BSc Artificial Intelligence

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Course: Brain Modeling

Computational Modeling of Neurodegenerative Diseases

Project Report

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1. Introduction

Project Overview and Objectives

In our project, we implement a computational brain modeling framework to simulate and compare three brains: one affected by Alzheimer's disease (AD), another affected by Frontotemporal Dementia (FTD) and one that is healthy.

We took inspiration from Monteverdi et al. (2023) [1], where the Virtual Brain was used to showcase network-specific signatures in connectivity and synaptic parameters across dementias. We adopt a similar strategy: we employ a "MiniBrain" model targeting disease-vulnerable regions by exploiting the Wilson-Cowan neural mass dynamics and a severity parameter (α) to control diseases' effects.

2. Model Reconstruction

Implementing MiniBrain and Brain Atlasing

In this phase, we focused on **constructing a reduced brain model (Mini-Brain)** from a standard structural connectivity dataset. The data and metadata are ready for subsequent simulation of healthy and pathological conditions.

Structural Connectivity Initialization

The foundation of the model is the structural connectivity (SC) matrix provided by The Virtual Brain, which encodes the physical wiring between 76 brain regions based on diffusion tractography data. After normalizing connection weights to [0, 1] and removing self-loops, we derive a reduced 10-node "mini-brain" by selecting regions particularly vulnerable in neurodegenerative dementias.

These nodes split into two groups based on their clinical relevance: the Default Mode Network (rCCP, rPCI, rPCIP, rPCM), which is among the earliest affected in Alzheimer's Disease, and the frontotemporal regions (rPFCM, rPFCDL, rPFCDM, rPFCORB, rPHC, rAMYG), whose degeneration defines Frontotemporal Dementia. The resulting reduced SC matrix and an associated metadata table linking each node to its network membership form the structural backbone for all subsequent simulations.

Disease-specific Structural Connectivity

Pathological SC matrices are generated by introducing a degradation parameter $\boldsymbol{\alpha} \in \mathbf{[0, 1]}$, which tunes disease severity from the healthy baseline to maximal structural damage. The degradation pattern differs between conditions: in AD it acts predominantly on DMN nodes, while in FTD it targets the frontotemporal regions. Sweeping alpha across its full range produces a collection of SC matrices that capture the structural evolution of each condition, which are then fed into the dynamical simulations.

3. Model Simulation

Wilson-Cowan Dynamics

Each node is modeled as a Wilson-Cowan excitatory-inhibitory unit. Local parameters are adjusted for each condition based on the pathological SC, and the network is integrated over 30s with input weighted by a global coupling **G parameter**. Simulations are run for HC, AD, and FTD across multiple alpha levels, producing time series for each node.

Phase-Plane and Stability Analysis

For each node, the effective network input (Ieff) is computed and nullclines are constructed in the E-I plane. Fixed points are characterized by Jacobian eigenvalue analysis, providing stability metrics (maximum real eigenvalue, damping time, local sensitivity). The central finding: phase-plane structure remains identical across HC, AD, and FTD — the I-nullcline is unchanged, confirming local dynamics are not intrinsically altered.

What changes is the effective network input, which shifts the operating point along the same manifold. HC nodes receive highest input and operate in steep, responsive regions; AD shows global reduction, pushing nodes toward flatter regions; FTD shows selective reduction in frontotemporal nodes while DMN nodes remain near HC levels. Pathology thus acts through network-level input modulation — altering where nodes operate on the same dynamical landscape — rather than changing intrinsic local dynamics.

Note on Graphical Representation

All dynamical and structural analyses described above were systematically visualized through code-generated figures and animations. These graphical outputs confirm the findings reported in the literature, particularly the preservation of intrinsic dynamics across conditions and the disease-specific modulation of network inputs. To maintain conciseness, such illustrations are not reproduced in this document but are directly inspected in the scripts.

4. Results and Conclusion

Functional connectivity and stability analyses reveal disease-specific network disruptions in Alzheimer's disease (AD) and frontotemporal dementia (FTD).

Spatial difference maps show that AD produces diffuse changes across both DMN and frontotemporal regions, whereas FTD causes focal frontotemporal alterations with relative DMN sparing.

Local sensitivity analysis demonstrates that pathology does not change intrinsic dynamics but rescales nodal reactivity. AD shows a global reduction in sensitivity, while FTD selectively reduces sensitivity in frontotemporal nodes.

Overall, both diseases diminish effective network responsiveness by placing nodes in regimes where identical inputs have reduced impact, indicating functional rescaling rather than a dynamical bifurcation.

5. References

[1] Monteverdi et al. (2023)
https://www.frontiersin.org/journals/aging-neuroscience/articles/10.3389/fnagi.2023.1204134/full?utm_source=chatgpt.com

[2] The Virtual Brain (TVB)
All structural connectivity data, modeling framework, and simulation environment used in this project are based on materials and methodologies developed within *The Virtual Brain* associated laboratories.

[3] Mean-Field and Neural Mass Modeling Frameworks
The Wilson–Cowan neural mass model and mean-field theoretical assumptions adopted in this work are consistent with implementations provided in The Virtual Brain laboratory.

[4] Brain Atlas Representation
Anatomical and region-to-node mapping were performed using the Harvard–Oxford volumetric atlas, as we have seen during laboratory activities.