

# CONNECTIVITY-BASED PARCELLATION OF THE CORTICAL SURFACE USING Q-BALL IMAGING

Pamela Guevara<sup>1,2</sup>, Muriel Perrin<sup>1,2,3</sup>, Pascal Cathier<sup>1,2</sup>, Yann Cointepas<sup>1,2</sup>, Denis Rivière<sup>1,2</sup>, Cyril Poupon<sup>1,2</sup> and Jean-François Mangin<sup>1,2</sup>

<sup>1</sup> CEA, Neurospin, Gif-sur-Yvette, France

<sup>2</sup> Institut Fédératif de Recherche 49, Gif-sur-Yvette, France

<sup>3</sup> GE Healthcare, Buc, France

## ABSTRACT

This work exploits the idea that each individual brain region has a specific connection profile to create parcellations of the cortical surface using MR diffusion imaging. The parcellation is performed in two steps. First, for each vertex of a cortical surface mesh, a connection profile is computed using a probabilistic tractography framework. The tractography is performed from q-ball fields using regularized particle trajectories. The raw connectivity matrix is smoothed over the surface to account for a reasonable uncertainty on the tractography result. A cortical surface parcellation in 36 large gyri is used to reduce the connectivity profiles dimension. For each vertex, interconnection with the gyri is determined, leading to a connectivity profile made up of only 36 connection strengths. These profiles are clustered on a gyrus by gyrus basis using a k-means approach including spatial regularization. The reproducibility of the results is studied for three subjects.

**Index Terms**— diffusion, connectivity, q-ball imaging, parcellation

## 1. INTRODUCTION

Diffusion Magnetic Resonance Imaging is a probe allowing noninvasive studies of the microscopic structure of brain tissues. For instance, inside white matter, preferential orientations of fiber bundle axonal membranes induce anisotropy of the local Brownian motion of water molecules. The fiber orientation can be inferred from this anisotropy. Hence, one of the most attractive applications of diffusion imaging is the tractography of white matter fiber bundles and the inference of brain connectivity.

Tractography has been developed first from diffusion tensor imaging (DTI) [1], a technique indicating for each voxel the direction of highest amplitude of the diffusion process. Assuming that this direction corresponds to the main fiber orientation inside the voxel, some of the tracts can be reconstructed step by step [2, 3, 4]. Unfortunately this simplistic approach can not resolve fiber crossings, which are numerous in the brain. The emergence of High Angular Resolution Diffusion Imaging (HARDI) provides the opportunity to model better water mobility in fiber crossing. Hence more reliable mapping of the corticocortical pathways can be achieved, which is exploited in this paper. There is no consensus yet on the best way to interpret HARDI data for tractography [5]. The main issue is the choice of the method used to build fiber orientation distribution functions (ODFs). In this paper, we explore the potential of q-ball imaging, a method pushing further than DTI the idea that the fiber

directions can be inferred from the local maxima of the amplitude of water molecule radial displacements [6, 7].

The network of anatomical connections linking the neuronal elements of the human brain is still largely unknown [8, 9]. Therefore, compiling the connection matrix or the “connectome” of the human brain represents an indispensable foundation for basic and applied neurobiological research [9]. One of the challenges faced by this research program is that the structural elements of the human brain, in terms of interesting nodes for the connection matrix, are difficult to define. Attempting to assemble the human connectome at the level of single neurons is unrealistic and will remain infeasible at least in the near future. Nevertheless, a higher scale of representation is more attractive: there is overwhelming evidence that human cognitive functions depend on the activity of large populations of neurons in distributed network. Unfortunately, brain areas and neuronal populations are difficult to delineate.

No single universally accepted parcellation scheme currently exists for the human brain. In the cerebral cortex, neurons are arranged in an unknown number of anatomically distinct regions and areas, perhaps on the order of 100 or more [10]. The most standard parcellation, which has been proposed by Brodmann one hundred years ago from cytoarchitectonic criteria, can not be mapped *in vivo*. Anyway, while cyto- and myeloarchitectonics are powerful methods to highlight anatomical segregation, animal studies have shown that further parcellations of architectonically homogeneous areas can be obtained using connectivity [11]. Therefore, the most promising avenue for parcellating the brain and compiling the brain connectome originates from the notion that individual brain regions maintain individual connection profiles [9]. What defines a segregated brain region is that all its structural elements share highly similar long-range connectivity patterns, and that these patterns are dissimilar between regions. These connectivity patterns determine the region’s functional properties [12], and also allow their anatomical delineation and mapping.

Tractography has been used previously to distinguish thalamic areas using a lobar parcellation of the cerebral cortex as input [13]. For this application, each thalamus voxel was attached to the lobe with the strongest connection. The idea that the whole patterns of connectivity can be used to identify areal boundaries has been demonstrated in the human medial frontal cortex [14]. First, connection strength from voxels within the medial frontal cortex to all other voxels in the rest of the brain were obtained. Connection profiles were then used to calculate a cross-correlation matrix, which was examined for the existence of distinct clusters of voxels with shared connection patterns. The resulting clusters matched an independent clustering of the same region obtained from functional

imaging.

In this paper, we extend further the idea of parcellating the cerebral cortex using connectivity profiles. The main difference with the work mentioned above is that we address the parcellation of the complete cortex. We refine a previous attempt performing this parcellation from a voxel-based segmentation of the cortical mantle [15]. In this paper the cortex is represented by a mesh of the interface between grey and white matter, which allows the method to embed the constraint that the parcellation should be constant across the cortical layers. Addressing our goal following the approach of the Oxford group would involve the difficult clustering of a huge cross-correlation matrix. To overcome this problem, our parcellation framework relies on an initial macroscopic parcellation of the cortex into 36 large gyri performed with a pipeline of processing [16] provided in BrainVISA framework (<http://brainvisa.info>). This initial parcellation is used to reduce each vertex connectivity profile to a short vector of 36 values, namely the strength of connection to each of the gyri. A second use of the gyral parcellation is to split the initial global clustering problem into 36 smaller problems: the gyri are clustered one by one. The justification leading to the use of a gyral parcellation to reduce the complexity of the problem lies in the strong link between this large scale division of the cortex and its functional and architectonic organizations [17]. An additional argument stems from the hypothesis that the fiber bundle organization is deeply related to the folding patterns of the cerebral cortex [18].

In the following, we provide first a brief overview of our data and of the fiber ODF choice. The next part describes our “probabilistic” tractography framework [19], dedicated to q-ball fields and based on regularized particle trajectories. Then, we describe the method dedicated to the clustering of the cortical surface vertices from the connectivity profiles, based on a k-means principle including a Markov Random Field regularization procedure. The method is tested in the right postcentral gyrus for three brains.

## 2. METHOD

### 2.1. MRI Data and Fiber Orientation Distribution Function

We worked with three subjects data of the NMR database [20]. This database provides high quality T1-weighted images and diffusion data acquired with a GE Healthcare Signa 1.5 Tesla Excite scanner. The diffusion data presents a high angular resolution (HARDI) based on 200 directions and a b-value of 3000 s/mm<sup>2</sup> increasing the contrast between crossing bundles. After several steps of distortions correction, the T1-weighted image and the diffusion-weighted dataset are perfectly aligned.

In order to use a probabilistic tractography algorithm, HARDI data have to be converted into a fiber ODF in each voxel. In this paper the ODF is simply a sharpened version of the q-ball [15], which is an approximation of the diffusion ODF provided by a spherical Radon transform [6, 7]. This approach assumes the equivalence between the local maxima of the q-ball and the local maxima of the fiber ODF. Pushing further the hypothesis of a strong equivalence between both ODFs, one can consider that the shape of the q-ball around a local maximum provides a good estimation of the uncertainty related to the orientation of the underlying fibers. This is the strategy chosen in this paper to sample the fiber directions during the probabilistic tractography.

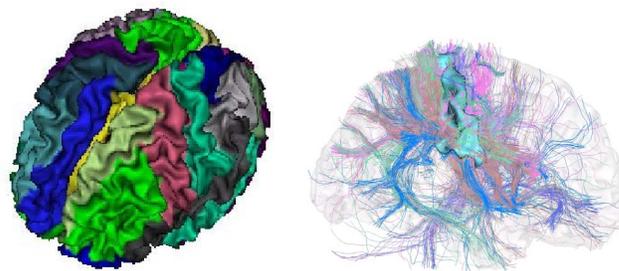
### 2.2. Probabilistic regularized tractography in q-ball fields

The fiber bundles were calculated using a “probabilistic” tractography framework [15] provided by BrainVISA. The implemented method is an extension of a previous algorithm [21] based on regularized particle trajectories performing Monte Carlo sampling of the white matter geometry. This method had been validated using a crossing phantom made up of sheets of parallel haemodialysis fibers and through the successful tracking of the primary auditory tract in the human brain. The last version includes the following refinements [15]:

1. A T1 image based mask of propagation is used to prevent the particles from spuriously crossing the cortical folds;
2. A local sharpening of the q-ball ODF is performed to concentrate the Monte Carlo sampling around the most probable fiber directions;
3. A processus creating children fibers during the tracking is used to improve the sampling of long bundles.

The behaviour of these refinements was illustrated using virtual phantoms of crossing computed via simulation of the random walks of the water molecules in a restricted geometric environment [15].

### 2.3. Connectivity-based parcellation



**Fig. 1.** (left) A gyral parcellation over the cortical surface mesh. (right) 5% of the fibers calculated for the right postcentral gyrus.

The tractography method introduced above is used to compute the connectivity profiles over the cortical surface. Similarities between these profiles are used to parcel the cortex into areas with stable profiles. The parcellation is computed in two steps. The cortical surface is first parcellated into large gyri, then each gyrus is parcellated into smaller entities according to the profiles of connectivity to the gyral parcellation.

*Gyral parcellation:* We use a gyral parcellation of the cortical surface in 36 gyri [16], computed from the T1-weighted image (see **Fig. 1 (left)**).

*Connectivity profiles:* In average about 200,000 putative fibers longer than 8 mm connect one gyrus to the other gyri (see **Fig. 1 (right)**). A connectivity profile was calculated for each vertex of a cortical surface mesh, extracted by BrainVISA from the interface between gray matter and white matter. Considering a gyrus of  $n$  vertices (a gyrus has an average of 13,000 vertices), the whole information is gathered into a  $m \times n$  raw connectivity matrix, where  $m$  is the total number of vertices of the cortical surface mesh. Connectivity is then smoothed over the surface to account for a reasonable uncertainty on the tracking result, as well as to ensure a better numerical behavior [22]. Each fiber contributes to two patches of vertices

with Gaussian weights evaluated from the geodesic distance to the extremities of the fiber. The Gaussian standard deviation is 10 mm.

The gyral parcellation is then used to build the  $n$  reduced connectivity profiles. A  $p \times n$  matrix is then obtained, where  $p$  is the number of connectivity strengths, namely the number of gyri. The columns of the matrix are normalized for the number of fibers in order to get comparable profiles. Hence, a connectivity profile looks like a probability distribution. Most of the vertices are connected to more than one gyrus, which justifies the idea of basing the clustering on the connectivity profiles.

*Clustering:* The nonsupervised clustering approach used to gather vertices with similar profiles is based on the classical k-means algorithm associated with a spatial regularization provided by a Markov Random Field model [23]. In order to stabilize the k-means approach, which is known for its high dependence on initialization, we use the maximum connectivity strength and an initial gyrus split into ten clusters. In this paper, the clustering of a gyrus is not performed subject by subject, like in the work of Perrin [15], but simultaneously on a merge of all the profiles gathered across the subjects. This choice increases the robustness of the clustering thanks to a better sampling of the space of connectivity profiles. Furthermore, the result is directly matched across subjects.

The Markovian prior of our clustering method is an adaptation of the standard Potts model to non uniform meshes. This model penalizes the length of boundaries between clusters. The underlying Gibbs distribution is based on potentials acting on order 2 cliques:

$$\begin{aligned} U_2(l_r, l_s) &= -\beta \quad \text{if } l_r = l_s \\ U_2(l_r, l_s) &= +\beta \quad \text{if } l_r \neq l_s, \end{aligned}$$

where  $l_r$  and  $l_s$  are the labels of two connected nodes. The a posteriori energy whose minimum is the target of the clustering is:

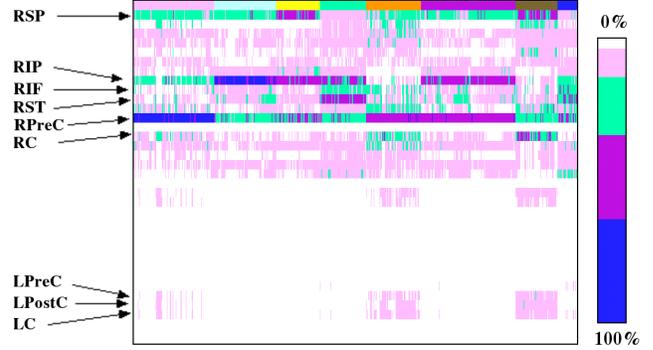
$$U(l|c) = \sum_{s \in [1, \Sigma n]} D(c_s, \mu_s) + \sum_{s \in [1, \Sigma n]} U_s(l_s),$$

where  $c$  are the connectivity profiles, the summations include all the subjects,  $\mu_s$  is the closest centroid to vertex  $s$ ,  $D$  is Euclidean distance and  $U_s(l_s)$  is the vertex  $s$  spatial regularization term, given by the sum of all the clique potentials  $U_2(l_r, l_s)$  on the vertex neighborhood. For each vertex, a different normalization is used to discard the effect of the neighborhood size. The energy is minimized alternating the standard ICM algorithm and the centroid update. The  $\beta$  parameter was varied in order to analyse the effect of the spatial regularization.

### 3. RESULTS

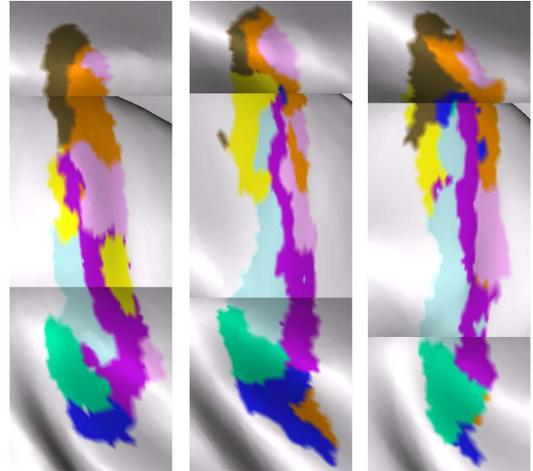
We present here the parcellation obtained for the right postcentral gyrus over the three subjects. **Fig. 2** shows a subset of the connectivity matrix calculated for subject 1. Each column is a vertex connectivity profile. Rows, excepting the first, represent the vertex connectivity strength to each of the 36 gyri. Connectivity profiles are ordered by clusters obtained by a simple k-means. The first row codes for the different clusters. We can see that the clusters rely mainly on the most important connectivity strengths. For space reasons only clustered matrix of subject 1 is shown but note that connectivity profiles from the three subjects are clustered together and present very similar clusters.

The resulting right postcentral gyrus parcellation is presented over an inflated cortical surface mesh in **Fig. 3**. We can observe that even without regularization, the parcels are often connected and



**Fig. 2.** Connectivity matrix of the right postcentral gyrus (subject 1). Connectivity profiles are ordered by clusters obtained from a simple k-means. The most connected gyri are: right superior parietal (RSP), right inferior parietal (RIP), right inferior frontal (RIF), right superior temporal (RST), right precentral (RPreC), right central (RC), left precentral (LPreC), left postcentral (LPostC) and left central (LC).

present a similar topography across subjects. Parcels across subjects (having vertices with similar connectivity profiles) have comparable positions and sizes in the gyrus.

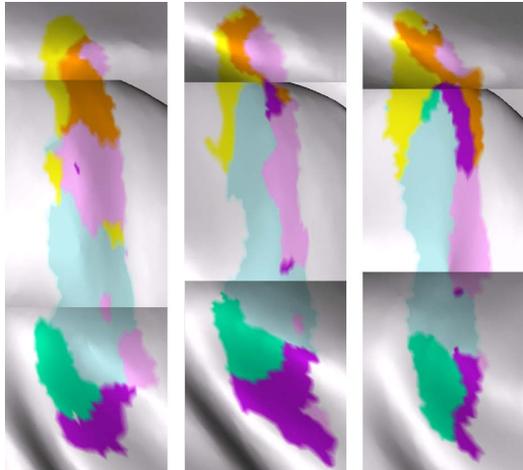


**Fig. 3.** Parcellation of the right postcentral gyrus obtained by simultaneous clustering of the three subjects using a simple k-means. The cortical surface mesh was inflated in order to facilitate the visualization.

The spatial regularization smooth the parcels and reduce their final number because of the fusion of clusters (see **Fig. 4**). However, parcels become less comparable across subjects because for a particular regularization parameter, the amount of fusion is different for each subject.

### 4. DISCUSSION AND CONCLUSION

The connectivity-based parcellation presented in this work is still largely exploratory but the results are very encouraging. We decided to proceed further with the exploration started by Perrin [15], keeping identical a large number of parameters, in particular, the tractography ones. Our cortical surface mesh approach notoriously reduce



**Fig. 4.** Right postcentral gyrus parcellation obtained by k-means clustering and spatial regularization ( $\beta = 0.0005$ ) across the three subjects. The cortical surface mesh was inflated in order to facilitate the visualization.

the number of connectivity profiles to be clustered and overcome the piling up of different clusters orthogonally to the cortical surface. In addition, the smoothing of the connectivity data over the cortical surface leads to more robust data. It is too early to decide if the connectivity matrices and the parcellations inferred from our framework are meaningful, but their level of reproducibility across subjects is impressive. It should be noted that according to anatomical knowledge, architectonic areas can double or triple in size from one subject to another [10]. Therefore, there is no simple way to quantify the reproducibility of our parcellations. The mandatory approach will be correlation of such connectivity-based parcellations with mappings obtained from functional imaging or postmortem anatomical studies.

## 5. REFERENCES

- [1] P. Basser, J. Mattiello, and D. Le Bihan, "Estimation of the effective self-diffusion tensor from the NMR spin echo," *J. Magn. Reson. B.*, vol. 103, no. 3, pp. 247–254, 1994.
- [2] S. Mori, B. Crain, V. Chacko, and P. Van Zijl, "Three-dimensional tracking of axonal projections in the brain by magnetic resonance imaging," *Ann. Neurol.*, vol. 45, no. 2, pp. 265–269, 1999.
- [3] P. Basser, S. Pajevic, C. Pierpaoli, et al., "In vivo fiber tractography using DT-MRI data," *Magn Reson Med*, vol. 44, pp. 625–632, 2000.
- [4] T. Conturo, N. Lori, T. Cull, et al., "Tracking neuronal fiber pathways in the living human brain," *Proc. Natl. Acad. Sci.*, vol. 96, no. 18, pp. 10422–10427, 1999.
- [5] M. Descoteaux, E. Angelino, S. Fitzgibbons, and R. Deriche, "Regularized, fast, and robust analytical q-ball imaging," *Magn Reson Med*, vol. 58, no. 3, pp. 497–510, 2007.
- [6] D.S. Tuch, T.G. Reese, M.R. Wiegell, and V.J. Wedeen, "Diffusion MRI of complex neural architecture," *Neuron*, vol. 40, no. 5, pp. 885–895, 2003.
- [7] D.S. Tuch, "Q-ball imaging," *Magn Reson Med*, vol. 52, no. 6, pp. 1358–1372, 2004.
- [8] F. Crick and E. Jones, "The backwardness of human neuroanatomy," *Nature*, vol. 361, pp. 109–110, 1993.
- [9] O. Sporns, G. Tononi, and R. Kötter, "The human connectome: A structural description of the human brain," *PLoS Comput. Biol.*, vol. 1, no. 4, pp. e42, 2005.
- [10] D.C. Van Essen, H.A. Drury, S. Joshi, and M.I. Miller, "Functional and structural mapping of human cerebral cortex: Solutions are in the surfaces," in *PNAS USA*, 1998, vol. 95, pp. 788–795.
- [11] D.J. Felleman and D.C. Van Essen, "Distributed hierarchical processing in the primate cerebral cortex," *Cerebral Cortex*, vol. 1, pp. 1–47, 1991.
- [12] R.E. Passingham, K.E. Stephan, and R. Kötter, "The anatomical basis of functional localization in the cortex," *Nat. Rev. Neurosci.*, vol. 3, no. 8, pp. 606–616, 2002.
- [13] T. Behrens, H. Johansen-Berg, M. Woolrich, et al., "Non-invasive mapping of connections between human thalamus and cortex using diffusion imaging," *Nature Neuroscience*, vol. 6, no. 7, pp. 750–757, 2003.
- [14] H. Johansen-Berg, T. Behrens, M. Robson, et al., "Changes in connectivity profiles define functionally distinct regions in human medial frontal cortex," *PNAS USA*, vol. 101, no. 36, pp. 13335–13340, 2004.
- [15] M. Perrin, *Imagerie de diffusion à haute résolution angulaire : étude du modèle q-ball par couplage simulations — fantômes et applications au suivi de fibres et à la parcellisation du cortex*, Ph.D. thesis, Université Paris XI, France, 2006.
- [16] A. Cachia, J.-F. Mangin, D. Rivière, et al., "A generic framework for parcellation of the cortical surface into gyri using geodesic Voronoï diagrams," *Med. Image Anal.*, vol. 7, no. 4, pp. 403–416, 2003.
- [17] W. Welker, *Cerebral Cortex*, vol. 8B, chapter Why does cerebral cortex fissure and fold?, pp. 3–136, Plenum Press, New York, 1988.
- [18] D.C. Van Essen, "A tension-based theory of morphogenesis and compact wiring in the central nervous system," *Nature*, vol. 385, pp. 313–318, 1997.
- [19] M. Perrin, C. Poupon, D. Rivière, et al., "Q-ball imaging simulation with a numerical diffusion fiber crossing phantom," in *HBM*, Florence, Italy, 2006.
- [20] C. Poupon, F. Poupon, L. Allriol, et al., "NMR: a free database dedicated to the anatomofunctional study of the human brain connectivity," in *HBM*, Florence, Italy, 2006.
- [21] M. Perrin, Y. Cointepas, C. Poupon, et al., "Fiber tracking in q-ball fields using regularized particle trajectories," in *IPMI*, Glenwood Springs, Colorado, 2005.
- [22] P. Cathier and J.-F. Mangin, "Registration of cortical connectivity matrices," in *MMBIA'06*, New York, USA, 2006.
- [23] S. Basu, *Semi-supervised clustering: Probabilistic models, algorithms and experiments*, Ph.D. thesis, University of Texas at Austin, USA, 2005.