A longitudinal MRI preprocessing pipeline of grey matter atrophy for modeling Alzheimer's disease progression

Kevin Mueller, Toan Tran, Gordon Erlebacher, Anke Meyer-Baese

Department of Scientific Computing, Florida State University

Abstract

Alzheimer's disease is thought to be primarily characterized by emergence of amyloid beta (Aβ) plaques and neurofibrillary tangles from an abundance of tau, that spread among the brain inducing large amounts of neurodegeneration. One approach for modeling the spread of the disease is as a diffusion process of anatomical MRI-derived atrophy along a graph created from the brain's structural connectome or functional connectivity. However, this diffusion approach requires longitudinal time-series data that is often highly corrupted due to noise introduced in the standardization process when registering to a common space among subjects. In this work, we create a custom pipeline that includes: creating a longitudinal template with corresponding Jacobian determinant maps, segmenting the template into grey matter voxel probabilities, normalizing the template into a standardized space, partitioning the Jacobian determinant maps into regions, and creating an atrophy time series for all subjects with respect to a baseline scan. We demonstrate the effectiveness of our pipeline by applying it to a large cohort of subjects with varying baseline diagnosis from the ADNI database, and by comparing the resulting data with idealized synthetic data of the diffusion process.

Introduction

Alzheimer's disease is a progressive and irreversible disease that causes significant memory loss, thinking, and eventually even the ability to carry out simple tasks. As such, there is a strong need to develop better models for accurate prediction of the severity and progression of the disease. Recently, longitudinal database have been released that can be used to mode the progression of the disease, however, due to significant preprocessing required to remove large amounts of heterogeneity in the data, i.e., motion artifacts, scanner properties, and post processing, it can be challenging to acquire useable data for longitudinal models, greatly harming the iterative process of researching new modeling paradigms.

Pipeline

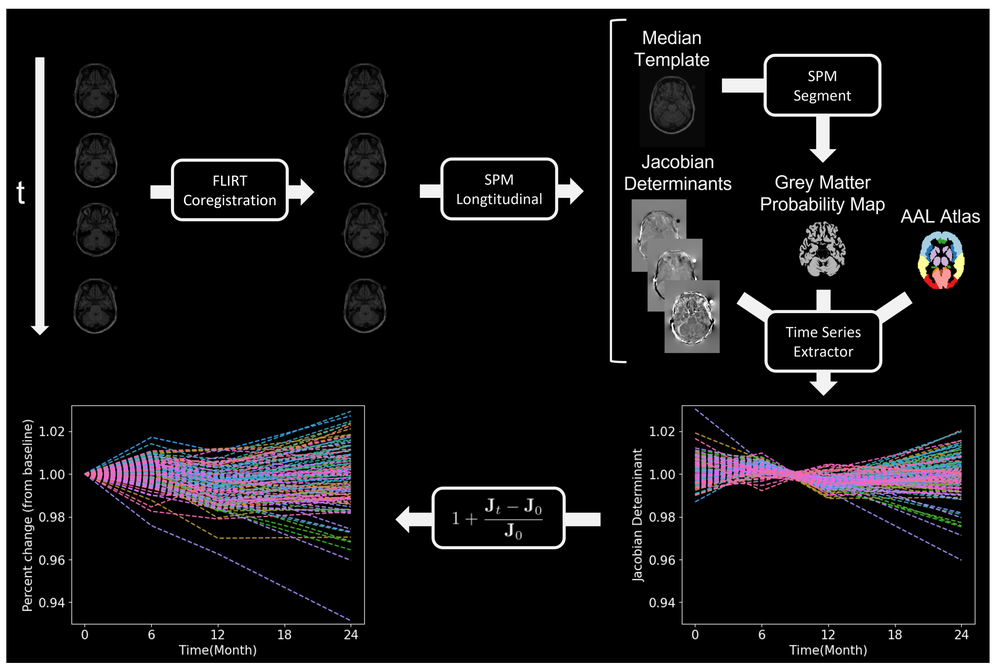

Figure 1: *A flow diagram of the graph encoder module for learning set of node embeddings and undirected edges.*

Figure 1 provides an overview of our pipeline from raw MRI images to final atrophy measures. In order to implement our pipeline. we wrapped various popular MRI preprocessing libraries with the help of nipype, a python library that provides higher level interfaces for neuroimaging preprocessing programs [2].

Our pipeline primarily consists of the following components:

- **FLIRT Coregistration**: Applies an affine transform to coregister all raw images greater than the baseline scan to the baseline. This is needed to account for basic motion artifacts and poorly aligned global coordinates encoded in the image's affine transformation matrix.
- **SPM Longitudinal** : The core longitudindal step that simultaneously creates a median temporal image and registers all other images to the median temporal image [1]. The registration procedure combines group-wise rigid-body and diffeomorphic registration with intensity non-uniformity correction. The optimization is performed by alternating between re-estimating the median template and estimating the 9 affine registration parameters. It outputs a set of Jacobian determinants that represent expansion if greater than 1 or contraction if less than one with respect to the median longitudinal image. These maps are the provide our measure of atrophy in the brain.
- **SPM Segment**: Utilizes a Bayesian strategy based on prior tissue maps to segment and create a deformation field of the median temporal image outputted from the SPM longitudinal pipeline. Only the grey matter (GM) probability map is kept for further stages in the pipeline.
- **Time Series Extractor**: Combines the atlas, GM probability map, and Jacobian determinant maps to create a set of time series for each region. The procedure can be summarized by the following equation:

$$J_r = \frac{1}{N(r)} \sum_{i,j,k} (\text{GM}_{i,j,k} > \tau)\ \text{Atlas}_{i,j,k,r} \text{Img}_{i,j,k}$$

where $N(r)$ is the number of voxels in the rth region of the atlas and above an arbitrary threshold τ. Since all the Jacobian determinant time series are defined with respect to a temporal median image that varies based on the temporal range of each subject, the Jacobian determinants cannot easily be compared across subjects. Therefore, we normalize with respect to the baseline scan as

$$1 + \frac{J_t - J_0}{J_0}$$

where J_t represents the vector of Jacobian determinants for all regions at time t.

Results

We apply out pipeline to AD and CN subjects from the ADNI dataset that consist of a baseline scan, and any subset of {m0,m12,m24}, which implies we only consider temporal data up to two years. This is primarily done due to the lack of data for AD subjects after two years. Figures 2 and 3 provide and overview of our results for single subjects and aggregated statistics over both cohorts. We use a masking threshold (τ) of 95%.

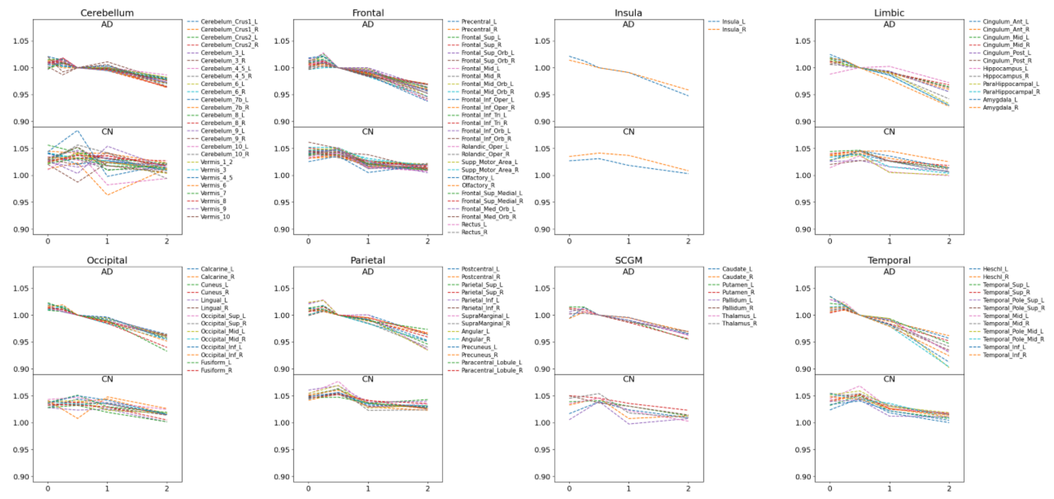

Figure 2: *Regional Jacobian determinant time series of 116 regions derived from the AAL-atlas arranged by temporal lobe applied to two subjects from the AD and CN cohorts.*

Figure 3: *Median time series for 41 important regions from the AAL-atlas of a percent atrophy from baseline measure for AD and CN subjects with corresponding 99% confidence intervals.*

Future Work

- Further clean the data to remove noise.
- Apply our pipeline to progressive mild-cognitive impairment (sMCI) and steady mild cognitive impairment (pMCI) cohorts.
- Use the outputted time series as training data for network diffusion models.

References

[1] John Ashburner Symmetric diffeomorphic modeling of longitudinal structural MRI arXiv:1802.04687 (2018).

[2] Gorgolewski K, Burns CD, Madison C, Clark D, Halchenko YO, Waskom ML, Ghosh SS. (2011). Nipype: a flexible, lightweight and extensible neuroimaging data processing framework in Python. Frontiers

[3] Kunio Nakamura, et al. Jacobian integration method increases the statistical power to measure gray matter atrophy in multiple sclerosis