Collaborative Research in Computational Neuroscience of the Stanford and RWTH Aachen University

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Dementia, especially Alzheimer's, are widely spread diseases in the sophisticated aging process of human beings. Commonly accepted are structural changes in white matter as reason or impact of it. Lately studies have shown that diffusion magnetic resonance imaging can identify structural changes in the hippocampus in affected brain regions. A main part of this approach is to describe the measured diffusion signal with so called diffusion models. The most popular one is the diffusion tensor model.
As an initial step this study wants to use other commonly known diffusion models, such as constrained spherical deconvolution, to identify similar indicators. Based on that, new diffusion models should be developed, which take a patient specific noise atlas into account. With the help of improved models, the subsequent fiber tacking algorithms are hoped to achieve better and more reveling results, with special attention to dementia diseases.

INTRODUCTION

Magnetic Resonance Imaging (MRI) is a well known medical imaging technique to acquire images of the anatomy and physiology of the human body. It was invented by Lauterbur in 1971 [14] under its previous name Nuclear Magnetic Resonance (NMR). Damadian reported first in [15], that tumors and normal tissue can be distinguished in-vivo and non-invasively with NMR. Stejskal et al. proposed in [17] a pulsed spin echo sequence, which allowed to measure the diffusion of water molecules [18]. Because the molecular diffusion process reflects interactions with obstacles like macromolecules, fiber or membranes, it can therefore reveal details about microscopic tissue structure. Bihan et al. finally introduced the proposed methods from Stejskal into MRI [16]. A scan is therefore called Diffusion Weighted MRI (dMRI). Basser proposed in 1994 the Diffusion Tensor Imaging (DTI) model based on Stejskal publications [19]. He used the direction dependents of the diffusion tensor coefficients to determine the process of fiber tracks in the human brain. Discovered by Tuch et. al, DTI, unfortunately, performs poor in brain regions with fibers in more than one directions [20]. To overcome this problem, Tuch publicized in [21] the High Angular Resolution Diffusion Imaging (HARDI). HARDI scans use more then the necessary 6 diffusion directions to resolve crossing fiber regions. Based on that, starting in the early 21st century, several research groups developed more complicated models to overcome this issue. Most of these models assume that the diffusion signal can be decomposed as a weighted sum of generic diffusion models, for example the Multi-DTI, Ball-Stick model or CHARMED. CSD, however,

DSI PASMRI

2002 ball and stick

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DTI bad in fiber crossing areas Tournier J. D., Calamante F., Gadian D. G., Connelly A. (2004). Direct estimation of the fiber orientation density function from diffusion-weighted MRI data using spherical deconvolution. Neuroimage

HARDI high angular resolution diffusion imaging (HARDI) [Tuch et al., 1999, Tuch et al., 2002]

"While the Gaussian assumption is adequate for voxels in which there is only a single fiber orientation (or none), it breaks down for voxels in which there is more complicated internal structure. This is an important limitation, since resolution of DTI acquisition is between 1 mm3 and 3 mm3 while the physical diameter of fibers can be between 1"m and 30 "m [Poupon 1999; Beaulieu 2002]."

Tracking fibers in the human brain (Mori et al., 1999; Conturo et al, 1999)

Except for some extensions of diffusion tensor models, such as the multi-Gaussian model [10] and the ball-stick model [11], most of the researchers using the HARDI method have used one of three general approaches: diffusion spectrum imaging (DSI) [12], decomposition-based methods [11, 13?18], and deconvolution-based methods [19?21].

Whether using multiple q-shellsand reducing the number of diffusion directions (to maintain the same acquisition time) would still be help-ful is a subject of current research.

GENERAL

The proposed study is a cooperative research project between the Stanford Center for Cognitive and Neurobiological Imaging (CNI, **CA**) and the Institute of Imaging and Computer Vision RWTH Aachen University (LfB, **AA**). The CNI is a shared facility in the psychology department of the Stanford University in California, USA, dedicated to research and teaching. The center provides resources for researchers and students in cognitive and neurobiological sciences, such as a 3 Tesla Magnetic Resonance Imaging (MRI) scanner from General Electric with a variety of different head coils, goggle system with eye tracker and audio as well as an EEG system or Mock scanner. The CNI team has high expertise in various pulse sequence developments which include, but are not limited to simultaneous multi slice in-vivo diffusion imaging pulse sequences. One of the latest publications arisen in this field leaded to the development of Multi-slice acquisition with Incoherent Controlled Aliasing (MICA) [9]. Another focus of the CNI is the MRI data management and reconstruction. Research in this field of study resulted in the development of the Neurobiological Image Management System [10].

The LfB, however, is part of the department of electrical engineering and information technology at the RWTH Aachen University, Germany. The research and teaching activities cover the whole range of image acquisition, image processing and visualization in medical, biological, industrial image processing as well as fundamental research. The latest publications refer to the exploration of crossing fiber regions in the brains white matter [11] and comparison of reconstruction algorithms for diffusion data [12]. The proposed cooperation wants to combine the expertise of both participating institutes to achieve a better result in the identification of dementia diseases. A successful partnership was already demonstrated during a cooperative master's thesis in novel model fitting approaches for incoherently aliased multi-slice diffusion [13].

The principle investigator of the whole project will be Prof. Dr. Dorit Merhof, who will also supervise the time being in Aachen. The research in Stanford will be mainly supervised by Dr. Robert F. Dougherty respectively. The outcome of this project should be the headstone to obtain the degree of Doctor in Engineering for Christian

Pötter.

TIMELINE

The proposed collaborative project has an estimated overall handling time of three years. This time can be subdivided into the two fundamental working fields MRI physics and image processing. The first one will be supervised by Dr. Dougherty in Stanford and will probably have a time frame of one year. This is followed by a transition period over to image post processing in Aachen, which is then the main responsibility of Prof. Merhof. A more accurate breakdown of the aimed timeline can be found in figure 1. Bold emphasized words in the following paragraph illustrate the chronological position of the explained topic in figure 1.

Starting in the end of 2014, a collaboration between the two institutes was established based on the common supervision of the **master's thesis** of Christian Pötter. One of the main outcomes of this collaborations was a voxel based parallel processing approach for diffusion image reconstruction, which was contributed to the dipy package [5]. Dipy is a free and open source software project focusing mainly on diffusion MRI (dMRI) analysis. It contains algorithms to all steps of the dMRI pipeline: reconstruction, model fitting and fiber tracking. To consolidate the successful collaboration, in the following quarter the publication of a common paper based on the Restriction Spectrum Sparse Fascicle Model (**RS-SFM**) developed in the master's thesis were initiated. This model had already proven to be useful during the white matter modeling challenge of the International Symposium on Biomedical Imaging 2015 in New York City. The new paper should compare the improved SFM [2] with already existing state of the art diffusion models. Therefore implementation and integration of the Persistent Angular Structure (**PASMRI**) [4] diffusion model into the dipy package was conducted. To follow this idea, one of the next steps is the upgrade of the SFM and Constrained Spherical Deconvolution (**CSD**) model to multi-shell capability. This might be done in cooperation with Dr. Ariel Rokem from the University of Washington, who is one of the main contributors to dipy and a close collaborator of the CNI.

Simultaneously initial steps for the **grant application** in Collaborative Research in Computational Neuroscience [1] between both institutes were made, which will be finalized until October 29, 2015.

Diffusion Tensor Imaging (DTI) followed by the application of fiber tractography algorithms is a useful tool to detect Alzheimer's disease in effected brains, as for example emphasized in [6]. In this junction among other things the Fractional Anisotropy (FA) and Mode of Anisotropy (Mode) are used as indicators. A weakness of the commonly used diffusion models is their small degree of freedom, as researched in [3]. We propose to develop **new diffusion models**, which overcome this weakness and result therefore in a better fitting. The main approach is to develop a patient specific **noise atlas**, which will be considered in the model and allow therefore a more complex parameter fit with more parameters. This noise atlas will be based on the thermal noise map estimation of Dr. Hua Wu from the Stanford Center of Cognitive and Neurobiological Imaging. To validate the new model, however, previously a **ground truth**, fiber based diffusion data set should be developed. A challenging approach for this is the construction of a mechanical fiber phantom, which accompanies with one of the newest projects in the CNI. An alternative ground truth approach includes the simulation of fiber tracks and their resulting noisy diffusion data.

Subsequently the current state in research in fiber tractography algorithms should be

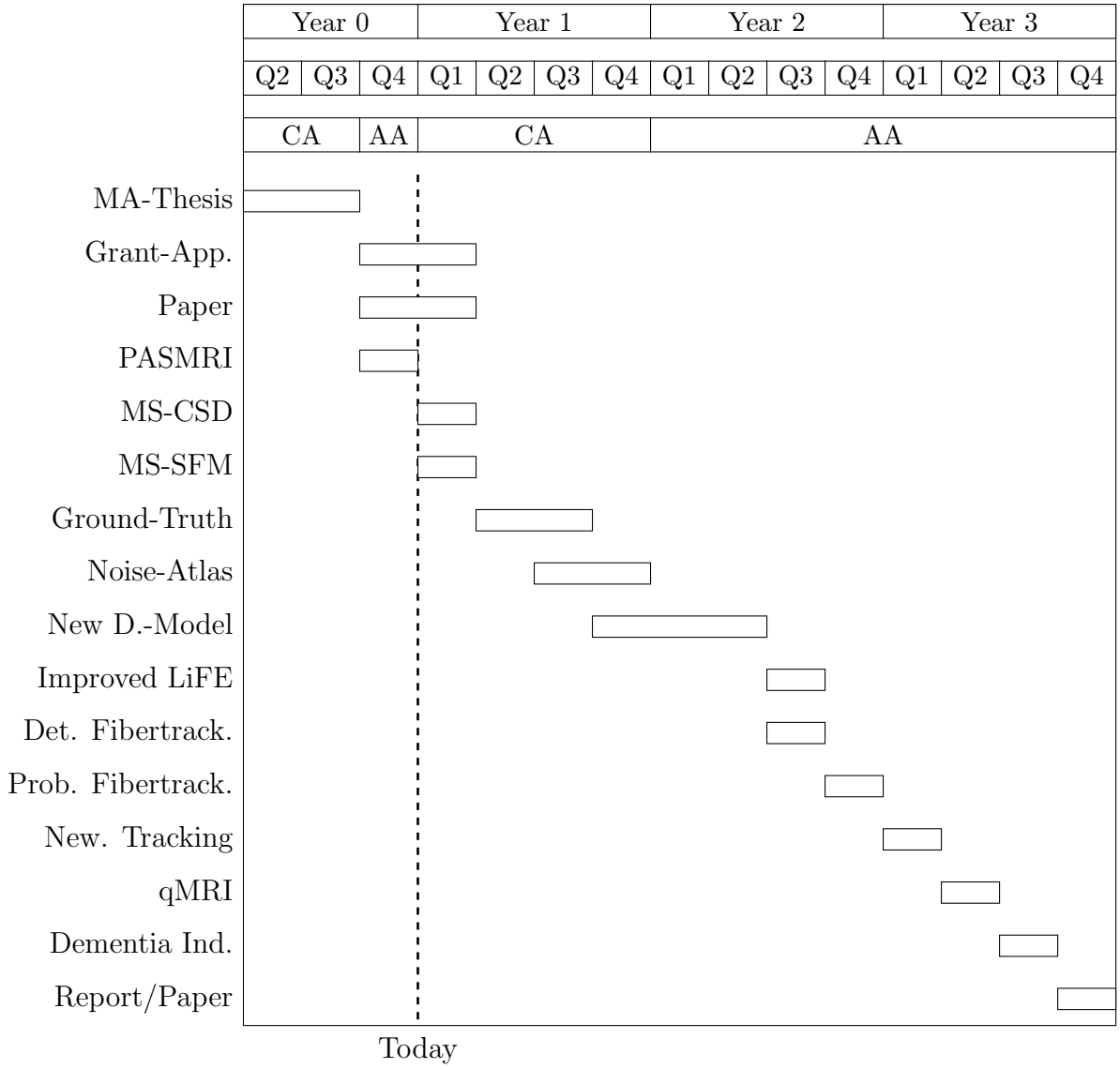

Figure 1: Estimated timeline of the collaborative project

examined. To compare the two latest developments in the main approaches **deterministic** and **probabilistic fiber tracking**, the Linear Fascicle Evaluation [7] (**LiFE**) model should be applied. While doing so, already existing improvements to the LiFE algorithm should be implemented in python and be uploaded to the dipy package. A final resulting study might lead to **new fiber tracking algorithms**, or at least improvements to the existing fiber tracking algorithms.

In any case the correlation between local tissue volume acquired via Quantitative MRI (**qMRI**) and DTI published in [8] should be used to examine new indicators for the Alzheimer's disease. In this proposed study, however, the more complex diffusion model developed in previous steps should be used instead of DTI to calculate this indicators. Last but not least the overall results of this collaboration should be validated with data sets from Alzheimer's patients against a control group.

Along the progress of the project new results will be summarized and published in journal articles or conferences. A final **report** will summarize and discuss all outcomes of

the cooperation in the end, and will give a perspectives for future research.

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