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Groupwise structural parcellation of the whole cortex: A logistic random effects model based approach

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ABSTRACT

Current theories hold that brain function is highly related to long-range physical connections through axonal bundles, namely *extrinsic connectivity*. However, obtaining a groupwise cortical parcellation based on extrinsic connectivity remains challenging. Current parcellation methods are computationally expensive; need tuning of several parameters or rely on ad-hoc constraints. Furthermore, none of these methods present a model for the cortical extrinsic connectivity of the cortex. To tackle these problems, we propose a parsimonious model for the extrinsic connectivity and an efficient parceling technique based on clustering of tractograms. Our technique allows the creation of single subject and groupwise parcellations of the whole cortex. The parcellations obtained with our technique are in agreement with structural and functional parcellations in the literature. In particular, the motor and sensory cortex are subdivided in agreement with the human homunculus of Penfield. We illustrate this by comparing our resulting parcels with the motor strip mapping included in the Human Connectome Project data.

1. Introduction

The human brain is arranged in areas based on criteria such as cytoarchitecture, functional specialization or axonal connectivity (Brodmann, 1909; Thirion et al., 2014; Thiebaut de Schotten et al., 2016). Parceling the cortex into such areas and characterizing their interaction is key to understanding how the brain works. Nowadays it is accepted that axonal connectivity plays a fundamental role in the interaction between brain regions (Schmahmann and Pandya, 2006). Moreover, current theories hold that long-range physical connections trough axonal bundles, namely *extrinsic connectivity*, are strongly related to brain function, for example, this has been shown in macaques (Passingham et al., 2002). Therefore, understanding how the cortex is arranged based on its extrinsic connectivity can provide key information in unraveling the internal organization of the brain.

Diffusion MRI (dMRI) enables the in vivo exploration of extrinsic connectivity and other aspects of white matter anatomy on the brain. However, in using diffusion MRI to infer long-distance connectivity, several challenges arise. A primary issue is the spatial resolution of diffusion imaging: it is several orders of magnitude coarser than axonal diameters (millimeters vs. micrometers) (Van Essen et al., 2014), making hard to infer some brain pathways. In addition, there is as yet no quantitative measure of the strength of connections from diffusion (Jbabdi and Behrens, 2013). Given these general limitations, obtaining a cortical parcellation based on extrinsic connectivity remains challenging (Van Essen et al., 2014; Jbabdi and Behrens, 2013). Moreover, most current parceling techniques compute either single-subject or groupwise parcellations. Single-subject techniques work by refining other parcellations (Clarkson et al., 2010), which introduces a bias in the resulting parcellation; parceling only part of the cortex (Lefranc et al., 2016; Roca et al., 2009; Thiebaut de Schotten et al., 2014, 2016) or using ad-hoc metrics to compare extrinsic connectivity (Moreno-Dominguez et al., 2014). Meanwhile, existing groupwise methods rely on average connectivity profiles (Clarkson et al., 2010; Roca et al., 2010), which prevents obtaining single subject parcellations; seek a matching across subjects after independent parcellations (Moreno-Dominguez et al., 2014), relying on possible noisy results, or need fine tuning of parameters, as the expected number of clusters to find (Parisot et al., 2015).

In this work, we present a parsimonious model for the cortical connectivity alongside an efficient parceling technique based on it. We summarize both contributions in Fig. 1. Our model assumes that the cortex is divided in patches of homogeneous extrinsic connectivity. That is, nearby neurons in the cortex share approximately the same long-range physical connections, we call this the *local coherence*

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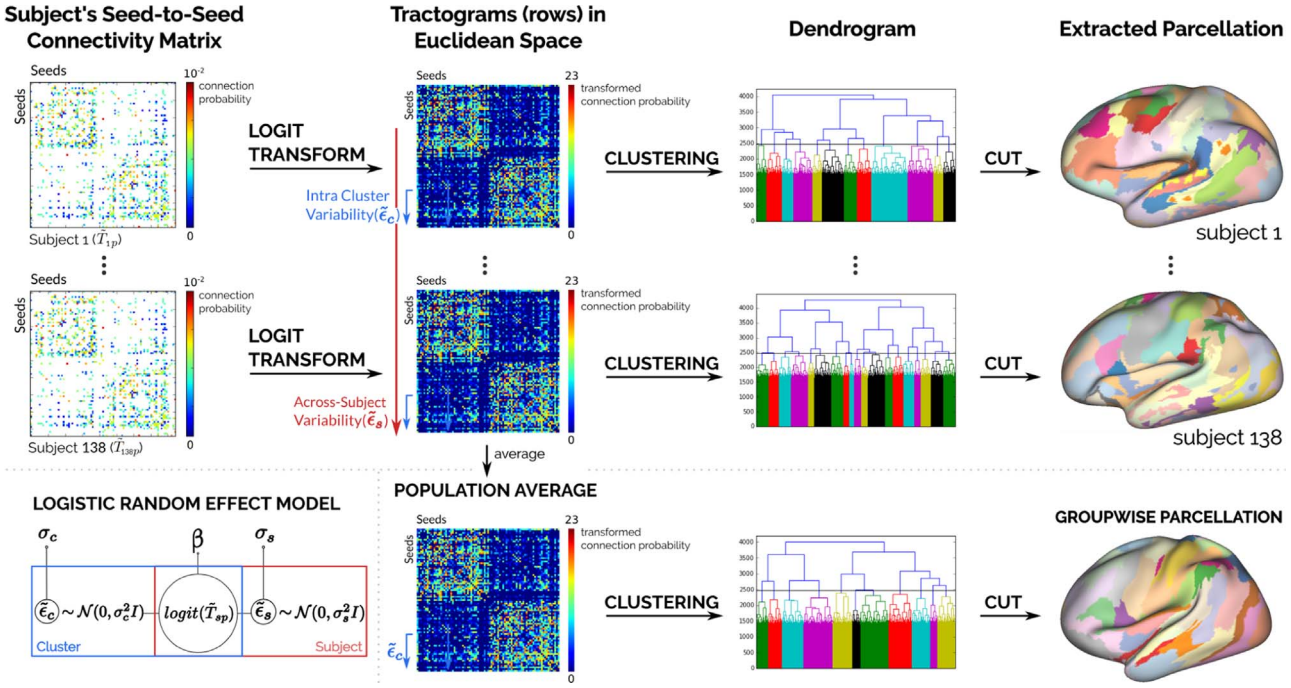

Fig. 1. Lower left corner: graphical model of the linear relationship between the tractogram of a subject s for a seed p ($\tilde{T}_{sp}$); and the intra-cluster ($\tilde{\epsilon}_c$) and across-subject ($\tilde{\epsilon}_s$) variability of the seed's patch. We transform the tractograms into a Euclidean space while explicitly accounting for the variability. This allows us to use well known clustering techniques and compress different levels of granularities for a same parcellation in a dendrogram.

criterion. Our assumption is based on histological results in the macaque brain (Schmahmann and Pandya, 2006). Inspired by statistical models for clustered data (Pendergast et al., 1996), our model accounts for the variability in the axonal connections of neurons within a patch and for variability in patch boundaries across subjects. Our parceling technique allows us to create single subject and groupwise parcellations of the whole cortex in agreement with extant parcellations.

We validate our technique by taking advantage of data available from the Human Connectome Project (HCP). Using our technique, we compute single subject and a groupwise parcellations. In this work we will focus on the groupwise case. For results of our method on the single-subject case please refer to Gallardo et al. (In press). Here, we first assess the consistency of our groupwise parceling technique by comparing the groupwise parcellations of three disjoint groups of 46 subjects from the HCP. We also show that our technique computes a similar parcellation to the one obtained by Thiebaut de Schotten et al. (2016) when parceling only the frontal cortex. Later, to test the functional specialization of our frontal lobe parcels, we use a database of meta-analysis of fMRI studies (Yarkoni et al., 2011), as in Thiebaut de Schotten et al. (2016). After, we show that our groupwise parcels subdivide some well-known anatomical structures by comparing our results against Desikan's atlas (Desikan et al., 2006). Also, we show the functional specialization of some of our parcels by comparing against results from Glasser et al. (2013). Finally, we compare our groupwise parcellation of 138 subjects against the multi-modal parcellation of Glasser et al. (2016). We show that, while the parcellations boundaries differ, our parcels show similar or better functional specialization, specially for motor related tasks.

This work is organized as follows: In the Section 2 we present our model for cortical connectivity and frame tractography within our model. Also, we present both our single-subject and groupwise case methodologies to parcellate the cortex. In the Section 3 we present our results on HCP data. We then discuss our results and position ourselves with respect to the state of the art in the Section 4. Finally, in the last section we provide our conclusions.

2. Methods

2.1. Cortical connectivity model and tractography

Our model assumes that the cortex is divided in clusters of homogeneous extrinsic connectivity. That is, nearby neurons in the cortex share approximately the same long-ranged physical connections, we call this the *local coherence criterion*. Our assumption is based on histological results in the macaque brain (Schmahmann and Pandya, 2006). As in clustered data models in statistics (Pendergast et al., 1996), we allow intra-cluster and across-subject variability in the connectivity. We formalize this concept as:

$$K = \bigcup_{i=1}^{k} K_i, \quad \forall_{1 \le i,j \le k}, \quad i \neq j \rightarrow K_i \cap K_j = \varnothing \wedge \mathrm{conn}(K_i) \neq \mathrm{conn}(K_j) \tag{1}$$

where the set of points on the cortex K is the disjoint union of each cluster K_i and $\mathrm{conn}(\cdot)$ is the extrinsic connectivity fingerprint of a cluster. We will make the notion of variability explicit in Eq. (3). In this work, the connectivity fingerprint of a seed-point in the brain is a binary vector denoting to which other seed-points it is connected through axonal bundles. That is, the physical connections of a point $p \in K_i$ in the brain are represented by its connectivity fingerprint $\mathrm{conn}(p) = \mathrm{conn}(K_i)$.

Currently, the most common tool for estimating the extrinsic connectivity fingerprint of a point in vivo is probabilistic tractography (Jbabdi and Behrens, 2013). Given a seed-point in the brain, probabilistic tractography creates a *tractogram*: an image where each voxel is valued with its probability of being connected to the seed through axonal bundles. One way of calculating these probabilities is with a Monte Carlo procedure, simulating the random walk of water particles through the white matter (Behrens et al., 2003). Each one of these paths is known as a streamline. If we model these streamlines as Bernoulli trials, where we get a value for the connection from our seed with other points (1 if they connected by the streamline, 0 if not) (Behrens et al., 2003), then, we can model the tractogram of the subject s in the seed-point p as: