Investigation, modelling and quantification of the brain response to external stimuli

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INVESTIGATION, MODELLING AND QUANTIFICATION OF THE BRAIN RESPONSE TO EXTERNAL STIMULI

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Abstract

No adequate mathematical model of the brain activity exists until today. This is due to the fact that the brain is an extremely complex non-linear system. This research work presents a novel mathematical model of the human brain response to external stimuli.

Using the basic laws of physics: the conservation of energy principle, the second law of thermodynamics and the least action principle, a phase-lagging diffusion model of a single neuron action potential has been proposed with validation. This model overcomes the paradox of instantaneous propagation in the classical diffusion equation by introducing a time lag. Applying the external stimuli, simulated as a series of Gaussian energy pulses, to this model has generated fractal time series similar to EEG.

Various functions describing concepts of the importance of information, relevance of information and information gain have been introduced. Measures like the Hurst exponent and the Jeffreys measure have been proposed to quantify the stimulus and its effects. Software has been developed to analyse the captured EEG signals from subjects and compute fractal measures of the signals. Analysis of the effects of different auditory, visual and olfactory stimuli on different subjects is performed and results have been provided with applications to real life.

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List of Abbreviations

ANS	Autonomous Nervous System
BOLD	Blood Oxygenation Level Dependant
CNS	Central Nervous System
CT	Computer Tomography
CWT	Continuous Wavelet Transform
DFT	Discrete Fourier Transform
DWT	Discrete Wavelet Transform
ECG	Electrocardiogram
EEG	Electroencephalogram
EPSP	Excitatory Post Synaptic Potential
FFT	Fast Fourier Transform
fMRI	functional Magnetic Resonance Imaging
FRATSAN	FRactal Time Series ANalyser
FWT	Fast Wavelet Transform
GUI	Graphical User Interface
hb	haemoglobin
IPSP	Inhibitory Post Synaptic Potential
IV	Intravenous
MCG	Magnetocardiogram

MEG	Magnetoencephalogram
MRI	Magnetic Resonance Imaging
ODE	Ordinary Differential Equation
PC	Personal Computer
PDE	Partial Differential Equation
PET	Positron Emission Tomography
PNS	Peripheral Nervous System
SCSI	Small Computer System Interface
SPDE	Stochastic Partial Differential Equation
SQUID	Superconducting Quantum Interference Device

List of Symbols

A, a, B, b, k, M_e, M_i	constants
A_K	maximum amplitude of Potassium flux
A_{Na}	maximum amplitude of Sodium flux
a_c	radius of cylindrical nerve
a_0, a_n, b_n	Fourier series constants
$C(n)$	computational advantage of FFT as compared to DFT
$C_e(k, l)$	number of excitatory synapses from the k^{th} pyramidal cell on l^{th} interneuron
$C_i(k, l)$	number of inhibitory synapses from the k^{th} pyramidal cell on l^{th} interneuron
C_M, C_m	capacitance of membrane
C_1, C_2	interconnectivity constants
c	velocity of propagation
c_0	velocity of propagation in case of pure wave motion
D	diffusion co-efficient
D_e	electric field density
D_q	fractal dimensions
D_0	diffusion-coefficient in case of pure diffusion
dA	differential vector element of surface area A

dl	differential vector element of length l
d_V	deviation of voltage from mean
d_i	decision
$f(t)$	function of time, t
$f_e(V), f_i(V)$	static non-linearities relating dendritic membrane potentials to pulse density
G	information gain
g	conductance of ion
$\bar{g}_K$	conductance of Potassium
$\bar{g}_{Na}$	conductance of Sodium
H	Hurst exponent
H_m	magnetic field
$h_e(t)$	transfer system representing EPSPs
$h_i(t)$	transfer system representing IPSPs
I	current
I_{ext}	extracellular current
I_{int}	intracellular current
I_{ion}	ionic current
I_m	transmembrane current per unit area
I_s	magnitude of applied stimulus
Im_i	importance of information
I_0	magnitude of threshold stimulus
$\mathcal{I}_0(z)$	modified Bessel function
i	counter
i_m	transmembrane current per unit length

i_p	current carried outside due to polarizing electrodes inserted in membrane
J	current density
$J(pj, qj)$	Jeffreys measure
j	imaginary number such that $j^2 = -1$
L	half the period of function $f(x)$
M	memory
m	mean of voltage values
Ne	need for information
n	number of values/events/items
n_{act}	number of neurons activated
$P(\xi, s)$	particular solution
$p(\xi, \vartheta)$	inverse Laplace tranform of $P(\xi, s)$
p_i	probability of occurence of event in i^{th} bin
pj_i	reference probability distribution
Q_{ae}	incoming excitatory potential
Q_{ai}	incoming inhibitory potential
Q_m	asymptotic maximum of sigmoid curve
Q_s	specific excitation due to stimuli
q_s	number of symbols
qj_i	probability distribution of the current sample of signal
R	relevance
R_H	range of voltage values
R_{int}	intracellular resistivity
Re	redundancy

R_2	specific resistance of axoplasm
r_{ext}	extracellular resistance
r_{int}	intracellular resistance
S	magnitude of sensation
$S(\omega), S(x, t)$	source/sink term
$\tilde{S}(\xi, s)$	Laplace transform of source/sink term
S_e	Shannon's entropy
s_H	standard deviation of voltage values
T_k	means of Gaussian pulses
t	time
$t_{max,K}$	time at maximum flux of Potassium
$t_{max,Na}$	time at maximum flux of Sodium
u	energy density
u_{th}	unit step function
V	voltage
$V_e(t)$	potential of pyramidal cell dendrite
V_K	voltage due to Potassium flux
V_l	voltage due to leakage flux
V_m	membrane potential
V_{max}	maximum voltage
V_{min}	minimum voltage
V_{Na}	voltage due to Sodium flux
V_{th}	threshold voltage
w_a	probability after application of stimulus
w_b	probability before application of stimulus

w_j	probability of event occurring
α	power exponent in Steven's law
δ_K	standard deviation of Potassium flux
δ_{Na}	standard deviation of Sodium flux
δV	size of self similar structure
η	informational distance
η_{act}	frequency of activation
θ	velocity of conduction
ϑ	time like variable
κ	term related to variation in cortex diffusivity
Λ	excess potential
$\tilde{\Lambda}$	Laplace transform of excess potential
λ	spatial frequency
μ	mean of Poisson distribution
ξ	distance like variable
ϖ_j	event
ρ	risk
$\rho(d_i)$	risk associated with taking decision
ρ_a	risk after information
ρ_b	risk before information
σ_k	standard deviations of Gaussian pulses
ς	dummy variable
τ	time lag
τ_K	time lag of Potassium flux
τ_{Na}	time lag of Sodium flux

v_m	voltage
$\dot{v}_m$	first derivative of voltage
$\ddot{v}_m$	second derivative of voltage
ϕ	flux due to ion movement across membrane
$\phi_{e,i}$	wave potentials
ϕ_{ext}	extracellular potential
ϕ_{int}	intracellular potential
ϕ_K	Potassium flux
ϕ_{Na}	Sodium flux
ϕ_0	amplitude of stimulus
ψ	function describing wavelets
Ω	Ohm (unit of resistance)
ω	temporal frequency
ω_n	Frequency

Chapter 1

Introduction

1.1 Background

The brain is a very complex organ in the human body. It is the central controlling organ of the body. It behaves like a super computer with many more functions [1]. It acts as the storage device. It acquires information from sensory neurons and responds to the stimuli.

Researchers have been trying to find out more about the enigmatic brain for centuries. A Sumerian scholar wrote about the effects of the poppy plant on the brain. But, the earliest recorded mention of the brain is in the Edwin Smith Surgical Papyrus[2, 3]. The Egyptians believed that the heart was the seat of intellect and thus discarded the brain during the embalming process. The Greeks recognized it as the seat of intellect but many of them also felt that the brain was only an organ to cool down the blood. Galen, a Roman physician, proposed that the brain was an organ that contained the four humors - blood, phlegm, choler and black bile. He also proposed that the brain was divided into faculties and that the mind resided in the brain. Then after a long period of no major advancement in the area of brain study, Andreas Vesalius published “De Humani Corporis Fabrica” which contained lavish illustrations of the brain and the nerves. After this vari-

ous researchers like Galvani, Franz Gall, Pierre Broca, Karl Wernicke, Parkinson worked on the brain and tried to pinpoint the various areas that control different functions of the body. Then in 1929, Hans Berger recorded electrical activity, ElectroEncephaloGram (EEG), from the human brain. After this, EEG became a very important tool in the research and the diagnostics of the brain. In 1963 and 1973, x-ray computerized tomography was developed independently by two different researchers. In the 1980s, Positron Emission Tomography (PET) was developed which studied neural activity by measuring the blood flow to the parts of the brain. In the 1990s, functional Magnetic Resonance Imaging (fMRI) was put forward to measure the neural activity by means of recording the oxygenation of blood[4–9].

After EEG started being used extensively to measure the brain’s electrical activity, various methods were developed to analyze it. The most extensively used method is called Fast Fourier Transform (FFT). But Kramarenko and Tan proposed that, since the brain is a complex non-linear system and FFT is a linear system, spectral analysis of the EEGs using FFT may mislead the neuroscientists. They also pointed out the inaccuracies that may occur if FFT is used on EEGs[10]. Wavelet transform as a method of spectral analysis of EEG was found to be better in detecting brain diseases as compared to FFT[11]. Kulish et al. proposed a method of viewing the EEGs as a fractal time series which can provide both amplitude and frequency characteristics of the EEGs[12]. The fractal series method is a nonlinear spectral analysis method and thus may be more suited for nonlinear signals like EEGs.

As the methods to measure and analyze the brain function grew, researchers also started getting curious about the modeling of the human brain in order to further understand how it uses sensory inputs. Freeman[13], Lopes da Silva[14], Rotterdam[15], Nunez[16], Wright and Liley[17, 18], Steyn Ross[19], Kulish and Chan[20] were some of the researchers who worked in this area. Various mathematical models were developed

which attempted to explain the functioning of the brain. From the first linear model to the present nonlinear models, all of them have improved on the previous one by adding various parameters to account for the complexity of the brain architecture and behavior.

1.2 Research motivation

Even though many researchers have worked on modeling the brain for years, there is no mathematical model which is adequate to model the brain functions accurately. The primary reason offered for the absence of such a model is the complexity and non-linearity of the brain. The relationship between an external stimulus and the corresponding brain response is also an area that has been vague. Such a model, when developed, shall be very useful in the area of brain research. It will open up various other avenues of exploration into the activities of the brain.

1.3 Research objectives

The research aims to develop a mathematical model which will begin by explaining the generation of action potential. The action potential is the most basic neuronal activity. This model shall then be expanded to be able to model EEG signals. We also develop a software to analyze EEG signals as multi fractal time series and extract information from it.

1.4 Preview of the thesis

The thesis is divided into 7 chapters. Chapter 1 gives a brief introduction of the thesis. Chapter 2 investigates the work done in the area of brain research and outlines the basics

of the area of work. The development of a novel phase-lagging model for a single action potential and its validation is detailed in Chapter 3. Chapter 4 is devoted to modelling the EEG from the brain and introducing key concepts. Chapter 5 gives the data acquisition methodology and describes the development of a novel software for analysis of EEG. Chapter 6 presents the results of data analysis and also the discussion about the results. Finally, Chapter 7 details the future work that can be done with this research work as basis.

Chapter 2

Literature Review

2.1 Review of the nervous system

The nervous system in the body is composed of the brain, various sensors and a high speed transmission system. Nerves that carry the information to the brain are called afferent nerves and those that carry information from the brain are called efferent nerves. The brain and the spinal cord form the central nervous system (CNS) as shown in Figure

2.1

Nerve fibers outside the central nervous system form the peripheral nervous system (PNS). The PNS mainly serves to connect the CNS to the other parts of the body. Afferent peripheral nerves are called sensory nerves and efferent peripheral nerves are called motor nerves. The PNS can be divided into the somatic nervous system and the autonomic nervous system.

The somatic nervous system consists of nerves that control skeletal muscles and sensory receptors. The system of afferent nerves that carries sensory information from the skin to the brain is called the somatic sensory nervous system. The visual pathway carries information from the retina and the auditory pathway carries information from the

Figure 2.1: The Central Nervous System (Source: National Library of Medicine (NLM))

auditory receptors to the brain. In the visual pathway, the light sensors - rods and cones - are located on the retina. Some of the sensed information is processed at the retina, and then sent to the optical cortex via the optical nerve. The rods are sensitive to dim light and the cones to colour. In the auditory system, the frequency of sound is coded in two different ways. After passing through the acoustical system into the inner ear, the sound excites the basilar membrane. At low frequencies, the entire membrane vibrates as a unit, and the sound frequency is coded into a spike discharge frequency by the hair-cell sensory neurons located along the membrane. Above a certain crossover point (about 4000 Hz); the frequencies distribute themselves along the basilar membrane. Thus, for higher frequencies, the frequency is coded according to which sensors are activated, whereas for lower frequencies, the coding is by spike discharge frequency. Auditory information from both ears is transmitted to the temporal lobes on both sides of the cerebral cortex. Tim-

ing devices are provided so that if a sound strikes both ears a fraction of a millisecond apart, the ear receiving it first inhibits the response from the other ear. This gives the person hearing the sound a sense of direction.

The autonomic nervous system (ANS), shown in Figure 2.2, is involved in emotional response and in maintaining homeostasis. It is composed of two subsystems - sympathetic and parasympathetic. The sympathetic system functions in actions that require quick responses like emergencies. The parasympathetic system functions in actions that do not require immediate responses thereby aiding in conservation. These two subsystems complement each other [21]. The red lines in the Figure 2.2 indicate sympathetic nerves and the blue lines indicate parasympathetic nerves.

Figure 2.2: The Autonomic Nervous System (Source: Gray's Anatomy)

2.2 Introduction to the brain

The brain is one of the most complex and important organs in the human body. As Hippocrates said about the brain in *On the Sacred Disease* in 400 B.C., “Men ought to know that from nothing else but the brain come joys, delights, laughter and sports, and sorrows, griefs, despondency, and lamentations. And by this, in an especial manner, we acquire wisdom and knowledge, and see and hear, and know what are foul and what are fair, what are bad and what are good, what are sweet, and what unsavory; some we discriminate by habit, and some we perceive by their utility. By this we distinguish objects of relish and disrelish, according to the seasons; and the same things do not always please us. And by the same organ we become mad and delirious, and fears and terrors assail us, some by night, and some by day, and dreams and untimely wanderings, and cares that are not suitable, and ignorance of present circumstances, desuetude, and unskilfulness. All these things we endure from the brain, when it is not healthy, but is more hot, more cold, more moist, or more dry than natural, or when it suffers any other preternatural and unusual affection. And we become mad from its humidity. For when it is more moist than natural, it is necessarily put into motion, and the affection being moved, neither the sight nor hearing can be at rest, and the tongue speaks in accordance with the sight and hearing. In these ways I am of the opinion that the brain exercises the greatest power in the man”. [22].

The brain is seated in the cranial cavity and is the main organ of control of the body functions. It weighs about 1.3 kg to 1.4 kg [23]. It has about one billion neurons, and about 10 times more glial cells [4].

2.3 Review of the anatomy of the brain

The brain is divided into four major parts as seen in Figure 2.3:

1. Cerebrum
2. Brain Stem
3. Diencephalon and
4. Cerebellum.

Figure 2.3: Cross section of the brain

The major parts of the brain are discussed below with a small description of their functions.

2.3.1 Cerebrum

The cerebrum is the most prominent and readily identifiable part of the human brain. It is divided into two halves called the cerebral hemispheres.

A detailed anatomy of the cerebrum is shown in Figure 2.4.

Figure 2.4: Parts of the cerebrum (Source: SEER)

The left hemisphere is dominant for language and the right is more for spatial and perceptual processing. They comprise of grey matter and white matter. Grey matter is the collection of the blood capillaries of the nerve cells and white matter is made up of the axons. The outer layer of the grey matter is called the cerebral cortex. It is very thin, about 2-3 mm thick, and is folded to a great extent. The ridges are called gyri and the raised parts are called sulci [4, 24]. The surface area of the cortex is about 2.5 sq.ft. (75 cm^2) [25].

The cerebrum is responsible for the complex intellectual functions of the brain. It

allows us to sense, perceive, remember, communicate, reason, plan, feel emotions and perform voluntary motor activities.

Each hemisphere is divided into four lobes:

1. Frontal lobe - It is involved with voluntary motor functions, concentration, verbal communication, decision making, planning and personality.
2. Parietal lobe - It is necessary for the general sensory functions.
3. Temporal lobe - It is responsible for hearing, interpreting speech and language, and smell.
4. Occipital lobe - It is involved with processing of incoming visual information and storing visual memories [24].

Brodmann in 1909 divided the cerebral cortex into 52 different regions based on his observations on the involvement of the region for each of the functions. Economo and Koskinas, in 1952, constructed another cytoarchitectonic scheme for the cortex [26]. Later researchers like von Bonin and Bailey used the scheme made by Economo et al. for their brain map and mentioned that Brodmann's scheme was inadequate [27].

2.3.2 Brain Stem

The brain stem is an enlargement of the spinal cord when it enters the brain. It consists of the medulla oblongata, pons and the mesencephalon as shown in Figure 2.5.

The medulla oblongata controls the vital functions like heart rate, blood pressure and respiration and also involuntary behavior like coughing, gagging, sneezing etc. Any damage to the medulla is fatal due to a disruption to the above functions. The pons regulates the rate of breathing. The mesencephalon is responsible for the visual and auditory reflexes and also regulation of movement. [4, 24, 28]

Figure 2.5: Parts of the brain stem (Source: SEER)

2.3.3 Diencephalon

The diencephalon is the region above the mesencephalon and consists of the epithalamus (pineal gland), thalamus and hypothalamus. These three parts of the diencephalon, shown in Figure 2.6, perform variedly different functions.

The epithalamus, which is represented as pineal gland in Figure 2.6, secretes the hormone melatonin which appears to regulate the circadian rhythm of the human body. The thalamus acts as the relay between the cortex and the CNS. It acts as a filter so that only the important information gets relayed to the cortex and other “noise (visual or auditory)” is blocked. It also informs the cortex on the source of the sensory information.

The hypothalamus is responsible for regulation of temperature, fluid balance and nutrient balance of the human body. By doing so, it maintains the homeostasis of the body. It is the master control of the ANS and the endocrine system [24, 28].

Figure 2.6: Parts of the diencephalon (Source: Become healthy now)

2.3.4 Cerebellum

The cerebellum or the “little brain”, shown in Figure 2.7, extends from the pons and is located between the cortex and the posterior of the brain. The most distinctive feature of the cerebellum is the presence of white matter distributed like the branches of a tree and is called the arbor vitae or tree of life.

The cerebellum is responsible for maintaining body posture and body equilibrium. It also coordinates and refines the muscle movements [24, 28].

Figure 2.7: The Cerebellum shown as a pink area (Source: Wikipedia)

In addition to all the parts mentioned above, the brain has a functional system called the limbic system which is made up of a number of scattered but interconnected structures in the brain, as shown in Figure 2.8. This system is supposed to allow humans to process and experience emotions. It is made up of cingulate gyrus, parahippocamal gyrus, hippocampus, fornix, amygdaloid body, olfactory bulb, mass intermedia along with other structures [4, 24].

Figure 2.8: Limbic System shown in red (Source: Wikipedia)

2.4 Review of various measurement methods

The brain is a very active organ. It processes a lot of signals and responds to them with the relevant and required output. This output and the brain activity are measured by various ways, some of which are elucidated below.

2.4.1 Electroencephalogram (EEG)

The measurement of the electrical activity of the brain is called Electroencephalography and the resulting traces are called Electroencephalogram (EEG). It measures the activity of a large number of neurons rather than a single neuron [4]. It is one of the early methods of measuring brain activity.

2.4.1.1 History

Richard Caton, in 1875, placed bare electrodes on the skulls of dogs and apes and measured the electrical activity using a sensitive galvanometer. This can be called the foundation to EEG measurement. After this, Einthoven developed the string galvanometer. Later Hans Berger in 1929 measured the first human EEG using Einthoven's string galvanometer. He was the one who coined the term *Elektenkephalogram*. He observed that the waking and sleeping EEGs are different. He is generally credited with the invention of EEG. His EEG recording is shown below in Figure 2.9.

Figure 2.9: First EEG recording, obtained by Berger in 1924 (Source: Wikipedia)

Berger's work was later expanded by Edgar Douglas Adrian. Ralph Gerard and Franklin Offner introduced concentric needle electrodes and developed the EEG equipment. The first EEG lab was set up in Massachusetts General Hospital in 1936. Neonatal EEG was introduced in the 1970s. Digital EEG began to gain prominence in the 1980s which was further substantiated by topographic mapping. The 10-20 system of electrode placement was taken as a standard for surface EEG recordings. Later, an extension of the 10-20 placement system was proposed which increased the number of electrodes from 21 to 74. This new system called the 10% system or extended 10-20 system has been widely accepted by the American Encephalographic Society and the International Federation of Societies for Electroencephalography and Clinical Neurophysiology [3, 29–39].

2.4.1.2 Methodology

The process of recording an EEG is very simple, non-invasive and painless. Electrodes are placed on the subject's scalp along with a conductive gel. At least three electrodes are required for the recording. Two of these are recording electrodes and one is called the ground electrode as it is connected to an electrically inactive part of the human body like the earlobe. The number of electrodes can range from 3 to 164. The electrodes should be securely attached to the scalp in order to reduce disturbances in the signal. The electrode cap, a stretchable cap with electrodes attached to it, is very useful as the electrodes placed on it are in accordance with the international placement system. The signals produced by neurons are usually very small, a few tens of micro volts (V) in amplitude. Different regions of the brain can be observed by selecting the relevant sets of electrodes. The recorded voltages are then fed into the amplifier, to amplify the signal, and a set of filters to give the EEG as output. This signal can be obtained on paper or on the monitor [3, 28, 40]. An example of the EEG signal is shown in figure 2.10.

Figure 2.10: EEG Signal (Courtesy: Hugo Gamboa Dez, Wikipedia)

The placement of electrodes on the scalp is governed by the international 10-20 standard for electrode placement. The Figure 2.11 below shows the system of placement.

Figure 2.11: International 10-20 standard of electrode placement

Each of the sites is represented by a letter and a number or another letter. The letters are as shown below in Table 2.1

Sr.No	Alphabet	Position
1	Fp	Front Polar
2	F	Frontal
3	C	Caudal
4	T	Temporal
5	P	Pareital
6	O	Occipital

Table 2.1: Naming of sites on the scalp for EEG

The even numbers represent the right side of the hemisphere while the odd numbers represent the left. The smaller the number, the closer it is to the midline. The letter ‘z’ refers to the electrode placed on the midline of the scalp [38, 39, 41].

2.4.1.3 Activity types

Rhythmic sinusoidal activity in the EEG often relates to the state of behavior. The following four types of rhythmic EEG activity are historically recognized [3, 28, 39, 42]:

1. Beta: These are the fastest rhythms and have a frequency greater than 14 Hz. These are seen when the cortex is active i.e. the subject is busy thinking or concentrating. They are shown in Figure 2.12

Figure 2.12: Beta waves (Courtesy: Hugo Gamboa Dez, Wikipedia)

2. Alpha: These have a frequency between 8 to 13 Hz and are seen when the subject is awake but rested and quiet. They are shown in Figure 2.13

Figure 2.13: Alpha waves (Courtesy: Hugo Gamboa Dez, Wikipedia)

3. Theta: These are between 4 to 7 Hz and are present during some sleep states, drowsiness, hypnotic states and trance. They are shown in Figure 2.14

Figure 2.14: Theta waves (Courtesy: Hugo Gamboa Dez, Wikipedia)

4. Delta: These are the slowest rhythms, with a frequency less than 4 Hz. They have very large amplitude. These are characteristic of deep sleep. They are shown in Figure 2.15

Figure 2.15: Delta waves (Courtesy: Hugo Gamboa Dez, Wikipedia)

Other than the four major rhythmic activities stated above, there are various other patterns noticed in an EEG signal too. They are [42, 43]:

1. Sensorimotor rhythm: It is a middle frequency, 12-16 Hz, which is associated with body stillness. It is shown in Figure 2.16

Figure 2.16: SMR Waves (Courtesy: Hugo Gamboa Dez, Wikipedia)

2. Gamma: It is the frequency range approximately 26-100 Hz. It appears in subjects performing higher mental activity like fear, problem solving and perception. It is shown in Figure 2.17

Figure 2.17: Gamma waves (Courtesy: Hugo Gamboa Dez, Wikipedia)

3. Spike and wave activity: This indicates a seizure disorder and may be visible in the EEG even though the patient is not having an epileptic seizure. It is shown in Figure 2.18

Figure 2.18: Spike and Wave activity

4. Psychomotor variant: This is an unusual form of brain activity that occurs as asymmetrical runs of theta or delta activity primarily in the temporal regions, lasting for a few seconds or as long as 30-45 seconds. This however does not correlate with a seizure disorder.
5. Mu: This waveform occurs in the central regions of the awake patient and has no pathological significance. It joins with motor activity of the contra lateral body (or the thought of such movement).
6. Benign Epileptiform Transients of Sleep: These are sharp, small waves that can be seen most often in elderly rather than children. They can be seen in both normal and epileptic patients.
7. Phantom spike and wave: These occur as bursts of miniature spike and wave complexes at 6 Hz rather than the usual 2-4 Hz.
8. Wicket spikes: These are another waveform with no pathological significance. They are rounded on one end and sharp on the other giving them an appearance like spikes.

2.4.1.4 Artifacts in EEG signals

The disturbances present in an EEG signal are called artifacts. These artifacts are signals that are non-cerebral in origin and are interference waveforms. The most common types of artifacts are [39, 42–45]:

1. Electrode pop: This occurs when the subject moves or even when the electrodes are settling down. This causes a reduction in the impedance of the given electrode and is characterized by a sudden spike in the EEG signal.
2. Alternating Current artifacts: This is caused due to poor grounding of the EEG electrodes. This introduces a 50 Hz or 60 Hz (depending on the laboratory's electrical supply) artifact in the signal. This can be eliminated by properly grounding the subject.
3. Intravenous (IV) drip artifact: This is more observed in clinics where IV drips are present near the EEG machine. They produce rhythmic, fast, low voltage bursts in the EEG signal. This can be eliminated by keeping all such IV drips away from the machine.
4. Electrocardiogram (ECG) artifact: This usually occurs when the ear electrode touches the skin behind the earlobe. This introduces a sinus rhythm in the EEG signal synchronizing to the QRS complex of the ECG channel. This can be eliminated by placing a cotton ball behind the subject's ear preventing any contact of the electrode with the skin.
5. Muscle artifact: This is present when the subject moves his/her muscles like clenching of jaw, shifting in the seat etc. This can be identified as the potential and duration of such artifacts is lesser than the EEG signal. This can be reduced by giving proper instruction to the subject and making them comfortable.

6. Eye movement artifact: Eye movements of the subject cause this artifact. Vertical eye movements like blinks or other reflexive movement of the eyeball (e.g. Bell's phenomenon) can be observed as upward or downward deflections. Such artifacts are present in all EEG measurements.
7. Respiration artifacts: The breathing of the subject can produce two kinds of respiration artifacts. One of them is the slow, rhythmic activity due to normal respiration by the subject and usually one electrode is affected. Sharp inhalation or exhalation can produce the other kind of respiration artifact. This has to be monitored by a device attached to the EEG machine or by the EEG technician.
8. Glossokinetic artifact: This is caused by the potential difference between the base and the tip of the tongue. The tip is negative with respect to the base of the tongue. Tongue movement by the subject also affects the EEG signals greatly.

2.4.1.5 Advantages and Limitations

Like every method, EEG has its advantages and limitations. The advantages of EEG are:

1. Simple method,
2. Non-invasive,
3. Painless,
4. High time resolution in terms of milliseconds and
5. Direct measurement of brain electrical activity.

The disadvantages of EEG are:

1. Not very sensitive to single neuron output,
2. Limited anatomical specificity,
3. Poor spatial resolution due to the skull acting as a filter and
4. Presence of artifacts.

In spite of all the disadvantages, EEG is a very useful method for monitoring the brain activity. It can be coupled with other methods like fMRI and PET to obtain high spatial resolution.

2.4.2 Magnetoencephalogram (MEG)

Magnetoencephalography is the detection and measurement of the small magnetic fields generated by the neurons using highly specialized equipment like Superconducting Quantum Interference Device (SQUID).

It is a well known fact in physics that whenever electrical current flows, a magnetic field is generated. This is in accordance to Maxwell's equations. So it follows that when neurons generate currents, they should produce a magnetic field given by the equation below

$$\oint_C H_m \cdot dl = \int_S J \cdot dA + \int_S \frac{\partial D_e}{\partial t} \cdot dA \quad (2.1)$$

where, H_m is magnetic field, D_e is electric field density, dl is the differential vector element, J is free current density and dA is the differential vector element of surface area A .

But the magnetic fields generated are very small with amplitude below 10-12 tesla. It is estimated that around 50,000 active neurons are required to produce a detectable signal [46–48]. The origin of the brain's magnetic field is shown below in Figure 2.19

Figure 2.19: Origin of the brain's magnetic field (Source: Wikipedia)

Since these magnetic fields are very small as compared to the urban fluctuating magnetic noise (about 10^{-7} tesla) and the earth's magnetic field (about 0.5×10^{-4} tesla), measurement is done with the highly sensitive SQUID and in a magnetically shielded room.

2.4.2.1 History

The first valid biomagnetic recording was done by Baule and McFee in Syracuse, New York. Later the first measurement of a MEG was done by David Cohen et al. at MIT in 1968. In 1962, B.D. Josephson discovered the Josephson Effect, namely the phenomenon of the current flow across two semiconductors weakly coupled and separated by a very thin insulating barrier. This phenomenon was used by Jim Zimmerman to invent the SQUID in 1969. The SQUID was used by Cohen to generate the first MEG measured by a SQUID. The advent of the SQUID allowed the researchers to generate very clear MEGs. The first fetal Magnetocardiogram (MCG) was recorded by Kariniemi et al. in 1974 [49–52].

2.4.2.2 Localization of source

After the recording of the MEG, it becomes necessary to locate the source of the magnetic activity. This will point to the location of the activity within the brain. This is called the inverse problem. Advanced signal processing techniques are used which attempt to establish the source of the measured magnetic fields. The problem with this approach is the lack of a unique solution. Localization algorithms are used for finding the possible solution to this problem. They use signal and head models (geometrical models of the head) for finding the likely location. Estimation algorithms ignore the inverse problem completely. Beamforming is one such approach and is used to concentrate on a required radiation and give a probability estimate of where the signal came from. The solution obtained by this method is then superimposed on the Magnetic Resonance Imaging (MRI) scans to give a localization of the activity source. But all of these methods have their own criticisms [53, 54].

2.4.2.3 Advantages and limitations of MEG

MEG also has certain advantages and disadvantages. It has been compared to EEG by Cohen et al. and it is an issue under dispute [53, 54]. The advantages of MEG are:

1. Non-invasive,
2. Painless,
3. No electrode implantation like in EEG,
4. High temporal resolution and
5. Direct measurement of the activity of neurons.

The disadvantages of MEG are:

1. Expensive equipment,
2. Spatial resolution lower than fMRI,
3. Localization of activity source problem - non-uniqueness of solution of inverse problem and
4. Complicated procedure.

2.4.3 functional Magnetic Resonance Imaging (fMRI)

functional Magnetic Resonance Imaging (fMRI) is the imaging of the brain activity by detection of the changes in the oxygenation of blood in the brain. Active areas of the brain have more blood flow than the inactive areas [3, 55].

2.4.3.1 History

As early as 1890, researchers discovered that changes in blood flow and other physiological processes are directly linked to neural activity. The phenomenon of magnetic imaging has been known since the 1940s and MRI has developed over the last 30 years. fMRI is a recent development. The first fMRI was done in 1991 by Belliveau and co-workers who injected a chemical into a patient and showed that the perception of visual stimuli increases blood flow in primary visual cortex [56–59].

2.4.3.2 Methodology

In the Blood Oxygenation Level Dependant (BOLD) method developed by Ogawa in 1990, the difference in magnetic susceptibility of oxyhaemoglobin and deoxyhaemoglobin is used. Deoxygenated haemoglobin (hb) is paramagnetic, whereas oxygenated hb is diamagnetic.

Diamagnetic materials have a very weak and negative susceptibility to magnetic fields. Under the influence of an external magnetic field, they produce a magnetization in a direction opposite to applied field. Paramagnetic materials have a very weak and positive magnetic susceptibility. They are attracted to an external magnetic field.

The subject is kept under strong external magnetic fields for observation. He/She is then asked to perform specific tasks. As oxygenated blood shows up better on MR images due to the presence of Oxyhaemoglobin, a MRI scanner which is sensitive to susceptibility changes is used and one can find out areas where there is an increase in oxygenated blood to locate areas of activity for a particular sense, emotion or motor movement [28, 58, 60–62].

2.4.3.3 Advantages and Limitation of fMRI

fMRI has been used to locate processing areas in the visual cortex, the motor cortex and Broca's areas of speech [59, 63–66]. The advantages of the fMRI are as below:

1. Non-invasive,
2. High spatial resolution,
3. No risk of radiation like in CT scan and
4. Painless

The disadvantages of fMRI are:

1. Expensive,
2. Poor temporal resolution as compared to EEG and
3. Models not accurate enough.

2.4.4 Comparison of methods

Three different measurement techniques have been described before. For this research work, EEG signals shall be used. The reasons being:

1. They have a very good temporal resolution as compared to the other methods. So, changes in the brain activity can be found out almost instantaneously. This can aid in further pin-pointing the specific response of the brain to a unique stimulus.
2. Brain activity can be adequately described by a fractional equation. The best technique that can be viewed as a fractal time series is EEG. So, EEG is very suitable to describe the brain activity.

Currently, EEG can be sampled in 256 or 512 Hz frequencies. But work is ongoing at Technion, Israel to enable measurement of EEG up to 40 kHz which will be very helpful in encompassing a wide range of brain activity and improve the resolution. This makes EEG to be a very suitable choice for this research work.

2.5 Method of analysis of EEG signals

EEG signals are a direct representation of the brain's activity. But it is still a raw signal which is influenced by various other factors as well. To obtain the information from the raw EEG signal, various analysis methods have been adopted. Initially, only a qualitative description of EEG was done which though clinically important, could not be used for those areas of brain research where quantitative data was required. This was to be the case till there was advancement in time series analysis and power density spectral estimation by researchers like Blackman and Tukey, Jenkins and Watts, Jones and others [67–70]. A few methods of analysis of EEG have been outlined below.

2.5.1 Fourier analysis

In 1822, Jean Baptiste Joseph Fourier published *Théorie analytique de la chaleur* (The Analytic Theory of Heat) which contained a series of sines and cosines that could express the heat conduction in solid bodies [71]. Though initially it was not accepted by the mathematicians and physicists, the Fourier series was later proved to be correct by the works of Dirichlet, Friedrich and others. If $f(x)$ is a function over a period $2L$, then its Fourier series expansion can be written as

$$f(x) = \frac{a_0}{2} + \sum_{n=1}^{\infty} \left[a_n \cos\left(\frac{n\pi x}{L}\right) + b_n \sin\left(\frac{n\pi x}{L}\right) \right] \quad (2.2)$$

where $a_0 = \frac{1}{L} \int_{-L}^L f(x) dx$, $a_n = \frac{1}{L} \int_{-L}^L f(x) \cos\left(\frac{n\pi x}{L}\right) dx$, $b_n = \frac{1}{L} \int_{-L}^L f(x) \sin\left(\frac{n\pi x}{L}\right) dx$ and $n = 1, 2, \dots$.

The Fourier Transform is a linear operator which decomposes a function into a spectrum of its frequency components. The Discrete Fourier Transform (DFT) is an application of the Fourier transform widely used in signal processing to analyze the frequencies in a signal. If the sequence to be represented is to be taken in finite duration, then the discrete Fourier transform is taken. For a sequence $f(t)$ as in Equation (2.2), the N point DFT is represented as [72–74]

$$F_n = \sum_{k=0}^{N-1} f_k e^{-j2\pi nk/N} \quad (2.3)$$

where, $k = 0, 1, 2, \dots, N-1$ and $j = \text{imaginary unity such that } j^2 = -1$.

But, the problem with the DFT is the amount of computation it requires. For computing the above DFT, N^2 complex multiplications have to be performed which is a tedious task. In order to alleviate this arduous task, the Fast Fourier Transform was formulated

by Cooley and Tukey in 1965 [75]. In fact, this algorithm had already been formulated by Gauss in 1805 but was not widely recognized till years after Cooley and Tukey published their paper.

The Fast Fourier Transform basically divides the DFT into much smaller portions that require lesser times of computations. So a DFT of composite size N is broken down into smaller DFTs of sizes N_1 and N_2 . This reduces the computations to $N \log_2 N$ size. The most popular form breaks the DFT into two parts and is called the radix-2 algorithm. So the DFT of size N becomes two DFTs of size $N/2$ each. This can be performed recursively to further reduce the size of the DFT. A DFT as in Equation (2.3) can be broken down into two DFTs of size $N/2$ [75]

$$F_n = \begin{cases} G(k) + W_N^k H(k) & 0 \leq k \leq N/2 - 1 \\ G(k + N/2) - W_N^k H(k + N/2) & N/2 \leq k \leq N - 1 \end{cases} \quad (2.4)$$

The computational advantage, $C(n)$, of the FFT as compared to the DFT can be represented by

$$C(n) = \frac{N^2}{N \log_2 N} = \frac{N}{\log_2 N} \quad (2.5)$$

If $N = 2^n$, then

$$C(n) = \frac{2^n}{n} \quad (2.6)$$

If $C(n)$ is plotted, as shown in Figure 2.20, it can be seen that the computational advantage rises for rise in n . This is the major advantage of the FFT as compared to the DFT.

Figure 2.20: Computational advantage of FFT to DFT

The FFT is a very fast algorithm for calculating the DFT of signals. It is used to analyze EEGs in order to obtain the frequency spectrum data. But, since the EEG is a non-linear signal and FFT is a linear algorithm, the data obtained from FFT of EEG may mislead neuroscientists [10]. In addition, the transform cannot be applied to non-stationary signals. For this, the researcher has to assume that the signal is stationary and look at a small window length from the original signal, which, in many cases like speech signals, is erroneous. Also, choosing the window length of the FFT is an issue. As the window length of the signal chosen decreases, the frequency resolution decreases. On the other hand, with a decrease in window length, time resolution increases. So, the choice of the window length is a trade-off between time and frequency resolution. Both of them cannot be good as their product is bounded according to Heisenberg's uncertainty principle [10, 76]. In spite of these issues, FFT still remains the widely used algorithm

for finding spectral characteristics of a signal.

2.5.2 Wavelet analysis

Wavelet analysis is the representation of a signal in terms of wavelets. Wavelets are fast decaying oscillating waveforms which should integrate to zero over the interval $-\infty$ to ∞ . Wavelets have been around since Haar formulated the first Haar wavelet which was a basic step function taking the values 1 and -1 at $(0,1/2)$ and $(1/2,1)$ [77]. Jean Morlet used the term wavelets to describe them for the first time. He then came together with Alex Grossman to develop the continuous wavelet transform. Later Mallat and Meyer developed the multiresolution analysis for wavelets. This allowed researchers to develop their own families of wavelets. Then Ingrid Daubechies constructed the compactly supported continuous wavelets which were called Daubechies wavelets [78].

The mother wavelet, the basic wavelet, is a wavelet from whose translations other baby wavelets are formed. For example, in the scale one frequency band, the mother wavelet function is

$$\psi(t) = \frac{\sin(2\pi t) - \sin(\pi t)}{\pi t} \quad (2.7)$$

A few other examples of mother wavelet are shown below in Figures 2.21, 2.22 and 2.23

Figure 2.21: Meyer wavelet

Figure 2.22: Morlet wavelet

Figure 2.23: Mexican Hat wavelet

The wavelets are used in methods like Discrete Wavelet Transform (DWT), Continuous Wavelet Transform (CWT) and Fast Wavelet Transform (FWT). In fact the FWT is faster than FFT because in FWT only N computations need to be performed as compared to the $N \log_2 N$ computations in FFT. Fourier analysis is localized in frequency and small frequency changes in Fourier Transforms will produce changes everywhere in the time domain. Whereas wavelet transform is localized in both frequency and time. Also, fewer basic wavelet functions are required to represent functions with discontinuities as compared to sine or cosine functions [79].

If orthogonal wavelets are applied to the EEG signals, then the evoked potentials can be determined. But further application revealed that the representation of the signal was not time shift invariant. This problem is solved in CWT but, then the compactness of the orthogonal wavelet representation is lost [80].

2.5.3 Fractal analysis

In simple Euclidian geometry, complexity of natural forms has been filtered out to give them simple shapes. But natural forms such as leaves, coastlines etc. are essentially very complex and of irregular shape. Fractals can describe this complexity of nature. A fractal is a rough or fragmented geometric shape that can be subdivided in parts, each of which is (at least approximately) a reduced/size copy of the whole [81]. The term fractal was coined by Mandelbrot in 1975.

A simple fractal has the following features [82]:

1. fine structure at small scales,
2. cannot be described by Euclidian geometry,
3. is self similar or has self affinity,
4. has a Hausdorff dimension greater than its topological dimension and
5. has a simple and recursive definition.

Fractals are not new to human civilization. They have been around for eons. Ancient craft work and paintings reveal fractal shapes in them. But the idea of self similarity was developed by Leibniz. Later, Karl Weierstrass found an equation with this non-intuitive property. In 1904, Koch, dissatisfied with Weierstrass' abstract equation, gave a more geometric definition which is called the Koch snowflake. But it was not until Mandelbrot published his book that fractals became well known. Figure 2.24 shows the Koch snowflake in various iterations.

Figure 2.24: The first four iterations of the Koch snowflake

Real life objects are not self-similar but rather self-affine i.e. they may be written as a union of rescaled copies of themselves, where the rescaling may be anisotropic or dependent on the direction. They can also be called as multi-fractals as opposed to simple fractals. These are the fractals used in fractal analysis of a signal.

In fractal analysis, the fractal spectrum of the signal is found out by finding the fractal dimensions for a known probability distribution. As mentioned above, the fractals used in the analysis are multi-fractals. If the probability distribution, p_i , is known, then the generalized fractal dimensions of a signal, D_q , are

$$D_q = \lim_{\delta V \rightarrow 0} \frac{1}{q-1} \frac{\log \sum_{i=1}^N p_i^q}{\log \delta V} \quad (2.8)$$

where, δV is the size of self similar structure and q ranges from $-\infty$ to $+\infty$.

Plotting D_q will give the fractal spectrum of the signal [10, 83].

Using fractal analysis on signals like EEG will give better temporal resolution than FFT. Also the fact that the signal is non-linear makes it even more sensible to use a non-linear analysis method as opposed to a linear method like FFT. But fractal analysis of EEG has been found to be affected by Gaussian noise greater than $0.5 \mu\text{V}$ and line noise greater than $2 \mu\text{V}$. This can however be remedied by using an adaptive notch filter such as the one described in [84–86].

Three methods have been discussed so far. Other than these, there is another method called the Empirical Mode Decomposition. It is a relatively new method which is still under development. A comparison of the methods is given below in Table 2.2 for easy reference

	Fourier Transform	Wavelet Transform	Empirical Mode Decomposition	Fractal Transform
Basis	Non - adaptive	Non - adaptive	Adaptive	Adaptive
Non-stationary	No	Yes	Yes	Yes
Non-Linear	No	No	Yes	Yes
Expertise required to work	Low	Medium	High	Low
Adaptation required	NA	NA	Needs to be individually adapted	Universally adapted

Table 2.2: Comparison of different EEG analysis methods

2.6 Measurement of senses and emotions

Measurement of senses is a very abstract concept. But there has been a lot of work done in this area which is now developed into a subject called psychophysics. A few of the laws proposed have been discussed next.

2.6.1 Weber-Fechner's law

Weber's work is one of the earliest researches into the measurement of senses. He proposed a law which was later theoretically discussed by Fechner and the law is now called the Weber-Fechner's law. This law states that the magnitude of psychological sense is proportional to the logarithm of the magnitude of physical stimulus [87]. It can be mathematically expressed as

$$S = k \log \frac{I_s}{I_0} \quad (2.9)$$

where, S is the magnitude of sensation, k is a constant called the Weber constant, I_s is the magnitude of stimulus and I_0 is the magnitude of threshold stimulus.

This law assumes that the just noticeable differences (smallest difference in a specified modality of sensory input that is detectable by a human being or other animal) are additive [88].

The Weber-Fechner law has come under a lot of criticism. Critics say that the development of the law doesn't describe intensity perception. There is a series of data which shows that the basic ratio of threshold difference to intensity is not constant but keeps varying. It was also found out that in case of loudness, the judged loudness did not grow as a logarithmic function as described by Weber-Fechner's law [89, 90].

2.6.2 Steven's power law

Stevens argued that Weber-Fechner's law will only work for prothetic sensations in which change in input takes place in the form of increase in intensity. It will not hold for meta-thetic sensations in which change in input takes place qualitatively rather than quantitatively. So he proposed his own psychophysical law which was later called Stevens' law. It states that the magnitude of a subjective sensation increases proportional to a power of

the stimulus intensity [91]. It can be expressed as

$$S = kI_s^\alpha \quad (2.10)$$

where, S is the sensation magnitude, k is proportionality constant, I_s is the stimulus intensity and α is the power exponent dependant on the nature of stimulus. Various values of α were reported by Stevens [90, 91].

Stevens used two methods to measure the sensation magnitude - magnitude estimation and magnitude production. In magnitude estimation, a standard stimulus is first fixed by the researcher and all subsequent stimuli are graded by the subject based on this standard. In magnitude production, a number and a standard stimulus are given and subjects produce a stimulus which is that number times the standard stimulus. Also sometimes he used cross-modality matching which involved the subject altering the magnitude of one physical quantity so that its perceived intensity is equal to the intensity of the stimulus given to him/her [91].

Stevens took data from several subjects, averaged them and then fitted them to a curve to develop his law. This basically ignores the fact that when individual respondents are considered, the law may not hold true which was proven later. Also, Stevens asserted that using the methods of measurement, subjects could make judgments on a ratio scale. This was used by Narens to suggest an axiomatic property which was summarily rejected by other peers. He also formulated a property without using the assertion which was proved to be right thereby suggesting that the assertion by Stevens is faulty [92–94].

2.7 Models of the human brain/cortical activity

Numerous models of cortical activity have been developed by researchers all over the world. On a microscopic level, the work done by Freeman in modeling the EEG arising from olfactory bulb of animals during the perception of odors is noteworthy. He developed a set of non-linear equations for this response [13, 95]. The basic module, the KO subset, is divided into two parts. The linear time-dependent part of the KO subset is written as

$$abF(v_m) = \ddot{v}_m + (a + b)\dot{v}_m + av_m \quad (2.11)$$

where $a=220/\text{s}$ and $b=720/\text{s}$ are fixed rate constants.

The non-linear time-invariant part of the KO subset is written as

$$\begin{aligned} Q &= Q_m \{1 - \exp[-(c^v - 1)/Q_m]\}, v > -u_0, \\ Q &= -1, v \leq -u_0, \\ u_0 &= -\ln[1 - Q_m \ln(1 + 1/Q_m)] \end{aligned} \quad (2.12)$$

where, $Q_m=5.0$ is the asymptotic maximum of the sigmoid curve.

A KI_e subset is formed with two KO_e subsets in feedback relation. A KI_i subset is formed with two KO_i sets in feedback and with inversion of the output voltage of each before input to the other. A KII subset is formed by feedback between a KI_e subset and a KI_i subset. Feedback between three KII sets gives the $KIII$ subset. Different small initiating pulses given to these subsets generate EEG like patterns [95].

When the microscopic models are extended to a macro level, then different methods are employed. Many of these models assume the cortical region to be a continuum. The first continuum model was proposed by Lopes da Silva et al. and Van Rotterdam et al. [14, 15]. In the model proposed by Lopes da Silva et al., two interacting populations of

cells were considered namely, the pyramidal cells and the local interneurons. These were characterized by two transfer systems - $h_e(t)$ representing the excitatory post synaptic potentials (EPSPs) and $h_i(t)$ for inhibitory post synaptic potentials (IPSPs). Two static non-linearities, $f_e(V)$ and $f_i(V)$ related the dendritic membrane potentials to their input pulse density. C_1 and C_2 were the interconnectivity constants representing the total number of postsynaptic connections between each pyramidal cell and the local interneuron, and vice-versa. The potential of the pyramidal cell dendrites, $V_e(t)$, was the signal to which the recorded EEG was assumed to be proportional. The nonlinearities $f_e(V)$ and $f_i(V)$ were converted to linearities. Then, $h_e(t)$ and $h_i(t)$ can be associated in the frequency domain with

$$H_e(j\omega) = \frac{Aa}{(j\omega + a)^2} \quad (2.13)$$

$$H_i(j\omega) = \frac{Bb}{(j\omega + b)^2} \quad (2.14)$$

where, $A = 3.25$ mV, $B = 22$ mV, $a = 100$ ms⁻¹ and $b = 50$ ms⁻¹.

This gives

$$V_e(j\omega) = \frac{Aa(j\omega + b)^2}{(j\omega + a)^2(j\omega + b)^2 + K^-} P(j\omega) \quad (2.15)$$

where, $P(j\omega)$ is a spectral component of $p(t)$ and $K^- = C_1 C_2 AaBbq_{e1}q_{i1}$.

Van Rotterdam et al. extended this model by assuming an infinite one-dimensional chain of interconnected pyramidal cells and interneurons. These interconnections were described by $C_e(k,l)$ denoting the number of excitatory synapses from the k^{th} pyramidal cell projecting on the l^{th} interneuron and $C_i(k,l)$ denoting the number of inhibitory synapses from the k^{th} interneuron to the l^{th} pyramidal cell. They then obtained a transfer function

for the temporal frequency ω and spatial frequency λ as

$$U(j\lambda, j\omega) = \frac{H_e(j\omega)P(j\lambda, j\omega)}{1 + q_{e1}q_{i1}H_e(j\omega)H_i(j\omega)C_i(j\lambda)C_e(j\lambda)} \quad (2.16)$$

These equations took into account the effect of inhibitory and excitatory populations of neurons. Inhibitory neurons are those that reduce the firing rate of other neurons and excitatory ones increase the same. With suitable adjustments, the model recreated the alpha rhythm. But the major issue with this model was that it did not include the nonlinear effects, axonal delays (delays due to finite propagation velocity of signals in the axons of neurons) and convolutions of the cortex.

After this, Nunez introduced the effect of axonal delays and proposed a model [16]. This model allowed wave solutions and also identified the alpha rhythm as being at the fundamental cortical eigenfrequency. Nunez also solved this model for a 1D loop cortex and for a two-dimensional cortex with boundary conditions.

Nunez's model had the following equations:

$$h_E(r, t) = u_E(r, t) + \int_0^\infty dv \int_S R_E(r, r_1, v) g\left(r_1, t - \frac{|r - r_1|}{v}\right) d^2r_1 \quad (2.17)$$

$$h_I(r, t) = u_I(r, t) + \int_S R_I(r, r_1, v) g(r_1, t) d^2r_1 \quad (2.18)$$

But this model neglected the inhomogeneity of the cortical connections and also the effect of the convolutions of the cortex as in Lopes da Silva's model.

Wright and Liley [17, 18] introduced a spatially discretized model. In this, the cortex was treated in 2D and was divided into patches. They used Green's functions to describe the interconnectivity of the patches. This model took into account nonlinear effects with axonal delays and dendritic delays but did not involve the convolutions and non-uniformity of the cortical connections. But this model could only be used for small systems or for

a coarser look at the larger systems as the Green's functions are very time consuming to evaluate.

Robinson et al. [96] took these equations and introduced a continuum wave model to replace the linear discrete parts of the equations. So, the Wright and Liley equations became

$$Q_{ae}(r, t) = M_e Q_z(r, t) + \mu_e Q_{ns} - a_{ei} Q_i(r, t) + a_{ee} \int d^2 r' \int dt' G(r, t; r', t') Q_e(r', t') \quad (2.19)$$

$$Q_{ai}(r, t) = M_i Q_z(r, t) + \mu_i Q_{ns} - a_{ii} Q_i(r, t) + a_{ie} \int d^2 r' \int dt' G(r, t; r', t') Q_e(r', t') \quad (2.20)$$

$$G(r, t; r', t') = G(|r - r'|) \delta(t - t' - |r - r'|/v) \quad (2.21)$$

Robinson et al. [96] then developed their own model based on the same fundamentals as Wright and Liley. These equations were

$$Q_{ae}(r, t) = M_e Q_s(r, t) + \mu_e Q_{ns} + a_{ee} \phi_e(r, t) - a_{ei} \phi_i(r, t) \quad (2.22)$$

$$Q_{ai}(r, t) = M_i Q_s(r, t) + \mu_i Q_{ns} + a_{ie} \phi_e(r, t) - a_{ii} \phi_i(r, t) \quad (2.23)$$

where Q_{ae} and Q_{ai} are incoming excitatory and inhibitory potentials respectively, $\phi_{e,i}$ are wave potentials, Q_s is a specific excitation due to stimuli and M_e and M_i are constants.

Robinson et al. also simplified the computation of dendritic lags. But this model did not consider the filtering effects of the skull on the EEG, which they claimed could be solved by using MEG with EEG.

Liley et al. [97] developed a set of non-linear continuum field equations which described the macroscopic dynamics of neural activity in the cortical region; namely,

$$\tau \frac{\partial h(x, t + \bar{\xi})}{\partial t} = h^r - h(x, t + \bar{\xi}) + \Psi_e(h)I_e(x, t) + \Psi_i I_i(x, t) \quad (2.24)$$

$$\left(\frac{\partial}{\partial t} + \gamma_e \right)^2 I_e(x, t) = \Gamma_e \gamma_e e \{ N_e^\beta S_e(h_e) + \phi(x, t) + p_e(x, t) \} \quad (2.25)$$

$$\left(\frac{\partial}{\partial t} + \gamma_i \right)^2 I_i(x, t) = \Gamma_i \gamma_i e \{ N_i^\beta S_i(h_i) + p_i(x, t) \} \quad (2.26)$$

$$\left(I \frac{\partial}{\partial t} + \bar{v} \Lambda \right)^2 \phi(x, t) - \bar{v}^2 \frac{\partial^2 \phi(x, t)}{\partial x^2} = \bar{v} \Lambda N^\alpha \left(\bar{v} \Lambda + I \frac{\partial}{\partial t} \right) S_e(h_e) \quad (2.27)$$

These equations were used by Steyn-Ross et al. [19, 98–100] who introduced noise terms into them to give a set of stochastic partial differential equations (SPDEs). They also converted the above Equations (2.24) - (2.27) into linearized ODEs. The equations in Steyn-Ross et al.'s model were

$$\begin{bmatrix} \tau_e & 0 \\ 0 & \tau_i \end{bmatrix} \frac{d}{dt} \begin{bmatrix} h_e \\ h_i \end{bmatrix} = \begin{bmatrix} h_e^{rest} - h_e \\ h_i^{rest} - h_i \end{bmatrix} + \begin{bmatrix} \Psi_{ee} I_{ee} + \Psi_{ie} I_{ie} \\ \Psi_{ei} I_{ei} + \Psi_{ii} I_{ii} \end{bmatrix} \quad (2.28)$$

$$\begin{bmatrix} \left(\frac{d}{dt} + \bar{v} \Lambda_{ee} \right)^2 \phi_e \\ \left(\frac{d}{dt} + \bar{v} \Lambda_{ei} \right)^2 \phi_i \end{bmatrix} = \bar{v} \begin{bmatrix} \left(\frac{d}{dt} + \bar{v} \Lambda_{ee} \right)^2 \Lambda_{ee} N_{ee}^\alpha \\ \left(\frac{d}{dt} + \bar{v} \Lambda_{ei} \right)^2 \Lambda_{ei} N_{ei}^\alpha \end{bmatrix} S_e(h_e) \quad (2.29)$$

$$\left(\frac{d}{dt} + \gamma_e \right)^2 \begin{bmatrix} I_{ee} \\ I_{ei} \end{bmatrix} = \left\{ \begin{bmatrix} N_{ee}^\beta \\ N_{ei}^\beta \end{bmatrix} S_e(h_e) + \begin{bmatrix} \phi_e \\ \phi_i \end{bmatrix} + \begin{bmatrix} \langle p_{ee} \rangle \\ \langle p_{ei} \rangle \end{bmatrix} \right\} G_e \gamma_e e + \begin{bmatrix} \Gamma_1(t) \\ \Gamma_2(t) \end{bmatrix} \quad (2.30)$$

$$\left(\frac{d}{dt} + \gamma_i \right)^2 \begin{bmatrix} I_{ie} \\ I_{ii} \end{bmatrix} = \left\{ \begin{bmatrix} N_{ie}^\beta \\ N_{ii}^\beta \end{bmatrix} S_i(h_i) + \begin{bmatrix} \langle p_{ie} \rangle \\ \langle p_{ii} \rangle \end{bmatrix} \right\} G_i \gamma_i e + \begin{bmatrix} \Gamma_3(t) \\ \Gamma_4(t) \end{bmatrix} \quad (2.31)$$

This model could predict the substantial increase in low frequency power at the critical points of induction and emergence. They later used this model to study the electrical

activity of an anaesthetized cortex.

Kramer et al. [101] started with the equations given by Steyn-Ross and co-workers and neglected the spatial variation and the stochastic input. This gave rise to a set of ordinary differential equations (ODEs) for modeling the cortical activity. They then showed that the results obtained from the SPDE model agree with clinical data in an approximate way. But they also stated that the spatial sampling of the cortex was poor because of inherent shortcomings in the equipment used. There is also ambiguity in the lead/lag relationships determined by the Windowed Cross Correlation that they used. But the paper did suggest that the seizing activity of the cortex may be understood as an example of pathological pattern formation.

Kulish and Chan [20] have suggested a novel method for modeling the brain response by the use of fundamental laws of nature such as energy conservation and the least action principle. Their equation is

$$\frac{\partial^\kappa u}{\partial t^\kappa} = D \frac{\partial^2 u}{\partial \eta^2} - S(\omega) \quad (2.32)$$

where $u = u(\eta, t)$ is the energy density, t is the temporal variable, κ is the term accounting for the variations in the cortex diffusivity, D is the diffusion co-efficient, η is the informational distance and $S(\omega)$ is the source/sink term.

The model equation obtained has been solved and the results show a good agreement with real EEGs. They also introduced the concept of distance in the informational space. Fractal spectra of EEGs and the solution of the equation show similarities [20].

2.8 Information theory and Dynamics of information transfer

Information is a term that shall be used quite often in the remainder of the thesis. Information can be defined as a measurement of system organization, opposite to uncertainty and entropy. It can also be termed as a sensory input. The basic unit of information is called bit. It is the amount of information that can be expressed or coded by one 0 or 1 only. The quantitative measurement of information ignores the quality of the information. The two messages - “Hello, how are you?” and “Quick, call an ambulance” - will take the same time to write or say and may have the same quantitative measure though the latter is more important.

An important measure of information is called informational entropy. It was described by Shannon in his paper “A Mathematical Theory of Communication” [102]. He defined entropy as a measure of the average information content associated with a random outcome. A measure of the information entropy satisfies the following criteria:

1. The measure should be continuous i.e. changing the value of one of the probabilities of the events by a small amount should alter the entropy by a small amount too.
2. If the outcomes of an event are equally likely, then the entropy should be a monotonic increasing function of the number of events. It will be maximal when the number of events, n , is definite and known.
3. If the outcome is certain i.e. probability is 1, then the entropy is zero.

Shannon’s formula gives entropy for a discrete random variable X , with possible outcomes $x_1, x_2, \dots, x_N$, as

$$S_e = - \sum_{i=1}^N p_i \log_2 p_i \quad (2.33)$$

where, S_e is the entropy and p_i is the probability of the i^{th} outcome of X.

At this point, the notion of redundancy comes into existence. This can be defined as one minus the relative entropy. Relative entropy is the ratio of the entropy of source to the maximum value it could have while restricted to the same symbols. If q_s is the number of symbols and S_e is the entropy, then relative entropy is given by $\frac{S_e}{\log q_s}$ and redundancy by

$$Re = 1 - \frac{S_e}{\log q_s} \quad (2.34)$$

Shannon found that the redundancy of the English language is 0.5. This means that half of the English written by a person is determined by the structure of the language while the other half is taken freely. But, redundancy is important for languages as this makes the language and subsequent information transfer via the medium of that language strongly resistant to noise. This enables information transfer even when noise is present in the information channel (the path of information transfer) [102].

Information transfer takes place in every living system. Information is transmitted in every living system, like the human body; the sensory systems collect information from the outside world to be transmitted via the nervous system to the brain. The brain, after some information processing (decoding and analyzing), sends commands, which are information too, to the muscles via neurons again. Although information itself is not matter, it can exist only as connected to matter. Only matter and its movement (energy) can carry information. A text of letters can be preserved only if it is carved into stone, written or printed on paper, or stored on a computer drive. A voice comes forth in the form of the movements of air molecules or on records, tapes, CDs, etc. The transmission of information between two points can happen via cable, with the help of electric current or electromagnetic waves. It is clear that our thoughts and memories can happen only in connection with matter, brain matter, that is, the chemical and electrical events of the

brain. So it follows that the speed of transmission of information cannot be arbitrarily great and it certainly cannot exceed the speed of light.

2.8.1 Concept of informational distance

In equation (2.32), η is the spatial variable in informational space. This is a new concept which involves distances in the informational space. This distance is based upon the informational interlinking of the two points in the space. These two points establish an informational channel between them and the length of this channel is called the informational distance. In the brain, the two points can be understood as two neurons.

The informational space is a metric space. So, the informational distance possesses the following properties (for every x, y, z being points in informational space) [103]:

1. $\eta(x, y) = 0$, if $x = y$ {identity axiom}
2. $\eta(x, y) + \eta(y, z) \geq \eta(x, z)$ {triangle inequality}
3. $\eta(x, y) = \eta(y, x)$ {symmetry axiom}

It also follows that $\eta(x, y) \geq 0$.

This informational distance should not be confused with the concept of spatial distance. Two neurons close together may not exchange information at all which means that $\eta \sim \infty$ in such a case. On the other hand, two neurons far apart in the brain may be closely interlinked to each other, exchanging information a lot which makes η very small. $\eta = 0$ means that it is a single location. So $0 \leq \eta < \infty$ is the range of values of η .

An information exchange will take place between two neurons in an informational channel when there is a potential difference along the channel. That is to say that the two neurons have different informational potential. This will cause a flux and the information exchange will continue till the gradient becomes zero. The information transfer will take

place from the neuron with higher informational potential value to the one with the lower value. Also, a large value of η (explicitly as $\eta \rightarrow \infty$) does not imply that the neuron is isolated. This neuron may still experience stimuli from the boundary.

Chapter 3

Phase-Lagging Model of Action Potential

3.1 Introduction

Several models for brain activity have been proposed in the literature [13–20, 95–100]. The methodology adopted by Kulish and Chan, namely to use basic laws to derive a model, has been seen as most promising and shall be adopted here.

This chapter details the derivation of a model from fundamental laws like Conservation Law, Ohm's Law and Kirchhoff's Laws. The paradox of instantaneous propagation of impulse is taken care of by introducing a finite propagation speed. The model is then solved to give the relation between the voltage and its spatial derivative at any moment in time and at any location in the domain of interest. This is then implemented for the specific case of the action potential. The plot of the solution is similar to the action potential observed in real life.

The chapter is organised as follows: Section 3.2 examines the Hodgkin-Huxley model of action potential briefly. Section 3.3 shows the derivation of the diffusion model as

described in Plonsey and Barr. The formulation of a phase-lagging model to overcome the paradox of instantaneous propagation in the neuron is given in Section 3.4. Application of the solution for the case of a single action potential is detailed in Section 3.5. A brief conclusion about the chapter is given in Section 3.6.

3.2 Hodgkin-Huxley model of action potential

The Hodgkin-Huxley model is the most well known model of action potential [104]. In this model, they view the neuron as an electrical circuit with a capacitor and three parallel series of batteries and variable resistors. One series represents the sodium flux, the second represents the potassium flux and the last one represents leakage current. The batteries represent the Nernst potential of each ion. The current, I , is a function of voltage and time - $I(V, t)$. Voltage, V is a function of time - $V(t)$. The current through this circuit was modelled as

$$I = C_M \frac{dV}{dt} + \bar{g}_K n^4 (V - V_K) + \bar{g}_{Na} m^3 h (V - V_{Na}) + \bar{g}_l (V - V_l) \quad (3.1)$$

where I is the current crossing the membrane, C_M is the capacitance of the membrane, V is the voltage, $\bar{g}_K$ and $\bar{g}_{Na}$ are the conductances of Potassium and Sodium respectively, n^4 and $m^3 h$ are the constants used to fit the curve for conductance changes as observed in voltage clamp experiments and V_K , V_{Na} and V_l are voltages due to Potassium flux, Sodium flux and leakage flux respectively. This equation can plot the action potential as observed in the neuron.

But, when it comes to propagated action potential, the equation changes to

$$\frac{a}{2R_2\theta^2} \frac{d^2 V_m}{dt^2} = C_M \frac{dV}{dt} + \bar{g}_K n^4 (V - V_K) + \bar{g}_{Na} m^3 h (V - V_{Na}) + \bar{g}_l (V - V_l) \quad (3.2)$$

where a is the radius of the nerve fibre, R_2 is the specific resistance of the axoplasm and θ is the velocity of conduction.

The constants used in equation (3.1) are arbitrary constants taken in order to make the plot generated by the equation fit the action potential plot. As stated by Hodgkin and Huxley themselves, any other set of equations with a different set of constants could also generate the same plot. Also, the equation (3.2) is a non-linear equation which does not have an exact solution.

The model to be proposed later in this chapter will be a linear equation which will be developed from basic laws. The plot from this model approximates the plot of an action potential to a good extent.

3.3 Derivation of the diffusion model for voltage change

The basic model shall be derived from simple laws like Conservation law and Ohm's law. The derivation of this model shall follow the derivations as outlined by Plonsey and Barr [105]. Let us consider the neuron as a cylindrical conductor. It is assumed that the conductor is axially symmetrical and that the current conducted by that neuron is also axial in nature. This means that the potentials and the currents in the neuron are functions of the axial coordinate, x . x is semi-infinite which is applicable as the length of the neuron cannot be infinity.

By Ohm's Law, the decrease in potential in the neuron per unit length must be equal to the IR drops along the neuron and are given by

$$\frac{\partial \phi_{ext}}{\partial x} = -I_{ext}r_{ext} \quad (3.3)$$

$$\frac{\partial \phi_{int}}{\partial x} = -I_{int}r_{int} \quad (3.4)$$

where, $\phi_{ext} = \phi_{ext}(x, t)$ is the extracellular potential, $\phi_{int} = \phi_{int}(x, t)$ is the intracellular potential, I_{ext} is the extracellular current, I_{int} is the intracellular current, r_{ext} is the extracellular resistance and r_{int} is the intracellular resistance.

By Kirchhoff's current law, we have

$$\frac{\partial I_{int}}{\partial x} = -i_m \quad (3.5)$$

where, i_m is the transmembrane current per unit length. This is in line with the conservation of current law which requires that the axial rate of decrease in the intercellular current must be equal to transmembrane current per unit length. This is because any loss in the intercellular current has to be due to the current crossing the membrane.

For extracellular current, any decrease in its value is due to current crossing the membrane along with the current that is carried out due to the electrodes inserted. So,

$$\frac{\partial I_{ext}}{\partial x} = i_m + i_p \quad (3.6)$$

where, i_p is the current that is carried outside because of the polarizing electrodes inserted in the membrane. Let I be defined as

$$I = I_{int} + I_{ext} \quad (3.7)$$

The membrane potential V_m is given by

$$V_m = \phi_{int} - \phi_{ext} \quad (3.8)$$

Differentiating the above equation (3.8) with respect to x and including equations (3.3)

and (3.4), we have

$$\begin{aligned}\frac{\partial V_m}{\partial x} &= \frac{\partial \phi_{int}}{\partial x} - \frac{\partial \phi_{ext}}{\partial x} \\ \frac{\partial V_m}{\partial x} &= -r_{int}I_{int} + r_{ext}I_{ext} \\ \frac{\partial V_m}{\partial x} &= -r_{int}I_{int} + r_{ext}(I - I_{int})\end{aligned}\tag{3.9}$$

From equations (3.5) and (3.6), we have

$$\frac{\partial I}{\partial x} = i_p\tag{3.10}$$

We also have

$$\frac{\partial V_m}{\partial x} = -(r_{int} + r_{ext})I_{int} + Ir_{ext}\tag{3.11}$$

Differentiating equation (3.11) with respect to x yields

$$\frac{\partial^2 V_m}{\partial x^2} = -(r_{int} + r_{ext})\frac{\partial I_{int}}{\partial x} + r_{ext}\frac{\partial I}{\partial x}\tag{3.12}$$

Substituting equations (3.5) and (3.10) gives

$$\frac{\partial^2 V_m}{\partial x^2} = (r_{int} + r_{ext})i_m + r_{ext}i_p\tag{3.13}$$

For an action potential on a single fiber, we must have no external polarizing current i.e. $i_p = 0$. Also, from equations (3.7) and (3.10), $I_{int} = -I_{ext}$. Under such constraints, equation (3.13) becomes

$$\frac{\partial^2 V_m}{\partial x^2} = (r_{int} + r_{ext})i_m\tag{3.14}$$

Also, the nerve is present in an extensive extracellular medium. This makes the extracellular resistance $r_{ext} = 0$. This approximation is also permitted by the Hodgkin-Huxley experimental chamber during their studies on the squid axon. The intracellular resistance per unit length r_{int} can be rewritten in terms of the intracellular resistivity, R_{int} as $r_{int} = \frac{R_{int}}{\pi a_c^2} \Omega/cm$ where a_c is the radius of the cylindrical nerve. So, i_m becomes

$$i_m = \frac{\pi a_c^2}{R_{int}} \frac{\partial^2 V_m}{\partial x^2} \quad (3.15)$$

The transmembrane current per unit area, I_m , can also be written as

$$I_m = \frac{i_m}{2\pi a_c} \quad (3.16)$$

From Equations (3.15) and (3.16), we obtain

$$I_m = \frac{a_c}{2R_{int}} \frac{\partial^2 V_m}{\partial x^2} \quad (3.17)$$

Equation (3.17) can be equated to the transmembrane current density from the Hodgkin-Huxley relations to give

$$\frac{a_c}{2R_{int}} \frac{\partial^2 V_m}{\partial x^2} = C_m \frac{\partial V_m}{\partial t} + \Sigma I_{ion} \quad (3.18)$$

where C_m is the membrane capacitance and ΣI_{ion} is the sum total of the ionic currents. The equation rearranged gives,

$$\frac{\partial^2 V_m}{\partial x^2} = \frac{2C_m R_{int}}{a_c} \frac{\partial V_m}{\partial t} + \frac{2R_{int}}{a_c} \Sigma I_{ion} \quad (3.19)$$

where $t \geq 0$ and $x \geq 0$.

If the equation is observed, it is noticed that this diffusion equation shall give rise to the

paradox of instantaneous propagation of action potential. This means that the equation suggests that the response to the stimulus signal is generated almost instantaneously. This is physically not possible as that would require an infinite speed of propagation. This paradox of instantaneous propagation exists for all such diffusion equations which becomes evident as the characteristic time gets shorter [106, 107].

In order to avoid such a paradox, the space time behaviour of the action potential should satisfy the wave equation i.e.

$$V_m(x, t) = V_m(x - ct) \quad (3.20)$$

where c is the velocity of propagation. Differentiating equation (3.20) twice and using the chain rule, we get

$$\frac{\partial^2 V_m}{\partial x^2} = \frac{\partial^2 V_m}{\partial t^2} \frac{1}{c^2} \quad (3.21)$$

Adding equations (3.19) and (3.21), we get

$$2\frac{\partial^2 V_m}{\partial x^2} = \frac{1}{c^2} \frac{\partial^2 V_m}{\partial t^2} + \frac{2C_m R_{int}}{a_c} \frac{\partial V_m}{\partial t} + \frac{2R_{int}}{a_c} \Sigma I_{ion} \quad (3.22)$$

3.4 Phase-lagging model of voltage change in the neuron: Overcoming the paradox of instantaneous propagation

The paradox of instantaneous propagation can be rectified by introducing a constant propagation velocity (required for uniform propagation of the action potential) and also by the presence of a time lag term which takes care of the lag between the occurrence of the stimulus and the rise of the subsequent action potential. The model to be written

shall do these two things. It shall also satisfy both the diffusion of voltage equation and the wave equation.

Considering the voltage in the neuron, we have

$$\frac{1}{c^2} \frac{\partial^2 V}{\partial t^2} + \frac{1}{D} \frac{\partial V}{\partial t} = \frac{\partial^2 V}{\partial x^2} + S(x, t) \quad (3.23)$$

The term V is the voltage in the neuron. The speed of propagation, c , is a finite quantity and is the speed with which the impulse travels through the neuron. The diffusivity term, D , is related to the resistance of the neuron to the electrical impulse. It is the property of the neural tissue and will dampen the impulse as it travels over the nerve. The source/sink term, $S(x, t)$ arises from the constant interactions between the neurons even in the absence of an external potential. It also accounts for the fact that the voltage is not conserved.

We shall now attempt to solve the equation (3.23) by using the method detailed by Kulish and Novozhilov [108] and Kulish et al. [109].

Rewriting the equation (3.23), we have

$$\begin{aligned} \frac{D}{c^2} \frac{\partial^2 V}{\partial t^2} + \frac{\partial V}{\partial t} &= D \frac{\partial^2 V}{\partial x^2} + S(x, t) \\ \tau \frac{\partial^2 V}{\partial t^2} + \frac{\partial V}{\partial t} &= D \frac{\partial^2 V}{\partial x^2} + S(x, t) \end{aligned} \quad (3.24)$$

where, $\tau = \frac{D}{c^2}$. The term τ is the time lag that avoids the paradox of instantaneous propagation.

Equation (3.24) is now solved in a semi-infinite domain. This is quite valid as the neuron cannot be infinite in length and is therefore a semi-infinite domain. The initial condition can be defined as $V = V_0$ at time $t=0$ which is the resting potential of a neuron and $\frac{\partial V}{\partial t} = 0$.

Three new variables shall now be introduced in equation (3.24); namely $\xi = \frac{x}{D^{\frac{1}{2}}}$, $\vartheta = \frac{t}{\tau^{\frac{1}{2}}}$ and $\Lambda = V - V_0$. The term ξ is the new distance like variable, ϑ is the new timelike variable and Λ is the excess potential. Now the equation (3.24) becomes

$$\frac{\partial^2 \Lambda}{\partial \vartheta^2} + \tau^{-\frac{1}{2}} \frac{\partial \Lambda}{\partial \vartheta} = \frac{\partial^2 \Lambda}{\partial \xi^2} + S(\xi, \vartheta) \quad (3.25)$$

The initial conditions in this case are $\Lambda = 0$ at $\vartheta = 0$ and $\frac{\partial \Lambda}{\partial \vartheta} = 0$.

Taking the Laplace Transform of equation (3.25) and rearranging the terms, we get

$$\frac{d^2 \tilde{\Lambda}}{d\xi^2} - s(s + \tau^{-\frac{1}{2}}) \tilde{\Lambda} + \tilde{S}(\xi, s) = 0 \quad (3.26)$$

where $\tilde{\Lambda}(\xi, s)$ is the Laplace transform of the excess voltage and $\tilde{S}(\xi, s)$ is the Laplace transform of the source/sink term.

The general solution of Equation (3.26) is

$$\tilde{\Lambda}(\xi, s) = C_1(s) \exp\{-\xi[s(s + \tau^{-\frac{1}{2}})]^{\frac{1}{2}}\} + C_2(s) \exp\{\xi[s(s + \tau^{-\frac{1}{2}})]^{\frac{1}{2}}\} + P(\xi, s) \quad (3.27)$$

The first two terms on the right hand side of the equation (3.27) are the general solution of the associated homogenous equation, when $\tilde{S}(\xi, s) = 0$, and $P(\xi, s)$ is the particular solution.

Since we are considering a semi-infinite domain, the solution has to be bounded as $\xi \rightarrow \infty$ so as to not violate the energy conservation principle. This requires that $C_2(s) \rightarrow 0$. Denoting $C_1(s) \equiv C(s)$, we get

$$\tilde{\Lambda}(\xi, s) = C(s) \exp\{-\xi[s(s + \tau^{-\frac{1}{2}})]^{\frac{1}{2}}\} + P(\xi, s) \quad (3.28)$$

Rearranging equation (3.28), $C(s)$ can be written as

$$C(s) = [\tilde{\Lambda}(\xi, s) - P(\xi, s)] \exp\{\xi[s(s + \tau^{-\frac{1}{2}})]^{\frac{1}{2}}\} \quad (3.29)$$

Equation (3.29) shall be differentiated with respect to ξ in order to eliminate $C(s)$ as shown by Kulish and Lage [110].

$$\begin{aligned} \frac{\partial \tilde{\Lambda}(\xi, s)}{\partial \xi} &= -[s(s + \tau^{-\frac{1}{2}})]^{\frac{1}{2}} C(s) \exp\{-\xi[s(s + \tau^{-\frac{1}{2}})]^{\frac{1}{2}}\} + \frac{\partial P(\xi, s)}{\partial \xi} \\ &= -[s(s + \tau^{-\frac{1}{2}})] \tilde{\Lambda}(\xi, s) + [s(s + \tau^{-\frac{1}{2}})] P(\xi, s) + \frac{\partial P(\xi, s)}{\partial \xi} \\ -\tilde{\Lambda}(\xi, s) &= [s(s + \tau^{-\frac{1}{2}})]^{-\frac{1}{2}} \frac{\partial \tilde{\Lambda}(\xi, s)}{\partial \xi} - [s(s + \tau^{-\frac{1}{2}})]^{-\frac{1}{2}} \frac{\partial P(\xi, s)}{\partial \xi} - P(\xi, s) \end{aligned} \quad (3.30)$$

From Abramowitz and Stegun (page 374-379, 1024)[111], it is found that the inverse Laplace Transform of $[s(s + \tau^{-\frac{1}{2}})]^{-\frac{1}{2}}$ is $\mathcal{I}_0\left(\frac{\vartheta}{2\tau^{\frac{1}{2}}}\right) \exp\left(-\frac{\vartheta}{2\tau^{\frac{1}{2}}}\right)$, where $\mathcal{I}_0(z)$ is the modified Bessel function of zeroth order.

Thus, taking the inverse Laplace Transform of equation (3.30) and applying the convolution theorem, we obtain

$$\begin{aligned} \Lambda(\xi, \vartheta) &= - \int_0^\vartheta \frac{\partial \Lambda(\xi, \varsigma)}{\partial \xi} \mathcal{I}_0\left(\frac{\vartheta - \varsigma}{2\sqrt{\tau}}\right) \exp\left(-\frac{\vartheta - \varsigma}{2\sqrt{\tau}}\right) d\varsigma \\ &\quad + \int_0^\vartheta \frac{\partial p(\xi, \varsigma)}{\partial \xi} \mathcal{I}_0\left(\frac{\vartheta - \varsigma}{2\sqrt{\tau}}\right) \exp\left(-\frac{\vartheta - \varsigma}{2\sqrt{\tau}}\right) d\varsigma + p(\xi, \vartheta) \end{aligned} \quad (3.31)$$

where $p(\xi, \vartheta)$ is the inverse Laplace transform of the function $P(\xi, s)$.

Restoring the original terms and rearranging the terms, equation (3.31) transforms into

$$V(x, t) = V_0 - \left(\frac{D}{\tau}\right)^{\frac{1}{2}} \int_0^t \frac{\partial V(x, t^*)}{\partial x} \mathcal{I}_0\left(\frac{t-t^*}{2\tau}\right) \exp\left(-\frac{t-t^*}{2\tau}\right) dt^* \\ + \left(\frac{D}{\tau}\right)^{\frac{1}{2}} \int_0^t \frac{\partial p(x, t^*)}{\partial x} \mathcal{I}_0\left(\frac{t-t^*}{2\tau}\right) \exp\left(-\frac{t-t^*}{2\tau}\right) dt^* + p(x, t) \quad (3.32)$$

This equation (3.32) gives the relation between the voltage and its spatial derivative at any moment in time and at any location in the domain of interest.

It is worth noting here that the traditional definition of voltage is the potential difference between two points. It may confuse one to see voltage being referred to here without a reference point. The voltage mentioned here in the text is actually the potential difference between the surface potential of the neuron membrane and the ground potential (taken as 0 V). Moreover, we are interested in the change in voltage and not the absolute voltage value. So, we can use V in the equation without having to keep including the ground reference voltage.

3.5 Validation of phase-lagging model - Modelling a single action potential

For an isolated neuron, we can get the model equation by taking $p(x, t) = 0$ in equation (3.32). This is because we are assuming that the neuron doesn't interact with other neurons i.e. its isolated. So, we have

$$V(x, t) = V_0 - \left(\frac{D}{\tau}\right)^{\frac{1}{2}} \int_0^t \frac{\partial V(x, t^*)}{\partial x} \mathcal{I}_0\left(\frac{t-t^*}{2\tau}\right) \exp\left(-\frac{t-t^*}{2\tau}\right) dt^* \quad (3.33)$$

The term $\frac{\partial V(x, t^*)}{\partial x}$ on the right hand side of equation (3.33) is a direct result of the external influence i.e. stimulus. It is related to the flux as $\frac{\partial V(x, t^*)}{\partial x} = -\frac{1}{g}\phi(x, t^*)$ where $\phi(x, t^*)$ is the flux and g is the conductance. This changes equation (3.33) to

$$V(x, t) = V_0 + \frac{1}{g} \left(\frac{D}{\tau} \right)^{\frac{1}{2}} \int_0^t \phi(x, t^*) \mathcal{I}_0 \left(\frac{t - t^*}{2\tau} \right) \exp \left(-\frac{t - t^*}{2\tau} \right) dt^* \quad (3.34)$$

Now, considering the effect of both sodium(Na) and potassium(K) as the driving ions for the action potential,

$$V(x, t) = V_0 + \frac{1}{g_{Na}} \left(\frac{D_{Na}}{\tau_{Na}} \right)^{\frac{1}{2}} \int_0^t \phi_{Na}(x, t^*) \mathcal{I}_0 \left(\frac{t_{Na} - t^*}{2\tau_{Na}} \right) \exp \left(-\frac{t_{Na} - t^*}{2\tau_{Na}} \right) dt^* \\ + \frac{1}{g_K} \left(\frac{D_K}{\tau_K} \right)^{\frac{1}{2}} \int_0^t \phi_K(x, t^*) \mathcal{I}_0 \left(\frac{t_K - t^*}{2\tau_K} \right) \exp \left(-\frac{t_K - t^*}{2\tau_K} \right) dt^* \quad (3.35)$$

The term $\frac{D}{\tau}$ is equal to c^2 where c is the velocity of propagation (21.2 m/s). The terms ϕ_{Na} and ϕ_K , the flux of sodium and potassium respectively, can be modeled as a Gaussian pulse. So, the term ϕ_{Na} can be taken as $\phi_{Na} = A_{Na}(x) \exp \left[-\frac{t - t_{max,Na}}{\delta_{Na}} \right]$ and the term ϕ_K can be taken as $\phi_K = A_K(x) \exp \left[-\frac{t - t_{max,K}}{\delta_K} \right]$, where $A_{Na}(x)$ is the maximum amplitude of the sodium flux, t is the total time, $A_K(x)$ is the maximum amplitude of the potassium flux, t is the total time, $t_{max,Na}$ is the time of maximum flux for sodium, $t_{max,K}$ is the time of maximum flux for potassium, δ_{Na} is the standard deviation of Sodium flux and similarly δ_K for potassium flux.

Substituting the above mentioned changes into equation (3.35), it becomes

$$V(x, t) = V_0 + \frac{c}{g_{Na}} \int_0^t A_{Na}(x) \exp \left[-\frac{t - t_{max,Na}}{\delta_{Na}} \right] \mathcal{I}_0 \left(\frac{t_{Na} - t^*}{2\tau_{Na}} \right) \exp \left(-\frac{t_{Na} - t^*}{2\tau_{Na}} \right) dt^* \\ + \frac{c}{g_K} \int_0^t A_K(x) \exp \left[-\frac{t - t_{max,K}}{\delta_K} \right] \mathcal{I}_0 \left(\frac{t_K - t^*}{2\tau_K} \right) \exp \left(-\frac{t_K - t^*}{2\tau_K} \right) dt^* \quad (3.36)$$

The equation (3.36) consists of both sodium and potassium fluxes which can be obtained by putting in the values relevant to sodium and potassium which are as follows

$$\phi_{Na}(x, t) = \frac{c}{g_{Na}} \int_0^t A_{Na}(x) \exp \left[-\frac{t - t_{max, Na}}{\delta_{Na}} \right] \mathcal{I}_0 \left(\frac{t_{Na} - t^*}{2\tau_{Na}} \right) \exp \left(-\frac{t_{Na} - t^*}{2\tau_{Na}} \right) dt^* \quad (3.37)$$

$$\phi_K(x, t) = \frac{c}{g_K} \int_0^t A_K(x) \exp \left[-\frac{t - t_{max, K}}{\delta_K} \right] \mathcal{I}_0 \left(\frac{t_K - t^*}{2\tau_K} \right) \exp \left(-\frac{t_K - t^*}{2\tau_K} \right) dt^* \quad (3.38)$$

The values to be substituted for the parameters involved are as given below in Table 3.1:

Sr. No.	Variable	Value	Units
1	V_0	-0.07	V
2	c	21.2	m/s
3	g_{Na}	1200	S/m ²
4	g_K	360	S/m ²
5	A_{Na}	5100	V/m
6	A_K	130	V/m
7	$t_{max, Na}$	0.0011	s
8	$t_{max, K}$	0.002	s
9	δ_{Na}	0.0011	s
10	δ_K	0.002	s
11	τ_{Na}	0.0445	s
12	τ_K	0.002	s
13	t	0 - 0.005	s

Table 3.1: Values of parameters to be substituted in equations (3.36), (3.37) and (3.38)

The Sodium flux can be plotted from equation (3.37) as given in Figure 3.1 below:

Figure 3.1: Sodium Flux as plotted from equation (3.37). The flux rises to a maximum value around 1 ms as expected and then goes down to 0 V/m

The Potassium flux can be plotted from equation (3.38) as given in Figure 3.2 below:

Figure 3.2: Potassium Flux as plotted from equation (3.38). The flux slowly rises to a maximum value around 2 ms and then gradually goes down to 0 V/m

It can be seen that the sodium flux rises to its maximum value near $t = 0.0011$ sec after which it reduces to 0 V/m. The potassium flux on the other hand slowly rises and reaches its maximum value near $t = 0.002$ sec after which it reduces to 0 V/m. This is the behaviour that has been described by various researchers when they performed experiments on the giant axon of the squid [112–115]. The opening and closing of the sodium and potassium channels leads to this variation in flux.

When the equation (3.36) is evaluated by substitution of values and plotted, we get the plot as shown in Figure 3.3 below.

Figure 3.3: Plot of evaluated equation (3.36) after substitution of values - A plot similar to action potential is generated

The Figure 3.3 shows the characteristic shape and values of the action potential. The resting potential has been taken as -70 mV. The potential rises to a maximum of + 30 mV before it falls down to around -80 mV and subsequently rises again to reach the resting potential value of -70 mV.

This is due to the fact that the sodium channels rapidly open up when the action potential is initiated leading to a sodium ion influx till the transmembrane voltage approaches a value closer to the sodium Nernst potential. The sodium channels then close and the potassium channels open to cause an efflux of potassium ions which continues till the potential approaches the potassium Nernst potential. This causes a slight undershoot, which is also called hyperpolarization. Later the ionic balance is restored, which leads to the transmembrane potential becoming closer to the resting potential value.

Equation (3.36) can accurately model the action potential when the exciting potential is above a threshold level. For sub-threshold levels, there should be no generation of action potential and there should be a passive spread like diffusion. This is called electrotonus. The threshold voltage, V_{th} is such that it will raise the potential of the neuron more than 15 mV above resting potential [116]. To incorporate this important aspect of action potential generation, equation (3.36) is rewritten as

$$V(x, t) = V_0 + \frac{c}{g_{Na}} \int_0^t A_{Na} \exp \left[-\frac{t - t_{max, Na}}{\delta_{Na}} \right] \mathcal{I}_0 \left(\frac{t_{Na} - t^*}{2\tau_{Na} u_{th}} \right) \exp \left(-\frac{t_{Na} - t^*}{2\tau_{Na} u_{th}} \right) dt^* \\ + \frac{c}{g_K} \int_0^t A_K \exp \left[-\frac{t - t_{max, K}}{\delta_K} \right] \mathcal{I}_0 \left(\frac{t_K - t^*}{2\tau_K u_{th}} \right) \exp \left(-\frac{t_K - t^*}{2\tau_K u_{th}} \right) dt^* \quad (3.39)$$

where, u_{th} is an unit step function with value unity when the threshold voltage is reached. u_{th} can be mathematically expressed as

$$u_{th} = H(V_e(x, t) - 15) \quad (3.40)$$

where H is the Heaviside step function and $V_e(x, t)$ is the exciting potential due to stimulus.

3.6 Conclusion

The proposed model incorporates the concept of finite propagation speed of the action potential in the neuron. This takes care of the paradox of instantaneous propagation, which is present in the diffusion model. On application of the required values of the parameters involved, a plot of a single action potential is generated by the model. The plots of Sodium and Potassium fluxes as provided by the model are consistent with the general behaviour of the ions inside the neuron.

Chapter 4

Macro Model

4.1 Introduction

The previous chapter introduces the phase-lagging model, which accurately models the single action potential. The behaviour of the sodium and potassium ions is also plotted. The introduction of the time delay helps solve the paradox of instantaneous propagation as well. The model now needs to be extended to be able to portray brain response.

The way in which information about the nature and strength of stimulus is transferred, through the nervous system is expounded in this chapter. This chapter shall also model the EEG by solving the phase-lagging model equation introducing the flux generated by external stimuli. This stimuli can be of any kind - auditory, visual and somatosensory. The influx of information to the individual, over a period of time, is huge in terms of quantity. The brain has to decide on the importance of specific information that it receives and this is very crucial for it to function properly. If the brain responded to every information that it receives, then it would shut down due to over load. This decision is done by estimating the importance of information for the brain.

The chapter is organized as follows: Section 4.2 describes the mechanism of information

transfer through the nervous system. The time lag in the phase-lagging model described in Chapter 3 is developed as a function of the Hurst exponent(H) in Section 4.3. This section also models the flux due to external stimulus and solves the phase-lagging model showing good correlation to EEG series. The concept of importance of information is explained in Section 4.4. Section 4.5 defines information gain due to a stimulus. A conclusion of the chapter is given in Section 4.6.

4.2 Stimulus to brain - The mechanism of information transfer

The path of information flow begins from the reception of the stimulus. The stimulus can be light, heat, sound, mechanical stress or chemicals. The stimulus is picked up by the relevant sensory receptor. These are [117]:

1. **Photoreceptors** - They detect the light stimulus. Ex. receptors in retina(eyes).
The receptors in the retina are made up of rods and cones. The rods are specialized for detection of light of light at low intensities and the cones for detection of different wavelengths which leads to detection of colour. The exact mechanism in which colour is detected is not known but it is agreed that the colour information is sensed as a combination of the primary colours.
2. **Mechanoreceptors** - They detect mechanical stimuli. Ex. auditory receptors in the ear. The auditory signals received by the ear in the form of waves and vibrate the eardrum. This vibration is transmitted through the middle ear where it is amplified by the levering action of the bones present there. The vibrations then pass through the fluid of the inner ear and reach the basilar membrane which has sensory hair cells. Different sections of the basilar membrane are vibrated

depending on the frequency of the auditory signal received. So, a signal consisting of different frequencies vibrates a different section of the basilar membrane which generate action potentials. All these different action potentials are integrated to provide the individual with a perception of sound at a corresponding pitch and loudness.

3. **Chemoreceptors** - They detect chemical stimuli. Ex. taste buds in tongue. Taste and odour are detected by the chemoreceptors in the tongue and nose, respectively. The detection mechanism is based probably on selective binding with molecules in the environment by the proteins in the receptors. The coding mechanism is not known exactly but the information is conveyed in the form of number of receptors and frequency of action potentials.
4. **Thermoreceptors** - They detect thermal stimuli. Ex. receptors in skin. Distinct thermoreceptors react to cold or heat. The coding mechanism is not known exactly too, but as in the case of chemoreceptors the information is conveyed in the form of number of receptors and frequency of action potentials.
5. **Nociceptors** - They detect tissue damage and are responsible for detecting pain. Ex. receptors in skin. The coding for these receptors is also a function of number of neurons and frequency of action potential generation.

A stimulus strong enough to generate an action potential in the neuron is called the threshold stimulus. Any stimulus stronger than the threshold stimulus is translated by the number of sensory neurons generating information about the stimulus and the frequency of the action potentials. If the intensity of the stimulus stays constant for a long period of time, some of the sensory receptors reduce the frequency of action potentials generated and this is called sensory adaptation. For instance, mechanoreceptors adapt to the feeling of a

chair when the person sits on it for long. Some sensory receptors, especially nociceptors, never adapt to stimuli. This ensures the safety of the individual by informing the brain about the constant harm being caused to the body.

After the action potential has been generated, it travels through the neural network to the brain. In various sections of the network and in the brain, integration of the signals takes place. Different areas of the brain respond depending on the kind of stimuli and the location of the stimuli. The brain sends out signals, which generate the response mechanism. The information that reaches the brain along with the response signal is involved in the creation of a memory through learning.

For reflex actions, such as jerking away from heat, the pathway is a simple loop. The afferent neurons from the receptor areas carry information to the grey matter in the spinal cord where the integrating interneurons simulate the efferent nerves to generate the response. Information about the stimulus is sent to the brain but even before the information reaches the brain, the reflex action has been completed.

4.3 Modelling brain activity(EEG) using phase-lagging model

The brain gets information from multiple neurons. All the signals come to the brain and get integrated. Each of the neuron is expected to behave like the single neuron that has been discussed in Chapter 3. This means that the action potentials generated in the multiple neurons has the same behaviour as the action potential generated in the single neuron. As described in the Section 4.2, integration of the various impulses from the myriad of receptors takes place in the interneurons. This integration is dependant on the type of stimulus that is acting and also on whether the various action potentials are

EPSPs or IPSPs. EPSPs are potentials that will raise the potential inside the neuron and IPSPs are potentials that reduce the potential inside the neuron. This integration of various potentials can be any kind of mathematical process like summation, weighted summation or any other process. The resultant signal will be dependent on the number of neurons activated (n_{act}) and the frequency of activation (η_{act}).

These signals from the multiple neurons reach the brain, which responds correspondingly. This response is observed as EEG. The EEG is a time series with varying Hurst exponent (H). This can be observed by computing the Hurst exponent dynamically for any EEG as done later in Chapter 6. The phase-lagging model has variable time lag (τ). In order to model the EEG by the phase-lagging model, we need to find a relationship between τ and H .

4.3.1 Relationship between τ and H

The behaviour of D and c is known for different cases of H . D has the following values:

$$D \rightarrow \begin{cases} \infty & H \rightarrow 0 \\ D_0 & H \rightarrow 0.5 \\ 0 & H \rightarrow 1 \end{cases} \quad (4.1)$$

where, D_0 is the value of diffusion coefficient in case of pure diffusion.

So, a formulation of D which satisfies all the above cases as given in Equation (4.1) is

$$D = 3.464 \times D_0 \left[\frac{(1-H)^2}{\sqrt{2H-H^2}} \right] \quad (4.2)$$

A plot of $\frac{D}{D_0}$ vs H , as per equation (4.2), is given in Figure 4.1.

Figure 4.1: Plot of Equation 4.2 - Values of $\frac{D}{D_0}$ for various values of H

c has the following values for H

$$c \rightarrow \begin{cases} 0 & H \rightarrow 0 \\ \infty & H \rightarrow 0.5 \\ c_0 & H \rightarrow 1 \end{cases} \quad (4.3)$$

where c_0 is the velocity of propagation when the system is completely under wave motion.

So, c can be modelled as

$$c = 0.25 \times c_0 \left[\frac{H}{(0.5 - H)^2} \right] \quad (4.4)$$

Plotting $\frac{c}{c_0}$ for various values of H gives Figure 4.2

Figure 4.2: Plot of Equation 4.4 - Values of $\frac{c}{c_0}$ for various values of H

The time lag, τ , can be formulated as per Equation (3.24) as $\tau = \frac{D}{c^2}$. So, we have

$$\begin{aligned}
 \tau &= \frac{D}{c^2} \\
 &= 3.474 \times D_0 \frac{(1-H)^2}{\sqrt{2H-H^2}} / 0.25 \times c_0^2 \frac{H}{(0.5-H)^2} \\
 &= 13.856 \times \frac{D_0}{c_0^2} \left[\frac{(1-H)^2(0.5-H)^2}{H^{3/2}\sqrt{2-H}} \right] \\
 &= 13.856 \times \tau_0 \left[\frac{(1-H)^2(0.5-H)^2}{H^{3/2}\sqrt{2-H}} \right] \tag{4.5}
 \end{aligned}$$

Plotting $\frac{\tau}{\tau_0}$ as per Equation (4.5), we get the following Figure 4.3

Figure 4.3: Plot of Equation 4.5 - Values of $\frac{\tau}{\tau_0}$ for various values of H

The values are in accordance with the theoretical classical law of diffusion where the propagation is considered to be instantaneous. But we should be aware of the fact that there does exist a very small value of time lag even in the case of pure diffusion which can be observed by experimentation. The values of D and c are in line with the values expected for pure diffusion ($D = D_0$ and $c = \infty$) and wave motion ($D = 0$ and $c = c_0$).

4.3.2 Generation of EEG plot by phase-lagging model

Multiple neurons provide information to the brain. The flux reaching the brain can be modelled by a series of Gaussian pulses [109] as

$$\phi(t) = \sum_{k=1}^N \phi_0(T_k) \exp \left[-\frac{(t - T_k)^2}{\sigma_k^2} \right] \quad (4.6)$$

where, ϕ_0 denotes the amplitude of the stimulus with values randomly distributed between -3 and 3 mV/m. T_k and σ_k are the means (time at which maximum stimulus is achieved) and standard deviations (time duration of stimulus) of the pulses respectively, modelled as Poisson distribution ($\sim \frac{e^{-\mu} \mu^k}{k!}$ where μ is the mean of the distribution).

Equation (4.6) is now substituted in equation (3.34) and a numerical solution is performed. The resultant plot is shown in Figure 4.4

Figure 4.4: Plot of the numerical solution of equation (3.34) with values of flux from equation (4.6)

Figure 4.4 looks very similar to an EEG which is a multi-fractal time series. But, in order to confirm this, we need to calculate the fractal spectra of the numerical solution as described in Section 2.5.3. This fractal spectra is given in Figure 4.5

Figure 4.5: Plot of the fractal spectra of the numerical solution of equation (3.34)

It can be seen from figure 4.5 that the fractal spectra of the solution is a widely spread Z shaped curve, which corresponds to a multi-fractal time series [81, 118]. Hence, the solution to the phase-lagging equation is capable of modelling multi-fractal time series like EEG signals, which are a result of brain response to external stimuli.

4.4 Importance of information

The amount of information contained in the stimulus or the meaning of information has to be defined before it can be analysed. The information that reaches us has meaning and importance if

1. it is relevant or required to the individual,
2. it reduces the risk associated with an event or action to be undertaken.

A brief description of both these quantities follows.

4.4.1 Relevance of information

Any incoming data to the individual has to be relevant to his/her needs. Even an important piece of information like “Call the ambulance” is irrelevant unless the individual needs it or recognizes it (has an understanding of what is being said). So, relevance of information is dependant on the need of the information and a memory/understanding of what has been said, heard or seen. Relevance is therefore defined as a function of need (Ne) and memory (M).

$$\text{Relevance}(R) = f[\text{Need}(Ne), \text{Memory}(M)]$$

Relevance has two possible states - 1 or 0. It takes a value of 1 when there is relevance and 0 when the information is irrelevant. Need takes the values of 1 and 0 when there is a need and when there is no need for the information, respectively. Memory has values of 1 and 0 too depending on whether there is prior memory or understanding of what is being conveyed. The various values of relevance for different values of need and memory are given as follows:

$$R = \begin{cases} 1 & Ne = 1, M = 1 \\ 1 & Ne = 0, M = 1 \\ 1 & Ne = 1, M = 0 \\ 0 & Ne = 0, M = 0 \end{cases} \quad (4.7)$$

The values of R for various conditions are very evident as the information only has relevance if the recipient has either need for that information and/or has a memory of what it means. Going back to the example of “Call the Ambulance”, the individual will only register the information if he either needs it like the person speaking it is someone he knows or he understands it if it is gestured or spoken in a language the individual is familiar with. In all other cases, it holds as much meaning to him as anything else.

4.4.2 Risk associated with event/action

Every event or decision taken has an inherent risk associated with it. The Royal Society defines risk as the probability that a particular adverse event occurs during a stated period of time, or results from a particular challenge [119]. Chicken and Posner define risk as “Risk = Hazard $\times$ Exposure”. Hazard is defined as the way in which a thing or situation can cause harm and exposure is stated as the extent to which the likely recipient of the harm can be influenced by the hazard [120]. Smith defines risk as decision expressed by a range or possible outcomes with attached probabilities [121]. Risk can also be defined as the threat or probability that an action or event will adversely or beneficially affect an organisation’s ability to achieve its objectives [122].

So, risk can be defined as

$$\text{Risk}(\rho) = \text{Probability of event} \times \text{Impact}$$

Let us now suppose a system chooses one among N possible decisions $d_1, d_2, \dots, d_N$ in an environment of M events $\varpi_1, \varpi_2, \dots, \varpi_M$ with probabilities $w_1, w_2, \dots, w_M$ respectively. $L(d_i, \varpi_j)$ denotes the losses in case of making decision i, if event ϖ_j takes place. The risk associated with making decision d_i can be expressed mathematically as

$$\rho(d_i) = \sum_{j=1}^M w_j L(d_i, \varpi_j) \quad (4.8)$$

4.4.3 Mathematical expression for importance of information

The importance of information (Im_i) can be defined as

$$Im_i = -R \log \frac{\rho_a}{\rho_b} \quad (4.9)$$

where, R is the relevance of information as given by equation (4.7), ρ_a is the risk after the information has been processed and ρ_b is the risk before the information was processed.

If the risk after the information is lower than the risk before, then Im_i takes a positive value. This means that the information is important and has increased the individual's knowledge to its benefit. This sort of information and the response to it will be stored in memory if the benefit is high enough.

On the other hand, if the risk after the information is higher than the risk before, then Im_i will take a negative value and this can be considered as misinformation. The information has, in fact, caused more harm than benefit. Such an information and the response may be stored in memory if a lot of harm was caused. This may also associate a bad memory to the source of the information in the brain of the individual.

In case the risk before and after are the same, then the information is not important and most possibly, the individual was aware of this information even before it was received.

It is to be noted here that information by itself has no meaning or importance unless it is processed by the individual. We can say that unless information gets processed and becomes knowledge, it has no meaning.

4.5 Information gain

Any information that has been processed by the user has to reflect itself as information gain. It will have increased the knowledge of the individual irrespective of whether it caused benefit or harm. But this gain will only happen if the stimulus is higher than the threshold stimulus. Threshold stimulus is the minimum stimulus that causes a change in the information state of the individual.

Information gain can be defined as the subjective increase in the information state of

an individual after a stimulus has been received. It can take the following values:

$$G = \begin{cases} 0 & S < S_0 \\ 1 & S = S_0 \\ f(C) & S > S_0 \end{cases} \quad (4.10)$$

where $f(C)$, the neuronal coding function, is a function of C which is dependant on the number of neurons activated and the frequency of generation of action potentials in response to the stimulus, S is the stimulus applied and S_0 is the threshold stimulus. The neuronal coding function can be assumed to have a similar form to Weber-Fechner's law or Steven's law or any other law. We can also observe that the gain in case of the brain will always be positive as the brain does not react to stimulus below threshold level.

4.6 Theory of quantification of stimulus

As stated in the previous section, any stimulus that is applied to the individual will generate a response from the brain if it is above the threshold level. This is the information gain and it is reflected in the EEG of the individual. This, in turn, presents us with an avenue to quantify stimulus based on the gain it causes and consequently the change in EEG that appears.

Considering Equations (4.8) and (4.9), we notice that $\log \frac{\rho_a}{\rho_b}$ should be proportional to $\log \frac{w_a}{w_b}$, where w_a and w_b are the probabilities of events after and before stimulus application, respectively. Now, this can be equated to the information gain by redefining it through the Weber-Fechner's law where w_a can be the probability for applied stimulus and w_b the probability for threshold stimulus. So, we can relate the importance of information to the information gain.

This interconnection will aid us in relating the physical stimulus through the quantifi-

cation of information gain to the meaning of information as processed by the brain. So, if the stimulus has meaning, it causes a change in the EEG and we can quantify it. We will now introduce a key measure for this quantification.

4.6.1 Jeffreys measure

Jeffreys measure is a measure of how much the signal diverges from the base signal [123, 124]. It can be computed as

$$J(pj, qj) = \sum_i pj_i \log(pj_i/qj_i) + \sum_i qj_i \log(qj_i/pj_i) \quad (4.11)$$

where, i ranges from 1 to n , $J(pj, qj)$ is the Jeffreys Measure, pj_i is the reference probability distribution and qj_i is the probability distribution of the current sample of signal.

The reference probability distribution in the EEG is the probability distribution of the signal when the subject is at rest.

If we look at the mathematical expression for Jeffreys measure, we can see that it is related to the logarithmic ratio of the probabilities in the EEG signal after and before the application of stimulus. This is similar to the interconnection that we have already discussed. So, we propose that this measure is a very good indicator of the gain in information due to the stimulus and hence can be used to quantify the stimulus and its effects.

Observation of the changes in Jeffreys measure dynamically can help us to quantify the stimulus and the software described in the subsequent chapter has been developed to measure Jeffreys measure dynamically among other measures.

We also observe that there are two terms in the formulation of Jeffreys measure. As mentioned above, one of the terms measures the information gain. The other term eliminates the noise due to background processes like other stimuli. This assists us in

observing the effects of a stimuli with greater clarity. So, Jeffreys measure can also be called a noise eliminating measure.

4.7 Conclusion

The path of information transfer from the point of application of stimulus to the brain begins from the receptors, goes through afferent neurons, gets integrated at interneurons and reaches the brain. Multiple inputs to the brain get integrated in the brain whose response can be observed as EEG. The flux due to the various inputs reaching the brain can be modelled as a series of Gaussian pulses and substituting this value in the phase-lagging model gives a plot which is a multi-fractal time series like the EEG. A relationship between the time lag and the Hurst exponent is developed in order to build the relationship between the theoretical phase-lagging model with varying time lag and the experimental data with varying Hurst exponent. Mathematical formulations for the importance of information and information gain have also been developed in this chapter. We have also suggested a way and a noise-cancelling measure to quantify the stimulus and its effects.

Chapter 5

Data Acquisition and Analysis

Methodology

Brain activity is measured by acquiring and analysing EEG signals from an individual. This chapter explains the procedure of data acquisition. The useful information in biological signals like EEG is nested inside noise and irrelevant brain activity. Hence, a method to analyse these signals and the development of a software, FRactal Time Series ANalyser (FRATSAN) for analysing the EEG data to extract information in the form of various measures is outlined in this chapter.

Section 5.2 gives details of the equipment setup used, subject preparation and stimulus introduction for acquiring data to be used later in Chapter 6 for analysis. Section 5.3 lists out the various measures that can be used to extract information from EEG signals and are given as outputs by FRATSAN. Section 5.4 gives an overview of FRATSAN and its outputs including various screenshots.

5.1 Experimental set-up and procedure

5.1.1 Equipment used

The following equipment were used for data collection:

1. Personal Computer (PC) - Windows PC with SCSI cable for Mindset 24 hardware. A software for capturing the EEG signal data and subsequent processing is installed on the machine.
2. Mindset 24 device - a 24 channel topographic neuromapping instrument. It can measure 24 channels of data with a sampling frequency of 256 Hz.
3. Electrode caps - 3 different caps for different head sizes. These caps have electrodes placed in them in the international 10-20 method of electrode placement. The 10-20 system has been explained in Chapter 2.
4. Ear electrodes - for grounding purposes. These are attached to the ear lobes of the subject.
5. Quick insert electrodes - temporary electrodes. These are used for overriding the cap wiring in case of a faulty electrode in the cap.
6. Impedance tester - used to test the impedance of electrodes in the cap.
7. Body harness - used to secure the subject and prevent unnecessary movement which may introduce artifacts in the EEG signals.
8. Electro gel - gel used to reduce the impedance between skull of subject and electrodes in the electrode cap.
9. Blunt needle syringe - used to fill the electrodes with electro gel. These are blunt nosed in order to reduce any chances of causing harm to the subject.

10. Measuring tape - nylon tape with various cap colours. This is used to measure the cap size required for subject.
11. Disposable sponge disks - sponge disks with holes. These are affixed on the subject's forehead to prevent the gel from running into his/her eyes.

5.1.2 Selection and preparation of subject

Subjects are students of the university, between 20-25 years of age. All of them are in sound mental health and ascertained to be not under mental stress or disease of any kind prior to the EEG measurement.

The subjects are briefed on the various tests that shall be done on them. They are informed that no physical harm shall be done to them and the procedure is entirely non-invasive. They are allowed to relax for a while and then prepared for the EEG measurement.

First, the body harness is put on the subjects with their arms outstretched across their chest. Then, ear electrodes are attached and filled with gel to reduce the impedance. The circumference of the subject's head is measured using the colour coded measuring tape. The size is measured on an imaginary line running through a point one inch above the nasion (depression between eyes above the bridge of nose) and one inch above inion (bony protuberance at base of the skull). The correct cap as indicated by the colour on the tape is used. Sponge disks are placed on either side of the center line from nasion to inion. The Fp1 and Fp2 electrodes inserted into these disks and then the cap is pulled over the subject's scalp. The bands on the side of the cap are then affixed to the body harness so that the movement of the cap is restricted and the electrodes are pulled tightly against the scalp.

The impedance of individual electrode is checked by connecting the impedance tester

to the cap. The impedance should be lower than 5 k Ω for proper measurement of EEG. If the impedance is higher, then electro gel is injected into the electrode using the syringe to bring it down to the desired value. In case the value of impedance refuses to fall below the required value even after application of gel, a quick insert electrode is inserted in the electrode and connected to Mindset 24. After all the electrodes have been checked, the cap is connected to the Mindset 24 machine.

5.1.3 Application of stimulus and data collection

Various stimuli like light, sound, odour or pressure were administered to the subjects at pre-set intervals. The time of application of stimulus was recorded for subsequent analysis of data. This procedure is endeavoured to insulate the subject from all other external stimuli. This ensures that the response measured in the EEG is primarily due to the stimulus applied.

Mindmeld24 software is used for collection of data from the subject using Mindset 24 machine. A sample screenshot of the Mindmeld24 software in use is given in Figure 5.1. The software gives data in the form of .bin files which can be processed to give text files (.txt) which are required for processing the data with FRATSAN.

Figure 5.1: Screenshot of Mindmeld 24 software in use

5.2 Measures for analysis of EEG signals

There are three useful measures for analysis of multi-fractal time series like EEG. These measures are Fractal Dimensions, Jeffreys Measure and Hurst Exponent.

5.2.1 Fractal dimensions

Fractal Dimensions have been discussed in Section 2.5.3. They can be computed as

$$D_q = \lim_{\delta V \rightarrow 0} \frac{1}{q-1} \frac{\log \sum_{i=1}^N p_i^q}{\log \delta V} \quad (5.1)$$

where, q ranges from $-\infty$ to $+\infty$.

D_0 is the Hausdorff-Besicovitch dimension. The range of this fractal spectrum, $D_{-\infty} - D_{\infty}$ is associated to the range of frequencies in the signal. The plot of the spectra indicates the unexpectedness of the signal. Steeper spectra correspond to time series in which the unexpected values are more dominant as opposed to a time series with flatter spectra.

5.2.2 Jeffreys measure

Jeffreys measure has been introduced in Section 4.6. It is a measure of how much the signal diverges from the base signal. It can be computed as

$$J(pj, qj) = \sum_i pj_i \log(pj_i/qj_i) + \sum_i qj_i \log(qj_i/pj_i) \quad (5.2)$$

where, i ranges from 1 to n , $J(pj, qj)$ is the Jeffreys Measure, pj_i is the reference probability distribution and qj_i is the probability distribution of the current sample of signal.

A large value of the Jeffreys measure will signify the onset and presence of a response to an event or stimuli.

5.2.3 Hurst exponent

Hurst exponent is a measure of the predictability of the signal. It is an indicator of the long term memory of the process generating the signal. It was formulated by H.E.Hurst after studying the Nile river [125]. The method widely used by statisticians and also used in FRATSAN for computing the values of Hurst exponent is called the Rescaled Range Analysis. Let us say that we have a set of n voltages - $V(1), V(2) \dots V(n)$. Let m be the

mean of all those values such that

$$m = \frac{1}{n} \sum_{i=1}^n V(i) \quad (5.3)$$

The deviations of the voltages from the mean can be calculated as

$$\begin{aligned} d_{V(1)} &= V(1) - m \\ d_{V(2)} &= V(2) - m \\ &\dots\dots \\ d_{V(n)} &= V(n) - m \end{aligned} \quad (5.4)$$

Next, the sums are calculated as

$$\begin{aligned} Y(1) &= d_{V(1)} \\ Y(2) &= d_{V(2)} + d_{V(1)} \\ &\dots\dots \\ Y(n) &= Y(n-1) + d_{V(n)} \end{aligned} \quad (5.5)$$

Range is defined as the difference between the maximum and minimum values of the sums.

$$R_H = Y_{max} - Y_{min} \quad (5.6)$$

The standard deviation of the set of voltage values is given by

$$s_H = \sqrt{\frac{1}{n} \sum_{i=1}^n [V(i) - m]^2} \quad (5.7)$$

It has been established that

$$\frac{R_H}{s_H} \sim kn^H \quad (5.8)$$

where k is a constant and H is the Hurst exponent. In order to compute the Hurst exponent from a set of values, we plot $\log\left(\frac{R_H}{s_H}\right)$ against $\log(n)$ and obtain the Hurst exponent value from the slope of the graph plotted.

The value of the Hurst exponent ranges from 0 to 1. If $H = 0.5$, then the process is considered to be truly random (e.g. Brownian motion). It means that there is absolutely no correlation between any values of the process. A value of H between 0 and 0.5 means that the process is anti-persistent. The trend of the value of the process at the next instant will be opposite to the trend in the previous instant. A value of H between 0.5 and 1 means that the process is persistent, i.e., the trend of the value of the process at the next instant will be the same as the trend in the previous instant.

5.3 FRATSAN

The **FR**actal **T**ime **S**eries **AN**alyser (FRATSAN) was developed to compute all the measures mentioned in section 5.2. It is written completely in Visual C++. A component called PlotLab was used for plotting all the graphs required [126]. It has a very intuitive interface. All the necessary files are supplied with the executable file of the program. The software requires no installation of any kind.

5.3.1 Analysis methodology

The software uses a dynamic method of analysis for all the measures. A sliding window is selected with a value equal to 10% of the total number of data entries. This sliding window is moved one data entry at a time to obtain all the measures. This makes the

computation very sensitive to slight changes in data, thereby giving the user an acute analysis of the data.

5.3.2 Description of functions and usage of FRATSAN

Upon starting the program, the user is greeted with a splash screen as shown in Figure 5.2.

Figure 5.2: Splash screen of FRATSAN

The main GUI of the program loads up as shown in Figure 5.3

Figure 5.3: Main window of FRATSAN

The user has to select the file he/she wants to process by using the browse button. The semi-width of the spectrum can be entered as 45. The total number of channels is to be entered by the user. If processing all the channels is needed, then 0 should be entered in the no. of channels box, otherwise the required channels are to be filled in. The user

has to select any measure to be computed in the drop down box. If any of these options is not filled in, the software warns the user to complete them and then proceed.

Once the software has been given the calculate command, it will display a splash screen informing the user that Stage 1 of the computations are over as shown in Figure 5.4. The software will also display the values of maximum voltage (V_{max}), minimum voltage (V_{min}), total number of data entries in the file and the size of the sliding window. The size of the sliding window is selected as described in Section 5.3.1. After this stage, the user has the option to continue the calculations till the end or terminate the program.

Figure 5.4: FRATSAN - Stage 1 completed

A progress bar indicates how much progress has been made by the program as shown in Figure 5.5.

Figure 5.5: FRATSAN - Progress bar

Upon finishing the calculations, the user can select to plot the computed values. He/She can also perform calculation of average and obtain a plot. All plots can be saved under user specified names.

FRATSAN prohibits an attempt to generate the plot of an analysis if the analysis is not the action last performed as shown in Figure 5.6 .

Figure 5.6: FRATSAN - Warning for plot generation attempt without calculation being last action performed by user. Here, the Fractal Analysis was performed and plot for Jeffreys measure was asked for from the software

A ‘clear all’ button clears all the fields for another computation if so desired by the user. The exit button terminates the program.

5.3.3 Outputs

A variety of outputs is given by FRATSAN for every operation performed by the user on the data file.

5.3.3.1 Fractal analysis output

Upon completion of the fractal analysis on the data file, two text files are generated by the program for each channel selected. The files are named ‘(name of data file)_DFS_CH_(Channel number)’ containing the entire D_q and ‘(name of data file)_DFS_CH_Short_(Channel number)’ containing values of $D_{-\infty}$, D_0 and $D_{+\infty}$.

The plot command will plot the values of $D_{-\infty}$, D_0 and $D_{+\infty}$ for each channel selected. Three graphs will be generated in total for the three measures. Sample plots are shown in Figures 5.7(a), 5.7(b) and 5.7(c).

(a) FRATSAN - Plot for $D_{-\infty}$ (b) FRATSAN - Plot for D_0

(c) FRATSAN - Plot for $D_{+\infty}$

Figure 5.7: Plots of fractal dimensions given by FRATSAN

If the average command is performed after this, the software averages the values for $D_{-\infty}$, D_0 and $D_{+\infty}$ over all the channels and generates a single plot with three distinct lines as shown in Figure 5.8

Figure 5.8: FRATSAN - Plot for average fractal dimension

5.3.3.2 Jeffreys measure output

After performing the Jeffreys measure calculations, FRATSAN generates a text file named ‘(name of data file)_Jeffreys_CH_(channel number)’ for each channel selected. The plot command will plot all values on a single plot as shown in Figure 5.9.

Figure 5.9: FRATSAN - Plot for Jeffreys Measure

The average command will average the values over the number of channels and time to give a single line plot as shown in Figure 5.10.

Figure 5.10: FRATSAN - Plot for Jeffreys Measure

5.3.3.3 Hurst exponent output

After the Hurst exponent analysis has been done, the software generates text files named ‘(name of data file)_Hurst_CH_(channel number)’ for each channel selected. Plot will plot all the values to give a multiple line plot as shown in Figure 5.11.

Figure 5.11: FRATSAN - Plot for Hurst exponent

The average command will average the values over number of channels and time to give a single line plot as shown in Figure 5.12

Figure 5.12: FRATSAN - Plot for average Hurst exponent

Chapter 6

Results and Discussion

A number of people were randomly chosen as subjects and consent was obtained to perform EEG experiments on them. A variety of stimuli were given to the subjects and the corresponding EEG recordings taken. We shall discuss three such stimuli in this chapter. They have been chosen so that we can cover auditory, visual and olfactory kinds of stimuli.

Section 6.1 will discuss effect of visual stimuli on EEG. Olfactory responses shall be discussed in Section 6.2. Section 6.3 will investigate the effects of auditory stimuli on EEG. Section 6.4 shall conclude the findings.

6.1 Visual stimuli - Colour

Various colours were shown to the subjects ranging from black to white. In all, sixteen colours were shown to subjects with varying values of red, green and blue. We present results for black, white, red, green and blue here for two subjects.

6.1.1 Subject 1

Average fractal dimensions for subject 1 viewing black, white, red, green and blue colours are given below in Figures 6.1(a), 6.1(b), 6.1(c), 6.1(d) and 6.1(e) respectively.

(a) Average fractal dimensions of subject 1 viewing black colour on screen. $D_0 = 5.3$

(b) Average fractal dimensions of subject 1 viewing white colour on screen. $D_0 = 5.3$

(c) Average fractal dimensions of subject 1 viewing red colour on screen. $D_0 = 5.5$

(d) Average fractal dimensions of subject 1 viewing green colour on screen. $D_0 = 5.5$

(e) Average fractal dimensions of subject 1 viewing blue colour on screen. $D_0 = 5.4$

Figure 6.1: Average fractal dimensions for subject 1 viewing various colours on the screen

A view of the values of average fractal dimensions for colours reveals a few interesting points. Green and red have the highest value of the Hausdorff-Besicovitch dimension. But, green has a lower value of $D_{-\infty}$ and higher value of $D_{+\infty}$. This means that green leads to a higher chaos level in the EEG signal as compared to red. Blue has a higher value of D_0 than black or white but a lower value of $D_{+\infty}$ as compared to black. So, blue and black can be considered to be nearly equal in their effects on the subject's brain. White has a lower value of D_0 and $D_{+\infty}$. Hence, white is the most calming colour of the entire spectrum presented.

Average Jeffreys measures for subject 1 viewing black, white, red, green and blue colours are shown in Figures 6.2(a), 6.2(b), 6.2(c), 6.2(d) and 6.2(e) respectively.

(a) Average Jeffreys measure for subject 1 viewing black colour on screen. $J = 0.06$

(b) Average Jeffreys measure for subject 1 viewing white colour on screen. $J = 0.055$

(c) Average Jeffreys measure for subject 1 viewing red colour on screen. $J = 0.19$

(d) Average Jeffreys measure for subject 1 viewing green colour on screen. $J = 0.18$

(e) Average Jeffreys measure for subject 1 viewing blue colour on screen. $J = 0.045$

Figure 6.2: Average Jeffreys measure for subject 1 viewing various colours on screen

Appraising the plots and values of the Jeffreys measure, we observe that green and red are the colours with the maximum values of Jeffreys measure. They have a very high value of 0.18 as opposed to the smaller values of other colors. This means that the EEG signal divergence from the rest state is very high for green and red. The value for black is in between lowest and highest but closer to the lower range. Blue and white are the colours for which the EEG signal stays closer to the resting state ~ 0.05 .

The Hurst exponent plots for black, white, red, green and blue are given in Figures 6.3(a), 6.3(b), 6.3(c), 6.3(d) and 6.3(e) respectively.

(a) Average Hurst exponent for subject 1 viewing black colour on screen. $H = 0.71$

(b) Average Hurst exponent for subject 1 viewing white colour on screen. $H = 0.77$

(c) Average Hurst exponent for subject 1 viewing red colour on screen. $H = 0.66$

(d) Average Hurst exponent for subject 1 viewing green colour on screen. $H = 0.64$

(e) Average Hurst exponent for subject 1 viewing blue colour on screen. $H = 0.74$

Figure 6.3: Average Hurst exponent for subject 1 viewing various colours on screen

The analysis and plotting of Hurst exponent for all the colours gives results which do not deviate much from what has been observed in the earlier measures. Red and green remain the colours with the lowest Hurst exponent and, in fact, have a drop which gives values closer to $H = 0.5$ (complete unpredictability). Red has a lesser drop than green and a higher value of H . So, green is the colour leading to highest unpredictability in the subject's EEG signal. Black again obtains a mid range value. Blue and white have the highest H values which indicate a memory effect.

6.1.2 Subject 2

Average fractal dimensions for black, white, red, green and blue are given in Figures 6.4(a), 6.4(b), 6.4(c), 6.4(d) and 6.4(e) below respectively.

(a) Average fractal dimensions of subject 2 viewing black colour on screen. $D_0 = 5.3$

(b) Average fractal dimensions of subject 2 viewing white colour on screen. $D_0 = 5.3$

(c) Average fractal dimensions of subject 2 viewing red colour on screen. $D_0 = 5.5$

(d) Average fractal dimensions of subject 2 viewing green colour on screen. $D_0 = 5.5$

(e) Average fractal dimensions of subject 2 viewing blue colour on screen. $D_0 = 5.3$

Figure 6.4: Average fractal dimensions for subject 2 viewing various colours on the screen

The average fractal dimensions show that green and red are the colours with the maximum value of D_0 . Green has a more chaotic signal as the range of values between $D_{+\infty}$ and $D_{-\infty}$ is lesser than that of red. Black and white seem to have nearly the same spectrum for this subject's EEG. Blue, though having the same value of D_0 as black and white, has the least chaotic signal with the widest spectrum.

The plots for average Jeffreys measure for black, white, red, green and white for subject 2 are shown in Figures 6.5(a), 6.5(b), 6.5(c), 6.5(d) and 6.5(e) respectively.

(a) Average Jeffreys measure for subject 2 viewing black colour on screen. $J = 0.045$

(b) Average Jeffreys measure for subject 2 viewing white colour on screen. $J = 0.0375$ (c) Average Jeffreys measure for subject 2 viewing red colour on screen. $J = 0.05$

(d) Average Jeffreys measure for subject 2 viewing green colour on screen. $J = 0.054$

(e) Average Jeffreys measure for subject 2 viewing blue colour on screen. $J = 0.045$

Figure 6.5: Average Jeffreys measure for subject 2 viewing various colours on screen

Assessing the various plots given previously shows us that green has the highest Jeffreys measure followed by red. Both of them have a value around 0.05. This means that the EEG signal diverges the maximum from rest state for these two colours. Blue and black have the same average value of Jeffreys measure but blue has a smoother rise of curve indicating a smaller section of EEG diverging from the rest state as compared to black. White has the least value of Jeffreys measure (~ 0.0375) as the EEG for the subject viewing the colour white has the least divergence.

The Hurst exponent plots for black, white, red, green and blue are given in Figures 6.6(a), 6.6(b), 6.6(c), 6.6(d) and 6.6(e) respectively.

(a) Average Hurst exponent for subject 2 viewing black colour on screen. $H = 0.74$

(b) Average Hurst exponent for subject 2 viewing white colour on screen. $H = 0.76$ (c) Average Hurst exponent for subject 2 viewing red colour on screen. $H = 0.71$

(d) Average Hurst exponent for subject 2 viewing green colour on screen. $H = 0.7$

(e) Average Hurst exponent for subject 2 viewing blue colour on screen. $H = 0.755$

Figure 6.6: Average Hurst exponent for subject 2 viewing various colours on screen

The plots for Hurst exponent show that green and red have the lowest Hurst exponent indicating higher unpredictability. In fact, both of their plots drop to near 0.676 for green and 0.7 for red. Black has a higher value at 0.74 in spite of a brief drop to 0.718. Blue and white have the highest Hurst exponent at 0.755 and 0.76 respectively.

6.1.3 Conclusions for visual stimuli

After evaluating all the plots for both the subjects for all the colours, we observe that white and blue are the colours effecting the least change in the EEG of the subject. So, we can surmise that they are relaxing colours, which do not agitate the subject. Black is a neutral colour. Its effect may depend on personal preference to the colour. Red and green are the colours causing the most shift and unpredictability in the subjects' EEGs. This is very evident from looking at the Jeffreys measure values which is a good indicator of the divergence of EEG from pre-stimulus state.

Hence, white and blue can be used in areas which require the viewer to be more relaxed like bedrooms, hospitals and hotels. Red and green can be used where the intention is to agitate, alert or intimidate the viewer. It has been established that sports persons wearing red outfits have a higher chance of winning. Red and green can also be used in situations requiring the viewer to be active like offices or reading rooms. Text could be written in green or red to ensure alertness from the viewer.

6.2 Olfactory stimuli - Odour

Six different odours were administered to the subjects. They were english rose, jasmine, lemon, orange, rose and sandalwood. The results for two subjects are presented in this section. Subject 1 is a female and subject 2 is male.

6.2.1 Subject 1

After analysis, the plots of average fractal dimensions for subject 1 at rest and inhaling english rose, jasmine, lemon, orange, rose and sandalwood are given below in Figures 6.7(a), 6.7(b), 6.7(c), 6.7(d), 6.7(e), 6.7(f) and 6.7(g) respectively.

(a) Average fractal dimensions for subject 1 at rest. $D_0 = 4.3$

(b) Average fractal dimensions for subject 1 inhaling english rose. $D_0 = 4.3$ (c) Average fractal dimensions for subject 1 inhaling jasmine. $D_0 = 4.4$

(d) Average fractal dimensions for subject 1 inhaling lemon. $D_0 = 4.5$ (e) Average fractal dimensions for subject 1 inhaling orange. $D_0 = 4.5$

(f) Average fractal dimensions for subject 1 inhaling rose. $D_0 = 4.3$ (g) Average fractal dimensions for subject 1 inhaling sandalwood. $D_0 = 4.4$

Figure 6.7: Average fractal dimensions of subject 1 at rest and inhaling different fragrances

All the fragrances register as changes in D_0 value over the reference state D_0 value. We can state that minute changes in the EEG are being picked up the method of analysis of fractal dimensions. Perusing the plots, we find that the subject has the most chaotic signal while inhaling the orange fragrance. Lemon is quite close to that effect too. Jasmine and sandalwood are nearly equal in their effect with sandalwood being a bit calming than jasmine. English rose is approximately the same as reference values and the change is registered as a small increase in D_0 value when the fragrance is introduced. Rose seems to have a calming effect on the subject and does not disturb the EEG signal.

The plots of the average Jeffreys measure for subject 1 exposed to english rose, jasmine, lemon, orange, rose and sandalwood is given in the following Figures 6.8(a), 6.8(b), 6.8(c), 6.8(d), 6.8(e) and 6.8(f) respectively.

(a) Average Jeffreys measure for subject 1 inhaling english rose. $J = 0.015$

(b) Average Jeffreys measure for subject 1 inhaling jasmine. $J = 0.02$ (c) Average Jeffreys measure for subject 1 inhaling lemon. $J = 0.026$

(d) Average Jeffreys measure for subject 1 inhaling orange. $J = 0.032$ (e) Average Jeffreys measure for subject 1 inhaling rose. $J = 0.014$

(f) Average Jeffreys measure for subject 1 inhaling sandalwood. $J = 0.021$

Figure 6.8: Average Jeffreys measure of subject 1 inhaling different fragrances

Examination of the plots tells us that orange and lemon fragrances have the highest Jeffreys measure (~ 0.03), thereby disturbing the EEG signal the most. Jasmine and sandalwood seem to be having approximately the same effect on the subject (~ 0.02). Rose and english rose cause the least disturbance in the signal and can be called as calming aromas (~ 0.014).

The average Hurst exponents for subject's EEG for english rose, jasmine, lemon, orange, rose and sandalwood are given in Figures 6.9(a), 6.9(b), 6.9(c), 6.9(d), 6.9(e) and 6.9(f) respectively.

(a) Average Hurst exponent for subject 1 inhaling english rose. $H = 0.88$ (b) Average Hurst exponent for subject 1 inhaling jasmine. $H = 0.89$

(c) Average Hurst exponent for subject 1 inhaling lemon. $H = 0.895$

(d) Average Hurst exponent for subject 1 inhaling orange. $H = 0.89$

(e) Average Hurst exponent for subject 1 inhaling rose. $H = 0.905$ (f) Average Hurst exponent for subject 1 inhaling sandalwood. $H = 0.895$

Figure 6.9: Average Hurst exponent of subject 1 inhaling different fragrances

The examination of the plots for average Hurst exponents does not show much of a difference in the values for all fragrances. All of them have Hurst exponents higher than 0.5 showing memory effect and influence of past events. Rose has the highest Hurst exponent of 0.905 and may be considered the least disturbing fragrance.

6.2.2 Subject 2

The average fractal dimensions for subject 2 at rest and breathing in english rose, jasmine, lemon, orange, rose and sandalwood fragrances is given below in Figures 6.10(a), 6.10(b), 6.10(c), 6.10(d), 6.10(e), 6.10(f) and 6.10(g) respectively.

(a) Average fractal dimensions for subject 2 at rest. $D_0 = 4.4$

(b) Average fractal dimensions for subject 2 inhaling english rose. $D_0 = 4.5$

(c) Average fractal dimensions for subject 2 inhaling jasmine. $D_0 = 4.5$

(d) Average fractal dimensions for subject 2 inhaling lemon. $D_0 = 4.4$ (e) Average fractal dimensions for subject 2 inhaling orange. $D_0 = 4.5$

(f) Average fractal dimensions for subject 2 inhaling rose. $D_0 = 4.4$ (g) Average fractal dimensions for subject 2 inhaling sandalwood. $D_0 = 4.4$

Figure 6.10: Average fractal dimensions for subject 2 at rest and inhaling different fragrances

All fragrances are registered in the EEG as changes in D_0 even if for a short while. This again underlines the sensitivity and resolution of the method of fractal dimensional analysis. Jasmine and orange appear to be the fragrances having the most chaotic signal. The effects of english rose are close to the two. Jasmine and rose have nearly equivalent effects and are close to the resting EEG. Sandalwood is relaxing to this subject and has the widest fractal spectrum.

Average Jeffreys measure plots for subject 2 inhaling english rose, jasmine, lemon, orange, rose and sandalwood are given in Figures 6.11(a), 6.11(b), 6.11(c), 6.11(d), 6.11(e) and 6.11(f) respectively.

(a) Average Jeffreys measure for subject 2 inhaling english rose. $J = 0.026$

(b) Average Jeffreys measure for subject 2 inhaling jasmine. $J = 0.0375$ (c) Average Jeffreys measure for subject 2 inhaling lemon. $J = 0.026$

(d) Average Jeffreys measure for subject 2 inhaling orange. $J = 0.026$ (e) Average Jeffreys measure for subject 2 inhaling rose. $J = 0.021$

(f) Average Jeffreys measure for subject 2 inhaling sandalwood. $J = 0.023$

Figure 6.11: Average Jeffreys measure for subject 2 inhaling different fragrances

The evaluation of the different Jeffreys measure plots shows that jasmine has the highest Jeffreys measure (~ 0.0375). This implies that the EEG for the subject inhaling jasmine diverges from the rest state by the maximum amount. English rose, lemon and orange are nearly equal in their effect with values of the Jeffreys measure very close to each other (~ 0.026). Rose and sandalwood have the lowest Jeffreys measure value with the EEG being close to resting state (~ 0.023).

Analysing EEG signals, average Hurst exponents for subject 2 inhaling english rose, jasmine, lemon, orange, rose and sandalwood are plotted in Figures 6.12(a), 6.12(b), 6.12(c), 6.12(d), 6.12(e) and 6.12(f) respectively.

(a) Average Hurst exponent for subject 2 inhaling english rose. $H = 0.88$ (b) Average Hurst exponent for subject 2 inhaling jasmine. $H = 0.845$

(c) Average Hurst exponent for subject 2 inhaling lemon. $H = 0.87$

(d) Average Hurst exponent for subject 2 inhaling orange. $H = 0.869$

(e) Average Hurst exponent for subject 2 inhaling rose. $H = 0.878$ (f) Average Hurst exponent for subject 2 inhaling sandalwood. $H = 0.899$

Figure 6.12: Average Hurst exponent for subject 2 inhaling different fragrances

The Hurst exponent plots and values for all the fragrances are very close to each other. All the values are higher than 0.5 showing influence of past events and departure from unpredictability. Sandalwood has the highest Hurst exponent showing high predictability and jasmine has the lowest Hurst exponent.

6.2.3 Conclusions for olfactory stimuli

In the case of subject 1, lemon and orange are the odours causing maximum activation of cortex exhibited as disturbances in the EEG signal. Jasmine and sandalwood cause nearly equivalent effects and are not very apart in their influence. English rose and rose are the most calming fragrances with rose being marginally better at calming the subject.

For subject 2, jasmine causes the maximum divergence from resting state for EEG and is the odour causing maximal activity in the cortex region. Orange is close to the effects of jasmine too. English rose, lemon and rose are equivalent in their effects. Sandalwood is the most calming fragrance for this subject.

Hence, we can suggest that lemon or orange flavours can be used in rooms where the subject 1 needs to be active and awake like the office or gymnasium. In similar conditions, subject 2 should use jasmine.

English rose and rose should be used in rooms where the subject 1 needs to relax like the bedroom or meditating rooms. Subject 2 would prefer sandalwood in such cases.

This information can also be used by perfume manufacturers and inclusion of lemon or orange may get the female subject interested in the person wearing the perfume. It will also make the person noticeable to the subject. Similarly, male subject prefers jasmine; so, they may be attentive to individuals wearing jasmine based perfumes.

6.3 Auditory stimuli - Music

Different genres of music were played for the subjects. We present results here for classical, rap and rock music for two subjects.

6.3.1 Subject 1

After subject 1 listened to the different kinds of music, we analysed the EEG signals obtained to get values for average fractal dimensions, average Jeffreys measure and average Hurst exponent.

The average fractal dimensions for classical music, rap and rock are given in figures 6.13(a), 6.13(b) and 6.13(c) respectively.

(a) Average fractal dimensions for subject 1 listening to classical music. $D_0 = 5.3$

(b) Average fractal dimensions for subject 1 listening to rap music. $D_0 = 5.5$

(c) Average fractal dimensions for subject 1 listening to rock music. $D_0 = 5.5$

Figure 6.13: Plots of average fractal dimensions for subject 1 listening to different kinds of music

As can be seen from the three previous figures, the Hausdorff-Besicovitch dimension of classical music is less than that for rap and rock music. This means that the EEG signal while listening to classical music is less fractal and chaotic than the other two. We can say that the subject is in a more relaxed state while he/she is listening to classical music.

The average Jeffreys measure for classical, rap and rock is given in Figures 6.14(a), 6.14(b) and 6.14(c) below.

(a) Average Jeffreys measure for subject 1 listening to classical music. $J = 0.026$

(b) Average Jeffreys measure for subject 1 listening to rap music. $J = 0.029$

(c) Average Jeffreys measure for subject 1 listening to rock music. $J = 0.029$

Figure 6.14: Plots of average Jeffreys measure for subject 1 listening to different kinds of music

The figures clearly show that for classical music the rise of Jeffreys measure is smoother than the other two. The value of the average Jeffreys measure is lower in the case of classical music (~ 0.026). The average measure for rock and rap remain equally high (~ 0.029). This means that the EEG diverges farthest from relaxed state in the case of rock and rap music with rap being more disturbing than rock music considering the slope and rise of Jeffreys measure values.

The average Hurst exponent for subject 1 listening to classical, rap and rock music is shown in the following Figures 6.15(a), 6.15(b) and 6.15(c) respectively.

(a) Average Hurst exponent for subject 1 listening to classical music. $H = 0.9$

(b) Average Hurst exponent for subject 1 listening to rap music. $H = 0.84$

(c) Average Hurst exponent for subject 1 listening to rock music. $H = 0.85$

Figure 6.15: Plots of average Hurst exponent for subject 1 listening to different kinds of music

The main value to be noted here is the Hurst exponent at the end of the processing. In all cases the value is higher than 0.5, which means that the system has some memory of past events and is influenced by the past events. The H value for rap and rock music is lower than that of classical which again reiterates the fact that rap and rock music affect the EEG more than classical music.

6.3.2 Subject 2

After collecting the EEG data for subject 2 listening to the three kinds of music, analysis led to the following observations for average fractal dimensions, average Jeffreys measure and average Hurst exponent.

Average fractal dimensions for subject 2 listening to classical music, rap music and rock music are given in Figures 6.16(a), 6.16(b) and 6.16(c) below.

(a) Average fractal dimensions for subject 2 listening to classical music. $D_0 = 5.3$

(b) Average fractal dimensions for subject 2 listening to rap music. $D_0 = 5.4$

(c) Average fractal dimensions for subject 2 listening to rock music. $D_0 = 5.5$

Figure 6.16: Plots of average fractal dimensions for subject 2 listening to different kinds of music

At first glance, there is not much of a difference between the values for all three cases. But upon noticing the maximum values, we see that classical music has a lower maximum D_0 value than the other two. Rock music has the highest maximum D_0 value. Hence, we can say that EEG for subject listening to classical music is the least chaotic and for rock music is the most chaotic.

The average Jeffreys measure for subject 2 while listening to classical, rap and rock music is given in Figures 6.17(a), 6.17(b) and 6.17(c) below.

(a) Average Jeffreys measure for subject 2 listening to classical music. $J = 0.026$

(b) Average Jeffreys measure for subject 2 listening to rap music. $J = 0.026$

(c) Average Jeffreys measure for subject 2 listening to rock music. $J = 0.03$

Figure 6.17: Plots of average Jeffreys measure for subject 2 listening to different kinds of music

The analysis of average Jeffreys measure produces a small surprise. The values for classical music and rap music are nearly the same (~ 0.026) and, in fact, rap music has a smoother curve and lower average valued as opposed to classical music. This subject's EEG diverges more for classical music than rap music. Rock music has the sharpest rising plot and the highest value (~ 0.03) among all three kinds of music. It can be surmised that the EEG is most disturbed for rock music.

Average Hurst exponent values for classical music, rap music and rock music are given below in Figures 6.18(a), 6.18(b) and 6.18(c) respectively.

(a) Average Hurst exponent for subject 2 listening to classical music. $H = 0.865$

(b) Average Hurst exponent for subject 2 listening to rap music. $H = 0.87$

(c) Average Hurst exponent for subject 2 listening to rock music. $H = 0.85$

Figure 6.18: Plots of average Hurst exponent for subject 2 listening to different kinds of music

In this case too, the average Hurst exponent value is higher than 0.5 suggesting a memory and history effect. The subject's average Hurst value for classical and rap music are nearly equal to each other. Rock music has the lowest value and hence has lesser predictability as opposed to classical or rap music.

6.3.3 Conclusions for auditory stimuli

In both cases, rock music emerged as the music disturbing the mental state of the individual the most and thus the EEG signal. Classical music emerged as the least disturbing with rap music being in the middle and dependant on individual preference.

Hence, classical music is the most relaxing and rock is the most activating. Classical music can be used in cases where the subject needs to relax and not notice the music like when he/she is doing work. So, classical music can be used while relaxing, trying to study or do work. Rock music can be used in cases where the subject has to be stimulated like exercising in the gym, running or any kind of intense physical activity.

This observation also reinforces the real life use of classical music in lounges and lifts and usage of rock music by fitness clubs.

6.4 Conclusion

The analysis of the effects of different stimuli on different subjects gives interesting insights into the preferences of the individual. The observations and conclusions made in each section can be used by companies or marketers for developing highly specific products. Any stimuli can thus be analysed by the usage of the analysis methods and software to gain an understanding into the workings of the brain. The Jeffreys measure in each case gives a very good understanding of the extent of effect of stimulus applied in a quantitative manner.

Chapter 7

Conclusions and Recommendations

Modelling brain response has been a field with sparse work. The main problem facing researchers is the introduction of a complete model. With that problem in mind, we have proposed a novel phase-lagging model built from basic laws. This chapter details our research contributions and also suggests some directions for future work

7.1 Research contributions

We have outlined the problems present in current single action potential models. To alleviate this, we proposed a phase-lagging model which is based on basic laws like Conservation law, Ohm's law and Kirchhoff's laws. This model introduces a time lag and a constant velocity of propagation which eliminates the paradox of instantaneous propagation plaguing other models and even the classical diffusion equation. Solving this model gives a relation between the voltage in the neuron to its spatial derivative at any given moment of time and location.

Considering a single neuron and substituting the flux due to Sodium ion movement and Potassium ion movement in the solution gives us a plot of the single action potential.

This is a very important validation of the model proposed by us. We also provide plots of change in Sodium flux and Potassium flux which are in accordance with the observed behaviour.

Multiple neurons need to be considered as carriers of information about the applied stimulus. A single neuron is unable to carry the entire data about the stimulus. So, multiple neurons are activated with different frequencies to convey the entire knowledge of the stimulus.

The flux resulting from input of multiple neurons is modelled as a series of Gaussian pulses with varying means and standard deviations. We introduce this flux into our model and generate a plot similar to the plot of a multi-fractal time series like EEG. This reaffirms the claim that this equation can model the brain activity as a response to stimulus.

We introduce measures like fractal dimensions, Jeffreys measure and Hurst exponent for analysing the EEG signals. We also develop a software (FRATSAN), coded in VC++, for processing multi-fractal time series like EEG to obtain these measures and use them for deducing information from EEGs about the characteristics of the applied stimuli.

This software has been applied to data gathered from human subjects administered various auditory, visual and olfactory stimuli. The results obtained validate certain established practices (usage of classical music in relaxing and rock music in agitating situations, usage of blue color in hospitals and red for signboards) and lead to some interesting observations (odours being relaxing or agitating based on personal preference and not in a universal manner). The software is also going to be used in clinical trials for processing data from Intensive Care Units (ICU) and the National Neuroscience Institute (NNI) as an additional method of analysing EEGs.

7.2 Recommendations for future work

This thesis has proposed a comprehensive model for brain response to external stimulus. With this work as basis and looking into the future, we recommend future work in the areas outlined below.

7.2.1 Phase-lagging model

The model manages to model single action potential as well as brain response to inputs from multiple neurons. It can be made more accurate by the following points:

- Better understanding of the coding mechanism of neurons - We have taken the flux from multiple neurons to be modelled as a series of Gaussian pulses. This is a fairly good assumption of the coding mechanism. But, further work done in deciphering exactly how neurons code the stimulus as action potentials can help in making the model output more relevant to the kind of stimulus applied.
- Inclusion of memory and emotions associated with stimulus - Human beings are emotional creatures. Every stimulus that we administer to the subject has a memory which leads to a emotional response. This does affect the brain output. Further work in understanding how these memories and emotions affect the brain response will help in building a specialised model.

7.2.2 Data collection

- Increased sensitivity of equipment - Currently, the Mindset 24 machine used for collection of EEG data has a data collection rate of 512 Hz. As mentioned before, TECHNION is working on a machine that can measure data at a rate of 40 kHz.

This will make pin-pointing the brain response more accurate and will yield a wealth of data that can be analysed to provide some interesting insight.

- Reduction of environmental influences - The lab in which the measurements are made plays an important role in the reduction of noise and artifacts in the EEG signals. Hence, a dark, insulated room with a controlled environment will lead to cleaner EEG signals.
- Inclusion of more stimuli and subject conditions - This work could benefit from inclusion of more subject conditions like sleeping, meditating, hypnotised and drugged. This could expand the database of EEG signals and also brain response under varying mental conditions.

7.2.3 FRATSAN software

- Multi-threaded processing - As more computers get equipped with multi-core processors, the processing time of the software can be reduced by reprogramming it for such processors. Multi-threaded processing will also managed to analyse huge amounts of data in shorter time periods.
- Detrending analysis - For computation of the measures, the signal could be made free of any trends or influences. Many methods like detrended fluctuation analysis or diffusion entropy analysis can be used to remove such trends to lead to a more accurate calculation of the measures.
- Introduction of multiple analysis methods - There are many methods to analyse data and obtain the same measures as used by us. For ex., we use rescaled range analysis for computation of Hurst exponent. There exist more methods like power spectral analysis, variogram analysis and roughness length analysis for obtaining

the same Hurst exponent. Introducing such varied methods could provide the end user with many options with which he/she can ascertain the various measures.

- Usage of different plotting component - We have used PlotLab for VC++ to plot the output from the program. This component however does not allow us to change the axes and the axes values to what we may need. Usage of a different plotting component may help the user to have a fair amount of control on the output plots.

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