Python Software Foundation

Implementing advanced diffusion kurtosis imaging techniques in Dipy

Google Summer of Code 2015

Sub-organization information

This proposal is directly relevant for the sub-organization DIPY (Diffusion Imaging in Python, http://nipy.org/dipy/), a free open-source library for the analysis of diffusion MRI data.

Student Information

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University Information

- **University:** University of Cambridge
- **Major:** Biological Science at the MRC Cognition and Brain Science Unit

- **Subject of Research:** Neuroimaging methods and applications to the study of healthy ageing
- **Degree:** PhD
- **Current Year:** 2nd year of the 4 years program
- **Expected Graduation date:** September 2017

Abstract

Diffusion-weighted MRI (dMRI) is a non-invasive technique that allows mapping of brain connections and quantification of tissue properties *in vivo*. Diffusion Kurtosis Imaging (DKI) is a new dMRI modality that overcomes the limitations of the dMRI techniques most widely used by the medical community. The objectives of this project is to implement DKI modules in Dipy. My vision is to improve the reliability and reproducibility of DKI studies by providing the first open source DKI modules.

Introduction

Diffusion-weighted MRI (dMRI) is a non-invasive biomedical imaging technique that allows us to measure the trajectory of neuronal connections in the living human brain (tractography), and to assess the physical properties of these connections *in vivo*. The most commonly used dMRI technique is the Diffusion Tensor Imaging (DTI), which quantifies the water diffusion in tissue microstructures by a second order tensor, known as the diffusion tensor (DT). DTI is used in both clinical applications, and in many research studies, however it is not always accurate. DTI ignores the non-Gaussian properties of diffusion in biological tissues and cannot account properly for the crossing of different populations of white-matter fiber connections.

Diffusion Kurtosis Imaging (DKI; Jensen et al., 2005) is an alternative dMRI technique that overcomes the major limitations of DTI. It quantifies the non-Gaussian properties of water diffusion in biological tissues by modelling the kurtosis tensor (KT). KT can be used to derive interesting and important measures of tissue heterogeneity, and has already been used in many brain studies. For example, in the context of the aging brain, KT standard measures were shown to provide unique information of tissue maturation and degeneration across different age decades (e.g. Neto Henriques, 2012b). By combining the information of both diffusion and kurtosis tensors, DKI can also be used to quantify concrete biophysical parameters as the density of axonal fibres and diffusion tortuosity (Fieremans et al., 2011). These latter measures have shown huge potential in distinguishing axonal loss from demyelination in brain pathologies, as in the context of Alzheimer’s disease (Fieremans et al., 2013). Relative to the DT, KT was also shown to offer a better characterization of the spatial arrangement of tissue microstructure and can be used as a basis for more robust tractography which is able to resolve crossing fibers (Jensen et al., 2014).

Despite the fact that DKI has significant relevance in both research and clinical applications, there is no free, and open-source implementation of the algorithms. Thus, DKI applications are still limited by the lack of reliability and reproducibility (André et al., 2014). Bringing DKI to an open-source software project as the Diffusion Imaging in Python (Dipy) is an important step, which will help bring these algorithms to wider use in research, and ultimately in the clinic.

Objectives

The first goal of this project is to implement, optimize and test the DKI reconstruction modules in Dipy. Then, the DKI modules will be expanded with recent advances including biophysical parameter estimation methods proposed by Fieremans et al. (2011) and the DKI based fibre estimate techniques proposed by Jensen et al. (2014).

Timeline

This project will be structured in 4 phases which are described below:

1 – Finalize DKI based simulations

- **Before 25 May** – At the beginning of the year, I submitted a pull request to Dipy with software implementations of simulations of the DKI signals (https://github.com/nipy/dipy/pull/582). These are useful both because they will help us generate synthetic data, and also because these simulations provide "ground truth" DT and KT tensor for different white matter fiber configurations. Thus, they provide an efficient way to test and debug the development of DKI-estimation algorithms. Before the beginning of the official coding time, I will be continuing the work on this PR. I will improve the code, format it according to the project coding standards, and implement automated unit tests, with the goal of having this PR merged into the "master" branch. This work will help me familiarize myself with Dipy's architecture, and with the development process.

2 - Finalize the DKI reconstruction modules (4 weeks)

- **May 25 to May 29 –** I will start working on the DKI reconstruction modules, based on some preliminary preparation work previously submitted by other Dipy contributors. At the end of the week, I intend to finish the first part of the DKI reconstruction modules - the KT estimation from diffusion-weighted signals. For this I will implement the standard ordinary linear least-squares (OLS) solution of DKI (Tabesh et al., 2011).

- **June 1 to June 5 –** Based on the KT obtained from the OLS solution, the standard measures of kurtosis tissue heterogeneity will be implemented during this week.

- **June 8 to June 12 –** This week will be reserved to fix remaining issues and optimizing the modules created so far. If time allows, I will add some new features on the DKI reconstruction modules as adding different types of KT fitting procedures (e.g., the weighted linear least square fits, the non-linear least square fit, or the constrained least square fit).

- **June 15 to June 19 –** After having the DKI reconstruction modules ready and optimized, I will improve documentation and create example scripts of usage which will be added in Dipy's gallery of examples.

  Note: The work done on this step will be reported on the midterm evaluations.

3 – Implement the biological measures based on DKI (4 weeks)

- **June 22 to July 3rd –** I will start implementing the biophysical measures from DKI as proposed by Fieremans et al. (2011). Particularly, during these weeks, I will implement the first steps of Fieremans algorithms which requires procedures to search the KT maxima value (Fieremans et al., 2011).

- **July 6 to July 10 –** During this week, I will complete the implementation of Fieremans et al. (2011) models, and work on benchmarking and optimizing this implementation

- **July 13 to July 17 –**This week will be reserved to improve the documentation regarding to all the work done on the third step of the proposal and create the example script to add in Dipy's gallery of examples.

4 – Implement the DKI-based fiber direction estimation methods (4 weeks + 1 week for documentation)

- **July 20 to July 24 –** I will start implementing the DKI based fiber direction estimate procedures. During this week, I will be focusing in implementing a reconstruction of a 3D probability function of the direction fibers based on the DT and KT (Jensen et al., 2014).

- **July 27 to July 31** - Based on the 3D probability function, the modules to extract the fibre direction estimates will be implemented. These will involve the use of optimization problems to finding maxima of functions described by spherical coordinates.

- **August 3 to August 7** - The objective of this week is to improve the fiber direction estimation modules and make them consistent to other fiber estimation procedures already implemented in dipy. In this way, the DKI fiber estimated will be compatible to the tractography methods already implemented in Dipy.

- **August 10 to August 14 -** In this week, I will write the documentation and the sample scripts for the use of DKI fiber estimates for Dipy's gallery example scripts. In particular, I will show how to combine the outputs of the developed modules with the Dipy's tractography modules. At the end of this week, I will have the first *in vivo* DKI based tractography reconstruction obtain from an open source software.

- **August 17 to August 21 –** As suggested by the Google summer of code website, this week will be taken to improve codes, tests and documentation.

Personal note and Biographical Information

The objectives of this proposal are ambitious, however I am confident that I will be able to accomplish them successfully due to the expertise that I already have on DKI.

I started working on DKI in 2011 as part of my final master's project in Biophysics and Biomedical Engineering (Faculty of Science of the University of Lisbon, Portugal). The objective of this project was to use DKI ad-hoc "in-house" procedures to analyse the data for a large collaborative aging project in Cambridge (UK) - the Cambridge Centre for Ageing and Neuroscience (CamCAN). As a visiting student at the MRC Cognition and Brain Science Unit (MRC-CBU, Cambridge, UK) my interests in DKI increased after seeing its potential in probing microstructural changes on brain healthy ageing (Neto Henriques et al., 2012a, 2012b). Therefore, after my graduation in 2012, I started a research position at the Institute of Biophysics and Biomedical Engineering (University of Lisbon, Portugal) where I explored in detail the 3D information provided by KT (Neto Henriques et al., 2013) and how to uses it on DKI based tractography algorithms (Neto Henriques et al., 2014). Currently, I am doing my PhD at the University of Cambridge based at the MRC-CBU. Despite being now expanding my knowledge to other dMRI techniques as the spherical deconvolution (e.g. Dell'Acqua et al., 2010), I still have a huge interest on DKI. Particularly, on my latest study, I explored the advantages of using

DKI based fiber estimates to obtain robust tractography maps of the corpus callosum and to estimate kurtosis measures not limited to the assumption of well aligned fibers (Neto Henriques et al., 2015).

With the google summer of code, I will finally have the opportunity to go beyond the work done based on ad-hoc "in-house" software, shared locally with my colleagues in the lab, and start sharing my knowledge with the broader neuroimaging community through free open-source software. At the same time I will have the opportunity to explore the details of all the implementation steps of DKI techniques, learn about open source software development, testing and engineering, and have experience in working on a collaborative project. Finally, I am also hoping having a lot of fun on discussing ideas with my mentors, other participants in the project and the wider medical image processing community.

Other Schedule Information

Week that I am expecting to take off:

June 1 to June 5 – During this week I have to attend the International Society for Magnetic Resonance in Medicine (ISMRM) annual meeting where I will be presenting my latest work in DKI at the scientific section "Diffusion Weighted Analyses". This will impact the second week of work of the second step of the project plan, however I am planning extra hours of work on the week before the official coding period and during the other weeks of the project's second step, to be able to accomplish all planned objectives for the midterm evaluations. Moreover, attending the ISMRM annual meeting will also be beneficial for the proposed project because I will have the opportunity to personally meet some of the Dipy developers.

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