Internship Report

By

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Abstract

This internship report encompasses the work that was learned and executed as a Research Intern at the Brain Inspired Neural Networks (BINN) Lab, Computer Science and Information Systems Department, BITS Pilani K. K. Birla Goa Campus under the guidance of Dr. Basabdatta Sen Bhattacharya from July 31, 2023 until September 23, 2023. The report explores the dynamic field of Computational Neuroscience, focusing on the utilization of The Virtual Brain (TVB) software for large-scale brain modeling during a research internship. Computational Neuroscience endeavors to understand the intricacies of the nervous system, from molecular interactions to cognitive processes, employing mathematical models and simulations. TVB offers a unique approach to whole-brain simulation by simplifying micro-level complexities to reveal macro-level brain organization, producing accurate neuroimaging signals. As a central tool in clinical trials, digital research infrastructure, and neuroinformatics initiatives, TVB has gained prominence, with a burgeoning user base and a substantial body of peer-reviewed research. This report highlights TVB's contributions to advancing our understanding of the human brain and its applications in healthcare and neuroscience.

Acknowledgement

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Chapter 1
Introduction

During the 8-week internship period I worked as a Research Intern in the field of Computational Neuroscience under Dr. Basabdatta Sen Bhattacharya at the Brain Inspired Neural Networks (BINN) Lab at BITS-Pilani, Goa campus.

The interdisciplinary field of Computational Neuroscience is the study of the development, structure, physiology, information processing and cognitive abilities of the nervous system. Computational neuroscience uses mathematical multi-scale models, theoretical analysis, and simulations of neural function from the perspective of molecules, cells and networks, all the way to cognition and behavior. Simulating the human brain is the holy grail of neuroscience – offering a pioneering tool for understanding how our brain works and how to deal with its disorders like stroke, epilepsy or neurodegenerative diseases like Alzheimer's or Parkinson's.

As a Research Intern, I was primarily tasked with working with The Virtual Brain (TVB) software which is used to simulate large-scale brain models. While several research initiatives simulate neurons and small brain regions at the cellular level on massively parallel hardware, they are still years away from clinical applications. The Virtual Brain (TVB) takes a different approach and reduces complexity on the micro level to attain the macro organization: a TVB model of a patient's brain generates sufficiently accurate EEG, MEG, BOLD and SEEG signals by reducing the complexity millionfold through methods from statistical physics. The key is TVB's hybrid approach of merging individual anatomy from brain imaging data with state-of-the-art mathematical modeling. Today, TVB is a reference tool for full-brain simulation. TVB serves as the simulation engine in the world's first clinical trial on predictive brain modeling in epilepsy surgery (EPINOV). TVB is also the choice of full-brain simulator in Europe's digital research infrastructure EBRAINS and directly links to other large-scale neuroinformatics efforts such as the Allen Institute's Mouse atlas or the Human Brain Project (HBP). A large, growing user base of clinicians and scientists are working every day with TVB, citing its scientific groundwork in well over 100 peer-reviewed publications. Dedicated research facilities at Charité in Berlin, AMU in Marseille and Baycrest in Toronto have constructed and simulated almost 1000 individual, Connectome-based brain network models and published their findings, clocking in upwards of 10 million CPU core hours.

Chapter 2
Institute Profile

BITS Pilani Goa has emerged as a hub for cutting-edge research in a wide array of disciplines. The campus boasts state-of-the-art research facilities and laboratories, facilitating pioneering work in fields ranging from computer science and engineering to biological sciences and interdisciplinary studies. With a diverse and dedicated community of researchers, faculty, and students, BITS Pilani Goa consistently produces groundbreaking research that contributes to the advancement of knowledge and addresses real-world challenges. This institution's research endeavors not only enrich the academic landscape but also have a meaningful impact on industries, communities, and society as a whole.

The Brain Inspired Neural Networks (BINN) Lab @ BITS Pilani Goa campus falls under the purview of the Data Science Research Group of the Department of Computer Science and Information Systems (CSIS). The lab comprises a small team of undergraduate students and Research scholars, led by Dr. Basabdatta Sen Bhattacharya (BSB), who are fascinated with the areas of neural networks and/or neuroscience in particular, and artificial intelligence in general. The research interests are two-fold:

1. Computational Neuroscience: Design and develop biologically inspired/informed neural circuits/models that can advance the understanding of brain disease and mental health. Towards this, we use lumped parameter neural networks that are known to emulate high level brain data such as Electroencephalogram (EEG).

2. Neuro-inspired Technology: Design and develop brain inspired/informed neural networks that can be trained for visual cognition and decision making. Towards this, Spiking Neural Networks (SNN) were used that have, thus far, been implemented on the SpiNNaker neuromorphic platform. Alongside, they are now looking into computation on GPU.

Chapter 3
Literature Review

3.1 Learning how network structure shapes decision-making for bio-inspired computing

Michael Schirner, Gustavo Deco & Petra Ritter

Objective:

The primary objective of this study is to investigate the relationship between brain network structure and intelligent behavior. To achieve this, the researchers employed a learning algorithm to create personalized brain network models for a cohort of 650 participants from the Human Connectome Project. The study aimed to measure intelligence using two key metrics: the G-factor (General Intelligence Factor) and fluid intelligence, assessed primarily through the Penn Matrix Reasoning Test.

Methodologies:

- **Brain Network Modeling:** The researchers utilized a learning algorithm to construct personalized brain network models based on structural connectomes estimated from diffusion-weighted magnetic resonance imaging (DW-MRI) data. These models integrated neural population dynamics and connectivity patterns.
- **Parameter Optimization Algorithm:** An algorithm was developed to fit these brain network models to empirical functional connectivity data. This algorithm adjusted parameters to match simulated functional connectivity with observed connectivity, emphasizing the balance between neuronal excitation and inhibition (E/I balance).
- **Excitation-Inhibition (E/I) Balance:** The study investigated the role of E/I balance in controlling functional connectivity. By manipulating this balance, the researchers modulated the synchronization and amplitude of synaptic currents, which in turn affected functional connectivity patterns.
- **Decision-Making and Working Memory Modeling:** The study explored the impact of input amplitude on decision-making and working memory processes. Models considered the dynamics of neural connections in the prefrontal cortex (PFC) and posterior parietal cortex (PPC), specifically in decision-making tasks. The study observed correlations between cognitive performance metrics and neural input amplitudes.

Findings:

- **Intelligence and Decision-Making:** Individuals with higher intelligence scores demonstrated a tendency to adopt a deliberate, thoughtful approach when faced with complex decision-making tasks. Conversely, they exhibited superior efficiency in processing speed tasks. This suggests that higher intelligence is associated with the ability to flexibly modulate cognitive strategies based on task demands.
- **E/I Balance and Functional Connectivity:** The research highlighted the importance of excitation-inhibition (E/I) balance in controlling functional connectivity within the brain. Manipulating this balance allowed the researchers to modulate synchronization and amplitude of synaptic currents, thereby influencing functional connectivity patterns.
- **Input Amplitude and Decision-Making:** Lower input amplitudes were associated with slower but more accurate decision-making processes, indicating deeper and more thoughtful information consideration. Higher input amplitudes, however, resulted in quicker decisions but with reduced accuracy due to increased susceptibility to noise.

Conclusion:

This study offers a comprehensive exploration of the interplay between intelligence, decision-making strategies, and functional connectivity within the human brain. It introduces the concept of E/I balance as a fundamental determinant of functional connectivity patterns and presents a novel algorithm for tailoring brain network models to individual empirical data. By shedding light on the role of E/I balance and its implications for network dynamics, this research advances our understanding of the neural mechanisms underlying human cognition. It also provides a promising framework for investigating neuropsychiatric disorders and cognitive processes grounded in network-based principles, thus contributing to the understanding of the brain's complexities.

To further understand the vital role of Excitation-Inhibition Balance in understanding several neurological disorders, a second paper was reviewed.

3.2 Excitation-inhibition balance as a framework for investigating mechanisms in neuropsychiatric disorders

Vikaas S. Sohal & John L. R. Rubenstein

https://www.nature.com/articles/s41380-019-0426-0

Objective

The paper "Excitation-Inhibition Balance as a Framework for Investigating Mechanisms in Neuropsychiatric Disorders" by Vikaas S. Sohal and John L. R. Rubenstein offers a comprehensive exploration of the concept of excitation-inhibition (E-I) balance and its implications for understanding neuropsychiatric disorders, particularly Autism Spectrum Disorder (ASD).

Inferences

The authors begin by acknowledging the foundational work of Rubenstein and Merzenich in 2003, which hypothesized that ASD might result from an imbalance in neural circuits' signal-to-noise ratio due to changes in E-I balance. The paper builds upon existing hypotheses and considers various neurobiological mechanisms that could contribute to altered E-I balance, including neuronal homeostasis, synaptic autoregulatory feedback, and developmental disconnection. It refrains from attempting to replace or replicate these studies but rather seeks to provide a comprehensive framework for understanding E-I balance's complexity. Initially, the authors simplify E-I balance, treating excitation and inhibition as singular entities, where an imbalance results in increased or decreased activity until balance is restored, primarily on long timescales.
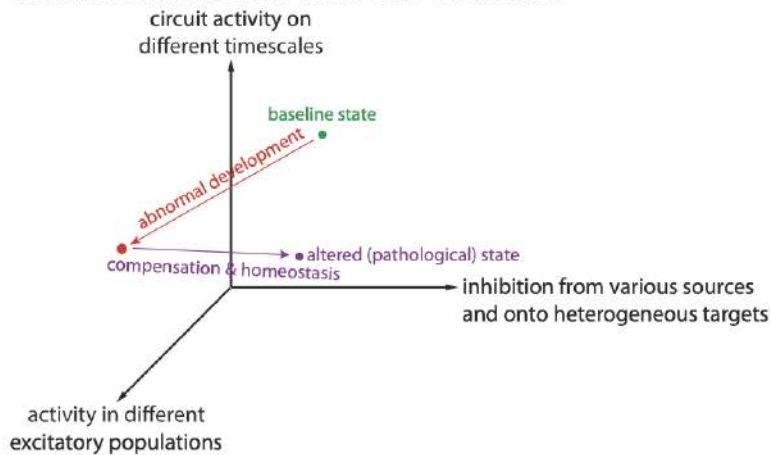
A multidimensional view of E-I balance:

Fig 3.1 Multidimensional view of E-I balance

However, they introduce a more nuanced definition, highlighting that E-I balance represents a stable global activity level within a circuit, acknowledging that specific neuron groups may exhibit temporary imbalances that change over time. This dynamic view emphasizes that even in balance, the active neuron set evolves, creating various configurations of E-I balance. Transitions between these configurations can occur due to external input changes or short-term synaptic plasticity, shaping the signal-to-noise ratio, as initially proposed by Rubenstein and Merzenich. Thus a multidimensional perspective of E-I balance is formed suggesting that various mechanisms, such as altered gene expression, protein translation, compensatory processes, etc., perturb circuits along multiple dimensions. These dimensions could be overall excitatory levels, inhibition levels, and circuit activity on different timescales. The paper then speaks about the developmental and genetic mechanisms that can lead to an increased E/I ratio in the cortex and hippocampus and the impact of defects in these processes on neural function.

Conclusion

In the conclusion, the researchers provide valuable suggestions for future computational studies to:

1. categorize the diverse "E-I imbalances" into manageable circuit derangement categories,
2. identify potential biomarkers indicating specific circuit derangements in individuals, and
3. determine whether identifying the type of E-I imbalance/circuit derangement can predict behavioral abnormalities and effective therapeutic strategies.

This paper provides a valuable framework for understanding E-I balance's intricacies and its relevance to neuropsychiatric disorders, offering important insights for future research in the field.
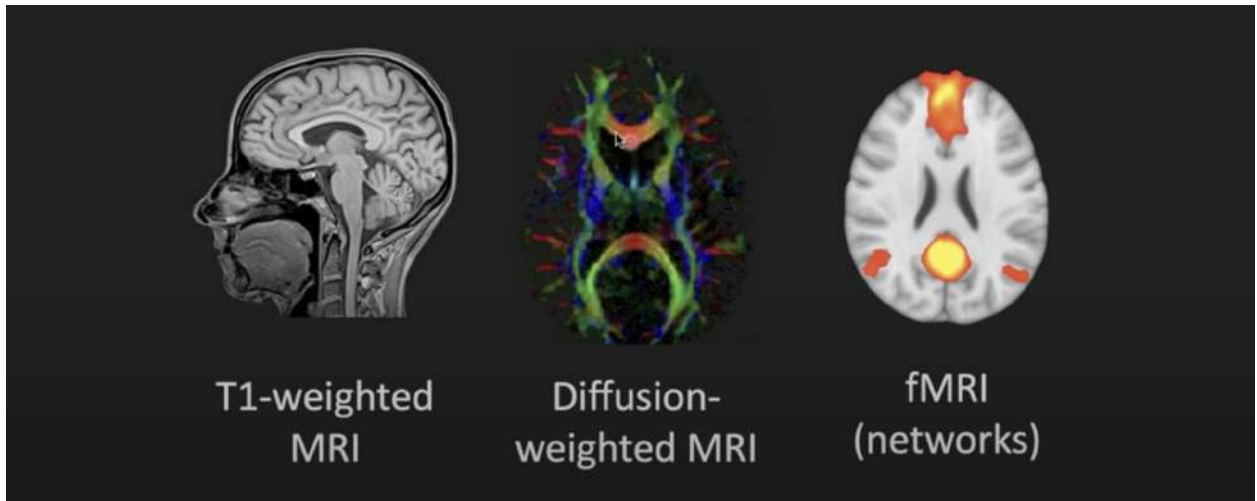
Chapter 4

Brain Imaging

Fig 4.1 Types of MRI used to create Brain Network Models

Magnetic Resonance Imaging (MRI) has proven to be pivotal in visualizing numerous aspects of the brain.

4.1 Types of MRI

TVB makes use of 3 different types of MRI to construct the Brain Network Models

1. **T1-weighted MRI**

   T1 weighted MRI is used to visualize and map the overall structure and anatomy of the brain. Using this mode of MRI, we are able to differentiate between white matter and grey matter which is a key to localizing function to certain regions in the brain

2. **Diffusion-weighted MRI**

   Diffusion-weighted MRI or dwMRI provides a visualization of the numerous white matter fiber tracts that act as the connections between different parts of the brain. It can help us to define how strongly two given regions of the brain are connected.

3. **fMRI (Functional Magnetic Resonance Imaging)**

   fMRI is a neuroimaging technique that measures brain activity by detecting changes in the magnetic properties of hemoglobin in blood. It is a non-invasive method that provides images of brain activity by capturing fluctuations in blood flow and oxygenation that occur in response to neural activity.

4.2 Processing of MRI data for TVB

TVB requires pre-processed data in order to build Brain Network Models. A pre-processing pipeline has been outlined by Michael Schirner et al (2015) which essentially converts raw MRI data into a form that TVB can interpret.
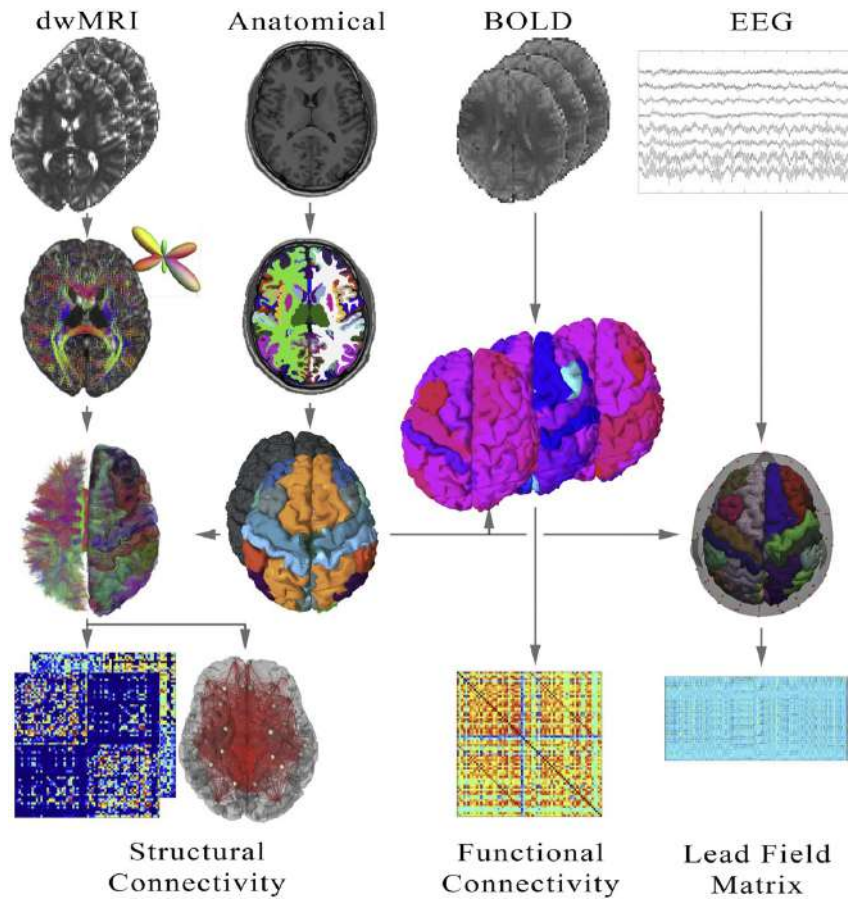
Fig 4.2 Processing Pipeline flow

4.2.1 Pipeline Notebook

A detailed Python notebook is available demonstrating a step-by-step procedure from uploading the MRI data to downloading the TVB-Ready data which is available on E-BRAINS, an open research infrastructure that gathers data, tools, and computing facilities for brain-related research. The pipeline makes use of other facilities of E-BRAINS such as the Drive and Collab to execute the pipeline.

4.2.2 The Need for High-Performance Computing

This pipeline is required to be executed on a supercomputer due to the intense computational power required to process the MRI data into an interpretable form.
Using the E-BRAINS platform it is possible to get access to the CSCS Piz Daint Supercomputer hosted in Switzerland. The pipeline notebook specifically shows the process for interacting with this supercomputer.

Table 4.1 CPU requirements to process one complete dataset of one subject

	Job	Cores	Walltime [h]	Memory [GB]	Total
HCP pipeline	Structural	1	24	12	
	Functional	1	12	24	
	Diffusion	1	30	24	
					= 66 core-h
Structural	Import	1	0.2	2	
connectome	Masks	1	0.4	2	
	Intensity	2	3	2	
	Response	8	1	12	
	Deconvolution	2	5	2	
	Tractography	36	20	72	
	Filtering	36	2	72	
	Aggregation	24	0.2	48	
					= 806.4 core-h
Functional	Cifti	1	1		
					= 1 core-h
				Total =	**873.4 core-h**

4.2.3 Goals of the pipeline

• Remove artifacts, distortions & blurring
• Preserve high spatiotemporal resolution
• Generate cortical surfaces
• Represent data using the natural geometry of cortical/subcortical structures
. Generate neurobiologically accurate segmentations/parcellations
• Generate precise within-subject cross-modal registration
• Generate surface/volume cross-subject / standard space registrations / transforms

4.2.4 Input to the pipeline

The pipeline requires that the MRI data be organized in a directory structure that is outlined by
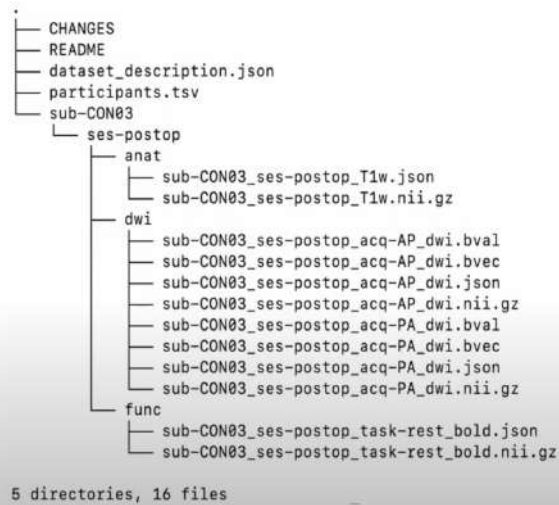BIDS (Brain Imaging Data Structure).

Fig 4.3 Directory structure of MRI data for input to the pipeline

After uploading MRI data to the supercomputer, the pipeline runs the three Docker containers

- bids/mrtrix3_connectome - for processing dwMRI, tractography
- poldracklab/fmriprep - for processing fMRI data
- thevirtualbrain/tvb_converter - for merging the output of the above two containers

4.2.5 Outputs of the pipeline

Once the pipeline processing is complete it will automatically provide the output data in 2 formats i.e. TVB-ready and BIDS. For our use in TVB, we will work with the first output format.

Table 4.2 Outputs of the processing pipeline

Level	Mandatory filename part	Description	Format	Output tvb-pipeline-converter
Minimum large-scale	weight	SC coupling weights	NxN	sub-_Connectome/ weights.txt
	tract	SC track lengths	NxN	sub-_Connectome/ tract_lengths.txt
	centres	Centers of brain regions	Nx4 column 1: region label columns 2 -4:3D coordinates	sub-_Connectome/ centres.txt
Extended large-scale	area	Surface areas (mm²)	Nx1	sub-_Connectome/area.txt
	cortical	cortical or subcortical	Nx1 1: cortical 0: subcortical	sub-_Connectome/cortical.txt
	orientation	orientation of the average normal vector	Nx3 3D coordinates	sub-_Connectome/ orientation.txt
	hemisphere	left or right	Nx1 1: right 0: left	sub-_Connectome/hemisphere.txt

Surfaces {"Cortex",	vertices	surface triangulation	Nx3 3d coordinates	sub-_/vertices.txt,
"inner_skull_surface", "outer_skull_surface", "outer_skin_surface"}	triangles	surface triangulation	Nx 3 vertex indices	sub-_/triangles.txt
	normals	surface triangulation	Nx3 3d coordinates	sub-_/normals.txt
Region-mapping	N/A	associates surface vertices with large-scale regions	Mx1 region label	sub-_region_mapping.txt
Sensors: EEG, SEEG, MEG	N/A	sensor locations	Kx4 o rKx 7 column 1: channel name columns 2- 4: 3d coordinates columns 5- 7: normals	sub-_EEG_Locations.txt
Projection matrix	N/A	mapping between regions/vertices and sensors	K x N or K x M	sub-_EEGProjection.mat

4.2.6 Key processes carried out by the pipeline

1. Surface triangulation

- This process involves dividing the brain's cortical surface into a network of interconnected triangles. While direct MRI imaging cannot provide a 3D representation of the brain's surface, using surface triangulation it is possible to reconstruct what the cortical surface of a particular patient's brain would look like.
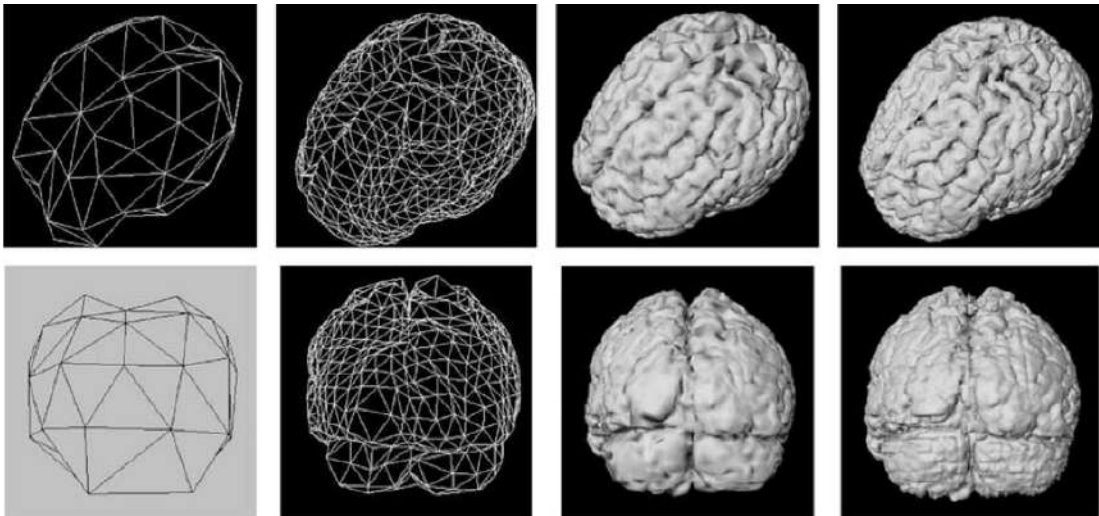

Fig 4.4 Surface triangulation of cortical surface

2. Parcellation

Parcellation is the process of dividing and mapping the brain into multiple regions. For this process, we make use of a tool called an atlas that is responsible for determining the number of regions and their boundaries that are to be mapped. Existing software tools like freeSurfer can automatically do this process.

3. Tractography

Tractography is computed from the dwMRI which is used to compute the connection weights and tract lengths between two regions. The weights are calculated by counting the axon bundles leaving one region and entering another. This is then assigned a relative number which is the 'weight' of that particular connection. The track lengths are the lengths of the white matter fiber tracts that connect the different regions of the brain. This information is vital to developing the Brain Network Model as it computes the time delay for a signal to travel from one region to another.

Together this data is represented as Structural Connectivity. It is represented as the weights and tract lengths as matrices as shown in Fig.
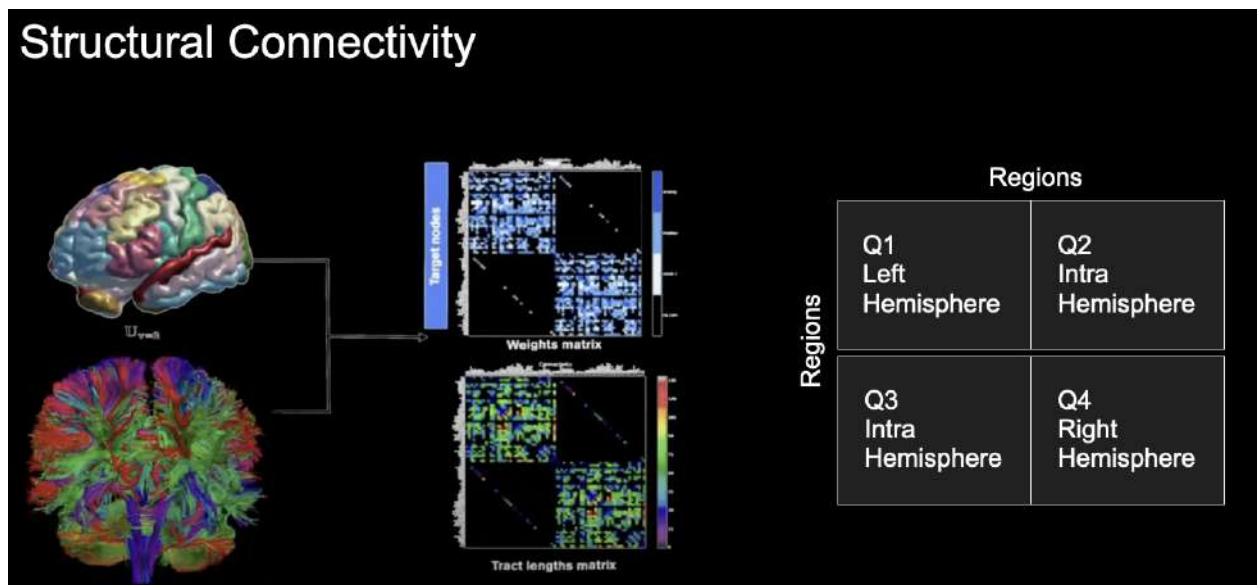

Fig 4.5 Parcellation and Tractorgrapyh used to compute the weights and tract lengths matrix

4.3 Types of Connectivity in TVB

TVB primarily distinguishes between 2 types of connectivity between nodes in a Brain Network Model (BNM).

1. **Global /large-scale connectivity**

   These track the axon bundles as they leave from one region to the other . These are heterogeneous in nature due to the time delay associated with each connection due to the varying lengths of the connection. Global connectivity is long-range (order of tens of cm).

2. **Local connectivity**

   It is the connectivity of one node to its neighboring nodes i.e. lateral axons that connect to the neighboring populations that applies **only to surface-based modelling.** Signal transmission via local connections is instantaneous and hence local connectivity is homogeneous in nature. We can define the range of local connectivity using spatial equations. Local connectivity is short-range (order of cm)

Chapter 5

Brain Network Models

5.1 Brain Network Model (BNM)

Brain Network Models simulate the brain as a network of relatively simpler units (nodes) that interact to produce brain activity. These 'simpler units' differ in their level of abstractions, depending on how detailed we need the simulation to be. By integrating real-world data into computational models, researchers can test and refine hypotheses, uncover hidden patterns, and gain insights into the intricate dynamics of brain networks. These models not only facilitate the interpretation of experimental findings but also allow for the exploration of hypothetical scenarios and the prediction of how the brain might respond under various conditions.

BNMs simulate the resting state of the brain. Multiple theoretical analyses have indeed confirmed the major role of the so-called resting state networks within the brain. Their complex oscillations on different time scales even provide the utter foundation of functional processes within the brain. Metaphorically speaking, the resting state of the brain can be pictured as a nimble, always vigilant tennis player, waiting on his baseline for the new service of his opponent (which would be an outside stimulus or a task being performed). Thanks to his constant motion, mindfully envisioning possible routes, he can react more readily to events from various directions.

5.2 Types of Brain Network Models

To compute a simulation, our goal is to simulate the activity of each node in the network as well as the interaction between the nodes of the network. The generic large-scale brain network equations effectively capture these various dynamics. TVB supports 2 types of models depending on how refined we need the simulation to be.
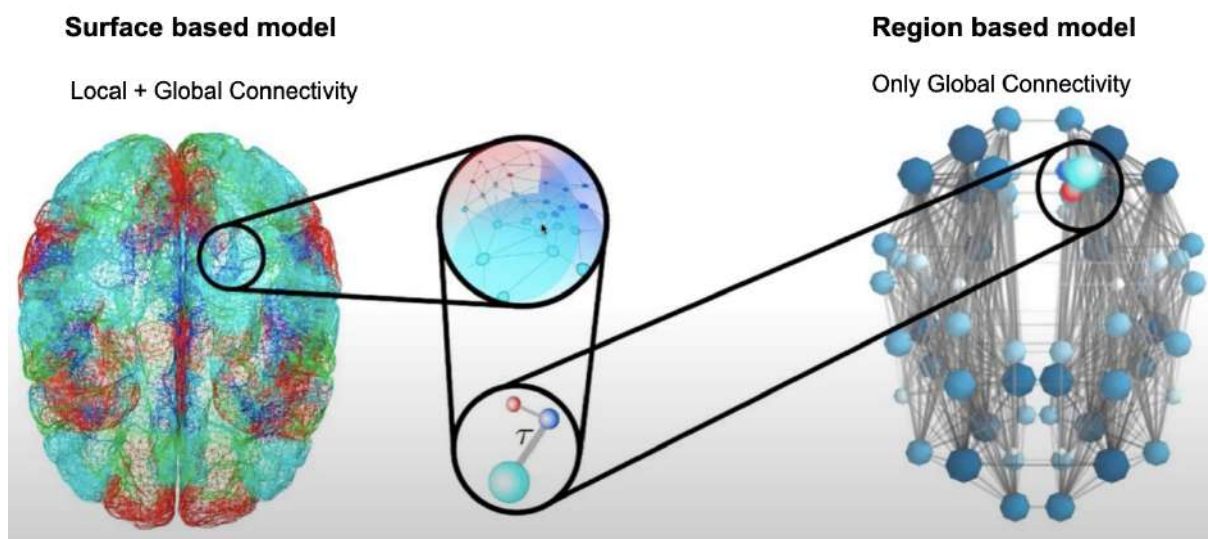

Fig 5.1 Types of Brain Network Models in TVB

1) Region-based model

Here each brain region is shrunk to its center of mass to form a node. Each node models the neural population activity of a brain region. There are no local interactions in this kind of model because the connections between regions are long-range.

Mathematical Representation

$$\psi(x_i, t) = N(x_i, t) + g\left(\sum_{j=1}^{n} W_{ij} x_j (t - D_{ij})\right) + I(x_i, t) + \xi_i(t)$$

In this equation:

- $\psi(x_i, t)$ represents the current state of state variable x (ex. Local Field Potential, Membrane Potential, etc) for region i at a particular time t
- $N(x_i, t)$ represents the intrinsic dynamics of the i-th region, describing how x_i evolves over time based on its own internal processes.
- The term $g\left(\sum_{j=1}^{n} W_{ij} x_j (t - D_{ij})\right)$ represents the influence of neighbouring regions on the i-th region's dynamics. Here, g is a scaling factor, n is the total number of regions, W_{ij} is the weight of the connection from region j to region i, and $x_j (t - D_{ij})$ represents the state of the neighbouring region j at a delayed time $(t - D_{ij})$.
- $I(x_i, t)$ represents external inputs or driving forces applied to the i-th region at time t. It can account for any additional factors or disturbances affecting the region's dynamics.
- $\xi_i(t)$ represents stochastic noise or random fluctuations in the i-th region's activity at time t, capturing inherent randomness or variability in neural processes.

2) Surface-based model

Here each vertex of the surface triangles is represented as a node. Cortical and subcortical areas are modelled on a finer scale, in which each point represents a neural population model. There are local interactions in addition to global interactions owing to the proximity of neighbouring nodes in the network. This provides for a more detailed, but computationally expensive simulation.

Mathematical Representation

$$\psi(x_i, t) = N(x_i, t) + g \left(\sum_{j=1}^{n} W_{ij} x_j (t - D_{ij}) \right) + \sum_{j=1}^{n} L_{ij} x_j (t) + I(x_i, t) + \xi_i(t)$$

In this equation:

- $\psi(x_i, t)$ represents the current state of state variable x for node i at a particular time t

- $N(x_i, t)$ represents the intrinsic dynamics of the i-th node, describing how x_i evolves over time based on its own internal processes.

- $g \left(\sum_{j=1}^{n} W_{ij} x_j (t - D_{ij}) \right)$ represents the influence of global interactions on the i-th node's dynamics. Here, g is a scaling factor, n is the total number of nodes, W_{ij} is the weight of the connection from node j to node i, and x_j represents the state of neighbouring node j at a delayed time $(t - D_{ij})$.

- $\sum_{j=1}^{n} L_{ij} x_j (t)$ represents the influence of local interactions. L_{ij} represents the weight of the connection between node j and node i within the neighbourhood of node i.

- $I(x_i, t)$ represents external inputs or driving forces applied to the i-th node at time t. It can account for any additional factors or disturbances affecting the region's dynamics.

- $\xi_i(t)$ represents stochastic noise or random fluctuations in the i-th node's activity at time t, capturing inherent randomness or variability in neural processes.

5.3 Neural Mass Models

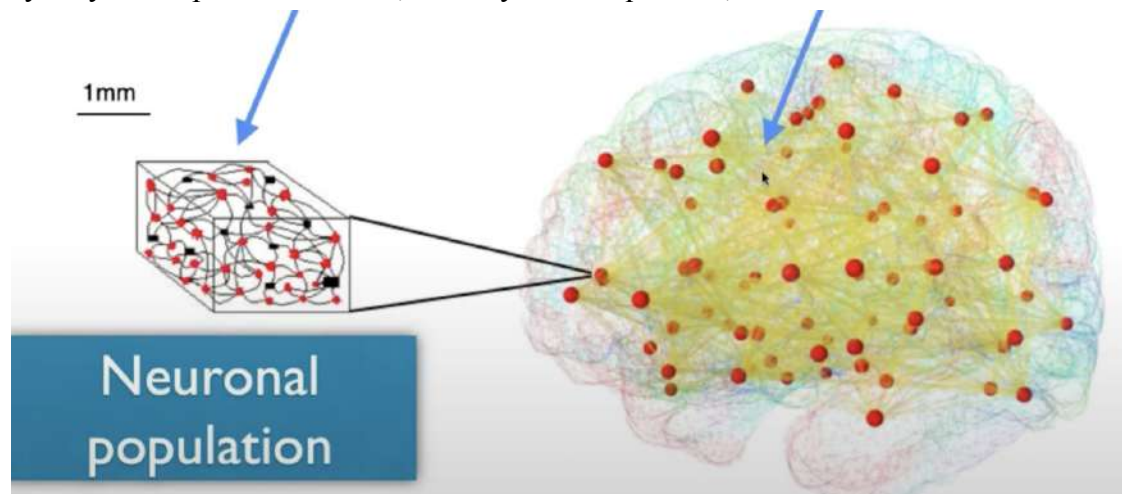Synonyms: Population models, local dynamic equations, mean field model

Fig 5.2 Illustration of the dynamics within a single node in a BNM

Neural mass models describe the activity produced **within** a single node (which can be a region in the case of the region-based simulations or a vertex of the surface triangles as in surface-based simulations). As previously mentioned, our goal is to simulate large-scale brain activity i.e whole-brain activity. Therefore it is not possible to simulate the activity of each individual neuron in the brain as there are roughly 86 billion of them in the brain. We instead group multiple neurons in what is called a **neural mass** or **neural population**. Within this grouping, we may look to differentiate neurons based on their type for ex. Excitatory and Inhibitory. We combine multiple neurons into a single coupled excitatory and inhibitory population. Therefore the activity of the neural mass can be expressed using a simplified model that describes the average/mean behaviour of each of the two groups.

Mathematically, the activity of these individual neural masses by expressing the model as a set of differential equations that describes the change of some biophysical quantity such as membrane potential, firing rate, etc. with respect to time. TVB supports several neural mass models such as Jannse-Rit, Wong-Wang, Wilson-Cowan as well as phenomenological models like the Generic 2D Oscillator, the wave pattern of brain activity.

Ex. Deco-Wang Model

Deco-Wang dynamic mean field model

Input currents

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

$$I_i^{(I)} = W_I I_0 + J_{NMDA} S_i^{(E)} - S_i^{(I)} + \lambda G J_{NMDA} \sum_j C_{ij} S_j^{(E)},$$

Firing rates

$$r_i^{(E)} = H^{(E)}(I_i^{(E)}) = \frac{a_E I_i^{(E)} - b_E}{1 - \exp(-d_E(a_E I_i^{(E)} - b_E))},$$

$$r_i^{(I)} = H^{(I)}(I_i^{(I)}) = \frac{a_I I_i^{(I)} - b_I}{1 - \exp(-d_I(a_I I_i^{(I)} - b_I))},$$

Synaptic activity

$$\frac{dS_i^{(E)}(t)}{dt} = -\frac{S_i^{(E)}}{\tau_E} + (1 - S_i^{(E)})\gamma r_i^{(E)} + \sigma v_i(t),$$

$$\frac{dS_i^{(I)}(t)}{dt} = -\frac{S_i^{(I)}}{\tau_I} + r_i^{(I)} + \sigma v_i(t),$$

Deco et al., 2014

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Chapter 6

The Virtual Brain

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The Virtual Brain software (TVB) is a computational framework for the virtualization of brain structure and function. This is accomplished by simulating network dynamics using biologically realistic, large-scale connectivity.

6.1 Graphical User Interface

Fig 6.1 TVB- Welcome screen

The TVB GUI has 6 navigation tabs.

6.1.1 Project Tab

In this tab, we can view our existing project data that has been pre-processed. One can visualise several surfaces generated like the cortical surface, skull surface, skull skin, and face. Additionally, it provides a visualisation of sensor placement, EEG Cap, Region Mapping, etc.
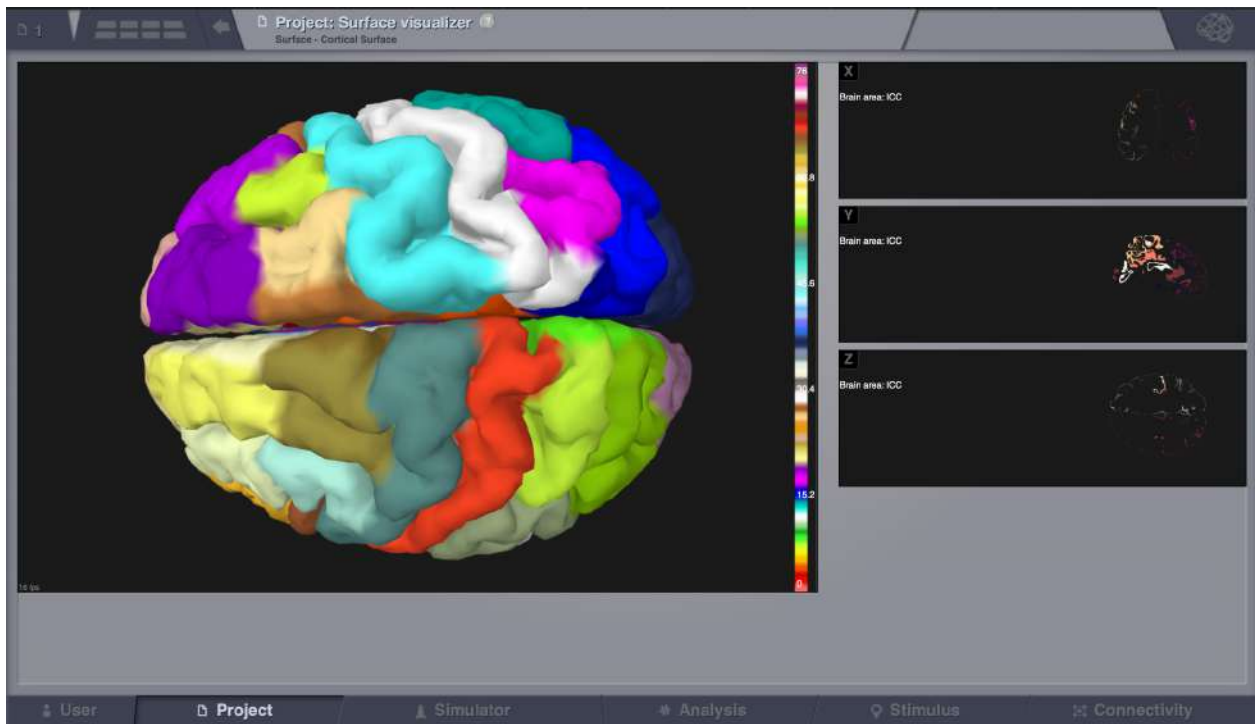
Fig 6.2 TVB- Project Tab

6.1.2 Simulator: Simulation Cockpit Tab

This is the main interface that allows you to set up the entire simulation. We are required to configure the following parameters:

- **Long-range connectivity**- Long-range connectivity is the pre-processed structural connectivity data
- **Conduction Speed**- Specifies the speed at which the signals can travel from one region to another
- **Coupling**- Allows the user to specify the global coupling scheme between nodes in the network
- **Cortical Surface**- If we want a Surface-based simulation it is necessary to load a cortical surface dataset. If we are performing a region-based simulation we leave this empty.
- **Spatiotemporal stimulus** -This allows us to specify some stimulus for the model that can be configured in the 'Stimulus' tab
- **Local Dynamic Model**- This allows us to choose one of the several neural mass models available in TVB. Additionally, we also set the values for the various parameters used in the model.
- **Integration scheme**- This allows us to choose the integration scheme that will produce a numerical solution to the set of differential equations of the neural mass model.
- **Integration step-size**- This defines how frequently a solution to the differential equation is to be produced. A smaller step size will result in better accuracy but an increased compute time.

- **Monitors**- Monitors allow us to specify what output we want the model to provide. TVB can output Raw Recording, Temporal Sub-Sample, EEG, MEG, Intracerebral / Stereo EEG BOLD, etc
- **Simulation length**- This defines how long the brain activity would be simulated for.
- **PSE (Parameter Space Exploration)**- Optionally TVB provides a feature to produce multiple simulations by specifying the range of values of particular parameters.
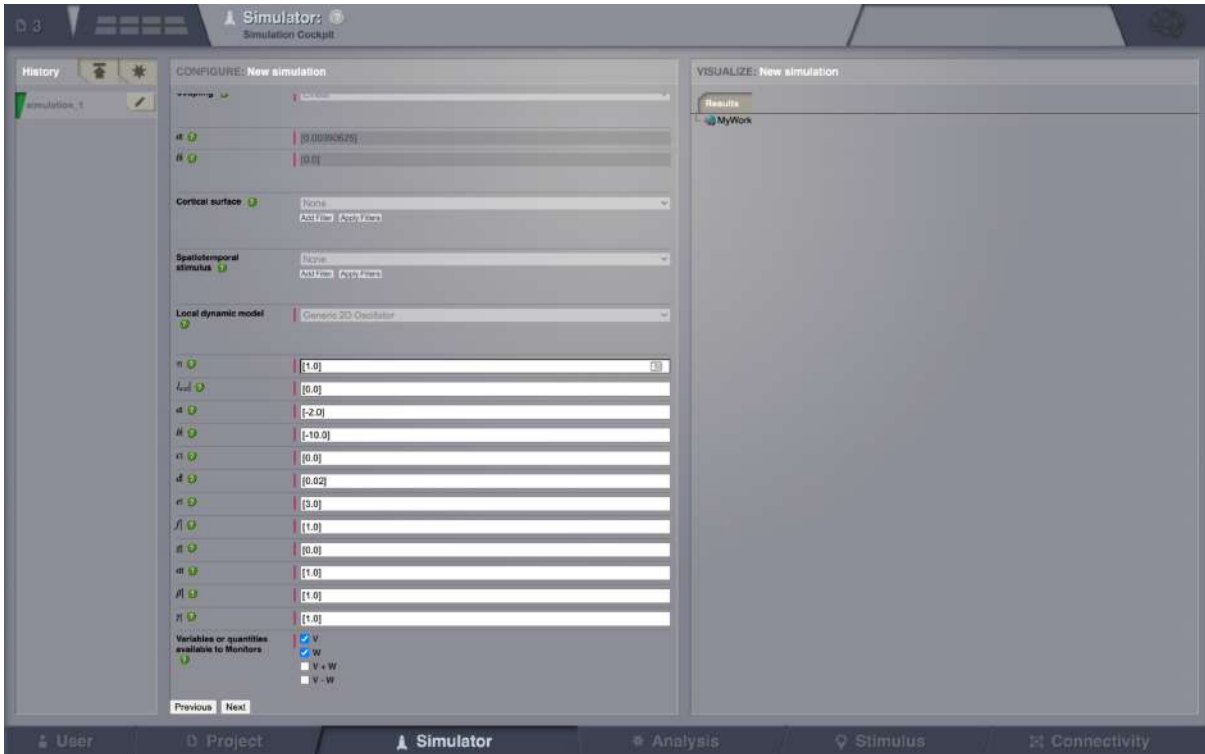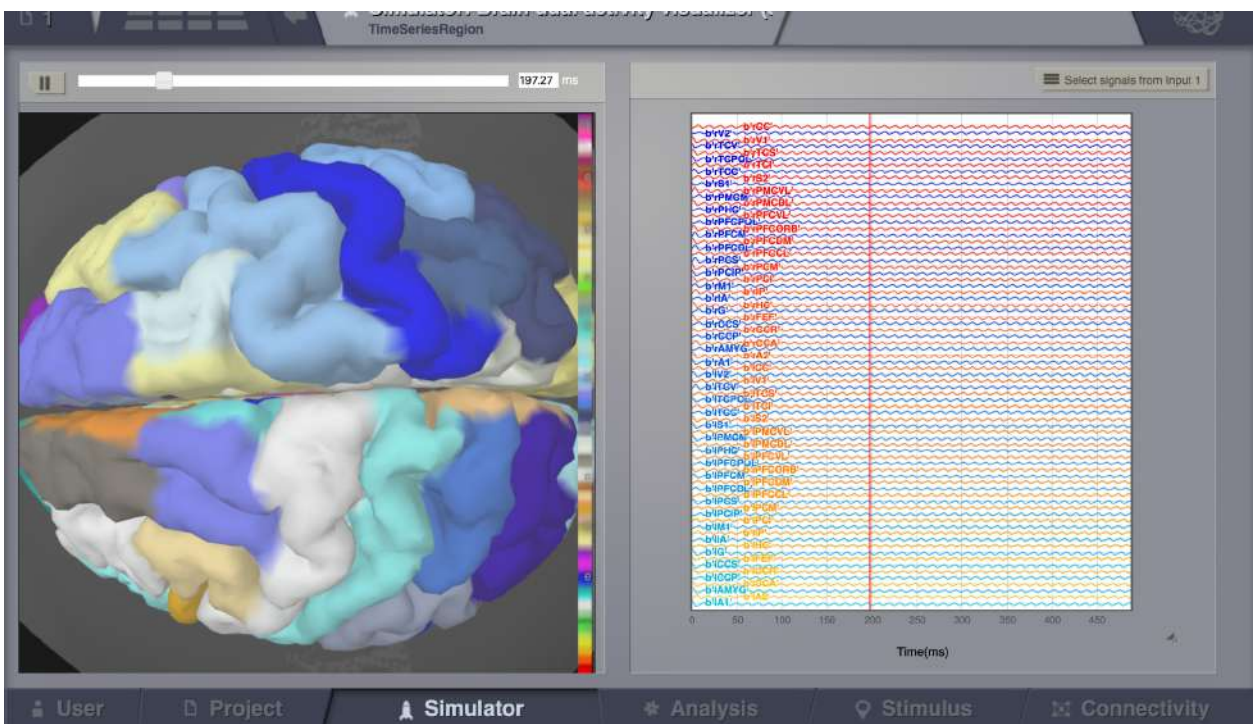

Fig 6.3 TVB- Simulation cockpit

Fig 6.4 TVB- Simulation result

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6.1.3 Simulator- Phase Plane Tab

This page allows you to observe how the dynamics of the neural mass model change as a function of its parameters. On the left column select the model you want to explore and set its parameters. The selected model will generally have a n-dimensional phase space. The right column shows a 2-dimensional axis cut of this space. If you click in the phase plane, a state trajectory will be computed which is useful to understand the oscillatory pattern that will be achieved as a result of the current parameters of the model.
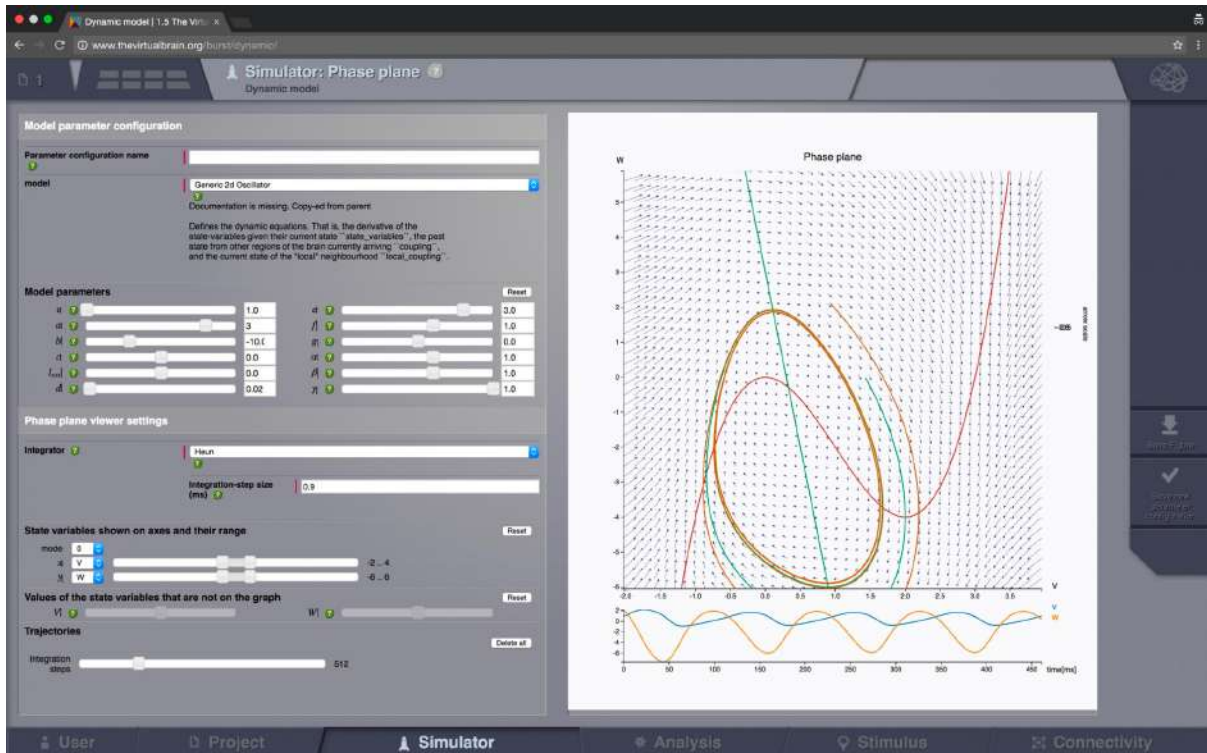

Fig 6.5 TVB- Simulator: Phase Plane

6.1.4 Analysis Tab

This tab allows us to perform various forms of data analysis after the time series has been generated as a result of the simulation.

Fig 6.6 TVB- Analysis Tab

6.1.5 Stimulus

Here using spatiotemporal equations, we can precisely define input stimulus by controlling its strength, the time at which it occurs, and the regions/nodes that it will act on. Depending on the type of model we are simulating, we can define a region stimulus or a surface stimulus
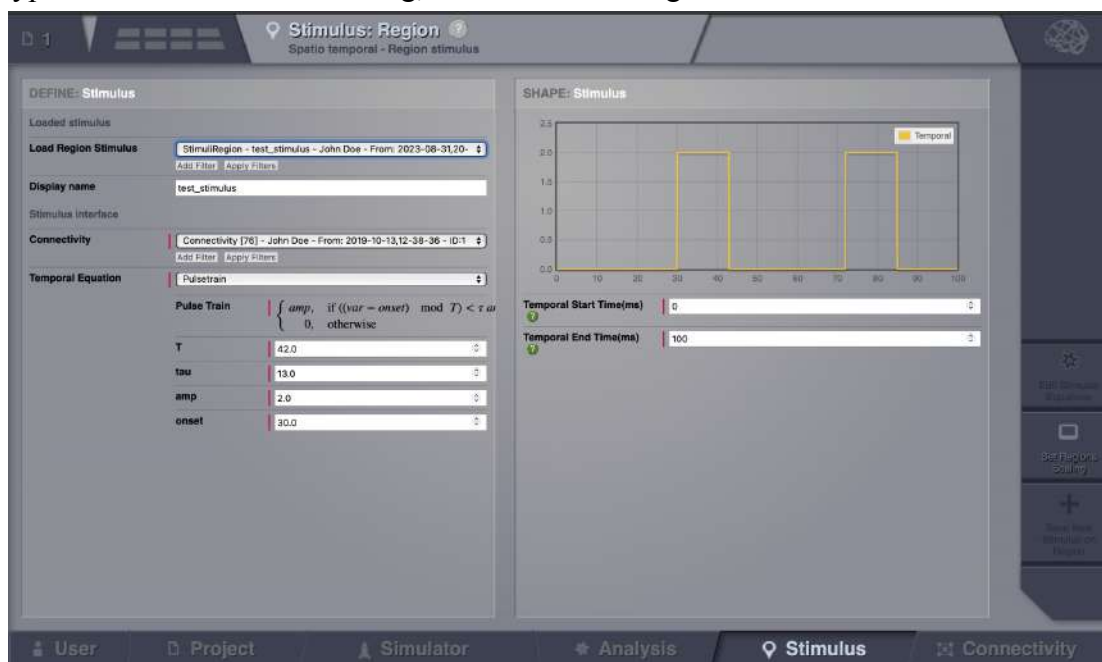

Fig 6.7 TVB- Stimulus Tab

6.1.6 Connectivity

In this tab, we can visualize the Structural Connectivity that has been generated as a result of the MRI preprocessing pipeline. It additionally allows us to alter certain connections or remove them altogether. This has found several clinical applications, especially in tumor-resection surgeries where the surgeon is able to visualize the effects of cutting out certain areas and the impact that it has on the overall functional connectivity.

We can primarily visualize 2 types of connectivity:

1. **Large-scale connectivity**

   This shows the network of nodes on the left. On the right half of the interface, we can view the weights and tract lengths matrix.
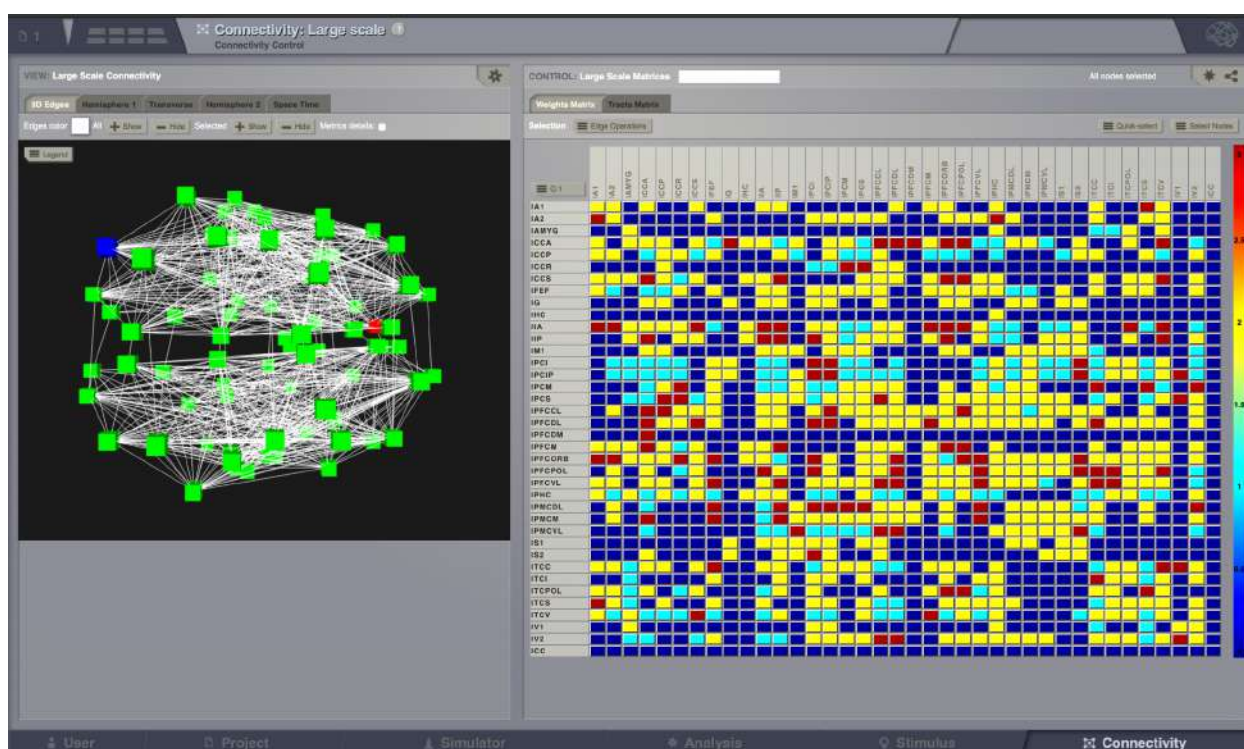

Fig 6.8 TVB- Large-Scale Connectivity Viewer

2. Local connectivity

Here we can precisely define using spatial equations the spread and intensity of local connectivity for surface-based models.
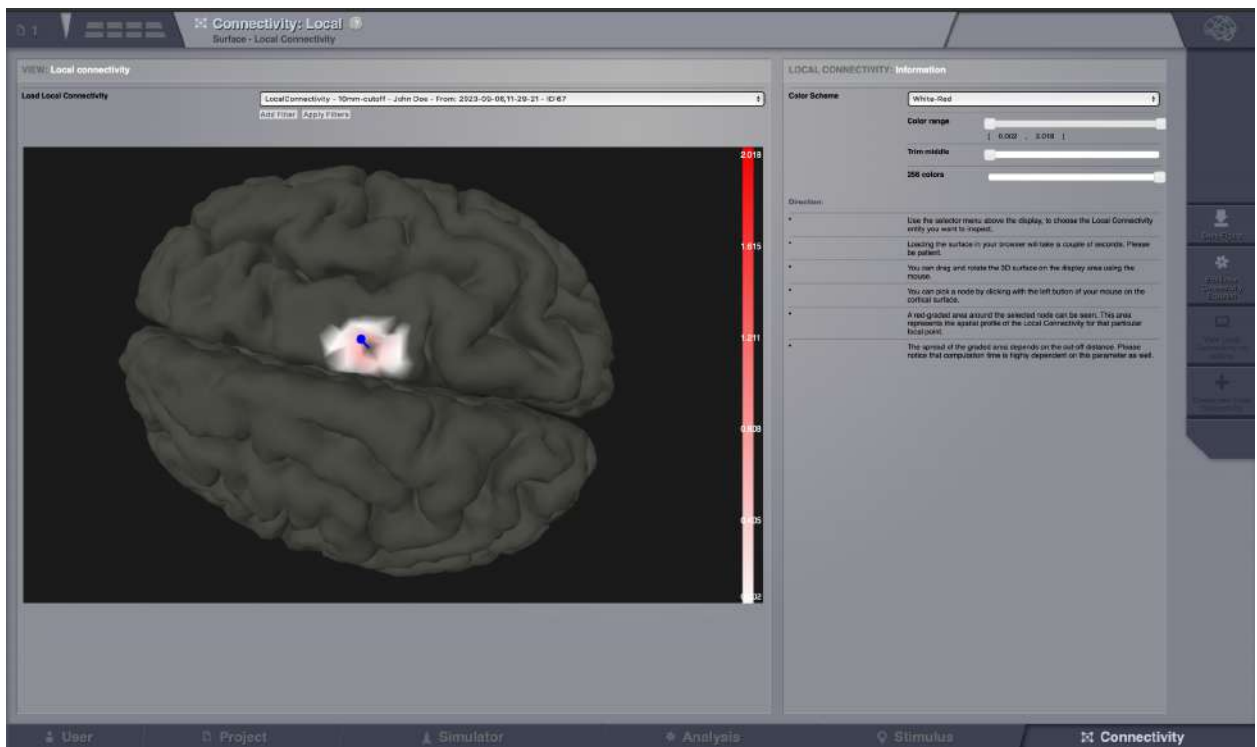

Fig 6.9 TVB- Local Connectivity Viewer

6.2 TVB- Console interface

TVB also supports a far more robust interface through a python notebook where the user has complete access to all the APIs of TVB. This provides for far superior post-simulation analysis as compared to the GUI for using existing python-based data analysis frameworks and libraries such as Numpy, SciPy, and many more.
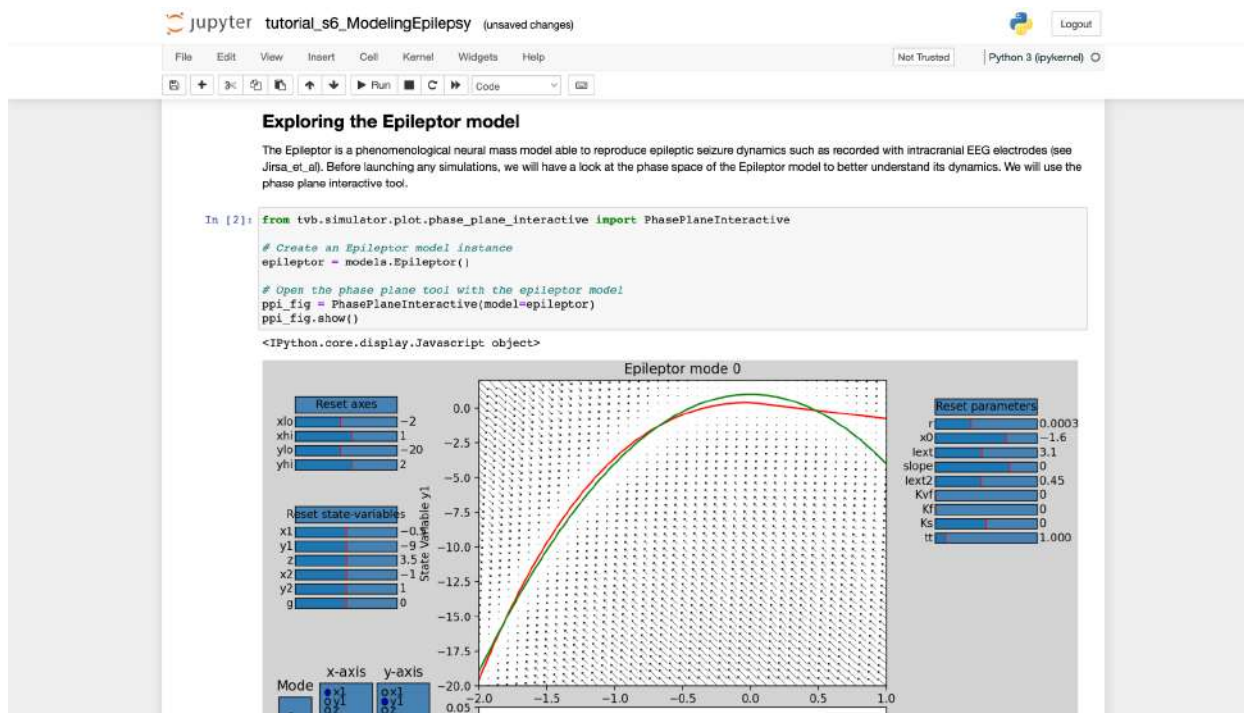

Fig 6.10 TVB- Console interface in Jupyter Notebooks

Chapter 7
Simulations

The following simulations were carried out in The Virtual Brain:

1. Region-based simulation using the Generic 2D Oscillator showing a damped oscillatory pattern for the simulated time series of state variable 'V'
2. Region-based simulation using Generic 2D oscillator showing the existence of a limit cycle in the phase plane as observed by the self-sustained nature of oscillations for the simulated time series of the state variable 'V'
3. Cortical Surface simulation using the Reduced Wong Wang Model for a coupled excitatory and inhibitory population
4. Region–based simulation using the Wilson Cowan model
5. Region-based simulation using the Jansen-Rit model
6. Region-based simulation using the Generic 2D Oscillator showing a single oscillation and the effect of Gaussian region stimulus applied at 100ms
7. Cortical Surface simulation using the Generic 2D Oscillator to view the effect of a sigmoidal surface stimulus
8. Effect of disconnection of left and right hemisphere using Generic 2D Oscillator model
9. Region-based simulation to view the increase effect of global interaction caused by increasing the global-coupling factor 'G'
10. Comparison on the effect of the size of integration step size on the simulated time-series
11. Comparison of Runge Kutta 4th Order and Euler's method integration scheme on the simulated time series
12. Effect of cutting connections to and from a region 'lPMCDL' and the resultant effect on brain activity of previously connected regions
13. Region-based simulation using the Generic 2D Oscillator and the stochastic Heun integration scheme to observe the effect of noise on the simulated time series.

Chapter 8
Conclusion

In conclusion, The Virtual Brain represents a remarkable advancement in the field of neuroscience and computational modeling. Two closely related research directions seem especially promising for clinical research with The Virtual Brain. One approach is to use brain network modeling in order to create a better understanding of the cell, circuit, and network mechanisms underlying an illness, with the goal to design and develop better diagnostic and therapeutic tools. Another approach is to fit TVB models with empirical data in order to find parameters that can be used as health status indicators for diagnosis, in order to predict therapeutic outcomes – to decide between therapy alternatives or to guide surgical intervention specifically and individually for each patient.

Active research in clinical applications of TVB

- **Epilepsy (EPINOV Project):** TVB is employed in a clinical trial involving 365 patients across 13 French hospitals to assist in planning surgery strategies for drug-resistant epilepsy, enhancing localization accuracy for surgical removal of seizure-origin areas.
- **Stroke Recovery:** TVB identifies biomarkers of stroke recovery in both adults and children, offering insights into functional mechanisms of recovery and suggesting that TVB coupling parameters could serve as individual biomarkers.
- **Alzheimer's Disease:** TVB parameters characterize brain network dynamics in Alzheimer's patients, with optimized models correlating significantly with cognitive measures, surpassing traditional structural and functional connectivity.
- **Neuroimaging Fusion:** TVB is combined with positron emission tomography (PET) to simulate hyperexcitability in Alzheimer's patients related to amyloid beta protein, aiding in personalized treatment strategies.
- **Brain Stimulation Therapy:** TVB provides a platform to explore the effects of brain stimulation, studying its impact on functional connectivity, synchronization, EEG power spectra, and network states.
- **Ageing:** TVB models help understand the effects of ageing, highlighting changes in resting-state fMRI time series and their departure from optimal dynamical working points in older adults.
- **Tumor Resection:** Patient-specific TVB models are used to differentiate brain regions affected by tumors, optimizing surgical strategies, and predicting postsurgical outcomes to explore various neurosurgical approaches.
- **Schizophrenia:** TVB investigates the influence of genetic polymorphisms on excitatory and inhibitory balance in healthy carriers, providing insights into the NRG1 gene's role in schizophrenia.
- **Additional Pathologies:** TVB is applied to ongoing clinical research projects across a range of conditions, including psychotic disorders, mild traumatic brain injury, lesions, hypoxia, and autism, aiming to uncover underlying pathomechanisms.

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