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# A flexible graphical model for multi-modal parcellation of the cortex

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ABSTRACT

Advances in neuroimaging have provided a tremendous amount of in-vivo information on the brain's organisation. Its anatomy and cortical organisation can be investigated from the point of view of several imaging modalities, many of which have been studied for mapping functionally specialised cortical areas. There is strong evidence that a single modality is not sufficient to fully identify the brain's cortical organisation. Combining multiple modalities in the same parcellation task has the potential to provide more accurate and robust subdivisions of the cortex. Nonetheless, existing brain parcellation methods are typically developed and tested on single modalities using a specific type of information. In this paper, we propose Graph-based Multi-modal Parcellation (GraMPa), an iterative framework designed to handle the large variety of available input modalities to tackle the multi-modal parcellation task. At each iteration, we compute a set of parcellations from different modalities and fuse them based on their local reliabilities. The fused parcellation is used to initialise the next iteration, forcing the parcellations to converge towards a set of mutually informed modality specific parcellations, where correspondences are established. We explore two different multi-modal configurations for group-wise parcellation using resting-state fMRI, diffusion MRI tractography, myelin maps and task fMRI. Quantitative and qualitative results on the Human Connectome Project database show that integrating multi-modal information yields a stronger agreement with well established atlases and more robust connectivity networks that provide a better representation of the population.

## 1. Introduction

In-vivo neuroimaging and its recent advances have significantly contributed towards a thorough understanding of the brain's organisation. The brain's anatomy and cortical organisation can be investigated from the point of view of several sources of information: functional and diffusion Magnetic Resonance Imaging (fMRI and dMRI respectively) have allowed to infer the brain's structural and functional connectivity, while cortical folding or myelination patterns can be extracted from structural MRI. In particular, dMRI, fMRI and myelin maps have been largely studied for mapping functionally specialised cortical areas (Glasser et al., 2013; Craddock et al., 2012; Moreno-Dominguez et al., 2014), an objective which has been prominent for over a century (Zilles and Amunts, 2010).

There is strong evidence that a single modality is not sufficient to fully identify the brain's cortical mapping (Eickhoff et al., 2015). Indeed, cortical areas are believed to be defined by their microstructure, their connectivity and their function (Passingham et al., 2002). Because of this, a specific modality might not allow identification of the boundaries of all cortical areas. An accurate delineation of all cortical areas requires multiple modalities to exploit their complementarity and confirm the existence of certain boundaries. Yet, most existing brain parcellation methods are typically developed and tested on a specific type of information. Several popular parcellations have been derived from cortical folding (Tzourio-Mazoyer et al., 2002; Destrieux et al., 2010) or cytoarchitecture (Brodmann and Garey, 2005). More recently, connectivity-driven parcellations, in particular from resting state fMRI (rs-fMRI), have attracted a growing interest (Baldassano et al., 2015; Arslan et al., 2015; Blumensath et al., 2013; Cohen et al., 2008; Shen et al., 2013; Gordon et al., 2016; Thomas Yeo et al., 2011). The idea is to regroup vertices on the cortical surface based on how similar their connectivity profiles are. This is linked to the fact that parcellation can also be approached from a dimensionality reduction point of view for the study of brain connectivity networks. An essential step for the

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construction of these networks is the definition of the network nodes, which is typically done using parcellation techniques, where each parcel corresponds to a node. Connectivity-driven parcellations are expected to provide more accurate nodes than anatomical or random parcellations as they are derived directly from the connectivity data (Sporns, 2011).

In addition to the fact that a single modality cannot provide accurate cortical areas, mono-modal approaches are plagued by modality specific noise and biases which can significantly decrease the performance of parcellation algorithms. For instance, myelin maps only provide information on a subset of the cortex (highly myelinated regions), while diffusion MRI is a very indirect measurement of structural connectivity which is sensitive to the tractography algorithm used to recover the white matter fibres (Maier-Hein et al., 2016). dMRI is also subject to a gyral bias and geometrical issues associated with tractography algorithms. For these reasons, such algorithms tend to terminate fibres in gyri over sulci and align parcel boundaries with cortical folding (Van Essen et al., 2014). In contrast to this, rs-fMRI has the potential to provide reliable information across the cortex, but the modality has a poor signal to noise ratio (SNR) which can affect the accuracy and reproducibility of parcel boundaries. While the influence of noise can be strongly reduced when doing analysis on large groups, biases in the data (e.g. dropout in fMRI susceptibility regions) will constitute another important issue. Combining multiple modalities in the same parcellation task has the potential to provide more accurate and robust parcellations, since the different modalities are intrinsically related.

Nonetheless, only a few methods have tackled the problem of combining multiple modalities in the parcellation task. A popular approach aims to combine structural and functional connectivity so as to construct a multi-modal connectivity matrix, typically with the aim of constructing less noisy fMRI connectivity matrices using dMRI information (Ng et al., 2012; Venkataraman et al., 2012). Assuming fMRI is directly dependent on structural connectivity, fMRI connections are only considered valid if they are supported by a physical connection measured by tractography. One of the main flaws of this approach is the fact that tractography itself can be unreliable and particularly prone to false positives (Maier-Hein et al., 2016), but also to false negatives. As a result, the functional connections estimated from structural support could be biased and inaccurate due to tractography errors. Furthermore, working directly on creating multi-modal connectivity matrices does not allow considering other types of information (e.g. myelin maps) for the construction of a multi-modal parcellation. Glasser et al. (2016) approached the problem differently and generated a group-wise parcellation using a semi-automated approach where an algorithm placed parcel boundaries based on expert decisions using aligned rs-fMRI, task fMRI, myelin maps, cortical thickness and topographically organised functional connectivity. Parcel boundaries were delineated if they were consistent across at least two modalities. This group level segmentation was then transferred to the single subject level using a classifier.

Markov/Conditional Random Fields (M/CRFs) offer a way of constructing very tunable models which is beneficial for the problem of parcellation in several aspects: control over the level of parcel smoothness, flexible model design, easy incorporation of prior knowledge and natural extension to multi-modal or group-wise analysis. MRFs have been used for a plethora of image processing applications, including image segmentation (Boykov and Funka-Lea, 2006), registration (Glocker et al., 2008) or image denoising (Geman and Geman, 1984). Through the MRF formulation, parcellation is cast as a labelling problem, where each label corresponds to a specific parcel and is to be assigned to a set of nodes in a graph representing brain geometry. In our setting, the vertices of the cortical surface mesh correspond to the nodes of the MRF model. This labelling problem is solved by minimising the MRF energy which comprises unary and pairwise terms. The unary terms describe the likelihood of assigning a node to a specific parcel (i.e. label) while pairwise terms model the interactions between neighbouring nodes and typically act as smoothing priors. A significant advantage of MRF models is that they do not make any assumption on the input data. In other words, several modalities can be considered and processed within the same framework. The use of MRFs for rs-fMRI driven parcellation has recently been the subject of several publications (Lashkari et al., 2010; Ryali et al., 2013; Honnorat et al., 2015; Parisot et al., 2015, 2016b). The proposed methods describe the likelihood of assigning a node to a specific parcel as the correlation to the parcel's average connectivity profile. Ryali et al. (2013) proposed an EM-like approach tailored for fMRI data that iteratively estimated the parcellation using graph cuts (Boykov and Funka-Lea, 2006) and estimated the unary cost's parameters based on the current parcellation status. Honnorat et al. (2015) introduced the notion of parcel centres which are associated with a representative connectivity profile of the parcel. The MRF unary cost describes the correlation of a node's profile with the parcel centre's profile. This approach considers all nodes as potential parcel centres, which can be computationally expensive and subject to noise. A connectedness prior is introduced in the form of a star shape prior. Both approaches determine the number of parcels using label costs that estimate the number of necessary labels given a penalty. Despite the appeal of inferring the number of parcels from the data, this setting boils down to replacing the intuitive choice of the number of parcels with a different parameter of unknown impact.

In Parisot et al. (2015, 2016b), we introduced Graph-based Multimodal Parcellation (GraMPa), an iterative MRF framework designed to handle the large variety of available multi-modal data: (1) We propose a set of modality specific unary cost functions that allow parcellating the brain according to different modalities and their properties. This allows to construct modality specific parcellations that can be compared without biases introduced by the use of different parcellation methods. (2) We extend the proposed framework to the context of multi-modal parcellation through the introduction of a multi-modal merging step. At each iteration, we obtain a set of parcellations from different modalities and fuse them based on prior knowledge of the modalities' reliabilities and their interactions. The fused parcellation is used to initialise the next iteration, forcing the parcellations to converge towards a set of coherent yet modality specific parcellations. This provides a framework that allows 1) to directly compare different modalities, 2) to construct a multimodal parcellation and 3) to increase the robustness of mono-modal parcellations through the introduction of additional and complementary information.

In Parisot et al. (2015, 2016b), we focused on parcellation at the single subject level. In this paper, we provide a more general and detailed formulation of the model and investigate the impact of the proposed method on group-level analysis. This allows to explore multiple multimodal associations and to compare obtained parcellations to well established atlases. In particular, we investigate the use of task activation maps as an additional source of information, which are too noisy to be used at the single subject level. We evaluate the ability of our framework to parcellate based on different types of inputs and exploit this property to provide an experimental set-up that quantitatively evaluates multimodal agreements. Additionally, we evaluate the impact of integrating multiple modalities on the delineation of cortical areas, as well as from the point of view of network analysis. Our experiments on data from the Human Connectome Project (HCP) database using rs-fMRI, dMRI, myelin maps and task activation maps show that GraMPa yields a stronger agreement between modalities and more robust connectivity networks that provide a better representation of the population.

## 2. Material and methods

The proposed iterative multi-modal model is illustrated in Fig. 1. In this section, we first introduce the mono-modal setting where one modality is parcellated using an MRF unary cost tailored for this specific input data. We then introduce the multi-modal extension, which is designed as a step that fuses information from multiple modalities. Finally, we describe the methodological details for our evaluation set-up.

We introduce below a set of notations that will be used throughout this paper. We aim to parcellate the brain's cortical surface into a set of $K$