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Sidong Liu

Multimodal Neuroimaging Computing for the Characterization of Neurodegenerative Disorders

Doctoral Thesis accepted by
the University of Sydney, Sydney, Australia

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Supervisor's Foreword

Neuroimaging has transformed the way we study the human brain under both normal and pathological conditions. The anatomical and functional information in neuroimaging data has an important role in both brain research and clinical management of neurological and psychiatric disorders. In order to extract such information, advance our understanding of brain disorders and accelerate its translational impact, we need to develop innovative computational algorithms and methods to process and analyze these high-dimension and high-volume neuroimaging data.

Multimodal neuroimaging data, acquired from the same subject with different neuroimaging techniques or protocols, such as PET/CT, PET/MRI and MRI/DTI, enables us to explore the different brain functions and structures at the same time. However, computing the information in multimodal data is even more challenging, due to the inconsistent image temporal / spatial resolutions, contrasts, and qualities. As a result, multimodal neuroimaging computing always involves pre-processing, feature extraction, pattern recognition, and visualization techniques, varying in applications.

This book covers many aspects of brain image computing methods, and illustrates the scientific understanding of neurodegenerative disorders cohering around 4 general themes of multimodal neuroimaging computing, including neuroimaging data pre-processing, brain feature modeling, pathological pattern analysis, and translational model development. It demonstrates how multimodal neuroimaging computing techniques can be integrated and applied into neurodegenerative disease research and management, with many examples and case studies. It also contains a number of interesting extension topics, including longitudinal neuroimaging study, subject-centered analysis, and brain connectome. In all, this book introduces a series of innovative approaches and fundamental techniques in neuroimaging computing, which will greatly benefit the neuroscience researchers and neurology practitioners who are interested in medical image computing and computer-assisted interventions.

Sydney
October 2016

A/Prof. Weidong (Tom) Cai

Abstract

Neurodegenerative disorders, such as Alzheimer's Disease (AD), Parkinson's Disease (PD), Vascular Dementia (VD) and Frontotemporal Dementia (FTD), will become a global burden over the forthcoming decade due to the increase of aging populations. The characterization of neurodegenerative disorders has an important role in patient care and treatment planning, especially in the early stage of the disease, since current disease modifying agents are mainly effective before the clinical symptoms appear.

The revolutionary non-invasive neuroimaging technologies have transformed the way we study the brain, and become an essential component in the management of neurodegenerative disorders. The growth of neuroimaging studies has spurred a parallel development of image computing methods, which focus on the computational analysis of the brain images using both computer science and neuroscience techniques.

Multimodal neuroimaging enhances the neuroscience research by compensating the shortcomings of individual imaging modalities and by identifying the common findings from different imaging sources. Multimodal neuroimaging has become one of the major drivers in neurodegeneration research due to the recognition of the clinical benefits of the multimodal data and better access to the imaging devices. There is an imperative need for the development of novel multimodal neuroimaging analysis methods to address the variations in spatiotemporal resolution and merge the biophysical/biochemical information in multimodal neuroimaging data, thus enabling more accurate characterization of the complex pattern of neurodegenerative pathologies.

This study aims to advance our understanding of neurodegeneration using the multimodal neuroiamging techniques. A series of models and methods were developed and further validated through a large-scale systematic analysis on the multimodal neuroimaging datasets acquired from over 800 subjects in the Alzheimer's Disease Neuroimaging Initiative (ADNI) cohort. We designed a set of pre-processing protocols to control the quality of the datasets, then proposed a number of hand-engineered and learning-based features to model the brain morphological and functional changes associated with neurodegeneration. We further designed a multi-channel pattern analysis approach to identify the key brain regions associated with different neurodegenerative pathologies, and a cross-view pattern analysis approach to predict the synergy between these features in joint analysis of multimodal data. Finally, two clinical applications were developed to translate the research findings into improved diagnostic tools, both showing great potential in the management of Alzheimer's disease and mild cognitive impairment. A few extensions of these methods, including longitudinal neuroimaging analysis, subject-centered therapy, and brain connectome, are also demonstrated and discussed in this work.

Parts of this thesis have been published in the following journal articles:

1. W. Cai, S. Liu, L. Wen, S. Eberl, M. Fulham, D. Feng, "3D Neurological Image Retrieval with Localized Pathology-Centric CMRGLC Patterns", *The IEEE 17th International Conference on Image Processing* **(ICIP 2010)**, 3201–3204 (2010). [Reproduced with Permission]
2. S. Liu, Y. Song, W. Cai, S. Pujol, R. Kikinis, X. Wang, D. Feng, "Multifold Bayesian Kernelization in Alzheimer's Diagnosis", *The 16th International Conference on Medical Image Computing and Computer Assisted Intervention* **(MICCAI 2013)**, LNCS8150: 303–310 (2013). [Reproduced with Permission]
3. S. Liu, W. Cai, L. Wen, D. Feng, "Neuroimaging Biomarker based Prediction of Alzheimer's Disease Severity with Optimized Graph Construction", *IEEE International Symposium on Biomedical Imaging* **(ISBI 2013)**, 1324–1327 (2013). [Reproduced with Permission]
4. S. Liu, S.Q. Liu, S. Pujol, R. Kikinis, D. Feng, W. Cai, "Propagation Graph Fusion for Multi-Modal Medical Content-Based Retrieval", *The 13th International Conference on Control, Automation, Robotics and Vision* **(ICARCV 2014)**, 849–854 (2014). [Reproduced with Permission]
5. W. Cai, S. Liu, Y. Song, S. Pujol, R. Kikinis, D. Feng, "A 3D Difference-of-Gaussian-based Lesion Detector for Brain PET", *The IEEE International Symposium on Biomedical Imaging* **(ISBI 2014)**, 677–680 (2014). [Reproduced with Permission]
6. S. Liu, W. Cai, L. Wen, D. Feng, S. Pujol, R. Kikinis, M. Fulham, S. Eberl, ADNI, "Multi-Channel Neurodegenerative Pattern Analysis and Its Application in Alzheimer's Disease Characterization", *Computerized Medical Imaging and Graphics* **38**, 436–444 (2014). [Reproduced with Permission]
7. S. Liu, W. Cai, S.Q. Liu, S. Pujol, R. Kikinis, D. Feng, "Subject-Centered Multi-View Feature Fusion for Neuroimaging Retrieval and Classification", *The IEEE International Conference on Image Processing* **(ICIP 2015)**, 2505–2509 (2015). [Reproduced with Permission]
8. S.Q. Liu, S. Liu, F. Zhang, W. Cai, S. Pujol, R. Kikinis, D. Feng, ADNI, "Longitudinal Brain MR Retrieval with Diffeomorphic Demons Registration: What Happened to Those Patients with Similar Changes?", *The IEEE International Symposium on Biomedical Imaging* **(ISBI 2015)**, 588–591 (2015). [Reproduced with Permission]
9. S.Q. Liu, N. Hadi, S. Liu, S. Pujol, R. Kikinis, D. Feng, W. Cai, "Content-based Retrieval of Brain Diffusion Magnetic Resonance Image", *The 37th European Conference on Information Retrieval Workshop on Multimodal Retrieval in the Medical Domain* **(ECIR MRMD 2015)**, LNCS 9059: 54–60 (2015). [Reproduced with Permission]

10. S.Q. Liu, S. Liu, W. Cai, H. Che, S. Pujol, R. Kikinis, D. Feng, M. Fulham, ADNI, "Multi-Modal Neuroimaging Feature Learning for Multi-Class Diagnosis of Alzheimer's Disease", *IEEE Transactions on Biomedical Engineering* **62(4)**, 1132–1140 (2015). [Reproduced with Permission]
11. S. Liu, W. Cai, S.Q. Liu, F. Zhang, M. Fulham, D. Feng, S. Pujol, R. Kikinis, "Multimodal Neuroimaging Computing: A Review of the Applications in Neuropsychiatric Disorders", *Brain Informatics* **2(3)**, 167–180 (2015). [Reproduced with Permission]
12. S. Liu, W. Cai, S.Q. Liu, F. Zhang, M. Fulham, D. Feng, S. Pujol, R. Kikinis, "Multimodal Neuroimaging Computing: The Workflows, Methods and Platforms", *Brain Informatics* **2(3)**, 181–195 (2015). [Reproduced with Permission]
13. S. Liu, W. Cai, S. Pujol, R. Kikinis, D. Feng, ADNI, "Cross-View Neuroimage Pattern Analysis in Alzheimer's Disease Staging", *Frontiers in Aging Neuroscience* **8(23)**, (2016). [Reproduced with Permission]

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Author's Declaration

I declare that the work in this dissertation was carried out in accordance with the requirements of the University's Regulations and Code of Practice for Research Degree Programmes and that it has not been submitted for any other academic award. Except where indicated by specific reference in the text, the work is the candidate's own work. Work done in collaboration with, or with the assistance of, others, is indicated as such. Any views expressed in the dissertation are those of the author.

October 2015 Sidong Liu

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