Chapter 7

Summary and conclusion

7.1 Discussion

In this thesis we investigated structural and functional brain connectivity by means of DTI, fMRI and EEG analysis. By focusing both on the analysis and on the visualization of the results, we tried to provide techniques that could be useful to improve the understanding of the complex system that is our brain.

In Chapter 2 we extended the application of DTI to the study of auditory pathways in tinnitus patients and controls. We considered DTI tracks that connect the inferior colliculus, the auditory cortex and the amygdala, and vice versa. Such an approach does not identify new connections, but it allows the quantification of properties of known connections in the brain. The first interesting result is the ability to track the classical auditory pathway, as the connections follow the expected pathway of the classical auditory system. In order to summarize the track properties, we computed three quantities for each connection in each subject: the fractional anisotropy, the weighted fractional anisotropy, and the connection strength. Although these three measures are the result of considerable data reduction, they allow for straightforward comparisons between subjects and subject groups. We found a number of differences and similarities between tinnitus patients and healthy controls, and results that indicate that the limbic system may play a major role in tinnitus. For the first time, an anatomical pathway that might function differently between tinnitus patients and normal hearing controls was shown.

In Chapter 3 we introduced an improved tracking technique that allows DTI streamlining to solve low-anisotropy regions and permits branching of trajectories. Our method performs interpolation for any low-anisotropy voxel met during tracking. Interpolation is computed in Log-Euclidean space and collects directional information in a neighbourhood of the voxel in order to reconstruct a tensor with a higher linear diffusion coefficient than the original. Also, in order to resolve multiple fiber orientations, we divide the neighbourhood of the low-anisotropy voxel in 26 sectors, and compute an interpolated tensor in each sector according to our weighted tensor interpolation formula. We tested our method on artificial, phantom and brain data, and compared with existing methods. Because our method can resolve cases of multiple fiber orientations in a single voxel, it can produce results that are similar to those provided by more powerful techniques such as probabilistic tracking with multiple fiber orientations.

In Chapter 4 we proposed the usage of force-directed graph layout as an explorative tool
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for connectivity-based parcellation studies, and showed how our method tackles some problems of the techniques proposed in the literature. With a representation of the data that intuitively shows relations among (groups of) seed voxels, our method can be used as an exploratory tool to analyse the dataset and eventually decide to apply a clustering method. The principal application of our method is the definition of the number of clusters in the dataset, which can be localised and enumerated by the inspection of the peaks in the density map and of the iso-density lines. The exploration of the density maps is performed using both the graph layout and the mapping of the densities on the brain, so that hypotheses on the presence of clusters can be verified before running any clustering algorithm. We applied our technique to the study of the premotor cortex and showed that substantial variability among subjects occurs, and that a subdivision into two well separated clusters (as reported in the literature) is not always straightforward.

In Chapter 5 we proposed a method based on inexact graph matching for quantifying differences between multichannel EEG coherence networks represented by functional unit maps. We defined a class of cost functions to compute the mean of two attributed graphs representing FU-maps of two subjects and extended the notion of mean graph to the case with multiple subjects. A visualization of the mean FU-map was used with a visual representation of the frequency of occurrence of nodes and edges in the input FUs. A feature of our method is the possibility to locate FUs which are common among all subjects. This may reflect which brain areas are mostly involved in certain tasks. The applications showed that the method can help identify dissimilarities between EEG networks that are obtained under varying conditions or in different groups of subjects. Our method still has a number of limitations and is proposed as a preliminary step towards a complete quantitative comparison of multichannel EEG networks.

In Chapter 6 we proposed a method, built upon a method previously used in multichannel EEG analysis, that allows the visualization of brain functional connectivity from resting state fMRI data. This method should be considered a “proof of principle” at this stage. We evaluated the potential of our method by performing interviews with four medical domain experts, who agreed that this method could provide insights in the localization of functional and cyto-architectonic brain areas via resting state fMRI.

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The study of the structural and functional behavior of the brain through the application of computer science methods is a fascinating and challenging topic in neuroscience, and will flourish in the next years as technology improves and new and more powerful techniques will allow us to investigate the marvels of our nervous system with more and more accuracy.

I think there are two major factors that could improve the quality of the research in the field of brain visualization. First comes a stronger collaboration between research scientists and medical experts. Neuroscience, intended here as the analysis and visualization of brain connectivity, is a highly interdisciplinary science in which both neurology and computer science play an important role: the expertise from both fields is needed for the generation and verification of high-quality hypotheses. Nowadays we see several scientific works in which clinical relevance is put aside in favour of beautiful visualizations: brain visualization is not an art, but a tool that should serve
the clinical needs. I believe that a strong collaboration between researchers in brain visualization and physicians experienced in the clinical environment would be beneficial for the generation and verification of interesting hypotheses, that could effectively help physicians both to propose a diagnosis and to find solutions. As an example, in Chapter 5 we proposed a visualization method for the comparison of multichannel EEG networks. The proposed visualization is very rich in information, quantitatively and qualitatively, both on the group results and on the individual differences. The method is very interesting *per se*, but I think that the most interesting results still have to be achieved. Further analysis of the results, detailed comparisons between subjects, and discussions about the medical relevance would yield both new medical hypotheses and improvements of the visualization method.

Second comes the synergy of different techniques: I believe that extensive per subject analysis is necessary to gain knowledge of the human brain. Trying to get the complete picture of the brain’s behavior by using all the available technologies will allow a better understanding of the complex functional and structural networks. Several studies have been proposed on the combination of fMRI and DTI results. Lately, a new branch of research is trying to acquire fMRI and EEG data simultaneously. A combined analysis using DTI, fMRI, EEG, as well as other imaging techniques such as, for instance, PET, SPECT, and CT would allow a better understanding of the brain networks. Also, when a collaboration between research and clinical environments is available, the results of invasive analysis could provide detailed information that would be beneficial to a better understanding of the results. As an example, in Chapter 4 we proposed a parcellation method of the premotor cortex based on DWI analysis. The results showed that a separation between SMA and preSMA is not always straightforward in single subject analysis, and that there is great variability among subjects. It is well known that both preSMA and SMA are easily distinguishable in task-related fMRI and in cyto-architectonic analysis: to understand the parcellation results, and to understand why the variability among subjects occurs, DWI analysis alone is not enough: only a combination of these three acquisition methods would allow a full understanding of the functional and structural differences in the region.
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