FMRI of Gameplay

By

Sayali Birari

(Under the Direction of Tianming Liu)

ABSTRACT

Video games have become an integral part of our lives. Studying the brain's responses to video games becomes more and more important for many aspects of video games. This thesis describes our effort in using neuroimaging techniques and computational approaches to study the brain's responses to gameplay-based stimuli. We have designed a car driving video game and carried out the functional magnetic resonance imaging (fMRI) of the human subject during the experiment. We present fiber centered Granger causality analysis (GCA) studies on fMRI datasets in order to elucidate the functional dynamics of GCA. Precisely, we first acquired the corpus callosum fibers, which are used as a structural communication channel between the left and right hemispheres of the brain. Then, we extract the fMRI BOLD signals from the two ends of a white matter fiber derived from diffusion tensor imaging (DTI) data, and examine their Granger causalities based on fMRI data. Our experimental results show reasonably good correspondence between the car driving directions and the Granger causalities in the fMRI data. Our studies revealed meaningful functional brain dynamics driven by the gameplay.

INDEX WORDS: fMRI, game play, video game effect on the brain, granger causality analysis, task based stimuli, brain image segmentation, game design, DTI, time series, brain state.

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DEDICATION

To my loving and caring parents,

Without whose encouragement and inspiration

this thesis would never have been written.

ACKNOWLEDGEMENTS

I would never be able to finish my thesis without the guidance of my committee members and support from my friends.

I would particularly like to express my deepest gratitude to my advisor, Dr. Tianming Liu, for all his excellent teaching and providing me with an excellent atmosphere for doing this research. And I also would like to thank Dr. Khaled Rasheed and Dr. Hamid Arabnia for their patient suggestions. I would like to thank the group members of Prof. Liu's lab including Xiang Li, Xi Jiang, Tuo Zhang and the Young Dawgs student Brandon Lee, for their help. Finally I would like to thank my friends for supporting me.

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CHAPTER 1

INTRODUCTION

Most previous fMRI studies have been in these three categories: resting state fMRI, task-based fMRI and natural stimulus fMRI of movie watching. However, it has been rarely explored how the human brain will respond when there is interaction between the human and the computer, e.g., during gameplay. This thesis project aims to explore this relatively new direction to study the functional mechanism of the brain during interactive gameplay.

Since the complexity and variability of the brain's response to gameplay is expected to be very high, we propose to design a very well controlled scenario: the subject will play a well-characterized and designed game of driving a car. The actions to be taken will only include two steps: turn left and turn right. In this case, we hypothesize that the communication between the left and right brain, in particular, in the motor systems, will be the major functional events that are of interest in the fMRI data. Therefore, we propose to extract the fMRI signals from the fiber-connected voxels in two hemispheres guided by diffusion tensor imaging (DTI) data. Then, the well-established Granger Causality Analysis (GCA) will measure the causality between the fMRI signals at the two ends, which will then be correlated with the turns in car driving video game.

The general hypothesis to be tested is: the Granger causality between the fiber-connected voxels will be following the left-right turns during the gameplay. The traditionally used general linear model (GLM) will be used to detect the level of similarity between the extracted fMRI signals and the paradigm curves during the gameplay.

We expect that this research project provides novel insights into the functional working mechanisms of the brain during gameplay, and stipulates new perspectives to the emerging new field of interactive and real-time fMRI.

After the IRB of the University of Georgia's approval, Brandon Lee, a member of the UGA Young Dawgs program, contributed to the Cortical Architecture Imaging and Discovery Laboratory under the guidance of Dr. Tianming Liu. He played an instrumental role in developing and implementing the game. Sayali Birari, a Master student and author of this thesis, initiated the experimental design, conducted the scans and performed the data analysis. Dr. Liu provided his excellent guidance and feedback.

1.1 Motivation:

For several decades, researchers have desired to understand and control the functions of the mind and the brain. It has now become probable to image the functioning of the human brain in real time using functional MRI (fMRI), and thus to access both sides of the interface of subjective experience and objective observations. Improvements in neuroimaging are now being translated into many new potential practical applications, including the reading of brain states, brain-computer interfaces, lie detection, and learning control over brain activation to modulate cognition or even treat disease.

Rarely has been rarely explored how the human brain will respond when there is interaction between the human and the computer, e.g., during gameplay. This project aims to explore this relatively new direction to study the functional mechanism of the brain during interactive gameplay. Since the complexity and variability of the brain's response to gameplay is expected to be very high, we propose to design a very well controlled scenario: the subject will play a well-characterized and designed game of driving a car. The actions to be taken will only include two steps: turn left and turn right. In this case, we hypothesize that the communication between the left and right brain, in particular, in the motor systems, will be the major functional events that are of our interest in the fMRI data. Therefore, we propose to extract the fMRI signals from the fiber-connected voxels in two hemispheres guided by diffusion tensor imaging (DTI) data. Then, the well-established Granger Causality Analysis (GCA) will measure the causality between the fMRI signals at the two ends.

The general hypothesis to be tested is: the Granger causality between the fiber-connected voxels will be following the left-right turns during the gameplay. The traditionally used general linear model (GLM) will be used to detect the level of similarity between the extracted fMRI signals and the paradigm curves during the gameplay. Our main motivation was to prove the correspondence in direction change using a mathematical analysis technique.

CHAPTER 2

RELATED LITERATURE WORK

In the neuroimaging field, there have been growing interests in investigating how the human brain responds to natural stimuli such as watching a video, listening to different types of music or task based stimuli such as video game play, puzzle solving and in studying if consistent response patterns exist across individuals.

This research project involved scrutinizing related work done in the task-based stimuli to the brain. As video games are directly related to human behavior it was very inspiring and motivational to work in this area. Granger causality analysis, a mathematical approach was studied to perform the statistical time series analysis of the results. In recent years, many researchers have used this method in several fields such as neuroimaging, economics, weather prediction, market analysis.

Brandon Lee, the participant of The University of Georgia Young Dawgs program played instrumental role in designing and implementing the gameplay requirements. We started with designing the game paradigm. Then we started focusing more on the fMRI process. We were interested in the functional MRI data. Under Dr. Liu's guidance I started using the Oxford FSL open source tool. After getting all the relevant permission from IRB and Human subjects office (HSO) we conducted the experiment at the Bio-Imaging research center (BIRC) of UGA.

The subjects signed the consent forms and participated in the experimentation. Immediately the fMRI datasets were pre-processed. Also during the experiment, the log data was generated during each fMRI run so that we can correlate the fMRI time series data with the gameplay data.

2.1 Brain Imaging and Mapping:

Brain Imaging incorporates the use of various techniques to either directly or indirectly image the structure and function of the brain. Neuroimaging is classified into two broad classes, structural imaging and functional imaging. The structural imaging deals with the structure of the brain, which helps, in the diagnosis of brain diseases such as tumors and injuries. Functional imaging is used to examine functional activities of the brain. Also, fMRI plays an instrumental role in cognitive psychology research and clinical studies.

2.2 What is FMRI (Functional Magnetic Resonance Imaging)?

FMRI is widely used and standard data-analysis methodology allows researchers to compare results across labs. It produces convincing images of brain "activation". The procedure is lower in cost with no potential medical related complications.

Functional magnetic resonance imaging or functional MRI (fMRI) is a type of specialized MRI scan used to measure the hemodynamic response which in other words is the change in blood flow related to neural activity in the brain [2]. It is one of the most recently developed forms of Neuro Imaging. The brain mapping field is dominated by fMRI owing to its features like effectiveness, lack of radiation exposure, and relatively wide accessibility

In addition, however, the rapidly developing MRI technology, largely driven by clinical applications and needs, has been a crucial factor that has made fMRI possible. This noninvasive technology has evolved to a point where relatively small regional signal changes can be detected and imaged over the whole brain with high reliability in localizing the sites of signal changes, and thus the sites of increased neuronal activity. There are many software packages available for analyzing fMRI data.

The fMRI technique allows images to be generated and recorded as a response that reflect which parts of the brain are activated and in what way during performance of different tasks or at resting state. The most important role of fMRI in investigating human brain function arises from the fact that brain function is spatially segregated and integrated.

This functional specialization can be defined and mapped by fMRI utilizing secondary hemodynamic and metabolic responses to alterations in neuronal activity. An important additional feature of fMRI is its capability to follow signal changes in real time, even though the temporal as well as spatial resolution of fMRI is dictated by the characteristics of the hemodynamic response. In this thesis project, we employed the natural stimulus fMRI. The major advantage is that the brain is naturally engaged in viewing and comprehension of gameplay and reflects the brain's continuous functional responses.

2.3 Importance and Effect of Video Games:

Interactive video game play is an exciting aspect of new media that has experienced considerable growth during the last several years. The subjective experience of video games and its impact on a person's behavior has been a topic of debate in the scientific field as well as in the social scenarios.

Experience of computer games can be assessed indirectly by measuring physiological responses and relating the pattern assumed emotional states or directly by introspection of the player. Researchers found that those who played the violent video games showed less activity in areas that involved emotions, attention and inhibition of our impulses.

Video game addiction, or more broadly used video game overuse, is excessive or compulsive use of computer and video games that interferes with daily life. Instances have been reported in which users play compulsively, isolating themselves from family and friends or from other forms of social contact, and focus almost entirely on in-game achievements rather than other life events.

Video games have developed into an integral part of our daily life and spread over a variety of genres. Frequently one tends to hear about a new video game or computer game launch and before you know it, there is news on the popularity of the game and launch of games that can be along. Computer gaming has become a $25 billion per year entertainment business since the first coin-operated commercial videogames hit the market 41 years ago. Researchers over time have been observing how games can change a person's brain, and a university research suggests that gaming can improve creativity, decision-making and perception [3]. On a more specific note, games can improve hand eye co-ordination and vision changes that boost one's night driving ability. The significant benefits of video games has propelled growing video gaming trend has increased my curiosity and eagerness to learn more about the impact on the human brain activity and our physical movements.

Our research is concentrated on monitoring the brain's functional responses to gameplay by studying the fMRI data. With this background we started investigating about designing a simple video game to conduct an experiment in which subject is watching, thinking, making a decision and interacting with the computer using a joystick. Our plan is to measure the brain activity when a subject plays the video game. The idea is to measure brain activity with functional magnetic resonance imaging data during the game play under the guidance of structural connections inferred from DTI data.

2.4 Objectives:

The ultimate goal of fMRI data analysis is to detect correlations between brain activation and the task that the subject performed during the scan. The BOLD signature of activation is relatively weak, however, so other sources of noise in the acquired data must be carefully controlled. This means that a series of pre-processing steps must be performed on the acquired images before the actual statistical search for task-related activation can begin.

2.5 FMRI Analysis:

For a typical fMRI scan, the 3D volume of the subject's head is imaged every one or two seconds, producing a few hundred to a few thousand complete images per scanning session. The nature of MRI is such that these images are acquired in Fourier transform space, so they must be transformed back to image space to be useful. Because of practical limitations of the scanner the Fourier samples are not acquired on a grid, and scanner imperfections like thermal drift and spike noise introduce additional distortions. Small motions on the part of the subject and the subject's pulse and respiration will also affect the images.

The most common situation is that the researcher uses a pulse sequence supplied by the scanner vendor, such as an eco-planar imaging (EPI) sequence that allows for relatively rapid acquisition of many images. Software in the scanner platform itself then performs the reconstruction of images from the Fourier space. During this stage some information is lost (specifically the complex phase of the reconstructed signal). Some types of artifacts, for example spike noise, become more difficult to remove after reconstruction, but if the scanner is working well these artifacts are thought to be relatively unimportant.

After reconstruction the output of the scanning session consists of a series of 3D images of the brain. The most common corrections performed on these images are motion correction and correction for physiological effects. Outlier correction and spatial and/or temporal filtering may also be performed. If the task performed by the subject is thought to produce bursts of activation, which are short, compared to the BOLD response time (on the order of 6 seconds), temporal filtering may be performed at this stage to attempt to [32] deconvolve out the BOLD response and recover the temporal pattern of activation.

At this point, the data provides a time series of samples for each voxel in the scanned volume. A variety of methods are used to correlate these voxel time series with the task in order to produce maps of task-dependent activation.

Chapter 3

EXPERIMENTAL SETUP

In a single experiment, a huge number of fMRI images ranging from tens to several hundreds is measured consecutively. These experiments can last from few minutes to an hour. The collected data are a time series of signal intensity from small volume elements or “voxels” covering regions of interest or the whole brain. Throughout the data acquisition period, inputs for brain activation are presented to the subject in the magnet at appropriate periods. The input can be sensory stimulation, sensory input–guided cognitive tasks, subject-initiated mental activity, or even spontaneous brain activity the subject may not be aware of. Images taken during the absence of these inputs are used as a control. Image signals responding to the input are then compared with the control image signal. In our case the external stimulus to the brain is the video game play. The following Fig1 explains the flow of the entire experiment. The video game play generates log data and fMRI data. Using Granger causality and statistical analysis the results are mapped to find correspondence.

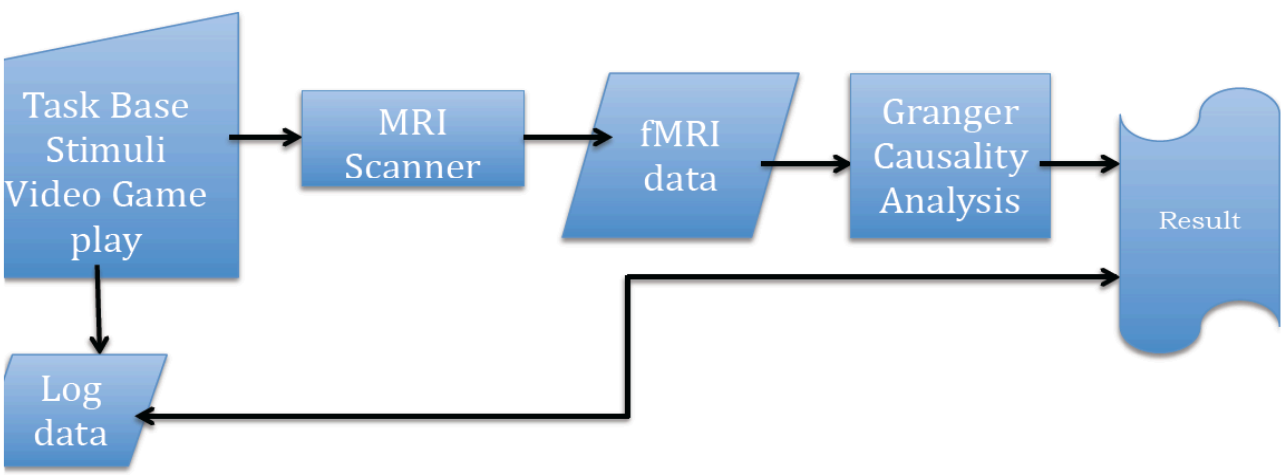


Fig 1: Overview of the Experiment

3.1 Designing the Game:

We have used open source free software called Alice [4] to design and implement the game. It is free of cost, easy to install and very flexible to use. Alice is an innovative 3D programming environment that makes it easy to create an animation for telling a story, playing an interactive game, or a video to share on the web. This is an NSF-sponsored educational research project developed at Carnegie Mellon University. Alice is an innovative programming environment to support the creation of 3D animations. The Alice project provides tools and materials for learning computational thinking, problem solving and computer programming. It uses 3D graphics and a drag-and-drop interacting interface to facilitate a more engaging, less frustrating first programming experience, where the instructions correspond to standard statements in a production oriented programming language, such as Java, C++, and C#.

Alice allows users to immediately see how their animation programs run, enabling them to easily understand the relationship between the programming statements and the behavior of objects in their animation. By manipulating the objects in their virtual world, users gain experience with all the programming constructs.

The following figure is a screen shot of the video game. As soon as the player starts playing he senses that the cone is in right direction hence he moves the joystick in the right direction. In this way player follows the instruction shown on the screen and completes the game by touching all the eight cones.

A car racing game is designed which is controlled by a joystick. The game is about the car following the track ad touching each of the cones. Time stamps is recorded when the car touches each of the cone. Also the duration from when the joystick is shifted from left to right is recorded.

We started with the basic components to create a world as a platform. The world consists of huge cones arranged in a Zig –Zag manner .The challenge in the game is to touch the car to the cones. The subject player will be controlling the car with the help of a joystick. The subject player follows the instructions and the game program moves the car forward at a constant speed to take that factor out of the equation and keep it to the left or to the right.

When the player touches a cone, the log displays the time to take between each cone. The game program also records how long the car is turning in each direction so that we can match the time curve with the fMRI signals. In total, we conducted 4 sessions and each session has 10 minutes. So the total time is about 40 minutes. When the experiment was started we used the "1 - 2 - 3 - GO!" approach. In between each session we waited for 1 minute to let the player know about the start and end each time.

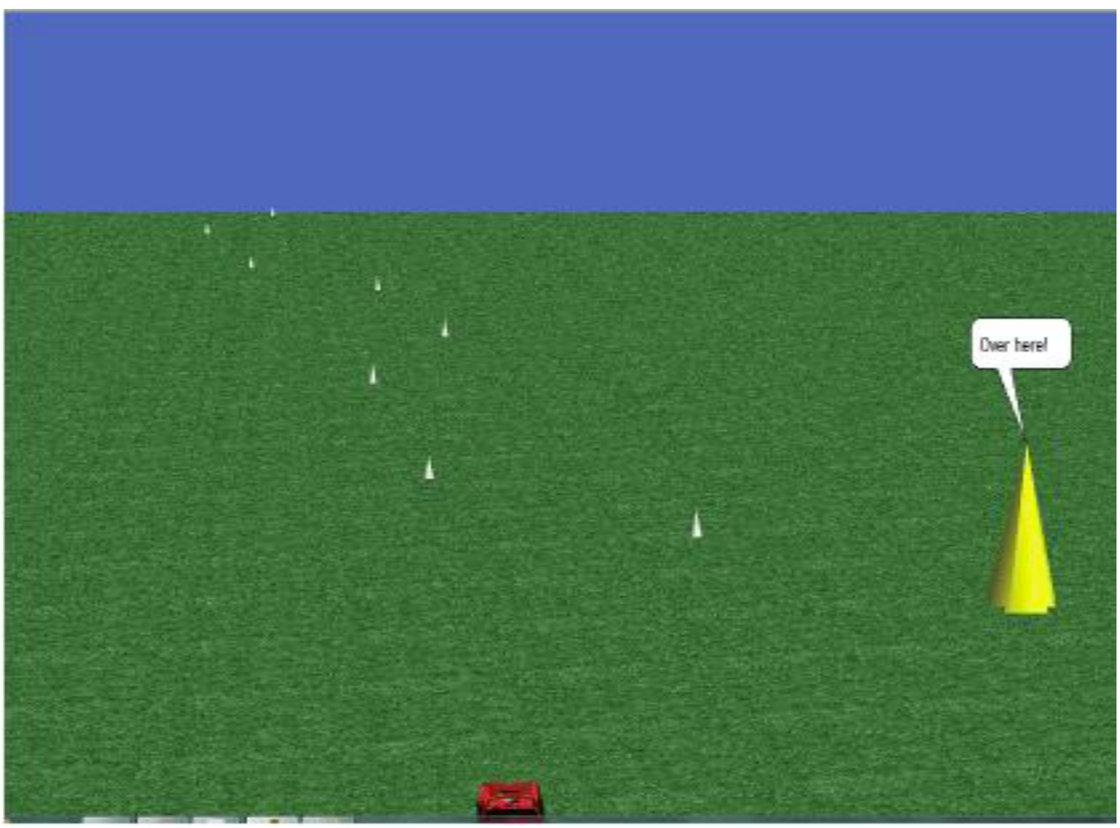


Fig 2: Actual Game Screenshot

3.2 Scanning Process:

Subjects participating in an fMRI experiment are asked to lie still and are usually restrained with soft pads to prevent movement from disturbing measurements. Some labs also employ bite bars to reduce motion, although these are unpopular as they can be uncomfortable. Small head movements can be corrected for in post-processing of the data, but large transient motion cannot be corrected. Motion in excess of around 3 millimeters or more results in unusable data. Motion is an issue for all populations, but most especially problematic for subjects with certain medical conditions (e.g. Alzheimer's Disease or schizophrenia) or with young children. Participants can be habituated to the scanning environment and trained to remain still in an MRI simulator.

Fig 3: Typical Scanning session at BIRC UGA

An fMRI experiment usually lasts between 15 minutes and an hour. Depending on the purpose of study, subjects may view movies, hear sounds, smell odors, perform cognitive tasks such as n-back, memorization or imagination, press a few buttons, or perform other tasks. Researchers are required to give detailed instructions and descriptions of the experiment plan to each subject, who must sign a consent form before the experiment.

Safety is an important issue in all experiments involving MRI. Potential subjects must ensure that they are able to enter the MRI environment. The MRI scanner is built around an extremely strong magnet (1.5 Tesla or more); so potential subjects must be thoroughly examined for any ferromagnetic objects (e.g. watches, glasses, hair pins, pacemakers, bone plates and screws, etc.) before entering the scanning environment.

During a typical functional imaging series, 30 images are acquired in a 90 sec run where the initial and last 10 images are baseline conditions and the middle 10 images (30 secs) are acquired during a task. For example, in the case of a typical task designed to identify eloquent brain tissue involved in hand and finger movement, the subject taps fingers and thumb during the activity epoch. The beginning and end of this activity period is cued by a visual or auditory signal and occurs at images 10 and 20, respectively.

Our imaging experimental setup is to perform fMRI brain imaging while participants play the game. Essential equipment includes a state-of-the-art 3T MRI imaging system (General Electric, Milwaukee, WI), an audio/video paradigm delivery system (Resonance Technology Inc., CA), and a joystick. A joystick is an input device consisting of a stick that pivots [5] on a base and reports its angle or direction to the device it is controlling. Analog joystick as used with many early home computer systems. The small knobs are for (mechanical) calibration, and the sliders engage the self-centering springs. The joystick is connected using a USB connection.

Fig 4: Joystick Used For Controlling The Car

We used freely available simulation program that is compatible with all the Windows machines called Xpadder. The Xpadder allows playing PC games with poor or no gamepad support. We chose this software as we have a windows machine running in synch with the MRI scanner and also the screen that the player will look at and play the game. The simulation is very efficient and the log data obtained is self-explanatory. It is installed as it simulates the keyboard, mouse using a game pad. It is designed for gamepads, joysticks, arcade sticks, steering wheels, dance mats and musical instruments like guitars, drum kits etc.

Fig 5: Computer used to control the task

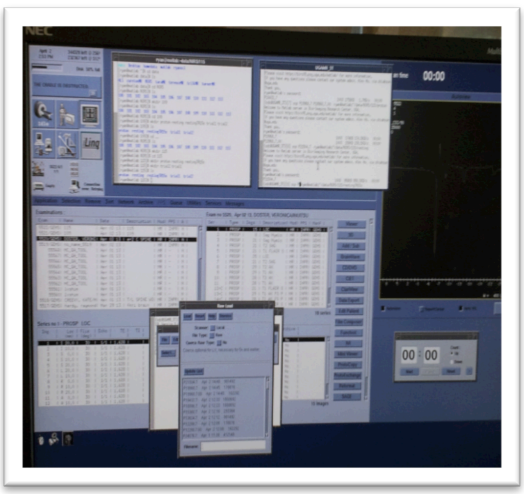


Fig 6: Interface used to get the fMRI signals in the study

During the experiment, the audio/video signals are delivered to the participant from the controller via the MRI-compatible transducers, goggles and headphones. The precise synchronization between media viewing and fMRI scan is achieved via the E-prime software [52] so that the fMRI time-series signals and gameplay time curves will be in strict temporal alignment.

Our image analysis framework is that we will extract quantitative measurements of the brain's responses to gameplay stimuli, and use them to correlate with the gameplay curves. Specifically, the methodologies in Dr. Liu's group's recent publication "Fiber-centered Granger Causality Analysis" in MICCAI 2011 will be used for this analysis. We will extract the fMRI signals from the two ends of a white matter fiber (connecting two hemispheres) derived from diffusion tensor imaging data, and examine their Granger causalities. Then, we will test the hypothesis: the Granger causality between the fiber-connected voxels will be following the left-right turns during the gameplay.

3.3 Subjects:

Two healthy young adults were recruited at The University of Georgia (UGA) under IRB approval to participate in this study.

The subjects for this experiment were students whose structural and functional brain network map was already mapped in a previous project called "Joint modeling of cortical folding and connectivity patterns". The experimental set up was conducted twice with different players each time. The duration was in total 60 minutes with regular intervals. In total, four runs with two 30 seconds and 60 seconds were conducted. The subjects did not have any prior knowledge about the game because of which accurate data is obtained. The players were given instructions in the form of dialogue message while progressing in the game.

3.4 Data Acquisition and Fiber Tracking Preprocessing:

In this study, fMRI data in resting state and task based stimulus were analyzed: OSPAN working memory tasked-based fMRI data [8], resting-state fMRI data [7]. The fMRI images were acquired on a 3T GE Signa scanner. The parameters used for the data procurement are as follows: fMRI: 64x64 matrix, 4mm slice thickness, 220mm FOV, 30 slices, TR=1.5s, TE=25ms, ASSET=2. Each participant performed a modified version of the OSPAN task (3 block types: OSPAN, Arithmetic, and Baseline) while fMRI data was acquired. In the task based (video game play) stimulus fMRI scan [8], the subject plays the game by following the instructions shown on the screen. The player does not have any prior knowledge about the game. The acquisition parameters were as follows: dimensionality 128*128*60*240, spatial resolution 2mm*2mm*2mm, TR 5s, TE 25ms, and flip angle 90. In the resting state fMRI scan [7], nine volunteers were scanned in a 3T GE MRI system. Resting state fMRI data were acquired with dimensionality 128*128*60*100, spatial resolution 2mm*2mm*2mm, TR 5s, TE 25ms, and flip angle 90 degrees. DTI data were acquired using the same spatial resolution as the resting state fMRI data; parameters were TR 15.5s and TE 89.5ms, with 30 DWI gradient directions and 3 B0 volumes acquired.

For preprocessing, we registered fMRI data to the DTI space by the FSL FLIRT tool. It should be noted that because DTI and fMRI sequences are both echo planar imaging (EPI) sequences, their distortions tend to be similar [7]. So the misalignment between DTI and fMRI images is much less than that between T1 and fMRI images [7]. DTI pre-processing included skull removal, motion correction and eddy current correction. Then fiber tracking was performed using MEDINRIA. Brain tissue segmentation was conducted on DTI data by the method in [9] and the cortical surface was reconstructed using the marching cubes algorithm. FMRI preprocessing steps included motion correction, spatial smoothing, temporal prewhitening, slice time correction, global drift removal, and band pass filtering [6] [7] [8] .

The next step after preprocessing was to use the white matter fibers to guide the fiber-centered GCA, which is the fMRI BOLD signals at the two ends of a white matter fiber, were extracted for the following Granger causality analysis.

The following figure 7 gives an overview of the fiber-centered Granger causality schema. The original data undergoes a series of processing. After carrying out the diffusion tensor image data process and the functional MRI data process mapping is done on each fiber. Then the granger causality regression is carried out on the data using the code.

Furthermore, significant correspondence is studied between the video game stimuli and the granger causality result. The model result is obtained using statistical analysis and task based stimuli. In the end the visualizations are achieved to show meaningful outcomes.

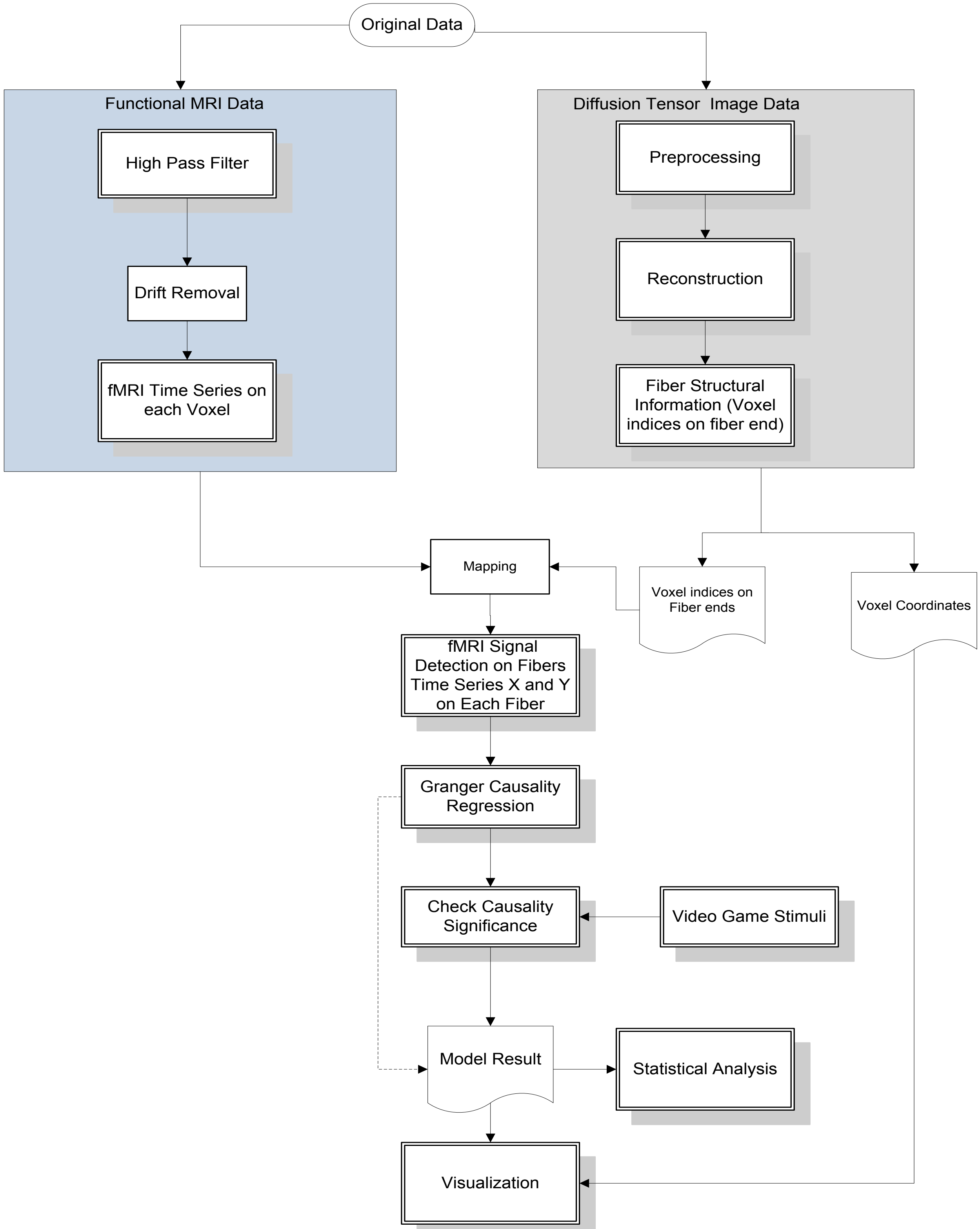


Fig 7: Flowchart of the fiber-centered Granger causality schema

3.5 Obtaining corpus callosum:

Corpus callosum (CC) is an important structure in human brain anatomy. The corpus callosum (CC) is a wide, huge, flat bundle of nerve fibers found in mammalian brains connecting the left and right cerebral hemispheres, and plays an important role in distributing perceptual, motor, cognitive, learned, and voluntary information to communicate between the two hemispheres [16]. It is composed of white matter that is, myelinated nerve cells, or axons, [17] [18], whose primary function is to connect grey areas together with neural impulses.

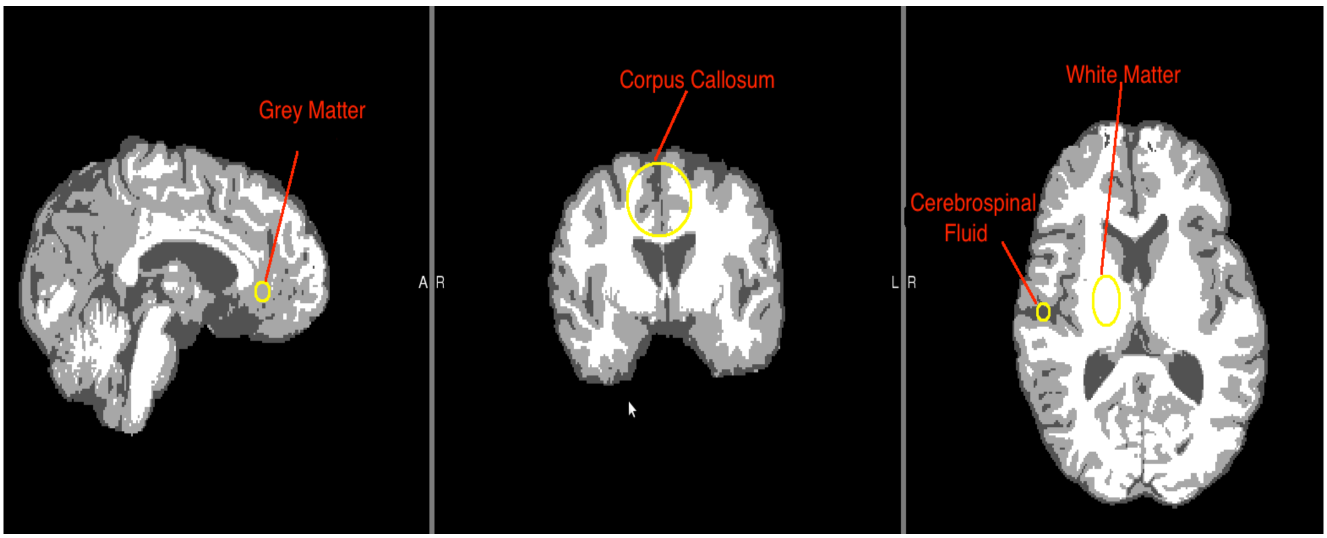
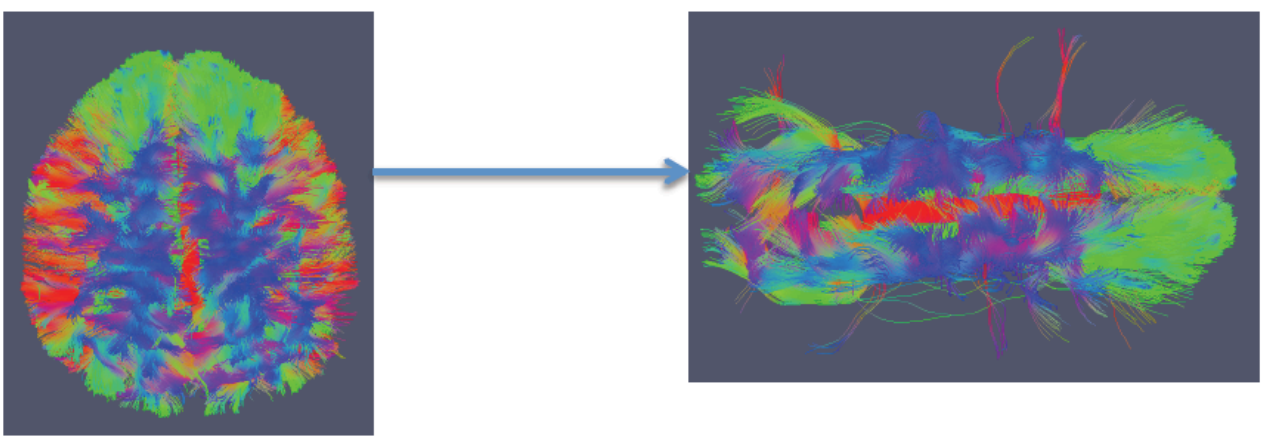


Fig 8: Various components of the human brain

The corpus callosum is the largest white matter structure in the brain, found in its interior. Grey matter occupies the periphery. Various neuroimaging studies indicate that the size, thickness and shape of CC are related to brain dysfunction [11, 12], gender [13], as well as intelligence [14, 15]. Manual delineation is typically used in clinical and neuroscience research practice. We used a fully automated and robust approach to extract corpus callosum from T1-weighted structural MR images.

Our method is composed of two key steps. In the first step, we find an initial guess for the curve representation of CC with the help of an open source software called Para-View [19]. It is an open-source, multi-platform data analysis and visualization application. Para-View users can quickly build visualizations to analyze their data using qualitative and quantitative techniques. The data exploration can be done interactively in 3D or programmatically using Para-View's batch processing capabilities. By using an expert research's judgment, manual extraction of the cutting plane that separates the brain into two complete hemispheres.

Further more in the second step, to obtain the specific data set, removal of fibers is done in detail. In this, the segments which cut through the plane obtained in step 1. More specifically, segment is defined to be a line segment consisting of two consecutive points on a fiber. We walk through a fiber from one end to the other until one segment cut through the plane. This part was done with the help of Matlab.



Raw Image Extracted Corpus Callosum Fibers

Fig 9: Obtaining the CC fiber

Chapter 4

DATA ANALYSIS

4.1 Time Series

A time series is a sequence of data points, measured typically at successive points in time spaced at uniform time intervals. Time series analysis comprises methods for analyzing time series data in order to extract meaningful statistics and other characteristics of the data. Time series forecasting is the use of a model to predict future values based on previously observed values. While regression analysis is often employed in such a way as to test theories that the current value of one time series affects the current value of another time series, this type of analysis of time series is not called "time series analysis".

4.2 General Linear Model:

The general linear model (GLM) is a statistical linear model. It is also written as [22] [23]

$$\mathbf{Y = XB + U,}$$

Here Y is a matrix with series of variable measurements, X is a design matrix. Matrix B is contains parameters that are usually to be estimated and matrix U contains errors and noise. The errors are usually assumed to follow a multivariate normal distribution. General linear model may be used to relax assumptions about Y and U if the errors do not follow a multivariate normal distribution. Regression and correlational methods, in turn, serve as the basis for the general linear model [24].

The general linear model has been an integral part of functional magnetic imaging analyses for the past 20 years. Over the time many methods have evolved rapidly, and most of the research papers published in this field have used this technique. Conceptually GLM is very simple and easy to implement and it uses standard statistics used in biomedical research which provide some answers to the most standard questions put to the data The main reason to use this model is applied for the analysis of multiple brain scans, where Y contains data from brain scanners, and X contains experimental design variables and confounds.

4.3 What is granger causality GCA?

The Granger causality test is a statistical hypothesis test for determining whether one time series is useful in forecasting another [1]. Normally, regressions reflect "simple" correlations, but, Economics Nobel prize winner Clive Granger argued that certain set of tests reveal something about causality [45]

A time series X is said to Granger-cause Y if it can be displayed, usually through a series of t-tests and F-tests on lagged values of X (and with lagged values of Y also included), that those X values provide statistically significant information about future values of Y [26].

Granger causality analysis (GCA) has been widely applied to analyze the relationships between time series. Briefly, a time series X is said to Granger-cause time series Y if the values of X provide statistically significant information about future values of Y. The GCA is very useful in functional MRI (fMRI) signal analysis, since different brain regions are supposed to connect together and have causal influence upon each other. [27]

Thus in recent years, it has been widely used in the brain-imaging field [28][29], in order to obtain a hierarchical understanding of the interaction and correlation between different brain regions. Despite wide application of GCA in fMRI, however, the structural underpinnings of

GCA remain unclear, e.g., how structural connectivity is related to Granger causality? In addition, many existing approaches of GCA on brain networks [28][29] assume temporal stationary, that is, Granger causalities are computed over the entire scan and used to characterize the causality strengths of connections across regions. However, accumulating literature [e.g., 14], have shown that functional brain connectivity is under dynamical changes in different time scales. In responses to the above-mentioned issues, this paper employs a fiber-centered GCA approach to examine resting state fMRI and natural stimulus fMRI datasets, in order to elucidate the structural substrates and functional dynamics of GCA.

Specifically, we extract the fMRI BOLD signals from the two ends of a DTI-derived fiber, and measure their Granger causalities. Our premise is that as axonal fibers are the structural substrates of functional connections between computational centers of cortical regions, and the fMRI time series along the fibers should reflect the functional causality between brain regions, if any such functional causality exists.

4.4 GCA analysis:

Assumed random processes X and Y, if they are stationary, each of the process can be expressed as an auto-regression of their lagged values:

$$X_t = \sum_{i=1}^{P} a_i X_{t-i} + e1_t \tag{1}$$

$$Y_t = \sum_{i=1}^{P} d_i Y_{t-i} + e2_t \tag{2}$$

where e1 and e2 are prediction errors and their variances describe the accuracy of the prediction. Assume that they have potential causality influences upon each other, there is:

$$X_t = \sum_{i=1}^{P} a_i X_{t-i} + \sum_{i=1}^{P} b_i Y_{t-i} + e3_t \quad (3)$$

$$Y_t = \sum_{i=1}^{P} c_i X_{t-i} + \sum_{i=1}^{P} d_i Y_{t-i} + e4_t \quad (4)$$

where e3 and e4 are prediction errors and a, b, c, d are linear regression coefficients. In order to study the dependency between X and Y, the null hypothesis $H0{:}\ \{b\}=0$ was made, which means Y will not significantly cause X. According to the null hypothesis, we can construct the F-statistics:

$$F_{Y \to X} = \frac{\mathrm{var}(e1)-\mathrm{var}(e3)}{\mathrm{var}(e3)} \quad (5)$$

When there is no causality caused by Y to X, the value of $F_{Y \to X}$ will approach zero since the additional Y terms will not influence the explanation power in Eq. (3). And if the value is greater than the given threshold, we will reject the null hypothesis, which means there is a significant causality caused by Y to X.

The original GCA model only gives the result of whether there is a causality or not, which is limited for the brain imaging research, since there are reciprocal polysynaptic connections between brain areas [11]. Here we applied the conditional GCA [7] which gives the magnitude to evaluate the causality strength:

$$CM_{Y \to X} = \ln\left(\frac{\mathrm{var}(e3)}{\mathrm{var}(e1)}\right) \quad (6)$$

where CM stands for causality magnitude. This value is used in the following analysis to evaluate the strength of Granger causality and in the visualization. Higher CM value indicates greater causal influence [30].

By evaluating directed functional connectivity from time series data is a key challenge in neuroscience. A powerful technique for extracting such connectivity from data is Granger causality (G causality)

One approach to this problem leverages a combination of Granger causality analysis and network theory. We have used the freely available MATLAB toolbox – 'Granger causal connectivity analysis' (GCCA) – that provides a core set of methods for performing this analysis on a variety of neuroscience data types including neuroelectric, neuromagnetic, functional MRI, and other neural signals. The toolbox was first introduced in 2005 and then later revised and extended versions of the software were released. It includes core functions for Granger causality analysis of multivariate steady-state and event-related data, functions to preprocess data, assess statistical significance and validate results, and to compute and display network-level indices of causal connectivity including 'causal density' and 'causal flow'. The toolbox is deliberately small, enabling its easy assimilation into the range of researchers. It is however readily extensible given proficiency with the MATLAB language.

4.5 Visualization:

Interpretation can be done easily if the causal networks are visualized effectively. The GCCA toolbox includes functions for generating simple graphical depictions of network causal connectivity. It is also incorporated of functions for generating data files that describe a network in a format suitable for importing into the network analysis software like Pajek, which contains many useful tools for network visualization and analysis. Functions such as cca_ plotcausality, ca_plotcausality_spectral, and cca_pajek enable causal network visualization.

In our experiment, we obtained six different results for each run. So we conducted two sixty seconds and thirty seconds each experiments. This gave us a scope to look for the best results.

Chapter 5

RESULTS

Interestingly, our experimental results showed that Granger causalities on white matter fibers are significantly stronger than the causalities between brain regions that are not connected by fibers, suggesting the structural underpinning of functional causality observed in resting state fMRI data. In addition, our experimental results of applying the fiber-centered GCA approach on task based video game stimulus fMRI data suggest that Granger causalities on fibers reveal significant temporal changes, offering new insights into the functional dynamics of the brain.

The GCA result is in the form of a huge matrix with 4322 columns and 381 rows. Normalizing the data was necessary hence the numbers were first sorted then the average of each column was taken. Then the log data obtained during the experiment and the normalized data obtained from the fMRI output is used to do the mapping. The graphical representation is shown below. The top 5% of the GCA output data is considered and plotted in the graph.

The log data recorded various timestamps. To simplify the analysis we denoted “0” of the player keeps driving straight “-1” if the player drives the car in the left direction and “1” if the car is going in the right direction. For easy graphical representation we denoted “100” when the car touches the cone. Also, each time the player sees a direction. Since the TR is 1.5 and each session of the experiment was 600 seconds long in duration, the total volume is 400. The time window length is 14 therefore in total there are 387 time windows (400-14+1).

Two GCA analysis results were acquired On each fiber, one was the F-statistics which could tell whether there was significant causality (given a significance value, here we use P=0.01) between the two time series at both ends of the fiber; the other was causality magnitude, which was the indicator for the level of causality. Since the GCA is bi-directional and we took the stronger value from the two directions. We used the F-statistics to select the fibers with significantly high causality

Hence we see that the result in figure 10 shows correspondence with color-coded fibers. The X-axis represents the time and the Y-axis represents the position the car attained. The figures 14, 15 give good resemblance of the log data and the data obtained from the granger causality analysis. Also the following figures 17 and 18 represent the results for the 30 seconds experiment, which was carried out second time so the similarity can be seen more as the player got an idea of the game. Furthermore the visual representation is concentrated on the corpus callosum area of the brain. The player goes straight, right, left and at times perceives a dialogue box. The data collected from two sessions of the subjects enabled us to compare the results and to see whether the inferred causalities were stable within subjects. All the results support the hypothesis stated above

Fig 10: Visualization of the processed data without using a color code in which each fiber has its own magnitude.

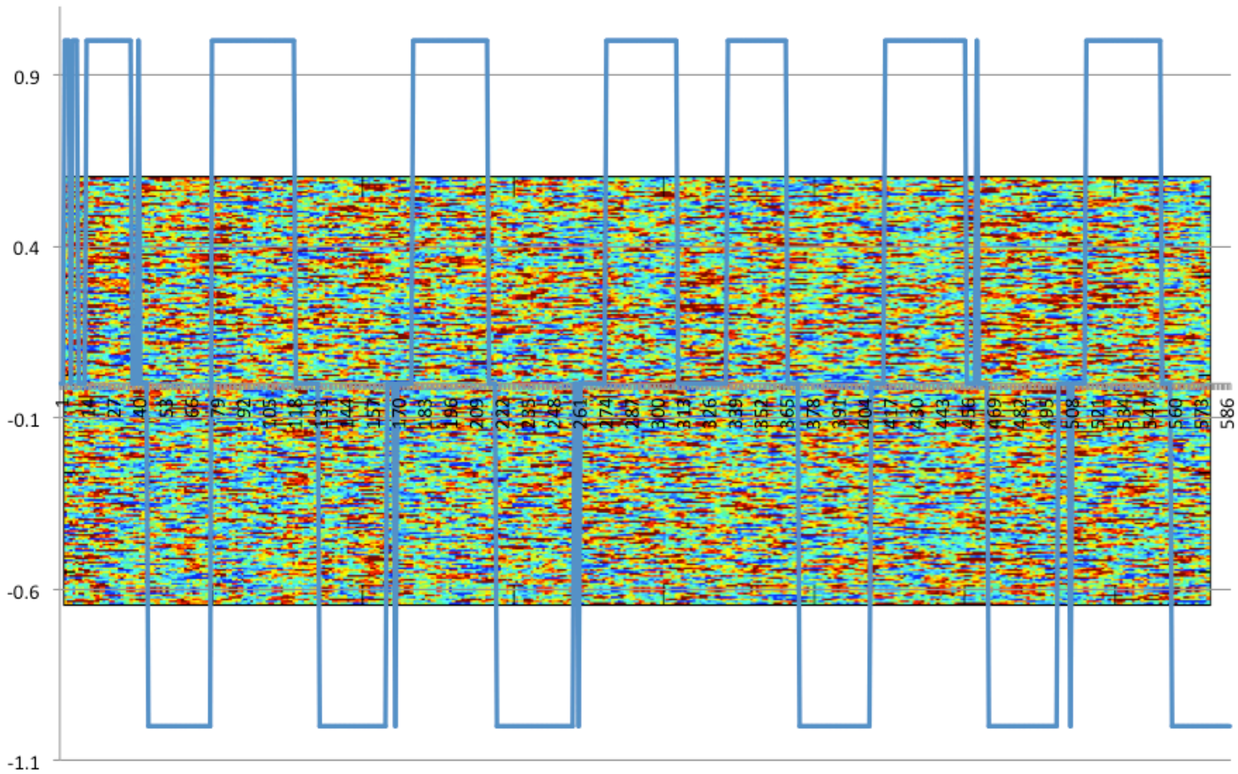


Fig 11: Visualization of Granger magnitude of all fibers in 387 sliding windows. Each row vector is the Causality Magnitude dynamics of one fiber through the whole time period, and each column vector is the causality magnitude state vector in that sliding window.

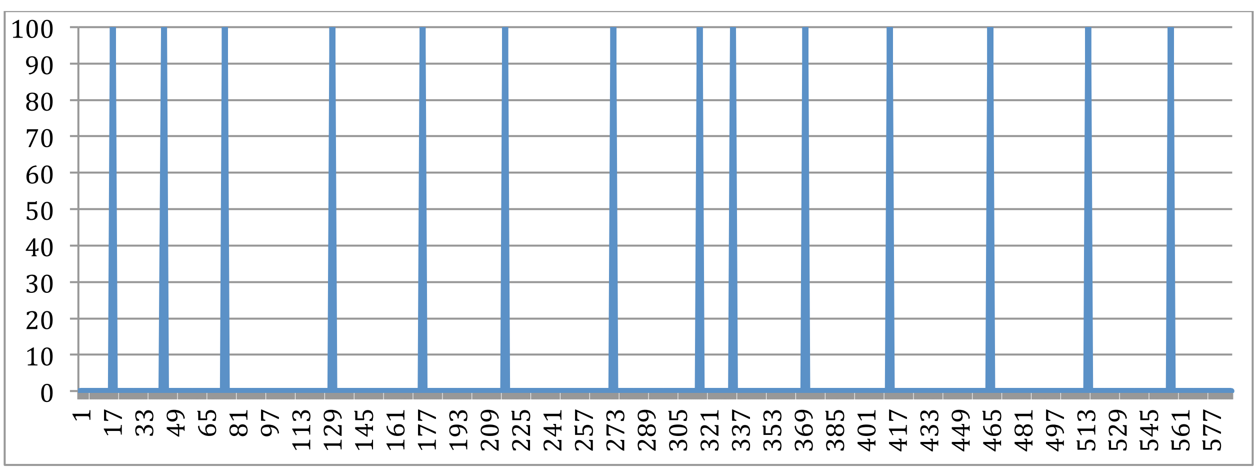


Fig 12: Graph representation of the instance when the car touched the cone in the game. The X-axis is the instance when the car touched the cone and the Y-axis represents the position the car reaches in each instance.

```
startRightTurn
the value of timer.time is 3.0
the value of timer.time is 4.0
the value of timer.time is 5.0
the value of timer.time is 6.0
the value of timer.time is 7.0
the value of timer.time is 8.0
the value of timer.time is 9.0
the value of timer.time is 10.0
the value of timer.time is 11.0
the value of timer.time is 12.0
the value of timer.time is 13.0
the value of timer.time is 14.0
the value of timer.time is 15.0
the value of timer.time is 16.0
the value of timer.time is 17.0
the value of convertibleCorvette.countRight is 15.175469  ( duration of the turn )
the value of timer.time is 18.0 ( Travelling straight )
the value of timer.time is 19.0
the value of timer.time is 20.0
the value of timer.time is 21.0
the value of timer.time is 22.0
the value of timer.time is 23.0
the value of timer.time is 24.0
the value of timer.time is 25.0
the value of timer.time is 26.0
the value of timer.time is 27.0
the value of timer.time is 28.0
the value of timer.time is 29.0
the value of timer.time is 30.0
the value of timer.time is 31.0
the value of timer.time is 32.0
the value of timer.time is 33.0
the value of timer.time is 34.0 ( touched cone one )
the value of timer.coneTimer is 0.0
car touch cone 1                ( dialogue box pops up gives the instruction to turn  )
startRightTurn
the value of timer.time is 35.0 (timer.time is basically the total time of the experiment )
the value of timer.time is 36.0
the value of timer.time is 37.0
the value of timer.time is 38.0
the value of timer.time is 39.0
the value of timer.time is 40.0
```

Fig 13: Screen shot of Log data generated during the experiment.

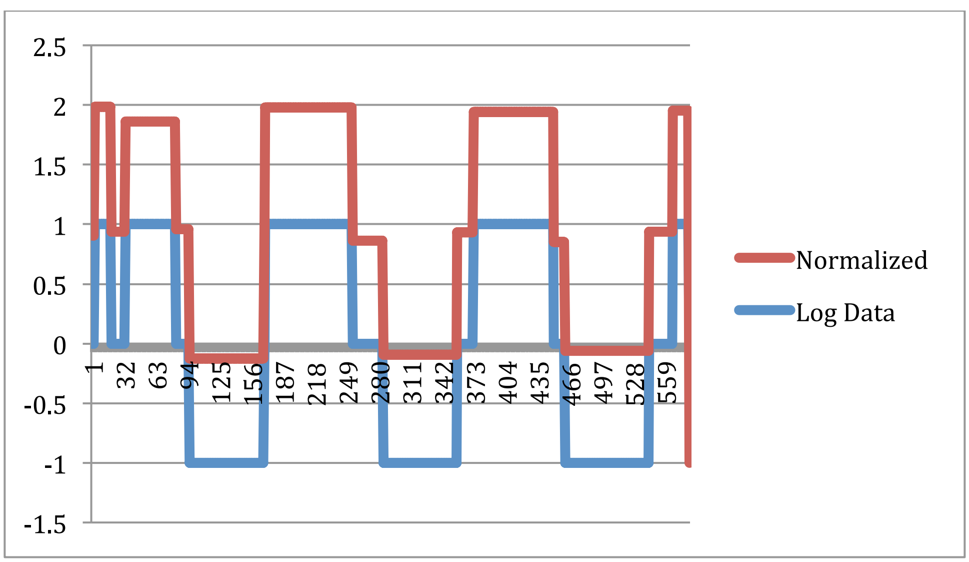


Fig 14: 60 Seconds test 2

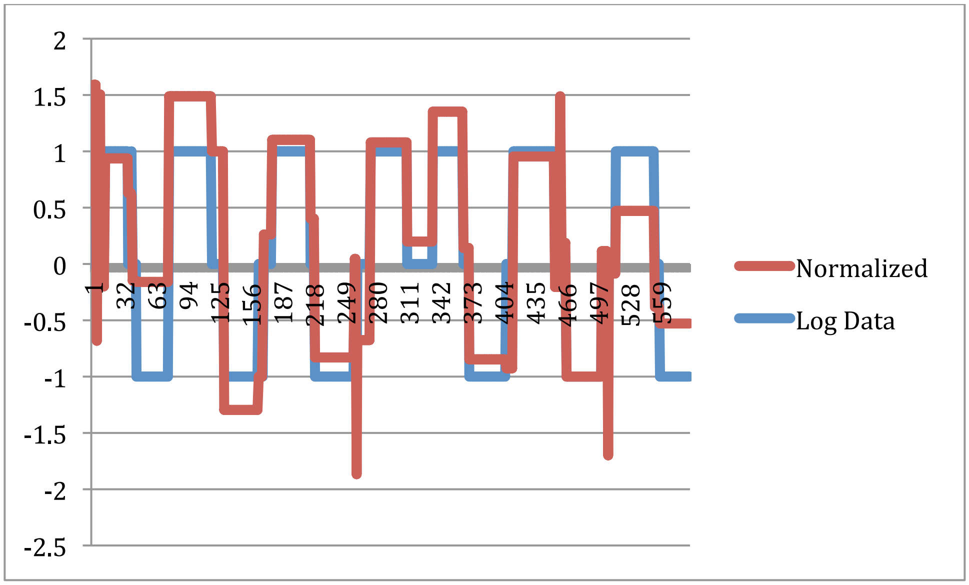


Fig 15: 60 Seconds test 1

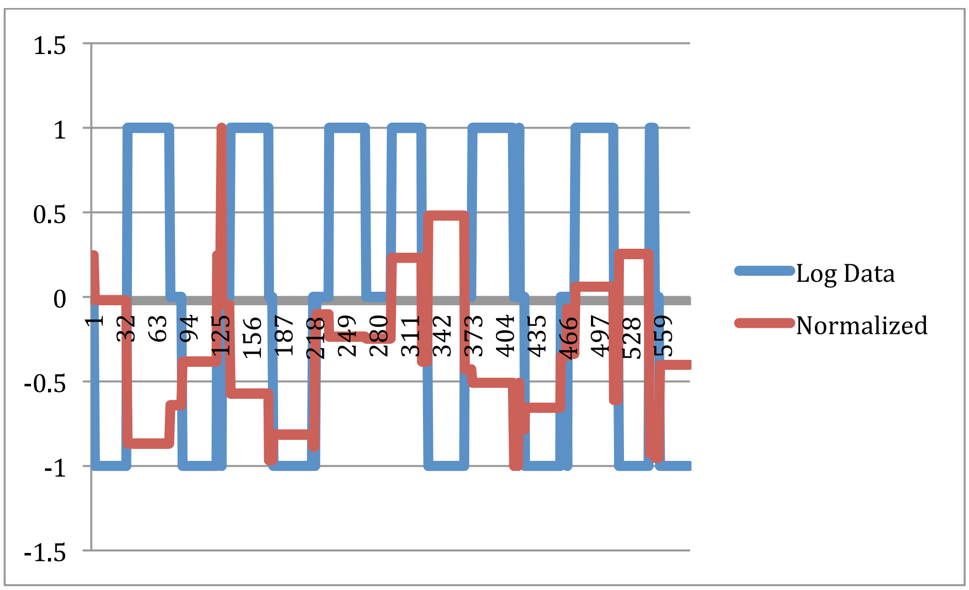


Fig 16: 30 Seconds Test1 (1_4)

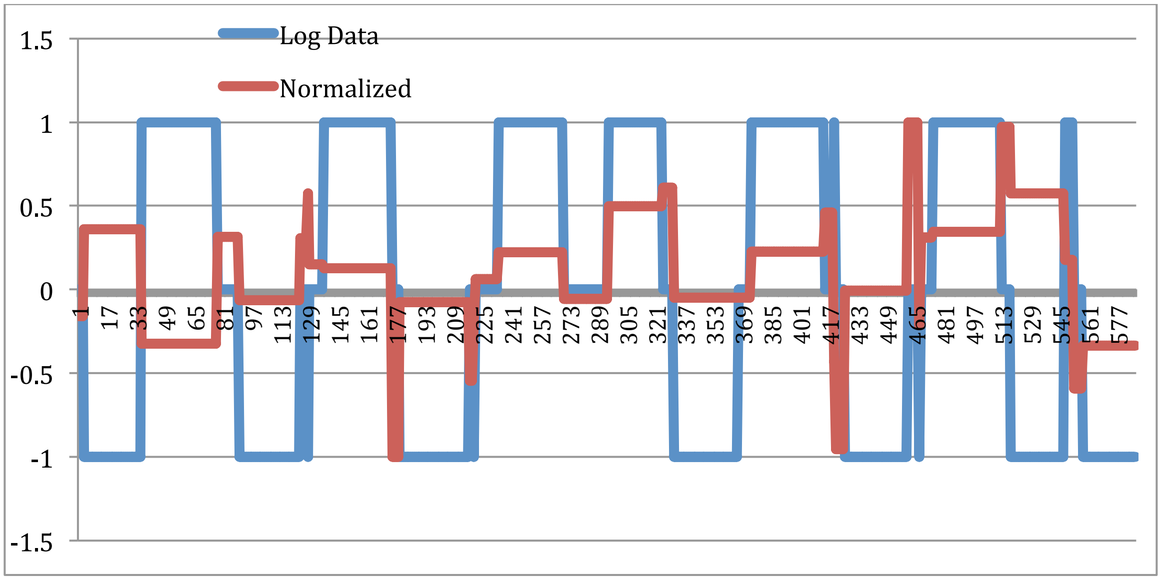


Fig 17: 30 Seconds Test 1 (1_1)

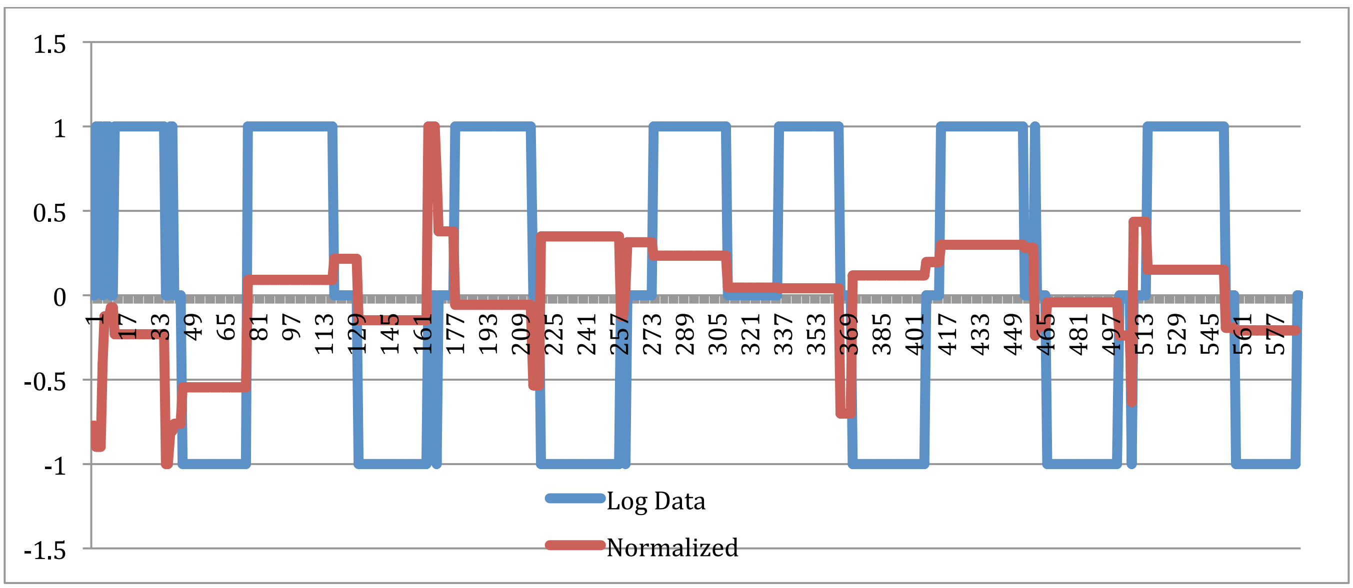


Fig 18: 30 Seconds Test 2 (2_5)

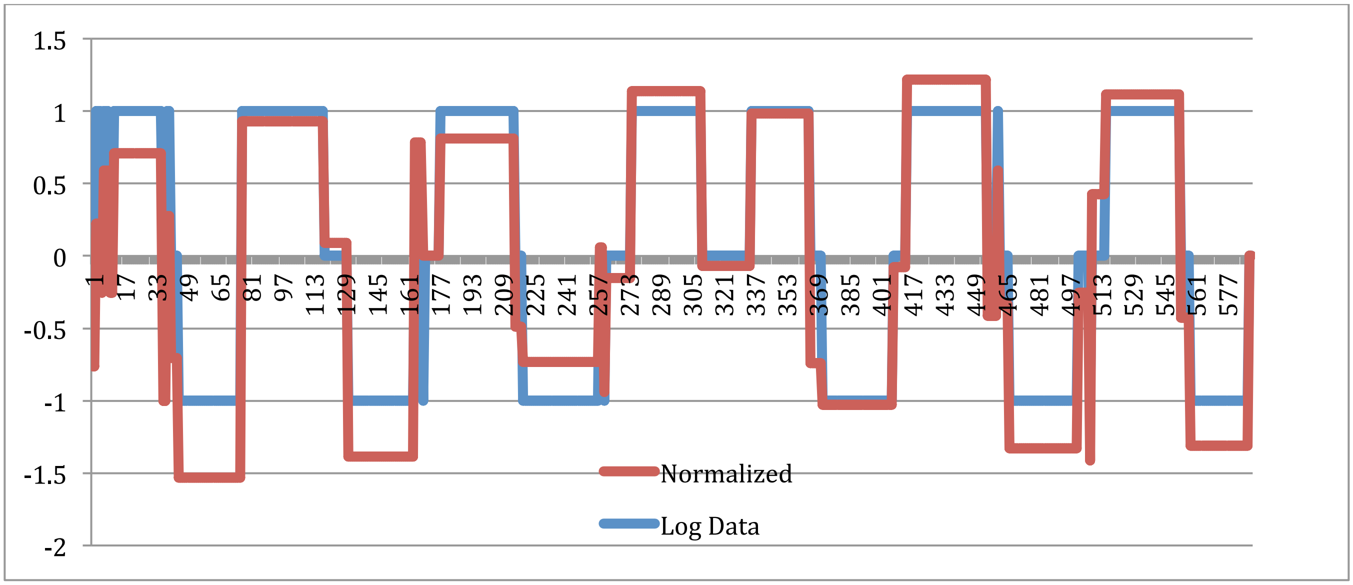


Fig 19: 30 Seconds Test 2 (2_3)

5.1 Graphs of data used for visualization:

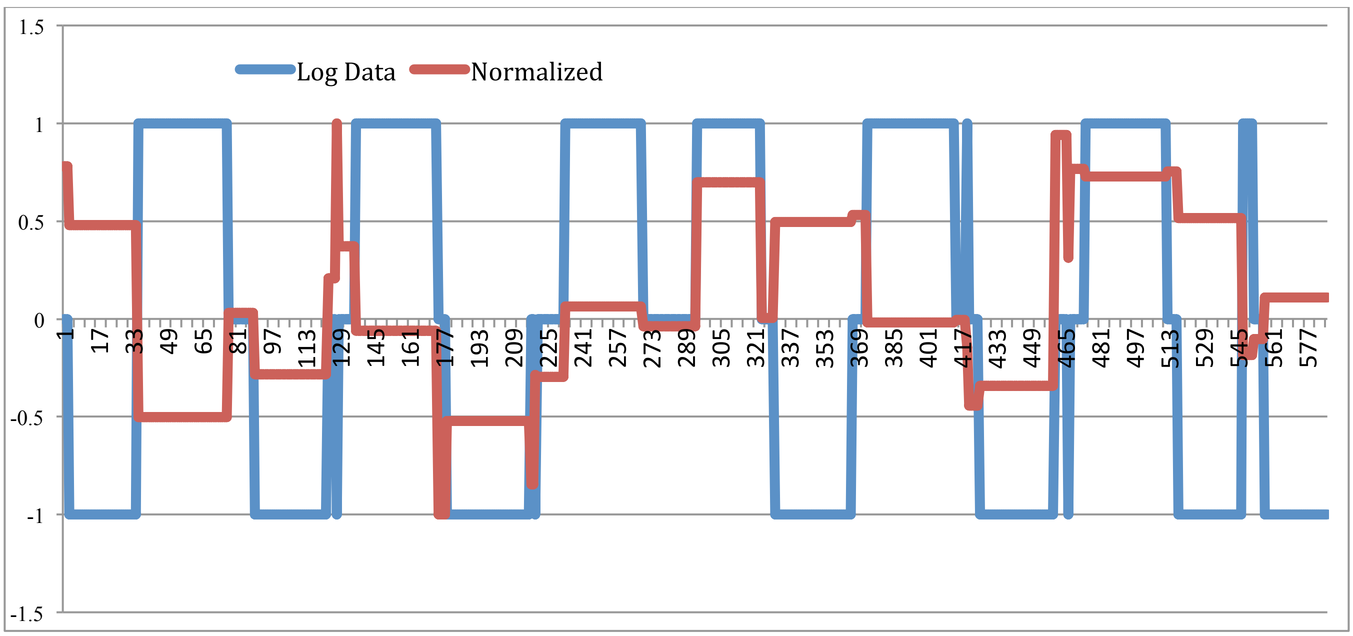


Fig 20: 30 Seconds Test 1 (Points considered are 37, 78, 296, 325, 129)

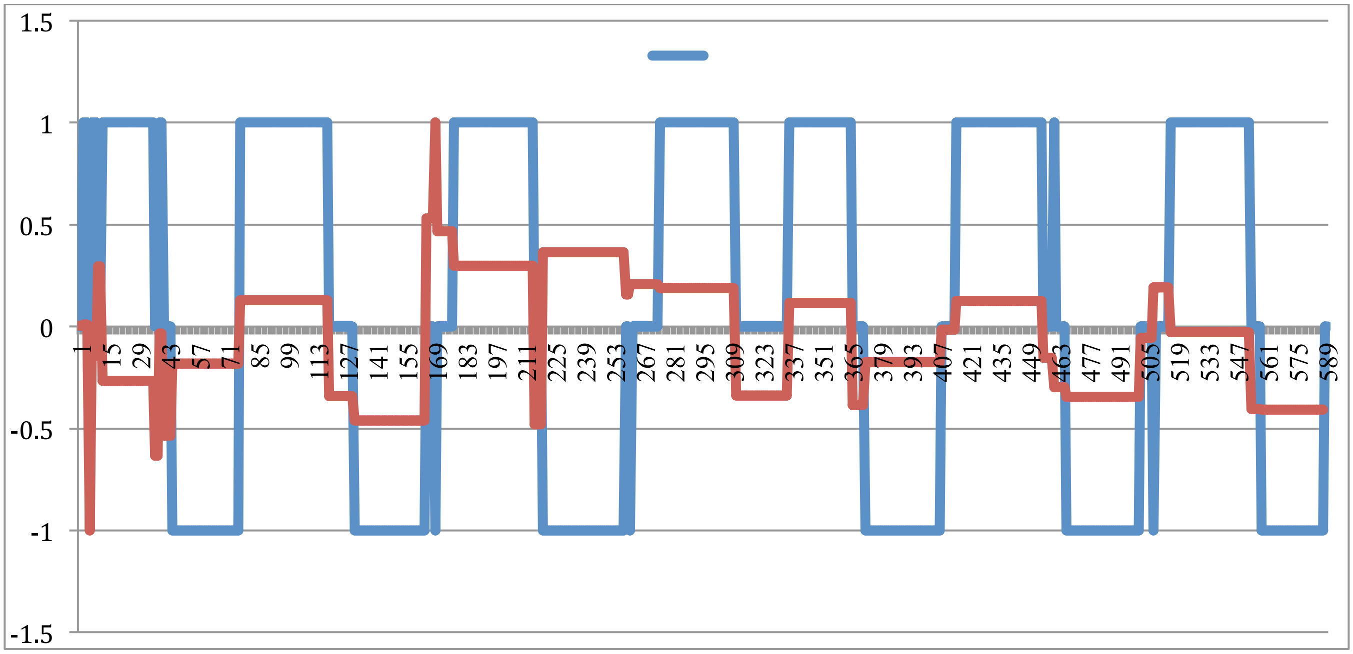


Fig 21: 30 Seconds Test 2 (Points considered are 7, 37, 78, 119, 170, 221, 259)

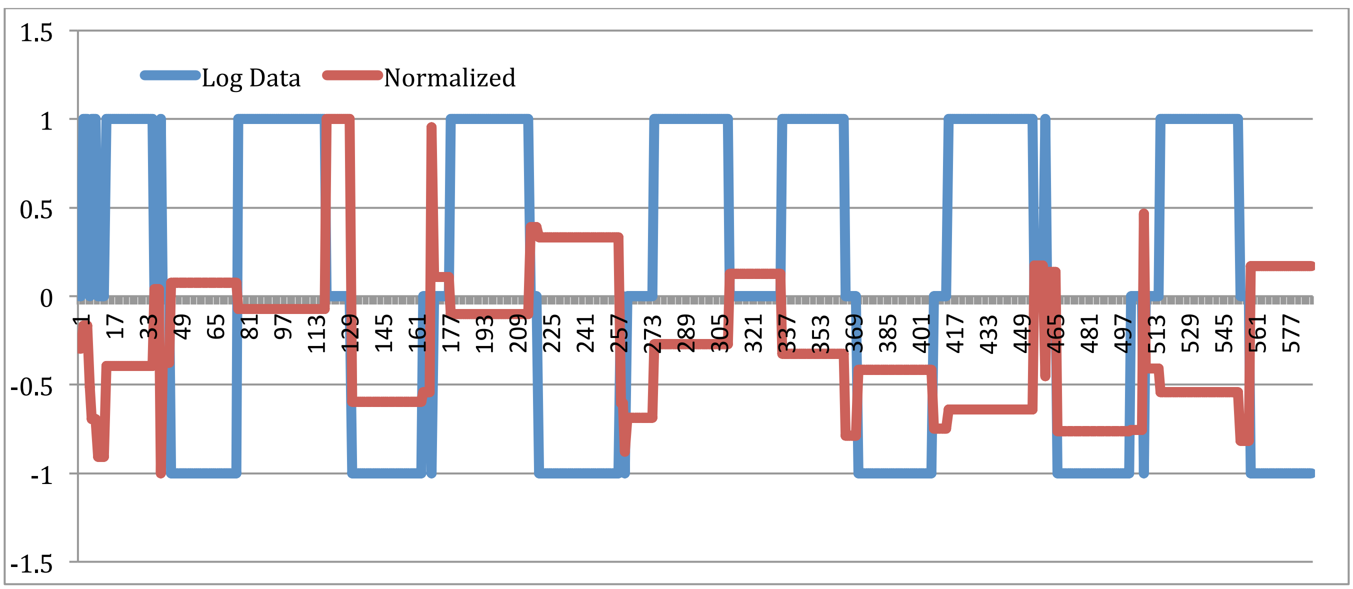


Fig 22: 60 Seconds Test 1 (Points considered are 41, 4,14, 46, 77, 78, 131)

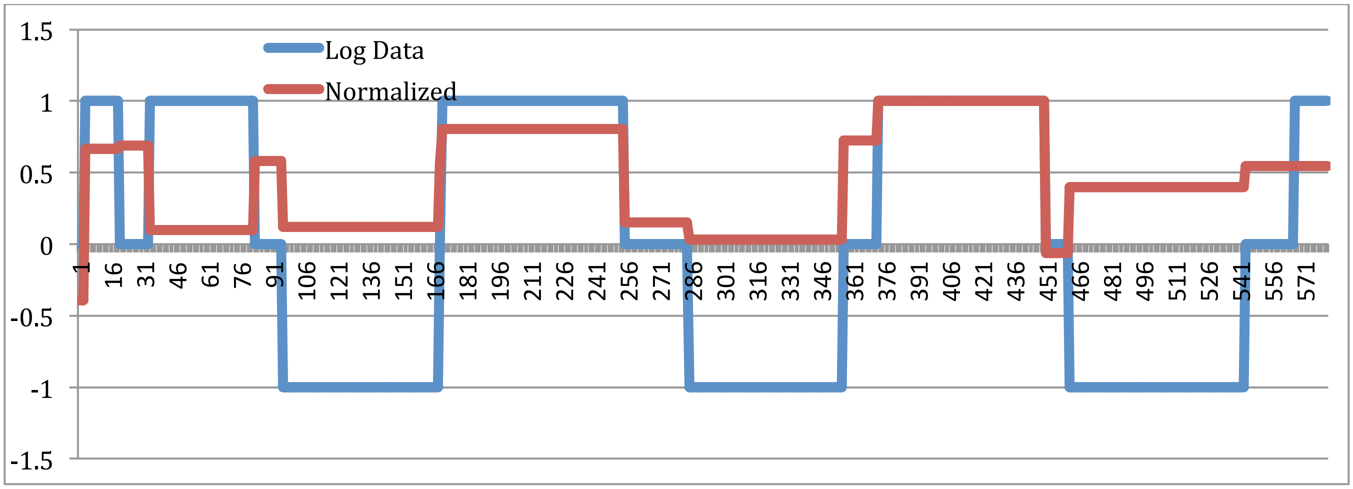


Fig 23: 60 Seconds Test 1 (Points considered are374, 451, 452, 462)

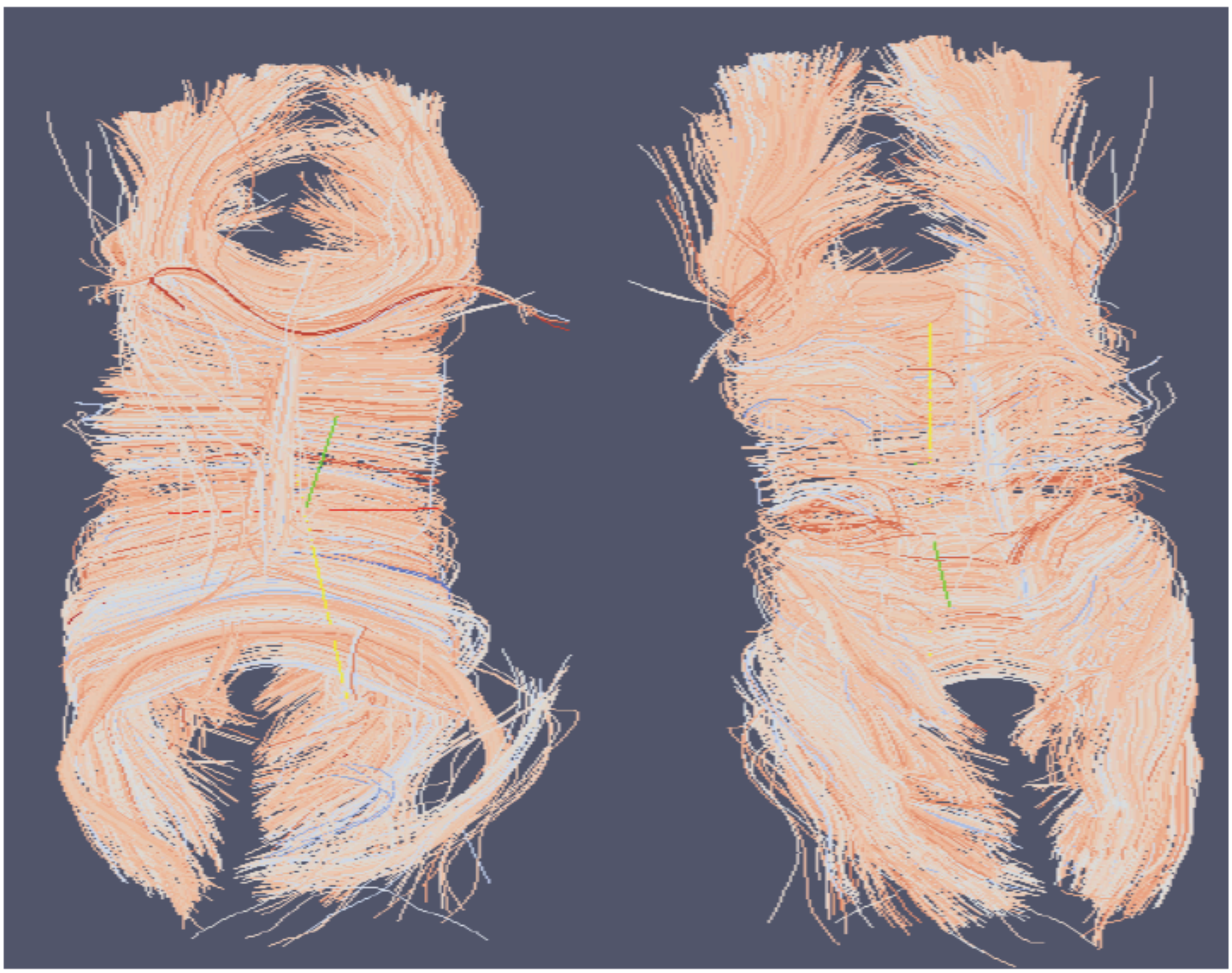


Fig 24: FMRI data visualizations when the player comes across the dialogue Box

Fig 25: FMRI data visualizations when the player completes a Right Turn

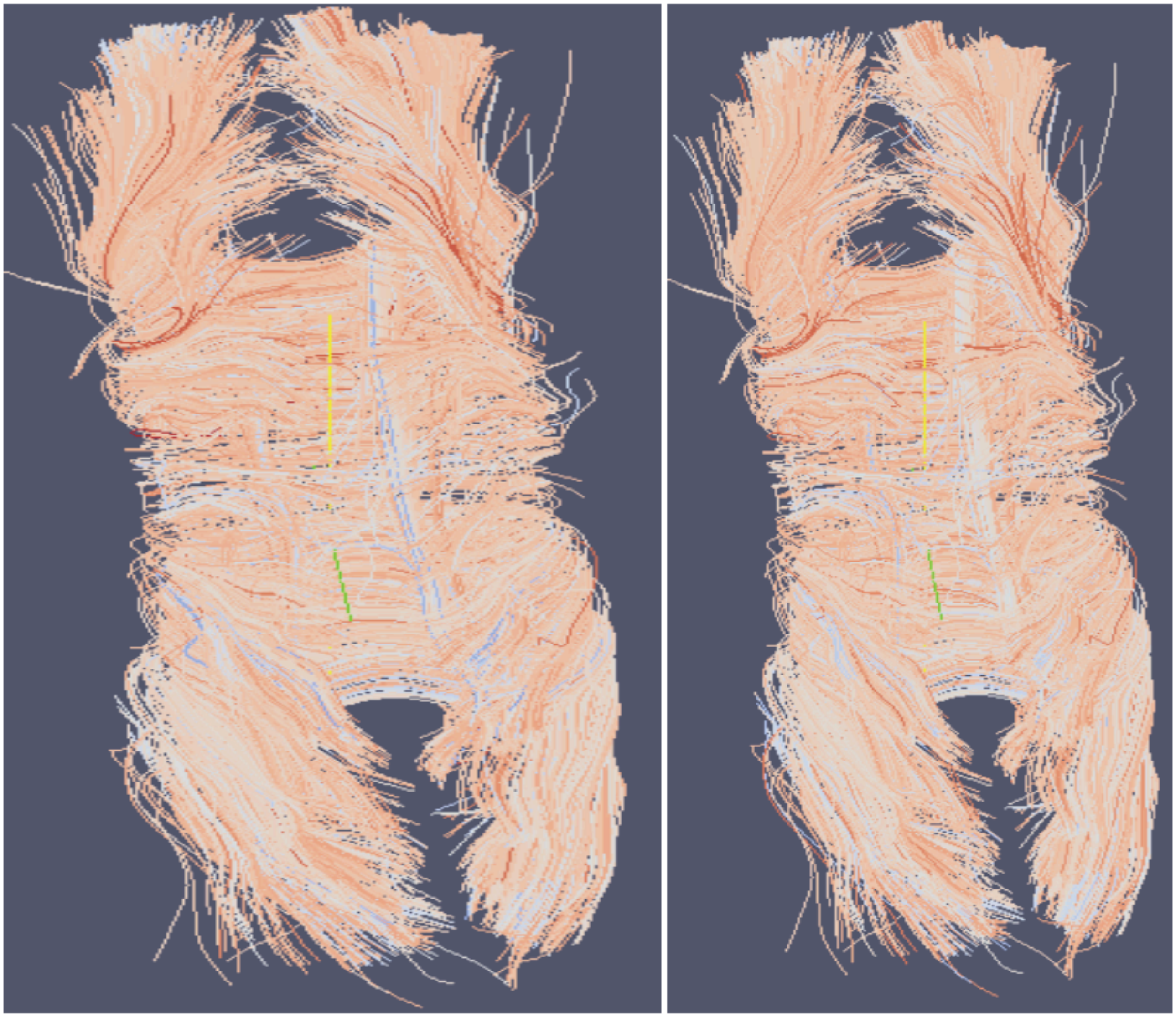


Fig 26: FMRI data visualizations when the player completes a Left Turn

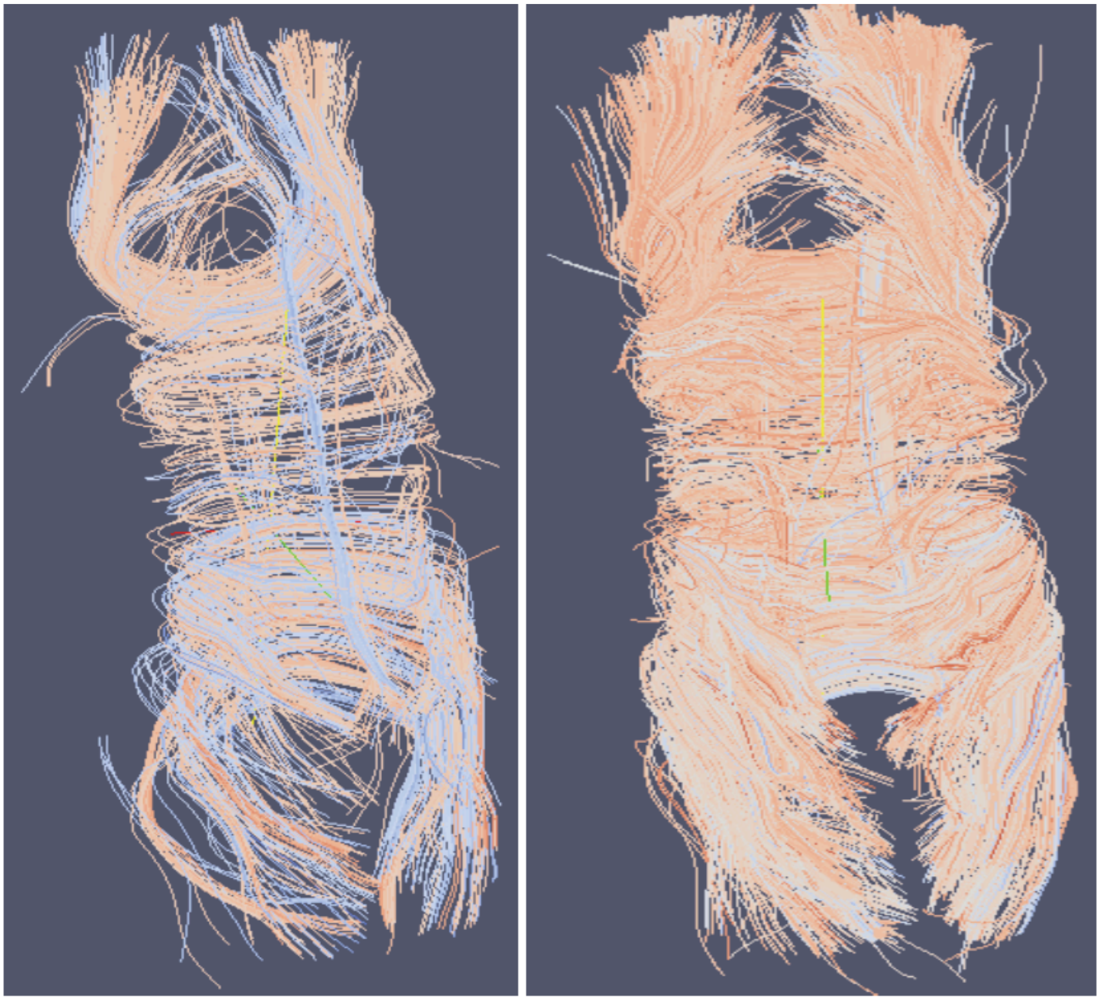


Fig 27: FMRI data visualizations when the player goes constantly in one direction

5.2 Conclusions and Discussion:

This research topic involved an innovative idea and use of cutting edge brain imaging technology in successful hypothesis results. We have worked on a novel and interesting idea of impact of video games on human brain. We developed a game and carried out the experiment using the MRI scanner. After the pre processing of the fMRI data, fiber centered granger causality analysis is done using the GCA toolbox. From the structural data corpus callosum is extracted. Later the log data and the GCA output are used for graphical representation and visualization. This project presented results of an experiment in which external stimulus in the form of video game is given to the human brain. With the use of fMRI datasets, structural underpinnings and functional dynamics of GCA convincing and interpreting results were obtained.

The methodology we followed in this research was to extract the fMRI BOLD signals from the two ends of a white matter fiber, which we obtained from the DTI data. After that we analyzed the granger causalities of the fibers. In total two subjects participated in two sessions with for rounds each.

The general hypothesis of finding the Granger Causality between fiber-connected voxels following the right and left turns during the game play and using the conventional general linear model to detect the similarity between the extracted fMRI signals and the paradigm curves during the game play is demonstrated.

Good correspondence was found in most of the result set. The proposed statement, that the communication between the left and right brain hemispheres is activated approximately in the motor cortex and sensory cortex.

5.3 Future Work:

This efficacious completion of the project has created a strong foundation for future studies in the task based stimuli field. We plan to improvise by designing a more complex game with detailed paradigm. We can use similar experimental setup and increase the number of subjects so that the findings can be replicated in cross session and cross subject comparisons.

In this game, car driving played a significant role. In future, we plan to design and use games and task that will involve features such as complex decision making, psychological behavior display, memory retention, educational interactivity.

Currently, only CC fibers were used for algorithm development and evaluation. In the future, we plan to apply the proposed method to other major fiber bundles such as cortico-cortical and cortical-subcortical pathways, and apply the methods for tract-based analysis of DTI datasets of the brain.

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