higher overlap (Jaccard indices) than state-of-the-art nonlinear image-based registration in the white matter. We also show how our novel method can be used to create bundle-specific atlases in a straightforward manner and we give an example of a probabilistic atlas construction of the optic radiation. In summary, Streamline-based Linear Registration provides a solid registration framework for creating new methods to study the white matter and perform group-level tractometry analysis.

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Introduction

The neuroscientific community today is very much interested in analyzing specific white matter fascicles like the arcuate fasciculus and the language pathways (Catani et al., 2005; Wakana et al., 2007; Catani and Thiebaut de Schotten, 2008), the corticospinal tract, the optic radiations or the recently discovered Aslant tract (Catani et al., 2013) to study sex differences, lateralization and many other connectivity applications. Hence, experts have been manually segmenting and more recently automatically segmenting or clustering white matter bundles from diffusion MRI (dMRI) tractography (Wassermann et al., 2013; Garyfallidis et al., 2012; O'Donnell and Westin, 2007; Guevara et al., 2012; Jin et al., 2014). Once bundles are extracted, the white matter anatomy can be studied. This domain is also known as *virtual in vivo dissection* of white-matter tracts (Catani et al., 2002a), where an expert will use regions of interest (ROIs) to filter out unnecessary streamlines and dissect a *bundle of interest*. After the bundles of interest have been obtained from different subjects, neuroscientists need to calculate statistics and do connectivity studies (Hagmann et al., 2003; Griffa et al., 2013). However, to date, there are very few computational tools

available to analyze and quantify these white matter bundles in the space of streamlines.

Existing white matter analysis techniques often map FA values or diffusion kurtosis indices or other macrostructure and microstructure indices (Assaf et al., 2013) on the streamlines of specific bundles. This is usually called *tractometry* (Bells et al., 2011). In tractometry, an average index value is calculated for every streamline in the bundle. Others project their indices into an average streamline (Corouge et al., 2006; Goodlett et al., 2009; Yeatman et al., 2012). These techniques are applied to individual bundles of individual subjects but most scientists are interested to study those for group comparisons. This is where registration of bundles becomes crucial and a challenging problem.

Registration is critical even though we may work with pre-segmented bundles because the correspondence problem is still not solved across subjects even for the same type of bundle. For example, as previously shown in Catani et al. (2007), notice the difference in shape and density for 5 arcuate fasciculi from 5 subjects shown in Fig. 1A. From our investigations, this is very common with real datasets.

Currently, when neuroscientists want to do group analysis of specific bundles of interest they still have to rely on full-brain image-based methods for registration (Groeschel et al., 2014). In particular, this is being used in a tract-based spatial statistics (TBSS) (Smith et al., 2006) and voxel-based morphometry (VBM) style analysis (Ashburner and

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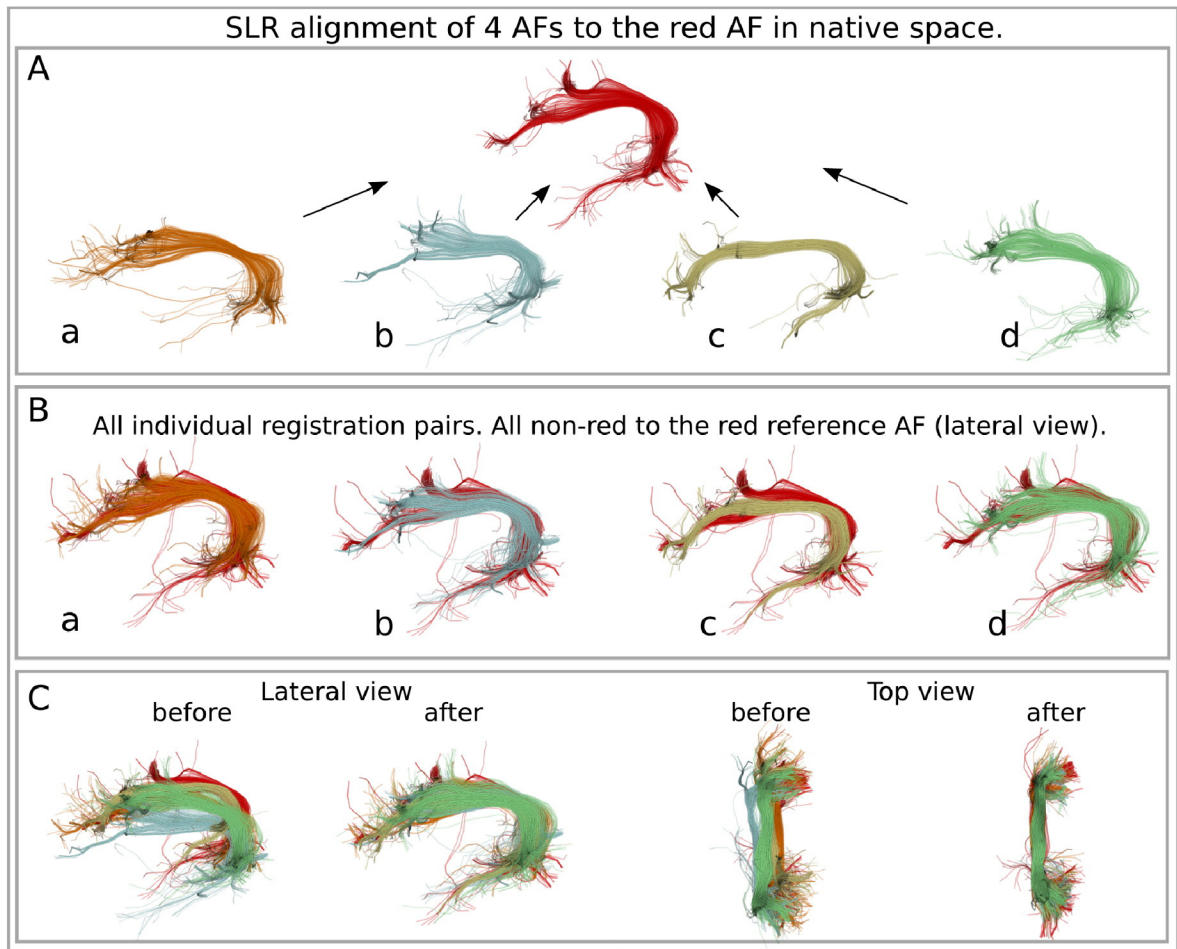   *E-mail address:* garyfallidis@gmail.com (E. Garyfallidis).

Fig. 1. A. Illustration of the concept of registration of 4 bundles to a reference bundle using Streamline-based Linear Registration (SLR). SLR registers all non-red arcuate fasciculi (AF) (moving bundles) to the red AF (fixed/reference bundle). All AFs are from different subjects of USherbrooke dataset. B. All registration pairs are shown in the space of red AF after SLR is completed. C. As they are in their native space coordinates, we show a lateral and top view of all the 5 AFs before and after registration as shown in A & B. For greater visibility, in B we show the individual registered pairs in lateral views. Although the bundles of interest have important shape differences, the SLR aligns them directly on the red AF. The streamlines shown here are visualized with semi-transparency to increase simultaneous visibility of both fixed and moving bundles.

Friston, 2000). In contrast, it is known that if landmarks have been extracted (in our case, the dissected bundles of interest), a landmark-based registration is more appropriate, as long as the landmarks correspond accurately across subjects (Sotiras et al., 2013).

Furthermore, some problems are truly challenging for volumetric methods such as used in VBM and TBSS. For example, there is an increase of *lateralization* studies (Lebel and Beaulieu, 2009; De Schotten et al., 2011), where several groups look at differences between left and right bundles of the same subject. For these studies, methods are needed which can register left and right structures of the same subject to study their differences in shape and integrity. Another example is with severely injured or diseased brains, where we can see large areas in the images with low intensity and contrast, e.g., because of a large tumor or inflammation. In these cases, the classical image-based registration techniques can fail because they use the entire extent of the brain (with the affected areas included) to drive the registration. However, if individual landmarks can be identified there is still the possibility for a successful registration of these landmarks.

In this paper, we show that using Streamline-based Linear Registration (SLR), we can efficiently and robustly register bundles of interest of the same subject for lateralization studies or from different subjects for population comparisons (see Fig. 1).

Going from a voxel-based registration to a streamline-based registration has some important advantages: a) Streamlines integrate information across many voxels. This is a property that can improve the alignment of the white matter as the points of the cortical mesh can improve the alignment of the gray matter in T1 images. b) Streamlines are defined in physical space coordinates (floating point coordinates) in contrast with standard MR images which are discretized on a grid with integer coordinates and need the application of interpolation when transformed. This can be advantageous for streamlines which do not require interpolation when transformed. However, such a representation raises computational challenges, illustrated in Fig. 2, which we summarize here:

- The streamlines in the bundles are often noisy and spurious.
- Even homologous bundles have locally large shape and density differences.
- The neighborhood of a streamline is not well defined.
- Comparing streamlines is a computationally expensive process.

To the best our knowledge, there has not been a simple, robust and efficient method to solve these problems. Our proposal consists on minimizing a cost function that takes into account both, local and global properties of the bundles, which can be computed robustly and efficiently directly in the native space of streamlines, even in the presence of missing data, noise and important shape differences.

Background

Many different approaches have been published during the last decades that can be used for registering dMRI datasets. We can divide