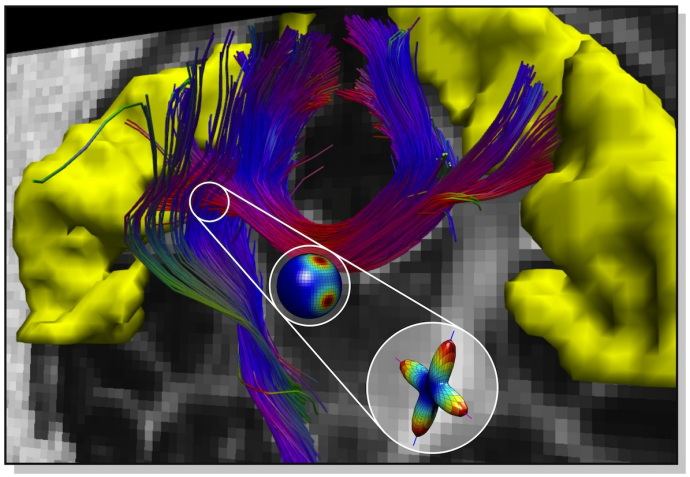
Towards micro-structure-based tractography for quantitative brain connectivity analysis

Signal Processing Lab (LTS5), École Polytechnique Fédérale de Lausanne, Switzerland



A **PhD research position** in diffusion MRI (see following project synopsis) is available at the Signal Processing Lab (LTS5), École Polytechnique Fédérale de Lausanne (EPFL), Switzerland. The EPFL is one of the two Swiss Federal Institutes of Technology. The main campus is located in Lausanne on the shores of Lake Geneva and at the foot of the Alps and as such offers a range of cultural and sporting activities.

We are looking for a highly motivated candidate holding a Master's degree or equivalent in computer science, physics, electrical engineering, or a related field with experience in computer vision and medical image processing. The ideal candidate has strong analytical skills and programming experience (preferably with Matlab, Python and C++). For a good working communication, oral and written fluency in English is required. It is essential that the candidate is willing to work in a multidisciplinary and international research team, as the work will be conducted in collaboration with the major international experts in the field. The project is supported by the Swiss National Science Foundation for a duration of at least three years.

Applicants should send their applications via e-mail, including an updated curriculum vitae and a letter of intent describing their motivation for this specific position. The project will be co-supervised by Dr. Alessandro Daducci and Prof. Jean-Philippe Thiran. The earliest starting date is *November, 1st 2014*.

For more information, feel free to contact:

- Dr. Alessandro Daducci, alessandro.daducci@epfl.ch
- Prof. Jean-Philippe Thiran, jean-philippe.thiran@epfl.ch

Project synopsis

Motivation Despite connectomics offers an exquisite tool to investigate non-invasively the architecture of the neuronal connections of the brain, the reconstructions recovered with *existing algorithms are not really quantitative*. In fact, the information recovered by diffusion MRI (dMRI) tractography is orders of magnitude coarser than the actual size of the axons and each of the recovered tracts represents an unspecified set of coherent real fibers. Consequently, the measures of structural connectivity between different brain regions estimated with existing tractography algorithms are only indirectly related to the actual properties of the underlying neuronal connections. On the other hand, dMRI is actually a quantitative modality by nature and several techniques have recently appeared to estimate biological micro-structural properties of the neuronal tissue, such as the average diameter of the axons in each imaging voxel. However, fiber-tracking and tissue micro-structure estimation have been considered so far as two separate problems. As a consequence, to date, nothing can be inferred from dMRI on the micro-structure of the fascicles themselves, ergo *today connectomics analyses are not truly quantitative*.

Objectives The project will focus on a novel linear formulation our group recently proposed in [1, 2] to combine tractography and tissue micro-structure estimation; the framework is called `COMMIT`, standing for "Convex Optimization Modeling for Micro-structure Informed Tractography". The introduction of convex-optimization as a way to express tractography and tissue micro-structure [1, 2] has actually opened the door for *quantitative and biologically-oriented connectivity analyses* to become practical.

The primary goal of the project is to further develop this unifying framework, not only to map the trajectories of the neuronal fascicles between different brain regions, but also to access more informative *micro-structural properties of the fascicles themselves*. For instance, the diameter of the axons in white matter fascicles is a particularly important morphological property to know, for it is directly related to the rate of information transfer of the fascicles themselves.

Multidisciplinary research will be required to accomplish our objectives. Substantial methodological development of the mathematical framework will be required to drastically improve the sensitivity and specificity of existing connectomics techniques. We will evaluate several multi-compartment models for the dMRI signal decay and also consider different regularization schemes to exploit properly all the prior knowledge we have on the brain structure. The effectiveness of the proposed approach will be evaluated through extensive validation procedures that will involve the acquisition of ex-vivo specimens on high-end MR scanners and comparison to histology. Finally, the applicability of this methodology will be tested for use on standard clinical systems and we will also evaluate its ability to cope with pathological conditions.

Impact Because of the multidisciplinary nature of the project, we strongly believe the work conducted in this context will lead to breakthrough contributions along several research themes. At the *methodological level*, the research involved in this project will lead to significant advances in the fields of numerical optimization and advanced signal processing for connectomics. This framework might have profound implications in a *fundamental neuroscience perspective*, as it will finally provide the community with a new paradigm to study quantitatively and from a biological standpoint the structural connectivity of the brain. In a *clinical perspective*, the availability of such a tool would open the door to develop new and extremely sensitive biomarkers of brain connectivity disruption and many important questions still unanswered might be investigated by means of quantitative and biologically-oriented connectivity analyses. Our framework will be general and flexible enough to be used to investigate and monitor the evolution of a wide range of pathologies, where brain connectivity is affected by local and/or global degenerative alterations of the tissue, ultimately leading to new imaging biomarkers having a more direct connection with the biological features of the tissue.

References

[1] A. Daducci, A. Dal Palú, A. Lemkaddem, and J.-P. Thiran. A convex optimization framework for global tractography. In *Proc. IEEE ISBI*, pages 524–7, 2013.

[2] A. Daducci, A. Dal Palú, A. Lemkaddem, and J.-P. Thiran. COMMIT: Convex Optimization Modeling for Micro-structure Informed Tractography. *IEEE Trans Med Imaging*, 2014. In press.