# Communication in Brain Circuits and Systems: a Primer

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***Abstract*—Communication in the brain is the key component underlying neural functions such as movement, memory formation and decision-making. In this primer, we characterize structural and functional mechanisms which implement communication at the cellular, network and system level. We then discuss data and computational models which can be used to study these mechanisms and provide hands-on examples implemented in Google Colab. Unifying the findings, we outline the structure of a computational model for testing the recently proposed spatial computing hypothesis, which describes memory encoding and retrieval in the prefrontal cortex.**

***Keywords—Neural Circuits, Oscillations, Biophysical Model, Spatial Computing, Reverse-engineer the Brain***

## I. Introduction

Communication in the mammalian brain covers a vast spatial and temporal range involving multiple neural levels ranging from molecular and cellular to network (single-region), systems (multiple-regions), and behavior. The brain is evolutionally optimized to have remarkable efficiency in performing sensory integration, computation and communication [1]. Perhaps somewhat surprisingly, the brain seems to have developed hardware for electronic and communication networks long before humans designed similar ones with metallic elements. However, we still do not understand brain 'software' and how it interacts with its hardware. The question of how networked neural elements and circuits intercommunicate and ultimately give rise to brain function is one of the most intriguing scientific challenges in reverse engineering [2]. The development of advanced tools to map and probe the brain has and is continuing to cause a deluge of data at multiple neural levels. This has led to growing collaborations between engineering/computer science researchers and neuroscientists to address the National Academy of Engineering grand challenge to 'reverse engineer the brain' [3]. How the human brain, with 86 billion neurons and 100 trillion connections, might represent a computer with its hardware and 'software' promises to be an exciting question that will challenge researchers in academia and industry in the coming decades, and provide curricular ideas for engineering educators [4].

This primer reviews the rapidly growing role of computational modeling at the cellular, network, and systems levels supporting this challenge, with a focus on communication as well as the retrieval and formation of memories. We highlight how oscillations play a key role in implementing all these 'functions'. We demonstrate these points with a set of open-source computational modeling examples implemented using Google Colab, which can run on any browser, providing a hands-on introduction for the interested reader uninitiated in computational neuroscience (https://github.com/cyneuro/neuro_communication).

## II. Brain Circuits, Systems and Communication

### A. Spikes, bursts and oscillations

Neural spikes, bursts, and oscillations represent different components of neural communication, each playing a distinct role. We begin by providing a short description of the physical nature of these entities.

A spike (or action potential) is an excursion of the neuron's membrane potential from the resting state (~ –70 mV) by about 100 mV (to ~30 mV), generated by salient inputs from other neurons. This excursion is transmitted as a voltage wave along the axon (much like a wave in an ocean) enabling it to engender similar spikes in its neighboring neurons. The mathematical dynamics of spikes was formalized in the celebrated Hodgkin-Huxley model (Box 1; [5]) for which the authors were awarded the 1963 Nobel Prize for medicine. Subsequent analyses showed how these dynamics involved a bifurcation mechanism [6], [7].

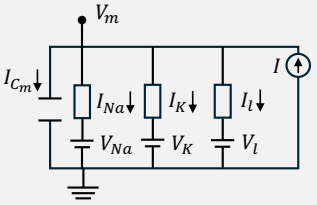
**Box 1. Hodgkin-Huxley model [5]**

$$I = C_m\frac{dV_m}{dt} + \bar{g}_K n^4(V_m - V_K) + \bar{g}_{Na} m^3 h(V_m - V_{Na}) + \bar{g}_l(V_m - V_l)$$

$$\frac{dn}{dt} = \alpha_n(V_m)(1-n) - \beta_n(V_m)n$$

$$\frac{dm}{dt} = \alpha_m(V_m)(1-m) - \beta_m(V_m)m$$

$$\frac{dh}{dt} = \alpha_h(V_m)(1-h) - \beta_h(V_m)h$$




where $I$ is the total membrane current, $C_m$ is the membrane capacitance, $V_m$ is the membrane voltage, $\bar{g}_X$ is the maximum conductance value for the ion channel $X$ ($Na$, $K$, leak), $V_X$ is the reversal potential of the ion channel $X$ ($Na$, $K$, leak), $\alpha_i$ and $\beta_i$ are rate constants for corresponding ion channels. See [5] for details.

Due to their transient and 'binary' nature, individual spikes cannot encode stimulus 'intensity'/significance and are not a reliable means of communication. It is believed that realistic communication mechanisms are executed via bursts, rapid

sequences of spikes occurring in a specific frequency band. Bursts give rise to neural oscillations, rhythmic patterns of neural activity that occur periodically at various frequencies; characterization of bursts in in vivo data is an active area of research due to its linkage to communication [8].

### B. Neural communication occurs at multiple levels

At the cellular level, the generation of an action potential involves communications within an elaborate dendritic tree with constant modulation by excitatory and inhibitory signals [9]; these communications are thought to implement computations at the soma. Although a detailed account of spike generation in a complex morphological cell is beyond the scope of this primer, the mechanism of spike and burst generation in a single-compartment cell is thought to be well-understood. Similarly, their role in communication with other neurons in close proximity seems to be clear (local network level).

However, communication across regions, particularly those separated by relatively large distances, is believed to be accomplished via oscillations, a topic that is only beginning to be understood, including via computational models, e.g., [10], [11]. While oscillations have been measured and documented extensively, including correlations with normal and pathological functioning, the mechanisms related to their genesis, or their role in implementing neural function, remain unclear. In particular, two important neural functions, memory formation and retrieval, are thought to be network phenomena arising from complex coordination of intricate circuits of neurons across several regions. Yet, it is unclear which structural and functional components allow the brain to produce, store and manipulate memories. There has been a recent surge in studies of the role of the *cellular and microcircuit* components involved in memory organization. Interestingly, this decomposition has also spawned a surge in investigations where researchers are translating the model from biological to artificial neural networks formulations to explore potential insights into neural function, as well as insights for the development of biologically inspired machine learning architectures [12].

### C. Oscillations play an important role in neural function, with dysfunction linked to pathology

Although not required for the knee-jerk reflex, motor learning and adaptation, and certain aspects of voluntary movement, oscillations play a central role in information processing for key neural functions including sensory, cognitive, motor, emotional/social and sleep/wakefulness functions (Table I). Here, we highlight the importance of oscillations to function via a few illustrative examples, and list how dysfunction in oscillations might underlie pathology.

*Sensory functions.* It has been demonstrated that the processing of sensory information from the environment, including visual, auditory, and olfactory signals, is enhanced by gamma band oscillations. Abnormal gamma oscillations can impair sensory processing and have been implicated in conditions such as the autism spectrum disorder [13].

*Motor functions*. Beta oscillations are seen in the motor cortex during the planning and execution of voluntary movement. Disruption in beta oscillations has been implicated in movement disorders such as Parkinson's disease, with symptoms such as motor tremors and rigidity [14].

*Emotional and social functions*. Theta and gamma oscillations are thought to be involved in processing and regulating emotions, with abnormalities linked to mood disorders such as depression and anxiety [15].

*Cognitive functions*. Oscillations, especially in the gamma band, have been linked to higher-order cognitive processes, including problem-solving and decision-making. Aberrant gamma oscillations are thought to underlie cognitive impairments in schizophrenia and Alzheimer's disease. Theta oscillations in the hippocampus have been shown to be crucial for memory encoding and retrieval. Similarly, alpha and gamma oscillations have been shown to play significant roles in focusing attention and filtering out irrelevant information, with alterations known to cause attention-deficit hyperactivity disorder and other attention-related disorders. Finally, oscillations were shown to help synchronize neural activity involved in language comprehension and production. In this case, dysfunctions have been linked to disorders such as dyslexia [15].

*Sleep and Wakefulness*. Various oscillatory patterns, such as delta waves during deep sleep and alpha waves during relaxed wakefulness, have been shown to be crucial for sleep cycles. Oscillations have also been demonstrated to be important in maintaining alertness during the day. Disruptions in delta waves can cause insomnia, and dysregulated oscillations can lead to conditions such as narcolepsy [15].

### D. Linking across neural levels via 'readouts'

Our understanding of brain oscillations and how they contribute to normal and pathological functions has been built largely through explorations involving rodents and non-human primates. While rodent studies afford accessibility and precise control of genetic and environmental conditions, e.g., [16], [17], non-human primates such as monkeys are closer to humans in brain structure and functions (e.g., compare frequency bands in Table I). These differences, in addition to evolving technical capabilities, motivated a variety of data recording techniques, each capable of capturing specific biological aspects. Here we characterize properties of data recorded at different spatial and temporal levels (Table II).

*Intracranial recordings*. Advanced probes such as Neuropixel [18] can simultaneously record from 384 channels (sites) at 30 kHz providing snapshots of neural activity at very fine temporal and spatial resolutions sufficient to capture spikes, bursts, and extracellular potentials (ECP, which is typically low-pass filtered at 500 Hz to yield local field potentials, LFP; the high frequency component of ECP is used to determine unit activity such as spikes and bursts). ECP signals can capture the activity of neurons within a few hundred micrometers of the electrode tip. The high sampling rate ensures that rapid changes in neural activity are included, making them suitable for studying oscillations. This information can be used to correlate behavior in rodents to functional roles of oscillations, e.g., [16].

*Noninvasive recordings*. Techniques such as magneto encephalography (MEG) and functional magnetic resonance imaging (fMRI) are often used in non-human primates in a manner that closely mirrors human studies. This enables translation of such findings to humans, facilitating the development of treatments for neurological disorders. Electroencephalography (EEG) is the most common technique used to study human brain function since it is non-invasive, has sufficient temporal resolution (in ms), and is cost-effective and portable [19]. It is presently used for clinical diagnosis, cognitive and behavioral research, and in brain-computer interfaces (BCIs).

## III. Computational Models

The neural data recorded using increasingly sophisticated probes provide insights into the functioning of single neurons and networks at unprecedented resolution in time and space. This deluge of high-fidelity data is driving research at all levels, including computational model development in both theory-driven (biophysical and reduced order) and data-driven (e.g., machine learning) domains. Computational models of neural circuits and systems are being developed at multiple levels including intracellular, cellular, network, multi-region, and behavioral levels (Table II). Here we provide a brief overview of biophysical models at single cell and network levels, with hands-on modules developed using the NEURON and BMTK simulators [20], [21]. The modules use Google Colab and can be executed directly in the browser or downloaded and run locally (https://github.com/cyneuro/neuro_communication).

*Single cell models*. A single compartment biophysical cell model under the Hodgkin-Huxley formalism (Box 1) illustrates one functioning type of spiking cells with three channels: sodium, delayed rectifier potassium, and leak. The user can change the maximal conductance of the channels and observe the corresponding effect on the soma voltage output.

*Network & oscillation models*. The single cell model can be replicated for other cell types and combined with synaptic models to develop neuronal networks. To illustrate oscillations, we use the canonical pyramidal-interneuron-gamma (PING) circuit model adapted from [6]. The network structure was adjusted to include clusters of densely connected neurons representing cell assemblies. The user can adjust the cellular and synaptic parameters (including time constants) to study how they impact characteristics of the rhythms including center frequency, bandwidth, and power.

*Machine learning (ML) models* [22], [23]. ML models are becoming essential to advance the frontiers of neuroscience for multiple reasons. ML models or architectures (particularly the deep-learning ones) are 'data hungry' and so are ideally suited to accommodate the rapidly growing large and complex datasets in neuroscience that exceed the limits of other modeling paradigms. Moreover, they have been shown to help uncover hidden patterns and develop predictive models for behavior and disease [24]. They have also been proven to be effective in real-time processing, which is critical for applications such as BCIs. As an example, we provide a workflow for emotion classification with EEG data.

*Example case of spatial computing in human prefrontal cortex (PFC).* Uniting the components above, we consider an example case where computational models can explore hypotheses regarding neural computing (Fig. 1). One such hypothesis, titled 'spatial computing' (SC), suggests that oscillatory bursts may selectively target one out of several representations of items held in working memory (WM) via top-down control, to activate cell assemblies (e.g., groups of neurons) to encode the memory of an item [25]. This paradigm describes the encoding and retrieval phase of a delayed match-to-sample WM trial [26]. According to SC, encoding of distinct items is accomplished by distinct patterns of gamma and beta bursting that dictate which item-selective assemblies represent specific items in network space. The readout after the delay period is performed by upregulating activity in the respective parts of the network. Moreover, mental representations can be updated over time by changing the imposed bursting patterns (i.e., the same item can be encoded in a different location with a different top-down bursting pattern).

To investigate this hypothesis, we are developing a 1000-cell biophysical network where we use oscillation-generated plasticity to encode memories of multiple items (mimicking the delayed match-to-sample WM task) and then recall them after a delay period. Such investigations can also inspire artificial neural network (ANN) architectures. For instance, our future work involves exploring an ANN architecture for the classification problem consisting of two sub-networks: a larger "storage" network and a smaller "controller" network. Training is performed in two stages: first, the controller network is trained to produce a unique stable pattern which selects parts of the storage network; second, the selected parts are trained to differentiate an item from all other items (one-vs-rest classification). We hypothesize that such a network will be able to separate memory features with enhanced accuracy.

## IV. Challenges and Future Research

Mimicking neurobiological circuits in biophysical models poses challenges due to their sheer complexity and scale. Although it is possible to generate viable models of single cells and networks, modeling 'communication' or interactions across brain regions is difficult due to the lack of data and hypotheses. Presently, it is an active area of research. As an example, at the cellular and network levels, research has shown how brain functions are modified by the release of neurotransmitters that are known to 'rewire' circuits, enabling a wide range of dynamic behaviors and adaptability [27] that directly affect communication. However, this 'rewiring' adds considerable complexity to both modeling and interpreting circuits, and thus typically ignored in current-day models. Extending biophysical models to the behavioral level also presents challenges due to the lack of data at the intermediate stages and is continuing to provide opportunities for machine learning models to 'fill the gap' via innovative hybrid schemes. Nevertheless, biophysical computational models represent an exciting and perhaps critical tool for advancing our understanding of the rich communication infrastructure in our brain.

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TABLE I. RANGES FOR CANONICAL FREQUENCY BANDS

| Wave | Description [28] | Rat (Hz) | Macaque (Hz) | Human (Hz) |
|---|---|---|---|---|
| Ultra/Infraslow | Results from fluctuations in resting state activity, most recorded in the neocortex and subcortical structures. | 0.02–0.6 [29] | <0.1 [30] | 0.02 - 0.1 [28] |
| Slow | The most prominent frequency during sleep as measured across the neocortex. | 0.5–1.5 [31] | 0.1–1 [32] | 0.1–1 [33] |
| Delta | Involved in the hyperpolarization state of slow waves, with roles in energy conservation and cortical silence. | 1–4 [34], [35] | 1–4 [36] | 1–4 [37] |
| Theta | Involved in several neural mechanisms, these waves tend to be involved in cross-frequency interactions including theta-gamma coupling. | 5–10 [37], [38] | 4–8 [39], [40] | 4–8 [41], [42] |
| Alpha | Characteristic of relaxed, waking brain states. There are 3 main types, arising after eye closure in primates, cessation of movement, and visualization of movement. | 8–12 [43], [44] | 8–12 [40] | 8–12 [44], [45] |
| Sleep Spindles | Occurs in slow wave sleep, and results from spiking synchrony in deep layers of the neocortex. | 7–14 [35], [46] | 12–18 [17] | 10–16 [47] |
| Beta | Occurs in motor areas of the neocortex during muscle contractions. | 15–30 [48] | 14–30 [49] | 13–30 [50] |
| Gamma | The most common rhythm present in most brain states and neocortical areas. | 30–80 [51], [52] | 30–60 [53] | 30–80 [54] |
| Ripples | Believed to replay neuron spiking associated with learning and memory in a rapid manner to aid in the consolidation of new memories. | 100–200 [55], [56] | 100–250 [57] | 80–140 [58] |

TABLE II. NEURO-LEVELS/TECHNIQUES AND CORRESPONDING MODELS

| Neuro-level Technique | Biophysical Models |
|---|---|
| ***Electroencephalography (EEG) Brain wide***<br>Temporal: <0.001 s, Spatial: 6,000–20,000 mm$^2$ (~30–500 million neurons) (Electrical measure of synchronized neuronal spiking activity at a population level) | Mean Field / Neural Mass [59], Human Neocortical Neurosolver [60], Harmonics based [61], Spectral Graph [62], Jansen-Rit Equations [63] |
| ***Magnetoencephalography (MEG) Large region***<br>Temporal: <0.001 s, Spatial: 3,000–4,000 mm$^2$ (Magnetic measure of synchronized neuronal spiking activity at a population level) | |
| ***Positron Emission Tomography (PET) Large region***<br>Temporal: 60–120 s, Spatial 4–5 mm$^2$ (Energy measure of neuronal activity, commonly via glucose metabolism) | Compartmental Models [64], [65], Reference tissue models [65], Tracer Kinetic Models [64] |
| ***Functional Magnetic Resonance Imaging (fMRI) Local/Large region***<br>Temporal: <4-5 s, Spatial: 3–4 mm$^2$ (~1 million neurons) (Energy measure of neuronal activity via blood oxygen concentrations) | Dynamic Causal Models (DCM) [66]<br>Connectome Models [67], [68]<br>Mean field models [69], [70] |
| ***Computed Tomography (CT) Local/Large region***<br>Temporal: 0.83–1 s, Spatial: 0.5–0.625 mm$^2$ (Indirect measurement of neuronal activity via x ray radiation and computer technology) | Tracer Kinetic Models [71], Compartmental Models [72], Deep learning models [73], [74] |
| **Electrocorticography (ECoG)** ***Local***<br>Temporal: <0.001 s, Spatial: <1 mm$^2$ (~500,000 neurons) (Electrical measure of summed spike activity in a small neuronal population) | Multicompartmental Neuron Models [75], Extracellular Potential Forward Models [76] |
| ***Single neuron recording Local***<br>Temporal: <0.001 s, Spatial: <1 mm$^2$ (1 neuron) (Electrical measure of spikes in a single neuron) | Hodgkin Huxley Model [5], Integrate & Fire [77] |

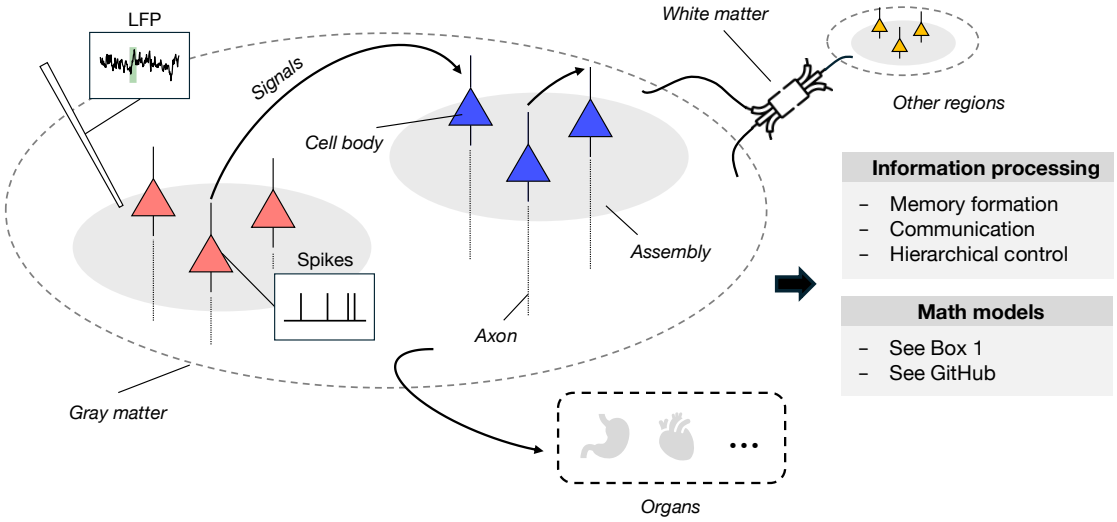


Fig. 1. Schematic of a computational model unifying different communication components.