PROJECT REPORT FOR GCS WEBSITE

Abstract

Recent studies associate schizophrenia to alterations in brain structure, function, and neurochemistry. However, such findings have not found their way into clinical practice, mostly due to the lack of biophysiological details about the processes that are behind such alterations.

To overcome such limitations, simulations of brain functioning using mathematical models can be used to describe brain functioning characteristics. Tunning such models' parameters, can produce simulations sufficiently similar to original brain functioning, which allows to infer about brain characteristics.

In this project, such techniques were employed to neurological data from patients with schizophrenia to investigate its effects in brain functioning mechanisms.

Report

The human brain is a very complex system, being composed of over 80 billion neurons, with each neuron being connected to over 1000 other neurons, thus resulting in a system with over 60 trillion neuronal connections. Such magnitude of complexity makes investigating brain disorders a challenge, specially when it comes to psychiatric disorders, which do not leave any visible marks on the brain, such as lesions, that can be observed through the usage of traditional brain imaging techniques such as Magnetic Resonance Imaging (MRI). Schizophrenia is a psychiatric disorder with a great impact on society, with approximately 1% of society being affected by this disease, and which imposes a great burden on individuals.

With no clear markers of this disease on the brain, recent studies investigated the effect of schizophrenia in brain functioning, combining information about the structure of the brain (structural MRIs, or sMRIs) and imaging of brain functioning (functional MRIs, or fMRIs). What was found in such studies, was that schizophrenia could be associated with alterations in brain structure, function, and neurochemistry in multiple brain regions.

None of these findings, however, have yet found their way into clinical practice nor have they contributed to the efficiency of psychiatric treatments, despite considerable scientific efforts. One possible explanation for this limitation is that traditional neuroimaging only provides us with a representation of the brain at a higher level, as 3 or 4-dimensional images. We lack, in such images, biophysiological details about the processes that underlie brain functioning, i.e., that are behind the observable functioning. One could think about the neurons as cities, the connections between neurons as the roads connecting such cities and the brain functioning as the traffic in such roads. What we see, with traditional neuroimaging would be the roads, and a temporal representation on how did the traffic flow happened on a specific time period. What we lack, is a view of what were the processes that caused the traffic to be as it was, during that specific ammount of time.

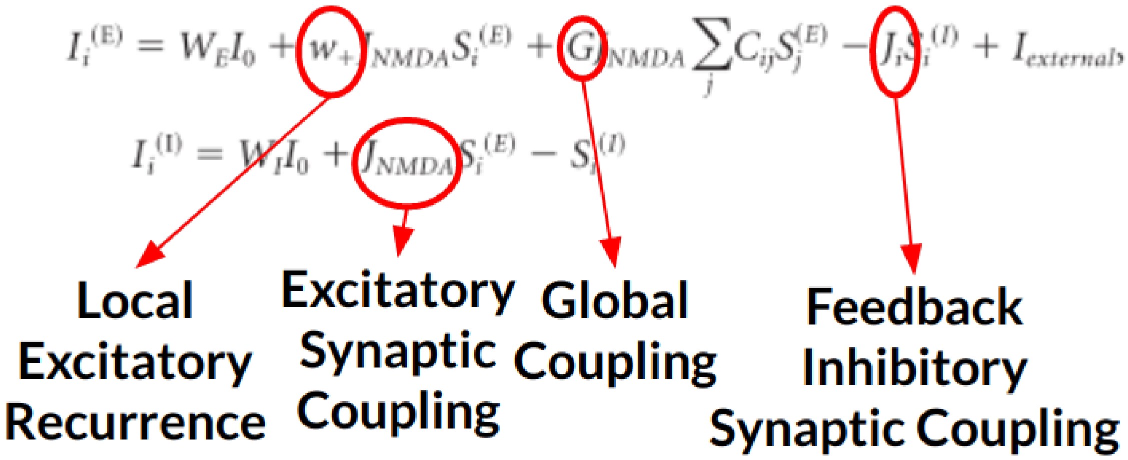
To overcome such limitations, one potential approach is to simulate brain functioning through the usage of mathematical models that represent brain's spatiotemporal dynamics. Through the usage of these so called “neural mass models”, we are allowed to simulate brain functioning constrained to its structural information. Such simulation models have parameters that describe brain functioning characteristics, and by tunning such parameters we can find simulations that are sufficiently similar to original functioning information, which then allows some inference about brain characteristics.

In the project “*Understanding Schizophrenia using Computational Modeling: Biological Simulations of the Brain’s Functional Connectome*” (registered at the GCS with the ID *Brainsim*), we employed simulation techniques to demonstrate the applicability of biophysical brain network models to neuropsychiatry. We investigated the mechanisms underlying whole-brain functional connectivity observed in patients with schizophrenia using a computational neuro-platform named “The Virtual Brain” (TVB). Our aim was to investigate the effects of schizophrenia in such brain mechanisms, thus shedding some light in the so far unknown effects of schizophrenia in brain dynamics.

This project was leaded and supervised by Prof. Dr. Joseph Kambeitz, from the Department of Psychiatry and Psychotherapy from the University of Cologne, and executed by the PhD Student MSc. Pedro Costa Klein, from the Department of Psychiatry and Psychotherapy from the University of Cologne, and used the infrastructure from GCS to perform such simulations in large-scale. The challenge of this project was to iterate over several combinations of model parameters, which quickly lead to a massive number of simulations. The GCS supercomputing system JURECA played a major role in this project, since it allowed the parallelization of such simulations, thus leading to a massive saving of computational time.

Results from these simulations are still under analysis, but such in depth analysis can potentially lead to interesting findings on schizophrenia, which can push forward the knowledge about this disorder and lead to improves in its treatment.

Images



$$I_i^{(E)} = W_E I_0 + w_+ J_{NMDA} S_i^{(E)} + G J_{NMDA} \sum_j C_{ij} S_j^{(E)} - J_i S_i^{(I)} + I_{external}$$

$$I_i^{(I)} = W_I I_0 + J_{NMDA} S_i^{(E)} - S_i^{(I)}$$

Figure 1: Equations for the model of brain dynamics. Models of brain dynamics can be interpreted as coupled dynamic mathematical equations, each equation containing parameters that are related to specific biophysiological brain mechanism.

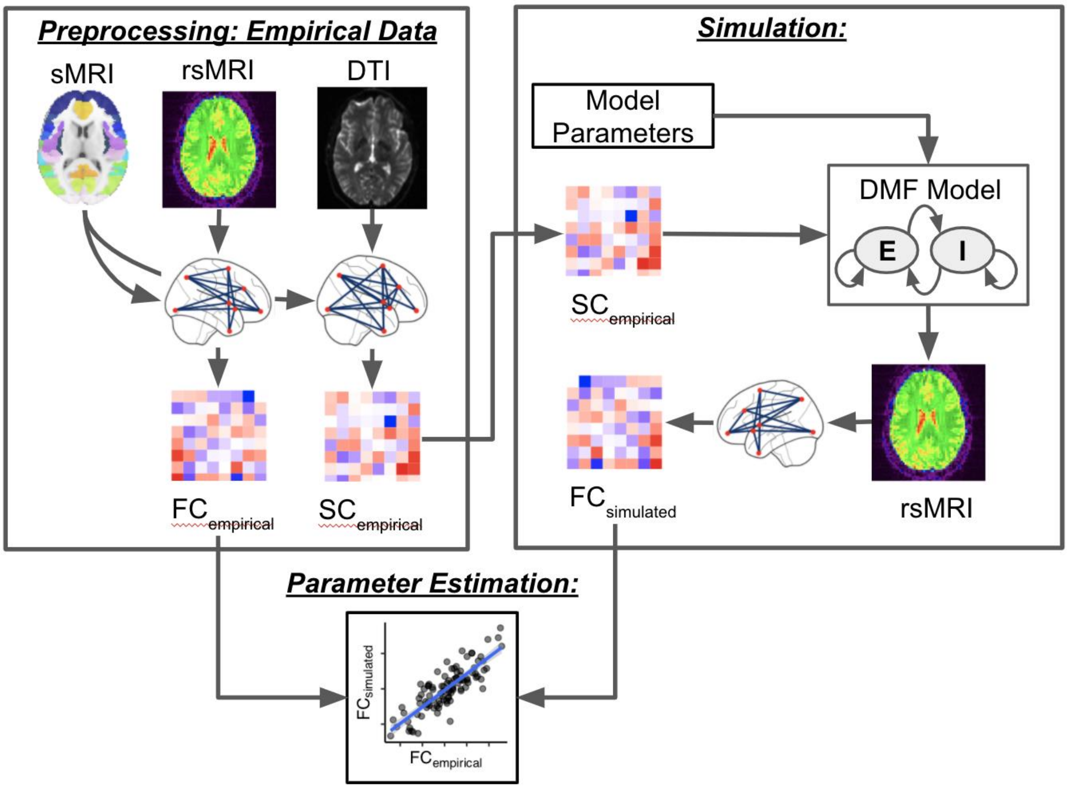


Figure 2 - Pipeline for the execution of the simulations. The pipeline for this work can be divided in two parts: Preprocessing and Simulation. For the preprocessing we collected MRIs with information about structure and functioning and generated individualized structural and functional connectivity representations. For the simulations, we used the structural connectivity representation along with space of parameters to be explored, containing all possible parameters combinations within a specific range. Then, for each parameter combination, a simulation was performed, resulting in a simulated functional connectivity. Finally, for each simulation, the simulated functional connectivity was compared to the original functional connectivity and the parameter combination that generated the simulation

mostly similar to the empirical data was then inferred as the actual parameters from a subject.