APPROACHING NEURODYNAMIC COMPLEXITY AND ITS INFORMATION CONTENT AS A COMPLEX DYNAMICAL NETWORK

A Thesis

by

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ABSTRACT

The human brain is a subsystem of nature's macroscopic ensemble whose time-varying behaviors serve to optimize the representation, manipulation, and even creation of information within its own structure to adapt towards the constraints of the environment. These dynamical characteristics serve to optimize the conditions of survival based on evolutionarily developed motivations, prior experiences, and instantaneous opportunities. To feasibly and efficiently perform these tasks the brain operates on a high degree of complexity resulting in its high level of adaptation towards the environment. As a result, the governing laws of nature is embedded in the brain's structure. It is infeasible to comprehensively represent these laws from any single perspective, therefore, to attain a more comprehensive understanding of how the brain functions and changes over time transdisciplinary approaches which consider the brain from multiple perspectives are absolutely necessary in painting a more complete picture of brain dynamics. Consequently, this study approaches the brain from its fundamental biology and the governing laws of physics which can be used to characterize complex network dynamics utilizing the general framework for complex networks. This methodology can characterize network dynamics at the macroscopic levels using information entropy and at the microscopic levels by establishing the dynamical energy level of individual constituent behaviors and their respectively time-varying interactions. Furthermore, the dynamic frequency components can be extricated at the microscopic and macroscopic level to establish the unique information content of the network (which is a product of a unique physical temporal evolution of frequencies). This approach aims to uncover the ambiguities in regard to the brains architecture and can not only aid progress in neuroscience but can provide a governing new philosophical approach towards assessing the highly nonlinear and potentially chaotic character of complex networks, ubiquitous in our world, thus having broad

reaching implications. This study provides a preliminary foundational framework to build upon towards achieving a deeper understanding towards complexity in the brain and further apply this philosophy towards complex network in general.

DEDICATION

I am nothing without my environment. Brief existence in this world (24 years as of the time of this writing) has blessed me with unique abilities and experiences as all humans have undergone. In my situation, these have made me realize, individual accomplishments and accolades are incomparably negligible to the grandiose scheme of our surrounding environment including the current state of society and its established knowledge and philosophies from the arts to the sciences building the quality of Mankind's existence. Therefore, to improve the state of things, one must further develop the overall knowledge and understanding to guide the progression of the current state of society for our future just as the giants, leaders, and innovators of the past (whose shoulders we stand upon) have done for us. My time has only begun as part of this cycle, and in recognizing this beautiful truth, I wish to dedicate absolutely every single moment of the precious ability bestowed to me in my finite life to contribute towards the relatively infinite legacy of our collective environment and in turn, maximizing my positive contribution towards the harmonious progression of life's macroscopic ensemble.

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NOMENCLATURE

DOC	Degree of Coupling
EMD	Empirical Mode Decomposition
FT	Fourier Transform
HHT	Hilbert-Huang Transform
IF	Instantaneous Frequency
IMF	Intrinsic Mode Function
LTD	Long-Term Depression
LTP	Long-Term Potentiation
STDP	Spike-Timing Dependent Plasticity
AMPAr	α-Amino-3-Hydroxy-5-Methyl-4-Isoxazolepropionic Acid receptor
NMDAr	N-Methyl D-Aspartate receptor
$\nabla\mu$	Electrochemical Gradient
α	Total Cross-Sectional Area of Available and Activated Ion Channels
J_{flux}	Diffusion Flux
q_{ion}	Charge per ion
R	Gas Constant
T	Temperature
Z	Ion Valency
F	Faraday's Constant
V_i	Voltage
Q_i	Charge
Ef	Electric force

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1. INTRODUCTION AND LITERATURE REVIEW

1.1 Overview

Nature's organization is understood by the brain through the underlying patterns of the environment's information content [1, 2]. Through limited observations, this is complex to say the least. Such inherent complexity is certainly not random or arbitrary and is governed by fundamental immutable physical principles rendering the emergence of intricate configurations of systems and subsystems from the macro to the micro scales which vary over time. Often, such dynamical complexity produces highly nonlinear or even chaotic behaviors making analysis, interpretation and understanding of such phenomena difficult, to say the least. Regardless, the brain is remarkably able to adapt and find stability in regard to a wide variety of scenarios by comprehending the information posed by the environment and generating a suitable response which typically optimizes its probability and conditions of survival. These neurological phenomena, along with established scientific fields ranging from biology and chemistry to physics and mathematics, are rooted in identifying certain underlying principles (patterns of information content as governing laws due to the intrinsic underlying order in highly nonlinear dynamical observations in natural phenomena [3]. Thus, the patterns of information content in Nature's organization are not only used by the brain but are qualitatively and quantitatively characterized in the established knowledge in our various fields of science and mathematics (e.g., branches of biology, chemistry, physics, mathematics, etc.) [4-6].

Furthermore, this conventional understanding has been developed by isolating various system components in highly specific testing and experimental conditions. Thus, foundational principles in neuroscience establish certain biological mechanisms of the brain. Furthermore, the sciences in general have developed foundational principles from the laws of quantum and classical

mechanics to preliminaries in cell and gene theory in biology are developed from this reductionist perspective [7]. Hence, a highly detailed understanding of certain individual components in the brain and natural phenomena is developed. Neuroscience, technological, medical, and even philosophical progress in society has been spearheaded by such approaches resulting in the current state of knowledge in society as it stands today.

Significant progress has been made in the past 200 years; however, more recently it is becoming implicitly apparent that a bottleneck of stagnation in progress is occurring. In other words, the current reductionist approaches are becoming insufficient and inefficient to sustain the next stage of progress [8]. That is because the true nature of natural phenomena in the brain and elsewhere rarely entails system components which can be perfectly isolated to manipulate and produce behaviors in an idealized experimental (or theoretical) scenario. Natural phenomena entail nonlinear macroscopic higher order systems which are composed of smaller-scale subsystems created from a variety of interacting components whose cumulative local interactions producing the global complexity commonly observed in weather trends, stock market fluctuations, and brain dynamics. Further detail upon this will be elaborated upon in future sections. Thus, despite significant progress in various fields of society, we are reaching the limitation of how far the current methodologies can take us displayed by the various impending bottlenecks limiting progress. This is seen in the classic Von Neumann computing architecture which has been the framework for computing since the days when vacuum tubes used to serve as transistors. Agreeably, computing performance has come a long way with incorporations such as the Harvard architecture; however, the fundamental philosophy is the highly similar limiting the maximum possible efficiency attainable resulting in bottlenecks for progress [9]. Advancements have certainly been achieved in our technological prowess in the past years and with much painstaking

effort and manipulation, society can reproduce and manipulate idealized scenarios observed in our tools today; however, this may not necessarily be the most efficient route or even a sustainable option to continue the propagation of progress in neuroscience and society in general.

The complex network dynamics exhibited by the brain enables producing far-more efficiently operating systems than achievable by current purely reductionist methods. For example, the information processing ability of the human brain is comparable to what is achievable by super-computers. Both are physical systems operating under fundamental constraints; however, power consumption of only a few watts by the brain achieves computing performance that rivals (and can beat) that of supercomputers which can consume enough power to supply a small city. This all is not meant to purely bash on reductionism as these past methodologies have garnered significant progress; however, it is clear that additional methodologies beyond pure reductionism is necessary for the next stage of progress in neuroscience and society.

Therefore, despite significant progress in neuroscience in establishing the details of certain fundamental physiological components within the human brain over the years, an overall understanding of brain dynamics is remarkable rudimentary. Patients with Alzheimer's, Parkinson's, or even different degrees of depression are given temporary cures which simply address symptoms and not the root pathological causes. Approximately 20% of American's experience a form of mental or neurological health conditions as reported by the National Institute of Mental Health. Beyond the negative personal impacts, these entail significant economic tolls as well. These issues are due to the current understanding of brain dynamics and function which are still in its early stages of maturing. This is a limitation to the propagation of research and innovation in a wide array of neuroscience applications. Therefore, it is the aims of this study to firmly establish that a transdisciplinary perspective upon the human brain is necessary to usher the next

stage of progress. Years of adaptations in the environment has embedded the complexity of Nature in the brain's own organization. In other words, evolutionary fine-tuning has directed neural cell populations and neural cells (themselves being a composition of subordinate individual parts such as protein subtypes and even smaller scale molecular components) to interact with one another from the microscopic to the macroscopic scales producing efficient global organizational structure observed as the human brain. It is becoming apparent that no one perspective alone is sufficient to comprehensively characterize the dynamical complexity present in the human brain, therefore this study approaches the brain from a variety of perspectives to attain a more universal understanding of neurological phenomena (which may also shed light on the highly nonlinear and sometimes chaotic nature of our world in general). Real-world complex systems (composed of smaller-scale subsystems which are composed of even smaller-scale constituent parts) such as the brain can be modeled as a complex network.

1.2 Literature Review

Complex networks [10] are ubiquitous in our world. From individual people interacting with one another composing social dynamics [11] to birds (or drones) flocking together producing self-organized swarm behaviors [12,13]. Such complex networks are macroscopic systems whose global behaviors are the result of its local microscopic properties (cumulative interactions between individuals). Self-organization [14] encapsulates the mutual collaboration of many individual parts to formulate a collective ensemble coordinated global dynamics offering greater chances of stability and even survival against external disruptions. Furthermore, despite the obvious differences in specific system, the nonlinear dynamical complexity present in emergent self-organization carries certain universal characteristics which are similar across different specific

disciplines [15]. This universality breaks the conventional pure reductionist approach to better comprehend complexity through a transdisciplinary perspective [16].

Complex networks exhibit similar characteristics and break the lines of separate scientific disciplines by unifying diverse seemingly unrelated fields with the underlying universal similarities of complexity and chaos [17]. Examples of complex networks are abundant in various disciplines. Technological networks such as power grids [18] to swarms of unmanned aerial vehicles [19], social networks [20] such as epidemic suppression [21] to political propaganda [22], and biological networks such as protein-protein interactions [23] to ecological patterns [24] all can be modeled, characterized and even controlled as complex networks provided that the inherent system dynamics, nonlinearities and constraints at the global and local levels are accurately accounted for. The brain, the focus of this study, is composed of around 100 billion neurons coupled with each other with 100 trillion synapses representing a monumental dynamic, nonstationary complex network. Due to the sheer size and complexity of the brain regarding its large number of individual constituents and possible connections and taking into account the dynamic nature of each of these components, the brain is one of the most complex and dynamic systems available. Therefore, the proposed methodology for improving the ability to understand and comprehend complex neurological phenomena can not only be a cornerstone for propagating research in neuroscience, but also a foundational cross-disciplinary framework for the characterization and control of complex networks in general which has ubiquitous applications in technological, biological, social and natural phenomena only to name a few. The focus of this thesis will be upon the human brain; however, it is emphasized that the underlying philosophies has far and broad reaching consequences beyond neuroscience which is a target for future studies and work.

1.2.1 The Brain as a Complex Network

The human brain is one of the most dynamically intricate networks molded by nature capable of performing a wide array of activities effectively and efficiently [25–28]. Operating on a high degree of complexity, brain dynamics consist of rapid reconfiguration of network states driven by interactions between network constituents to optimize temporal global evolution [29,30]. Constituents from the micro to the macro scale, such as neural cells, cluster to brain nuclei, and regions interplay with one another to compose an instantaneous, dynamical form of the brain, which serves to interact with the environment [31,32]. Brain dynamics are unified across its spatiotemporal scales to work in concert to coordinate an instantaneous current representation while simultaneously maintaining active recollections and processing of prior experiences, along with evolutionary developed, primal, raw, emotional contexts, which can influence future trajectories and goals for the brain [33, 34]. Constituent parts or subsystems of a network have unique responsibilities in contributing towards the overall time evolution of a network [35,36]. Thus, components of the brain cooperate and, in some cases, compete with one another from the micro to macro scales to direct and determine temporal evolution of the network's global behaviors [37]. Examples of these include neocortical modulation of amygdala activity to initiate higher-order cognitive regulation upon potentially fearful stimuli [38]. This interaction illustrates how activity produced by limbic regions (amygdala and associated areas), which provide primal emotional motivations such as fear, is regulated by contributions from the neocortex, which provides more complex forms of information manipulation, rendering higher cognitive thought to assess the initial appraisals of emotional response (such as fear) with more logic [39]. Furthermore, local activity from these regions are routed to one another via the thalamus, a relay center in the brain capable of coupling neocortical activity with a variety of localized subcortical structures.

The resulting collaboration (or competition), sways global network trajectory towards a particular path [40]. The brain must simultaneously organize and process these various modes of information to construct an instinctual network system reaction, ensuring coherent brain behavior. Information is physically transmitted via configured patterns of electrophysiological neural activity. Upon accomplishing this, the brain can contextualize its network state within the time-varying environment. Learning from previous experiences, executing current actions, and preparing future expectations consists of these dynamical capabilities, enabling the brain to optimize the variety of possible opportunities posed by the time-varying environment, ranging from scavenging food to maneuvering social situations and assessing potential sexual partners.

Naturally, these tasks are highly multidimensional, necessitating the brain to operate with a substantial degree of complexity to not only participate but excel at such behaviors [41,42]. Furthermore, the brain itself is not a single, one-dimensional entity; it is a multidimensional macroscopic network ensemble consisting of smaller-scale constituent parts. Consequently, it is the cumulative interactions of these subordinate parts or subsystems that direct global brain behaviors towards replicating multidimensional forms that can recognize, interpret, and react by generating a desirable system action that influences or manipulates external factors, such as the environment or other constituents. Typically, these actions are not arbitrary but correspond to attempts to benefit the probability and conditions of an individual's survival (not excluding interactions/relations with external stimuli). To successfully coordinate this, neural architecture must be capable of filtering and translating relevant information from the environment in its own time-varying structure to comprehend and react to its surroundings [43–47]. Cytoarchitecture of the brain can represent this multidimensional variation of information over time within its own dynamical form by orchestrating the activity of ensembles of neural populations. Information is

encoded within the unique firing patterns of such neural circuitry that represent individual recognition, understanding, and action in the environment. Thus, information representation capable of storing experiences and underlying motivations, as well as initiating actions, is embedded in the dynamical variation of unique patterns of electrical activity in the brain supported and modulated by neural, physiology providing stability for these dynamics [48].

Controlling the microstate configurations of neural biology corresponds to producing unique macrostate emergent behavior or representation of information by altering the interactions of unique patterns of local electrical activity, giving rise to diverse global behaviors. Thus, by fine tuning the coupling (interactions) between neural cells through various modes of plasticity (synaptic, axonal, and dendritic), microstate reconfigurations can modulate and refine macrostate behaviors on a variety of time scales corresponding to the speed of the various biological mechanisms [49]. The dynamical interplay of billions of neural cells coordinated by trillions of connections fosters effective and directed information transfer necessary for undertaking brain activities while balancing stability (to maintain a particular global form) and plasticity (being able to change, refine, and adapt global forms) [50]. The brain can control and steer the various possible configurations of a network to encode information pertinent to its conditions of survival.

1.2.2 Information Representation by the Brain

Complex information can be expressed physically as a unique composition or pattern of dynamical behavior. In the brain, this composition consists of the unique temporal and spatial evolution of neural activity [51,52]. Illustrated in the time evolution and distribution of neuron action potential firing rates across the brain, neural cells (including glia) are responsible for directing this time-varying evolution at the microscopic scale. Furthermore, individual neuron

action potentials do not operate in isolation but can influence or be influenced by other connected neural agents (individuals to population). If every single constituent were operating with disregard to its coupled neighbors, the emergence of higher-order patterned behavior would be difficult to produce. However, if agents can coordinate their behaviors, the collective effort is able to much better steer and influence global dynamics. Thus, neural individual agents act collaboratively to form higher-level neurodynamic rhythms [53]. In other words, the coalescence of individual neural firing mediated by connections between individual agents creates larger-scale brain rhythms commonly seen in global patterns, such as the bands of frequencies of electrical activity (corresponding to the rate and distribution of action potential activations of neurons) in the brain. Therefore, the form of higher order emergence such as local synchronization amongst populations of synchronized neural cells and global distribution of multiple synchronous modes (and sometimes asynchronous interactions) is essential to better define (and potentially control) overall network trajectory.

Information, encoded in the rate and time evolution of electrical activity in the brain, is fueled by patterns of collaborative and competing frequencies of action potentials. Synchronous agents collaborate with one another to achieve higher levels of stability and influence while asynchronous dynamics compete with each other battling for influence in directing overall network directions. These are necessary to consider and filter all forms of relevant information to determine what action must be taken to optimize survival in the environment (by exciting and depressing respectively relevant and irrelevant information). A helpful analogy follows to aid clarity in how information representation is accomplished via patterns of neural activity: fundamental letters in the alphabet in particular configurations can produce a large variety of words, and these words enable configuration of further complex forms, from sentences to books, conveying information.

Similarly, neuron action potentials are a fundamental building block for the dynamical repertoire of the brain, enabling higher-level information to be expressed as a unique patterned time evolution and spatial distribution of action potential firing. For example, raw sensory information is initially converted into electrical impulses capable of being transmitted to the central nervous system for further processing. Acquired sensory input is collected and translated into comprehensible information in the form of neural firing patterns. Broad information is then functionally segregated as specialized regions of the cortex process sensory stimuli to extract relevant features, such as visual and auditory information [54]. Upon sensory identification of the state of the environment information, the brain incorporates this information to form a global contextualization of the network regarding previous experiences and the current situation to determine a suitable response [55,56]. In other words, appraisal of external influences allows complex phenomena to be further dissected and understood with respect to internal network states. The physical medium for such information transfer is via activation of distinct patterns of neural activity.

From this, brain dynamical responses integrate discretized meaning into fluid understanding to formulate a suitable response. In other words, brain organization is structured to segregate information (assess sensory input) and integrate information, constructing an instinctual network system reaction, ensuring coherent and directed brain behavior [57]. This qualitative form is precisely quantified by the unique spatiotemporal spectra of frequencies in the brain representing information necessary to process input and contextualize said input with prior memories and evolutionary fine-tuned motivations to formulate a desirable system response observed and experienced in brain dynamics.

Qualitatively speaking, information contains meaning and can be physically represented [58]. Quantitatively, unique statistical signatures, such as variations of probability distributions

(different standard deviations of the normal distribution), define degenerate forms, of which one can exist at an instant in time as a physical manifestation to encode distinct forms of information. The brain aims to generate unique statistical distributions to identify internal or external stimuli. Thus, to differentiate objects and scenarios and annotate meaning towards unique conditions, the brain must be capable of producing unique configurations that are able to differentiate one piece of information from the next while ensuring survival in a time-dependent environment. In other words, the same pattern of neural activity cannot be used to represent two different forms of information. Sufficient differentiation (based on the capabilities of the brain) between patterns of neural activity is necessary to respectively distinguish different phenomena. This includes wielding different dynamical states (spatiotemporal distribution of neural activity) in recognizing emotional states, varying from fear to hope to external scenarios, such as predatory or friendly encounters. Distinct dynamical states (active network configurations) are necessary to distinguish scenarios from storing memories and executing actions to future planning and wielding subcortical motivations. Naturally, performing these tasks requires resources in the form of energy. This certainly has limitations, as physical energy constraints cannot create a limitless possible combination of stable configurations. With respect to energy conservation, hierarchical structures confer the efficient ability to organize the brain in a manner optimizing the finite number of relevant functional states the brain can morph into from stable physiological structure to produce wide-ranging adaptability [59]. Such architecture of complexity for dynamical configurations carries unique statistical signatures or characters at an optimal point between changing form and maintaining a current state. In other words, certain fundamental characteristics are held constant to minimize energy use while higher resolution refinements are built upon this structure resulting in a hierarchical architecture. Therefore, hierarchical structures are conducive towards

coordinating state transitions which minimize energy use and maximize the amount of relevant information representation. This can optimize information detection (input) and information presentation (output) from and towards the external environment (and internal states) in attempts to optimize survival. In seeking such unique dynamical configurations, self-similar structures emerge in the brain across scales to efficiently produce broadly adaptable dynamic behaviors. Self-similarity seeks to optimize network stability and plasticity by reinforcing network coupling configurations which correspond to efficiently being able to change or adapt dynamics while simultaneously maintaining reliable, stable forms in the face of adversity (battling a competitor for resources). In other words, a hierarchical structure confers efficient adaptability to the wide range of perturbations that may seek to disrupt the brain. Statistically self-similar (or fractal) structures can be found throughout the brain, conferring these necessary attributes and ensuring successful survival [60]. Qualitatively speaking, this can be thought of as producing the distinctive style or personality of an individual brain network in terms of the unique route an individual may choose to take in terms of isolating a single path towards a solution to a problem with many possible solution routes. In other words, this allows the brain to filter the variety of information present in the environment to direct energy towards relevant stimuli and consequently adapt in a way that attempts to minimize the action required to change form by holding certain fundamental signatures in the brain as statistically similar throughout its spatiotemporal scales. The medium for filtering information by the brain is fine-tuned and refined since birth (and even prenatal development) and is absolutely important to ensure efficient operation within the environment as there is often superfluous amounts or forms of information which may not be relevant (or even distracting) in regards towards optimizing the conditions of survival. Fine tuning this information processing ability is accomplished through neuroplasticity mechanisms over years and as all dynamic events

(time-varying phenomenon), this requires precious energy to perform. To conserve the most valuable resource of energy, this fundamental information processing and filtering ability of the brain needs to operate upon a self-similar architecture to efficiently fine-tune its underlying physiology towards a configuration which optimizes information interpretation and even modification from and towards the environment respectively. Optimizing information processing through neuroplasticity is observed as the brain performing or seeking tasks which improves its conditions of survival. The result of this underlying phenomena is the underlying values, morals, principles and in essence "the way of thought" of an individual's brain network seen by a distinctive personality. It is important to note that the brain's selected distinctive path may not necessarily be the absolute theoretical path of least action; however, it is a path chosen based on prior successes (through individual experiences or evolutionary fine-tuned configurations in neural architecture). Therefore, neural dynamics may not always perform perfect calculations which use the absolute theoretical path of least action in performing tasks. However, it is noteworthy that despite its imperfections, fundamental architecture of the brain tends towards finding the optimal path of least action as this is the asymptotic limit for maximizing efficiency and optimizing survival within the environment. Millions of years of evolutionary pruning has likely eliminated network configurations which deviate significantly from such efficiency (as they were less likely to survive and reproduce due to lower levels of efficiency in neural information manipulation). The following paragraphs give an overview of tools and methods which can be used (and have been used) to better understand such neurodynamical complexity.

The concept of information is useful in ascribing meaning entwined with logic towards different variations or patterns observed in the environment. As all things in nature, these variations of patterns are supported by the underlying energy distribution. In its most fundamental

form, energy takes the physical form of quantum particles, and their interactions compose the higher-order structured patterns and phenomena ranging from variations of molecular components to enzymes, proteins, cellular components to living organisms and even large-scale social networks commonly observed. Clearly, the overall amount of information in such a macroscopic system is significantly large. In fact, a complete illustration of the underlying information content in the environment is not feasible for analysis under reasonable means by the human brain. Despite these limitations, the brain is still able to operate, survive and thrive within the environment as it has adapted to filter the wealth of available information and devote its precious finite limited resources and time towards information which is most relevant to its survival conditions. Thus, brain capabilities have been geared towards a variety of relevant phenomena which filter the large amounts of available information to extract the most important perceived properties from the environment. For example, these include developing abilities which are proficient in select areas such as recognizing facial cues that can steer the quality of social encounters and consequently sway social status which significantly influences conditions of survival.

Fundamentally, these computational abilities of the brain are geared around optimizing representation, manipulation and even reorganization of information (represented by a unique time evolution of underlying frequencies within the brain's dynamical properties). The ability and degree of proficiency in learning new forms or patterns of information and even creating new patterns of information efficiently is qualitatively characterized as intelligence. If there were no energy constraints, relevant information can be represented by a variety of distinct physical configurations; however, energy is finitely distributed. Hence, encoding information by distinct physical configurations (which costs energy) must be efficiently done. Therefore, a self-similar structure is utilized to efficiently construct the wealth of information the human brain can process

as this architecture minimizes creating distinct physical configurations (minimizing energy use). It must be noted that despite similarities, a self-similar structure implies small differences and these small differences (while minimizing energy use) are manipulated to capture, represent or even create new forms of information. Therefore, an optimization point between minimizing energy consumption and maximizing information representation is found by the brain. As described previously, information is represented via a unique time evolution of frequency response within the brain's dynamics. Different patterns of frequencies in different contexts encode respectively distinguishable forms of information. Thus, information capacity is maximized within the energy capabilities of the human brain to improve the efficient operation of a neural network within the constraints of the environment. The ability of optimizing information representation is at the heart of the phenomena of intelligence. A distinct pattern of information can be identified by a network macroscopic and microscopic state along with the unique time evolution of the networks underlying frequency components at the ensemble (macroscopic) level and constituent (microscopic) level. This implies that advancements in producing intelligence (such as creating artificial intelligence more like human intelligence or even greater) lies within uncovering the intricacies behind the aforementioned phenomena. To summarize the above, as the brain adapts within the environment, rather than reorganizing its structure from scratch (for different adaptative behaviors), refinements are simply built upon the same fundamental structure rendering a unique style or personality for an individual's neural network to operate efficiently. The quantitative underpinning of this phenomena will be described in the later sections.

1.2.3 Complex Brain Network Dynamics Characterization

Concepts from statistical mechanics can define global dynamics by establishing relations between the microscopic and macroscopic state. A complex network is indeed a statistical mechanical system with energy distributed amongst constituents and their couplings. Therefore, the total energy can be defined by a probability distribution function, which changes over time with respect to the energy variation of individual ensemble constituents and their connections (consequently portraying the global state of the ensemble). The probability distribution of energy can be further defined using information entropy (or Shannon entropy) to describe the state of a complex network. Hence, stability or instability can be quantified with the corresponding information entropy and how it varies or fluctuates over time. Additionally, higher values of entropy correspond to a wider range of distribution, indicating less orchestrated collective behavior, whereas the opposite indicates more ordered ensemble dynamics gearing towards synchronized behaviors. Thus, information entropy can be used as a quantitative metric to assist bridging the character of global network states stemming from local behaviors. A further detailed description can be found in the referenced literature [61].

Brain dynamics are defined as the global neural processes that direct the network's evolution in time, commonly seen and experienced by the processing of sensory input and formulating a corresponding output [62]. These are typically observed in the change of the characteristics of the brain seen in the time-varying properties of the cumulative neuronal assemblies [63]. Experimental approaches observe this in the electrical activity of groups of neurons through electroencephalography (EEG) measurements or blood flow across brain regions through blood oxygen level dependency (BOLD) analysis via functional magnetic resonance imaging (fMRI) and how these properties change with exposure to new input [64,65]. It must be

noted that these methods do not explicitly isolate component neuronal activity. For example, fMRI detects changes in blood flow related to brain activity (formally described as BOLD analysis). Naturally, as the brain evolves over time, resources are redistributed by altering blood flow, which is detectable through fMRI; however, the resolution of this observable change is not sufficient to delineate the firing properties and patterns down to the scale of individual neurons. In addition to limitations of spatial resolution, fMRI-centered BOLD analysis lacks the temporal resolution to identify the time evolution of a neural component's firing patterns at the millisecond scale [66]. On the other hand, it is also difficult to isolate component neural activity at sufficient resolutions using EEG, as the detected EEG waveform is a superposition of dynamic electromagnetic activity, including local field potentials generated through the cumulative ionic flux in and out of the cellular space [67]. Additional techniques using magnetoencephalography (MEG) detect changes in magnetic fields resulting from dynamic electrical currents produced in the brain from neuronal activities. These represent examples of observed changes in brain structure and function [68]. The interpretations of these methods have been refined over the years with the addition of advanced techniques [69,70]. Whereas concrete claims remain elusive due to a lack of temporal or spatial resolution, a commonly observed theme is that there is no stationary state of the brain [71]. For example, classical EEG experiments have framed brains as nonequilibrium systems along with the observation that unique patterns of EEG waveforms acquired from the olfactory bulb correspond towards information processing of specific odors [72]. These established studies make it apparent that the brain does not remain in a static configuration; its form changes to varying degrees over time. Therefore, the brain is fundamentally a nonstationary system without an equilibrium point that utilizes its biological capabilities to detect, interpret, and respond to the dynamical environment. Portions of this complexity are apparent through observable neurodynamic rhythms

seen in EEG or fMRI recordings. Despite this recognition, the exact underpinnings of this substantial degree of complexity are among the core questions, ambiguities, and mysteries of modern neuroscience.

It must be recognized that significant understanding has been achieved through the earliest developments in neuroscience accomplished by Cajal and Broca, along with more recent undertakings utilizing the tools developed in network sciences, which have contributed to the development of a transdisciplinary perspective. Neuroscience research has been traditionally led by animal models, advanced neuroimaging techniques, brain tissue sampling, and separation methods [73–75]. These procedures have generated notable accomplishments, such as having a fundamental knowledge in identifying neuronal cell-mechanisms, structures, and functions, including dendritic and synaptic regulation, to identify and classify individuals, connections, and populations of neurons. Conventional approaches in neuroscience have led this progress; however, a comprehensive understanding of brain dynamical phenomena is still lacking in terms of how local and global cognitive mechanisms interplay simultaneously across multivariate scales.

A transdisciplinary field of network sciences has emerged over the past 20 years in attempts to address complexity in the brain and other complex networks and has met with limited success, particularly in helping to realize that a transdisciplinary perspective is necessary to guide the next level of progress in neuroscience. A review of the merits and limits of conventional network sciences follows. Traditional network science has been spearheaded by graph theory, defining individuals in a network as nodes and their interactions as edgewise connections between nodes [76]. It is important to note that this is purely a mathematically driven formalism that is not necessarily driven by fundamental physical law. Small-world and scale-free network models have influenced the development of established network theories over the past 20 years [77 54,55]. For

example, graph theory developments have been used to topologically describe networks and have been translated into anatomical and functional brain networks [78]. These are suited to capture small-world topology, such as highly interconnected hubs and modularity prevalent in the brain [79]. Additional topological properties of complex networks, such as hierarchies, centrality, and network hub distribution, have also been realized in this process [80]. Using serial reconstructions of electron microscopy, a complete connection matrix of the nematode C. elegans has been accomplished and described as a small-world network [81]. Furthermore, using combinations of physiological and anatomical techniques, multielectrode activity recordings have generated reconstructions of cellular networks in the neocortex, and diffusion tensor imaging has developed a map for cortical and basal brain gray matter areas [82]. The interplay of these methods has inspired a plethora of studies, models, and reviews [83–86]. These archetypes represent characteristics observed in networks under limitations. The assumptions underlying these limitations for small-world and scale-free networks must be considered when determining real-world applicability. For example, the network description is time-invariant, which neglects the dynamical elements inherent in all complex networks. Misrepresenting the dynamics can lower the accuracy of analysis at best or lead to catastrophic failure at worst. If the local interactions in a network are static, the global dynamics are adulterated and insufficient. Temporal networks are developed in attempts to compensate for this [87]. These models help represent the time-varying qualities of network structures, such as multilayer dynamics [88,89]. Whereas these help in developing tools better geared towards the dynamical aspects of complex networks, many of these methods still are plagued with the limited applicability of graph theory. For example, interactions represented by stationary edgewise connections between individuals lack the highly nonlinear features present in networks with diverse connections between individuals, groups, and large

populations (composed of smaller groups and individuals) [90]. Misrepresentation of this fundamental nonlinearity and dynamics renders traditional methods inept for comprehensive analysis and control. Additionally, a pure mathematical representation of a network ensures quantitative precision; however, the current state of network sciences does not necessarily intertwine this foundation with fundamental physical laws, compromising its comprehensive accuracy.

Without dispute, these advancements have led to significant developments in understanding human brain physiology and function; however, the consensus in the literature and scientific community is that a comprehensive fundamental and intuitive understanding is still amiss for human brain phenomena. Progress is limited, as the complete characterization and interpretation of coupled neuron activity is still in its rudimentary stage, and the current practices are not able to capture a comprehensive picture of the ensemble of neurons within the human brain. This barrier prevents advanced progress in neuroscience research, pathology, and a general, intuitive understanding of brain functional processes. A prime reason for this is that these methods either do not have the resolution needed to analyze the detail within the brain or they do not comprehensively account for the inherent time-varying nature of the neurons and their respective dynamic connections. Additional impediments in this challenge are not only due to brain intricacy but also the sheer size and scale of complexity of the human brain. With around 100 billion neurons and 100 trillion connections, mapping out a comprehensive dynamic model of the human brain remains an elusive asymptotic goal with the current methodologies. Simply put, the conventional practices are not made to address the grandiosity present in brain dynamics described previously. Therefore, a new method from a unified perspective with the capability of analyzing the characteristics of the spatiotemporal spectra of dynamical brain physiology is imperative to attain

a more comprehensive qualitative and quantitative understanding of neurological phenomena. A truly modern outlook on the brain surveying and observing its biological evolution under the physical constraints and laws of nature is amiss. Therefore, this study aims to provide a transdisciplinary perspective on the human brain in the hopes to inspire truly universal, comprehensive studies upon the brain to help aid progress in neuroscience.

1.3 Research Objectives and Deliverables

Therefore, the motivation of this study is to investigate the human brain to attain a deeper recognition of its underlying complexity in terms of its biological mechanisms and the governing laws of physics which determine the character of time-varying phenomena in nature. Therefore, a transdisciplinary approach is necessary to ensure the relevant physiology and governing physical laws are properly (and feasibly) accounted for to compose a more comprehensive illustration of brain dynamics and behavior. Furthermore, the knowledge and philosophies attained from this study can provide valuable information to fields beyond neuroscience. Apart from its implications in neuroscience, a deeper comprehension of the nonlinear dynamical complexity of the brain can be applied upon real world macroscopic network systems which entail highly nonlinear and even chaotic characteristics. A comprehensive, universal, and intuitive methodology upon such macroscopic complexity is sorely amiss with the current practices. As aforementioned, real-world phenomena rarely entail specific experimentally or theoretically idealized isolated individual components. Experimental conditions can be replicated in real-world applications with much painstaking (or even inefficient) energy expenditure. However, macroscopic dynamics seen in the time-evolution of real-world complex network systems entail of a variety of diverse interactions components with complex structures across hierarchical scales (from the micro to the macro levels)

rendering highly efficient performance displayed in the operation of brain dynamical physiology. Thus, a new approach is necessary to understand and even control such complex architectures which can be manipulated to improve the efficiency of society's current technological prowess and even philosophical ideologies. Efficiency is of paramount importance. In a world of finite distribution of resources, the degree of efficient distribution of resources ultimately dictates the quality and standards of overall societal living conditions and consequently, the degree of human suffering and happiness. Insight upon the details between the emergent properties of intelligence exhibited by the brain can elucidate on how to improve the efficient organization of information prevalent in a variety of disciplines.

Hence the implication and scope of this study are general to ultimately investigate the efficient biophysical complexity within the human brain to provide the foundational knowledge necessary towards optimizing the efficiency of our current practices. The established research and knowledge achieved in neuroscience is vast to say the least. It is infeasible to capture all of this information; therefore, the scope of this study is to focus on the most essential points to form a foundational approach which can be built off of for future further refined studies. The main findings are to be quantitative equations based on fundamental physical principles to represent the dynamical biology within the brain. This model is unique and diverges from the methodologies of previously attempts at characterizing the brain. Therefore, the deficiencies prevalent in these prior attempts will be resolved upon the completion of the proposed foundational model of the brain. Furthermore, these equations will be implemented in a numerical computational simulation and analysis of the generated data and results will be displayed to precisely pinpoint tools and patterns of information using a quantitative metric of time-frequency characteristics. Hence, the feasibility of the proposed approach (including the quantitative equations and metrics) upon the human brain

will be displayed by the analysis of the results. Furthermore, the exact analysis of different patterns of information will be displayed by a unique patterned time evolution of the frequency components of a network at different levels (microscopic and macroscopic). This is to show that encoding of information is physically represented by a distinct time-evolution of frequency components. Encoding different forms of information is naturally done by correlating different types of time-frequency components as the same physical patterns in the same context cannot be utilized to represent different forms of information.

2. METHODOLOGY AND APPROACH

2.1 General Framework for Complex Networks

To address this, a novel methodology to characterize and control the brain as a complex dynamical network is proposed in the following using the general framework for dynamic complex networks as follows. Complex dynamical networks are systems whose collective emergent global properties are the result of the nonlinear culmination of its local individual constituent behaviors and their dynamic couplings. The individual (local) constituents which compose the network ensemble exhibit dynamic, nonstationary behaviors and are coupled with each other to generate an amalgamation of overall (global) synchronous and asynchronous emergent patterns based on a desired objective and physical system constraints. The individual constituents and their respective couplings are intrinsically dynamic and transient with a particular degree of variance in the time and frequency domains. This dynamic nature of the local system properties is the foundational basis that allows the global collective properties of the system to have a high degree of adaptability and robustness to complex, time-varying environments or external perturbations to maintain the overall system stability and accomplish specific goals or tasks. In regard to the human brain, this pertains to how neuroplasticity, synaptic plasticity and even neurogenesis regulate the transient organization of neuron ensembles and their respective coupling strengths. From these arise complex functions such as learning and the storage and recall of information through the adaptation of synaptic coupling strength between neurons. This is a foundational basis for encoding information in the physical form of the creation of new thought, the ability to learn and memory retention and recollection. Likewise, other functions such as the processing of external sensory stimulus, sleep regulation including rapid eye moment (REM) sleep, involuntary body functions (temperature, breathing, blood pressure, heart rate regulation etc.), and the actuation of

physical movement are the results of the dynamic nature of neurons and their respective time-varying couplings. Consequently, a comprehensive understanding of a wide-array of human brain functions can be achieved if these neuronal dynamics are incorporated at the local and global levels. To actualize this, neural network system stability, characterization and control can be quantitively and qualitatively classified by implementing concepts from statistical mechanics which can characterize the local (microscopic) and global (macroscopic) system properties along with local and global system constraints simultaneously. Therefore, a relationship between the ensemble level (macroscopic) and individual constituent level (microscopic) must be defined to establish how the cumulative nonlinear interactions across scales (from the micro to macro levels) produces the emergent behaviors commonly observed in complex networks.

Thus, the exact configuration of a network structure is classified by the interconnectivity amongst the constituents of a network ensemble. These local connections (or couplings) must be dynamic to produce time-dependent global ensemble properties. Dynamic (time-varying) properties are fueled by energy. Thus, coupling strength (the magnitude of influence a constituent has upon another), must be defined fundamentally in terms of energy for all networks operating under the constraints of nature. Therefore, the local time-varying couplings in addition to the individual constituent dynamics can be defined in terms of energy. This establishes the network properties of energy at the microscopic level.

Due to limitations on resources, it is not feasible to determine ensemble dynamics by time integration of every single individual constituent behavior and interaction. Hence, an alternative option which has lower computational demands is necessary to create a much more feasible approach towards analyze real-world macroscopic networks with significant degrees of complexity.

Therefore, additional constraining factors at the global ensemble level is necessary to more comprehensively define network architectures. It is known that the cumulative energy of individual constituent behaviors and their connections results in a global networks probability distribution of energy. This feature can constrain and define macroscopic level network properties. Thus, the energy fluctuation for each individual constituent and their respective couplings must be constrained by the overall network's probability distribution of energy at all times. Furthermore, this ensemble level network property can be quantified by calculating the corresponding information entropy. Thus, information entropy can serve as a quantitative metric to define and constrain the global level network dynamical state. Therefore, ensemble level (macroscopic) emergent network properties can be determined using information entropy. The exact value of information entropy and the properties of its variation over time defines a unique state and temporal evolution of the emergent ensemble level network properties. Hence, information entropy and its variation over time can be used to determine, classify and target a global network state. As information entropy is a function of the distribution of energy, the underlying local constituents' behaviors and interactions within the network must be allowed to evolve and change within the constraint of information entropy (and how entropy changes over time). In other words, the local levels of energy for individual constituents and their dynamic couplings can only fluctuate amongst energy values which are confined by the global networks probability distribution of energy that is defined by information entropy. On the one hand, information entropy and its variation over time defines the emergent dynamical state of a network. On the other hand, information entropy is a function of the probability distribution of energy. Therefore, for a network system, local individual constituent time-varying behaviors and coupling dynamics must be constrained to particular

energy values that obey the constraints within the global ensemble's probability distribution of energy.

To summarize, all network systems evolution over time is fueled by energy. This macroscopic distribution of energy is not arbitrary but is normally distributed. Furthermore, the information entropy of the corresponding distribution of energy is a quantitative metric to define the overall dynamical state of a network ensemble. Therefore, upon establishing the information entropy of a network ensemble, the resulting distribution of energy can be found. Finally, constituent and connection strength energy levels must be allowed to fluctuate within this normal distribution as defined by information entropy. Thus, to incorporate the general framework correctly upon a dynamic complex network, the network must be defined in terms of energy. Hence a detailed understanding of the time-varying underlying biological mechanisms is necessary to feasibly characterize the energy distribution in a brain network.

The distribution of energy, and its respective information entropy, is a global network property to determine the dynamical state of a network whose underlying local constituents and their interactions are intrinsically nonstationary with a particular degree of variance in the time and frequency domains. This dynamic nature of the local system properties is the foundational basis that allows the global collective properties of the system to have a high degree of adaptability and robustness to complex, time-varying environments or external perturbations to maintain the overall system stability and accomplish specific goals or tasks. Thus, to apply this logic upon the brain, an understanding of the brain's fundamental local properties and how they change over time is necessary.

2.2 Biological Preliminaries

In human brain neural networks, this time-dependent process of adapting local configurations occurs in the form of synaptic plasticity [91] which is the change of connection strength (degree of coupling) between neurons over time (a more in-depth biological review is presented in later sections). The change of synaptic strength (analogous to connection strength) changes the interactions between the dynamics of individual neurons (neural firings rates) by adjusting the efficacy of neural information transfer (i.e., synaptic transmission). The connections between neurons are referred to as synapses and the presynaptic neuron is responsible for transmitting information while the postsynaptic neuron receives the transmitted information through its receptors. Therefore, the synaptic strength is a combination of how effective these two aspects function together. It is noteworthy that synaptic plasticity is one form of modulating coupling strength between brain network constituents. There are other forms of neuroplasticity which can occur on larger scale structures such as dendrites, axons and even groups of axonal fibers. For the scope of this study and this section, the focus is on synaptic plasticity; however, in the later sections other forms of plasticity will be discussed. In regards, to synapses, information is transmitted by the release of neurotransmitters by the presynaptic neuron. These bind onto the receptors of postsynaptic neuron, triggering an influx of ions which control the voltage of the cell and effect the probability of the postsynaptic neurons firing patterns. The change in the efficacy of synaptic transmission is bidirectional and can result in long-term potentiation (LTP, the increase in synaptic transmission) or long-term depression (LTD, decrease in synaptic transmission) [92]. This change of interaction between local neurons (interaction of individual neural firings) leads to a respective change in global dynamics by changing collective neural frequency firing rates [93]. The chaotic [94] dynamics represented by a change in the bandwidth of neural frequencies allow

for adaptations to external or internal stimuli which can result in the higher-level manifestations such as, evolutionarily adaptive behaviors, the solidification of memories and the formation of higher cognitive thought [95]. This changes the particular clusters of neurons which synchronize their firings thus altering the rate of activation of different neural circuits resulting in a modulation of the emergent asynchronous band of neural frequencies in the brain (the different emergent brain waves and their frequency components). These global system adaptations are the results of the nonlinear interaction of microscopic nodal dynamics in terms of information transmitted and received between constituents in a neural network. Long term synaptic plasticity refers to the bidirectionally adjustment of synaptic strength by increasing or decreasing connectivity leading to long-term potentiation (LTP) or long-term depression (LTD) respectively. Presynaptic plasticity controls an increase or decrease in neurotransmitter release while postsynaptic plasticity facilitates of the number and permeability of the receptors. The amount of information transfer is proportional to the amount of neurotransmitter release and the cumulative permeability of the postsynaptic receptors. Therefore, presynaptic and postsynaptic plasticity mechanisms consequentially control the change in the efficacy of information transmission and reception between neurons. By this, synaptic plasticity adapts the connection strength between two neurons to influence a change in global neural system dynamics and encode information. The connection strength is proportional to the magnitude of influence a neurons dynamic has on its coupled neurons. A brief overview on neuron physiology [96] follows for clarity and a detailed explanation will be conducted in the later sections. Neurons have semipermeable membranes which allow them to control their membrane potential in terms of voltage by controlling the influx and efflux of ions from the extracellular to intracellular space through ion channels. Neurons maintain an electrochemical gradient through having higher K^+ intracellular concentrations and higher extracellular Na^+ , Cl^- , and Ca^{++}, ionic

concentrations. This electrochemical gradient serves as the driving force for ionic flux in and out of the membrane which controls the overall membrane potential of the cell. Therefore, neurons communicate through voltage impulses (action potentials) through the transport of ions by ion channels across the cell membrane which result in sharp membrane potential depolarization and repolarizations activated at the cell body (soma) and travel in one direction along the axons of neurons to their axon terminals. At the axon terminals, synapses form the connection to the dendrites of different neurons (in general). Synapses serve as the medium for neural communication and the synaptic cleft consists of the presynaptic and postsynaptic sites. The presynaptic sites consist of the presynaptic membrane which is the point where action potentials traveling along the axon of neurons arrive to trigger the release of neurotransmitters into the synaptic cleft. The postsynaptic sites, built off the dendrites of neurons, consists of neurotransmitter receptors on the postsynaptic membrane. Released neurotransmitters from the presynaptic site bind to their respective neurotransmitter receptors on the postsynaptic sites and results in the processing of information in the form of excitatory or inhibitory postsynaptic voltage potentials. This refers to the increase or decrease in postsynaptic membrane potential. Thus, postsynaptic neurons receive information from neurons in the form of voltage changes through postsynaptic receptors. The dendrites collect these postsynaptic potentials relayed from the axons of connected neurons across synapses and this results in the overall change of the membrane potential of the neuron.

The postsynaptic neuron integrates the cumulative postsynaptic potentials received by its synapses from the presynaptic neurons which results in the overall postsynaptic neuron membrane potential (which has implications on the activation of neural firings). The initiation of action potentials (firing) of neurons is done by controlling the voltage of the cellular membrane potential.

The neurons resting membrane potential is held at ~ - 70 mV and if it receives sufficient excitatory postsynaptic potentials to elevate the membrane potential of the cell to a threshold voltage (~ -55 mV), an action potential is triggered. Excitatory or inhibitory postsynaptic potentials respectively increase or decrease the probability of activation of an action potential in the postsynaptic cell by bring the membrane potential of the cell closer or further from the threshold voltage. If activated, action potentials consequently travel along the axons to release neurotransmitters in their synaptic clefs which relay information to the dendrites of connected neurons in the form of excitatory or inhibitory postsynaptic potentials influence the probability of the firing of those neural action potentials. This is how information can be communicated throughout a network, through the firing, reception and transmission of electrical impulses by action potentials. These biological mechanisms and how they pertain to the magnitude and change of information transfer will be further elaborated upon in the later sections. Consequently, the synapse is the medium for information transfer between neurons by the transmission and reception of neurotransmitters. This can be qualified as the combination of neurotransmitter flux density by the presynaptic sites and the magnitude of reception by the number and permeability of the receptors on the postsynaptic site. Changing the efficacy of information transfer (i.e., changing the combined flux of neurotransmitters and their reception) is the basis of synaptic plasticity by changing the interaction between individual neurons. Therefore, this change in degree of coupling over time is the foundational basis for adaptation (i.e., the reorganization of a systems microscopic properties which correspond to stable global system dynamics.).

An understanding of how local individual dynamics effect coupled constituents and these local interactions influence the global organization of nodal behaviors is essential for a more comprehensive understanding of the stochastic nature of complex networks. The interactions

between individuals can be viewed, described and understood as the efficacy of information transfer between nodes in a complex network. Therefore, defining the degree of coupling in terms of how effectively information is transferred, is essential. General parameters to define this is how transmissive and receptive nodes in a network are. For neurons in the human brain, this unfolds as the cumulation of the flux of neurotransmitters by the presynaptic neuron and their reception by the receptors of the postsynaptic neuron. As briefly mentioned before, neural dynamics occur via the modulation of cellular membrane potentials in terms of voltage fluctuations. The cell membrane is semipermeable and lined with ion channels which (upon activation) allow for the influx and efflux of ions to change the membrane potential in response to stimuli from presynaptic neurons. At resting states, an electrochemical gradient is established. Typically, this results in elevated intracellular K^+ concentration and a higher extracellular Ca^{++}, Na^+, and Cl^-, concentrations. The electrochemical gradient serves as the driving force for passive ionic influx and efflux (which controls the membrane potential of the cell) upon the activation (opening) of cellular ion channels. Additionally, this gradient results in a resting potential. Neurotransmitters from presynaptic neurons bind on the receptors of the postsynaptic cell which activate the opening of chemically gated ion channels that allow the influx of ions causing excitatory or inhibitory postsynaptic potentials. Specific neurotransmitters bind to specific receptors which can result in the influx (or efflux) of positively or negatively charged ions thereby controlling the voltage of the cell with excitatory or inhibitory stimuli. If the neuron is sufficiently excited to a threshold voltage an action potential is triggered by the opening of Na^+ voltage-gated channels. Due to the previously established electrochemical gradient (a higher extracellular Na^+ concentration), Na^+ flows inside the cell resulting a sharp depolarization. Once the membrane potential is sufficiently depolarized, voltage-gated K^+ channels open. As there is a higher intracellular K^+ concentration, K^+ flows out

of the cell resulting in a cellular repolarization. This activated action potential starts at the cell body and travels along the axon of the neuron by the influx and efflux of Na^+ and K^+ respectively. Once the action potential reaches the axonal terminals, it arrives at the presynaptic membrane and activates the opening of voltage gated calcium channels. From the established Ca^{++} electrochemical gradient, Ca^{++} flows inside inducing the exocytosis of vesicles containing neurotransmitters by the binding of these vesicles on the presynaptic membrane to release neurotransmitters into the synaptic cleft. The amount of neurotransmitter release is proportional to the availability of a pool of readily releasable vesicles within the presynaptic membrane and the intracellular concentration of Ca^{++}. A higher concentration of Ca^{++} and higher amount of readily releasable vesicles (containing) neurotransmitters subsequently results in a higher concentration of neurotransmitters in the synaptic cleft. Furthermore, the concentration of neurotransmitters is affected by their diffusion out of the synaptic cleft into the ambient extracellular space, their degradation by enzymes and their reuptake by the presynaptic neuron to be reused for future vesicular release. As the neurotransmitters diffuse across the synapse, they bind to their specific neurotransmitter receptor on the postsynaptic membrane. Based on the type of neurotransmitters, this activates the opening of specific chemically gated voltage channels allowing for the influx of specific ions that can raise or lower the membrane potential (i.e., generate the excitatory or inhibitory post synaptic potential) based on the difference of voltage between the type of ion (K^+, Cl^-, Na^+, Ca^{++}, etc.) and the membrane potential. The influx of ions is a product of the number and permeability of receptors. A higher number and permeability of receptors results in a higher influx of ions which creates a greater magnitude increase in change of membrane potential and vice versa. The total number of receptors changes over time with respect to the transient change in intracellular postsynaptic Ca^{++} concentration. A higher intracellular Ca^{++} concentration results in an increase in

the number of receptors. Furthermore, the permeability of receptors is voltage dependent. Therefore, their availability for the influx of ions is nonstationary and depends on the membrane potential of the cell. The modulation of the efficacy of information transfer between neurons by adjusting the aforementioned mechanisms alters how local neuronal dynamics interact to reorganize their configurations and produce desirable adaptive group behaviors. This is done by changing the magnitude of neurotransmitter flux density and its reception in the synapse between two neurons. These two factors determine the efficacy of information transmitted and received between coupled neurons. As the field of neuroscience is constantly changing and developing with new research, the proposed equations provide a conceptual framework as a foundational basis to model and refine upon with further discoveries for more accurate brain simulations (or even experimental implementation).

2.3 Nonlinear Biological Interactions

This section will express the nonlinear nature of local interactions and how these contribute towards global network properties. After this section, details on global network properties (including the form and structures of higher order neurodynamic complexity) will be reviewed in detail. For now, the global state of brain phenomena is a time-varying ensemble, consistently changing to different degrees in accordance with factors within and without. Thus, brain phenomena are consistently nonstationary to different degrees in accordance with different environmental perturbations navigated through nonlinear interactions, propelling a wide repertoire of dynamics [97]. The properties of these local interactions determine global form and function. Therefore, to better understand the macroscopic brain, one must begin first with the brain's auxiliary local interactions. As they cumulatively dictate global function, local interactions

represent physical connections (or interactions) that deem the magnitude and direction of influence one agent has on another in a network and can be viewed as degrees of coupling [98]. These local interactions between connecting agents, regions, and subnetworks in the brain allow smaller-scale subsystems to coordinate with one another, composing coherent global forms by promoting coordinated local interactions, which engender stable global brain dynamics [99,100]. Thus, dynamical overall brain activity is nurtured through flexible configuration of local connectivity capable of generating a diverse variety of brain behaviors [101]. These include axonal architectures [102] with adaptive myelination [103], complex configurations of dendritic branching [104] and dendritic spine morphology [105], as well as the dynamic synapse [106], housing a multitude of pre- and postsynaptic mechanisms [107]. Importantly, each of these mechanisms is nonstationary and capable of dynamically influencing neural interactions along a wide range of spatiotemporal scales. Thus, local interactions range from (1) microscopic interactions between individual neurons and glial cells to (2) interplay between clusters of nuclei in the brain to (3) mesoscopic relations between different regions of the brain, to highlight a select few (out of the many scales in the brain). The cumulation of these interactions, along with others not mentioned or yet to be discovered, is built to fine-tune connections between local brain regions operating on a variety of temporal and spatial scales. Due to these diverse factors of coupling, which can change on a variety of time scales, interactions are fundamentally nonlinear in the time-domain. Furthermore, nonlinearity, observed in the dynamical interactions amongst a wide distribution of neural frequencies, engenders highly nonlinear characteristics simultaneously in the frequency domain. Moving forward, these produce highly nonlinear characteristics in overall spatiotemporal brain dynamics, enabling the unprecedented level of network reconfiguration observed and experienced in the human brain. Thus, the simultaneous nonlinearity in the time and frequency domains elicits

signature characteristics of chaos, which are essential for rapid reconfiguration of brain network states [108]. It must be borne in mind that the level of global complexity in the brain is a product of its local nonlinearities at the fundamental level. In other words, the flexible nature of the connections (interactions) between individual parts of a brain network across its many scales and modes of operation provides the network with multiple routes to efficiently and effectively reorganize itself to detect, interpret, and react within its environment. The following will provide an overview of the biological mechanisms which steer the nature of local nonlinear interactions (culminating into complex global emergence).

2.3.1. Synaptic Plasticity

The following is a biological review of the various modes of connectivity and plasticity in the brain engendering nonlinear interactions. Although by no means exhaustive, our review represents a fundamental foundation with references that convey the necessary important takeaways, that is, the variety of biological mechanisms for connectivity and how they can change over time to support dynamic brain function. Synapses are not stationary over time. They are highly dynamic, entailing a variety of presynaptic and postsynaptic mechanisms capable of changing over time to fine tune the overall efficacy of synaptic transmission and corresponding synaptic strength [109,110]. Thus, synaptic plasticity confers the highest-resolution modus operandi in the brain for controlling and modulating interactions between constituents with the smallest temporal and spatial scales possible. Presynaptic plasticity includes modulation of presynaptic intracellular Ca^{++} concentrations. This is primarily controlled by the function of voltage-gated calcium channels, which, when activated upon an incoming action potential, allow for the influx of Ca^{++} inside the cellular presynaptic domain. Correspondingly, Ca^{++} serves as a

secondary messenger [111]. As calcium has a high reactivity with a variety of substances, it serves as the ideal secondary messenger to relay information. Thus, biological form manipulates Ca^{++} reactivity to engender binding affinity upon different calcium-binding proteins. In the presynaptic cell, calcium forms a large signaling complex with SNAREs and associated proteins, triggering the binding of synaptic vesicles (containing neurotransmitters) with the membrane and consequent release of neurotransmitters within the vesicles [112]. Thus, regulation of voltage-gated calcium channels in the presynaptic domain has a significant influence on synaptic strength [113]. Furthermore, residual Ca^{++} from prior activity can influence vesicle release [114]. The quantal release of neurotransmitters freely diffuses across the synaptic space. Diffusion of neurotransmitters implies that they stochastically bind upon receptors in the postsynaptic domain. Probability of neurotransmitter binding is dependent on total amount or concentration of neurotransmitters [115]. Larger amounts of released neurotransmitters result in a higher concentration of neurotransmitters in the synaptic space, corresponding to an increase in the probability of greater numbers of activated receptors, resulting in an interaction with greater magnitude between pre and postsynaptic cells. Therefore, factors such as Ca^{++} concentration modulate synaptic strength by influencing vesicle release and, correspondingly, the total quantal number of released neurotransmitters. Furthermore, within the presynaptic domain, a pool of readily releasable vesicles is maintained to, as the name suggests, be released at a moment's notice upon action potential arrival (triggering Ca^{++} influx and consequent release of vesicles) to pervade the synaptic cleft with neurotransmitters. If these stores are exhausted by repetitive, higher-than-normal action potential firing, this may result in an overall decrease in the number of vesicles released, consequently reducing the concentration of neurotransmitters and vice-versa; factors that replenish or sustain a larger pool of readily releasable vesicles can increase the concentration of

neurotransmitters [116]. Extrapolating from this, synaptic strength can be influenced by factors that control the concentration of neurotransmitters in the synaptic cleft. Thus, enzymatic machinery responsible for reducing the neurotransmitter concentration in the synaptic cleft to reduce the neurotransmitter activation time also influences the time course of synaptic strength [117]. This is an essential mechanism to terminate a signal, thereby offering additional degrees of flexibility in fine tuning synaptic dynamics.

Furthermore, there are multiple neurotransmitter reuptake mechanisms (or neurotransporters) responsible for removing neurotransmitters in the synaptic cleft [118]. These can also be utilized for future neurotransmitter release; thus, while influencing the concentration of neurotransmitters in the synaptic cleft, they can also alter the storage of readily releasable vesicles, consequently influencing the possible concentrations of neurotransmitters in the future. Reuptake can be undertaken by neurons and glia cells alike and is driven by neurotransporters, which can offer additional degrees of freedom to modulate synaptic connection strength by altering neurotransmitter concentrations [119,120]. Additionally, it must be recognized that non-neuronal glia cells (such as astrocytes [121]) can also modulate synaptic transmission [122,123]. Their importance, along with that of other types of glial cells, such as astrocytes, oligodendrocytes, and microglia, has recently come to light, and as research progresses, this further illuminates the importance of a variety of cells (having clear dynamical roles) previously considered to have relatively stationary roles in the dynamical ensemble of a neural network [124–126].

Synaptic strength modulation by postsynaptic mechanisms is accomplished by controlling the availability and number of receptors on the synaptic site. A greater number of available receptors results in a higher probability that freely diffused neurotransmitters 1) bind upon receptors and 2) elicit a post synaptic response. In other words, receptor amount and availability are directly

correlated with synaptic strength. Therefore, postsynaptic plasticity mechanisms operate by modulating the properties of postsynaptic receptors. Receptor subtypes such as AMPAr and NMDAr play significant, dynamical roles in controlling factors such as receptor expression and availability [127]. Intracellular Ca^{++} concentrations once again play a large role as secondary messengers in modulating the expression of receptors. CaMKII and calcineurin are two examples of calcium-binding proteins, where the former typically initiates phosphorylation, typically resulting in long-term potentiation (synaptic strengthening), whereas the latter initiates dephosphorylation events that often lead to long-term depression (weaking of synapses) [128,129]. Of utmost relevance to synaptic plasticity, the intracellular Ca^{++} concentration regulates the expression of receptors. A higher Ca^{++} concentration increases the probability of Ca^{++} binding and activating protein units, resulting in AMPAr exocytosis [130]. A larger number of AMPAr results in a greater cumulative cross-sectional available area of receptors. Ergo, the flux of ions across the membrane multiplied by the cumulative greater cross-sectional area of the receptors (due to AMPAr exocytosis) results in an overall larger increase in postsynaptic potential, that is, a greater level of influence between neuron cells through a stronger degree of coupling [131].

NMDAr Mg^{++} blockage and relief of blockage via membrane potential excitation are at the core of controlling the direction and magnitude of plasticity [132]. This is based on temporal correlation of presynaptic and postsynaptic neuron firings [133]. Thus, the timing of interactions between presynaptic and postsynaptic neurons determines the overall amount of available NMDAr (relieved of Mg^{++} blockage). This is reflected by Hebbian learning rules illustrated through spike-timing-dependent plasticity (STDP). The general takeaway is that neurons that fire together wire together by increasing their mutual coupling strength [134]. The subtlety of this phenomenon has been pruned over time, and whereas the popularization of STDP clarifies how temporal correlation

of pre- and postsynaptic firing coincidence directs synaptic strength, it must be understood that this is a simplification of the actual underlying molecular and cellular mechanisms [135,136]. Although this simplification can be a helpful analogy, neglecting the fundamental details obscures the full repertoire of nonlinear dynamics supplanted by synaptic mechanisms. Imprecise truncation of the local nonlinear interactions renders severe alterations in global form and function, as opposed to more comprehensive incorporation of the full repertoire of nonlinear local interactions. When a postsynaptic cell fires after the presynaptic cell, there are greater numbers of unblocked NMDAr on the postsynaptic site that increase the overall receptor cross-sectional area for this uniquely Ca^{++} permeable receptor. Therefore, if presynaptic neuron firing releases neurotransmitters that diffuse across the synaptic site at the time when NMDAr are unblocked, ligand activation of the NMDAr results in an increased level of Ca^{++} influx. Consequently, intracellular Ca^{++} levels rise, increasing the probability of Ca^{++} secondary messengers activating AMPAr exocytosis. In some situations, different subtypes of AMPAr increase on the membrane that are also permeable to Ca^{++}, thereby increasing the probability of elevated Ca^{++} levels [137]. Furthermore, intracellular Ca^{++} concentrations can be modulated by internal release of calcium from intracellular stores. These can be controlled by metabotropic receptor activation [138]. Additionally, multiple types of receptors are expressed, offering a variety of mechanisms across a range of time scales. Of these, ionotropic and metabotropic receptors [139] are some of the most prevalent and widely studied. Ionotropic receptors (or ligand-gated ion channels) typically operate on a shorter time scale, whereas metabotropic (or G-protein-coupled receptors) have longer activation times and work over a longer time-period due to the additional metabolic steps necessary in between agonist binding and elicited postsynaptic response via ion flux. The variety of receptors operating on different time scales further engenders nonlinear interactions amongst constituents.

There is a wide multitude of forms of synaptic plasticity used in a variety of brain regions. The objective of this paper is not to provide a comprehensive description of all these forms but simply to provide the general foundations for the various modes of synaptic plasticity in the brain; references [140–143] provide more comprehensive reviews of synaptic plasticity. Magnitude of interaction is determined by concentration of neurotransmitters and cumulative availability of receptors. Direction of interactions (excitatory or inhibitory) is typically controlled by the type of neurotransmitter released. Thus, factors that influence these parameters control synaptic strength. As synapses are housed on axonal and dendritic structures, their properties also have significant influence on synaptic strength.

2.3.2. Axonal and Dendritic Structural Plasticity

Axonal and dendritic physiology further provide additional degrees of freedom to modulate connections between neural agents via structural plasticity [145,146]. For example, synapses are housed on dendritic spines, which offer stability to the synapse while supplying it with essential resources to support its activity. Thus, dendritic spine growth must follow synaptic dynamics. Should a synapse be particularly active, dendritic spine growth must increase to support a power-hungry synapse and vice-versa [147]. Dendritic spines provide structural support to synapses and can supply necessary resources which help in facilitate dynamical receptor functions (e.g., modulating receptor expression). Furthermore, dendritic spines help transmit electrical signals to the neuron's cell body, helping process input further. On the presynaptic end, axonal boutons also support presynaptic sites to supply synapses with resources, such as neurotransmitters, thus supporting synaptic strength [148]. Furthermore, dendritic branching [149] offers additional degrees of computation to neurons, increasing the degree of freedom with which neural

connectivity can maneuver. Axons confer additional methods for plasticity on a larger scale [150,151]. The axon is responsible for transmitting an action potential from cell body to axon terminal at its presynaptic sites. Myelin sheaths, produced by oligodendrocytes, are insulating layers encompassing axons made of protein and fatty substances that coat the axon to speed up action potential transmission through saltatory conduction. Naturally, the distribution of myelin carries significant implications for the temporal evolution of signal transmission throughout the brain. Axonal arborization can be particularly extensive, connecting a variety of brain regions. Hence, manipulating the signal transmission speed along axonal white matter tracts by controlling the distribution of myelin confers the ability to drastically change firing pattern interactions between relatively larger-scale (with reference to synaptic mechanisms) brain regions [152]. This from of plasticity is highly prevalent to adaptation in the adult brain [153]. Adaptive myelin plasticity modulates the growth and formation of myelin along axon bundles throughout cortical regions to modulate the speed and efficacy of information transfer. In other words, this can change the character of spatiotemporal frequencies of brain activity. High-resolution synaptic connections have been pruned through earlier experiences, restricting how flexible conformation changes can occur at this level. However, adaptive myelination is a form the adult brain commonly uses to refine signal transmission, albeit at a lower spatiotemporal resolution. This explains how young children, with fresh synapses, can learn new concepts to such a high level of resolution. Adults are still capable of learning through adaptive myelination; however, due to synaptic pruning in their youth, the resolution of detail that they can learn is not as refined. For example, an adult can learn a new language; however, it will be far more difficult to learn and achieve the subtleties of a native language speaker's accent.

The direction of such interactions is typically determined by the type of neurotransmitter used. For example, glutamate is used in excitatory neurotransmission, whereas GABA is used in inhibitory interactions. Furthermore, neurotransmitters can elicit modulatory responses. These can entail a combination of excitatory and inhibitory action [154,155] by being able to release multiple neurotransmitter types.

It must be noted that the preceding mechanisms are only the tip of the iceberg, providing a fundamental foundation to describe the various levels of intricate, detailed manipulation in neural connections fueling the emergence of complex brain dynamics. For a more comprehensive review where this subject matter is the main focus, the literature referenced above is recommended. In the context of this work, it is important to recognize that the variety of biological connectivity entails a wide range of capabilities in precisely fine tuning the nature of nonlinear dynamic interactions across the dynamical hierarchy of the brain.

Furthermore, previous studies have established a preliminary qualitative understanding regarding the underlying biological machinery of the brain. However, to develop further refined insights, these qualitative biological interactions must be quantitatively expressed to precisely encapsulate the inherent nonlinearity and coupling. This can enable further progress by addressing current limitations. For example, current methods lack the resolution and quantitative precision of enumerating global brain dynamics. A theoretical, numerical model describing coupling at the level of synapses can aid in providing a more precise quantitative description. As these global properties are a result of the nonlinear couplings between constituents, defining the degree of coupling (measure of influence between constituents) can aid in producing refined models and, consequently, a deeper understanding of the brain.

2.3.3 Local Interaction Induces Global Characteristics

As described, there is a broad distribution of plasticity mechanisms influencing functional, structural, temporal, and spatial behavior of neural interactions from the micro to macro scale. Furthermore, these mechanisms are not implemented in isolation but incorporated simultaneously, enabling different degrees of maneuverability in connection strength and direction. Consequently, these local interactions are highly nonlinear [156]. When combining these various components, global network dynamics are consequently nonlinear and, when undergoing complex dynamical evolutions, can display chaotic characteristics [157]. These are necessary for fluid multivariable adaptation, as the environment consists of a variety of nonstationary conditions requiring complex physiological form to not only ensure survival but to optimize conditions of survival (e.g., subcortical motivations, steering the quality of life, and gauging reproduction thresholds). Evolutionary adaptation has encoded a fundamental configuration for neural connectivity within the brain, resulting in its natural hierarchical order from birth. Life experiences over time fine tune neural connectivity with adaptive plasticity mechanisms to mold the adult brain. This refines a neural network's instinctive response to environmental stimuli in attempts to optimize its survival. From a higher-level perspective, global brain dynamics are the processes that steer the network to adapt within the constraints of nature. These are not static in time but highly time-variant from the micro to macro scale, structured in intricate layers of modular connectivity, allowing for coordinated, efficient, dynamic organization [158–162]. Therefore, unique microstate configurations (the exact individual behaviors of network constituents and the degree coupling between these network nodes produced by physiological configurations) determine the global macrostate emergent forms. Thus, the brain is a highly adaptive network whose characteristics change over time to interact with a nonstationary environment. Adaptation entails changing the

global properties of a network system over time in response to varying external input posed by environmental conditions. These macroscopic dynamics exhibit transitions from distinct states of global brain function to ensure stability (i.e., survival) in accordance with external situations. Different environmental scenarios, such as scavenging for resources, such as food and water; reading social communication cues; fight or flight response towards predators; sleep; and abstract conceptual thinking, necessitate a variety of distinct global brain functions created by respective microstate configurations of cumulative local neuron interactions [163]. As previously mentioned, the variety of macroscopic distributions (global brain states) is the result of the microscopic configurations of the ensemble's constituents, i.e., the cumulative behaviors and interactions between neurons mediated through their connections with one another, which regulate neural dynamical activity. Therefore, brain macrostate transitions in the form of adaptations to new environmental stimuli are also facilitated by changing the respective microstate configurations. In other words, this corresponds to changing the biological mechanisms between neurons and glia cells by changing the expression or availability of receptors between neurons or adjusting the concentration of neurotransmitters in the synapse. This is similar to how global phase transitions are facilitated by a change in the interactions between molecular constituents [164]. Brain network state transitions are directed by modulating the strength of synaptic and structural couplings between neurons, steering the magnitude and direction of local neuronal interactions that culminate into emergent dynamical trajectories [165]. The governing philosophy of a brain network is that the global level forms and their changes over time are the result of the local-level dynamical interactions of the constituents that compose the ensemble. Hence, the particular microstate configurations in terms of the exact myelin distribution across white matter fiber tracts, dendritic branching, and spine characteristics, along with synaptic efficacy determined by the product of

neurotransmitter concentration and receptor availability, cumulatively engender highly nonlinear connectivity. These relationships between network constituents are highly nonlinear and recursively couple upon one another across the temporal and spectral scales of brain activity capable of producing chaotic characteristics.

2.4 Complex Global Multimodal Synchronization from Local Properties

The hallmark of a brain network or any dynamically evolving macroscopic system is the ability to orchestrate collective, larger-scale action by coordinating constituent behaviors, generating higher-order levels of influence and stability (as opposed to isolated, uncoordinated individual actions). Interactions between network agents permit coordination of self-organized emergence. Furthermore, the highly nonlinear local properties of interactions allow for stable creation of a wide range of dynamical coupling levels. On the higher-order global levels, this enables flexible creation of a wide repertoire of neuronal circuit types necessary to determine the overall configuration and character of collective, larger-scale network states. Local interactions enable coordination in the form of creating larger-scale forms via gradients of constructive influences (mutually creating a stronger presence together) or destructive influences (interactions that inhibit one another) by controlling the alignment of individual action with reference to each other. For a multiagent network system with the sheer scale and complexity of the brain, ensuring stability or wide-ranging adaptability is directed by fundamental self-organizational principles that promote coordination (in the form of constructive or destructive interactions) amongst individual network components to achieve global network configurations that resonate towards external influences. Accordingly, interactions between multiple agents foster coordination and neuronal collaborations, which set the stage for global dynamical presence (from local collaboration). In

other words, interactions between neurons through their various modes of connectivity drive forms of emergence and self-organization. Hence, individual local individual component neural action, through collaboration with other agents, culminates into global brain rhythms and oscillatory activity, which have been recognized and established as hallmarks of brain activity for decades. Therefore, the particular configurations of connectivity across the brain determine how local neural activity interacts to respectively produce unique compositions of overall global network trajectory (quantitatively recognized as nonperiodic behavior [166]. Furthermore, it is known that the cumulative neural interactions compose a brain ensemble's collective global form in terms of neurodynamical oscillations of electrical activity supported by brain physiology. However, a detailed underpinning of how such global behavior is produced through local interactions remains ambiguous. Conventional studies emphasize local configurations, such as small-worldness and modularity, denoting respectively short average path length with high local connectivity and modularity describing dense intrinsic connectivity within a module, with sparse, weaker connections between multiple modules [167,168]. The idea that rich-club hubs (heavily connected nodes) promote global communication among modules has also been proposed, identifying a similar organization in a variety of neuronal systems ranging from the C. elegans nematode to the human brain [169,170]. Furthermore, this characterization suggests that structural architecture of the brain compromises wiring cost and its necessary computational ability. Additionally, a hierarchical organization promotes the effective and efficient function of such structures. Thus, past methods have identified the stationary emerged global form using small-world and high modularity descriptions, with scholars hypothesizing as to why such emergence occurs. However, this still does not explicitly identify how such complex global organization emerges in the brain. Furthermore, it does not comprehensively define the dynamical transition between these

stationarily defined states. In other words, a fundamental understanding of how complex dynamic collective organization is accomplished through local interactions in the brain is sorely lacking. Furthermore, a small-world and modular structural configuration is not explicitly correlated with the dynamical function of the brain in the previously mentioned literature. Small-worldness is ubiquitous in a variety of networks throughout nature. Simply recognizing this in the brain, therefore, does not elucidate significant unique meaning in neuroscience advancing our comprehension of the brain [171]. What it does imply, however, is that there are fundamental universal laws that govern the nature of complex networks, including the brain. However, a broad assessment of small-worldness does not explicitly convey why such emergence occurs and is necessary to support complex the collective dynamics observed in the brain and complexity in general. Therefore, in the following, section, we aim to provide a more detailed understanding as to how global dynamical brain phenomena fundamentally emerge from local configurations, as well as how this structural form is necessary to maintain stability towards a variety of internal and external scenarios by engendering a variety of complex functional spatiotemporal phenomena, a hallmark of healthy brain activity. This has yet to be clearly identified in the brain and must be fully understood to sustain progress in neuroscience. Understanding synchronization would help to assess the emergence of the broad spectrum of neurodynamical frequencies across scales [172].

2.4.1 Synchronization

The context of synchronization phenomena provides a backdrop for understanding how such emergent self-organization can occur [173]. Synchronization is a fundamental form of collective organization where local interactions amongst oscillators, biological or otherwise, result in coordinated global behaviors [174,175]. Emergence of this form typically carries a higher level

of influence and stability as opposed to the uncoordinated actions of isolated individuals. Characteristics of synchronization amongst a population of oscillators are determined in the brain by the physical connections through which neural cells interact. Thus, plasticity mechanisms that can modulate the magnitude and direction of local network interactions can control the global, self-organized forms of synchronization. Synchronization was first formally observed in the 17th century in the undulatory interactions of pendulums placed within close vicinity of each other. Regardless of asynchronous start times, two pendulum clocks, when placed next to each other mounted on a beam, synchronized their oscillations exactly in phase with each other. Their individual motions were not isolated but coupled to one another via the physical mount they were placed upon. Thus, individual oscillatory motions of each pendulum were transmitted as vibrations through the physical mount, interacting with one another. Through interactions, a dominant, emergent frequency of synchronized physical action was displayed by the oscillators. In this scenario, physical coupling led to the constructive and destructive wave interferences, resulting in an emerged synchronized frequency. Over time, further research was conducted to characterize biological oscillators and how this mutual interaction could be used to produce stronger group collective efforts, increasing probability of survival, as the oscillatory rates amongst a population of coupled nodes is typically normally distributed about a center frequency [176].

Synchronization is ubiquitous in nature, as it allows for the creation of global patterns of coordinated movement at a particular frequency (rate of oscillation over time) [177,178]. Self-organization emerges from the cumulative interactions of numerous constituents. Therefore, synchronization is a type of interaction amongst a population of agents who align their individual behaviors by adapting their coupling strengths to constructively amplify their dynamics as a group. This is an efficient method for creating global organization, as multiple agents' collaboration

directed towards a common goal can accomplish a task with more stability and persuasion than uncoordinated individual actions. This constructive interaction creates a stronger collective presence as a group capable of withstanding larger external disruptions and with greater influence to steer overall network dynamics.

Strongly coupled neural cells have a greater level of influence upon each other. They can more significantly sway the inherent probabilistic nature of action potential firing in one another. Such neurons can align their dynamics to amplify the activity of their firing frequency, which has a greater probability of influencing other coupled constituents and their behaviors. With larger numbers of synchronized neural oscillators, the amplified action potential frequency is much more capable of altering the trajectory of the global network, as opposed to isolated, undirected individual neuron activity. Therefore, self-organization in the form of synchronization amongst neural cell bodies is a common pattern observed in oscillators to produce stable dynamics that can have heightened impact on molding global network behaviors or better withstanding external and internal attacks. From these, it is observed that synchronization is one of the most fundamental means of creating global order in multicomponent systems. By adjusting the frequency of individual neural firings by adapting the connectivity between constituents, neurons can effectively shift their frequency timings to align their phases and collaboratively produce higher and more stable levels of influence in a neural network. In the human brain, the active adaptation of coupling strength between neurons is accomplished through synaptic and structural plasticity mechanisms [179].

Furthermore, this mechanism changes the degree of coupling (connection strength) and alters the frequency of synchronization (rate of neuronal firing) by which different forms of information are encoded. Thus, synchronization is a desirable form of organization to provide

order amidst highly nonlinear and potentially chaotic brain phenomena [180,181]. This is an efficient method for creating global organization, and such dynamical phenomena are supported by highly interconnected nodes, resulting in small-world structures. Highly interconnected nodes representing a particular module synchronized about a particular center frequency confer an efficient mode of collective organization, conserving wiring costs. This can explain the dynamical form and function of a structural population or cluster of highly interconnected neural cells. Synchronization can make an explicit local correlation between structural configuration and dynamical function (frequency of neural potential firing) [182]. As synchronization is a foundational building block for creating unified order amongst a population of neural cells, a richer understanding of synchronization can aid in better comprehension of complex phenomena, such as perception and even consciousness [183]. Quantifying synchronization in terms of frequency can aid in attempts to bind different perceptual features processed in the brain with mathematical precision [184,185]. A description follows in the next sections of how synchronization is used as a foundational local element to create further complex global forms in the brain.

2.4.2. Multimodal Synchronization

Whereas the previous can explain the emergence of a single mode of action capable of being represented by a respective frequency, the brain needs to operate on additional degrees of freedom to meet the variety of environmental needs, necessitating further developed complexity. The external environment is often complex, with multiple variables perturbing a network system at different time scales, requiring the simultaneous processing and activation of different spatiotemporal behaviors. For survival, these diverse conditions necessitate higher ranges of adaptability encompassing diverse temporal and spectral scales. Therefore, whereas

synchronization is a fundamental form of collective organization amongst numerous individuals (typically at one or a limited scale), brain complexity necessitates multiple forms of collective organization (across multiple scales) to direct the various modes of information internally encoded in the wealth of evolutionarily gifted underlying motivations in subcortical structures to more recently developed cognitive manipulations housed in the neocortex [186–188]. Synchronization gives insight into how small-scale interactions can produce large-scale behaviors capable of accomplishing specific tasks with a larger persuasion to withstand adversity through environmental disruption to maintain local stability. However, the magnitude and direction of this local influence at any one point in time is limited. Broad-bandwidth adaptation, or stability in a variety of scenarios, is produced through higher degrees of complexity. As the brain is responsible for simultaneously performing multiple tasks and handling internal and external dynamics, multiple modes of synchronization emerge to take appropriate actions across different temporal scales to incur broad-bandwidth stability [189]. Hence, at the cost of more expansive and diverse forms of wiring, brain physiology produces high-modularity structures capable of supporting multiple local modes of synchronization. The cumulative interactions of multiple modes of localized synchronous activity are necessary to produce the rich repertoire of the global ensemble of brain activity. Thus, clusters of synchronized populations of neurons are necessary to reliably perform tasks, relay information, or interpret sensory stimulus while withstanding a range of external or internal perturbations [191,192]. Brain nuclei, neuronal assemblies, and circuitry responsible for specialized roles in relaying unique patterns of neural activity with larger levels of collective influence emerged through these fundamental characteristics. Mutual interactions of multiple agents are driven by synchronization to create influential coordination (indicated by higher-power spectral response at a given frequency), which can be directed to initiate or trigger

communication between brain regions. Through a simple analysis of EEG or fMRI fluctuations, it is obvious that there is no one dominant global frequency of synchronization. However, there is a diverse distribution of multiple modes of synchronization at nonstationary amplitudes and frequencies interacting with one another to perform the beautiful dynamical evolution observed and experienced in the brain. Potentiation or depression of neural connections through plasticity mechanisms allows for changing of the amplitude of rhythms in the population of neurons to project their frequency information (AP firing rate) at altered spectral powers [193]. Furthermore, these projections alter the dynamics of larger-scale recipient neural assemblies and can gain enough collective strength to influence other cortical regions by recruiting synchronous neurodynamics. Thus, individual neuron firing can influence the firing patterns of other neurons across scales [194] if met with sufficient excitatory actions.

This increases the range of dynamical abilities for the brain, as synchronous populations of neural oscillators project information to excite or inhibit one another, competing for influence in directing global network trajectories. Different modes in certain configurations can represent different forms of information, from generating basic emotions from sleep or hunger to more complex forms in higher-order thoughts. Based on sensory input from the environment, along with internal interactions, a dominant pattern of neural activity emerges corresponding to a selected global network configuration, which corresponds to optimizing network stability. The coalescence of this neural firing mediated by connections (or interactions) between neurons creates such larger-scale brain rhythms commonly seen in global patterns, such as the frequencies of electrical activity in the brain. Naturally morphing this band of frequencies into a variety of possible distributions is difficult; however, certain hallmarks of nonlinearity and chaos enable highly effective and efficient reconfiguration of a neural spectral bandwidth by manipulating chaotic bifurcations towards

desirable transient states [195]. Thus, this dynamical flow of information representation as neural action potentials is not arbitrary but highly patterned, with rich underlying order that requires a hierarchical, multimodal form to efficiently coordinate rich dynamical phenomena. Efficient organization of this renders highly effective levels of computation, performance, and precision in multidimensional execution driven by biological wave interference constrained by the subtlety of neural action potentials [196,197].

2.4.3 Complex Forms of Self-Organization

Self-organization through multimodal synchronization directs this macroscopic ensemble as specialized populations of neurons synchronize to particular frequencies across the scales of the brain, producing global, asynchronous, multimodal neural frequencies (i.e., neurodynamic brain waves) [198,199]. The time-varying frequencies of these populations are modulated through the respectively dynamic interactions of connected constituents. Furthermore, different modes at respective spatiotemporal scales serve to encode dynamical information in terms of time-varying frequencies of brain activity to interpret, react to, and survive in an environment that also contains a variety of spatiotemporal perturbations [200]. These processes interact with one another to produce a bandwidth of neural frequencies (brain waves) that attempt to optimize interactions with external disturbances imposed by the environment. Brain physiology and anatomy facilitate these dynamical characteristics to ensure the flexibility of the neural ensemble to locally synchronize while also being able to globally influence the synchronous firing rate (frequency) of other neural populations through connectivity (e.g., properties of axonal arborization, dendritic branching, and synaptic efficacy) [201,202]. These are necessary to maintain stability amidst external attacks by adjusting the power of different frequency responses to excite or inhibit information via neural

signals, resulting in the performance of adaptive behaviors. Certain neural populations are synchronized to corresponding frequencies [203]. The unique interactions of these multicomponent dynamics enable modulation of frequency distribution and amplitude to encode different types of information [204,205]. Environmental interactions generally incorporate a variety of diverse phenomena, necessitating unique forms of information to distinguish certain attributes, i.e., distinguishing different frequencies of light, spatial curvatures, sounds, and moods of thought [206]. Consequently, a unique multimodal distribution of neural frequencies across the spatial and temporal scales quantifies the dynamical form of information representation. The cumulative interference of these spectra throughout the brain results in the overall composition of brain dynamics. The manifestation of previous experiences, current representation, and future trajectories is stochastically embedded within these spatiotemporal spectra [207]. Furthermore, the objective of the brain is to refine its possible instantaneous frequency distributions to optimize its performance in the environment. Thus, the overall goal of the brain is to steer its instantaneous spatiotemporal distribution of frequencies over time to optimize its conditions of survival by adjusting its interaction within the environment. This includes planning for future expectations based on previous experiences. Furthermore, these dynamical characteristics are supported by the evolutionarily fine-tuned microstate configurations of a neural network whose coupling configurations are further pruned by earlier developmental experiences, resulting in a unique physiological structure and thus the distribution of myelin, axonal, and dendritic organizations, along with the synaptic efficacy observed in the hierarchical and functionally specialized regions of the brain. Illustrated in specialized regions of the brain, these enable the coordinated emergence of synchronous populations responsible for unique roles in transmitting certain patterns of neural activity that collaborate in composing the overall behavior of the brain [208].

Thus, the brain can be conceptualized as a complex information processing unit, molding its neural physiology as an analog neural network [209]. Processing information through a medium of intricately coupled local action potential interactions (culminating into complex global trajectories), neural circuitry orchestrates interactions across the hierarchical scales of the brain, which combine individual action into collective group order. The latter is typically seen in overall brain activities and behaviors and can be quantified by multiphase, multiscale structures. In the context of memory, different scales of memory structures (working memories and past historical memories) are embedded across spatial scales (from the micro to the macro) and are dynamically observed at different frequencies (high to low). The range of dynamical frequencies are seen in brain behaviors from circadian rhythms occurring on the scale of days to cellular interactions operating on the scale of milliseconds. To encode different forms of information (from memories, or overall shifts in brain behavior), the pattern of dynamical frequencies orchestrated by the brain must be modified.

These modifications are facilitated through the nonlinear connections between constituents in a network [210,211]. Changing local connections (interactions) and their strength between neurons collectively incurs a shift in the global brain state to a potentially more stable (adaptable) form. Changing the degree of coupling between nodes can alter the spatiotemporal characteristics of information flow by altering neuron synchronization characteristics. In other words, this steers the information content of the brain, directing the trajectory of a neural network. As new signals from the environment change the input into the brain, different neural circuitries are activated to represent the new information and relay this throughout the brain [212]. As mentioned previously, this changes the time-varying properties of neural firing in the brain. Hence, over time, dynamical neural frequencies can establish different synaptic weight distributions across cortical regions

[213,214]. On a more general sense, the overall connectivity distribution (controlled by axonal and dendritic structures) can also be manipulated to further refine information representation (via altered neurodynamic spectra). This results in different modes of synchronization and a fundamentally distinct spatiotemporal distribution of neural frequencies. Qualitatively, we feel this fundamentally distinct state as the encoding of memories and experiences by our neural network. Furthermore, these can alter subcortical neural connections, slowly fine-tuning habits and personal preferences over time. The brain's mode of encoding information in the spatiotemporal dimensions of brain behavior involves adapting its frequency response accomplished by modifying the variety of locally synchronized clusters, producing global asynchronous dynamics capable of integrating the variety of information a brain network considers when directing its collective form [215]. There is no static state of the brain. The trajectory of a dynamical brain network is consistently being steered by different frequency components of neural firings (projected by synchronized nuclei) interacting and controlling the distribution of the spectral bandwidth, producing brain behavior.

2.4.4 Examples Observed in the Brain

To initiate sleep, the cortex inhibits afferent higher-frequency neural activity that is typically routed from the thalamus and activated by other brain regions. This assists the brain to inhibit afferents and the tendency towards falling asleep by reducing the power of higher-frequency neural oscillations and increasing the power of lower-frequency delta rhythms [216]. Transitioning into this spatiotemporal distribution of frequencies results in a global transition towards sleep. Processing and generation of information occurs over time to detect, interpret, and act within the environment [217]. Additionally, these neural frequencies serve to potentiate or inhibit information to excite or depress characteristics that determine global network stability.

Therefore, the frequency spectrum of brain rhythms serves to encode and propagate needed temporal brain behavior by processing environmental input and generating a global response.

Hippocampal memory index theory also illustrates how dynamical information exchange via spatiotemporal frequencies can be used to encode information to store memories. Neocortical activity projects and encodes unique connectivity configurations in the hippocampus. These can be stored and served as an index to the pattern of the respective neocortical activity by which higher-order thoughts encode the unique connectivity configuration. Thus, future scenarios can potentially activate this index, which, in turn, activates the corresponding neocortical patterns, resulting in an active retrieval of these memories [218]. This allows the brain to revisit past spatiotemporal distributions of frequencies (i.e., previous memories). Furthermore, due to the considerable manipulation of information by the neocortex, upon revisiting these prior memories, higher cognitive thought can review these situations they performed and potentially administer reappraisal to these memories [219]. Reappraisal is a method of reconfiguring these connections, which can enable an individual to potentially learn from prior memories and better adapt in the future (based on potential previous mistakes). Furthermore, this can reconfigure connectivity throughout the global distribution of the brain between the neocortex and other limbic regions.

Across these regions, hierarchical, modular, and fractal brain organization emerges to facilitate multimodal neural synchronization [220]. Such cytoarchitecture exhibits regions of statistical-self similarity to efficiently support the emergence of multiple modes of synchronous populations seen in repeated clusters of highly interconnected modalities [221,222]. In the cortex, this allows the brain to segregate sensory input into discernable and useful meaning as different modes at different spatiotemporal frequencies encoding information. Furthermore, a self-similar configuration allows the brain to reuse fundamental architectures and dynamical forms to conserve energy in

reproducing a variety of different brain states. This self-similar recursion of neural structures is also identified in the columnar organization of the neocortex, giving rise to higher levels of efficient information manipulation necessary to sustain fluid higher-order thought. Additionally, the entire domain of the brain (spatially and temporally) does not have identical degrees of self-similarity [223]. Different regions can have different degrees or dimensions of fractality necessary to support individual responsibilities. Modular brain hierarchies compose these regions to integrate respective information, forming appropriate brain dynamical responses [224]. This complexity is dynamically apparent in the brain through the emergence of bands of synchronized neural frequencies, each mode processing its respective received information and transmitting it to influence its coupled constituents, which cumulatively manifest into the dynamical structure of the brain. Specialized brain regions with unique roles and responsibilities collaborating with one another emerge from these properties. Each region consists of multiple modalities structured in unique ways to perform distinct roles. These regions communicate with one another to steer the global network evolution. Quantitively, this is represented by the bandwidth of neural frequencies (i.e., the frequency components of global brain rhythms) observed in different spatial regions of the brain. Dynamically, these produce brain waves from the delta, theta, alpha, beta, and gamma ranges, spanning from below 4 Hz to above 30 Hz, highlighting the variation in the spatiotemporal scales of a dynamical complex brain network [225]. Functionally and anatomically distinct brain regions with specialized capacities emerge from these principles. Therefore, multimodal functional integration is typically observed as the interaction of different frequencies (corresponding to the representation of forms of information). Large-scale integration producing a dynamical brain state is conducted through the coalescence of different frequencies mutually interacting to produce a bandwidth of neural frequencies at any one point in time. It is noteworthy that to maintain stability,

this band of frequency responses must be able to constructively interact with each other and environmental perturbations to optimize the probability of survival. In other words, unique synchronized modalities and systems with distinct roles emerge in a mutually beneficial relationship with each other to nurture a global composition of neural frequencies, which serves to constructively interfere with the disruptions imposed by the environment [226].

Globally, canonical circuits are recursively exercised to facilitate the flow of synchronous and asynchronous neural activity at different frequencies to compose ensemble brain cell dynamics. A modular organization facilitates the formation of different modes of synchronization [227]. These smaller units (modules) are where similar neural circuitry is iteratively repeated, forming a columnar organization, allowing for basis multimodal synchronous activity throughout modules enabling effective information transfer across scales [228]. Different modules (at different synchronized frequencies) can interact with one another to influence dynamical characteristics, thereby further processing information across scales. A structure of this nature allows for segregation or integration of complex, multi-scaled information, as previously mentioned. This fundamental cytoarchitecture is implemented from the micro to macro scales of the brain. That is, nuclei of brain regions and larger-scale structures serve unique roles and collaborate with one another through their interactions to produce a global dynamical brain state similar to how microscale columnar modules produce multiple modes of synchronous neural activity and interact with one another to process information. Thus, statistical self-similarity is exhibited across scales of the brain [229]. Spatially, this is observed in modular organization of neural populations, resulting in larger-scale brain nuclei and consequently producing different brain regions with respective degrees of statistical self-similarity. For example, the most recently evolutionarily developed part of the brain, the neocortex, is responsible for higher cognitive

thought [230]. This largest part of the cerebral cortex is organized into multiple layers of interconnected neural populations to facilitate efficient information transfer necessary to drive flexible conscious thought [231]. This region will have a different degrees of fractal dimension for respectively unique tasks (represented by distinguishable forms of information). The different lobes of the cortex are responsible for processing different types of information (sensory input, such as sight or touch, and sending out physical action output). Each type of sensory input is inherently composed of multiple components. Consequently, multicomponent inputs are segregated by cortical structure to discern valuable meaning with reference to what the brain already knows. After relevant information is extracted and understood by the brain, this dynamical organization of the cortex integrates this information with meaning attached to it to formulate an appropriate collective response. The brain interprets this information as a unique distribution of neural firing frequencies over time to understand the environment. Sensory input, in the form of a unique pattern of activity, interacts with cortical structures, eliciting a unique response by interacting with and then activating a unique pattern of neural firing frequencies. Unique synaptic weights (or microstate coupling configurations) create this macroscopic distribution of frequencies. As previously mentioned, these different forms of information are encoded via multiple modes of synchronized neural frequencies [232,233]. Different frequencies bifurcate to segregate information and contrastingly coalesce to integrate information. Thus, the organization of cortical physiology is responsible for accomplishing these tasks and interpreting and transmitting information. This distinct spatial organization created by layers of highly interconnected neurons facilitates the generation of synchronized neural firings amongst highly coupled clusters and fosters the interplay of multiple modes of synchronized neural clusters generating complex spatiotemporal neurodynamics [234]. Furthermore, these neocortical

dynamics are also influenced by subcortical activities. The neocortex receives sensory information routed from the thalamus [235,236]. These excitatory projections encode specific forms of information in signal attributes, such as the frequencies of action potential excitations. Upon this, a preliminary assessment of sensory input is generated. Consequently, the cortex can send projections back to the thalamus to process higher-order cognitive manipulation, which allows different layers of cortical connectivity to process information together. Furthermore, through the thalamus, the neocortex can send or receive information to and from subcortical structures (e.g., limbic regions, such as the amygdala) through higher-order relays to influence underlying motivation, emotion, bias, and perception [237,238]. Thus, thalamocortical and corticothalamic loops represent one example of how different regions of the brain collaborate with one another [239]. Importantly, the basis for information transmission by these regions is synchronized neural action potential activities. Additionally, these processes are modulated through the degree of coupling between constituents, by which the spectral power of neural activity is controlled across spatiotemporal scales over time. Therefore, structural and synaptic plasticity mechanisms excite (or depress) connectivity, propagating (or inhibiting) frequencies of synchronized populations recursively across the modular spatiotemporal organization of the brain. The interplay of these mechanisms allow for potentiating or inhibiting certain behaviors. These collectively produce (and adapt if need be) the multimodal dynamical ensemble of the brain. In other words, neural physiology is responsible for simultaneously providing stability to neural brain dynamics and degrees of plasticity when global dynamics must change or refine its organization [240,241].

Perhaps one of the most frequently observed brain characteristics representing how different regions of the brain communicate and interact with each other is neuronal ensemble oscillations (resulting from neural AP interactions), producing the vast degree of complexity in

neurodynamical phenomena [242]. The temporal correlation of activity across these brain regions (from the micro to macro scale) determines how strongly certain functional configurations are reinforced from the possible range of configurations produced by physiological structure. Multimodal synchronization allows for the complex algorithmic manipulation of information by creating centralized regions responsible for unique roles. For example, neuromodulator systems work in concert with one another to direct higher cognitive thought in prefrontal cortex activity [243]. These incorporate noradrenergic, dopaminergic, serotonergic, and cholinergic systems influencing each other while projecting and receiving signals to their respective targets. Having multiple systems responsible for specialized roles and coordinating their action amongst gives higher degrees of freedom for a system to encode information into meaning to perform a task. Together, these shape prefrontal cortex activity, which consists of a variety of subregions that send and receive information (via the thalamus) to and from other subcortical structures, from motor and sensory systems to memory and motivational state processing sites [244]. The magnitude, direction, and rate of these global spectral signals are manifestations of local constituent interactions.

The brain incorporates multiple mechanisms in performing a variety of tasks and effectively changing these tasks in accordance with its environment. These include initial appraisal of sensory input, discerning meaning from processing this information, and planning future action (or thought) based on the understood meanings. For example, as an individual is reading and taking in sensory input, the brain is simultaneously transforming the images of words into semantic meaning and cross referencing this information with previously known conceptions and new innovative ideas. (It is noted that this does not consider the simultaneous regulation of basic physiological processes, such as heart rate and circadian rhythms, to more complex refining of

subcortical motivations and primal instincts.) Clearly, the brain's complexity serves a necessary purpose of performing a variety of tasks briefly elucidated above. This enables integration of the vast amount of information present in the brain encoding personal experience, as well as previously embedded evolutionary adaptation constituting inherent predisposition to formulate a coherent system response encrypted and administered through the characteristics of spatiotemporal dynamical neural firing [245]. Sensory input is translated into meaning via a unique pattern of neural firing. The neurodynamic rhythms influence and interact with other brain regions, eliciting a sufficient response.

Furthermore, the structural network configuration produced by brain physiology must be functionally degenerate [246]. In other words, particular structural configurations must be capable of supporting a wide repertoire of functional dynamics to support brain function with respect to various environmental scenarios. These are supported by intricate structural configurations fine-tuned through developmental and experiential plasticity. Studies have identified this structural–functional degeneracy [247]; however, a clear explanation of how a single functional dynamical global state is selected out of the many possible states is lacking, and why this structural–functional degeneracy is necessary for the brain to reconfigure and adapt rapidly is unclear.

2.5 Defining the Brain Quantitatively

To be clear, a precise characterization of the brain in terms of quantitative metrics is absolutely necessary to develop a comprehensive understanding of the brain which can inspire progress in developing therapeutics or even support the implementation of brain machine interfaces. Thus, the global state of the brain can be described in terms of the emergent oscillations of neural activity [248]. This system is consistently perturbed by internal and external stimuli.

Internal stimuli can be patterns of local activity that interact with critical regions, gain influence, and threaten to sway the overall neural network trajectory for better or worse. This can be qualitatively observed as an individual thought that inspires significant change or, in pathological conditions (e.g., hallucinations, schizophrenia) where internal disruptions are not properly mitigated, may lead to network collapse [249,250]. External stimuli are typically in the form of sensory input. Processing of a variety of sensory information is accomplished by encoding raw sensory stimuli as unique patterns of neural activity that can trigger unique distributions in global neural activity [251]. This quantitative form encodes understanding, behaviors, and reactions in the global network. For example, sensory systems are hierarchically organized to extract relevant multicomponent information. Hierarchical organization is conducive to facilitating interactions between multiple frequencies of neural activity and is thus capable of efficiently harboring, processing, and morphing spatiotemporal spectra of activity across scales [252]. Sensory input, once converted into patterned electrical activity, thus activates unique compositions of the spatiotemporal spectra activity, encoding unique sensory information. Consequently, different types of sensory information are expressed as different spatiotemporal patterns of neural activity. These inherent variations, small differences in initial conditions of different types of sensory information, can elicit dramatic deviations in the processed results. Identification of an environmental scenario is represented by a particular pattern of activity, which is a construct of multimodal synchronous neural populations [253]. This composition of frequencies and various amplitudes (conveying sensory information) interacts with the activity of other brain regions (which are also producing a unique composition of neural frequencies and amplitudes). The consequent quasi-biological wave interference produces an emergent neurodynamical form of activity corresponding to reaction towards sensory input. In reaction to a threat in the environment,

this can produce spatiotemporal neural activity correlated with a fight-or-flight response. Small variations in initial sensory input and internal motivations, once processed throughout the cortical structure, result in the possible emergence of a variety of functional states corresponding to a possible fight-or-flight reaction. This selection of functional states occurs for a variety of scenarios, from simply deciding what foods to eat to determining a response in a social scenario. Additionally, the possible selected states may be chosen based on free-energy minimization principles to optimize network efficiency by conserving precious energy and maximizing productivity [254]. Furthermore, brain network structure degeneracy is limited [255]. Only a finite number of functional states can be represented (due to energy limitations); however, fine tuning of structural physiologies through plasticity mechanisms can enable the brain to refine its possible functional states and learn new configurations. Encoding new configurations (via plasticity mechanisms) occurs at a cost; however, utilizing a hierarchical structure can maximize the number of functional states that can emerge from a selected coupling configuration throughout a neural network. Naturally, selecting which structural configurations are necessary is dependent upon which functional states efficiently optimize an individual's survival. It is noteworthy that this reaction is almost instantaneous, as an instinctual response is orchestrated upon immediate detection of sensory stimuli. Thus, this is a highly efficient way to rapidly produce a global system response immediately upon interacting (or interfering) with the environment. Due to the resolution limitations of biological figures such as the brain, the response is not instantaneous, as there is always an inherent temporal lag in the brain network processing, interpreting, and reacting to the environment. Despite this, global system response occurs on the scale of milliseconds.

Thus, brain physiology refines its form through neuroplasticity to better adapt its degenerate functional dynamical forms, that is, its instantaneous spatiotemporal distribution of frequencies.

For example, the particular configuration of connectivity in evolutionarily older brain systems, such as the limbic regions, quantitatively provides different patterns of neural activity, which are qualitatively felt as aspects of emotional processing capable of projecting influential information upon the cerebral cortex and swaying the higher-order processing of emotion [256,257]. Complex forms of information manipulation accomplished by the neocortex allow for review of such fundamental raw emotions to better reconfigure towards a logical assessment should this lead to more optimal survival conditions. Orchestrating a complete physical reaction takes less than a second [258]. Purely cognitive reactions (mentally recognizing an environmental scenario) can take even less time.

Such agglomerations of different forms of neural activity mutually interact with each other to manipulate the flow of information in an attempt to direct a beneficial collective ensemble response. This entails creating a network structure which is capable of higher degrees of adaptation (in accordance with unique environmental situations) to better optimize all the opportunities external conditions may pose. Qualitatively, this can be thought of as the different aspects of consideration an individual recognizes when deciding what action or route to take. The harmony of these multimodal processes is essential to efficiently direct the trajectory of the ensemble towards obtaining dynamic stability in time with respect to the dynamical environment. In other words, these specialized modes of synchronization do not work in isolation but co-operate with each other with specialized roles to process and relay relevant information throughout the brain. Cross-modal reliance causes the distribution of synchronized frequencies to be highly sensitive to external and internal influences and changes [259]. For example, a slight variation in information transfer in one cortical area (new sensory stimulus) modifies the interactions with other cortical and subcortical regions. Thus, through cross-modal reliance, new information being transmitted

by a particular modality can have a cascading, rippling effect across the spatiotemporal scales of a network, which influences the reorganization of the macroscopic ensemble's frequency response, resulting in a global configuration towards a (in healthy brain function) desirable state [260].

Multimodal synchronization, observed as multiple frequencies of neural clusters mutually interacting, results in highly complex and nonlinear behaviors [261,262]. Scenarios ranging from chimera states to neuronal avalanches to explosive higher-order simultaneous synchronous and asynchronous states in dynamical networks are highly critical states that stem from different spatiotemporal scales of synchronization present in the brain [263,264]. The criticality of these states (stemming from the inherent nonlinear nature of the brain) is necessary to enable effective adaptation by changing the distribution of multimodal activity to better adapt to new deviations in a situation that necessitates a different form of emergent brain dynamics to maintain stability [265]. In critical states, certain perturbations or influences can bifurcate frequency responses and trigger neuronal avalanches [266,267]. In pathologies, these are not regulated and can rapidly deteriorate the state of the brain. However, in normal cognitive function, this is directed to produce a new brain state that is adaptable to the new environmental disturbances. Therefore, environmental input not resonating with the current state of the brain can engender network deterioration due to highly nonlinear and critically dynamic forms breaking down the previous functional states, allowing for new functional states to take place. If directed properly, transitions can be facilitated effectively to rapidly adapt brain form and function to create desirable configurations. Fight-or-flight response, high-pressure social communication, or simply waking up from a deep sleep in response to a loud noise are examples of global transitions that are highly nonlinear and effectively directed in most healthy brain networks [268]. There do exist certain pathologies that compromise the biological

mechanisms of brain function preventing the effective facilitation of these dynamical transitions [269].

Thus, the local degree of couplings between neurons controls global brain dynamics by changing the interactions between neural firings resulting in potentiating or depressing information. Increasing the degree of coupling (stronger connection) can reinforce particular patterns of neural frequencies to result in an increase in the influence of the corresponding spectral response in the global bandwidth of neural frequencies. Contrastingly, neural firings can also diminish the influence of certain spectral responses by depressing certain connectivity's. The emergence of these types is mediated by different degrees of coupling (interactions) to project or inhibit information based on whether it is desirable for the survival of the collective. Thus, broadband collaboration between constituents is the fundamental basis for complex behaviors commonly seen in the interplay of neural frequencies throughout the time evolution of a network ensemble. Neurons coordinate their individual actions with one another through their interactions to produce macroscopic oscillations across the spatiotemporal scales of the human brain. Based on assessment of the produced macroscopic interactions with the environment (in the form of how successful the brains distribution of neural activity is in accomplishing a task), neuroplasticity mechanisms can alter couplings to further refine the global distribution of neural activity if necessary (if performance improvement or change is needed).

Hence, a bandwidth of neural frequencies (quantifying the dynamical state of the brain) is simply the interaction of multiple synchronous clusters representing different components of information across the scales of the brain. The combined collaboration and competition amongst these dynamics produce the emergent dynamical features of the brain. Time-varying properties that dictate the trajectory of a neural network's behaviors are determined by the microstate

configurations of connectivity (degree of neuronal coupling distribution). The exact character of synapses, dendrites, axonal architectures, and myelin distribution, along with other physiological factors controlling coupling in a brain network, determine how individual components, from single cells to clusters and regions of the brain, interact with one another to manifest the overall dynamical form of the brain. An emerged frequency distribution of the brain, produced by its cumulative subordinate interactions, serves to interact with the external environment. Resulting environmental interactions are processed by the brain to assess its own performance and administer changes if needed to better manipulate its dynamical repertoire for seizing opportunities posed by the environment. Environmental opportunities may change at a moment's notice, necessitating the brain to shift its frequency distribution (spatiotemporal spectra of neural action potentials). Consequently, changing the bandwidth instills degrees of nonlinearity, including route-to-chaos [270]—both are dynamical evolution characterized by bifurcation of spectral response. Relationships between network constituents are highly nonlinear and recursively couple upon one another across the temporal and spectral scales of brain activity, capable of producing chaotic characteristics. Despite experiencing dynamic instability to different degrees, the brain is remarkably adaptable to finding stability. Therefore, uncovering the fundamental nature of how the brain maneuvers its "route to chaos" can be applied to a plethora of real-world systems that exhibit nonlinear and chaotic characteristics. Instability is typically characterized by unprecedented levels of change in the system. Typically, such a high degree of changes is viewed as undesirable, as bifurcation increases the probability of system instability. However, if instability is controlled, the degrees of changes can facilitate highly efficient reorganization towards a desirable state. The brain manipulates its high degrees of nonlinearity in its favor. From a plasticity point of view, these can enable the brain to rapidly reconfigure and adapt to new scenarios more

effectively than a highly statically stable network system with strongly reinforced configurations (as it may be more difficult to break out of these prior conventions and adapt to a new global state). Therefore, characteristics of instability exhibited by bifurcation of dynamics represented in the brain through the criticality of neural activity are manipulated by the brain to enable its proficient ability to adapt. This is further exhibited by the various modes of functional forms a neural network can assume from a fundamental physiological structure capable of performing a wide range of activities. Neural bifurcations are effectively directed towards rapidly reconfiguring the spatiotemporal distribution of frequencies in the brain toward a state that is better able to adapt in the environment. The number of possible network configurations is very large, to say the least. However, the brain isolates, refining a finite number of network configurations using a canonical, self-similar pattern and structure across its temporal and spatial scales. This directly corresponds to the statistically self-similar fractal nature of the brain. In qualitative terms, this directly correlates with the unique style, personality, or character of a brain network in terms of having a fundamental go-to protocol, method or philosophical way of thought (unique pattern of neural activity), which is administered recursively upon the variety of scenarios the environment poses. Self-similarity across the multivariate scales of the brain is therefore essential in supporting efficient dynamical transitions by directing chaotic bifurcations in its own hierarchical structure to effectively filter information throughout the scales of the brain while conserving resources through a self-similar organization [271,272].

2.6 Summarizing Points

The aforementioned information serves as a general overview of our understanding of how brain form and function changes over time within the constraints of nature. This review is by no

means complete. For example, the exact form of emerged spatiotemporal brain dynamics is unknown. According to literature reviews, brain structure and physiology enlist small-world structures to create multiple modalities of highly connected populations internally synchronizing and externally interacting with other populations in aperiodic characteristics. Hence, this biological structure engenders fundamental dynamical building blocks of synchronized neural populations. When these pieces are put together from the micro to the macro scales of the brain in unique configurations (gifted by evolutionary fine tuning) and molded by developmental and experiential plasticity, simple local activity can coordinate complex higher-order global forms, directing the trajectory of a brain network. Structurally observed in high-degree modularity, functionally, this enables the interaction of multiple modes of synchronized clusters. Local fundamental building blocks center around respective single-frequency components interacting with one another to create complex spectral distributions (multiple-frequency components). This spectral distribution inherently changes over time to support survival needs. Different regions of the brain have different connectivity configurations, enabling production of unique patterns of neural activity. Consequently, the amalgamation of these structures from the most fundamental constituent to the global level of the brain produces a unique spatiotemporal spectral distribution with an aperiodic trajectory that encodes information in the brain, incorporating abilities to (1) acquire and process sensory input and (2) initiate response (not necessarily physical). Quantitatively, this can be represented in terms of the spatiotemporal distribution of neural action potential frequencies, where the evolution of this distribution over time encapsulates the dynamical state of the brain. Therefore, brain dynamics (experienced and observed) can be concisely, consistently, and precisely defined as how this functional spatiotemporal distribution of neural activity morphs over time with the support of fundamental neural biological mechanisms. Global neural activity is not

random but highly ordered and supported by hierarchical structures. This form is recursively implemented from the micro to the macro scale and allows the brain to effectively produce complex forms of information representation (by composing unique spatiotemporal trajectories of neural dynamics), enabling performance of a wide range of activities while efficiently consuming precious resources necessary to sustain such dynamics. Furthermore, these forms entail self-similarity to optimize energy consumption in balancing and keeping certain network attributes similar (minimizing energy expenditure) while being required to change other network attributes (to adapt in the environment). Hence, a potential solution towards addressing neurodegenerative diseases and implementing brain–machine interfaces is to administer active control upon a neural network's spatiotemporal distribution of frequencies. Moving towards a more general step, effectively administering control of the complexity present in the brain can also provide insights towards the nature of complexity in our universe.

Due to our lack of understanding of the nature of brain dynamics and resolution limitations of current approaches, the precise form of the brain's spatiotemporal distribution of activity has yet to be comprehensively defined or modeled. The precise understanding of the following remains unclear: (1) what is the exact temporal evolution of neural activity in one region of the brain (for example, the thalamus routing information from the amygdala) and (2) how this interacts with the temporal activity of another region of the brain (the neocortex), producing emergent neurodynamic frequencies qualitatively observed or experienced as processing and acting upon fearful stimuli elicited from the amygdala. It is known that these are produced through the fundamental coalescence of individual neural activity coupled nonlinearly upon one another. However, to attain an improved understanding of brain dynamical phenomena and potentially administer active control, a more precise definition is necessary. Specifically, this means being able to (1)

mathematically represent a spatiotemporal spectral distribution of neural activity and (2) establish a governing dynamical law that can describe how such distribution changes over time. Mathematical representation ensures precision and entwining this with fundamental physical laws governing dynamical interactions ensures the creation of a comprehensive model that can comprehensively encapsulate complexity in the brain. A more precise interpretation not only renders higher levels of comprehension towards the subtleties behind spatiotemporal spectral distribution of neural activity but can also enable active control of such phenomena towards more desirable trajectories.

3. PRELIMINARY BRAIN NETWORK MODEL AND DATA ANALYSIS

Naturally, the dynamical biophysical complexity of the brain incorporates a variety of topics necessitation transdisciplinary collaboration from a variety of fields to compose a more comprehensive understanding. Fulfilling this completely is not feasible within the scope of this master's thesis; however, this work is written in the hope that it provides convincing information (along with a solid foundational start to build upon) to ignite transdisciplinary collaboration that can more completely characterize the brain in future work which has far reaching consequences beyond neuroscience as well.

To begin, one the most relevant dynamical property of the brain is its ability to compose unique waveforms and patterns of neural frequency (aforementioned as the instantaneous spatiotemporal bandwidth of neural frequencies). This time-varying property is in the form of voltage fluctuations and is the product of the cumulative nonstationary interactions of neural cells. Thus, modeling these local interactions between constituent neuron cells is an essential first step in being able to construct a global depiction (and potential control) of brain dynamics.

The following section will display a dynamical equation to model the postsynaptic potential voltage fluctuations of a neuron cell due to presynaptic interactions.

3.1 Quantifying Dynamical Local Coupling

With the established preliminaries above, it is apparent that the first step in creating a preliminary brain network model is to determine the dynamical interactions between individual constituents. Local constituents in the global brain can occur on a variety of scales from different regions of the brain, subnetworks down to different populations or clusters of neural cells to even individual neuronal constituents (if we keep going further we reach the scales of sub-clusters of

proteins down to individual molecules and their constituent atomic parts). However, due to finite limitations on resources; we will begin starting with an individual neuron cell and quantifying its dynamics in terms of its voltage fluctuations due to interactions with other connected neuron cells as a start. The governing equations below will focus on excitatory glutamate neurotransmitter driven interactions between neurons with special consideration and use of AMPAr and NMDAr as data is most widely available for this biological machinery. This will be the focus for the current model and provide as a foundation for future studies to be built upon.

Coupling strength, or interaction magnitude, at the synapse is determined by a combination of highly nonlinear processes, such as 1) the concentration of neurotransmitters in the synaptic cleft and 2) the total number and availability of receptors on the postsynaptic site. Neurotransmitter binding upon receptors is not deterministic but inherently stochastic. Therefore, the concentration of neurotransmitters in the synaptic cleft and the total number of available receptor binding points on the postsynaptic membrane can be used to generate a probability of receptor activation.

The concentration of neurotransmitters in the synaptic cleft can be approximated by considering 1) the amount of neurotransmitters released due to presynaptic depolarization and consequent vesicle exocytosis, 2) approximate rate of neurotransmitter degradation by enzymes in the synaptic cleft, and 3) the rate of neurotransmitter reuptake by transporter mechanisms. From studies identifying these parameters [273-275], the approximate volume of neurotransmitters (NT_v) can be found. Consequently, an approximate volume of the synaptic cleft (S_v) can also be determined. The volume of neurotransmitters divided by the volume of the synaptic cleft gives a probability ratio that a neurotransmitter will contact a postsynaptic site. Furthermore, a probability ratio calculation on the postsynaptic site is necessary to determine the probability that a neurotransmitter will make contact and bind upon a receptor on the postsynaptic site. Thus, the overall cross-

sectional area of receptors (α) divided by the overall cross-sectional area of the post-synaptic site (S_a) can determine a probability ratio of contacting a postsynaptic receptor. It must be noted that for this study, only ligand-gated ion channels (ionotropic receptors) from the AMPA and NMDA subtypes are considered. Metabotropic (or G-protein coupled receptors) are not included for this study and is the topic for future work. Thus, the probability ratio of 1) there being a receptor on the post synaptic site is multiplied by the probability ratio of 2) there being a neurotransmitter within the synaptic volume to calculate a probability of neurotransmitter binding and activating a receptor. This culminates into P_r shown in equation (1), the probability of a neurotransmitters within the synaptic cleft making contact and assumed to bind upon a receptor on the postsynaptic site.

$$P_r = \frac{R_a}{S_a} * \frac{NT_v}{S_v} \quad (1)$$

Therefore, the calculated probability above is multiplied by the maximum cross-sectional area of a receptor type to determine the overall cross-sectional area of receptors which are allowing for the influx of ions. The area of activated and unblocked NMDAr (α_{NMDA}) numerical equation will be shown later to incorporate the effects of Mg^{++} blockage. For now, the cross-sectional area of NMDAr which receive a neurotransmitter is signified by A_{NMDA}; however, this does not incorporate the effects of Mg^{++} blockage yet. Therefore, the expression for α_{NMDA} is not shown yet. α_{max} terms correspond to the overall cross-sectional area of the receptor type on the post synaptic cleft. This is approximated by the average cross-sectional area for one receptor multiplied

by the average number of receptors housed in a synapse whose approximate values are found from a variety of experimental approaches [276-278]. These are shown in equations (2).

$$\alpha_{AMPA} = P_r * \alpha_{max\_AMPA}$$

$$A_{NMDA} = P_r * \alpha_{max\_NMDA} \quad (2)$$

$$\alpha = \alpha_{AMPA} + \alpha_{NMDA}$$

The probability of receptor activation can be expressed in terms of the total cross-sectional area of receptors that allow for the influx of ions. Using fundamental diffusion principles formulated through Fick's laws [279], the flux of ions can be quantified regarding the established electrochemical gradient between the intra and extracellular space. Thus, the flux of ions multiplied by the total cross-sectional area of receptors corresponds to the total amount of ion influx across the membrane. Incorporating this value with the electrochemical gradient, temporal iteration time and charge for corresponding ion species summed over all synaptic points can represent the voltage fluctuations of a neuron over time. Equation (3) provides a preliminary governing dynamical equation to quantify coupling in terms of postsynaptic potentials. This can serve as foundational coupling law to determine whether a neuron will fire or not based on its synaptic inputs. Voltage (V_i), the energy per unit charge at the next time step, is equal to the voltage at the previous time step plus the summation (over all synapses and ion species respectively for connected neural cells) product of the electrochemical gradient ($\nabla\mu$) in [$\frac{\text{joule}}{\text{mol}}$].; the total cross-

sectional area of the open ligand-gated channel (α) in [m^2].; the flux of ions per area per unit time, [J_{flux}] ; and the charge per ion species, [q_{ion}]. This coupling law defines the dynamical voltage fluctuations of a neuron with reference to its synaptic inputs. Furthermore, this coupling law will be applied to the ion flux regarding K^+, Na^+ and Ca^{++} for this preliminary brain network model. Additionally, the term within the summation signifies the magnitude or strength of interaction between neurons. In other words, this part of the equation determines the magnitude of voltage fluctuation a single neuron has due to the interactions with it coupled constituent neuron cells.

$$V_i(t+1) = V_i(t) + \sum_{s}^{S} \sum_{ion} \frac{\nabla\mu * \alpha * J_{flux} * \Delta t}{q_{ion}} \quad (3)$$

The electrochemical gradient ($\nabla\mu$) corresponds to the free energy available to be converted into work due to the combined imbalance in the chemical and electrical gradient with respect to the intra and extracellular spaces [280].

$$\nabla\mu = RT * \ln\left(\frac{c_{out}}{c_{in}}\right) + Z * F * V_i \quad (4)$$

In the above equation (4), the right-hand side of the electrochemical gradient for an ion species corresponds to the chemical gradient where the interior of the logarithm term encompasses the ratio of the extracellular ion concentration (c_{out}) to the intracellular ion concentration (c_{in}) for a particular ion species. R stands for the gas constant and T stands for temperature. This gives the chemical gradient in units of [$\frac{joule}{mol}$]. The left-hand side of the equation incorporates the electrical gradient also in units of [$\frac{joule}{mol}$] where Z is the valency of the ion species, F is faradays constant

and V_i is the voltage potential of the membrane. Cumulatively, addition of these two terms gives the overall electrochemical gradient.

Equation (5) below signifies J_{flux} in units of [$\frac{mol}{s*m^2}$] and is derived from Fick's first law of diffusion.

$$J_{flux} = D\left(\frac{\partial \Psi}{\partial x}\right)$$	(5)

In the equation above, D stands for the diffusion constant for a particular ion species and the partial derivative term correspond to the concentration gradient for that ion species. It must be recognized that the electrochemical gradient and flux due to diffusion are relatively stationary. Hence, the term that relatively represents the dynamical nature of coupling to a higher degree is α, the overall cross-sectional area of activated receptors shown in equation (6). For the scope of this study, this incorporates the overall cross-sectional area of activate ligand gated channels, particularly for AMPA and NMDA receptors as their behaviors and implications in synaptic plasticity are most widely studied and known. Consequently, realistic modeling of their behaviors and implications in modulating coupling strength via plasticity mechanisms is far more feasible.

$$\alpha = \alpha_{AMPA} + \alpha_{NMDA}$$	(6)

This term is fundamentally nonlinear, as it is equal to the total cross-sectional area of the open ligand-gated channels, which is simultaneously dependent on pre- and postsynaptic mechanisms, such as the concentration of neurotransmitters which probabilistically bind upon postsynaptic

receptors that may or may not have a voltage-dependent Mg^{++} blockage (for the NMDAr in particular).

To incorporate the effects of Mg^{++} blockage upon the NMDAr, the following equation (7) is used which incorporates an approximate location of Mg^{++} ion blockage to determine the overall cross-sectional area of available NMDAr.

$$\alpha_{NMDA} = A_{NMDA} * (1 - \frac{y}{y_{max}})$$	(7)

Upon negative membrane potentials, the Mg^{++} ion is attracted deep within the NMDAr ion channel resulting in blocking ionic flow. The full depth of the deep site of the NMDAr where the Mg^{++} ion blocks the ion channel is defined as y_{max}. The location of the Mg^{++} ion is defined as y. A_{NMDA} corresponds to the total cross-sectional area of NMDAr (regardless of availability). Thus, it can be observed when the location of the Mg^{++} ion (y) is equal to the full depth of the deep site of the NMDAr (y_{max}), $\frac{y}{y_{max}}$ will equal unity (1) and the right-hand side will be zero rendering the available area of the NMDAr also equal to zero signifying blockage of ion flow. Consequently, when the location of the Mg^{++} ion is not at the deep site of the NMDAr, $\frac{y}{y_{max}}$ will become smaller than 1 (and grow even smaller as the Mg^{++} ion gradually starts to unblock the NMDAr) causing the overall availability of the NMDAr to approach its maximum value. To accurately represent this, dynamical equations based on electrical force between Mg^{++} ions and the neural membrane are shown below which can be used to find the position (y) of the Mg^{++} ion. First, the electrical force (Ef) in Newtons must be calculated as shown below using Coulomb's Law [**Error! R eference source not found.**] in equation (8).

$$Ef = K\frac{q_{ion}Q_{membrane}}{r^2}$$	(8)

Charge of the membrane ($Q_{membrane}$) in coulombs can be calculated using the capacitance (C) of the membrane [**Error! Reference source not found.**] by its voltage in equation (9).

$$Q_{membrane} = C*V_i$$	(9)

The known values enable calculation of electrical force (Ef) in Newtons. As a result, Newton's laws enable calculation of Mg^{++} ion acceleration (a) based on the mass of the ion ($M_{Mg^{++}}$) in equation (10).

$$\frac{Ef}{M_{Mg^{++}}} = a$$	(10)

Upon finding the acceleration, trivial double integration can be applied to approximate the location of the Mg^{++} ion within the pore of the NMDAr and this information can be used to determine the overall cross-sectional availability of the NMDAr consequently directly modulating the values of α which directly modulates the magnitude of voltage fluctuation (interaction strength) due to neuronal synaptic interactions. Hence, the intricacies of spike-timing dependent plasticity can be incorporated in this preliminary first model.

Hence, as a product of the variety of plasticity mechanisms, α is stochastic and highly nonlinear. It can be significantly influenced by: (1) the concentration of neurotransmitters and (2) the number and availability of receptors on the postsynaptic site. It must be noted that this equation

is a foundational factor in quantifying coupling in the brain, particularly on the micro scale. Additional coupling terms which include additional factors (e.g., dendritic spine dynamics and/or adaptive myelination), must be incorporated to comprehensively account for coupling on a larger scale. Furthermore, additional revisions are required to explicitly incorporate and quantify the various biological mechanisms that modulate the dynamical trajectories of neural postsynaptic potentials. Regardless, quantifying coupling at the microscopic scale is a necessary first step towards a more complete model. Thus, the underlying philosophy of this equation can be utilized to aid in quantifying complex local voltage fluctuations due to interactions amongst neuronal constituents.

Furthermore, the quantification of the above biological mechanisms must be further described in terms of energy to formally constrain the system under the global distribution of energy along with the corresponding information entropy value as described previously by the general framework.

3.2 Network System in Terms of Energy

To begin, the total energy (E_i) of the i^{th} constituent can be discretized into its potential energy (PE_i) and kinetic energy (KE_i) terms as shown in equation (11) below.

$$E_i = PE_i + KE_i$$	(11)

In the case of a neuron, the potential energy can be described by the accumulated charge (Q_i) in coulombs within a neuron multiplied by the total voltage (V_i) of that neuron shown in equation (12).

$$PE_i = Q_i * V_i$$	(12)

The kinetic energy can be described by the rate of change of charge ($\frac{dQ_i}{dt}$) within a neuron multiplied by the total voltage (V_i) over a time step (Δt) of that neuron shown in equation (13).

$$KE_i = \frac{dQ_i}{dt} * V_i * \Delta t$$	(13)

Finding these values were implied in the equations above; however, will be explicitly reinforced below. The rate of change of charge across the membrane of neuron can be determined using diffusion flux from Fick's Law's (J_{flux}) in units of $[\frac{mol}{m^2}]$ and the overall cross-sectional area of activated ion channels which are capable of allowing ion flux (α) in units of $[m^2]$. Multiplication of J_{flux} with α results in the overall amount of ion flow in mols. Thus, this total amount of ion flow in mol multiplied by the ion valency (Z) and Faraday's constant (F) in charge per mol for each particular ion species results in the overall amount of charge efflux or influx across the membrane of a neuron. This charge flow per unit time is shown below in equation (14).

$$\frac{dQ_i}{dt} = J_{flux} * \alpha * F * Z$$	(14)

Upon establishing the rate of charge flux, multiplication with time can establish the overall charge accumulation across the neuron membrane shown in equation (15).

$$Q_i = \frac{dQ_i}{dt} * \Delta t$$	(15)

These values can be used to determine the kinetic and potential energy components consequently producing the overall energy expenditure of a constituent neuron.

From the implementation of these equations based on fundamental biophysical principles, a neurons membrane potential fluctuation over time can be delineated in terms of energy. Thus, a local microscopic description of neuron dynamics and their coupled interactions is established in terms of energy.

3.3 Macroscopic Information Entropy

For a comprehensive characterization of a complex network, macroscopic ensemble level network description is necessary to constrain the time-evolution of microscopic constituent dynamical interactions. The global probability distribution of energy, and its respective information entropy content, provides a macroscopic ensemble level description. The ensembles probability distribution of energy must be normally distributed as shown in equation (16)

$$\mathbf{P}(E_i) = \frac{1}{\sigma\sqrt{2\pi}} e^{-\frac{1}{2}(\frac{E_i-\mu}{\sigma})^2}$$	(16)

Furthermore, the resultant macroscopic ensemble network state is determined by the information entropy [283] which is a function of the probabilities of energy shown in equation (17).

$$\mathbf{S} = \sum_{i=1}^{n} \mathbf{P}(E_i)\ln[\mathbf{P}(E_i)] \quad (17)$$

These equations are utilized in generating a preliminary brain network model to serve as a foundational basis for analyzing the network properties of the brain. Furthermore, additional mathematical tools are utilized to extract the underlying time-frequency content of dynamical networks to provide a precise quantification for unique patterns of information representation.

3.4 Time-Frequency Analysis to Identify Information Content

As aforementioned, unique patterns of information in a network can be generated by a respectively distinct unique physical characteristic. To be clear, this distinct unique physical characteristic occurs in the form of unique time evolution of underlying frequencies. To pinpoint this phenomena, mathematical analysis is necessary. Fourier analysis is usually used to extract frequency components from a time-series data set or signal [284]. However, Fourier analysis is done upon data with the underlying assumption that the time-series is stationary. As real-world complex network dynamical frequencies are nonstationary, conventional Fourier analysis is insufficient [285]. Nonstationary, nonlinear responses are intrinsically transient in the time and frequency domains. Hence, canonical functions based on Fourier analysis are insufficient as the basis frequency functions are do not vary over time. In other words, these basis frequency functions are not localized and extend off to infinity without changing the underlying frequency components. Therefore, Fourier methodology typically involves a complete conversion of time domain

information into the frequency domain rendering stationary temporal analysis. Consequently, an extraction of frequency information using Fourier analysis loses temporal information of the signal. Therefore, Fourier analysis allows extraction of only frequency domain information and is not capable of determining how frequency components vary over time which is an essential feature for dynamical complex networks as aforementioned. Hence, a simultaneous time-frequency analysis is not feasible using the Fourier Transform. Thus, spectral time-evolution can be misrepresented in the Fourier domain. Fundamentally, the Fourier transform is mathematically linear while the spectral characteristics of real-world complex network dynamics are fundamentally nonlinear rendering the inadequacy of applying Fourier methods.

Hence the concept of instantaneous frequency (IF) must be incorporated to resolve the underlying frequency components as a function of time of a time-series signal [286]. A time-varying signal typically entails an amplitude modulation term ($a(t)$) and a phase modulation term ($\Phi(t)$). The instantaneous frequency is found by the derivative of the instantaneous phase ($\Phi(t)$).

$z(t) = a(t) * e^{i\Phi(t)}$	(3)

A key caveat to instantaneous frequency is that it can only be applied upon monocomponent signals. Real-world complex signals (time-series) typically contain multiple components (which is a sum of multiple monocomponent signals.

Therefore, in addition to IF, a multicomponent time-series must be broken down to its intrinsic monocomponents. This method can be accomplished by the empirical mode decomposition by application of the Hilbert-Huang Transform (HHT) [287]. The underlying assumption is that any time-series signal consists of multiple simple intrinsic modes of oscillations. The inherent

oscillation can be classifieds into intrinsic mode functions (IMF) where each intrinsic mode function (IMF) represents a simply oscillatory mode as a monocomponent signal. Thus, decomposing a multicomponent signal using the Hilbert-Huang Transform allows extracting monocomponent signals in terms of the intrinsic mode functions. Finally, the concept of instantaneous frequency can be applied upon the monocomponent intrinsic mode functions enabling the extraction of simultaneous time-frequency information upon a time-series data set. As a result, the underlying information content of the dynamical properties of a network can be precisely determined by the intrinsic time-frequency content. These mathematical formulations were implemented using MATLAB's Time-Frequency Toolboxes.

3.5 Results and Data Analysis from Network Model

The previously described foundational equations and underlying philosophies were used to generate a preliminary neuron network model. The objective of this model is to model a brain networks dynamics from the microscopic to the macroscopic scales. In other words, the objective is to establish the time-varying characteristics of the brain network model at the macroscopic ensemble level by identifying global system information entropy and its fluctuation while simultaneously establishing the time-evolution at the microscopic constituent level regarding the dynamic variation of individual neuron membrane potentials. Furthermore, it must be noted that the dynamic changes in neuron voltage (membrane potential) are due to the time-evolution of even smaller scale coupling terms displayed within the summation of equation (). Additionally, the results from this brain network model can be used to analyze, determine, and quantify the underlying information content of the network model in terms of the time-frequency components of the resultant data sets. Furthermore, due to the computational demands and limitation on

resources, the preliminary neuron network model is limited to modeling 6 individual neurons and their interactions. While this is certainly not at the scale or full repertoire of the human brain, the fundamental methodology can be used to build support for the aforementioned philosophies and assumptions to garner the support justifying the merits of utilizing additional resources to produce further refined and complex studies based on the very same foundational principles. To begin, the next section will display results of the membrane potential dynamics and display the character of this is similar to what is observed in electrophysiological studies [288] adding credence to the claims and assumptions aforementioned.

3.5.1 Microscopic Brain Network Analysis and Information Content

Below the time-evolution of the voltages of 6 neurons in a 6-neuron network model is shown in Figure 1.

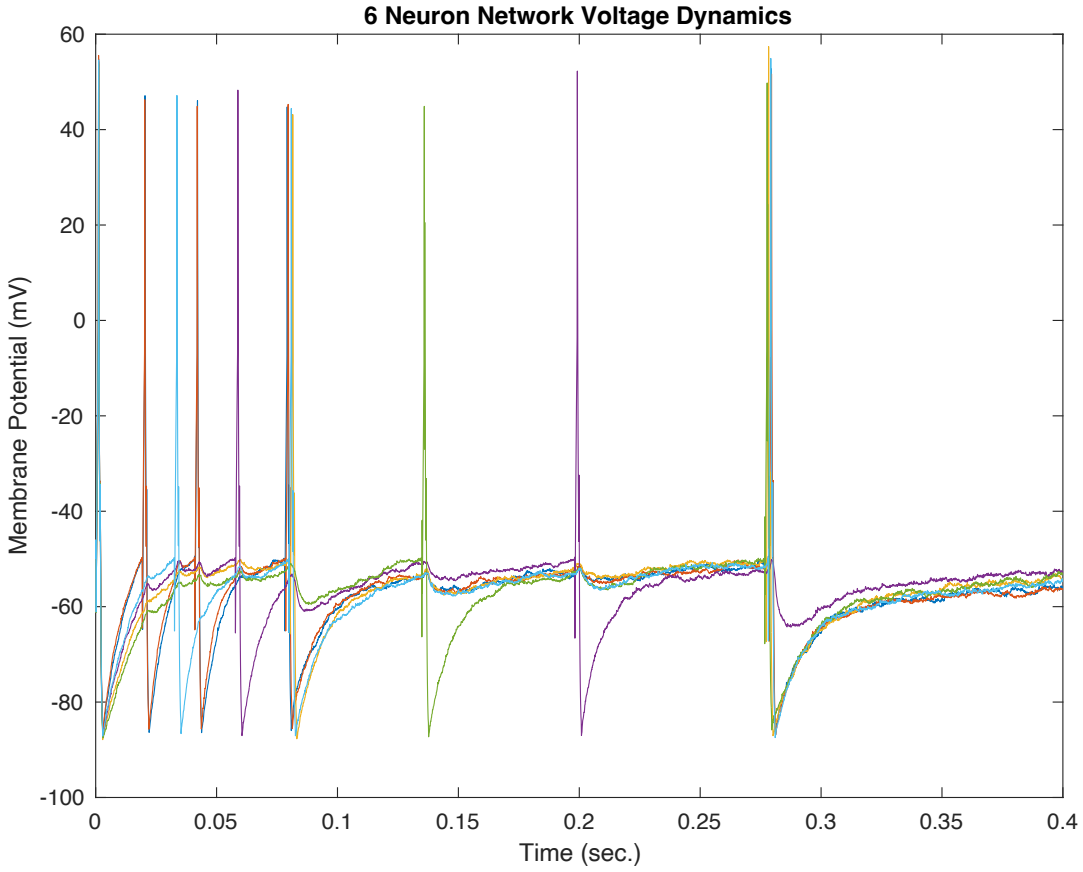

Figure 1: 6 Neuron Voltage Dynamics

The figure above displays the dynamical voltage fluctuations of six neurons interacting with one another eliciting an excitatory response. This data was generated from "An Energy Based General Framework for Dynamical Complex Networks – dissertation from Chun-Lin Yang" using the equations from the preliminary brain network model and philosophies described previously. The general character of these action potential waveforms are within the ranges found from electrophysiological studies supporting the validity of the equations and methodologies aforementioned in generating a preliminary brain network model. Each waveform is not completely identical; however, this inherent variability is necessary as in real brain networks all

action potential spikes are not the same due to intrinsic variation and uncertainty in underlying physiological machinery.

Furthermore, the characteristics of neuronal activity can be further delineated by extracting the intrinsic frequency components of a neurons voltage and displaying how these frequencies change over time. This is necessary to pin-point the exact patterns and forms of information represented by this individual neuron. Simultaneously extracting the time-frequency character of a neurons activity allows pin-pointing the underlying unique patterns of information. As a reminder, the time-frequency components were extracted upon applying the empirical mode decomposition using the Hilbert-Huang transform upon the multicomponent signal of a neuron's behavior in terms of its voltage fluctuation over time. This extracted monocomponent intrinsic mode functions allowing the application of instantaneous frequency upon the resultant data to produce a simultaneous time-frequency representation of the signal. The figure below shows the extraction of the underlying time-frequency components of a single neuron's (neuron 1) activity. It is important to note that this defines the information content (in terms of time-frequency components) at the microscopic individual neuron constituent level.

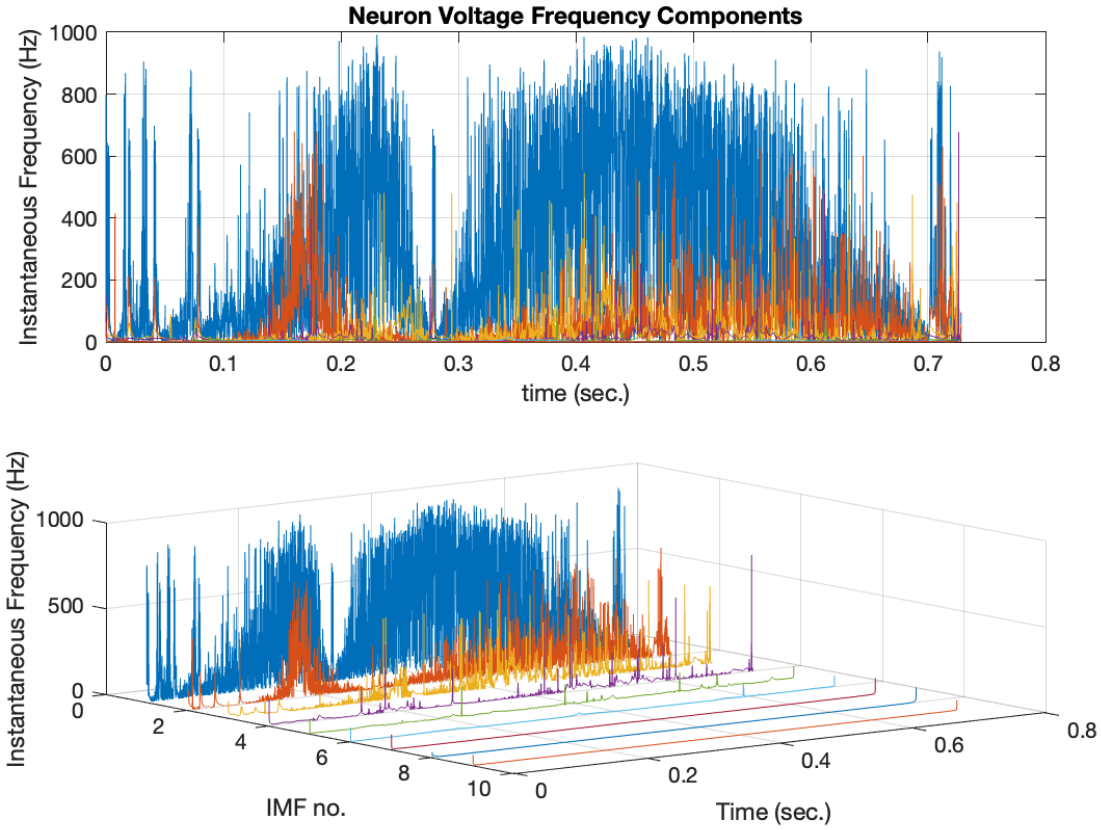

Figure 2: Neuron 1 Time-Frequency Components to Quantify Information Content

As is shown in figure 2 above, the monocomponent intrinsic mode functions (IMF) of neuron 1's multicomponent voltage response over time is extracted and the instantaneous frequency components as a function of time is displayed. Thus, this shows a signature information content for neuron 1 in terms of the underlying time-frequency components of its dynamical response. Furthermore, every single neuron is not identical in terms of the dynamical response. While it is difficult to establish the subtle differences, such complexity is absolutely necessary to ultimately encode diverse forms of information (observed in the diverse forms of physical activity and action of coupled neuronal activity). Time-frequency analysis can be applied to illuminate and pin-point these differences by representing the respective information content of a neuron in terms of the

time-evolution of its underlying frequency components. Thus, time-frequency analysis was applied upon neuron 6 (while the previous analysis was applied upon neuron 1) displaying a fundamentally distinct repertoire of frequency components corresponding to the unique physical behaviors of that particular constituent neuron. The underlying frequency components (corresponding to encoding a distinct form of information) is shown below.

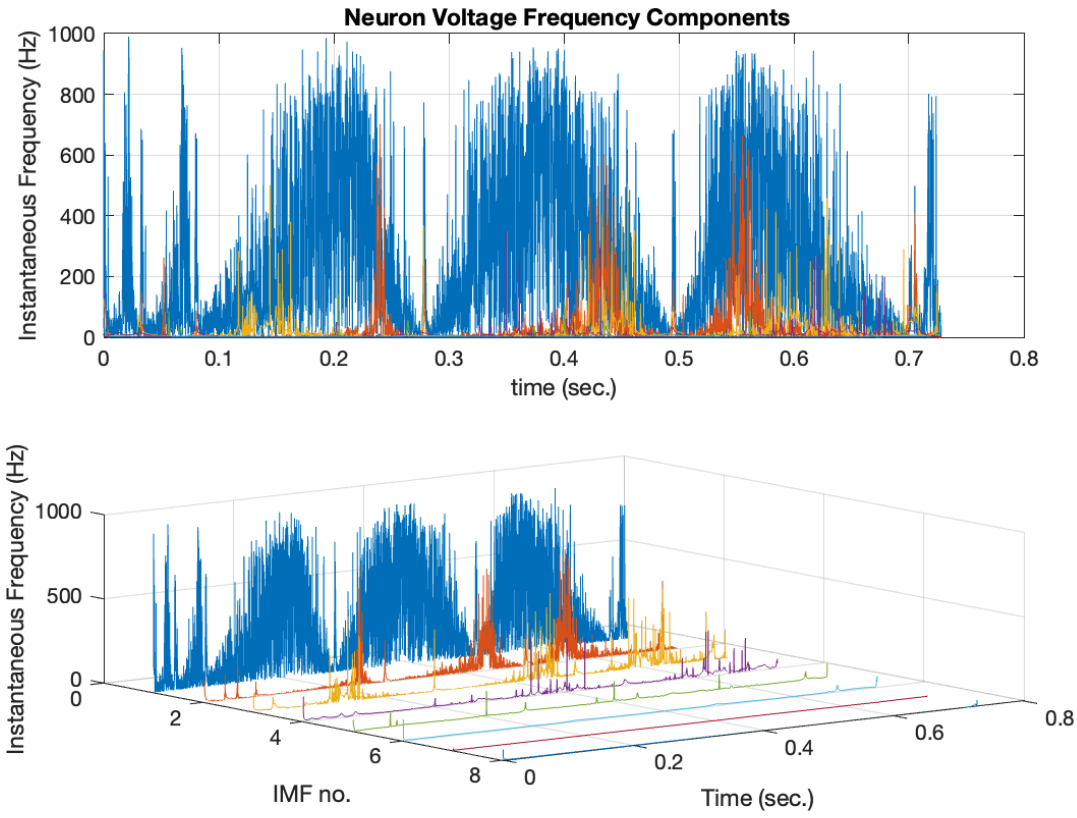

Figure 3: Neuron 6 Time-Frequency Components to Quantify Information Content

The figure above displays the unique time-frequency components in the dynamical response of neuron 6 corresponding to a representation of a different form of information. For the curious reader, time-frequency component analysis was done for all 6 neurons shown in Appendix A. Once again, it must be recognized that information description at this microscopic level of neurons is certainly ambiguous as it is not clear what relations they have to global brain behaviors. It is outside

of the scope of this thesis to completely establish this connection between information content at the microscopic level and information content and dynamics at the global level of a brain with billions of neural cells and trillions of connections. A complete answer to this would resolve the major questions in neuroscience (along with other network systems with complex architectures similar to what is observed in the brain). What is within the scope of this thesis; however, is that information can fundamentally be extracted without ambiguity using the unique spatiotemporal evolution of frequency components and this understanding can serve as one of the foundational principles (in addition to the in-depth reviews previously described) to aid in working towards a more complete understanding of the human brain which is currently missing in current approaches. Furthermore, as will be described in the following sections and figures, despite the simplicity of this preliminary brain network model, unique patterns of information in the time-evolution of distinct components at the macroscopic and microscopic levels are identified. In the bounds of this model, the microscopic level refers to the individual voltage dynamics of a single neuron. The results and data analysis displayed above describes the dynamical state and underlying information content of a neuron network at the microscopic constituent level in terms of voltage fluctuations over time. While these uncover characteristics at the microscopic scales, further analysis upon macroscopic level network properties is necessary to characterize network dynamics more comprehensively.

Going further down the microscopic level to the underlying ion flux driving the voltage fluctuations due to the interactions from coupling between neurons, analysis of the underlying time-frequency components is shown below. Furthermore, analysis of the underlying accumulated charge time-frequency components is also shown.

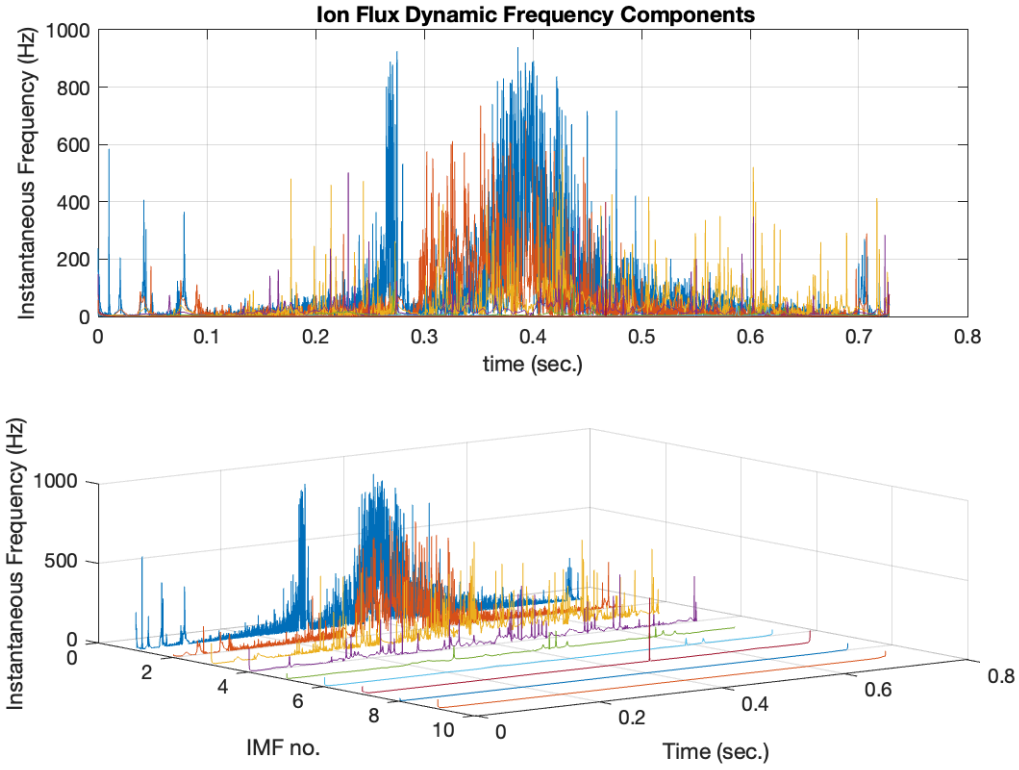

Figure 4: Neuron 1 Ion flux Time-Frequency Analysis

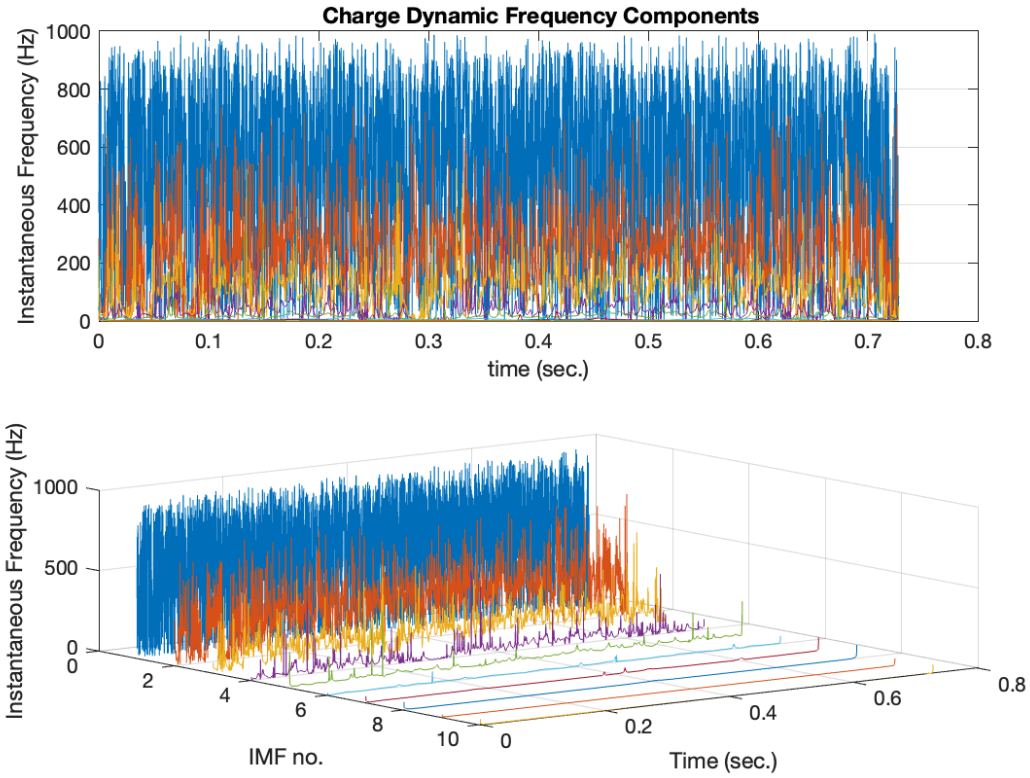

Figure 5: Neuron 1 Charge Time-Frequency Components

These figures show the dynamical components pertaining to the coupling interactions between neuron cells in regards to ion flux and accumulated charge respectively. It is clear that the underlying frequency components are significantly different than that of the neuronal voltage dynamics shown previously representing a different form of information at this microscopic scale. The cumulative interaction of these different forms of information placed in a particular context creates the overall dynamical characteristics of a network at the ensemble level. Thus, information content at the macroscopic and microscopic level can be precisely defined using these time-frequency tools.

3.5.2 Macroscopic Brain Network Analysis and Information Content

The overall macroscopic level information entropy of the network and its underlying time-frequency components can determine the dynamical state and information content of the network ensemble. To begin, the neuron network ensemble information entropy variation over time is displayed in figure 6 below.

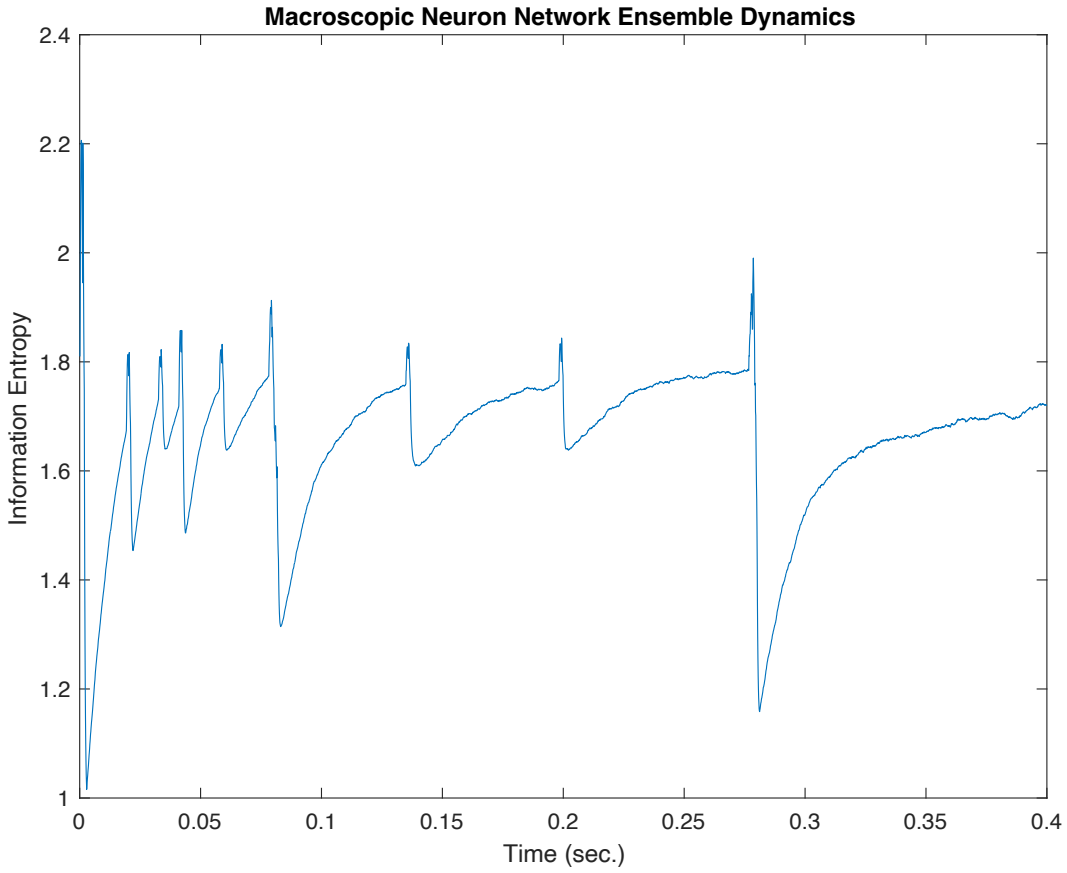

Figure 6: Macroscopic Neuron Network Information Entropy Dynamics

It is noteworthy that the character of the resultant entropy fluctuations reflect the underlying spikes in neuronal voltage thus exhibiting direct correlations between the ensemble (macroscopic) level and constituent (microscopic) level. Hence, the global variation of entropy over time reflects the dynamical state of the network ensemble and reflects the fluctuations of the microscopic level

constituent behaviors. Furthermore, figure 7 below displays the underlying frequency components for the macroscopic information entropy of the 6-neuron network model. Despite, showing similarity in time domain trajectories, the repertoire of the two levels (macro and micro) have clearly distinct underlying time-frequency components.

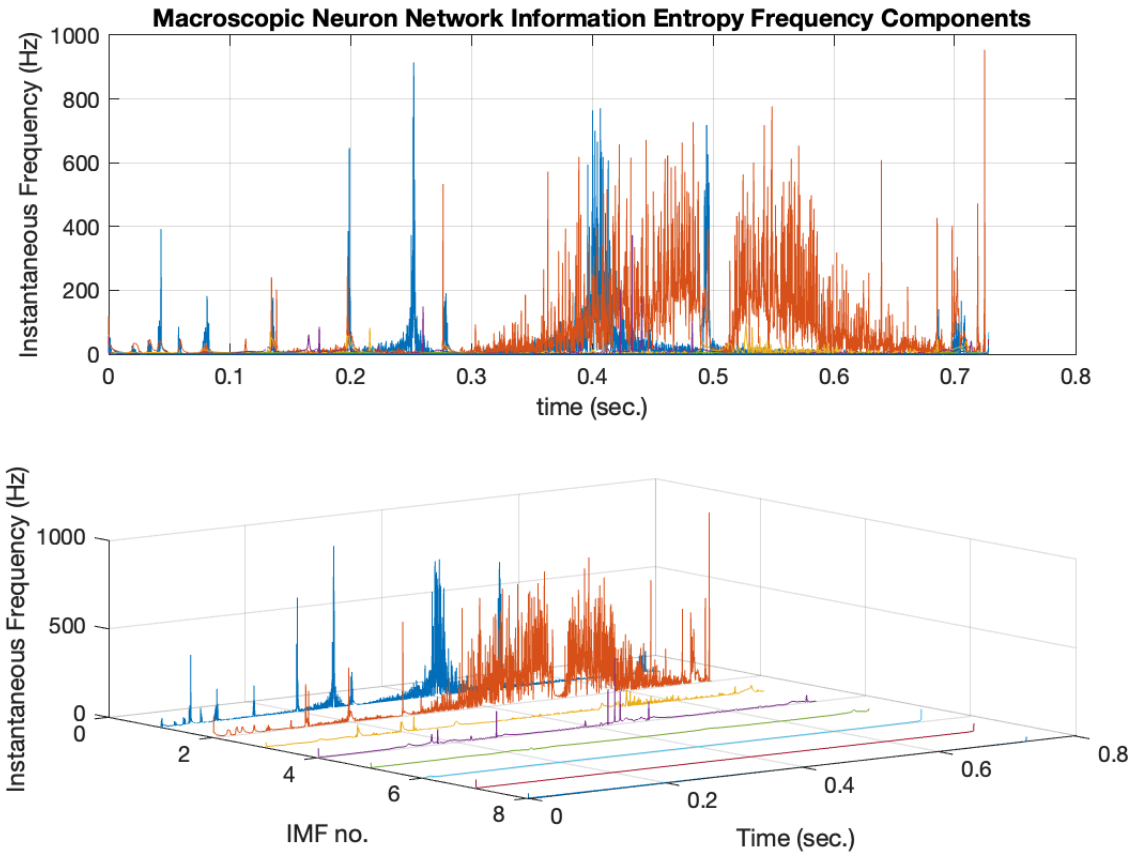

Figure 7: Information Entropy Dynamical Frequency Components

Thus, it is immediately recognizable that at the macroscopic scales a distinct patterned time evolution of frequencies is observed in regards to the information entropy of the network model. This, of course, corresponds to encoding different type of information (physically represented by a different dynamical state). Therefore, the analysis above shows the time frequency analysis can

be feasibly used to precisely identify he the unique patterns of frequencies. Furthermore, these unique patterns of frequencies correspond to respectively distinct types of information content.

The analysis above displays the time-varying properties of a 6-neuron network model at the macroscopic and microscopic levels along with the respective information content described by the unique time-frequency components of the network's global information entropy signature and its local neuron voltage dynamics and coupling interactions.

While the figures and analysis above describe the characteristics of one particular network type, a comparison must be made to a different network configuration to display that a different network composes another unique pattern of time-frequency components which can be used to encode different forms of information. Furthermore, analysis of upon a different network configuration must be similarly done upon the macroscopic and microscopic levels. Additionally, this analysis must be performed to display that the underlying methodologies and philosophies can be applied to networks beyond the human brain, rendering the aforementioned ideas generally applicable to network complexity within nature's ensemble in analyzing unique forms of information content (by the underlying time-frequency components).

3.5.3 Macroscopic 20 Point Mass Network Information Content Analysis

For further comparison in establishing a unique time evolution of frequencies for a particular network configuration (which encode different forms of information), the previously displayed results are compared to that of a 20-point mass network model. The intrinsic differences in this network underlying architecture from the micro to the macro scales renders a unique evolution of frequencies over time. In other words, this creates a distinct type of information. Furthermore, this exhibits how the precise characterization of unique patterns of information can

be quantified using such time-frequency tools to better understand (and even manipulate) various forms of information. Mathematical analysis of data must be performed to corroborate these claims.

The initial conditions of this network model start with 20-point masses oriented at different positions in a concentric circle in 3-D space. Each point mass was coupled to one another. The degree of coupling in this network configuration is signified by K and J to signify the magnitude of coupling strength between the point masses. The nature of coupling dynamics in this network system results in a network evolution towards synchronization. This is analogous to the terms within the summation of the dynamical equation for a neurons voltage which signified the magnitude of ion flux corresponding to the strength of interactions and respective degree of coupling between neurons. The key takeaway for the following analysis is to identify that a different network structure is capable of encoding different forms of information which is precisely quantified by its underlying time frequency content. To begin, we start of with the macroscopic dynamical state of this network ensemble dignified by the information entropy characteristics and an analysis of its underlying frequency components in figure 8 below.

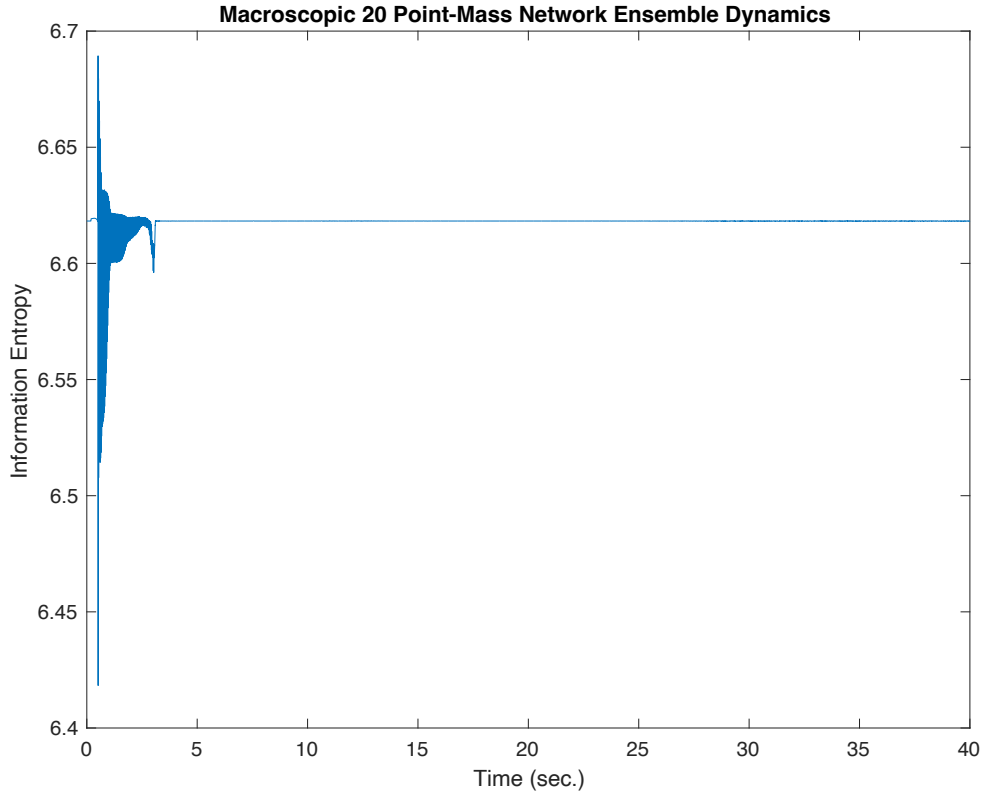

Figure 8: 20 Point-Mass Information Entropy Time Domain Fluctuation

As the network's trajectory evolves towards synchronization, entropy fluctuation is significant in the beginning time steps; however, reduces significantly once synchronization is reached. In addition to time-domain information, frequency domain information is extracted and shown below in figure 9.

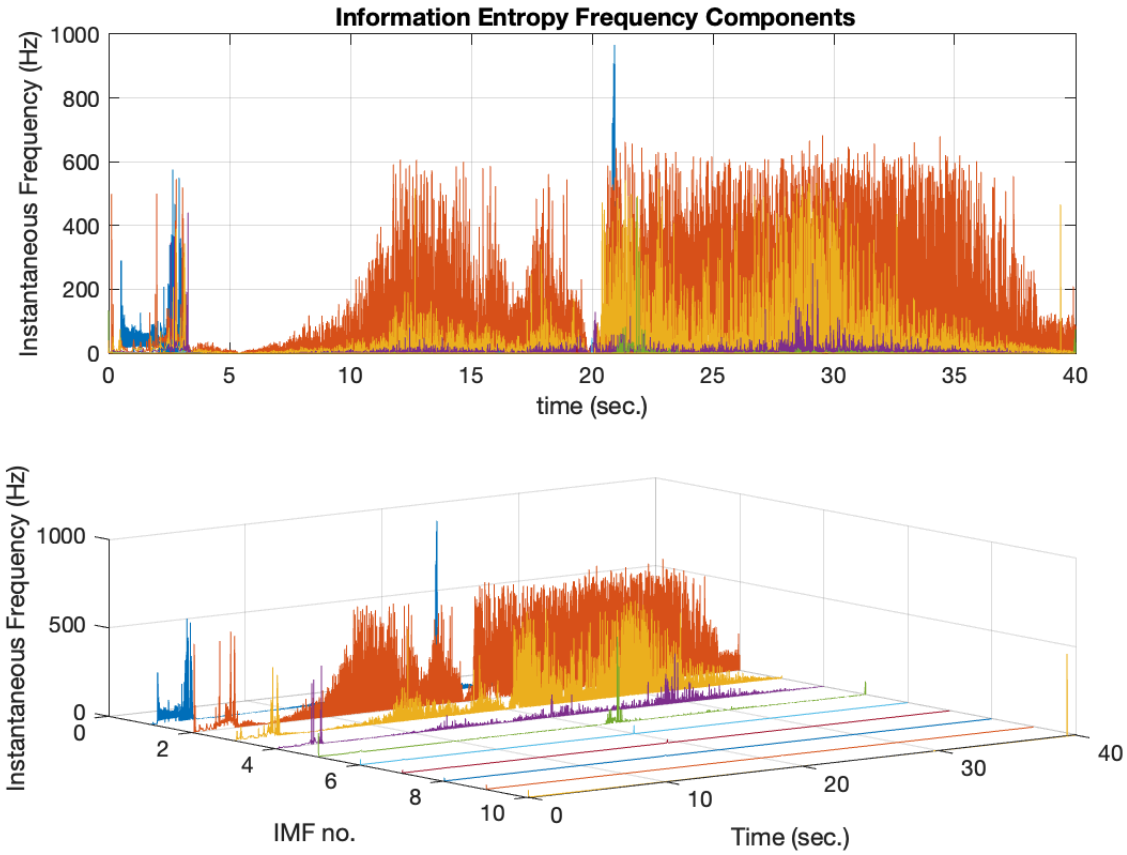

Figure 9: 20-Point Mass Network Time-Frequency Components of Information Entropy

It can be seen that far more information can be extracted from the simultaneous analysis of the time-frequency components. Therefore, this tool enables characterizing different forms of information content to a much higher degree than pure time-domain or pure frequency-domain analysis. Furthermore, the dynamical macroscopic ensemble state of this network and its underlying frequency components are distinctly different from that of a brain network model. Naturally, a neuron network model and a 20-point mass constituent model will have different characters; however, this is still shown to explicitly convey that these unique forms of information (a rather ambiguous term) can be precisely pin-pointed by analysis of the underlying dynamic frequency components. This formalization of information representation is necessary to enable the

advancement of future refined studies. Furthermore, these results indicate that neuron networks trial cases with different underlying parameter configurations would produce distinctly different time-frequency characteristics. In other words, alteration in underlying parameter configurations (such as interactions strength denoted by overall cross-sectional area of receptors) would inflict a change of the dynamical repertoire of a neuronal networks character enabling encoding different forms of information. This phenomenon is recognized as synaptic plasticity and can be quantitatively pinpointed with mathematical precision using these time-frequency tools. In the next section, the microscopic network level characteristics will be assessed for comparison as well.

3.5.4 Microscopic 20-point mass Network Information Content Analysis

Further analysis is done upon the microscopic level network characteristics. For this network system, the microscopic level dynamics is the velocity for a single constituent. The velocity of single constituent in a 20-point mass network model defines the driving state of an individual constituent. Hence, velocity in this network configuration is analogous to the voltage of a neuron for the 6-neuron network model. The velocity profile of a single constituent is show below in figure 10.

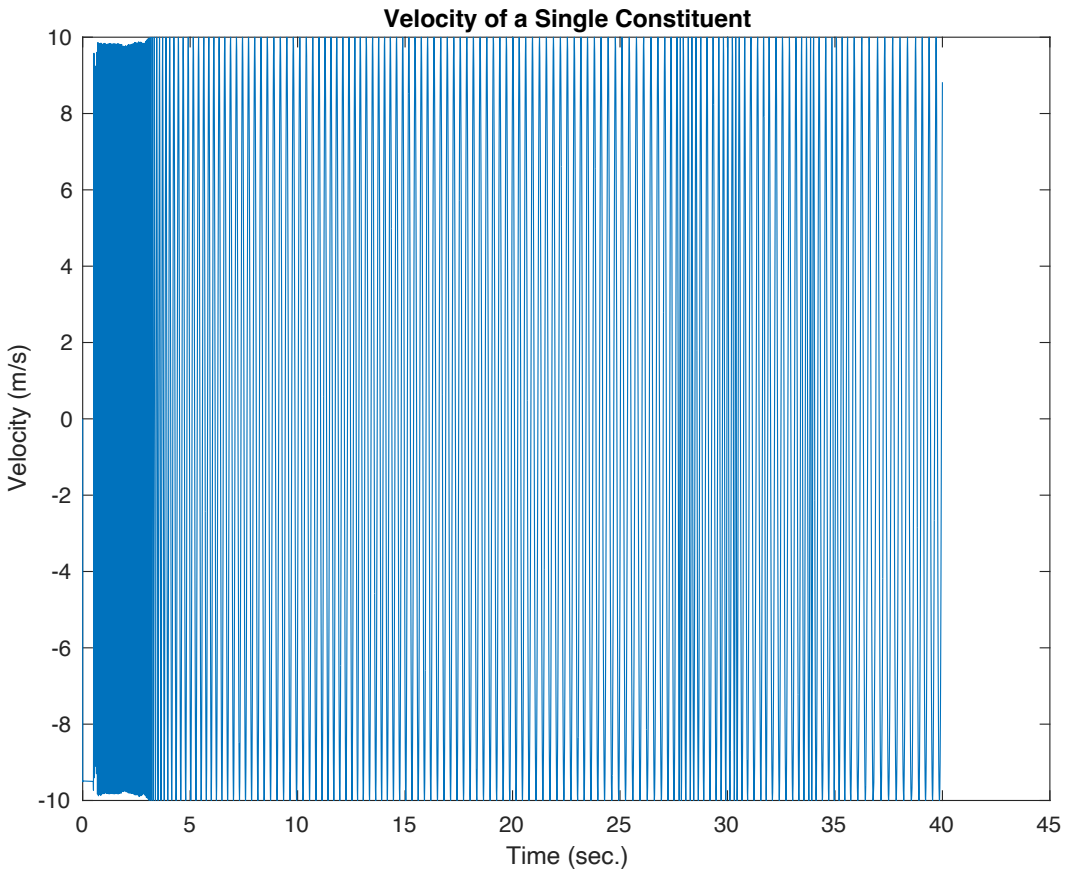

Figure 10: Velocity of a Constituent in 20 Point-Mass Network

As the 20-point mass network configuration is relatively simpler compared to neuronal dynamics, the resulting driving velocity has minimum variation in terms of its frequency spectrum over time as shown in the figure below. The time series displays the most significant dynamic features in the transition qualitatively observed between 0 to 5 seconds. This is shown in the corresponding time-frequency analysis below as the most significant changes are shown in between 0 to 5 seconds. There are smaller fluctuations from normal behavior throughout the signal shown in subtle jumps in the time frequency analysis as time continues. Still, it must be noted the overall level of information variation is minimal as compared to a neuron's dynamics due to the relative simplicity of a 20-point mass network model.

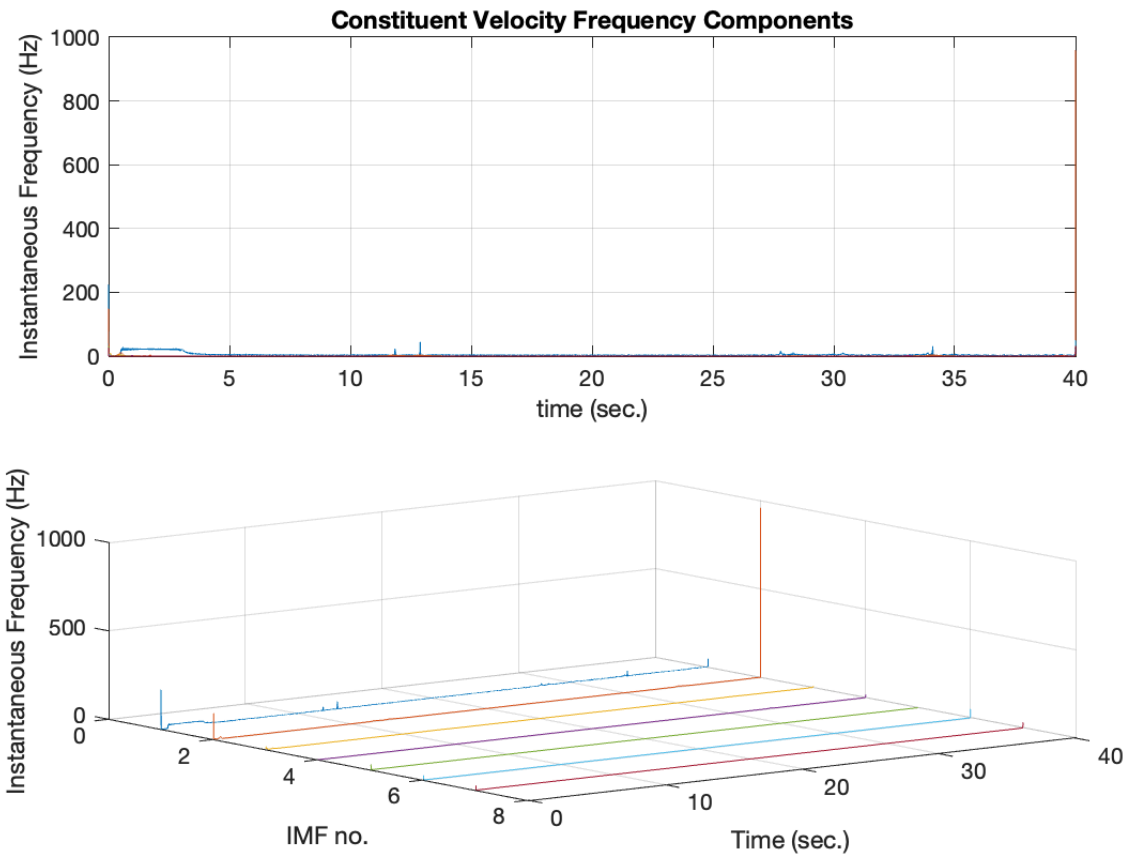

Figure 11: Velocity Time-Frequency Components of a Constituent in 20 Point-Mass Network

Thus, the information encoding scheme is displayed in the subtle yet non-negligible variation in physical characteristic of the velocity fluctuations over time. This is shown in the subtle spikes of frequency components displayed in the time-frequency analysis. The level of dynamic fluctuation is not as rich as a neuron networks individual voltage; however, the underlying information content (represented by the dynamical character of the velocity) can still be extracted using these time-frequency tools. Furthermore, this 20-point mass network model explicitly conveys coupling in

terms of degrees of coupling K and degree of coupling J. Analysis is shown in the following figures 12-13.

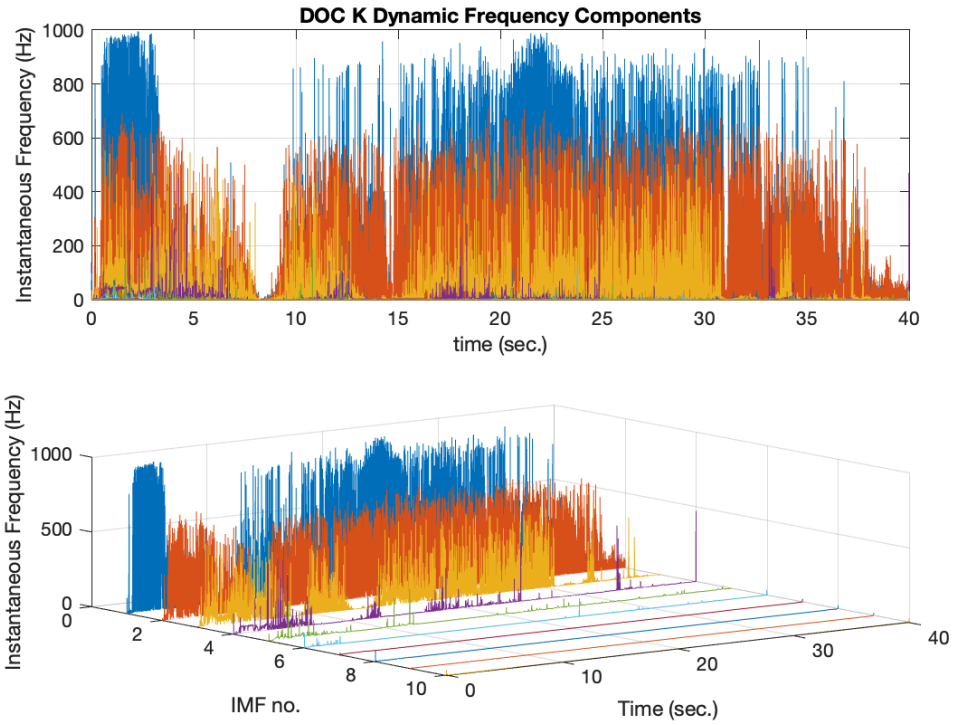

Figure 12: Time-Frequency Components for DOC K

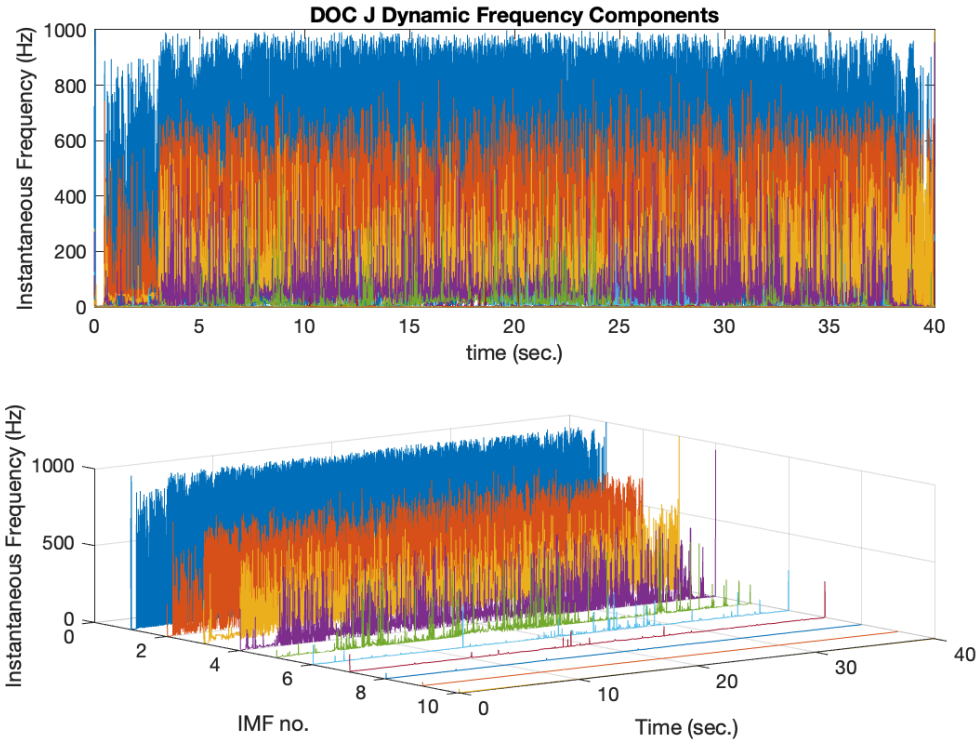

Figure 13: Time-Frequency Components for the DOC J

The degrees of coupling K and J in this 20-point mass neural network model signify the interaction magnitude between constituents. The degrees of coupling K and J are analogous to the accumulated charge within a neuron and the ion flux occurring across the membrane of a neuron. Analysis of the intrinsic frequency components and how they change over time shows a unique encoding of formation distinguished by these frequency components further corroborating the ability to extract different types of information using time-frequency tools. Furthermore, it is noteworthy that in this network configuration, the characteristics and evolution of the degree of coupling displays a richer repertoire of information content as opposed to the velocity of the constituents. Consequently, information encoding in this network architecture is significantly represented by the degree of coupling between network constituents. In other words, the magnitude of influence network constituents has upon each other and the time-varying properties of this

feature is capable of encoding complex forms of unique information. Thus, information content at the microscopic or macroscopic scales of a network can be distinctly identified by the underlying time-frequency content. Furthermore, the information content at the micro and macroscopic levels along with the coupling interactions between constituents is distinctly unique at all levels for the 20-point mass network model and the 6-neuron network model. This further dignifies the unique information character represented by distinctly different physical attributes which is precisely identified by extracting the instantaneous frequency components and comparing their temporal evolution.

4. SUMMARY, CONCLUSIONS AND FUTURE WORK

Through thorough literature review, current approaches in attaining a general understanding of human brain dynamics are insufficient. Significant knowledge has been attained; however, to sustain the next level of progress a new approach is necessary. Therefore, it is the aim of this study to build the foundations of a new approach towards understanding the human brain With the established theoretical framework and governing numerical equations implemented upon network models of different configurations and analysis of the resultant data, the feasibility of this approach is demonstrated in being able to model the underlying dynamics of the human brain using fundamental physical laws as established by the general framework for complex networks. This establishes network dynamics at the macroscopic levels through information entropy and at the microscopic levels through individual constituent energy fluctuations (manifested in the physical form of neuron voltage in the one hand and velocity of a point mass on the other hand) along with energy attributed to individual degrees of coupling. Each level (macro and micro for global network state and individual behavior and coupling dynamics) contains a unique spatiotemporal spectrum of information content. Furthermore, upon generating dynamical data, identification of a unique time-evolution of frequencies in the dynamical characteristics of a network can be accomplished to uncover the previously ambiguous notion of information content. This can be used to precisely quantify the information content of a complex network such as the brain to help uncover a deeper comprehension towards neurodynamic complexity. Additionally, mathematical tools and concepts such as empirical mode decomposition using the Hilbert-Huang Transform are useful in feasibly extracting instantaneous frequency components to determine the time-frequency character (information content) of a physical signal. Furthermore, the two different network

configurations displayed unique time frequency components signifying the encoding of respectively distinct forms of information at the microscopic and macroscopic levels.

In the case of a brain network analysis was done only upon a 6-neuron network model For neuron networks with larger numbers of constituents and greater diversity in the underlying attributes of each constituent, it is feasible to consider that various diverse forms of information can be encoded and the physical manifestation of a unique time evolution of underlying frequency content. Furthermore, encoding different forms of information is possible through adapting underlying network parameters. In brain networks, this phenomenon is displayed through the various modes of plasticity. Due to the sheer scale and degree of complexity in the brain, small changes in underlying network parameters (different forms of sensory information or underlying motivations) can dramatically alter the overall time-frequency characteristics of an instantaneous brain network response steering adaptive behaviors. For example, different adaptive behaviors from identifying valuable resources and recognizing beneficial opportunities to assessing the safety of certain tasks and even initiating fight or flight responses; throughout development, the brain wields its dynamical characteristics in mastering 1) the recognition of such a variety of scenarios and 2) the reaction towards each respective scenario to optimize conditions of survival. As described in detail, these dynamical characteristics can be defined through the macroscopic level of information entropy, the microscopic fluctuations of energy levels in regard to constituent behaviors and interactions and the underlying time-frequency content of both the macro and microscopic network state. It is necessary for the brain to operate on these principles to efficiently survive and thrive in a world with finite resource limitations. Thus, the feasibility of the philosophies of this study are generated from a throughout literature review on brain dynamics to a qualitative assessment on the nature of how the brain operates to generating a precise quantitative

metric to measure biophysical brain complexity across its multiple scales of action (micro to macro).

Therefore, future studies aim to build upon this foundation and conduct numerical experiments upon neuron network models with different configurations for the underlying physiological parameters of these neuron. Variation in underlying physiological parameters would be done by altering the interaction parameters between neurons via modulating the number and overall cross-sectional area of receptors (not limited to just this factor) changing the underlying configurations can change the dynamical characteristics and this alteration and physical response can encode different forms of information much like how synaptic plasticity and other modes of plasticity work in the human brain. Furthermore, the implementation of more efficient computing strategies and algorithms will be utilized to increase the scale and computation complexity of testing neuron network models with the aims of uncovering additional information. Additionally, more comprehensive incorporation of the various forms of plasticity can render generating richer brain network models. Additionally, future study in this area is open to transdisciplinary collaboration and even merging the developed understandings upon experimental application to further refine the merits and foundations of our research work. Experimental application to model the human brain is a complex task; however, a thorough understanding of the underlying knowledge gives the ability to conduct experimental studies with more efficiency and promise. Ultimately, the generated theory and computational simulations must be validated by physical experimental application to refine the validity of the developed knowledge to the next level.

Hence, this study serves to provide a foundational approach in assessing the human brain which sheds the inhibitions of conventional practices to bring together all the distinct field methodologies and garner a modern transdisciplinary perspective upon the human brain. A new

approach is necessary to attain a more comprehensive understanding which can illuminate new insight in neuroscience while simultaneously having implications upon organizing the optimal representation of information in our society. Furthermore, the precise architecture for optimizing the efficient representation of information is accomplished through a statistically self-similar or fractal structure. Quantitatively establishing this organizing principle comprehensively is the goal of future studies that can be built upon the foundations of this research.

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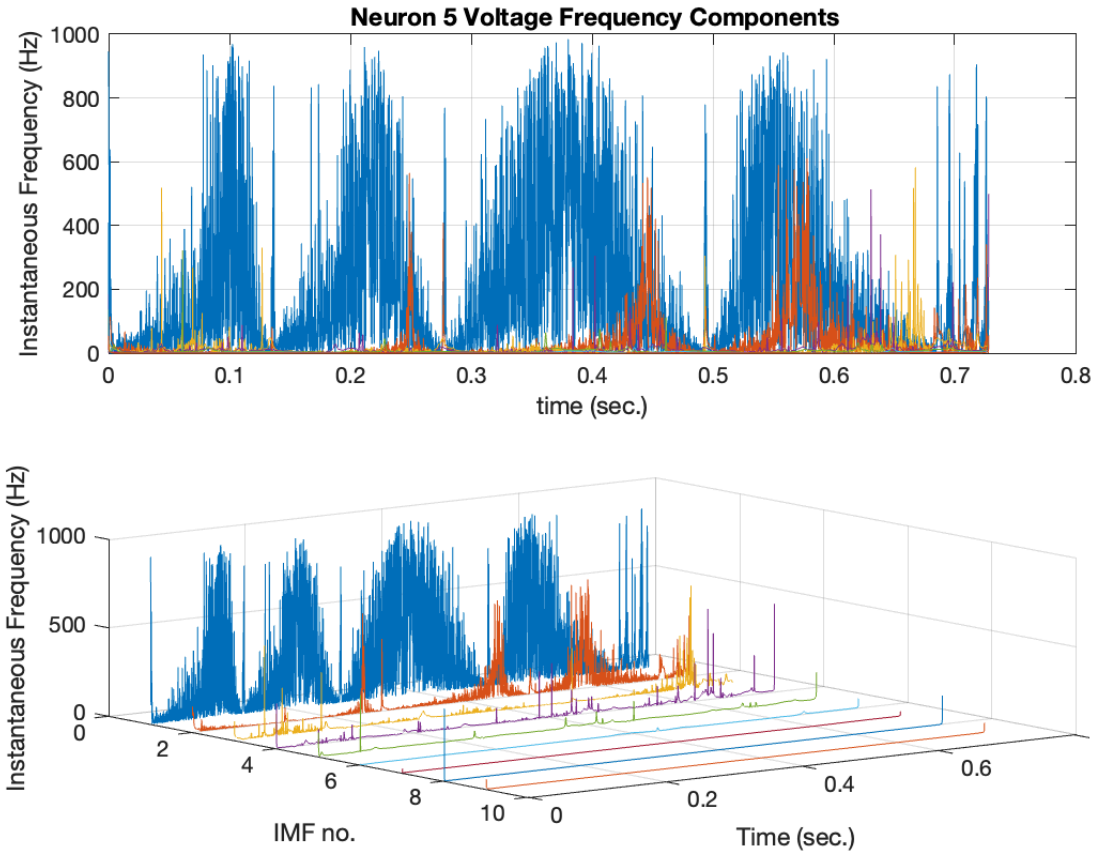
Neuron 5 Voltage Frequency Components
Instantaneous Frequency (Hz)
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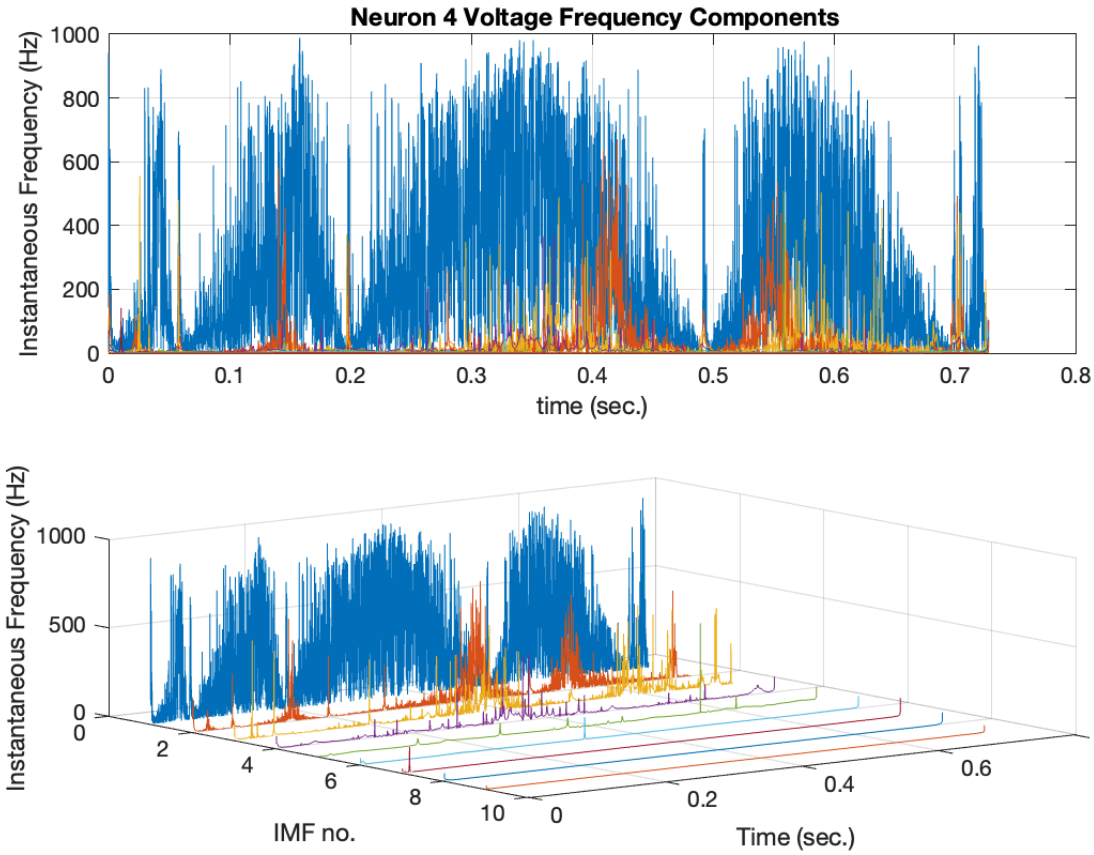
Neuron 4 Voltage Frequency Components
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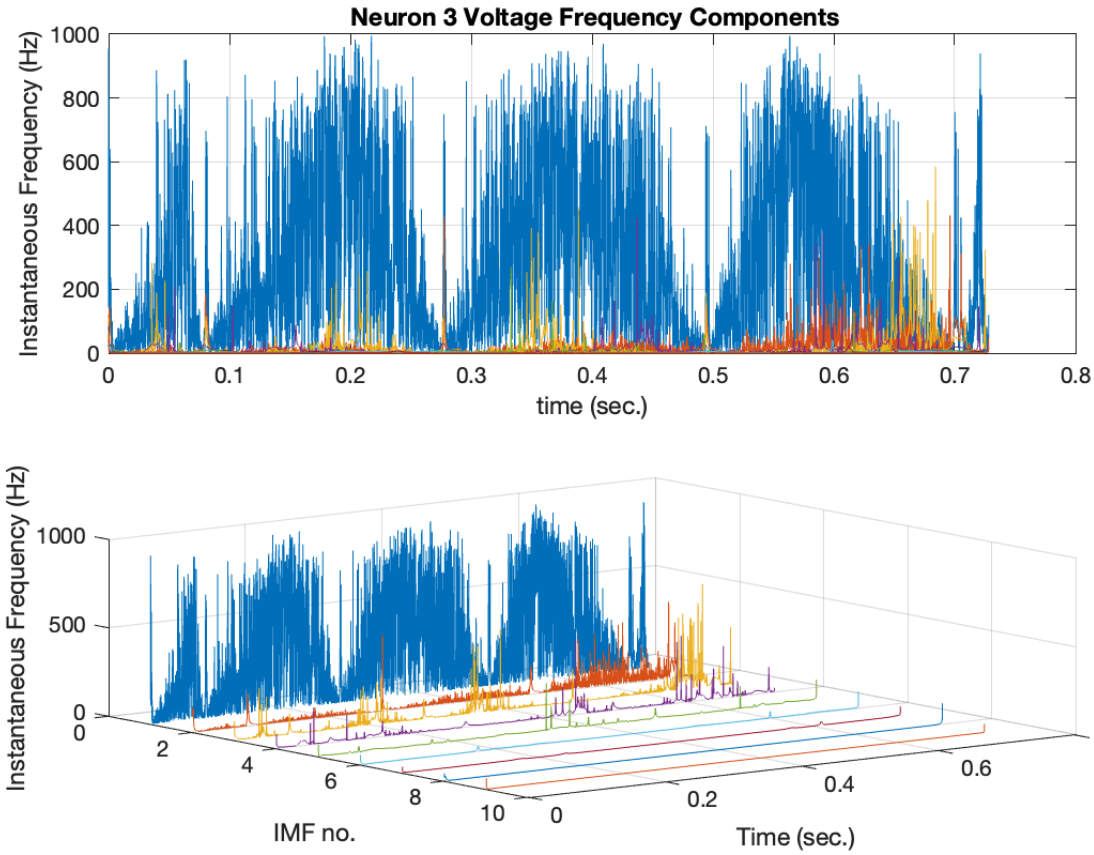
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time (sec.)
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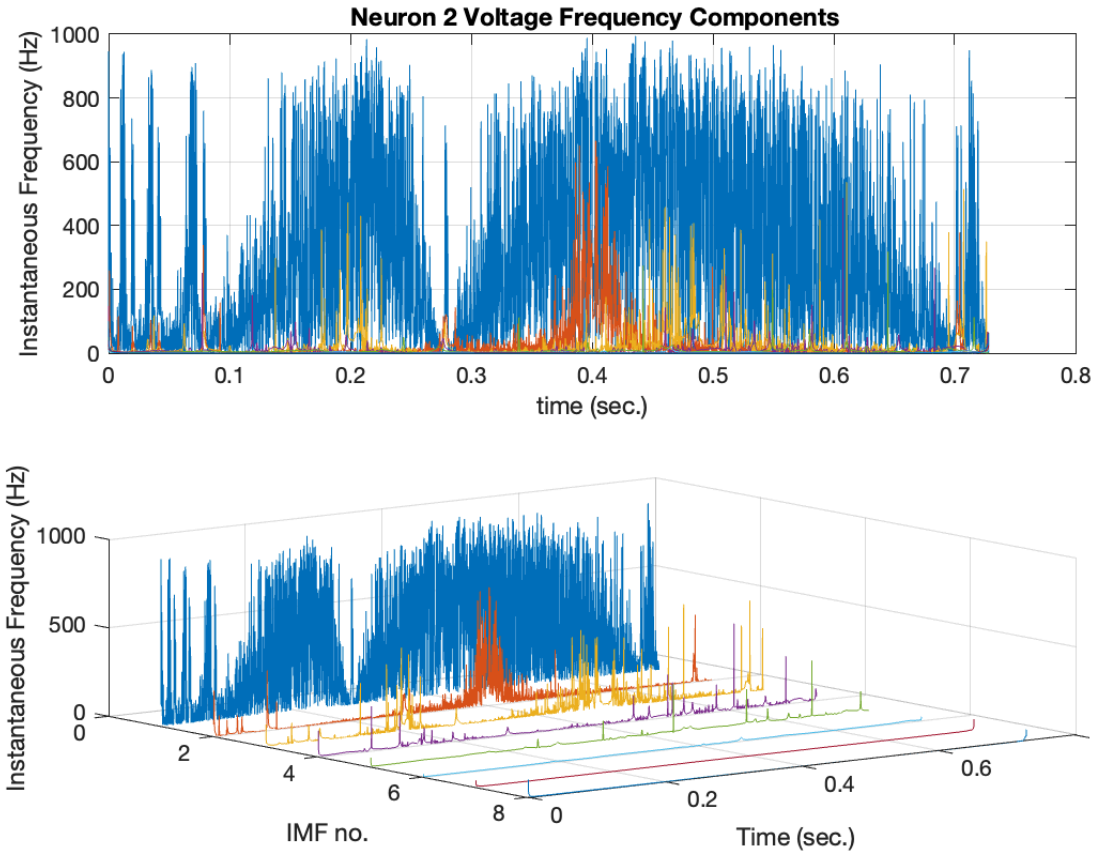
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