**Leveraging Neuromorphic Computing for Low-Power Detection of High Frequency Oscillations in the Hippocampus**

**Bachelors of Bioengineering qualification**

Histograma

Descripción generada automáticamente con confianza media

Autor **Marcos Oriol Pagonabarraga**

Director [Nombre y Apellidos]

Presentation Date [dd/mm/aaaa]

# Acknowledgements

The authors were very grateful for having the chance to demonstrate that…

**Table of Contents**

[Acknowledgements 2](#_Toc167036619)

[Abstract 4](#_Toc167036620)

[List of Tables 5](#_Toc167036621)

[List of Figures 5](#_Toc167036622)

[List of Abbreviations 5](#_Toc167036623)

[Objective 6](#_Toc167036624)

[Hypothesis 6](#_Toc167036625)

[Introduction 7](#_Toc167036626)

[State of the art 8](#_Toc167036627)

[Current stage of research in neurological diseases 8](#_Toc167036628)

[Drug Treatments 8](#_Toc167036629)

[Electrical Treatments 9](#_Toc167036630)

[The hippocampus 10](#_Toc167036631)

[Hippocampal subregions 10](#_Toc167036632)

[Memory consolidation 11](#_Toc167036633)

[Sharp Wave Ripples (SWR) 11](#_Toc167036634)

[Neuromorphic Computation 13](#_Toc167036635)

[Applications of NC 13](#_Toc167036636)

[Spiking Neural Networks 15](#_Toc167036637)

[Neuron models 15](#_Toc167036638)

[SNN Learning Mechanisms 16](#_Toc167036639)

[Materials and Methods 18](#_Toc167036640)

[References 23](#_Toc167036641)

# Abstract

With great advances…

# List of Tables

# List of Figures

# List of Abbreviations

# Introduction

## Neuromorphic Computation

Neuromorphic computation could be described as a “*computing paradigm designed to mimic the structure and function of the human brain”*. It involves the use of hardware and software systems that replicate the neural architecture and operational principles of biological neural networks.

The human brain is posed as the most intelligent and efficient machine. It is built by billions of neurons connected between them on an average of more than ten thousand synapses per neuron[1]. Its outstanding intelligence and efficient computation have inspired researchers to develop the working principles of AI, namely ANNs, where intelligence is achieved by small computing nodes forming a network capable to learn patterns. Following inspiration by nature, NC raised as another approach to recreate intelligence through a deeper emulation of the biological neural system [2]. At all ends, ANNs achieve intelligence by simulating the inputs and outputs of the nodes allocating values in memory and performing operations between them, which is not very efficient and needs more energy than biologically needed to perform simple tasks. In contrast, human brain has physical nodes with real connections and weights which make it way more efficient than our digital technology in spatial and visual tasks (a 10 million factor approximately [3]). That said, the main advantage of NC against deep learning is that it aims to build the neural structure physically. That is, designing electronic neurons and synapses at a microscopic scale, which are connected as a circuit recreating a neural network. Essentially, NC aims to reinvent computing machines making them fundamentally different from current digital computers.

### Strengths and weaknesses

Digital computers work with algorithms and calculations performed by arithmetic circuits[[1]](#footnote-1). Moreover, information is encoded in binary values by analogue-to-digital converters, working with zeros and ones. These values were first computed serialized (like a queue of values) controlled by timesteps set by an oscillating crystal inside the processing unit. Each timestep was able to perform a single operation. With the advances in the field, more parallel computation has been pursued and implemented. However, it supposes a hurdle and limits its capabilities. These limitations observed in the working nature of digital computation are overcomed in NC. Physical electronic nodes and synapses allow to process information in a decentralized manner, so the computation is much more parallelized. Moreover, a major part of the process happens by analogous electrical circuit operations which increase notably the speed compared with time step guided operations. Furthermore, as a consequence of parallel operation and improved efficiency in performing operations, much less energy is required to achieve the same computation.

Of course, recreating the physical circuits to mimic brain neural network architecture is much more complicated than building a silico microprocessor unit. In addition, NC cannot produce so small processing units as in silico processors. Currently, transistors are in the nanometric scale whereas electronic neurons are in the range of micrometres, limiting their capability to form so complex processing systems as we see in silico computation, because they would need much more space.

Considering the abovementioned features of NC, it can be understood why this computation paradigm have not replaced yet the silico industry. Further steps of tailoring and nanoscale electronical neurons would be required for its widespread implementation in our society.

### Applications of NC

Gráfico, Diagrama, Gráfico radial

Descripción generada automáticamenteIts broad potential due to parallel processing and low-latency operations make it suitable for tasks involving real-time analysis of streaming data from various sources, such as sensors, cameras , IoT devices… Its main strength could be assessed as instant decision making. This capability is often demanded in industries such as autonomous vehicles, predictive maintenance systems and healthcare devices.

**Figure4.** Applications of neuromorphic devices in real-time analysis of biological signals. Among the most relevant it can be found applications for: Deep Brain Stimulation closed-loop systems, cancer detection from biomarkers, and cardiac anomalies detectors within the realm of wearable biosignal analysis, and imaging advances for high computation cost imaging techniques.

In healthcare industry, there is a growing demand for low power, non-invasive quick treatments for handling biosignal analysis [4]. Current implantable devices which attempt to perform real time deep neural network (DNN) applications often end up needing cloud computing due to the required processing power. This constrains limit their applications in such sensitive fields due to risks associated with communication interferences and delays [5]. Unlikewise, hardware-based neuromorphic systems address these limitations by offering implantable devices capable to perform DNN computations locally in real time [5].

In signal detection applications, it is very usual to process the input signal before feeding the network for classification. This helps to overexpress the features wanted to be detected, which in consequence improve the accuracy of the model. A hurdle in the implementation of NC for real-time signal classification is this first process of signal filtering and preparation for the network. In digital computers is very easy because a complex code can be compiled to perform any modification to the signals.

However, in NC an equivalent electronic circuit must be developed and integrated in the system to feed a Spiking Neural Network (SNN) [[2]](#footnote-2). Fortunately, there is a wide knowledge and years of research in filtering circuits which are used by the community as preprocessing in real time [6], [7]. These include bandpass filters and analogue-to-digital converters.

## Hardware Neurons

In order to realize highly efficient neuromorphic computations that can be comparable to biological systems, bioinspired computing frameworks, involving biorealistic artificial synapses and neurons need to be developed. A circuit consisting of at least ten transistors is required to achieve the function of one biological synapse[1]. This makes the implementation of neuromorphic computation very difficult for large networks. Fortunately, another realm for electronic circuits have been tailored to mimic the electrical inputs and outputs of neurons. To achieve this, profound research in materials and physics has been done[1].

To recreate the brain environment, two electronic systems have been developed to define an electronic neuron. First, the cell body (e-cell), which computes the electrical inputs from the presynaptic neuron and regulates the state of its membrane potential (determining when to fire a spike) and second, the neuron axons (e-axon), which transmit the electrical pulses generated in the core of the cell. The electrical circuits defining the axons also mimic how synapses retain synaptic strength, enabling the natural learning method behaviour of biological neurons to happen in hardware, namely Spike-Timing-Dependent Plasticity (STDP).

These two building blocks are sufficient to construct complex networks with high level of fidelity, in the way of processing information, to a biological neural network. E-cells and e-axons circuits can be configured together to mimic the architecture of neural networks that, up to date, could only be simulated. The level of resemblance to biological neurons obtained by the development of e-cells and e-axons, have made this computing paradigm much more energy efficient and fast than transistor-based computation[8], [9], [10]. Furthermore, previous e-neurons and e-axons trials integrating many transistors suffered from high leakage power dissipation and difficulty in integration due to increased space needed.

### Building the blocks

The key to overcome traditional methods mimicking neurons behaviour (transistor based) was the discovery of memristors. They were conceived in 1971 as a theoretical concept, but they were not applied to physical devices until 2008, by Hewlett-Packard (HP) lab [11]. The word memristor states for “memory” and “resistor”. Basically, is a resistance with memory. So, the value of the resistance, therefore also of the conductance, depends on the last current applied to it. This feature makes them capable of working as non-volatile memory. In other computing frameworks, static random-access memory is used as non-volatile memory framework. With memristors, a resistance random-access memory (RRAM) can be achieved.

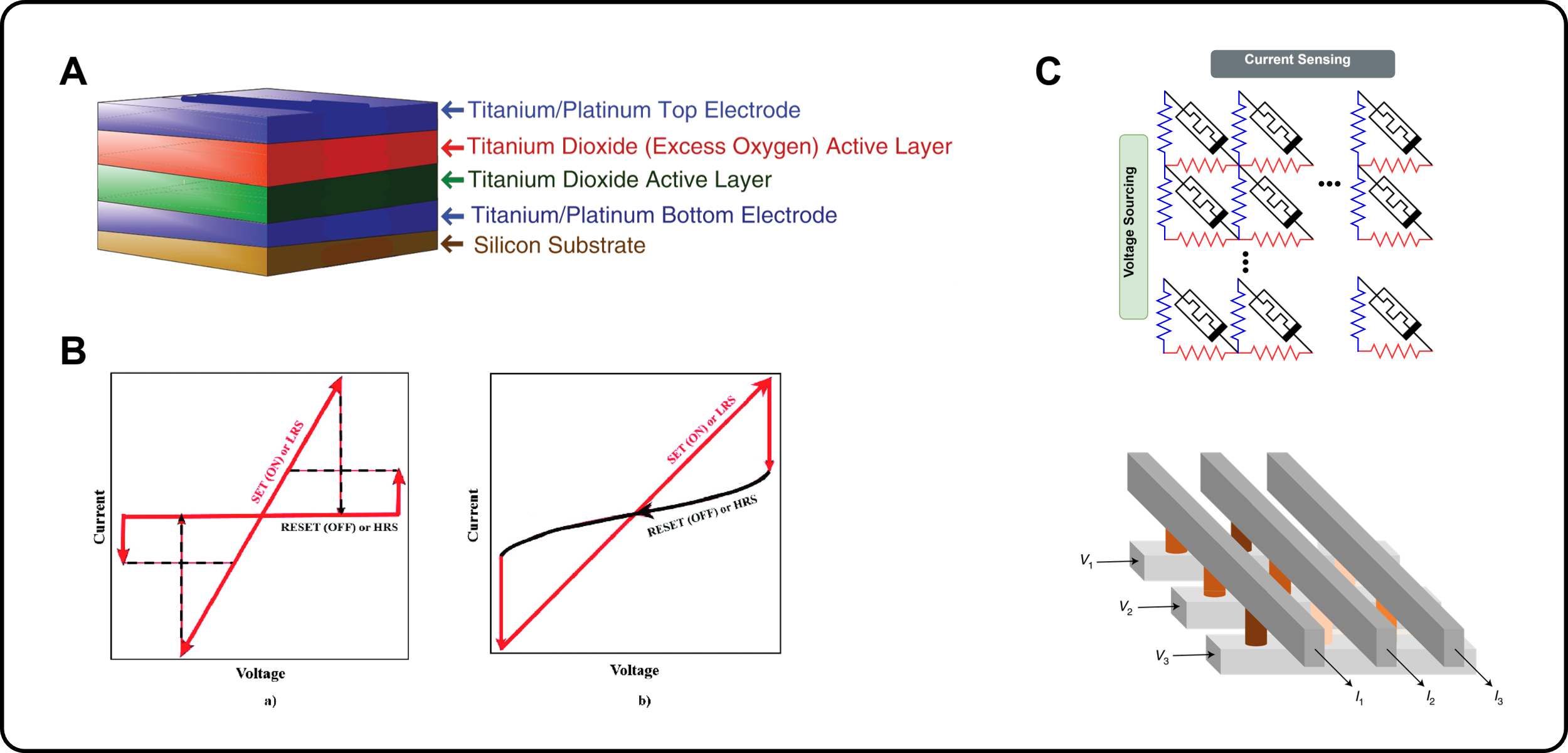
**Working principle of memristors**

Memristors are, indeed, very simple structures. They are composed of two-terminal metal-insulator-metal (MIM). The outer layers are conductive metals, and the inner layer is made of an insulating material. This insulating layer can change its resistance based on the history of voltage applied across the terminals, effectively "remembering" past electrical activity. When a voltage is applied, ions or charge carriers within the insulator move, altering its resistance [12]. Different insulating materials can be used to achieve memristive behaviour. TiO₂ memristors consist of a central insulating layer of titanium dioxide (TiO₂). The TiO₂ layer contains regions with oxygen vacancies, which can migrate under an electric field, altering the material's resistance. When a positive voltage is applied, these vacancies form conductive pathways, switching the device to a low resistance state (LRS). Reversing the voltage causes the vacancies to disperse, returning the device to a high resistance state (HRS) [11].

**Figure 1.** **Memristors Overview.** How memristors materials are distributed and their behaviours to electrical stimulus. **A)** Spatial distribution of a memristor layers. The choice of silicon substrate can impact factors such as thermal conductivity, mechanical strength, and integration with other semiconductor technologies, top and bottom electrodes establish electrical contact with the memristor and enable flow of current. Finally, Dioxide layers undergo reversible changes in its resistance in response to applied electric fields or currents. **B)** Current-Voltage characteristic curves of memristor, showcasing their hysteresis behaviour.

## Spiking Neural Networks

Neural communication is well known to be mediated by spikes [[3]](#footnote-3). The neuroscientiphic research community have widely debated whether if neural communication primary relies on the shape of spikes or the spike rate. Initially, some theories suggested that the precise shape of an action potential might carry important information. However, contemporary research tends to emphasize the importance of the spike rate over the plain shape of individual spikes for neural encoding [13].

Rate-based coding theories propose that the frequency of spikes over a period is the primary way neurons encode and transmit information. This approach is supported by evidence showing that many neural functions, such as sensory processing and motor control, correlate strongly with changes in spike rate [13], [14]. In these theories, the spike rate reflects the amount of information transmitted and is crucial for understanding neural activity.

Additional theories highlight the significance of the precise timing and patterns of spikes, arguing that the exact timing of spikes, in relation to each other, can carry additional layers of information that might be missed if only the rate was considered [14], [15]. One notable example is the “chronotron (Florian R et al 2012)”, which is a model of neurons that learn to fire at specific times [16]. This model demonstrates how precise timing of spikes can encode information. Overall, the consensus in modern neuroscience is that both spike rate and riming play roles in neural communication. In contrast to older theories, shape of the spike seems to be irrelevant in the task.

Discovering that biological neurons process information with spike timing independently of the I nformation of the spike led to the idea of event-driven computation. Spikes are the events and neurons act in response to them. When a stimulus is provided to the biological network through sensors (touch, vision, noise), the neurons propagate the stimuli through the corresponding areas of the brain in the form of events (spikes). The rate and time patterns of events encode the information, ultimately leading to an output. This process can involve more or less neuronal complexes. Similarly, artificial SNNs have been developed to process information in an event domain. An architecture of spiking neurons can be engineered to mimic the processing task that biological neurons would do in the brain. To achieve such task, neuron models have been proposed and tailored to behave as neurons.

### Neuron models

Neuron models are the main variable in SNNs. How the nodes of the network will communicate between them provide notable insights of the network behaviour. In the literature there are many neuron models reported and some of them have been widely used for different applications [17], [18].

**Leaky Integrate-and-Fire (LIF)**

Popular due its simplicity and efficiency. It captures the essence of neuronal behaviour by integrating incoming signals (synaptic inputs) over time. When the accumulated membrane potential reaches a specific threshold, the neuron fires a spike, and the potential resets, beginning the integration process. This model, with its straightforward threshold mechanism and leaky integration, has been foundational in many SNN applications, offering a balance between biological realism and computational manageability. []

**Hodgkin-Huxley**

Developed through Nobel Prize-winning research, this model describes how action potentials in neurons are initiated and propagated, based on detailed ionic currents through the neuronal membrane. The Hodgkin-Huxley equations capture the dynamics of voltage-gated ion channels, offering an unparalleled level of detail. Although computationally intensive, this model is useful electrochemical mechanisms underlying neural activity need to be considered. []

**Izhikevich**

Aiming to bridge the gap between the simplicity of the LIF model and the complexity of the Hodgkin-Huxley model, the Izhikevich model was introduced. This model combines biological plausibility with computational efficiency, capable of replicating a wide variety of neuronal firing patterns observed in real neurons. By using fewer computational resources, the Izhikevich model captures complex spiking behaviors, making it a versatile tool for simulating large-scale neural networks without compromising on realism​. []

**Adaptative Exponential Integrate-and-Fire (AdEx)**

AdEx enhances the LIF framework by incorporating adaptation mechanisms. This model can replicate the adaptative behaviour of real neurons, such as frequency adaptation and spike-frequency adaptation. The AdEx model’s ability to adjust its response based on prior activity provides a more refined simulation of neuronal behaviour, being able to capture the dynamic nature of neuronal adaptation observed in biological systems. []

### SNN Learning Mechanisms

The training process of SNNs is still at the stage of development because of its novelty and lack of deployment in our society. There are several methods which enable the network to learn patterns, but there is a lot of improvement to be done. ANNs are able to achieve better performances than SNNs in many workloads [19].

Learning in neural networks implies changing the weight connections between nodes []. In ANNs these nodes are responsible to modify the input signal throughout the layers to enhance “invisible” pattern features so that finally a simple operation can determine the correct label of the input. These modifications rely on “values as inputs”. For example, an image as the input of a convolutional network, will experiment kernel operations on its pixel values that will change the image itself through the layers. However, in SNN, the inputs are not values, but spikes. Therefore, the network must be able to modify the strength of neuron synapses to learn time domain patterns within inputs[20], [21]. The network will have a response for each sample. That is, in the context of detecting a ripple, the 100 samples it may last, each sample will modify the membrane potentials of neurons and the network will produce spikes (or not). The shape of the ripple will therefore cause that the network fire at higher frequency. Thus, setting a rate threshold for detection, in this case a ripple, can be done [22], [23]. As it is showcased, the rationale behind learning is notably different within ANNs and SNNs.

**Spike-Timing-Dependent Plasticity (STDP)**

This unsupervised learning rule adjusts the synaptic weights based on the precise timing of spikes from pre- and post-synaptic neurons. If a presynaptic spike precedes a postsynaptic spike within a certain time window, the synaptic strength is increased (long-term potentiation, LTP). If the presynaptic spike follows the postsynaptic spike, the synaptic strength is decreased (long-term depression, LTD) [20], [23].

**Surrogate Gradient (SG) Methods**

Due to the non-differentiability of spike events, traditional gradient-based optimization is challenging for SNNs. Surrogate gradient methods approximate the gradient of the spike function, enabling the use of backpropagation [[4]](#footnote-4). This approach has been effective in training deep SNNs directly and handling temporal data efficiency [24].

**ANN-to-SNN Conversion**

Another approach involves converting a pre-trained ANN into an SNN. This is done by replacing the activation functions of the ANN with spiking neuron models. While this method can quickly yield SNNs, it often relies on rate coding and might not fully exploit the temporal dynamics of SNNs [24], [25]​.

The training framework sounds quite straightforward until now. In fact, it is just required the code to recreate the mentioned behaviour, which we, as humans, are perfectly capable of. The problem comes when switching from software to hardware. That is, trespass the equivalent network to a physical network of electrical neurons. What are the electrical circuits that behave as neurons and synapses?

## Neuromorphic Framework

### Lava Neuromorphic Computing

Lava[[5]](#footnote-5) is an open-source software framework developed by Intel. It is designed for developing neuro-inspired applications and mapping them to neuromorphic hardware. Lava provides developers with tools to harness the principles of neural computation, enabling neuromorphic platforms to process, learn, and respond to real-world data efficiently and quickly compared to other computer architectures.

Lava has a versatile structure, allowing researchers to integrate a wide range of algorithms and build complex neuromorphic applications. It supports the definition of processes, such as individual neurons, neural networks, and interfaces to external devices, which can be encapsulated into modules and aggregated to form sophisticated systems. Communication between processes in Lava uses event-based message passing, facilitating the simulation of neural interactions.

Moreover, Lava allows applications to be run on conventional CPUs/GPUs and deployed to various neuromorphic chips, such as Intel’s Loihi. This flexibility is enhanced by a low-level interface called Magma, which aids in compiling and executing processes across different backends. Lava aims to unite the neuromorphic computing community, providing a common framework to facilitate collaboration and innovation in the field​.

### Lava Workflow

Lava framework is divided in two branches:

**Lava-nc** is the main branch and it is used to compile and run lava processes, as well as migrate them to physical neuromorphic chips.

**Lava-dl** is an independent module used to create neuron models and networks. It also provides SNN training as well as functions to convert network to lava process, which can be compiled and mapped to neuromorphic hardware.

**SLAYER**

Spike Layer Error Reassignment in Time is the tool used by lava-dl for training SNNs. It enhances a more effective learning by improving the network’s ability to recognize patterns and make decisions, mimicking the way the brain processes information. By implementing a temporal credit assignment policy, SLAYER enables errors to be backpropagated through the network layers, addressing the challenge of non-differentiability in spike generation [[6]](#footnote-6). This allows for the adjustment of synaptic weights and axonal delays, ultimately leading to better performance in tasks like pattern recognition and decision-making, similar to biological neural networks.

Slayer built-in tool from lava

**LAVA-DL**

### Loihi2

## Neuronal Electrode Systems

To effectively interface with the brain and record neural activity, a good and reliable recording system is required. It is as important to have good quality signals as to being able to detect them. Since we know that the brain has electrical activity happening within its tissue, many trials have been done aiming to undecipher their meaning. Currently, many recording systems are enabling neuroscientific community to learn many insights from neuronal signals, thus boosting the appearance of new technologies and advances. Electrodes implanted in the brain have created a renaissance in the study of normal and pathological brain function. These devices are being developed to treat a growing number of medical conditions, including Parkinson’s disease, paralysis, Alzheimer’s disease and depression [26]. These systems range from non-invasive to invasive techniques, each offering different levels of spatial resolution and specificity.

### Novel technologies

Common and traditional methods such as electroencephalography (EEG) and magnetoencephalography (MEG) are widely used for their ability to monitor brain activity without the need for surgical intervention. EEG measures electrical activity through electrodes placed on the scalp, while MEG detects magnetic fields produced by neuronal activity. Both methods provide interesting insights into brain function but are limited by their relatively low spatial resolution.

Other newer more invasive techniques include Electrocorticography (ECoG), which involves placing electrodes on the surface of the brain, typically during neurosurgery. This approach offers better spatial resolution than EEG and MEG, allowing for more precise localization of neural activity. Some works have relied on this technique to assess epileptogenic tissue areas during brain interventions [27]. The more precise recorded signals provide with a higher signal-to-noise ration and the detection of biomarkers results to be more accurate. In epileptic patients, high frequency oscillations originating from epileptogenic tissue can be detected by filtering the signal in its frequency band and training a simple network to detect them[28].

More invasive methods involve implanting electrodes directly into brain tissue, providing the highest spatial resolution and the ability to record from individual neurons or small groups of neurons. These include:

*Single-Unit Recording* uses fine microelectrodes to record the activity of single neurons. It offers unparalleled detail but can only sample a limited number of neurons at a time. This type of electrodes can be found in patch clamp method, a powerful technique widely used in electrophysiology to study the ionic currents flowing through individual ion channels on the membranes of neurons.

*Multi-Electrode Arrays (MEAs)* consist of multiple electrodes arranged in a grid, allowing simultaneous recording from many neurons. This approach is valuable for studying neural networks and their dynamics [29]. MEAs can be valuable to study 2D distributed cell populations. Being able to place electrodes uniformly as a “matrix” through the cellular space can assess signals flowing through the network and population oscillations. Nevertheless, they may not be suitable for deep tissue recordings due to their limited capabilities of being embedded in a 3D cell complex []. MEAs are primarily applied in vitro. Where neurons are delivered in top of the electrodes to grow in top of them. Recordings are directly in contact with neuron membranes, leading to much less interferences and pure raw signals []. Although, they have also been used in vivo [[]].

*Shank [[7]](#footnote-7) Invasive Electrodes*, such as silicon probes, are a specific type of invasive electrode designed to penetrate brain tissue and record from multiple sites along their length (***see Figure 6)***. These electrodes can sample from different layers of the brain, providing detailed information about neural activity in various depths. Shank electrodes have been instrumental in advancing our understanding of complex neural circuits and their role in behaviour and cognition[]. Their appearance was driven by the need of recording deep areas of the brain with high resolution. []

In applications where the goal is to study deep brain complexes, invasive technologies show better outcomes compared to superficial ones []. In neurodegenerative diseases where structures such as the hippocampus and temporal lobe are object of study, shank electrodes, despite their invasive damage, are worth the resolution they provide at the local site [].

### Key advances in recent systems

In top of improvements in recording methodologies, advances in electrode materials and physics and logics have also been done. Softer, less invasive, and more broadly distributed approaches outperform older technologies []. It has been well reported that traditional metal and silicon probes often cause an undesirable immune response, being reflected in local neural loss and glial reactivity [30], [31]. Improved electrodes influenced by underlying concerns reveal the well known “Michigan” style arrays. These devices consist mainly in on silicon with iridium or platinum recording sites embedded in the silicon shank[32], [33]. Their main advantage is the possible different configurations easily achieved with them [26].

Another key point in neural recording is the electronical advancements. These made possible to overcome a limitation which was the low capability of multiplexing [[8]](#footnote-8). Previously, this low capability limited the number of simultaneous recordings that could be obtained from neural electrode systems [34]. With modern electronic advancements, it is now possible to combine and transmit multiple signals from different electrodes through a single channel [34]. This has allowed researchers to record neural activity from many more sites simultaneously, greatly enhancing the ability to study complex neural networks and brain functions in greater detail [35], [36], [37].

### Prospects for learning and memory in NDs

Recording oscillatory behaviours, such as ripples in the hippocampus, in local parts of the brain is a thoroughly studied realm and has let to the understanding of cognitive processes (see “*Memory Consolidation section").* However, there are still many gaps and unclear processes that limit the development of more efficient treatments for NDs. NeuroGrid electrodes were able to determine anatomical locations of ripple-generating cortical areas [38]. Furthermore, Neuropixel electrodes, a kind of deep implanted shank electrodes, achieved to record simultaneous activity of multiple cortical areas (with the outstanding number of > 2000 neurons per site) and deeper brain structures[39], [40]. Further investigation works to deeper understand the transfer of memory traces and consolidation of memory could be achieved by combining these two recording systems simultaneously, because information of subcortical and cortical areas would be obtained at the same time, thus being able to relate patterns within deeper and surface observing points [35].

## Current stage of research in neurological diseases

At the current stage of scientific research, Alzheimer’s Disease (AD), the most common form of neurodegenerative disease (ND), representing the 60% to 80% of all cases [41], has no efficient treatment. This is mainly due to the late manifestation of its symptoms. When they first start appearing, many parts of the brain are already damaged without the possibility to recover[42]. Similarly, Temporal Lobe Epilepsy (TLE) show the first symptoms years after the onset of the disease.

NDs are becoming a major health and economic issue due to the aging and lifestyle of the society. Currently, over 50 million people worldwide suffer from a ND. This number is expected to triple in 2050 if no effective preventive measures are found[41].

Throughout the years, the research community has tried to approach and counteract the downsides of NDs by many different techniques, leading to greatest advances and improvements in the lifestyle of patients.

### Drug Treatments

Current treatments for AD are symptomatic-based rather than curative, trying to limit the progression of cognitive, behavioural and psychological symptoms of dementia. There are two main families of drugs approved on the market: Anticholinesterase inhibitors and anti-glutaminergics. Both are drugs that when enter the central nervous system (CNS) provoke a desired effect. Anticholinesterase inhibitors are molecules designed to increase acetylcholine levels in the brain and antiglutaminergics regulate the high levels of glutamate observed in persons with AD, which impair learning and memorization [43].

Although these treatments are not curative, they improve the quality of life of the patient by enabling them to maintain independence. Unfortunately, these drugs have a modest effect compared to their potential because of the difficulty in reaching the CNS. The drug present in the bloodstream targeting neurons must trespass many hurdles. The endothelial cells in the walls of the vessels of the CNS are joined tighter together, sealing possible gaps where drugs may go through. Furthermore, their efflux transporters that pump out undesired molecules also minimizes the effect of the drug.



**Figure 2.** Schematic representation of BBB complex interaction with inorganic and polymeric nanoparticles [43].

To overcome all these obstacles from the blood to the CNS, known as blood brain barrier (BBB), researchers have developed encapsulation methods such as lipids and exosomes [44], [45]. Moreover, other delivery routes were explored to overcome traditional ones. Intranasal delivery (IN) administration provides an alternative to intravenous administration[46]. It is non-invasive, painless, and easy to administer without a medical specialist. Furthermore, the IN route bypasses the BBB, enhancing drug bioavailability by avoiding first-pass metabolism and intestinal degradation[47].

With all the proposed techniques significant advances with improving results were obtained. However, any of them was able to revert the progression of the disease nor neutralize its primary cause. Furthermore, they were not able to restore the damage. As a result, dealing with ND implied long-term treatments without foreseeable total cure.

Drug therapies are thought to be more effective in the early asymptomatic stage before the process of neurodegeneration occurs [43]. *Cummings et al. (2018)* claim the need for better diagnosis in the early stages of AD using additional biomarkers to improve their prospects [48].

### Electrical Treatments

Since achieving fair effectiveness of drug therapy in the CNS has been a major challenge, other therapy methods have been explored. Patients with Parkinson (PD), AD and TLE have shown good response to determined electrical stimulus in specific regions of the brain [49].

There are several types of electrical stimuli applied to brain tissue [50]. Their main goal is to induce some controlled neuronal activity that will improve the condition of the disease. It was first applied in the mid 20s. Olds J. et al (1954) observed positive reinforcement in rats by electrical stimulation on septal area [51], Mcintyre et al (1969) reported changes in rats behaviour as a result of daily brain electrical simulation [52]. This opened a new realm in the context of therapies for neurological diseases. Since then, many electrical stimulations methods have been explored.

**Brain Stimulation Systems**

Nowadays, there are some methods that have garned higher relevance and are more often used.

*Deep brain stimulation (DBS)* has been approved for the treatment of Parkinson's disease, essential tremor, and dystonia. Research is ongoing to explore its potential in other neurodegenerative disorders such as AD and Huntington's disease[41], [49], [53].

*Transcranial Magnetic Stimulation (TMS)* is non-invasive and uses magnetic fields to induce electrical currents in targeted brain regions. It is primarily used as a treatment for depression but has also shown promise in conditions such as Parkinson's disease and Alzheimer's disease [54].

*Transcranial Direct Current Stimulation (tDCS)* delivers a low-intensity direct current through electrodes placed on the scalp, modulating the excitability of cortical neurons. It is a non-invasive technique that has been investigated for various neurodegenerative diseases, including Parkinson's disease, Alzheimer's disease, and multiple sclerosis.

DBS consists of electrodes implanted in deep areas of the brain and connected to a pacemaker-like device placed in the chest or abdomen. These electrodes emit regular electrical impulses to modulate neuronal activity. It is primarily used as a treatment for chronic neurological disorders such as PD, AD, obsessive-compulsive disorder (OCD), dystonia, essential tremor, epilepsy and depression [55].

The working principle of DBS is not fully understood. However, there are some neuronal behaviours strongly linked to DBS. The main hypothesis is that high-frequency DBS helps to normalize dysfunctional neuronal firing patterns in the brain[56]. It may disrupt pathological oscillations, synchronize neuronal activity, and induce plastic changes in neural circuits, ultimately leading to therapeutic effects. Supporting research include the work of *Castro D et al (2024)*, who has proposed a closed-loop system to detect abnormal high frequency oscillations in the hippocampus and perform local electrical stimulation to restore normal firing activity [57].

Dysfunctional neuronal firing patterns are one target for DBS regarding PD and epilepsy[49]. The high frequency oscillations of the electrodes end up exhausting the synapse neurotransmitters of nearby neurons and block the pathway to subsequent action potentials of the pathological network. This disrupts excessive oscillatory synchronization leading to normal brain function.

Depending on the frequency of stimulation and other parameters, different outcomes can be achieved on the target tissue. It has also been reported increased neuroplasticity resulting from DBS [55], [58], [59]. This neuroplasticity enhanced a notable recovery of damaged tissue on neurodegenerative diseases, where most of the times the affected areas cannot achieve tissue recovery.

Overall, DBS and other types of electrical stimulation devices have opened another realm for approaching NDs. This realm probably boosted the field of neuronal signal processing. The bound line between stimulating and measuring is very thin. If a cable can be introduced precisely to deliver controlled currentDiagrama

Descripción generada automáticamente same can be achieved with an electrode to measure. So, with the development of DBS, local invasive electrodes have also gone through a process of tailoring [35]. The combination of measuring and stimulating provides another degree of freedom and control in the context of electrical stimulation as a therapy for NDs, where stimulations can be intelligently delivered in response to known biomarkers [57], [60], [61]. Some of these biomarkers are localized in specific parts of the brain, namely the hippocampus[62]. The hippocampus has shown to play an important role in ND. Oscillation patterns within its networks show to mediate important tasks related to memory[63]. Studies in the literature involve numerous recordings and analysis of signals within its neural populations[64].

**Figure 3.** Transversal axis sliced view of the hippocampus showcases its subregions and their spatial distribution. Entorinal Cortex (EC) and Dentrite Gyrus (DG) are sandwiched between them creating the collectively known "hippocampal formation".

## The hippocampus

The hippocampus is one of the most thoroughly investigated parts of the brain. As a complex brain structure, it is found embedded into the temporal lobe and is involved in many processes of learning and memory. Since the famous report of the case study H.M. [[9]](#footnote-9), who lost the ability to acquire new memories after the removal of the hippocampus in a desperate approach to suppress invalidating epileptic seizures, it has been posed at the center of research in memory consolidation [65]. The intense research has raised the discovery of several subregions, with a complex interplay between them (firstly defined as trysinaptic loop), where input information from sensory systems is processed following a specific path (see “*Hippocampal Subregions”*), thus providing the brain with a spatiotemporal framework where memories can be stored and consolidated.

### Hippocampal subregions

The hippocampus is divided into two main complexes: Entorhinal Cortex (EC) and Dentate Gyrus (DG). EC provides the major cortical input source to the hippocampus. As information flows through it, different subregions (CA1, CA2, CA3, CA4) are distinguished [66], [67], [68] (see ***Figure 3***). It is said to mediate neural communication between neurons from hippocampus and neocortex. It primarily targets Dentrite Girus (DG), which then targets Cornu Ammonis 3 (CA3), finally leading to CA1, which will project back to neocortical neurons, through EC, to complete the loop [67], [68]. Apparently, the hippocampus seems predictable, each part doing a defined job. However, later it was found that the complex was not so stratified into separate regions. Simultaneous activity, parallel processing and widespread connectivity was revealed in further studies[63], [66], [67], [68].

### Memory consolidation

These processes happening within different subregions of the hippocampus are believed to somehow encode the lived experiences in a way that later the sense of it can be recreated in our brain with conscious awareness (known as declarative memory). When exposed to an experience, the learned material remains vulnerable to interference for a period of time before consolidating in other cortical areas or getting replaced by new ones [63]. In the literature it has been reported two types of declarative memory[63]:

***Episodic*** memories are those related to events that happened in a specific place and time throughout the day. They are easily forgotten. For example “this morning I closed the door when leaving”.

***Semantic*** memories are stored as general knowledge about the world. For example “if you touch the fire you get burnt”. Also referred to as “long-term memory”.

Many researchers believe that the hippocampus is specifically important for forming new episodic memories, whereas other parts of the temporal lobe and neocortex are more critical for semantic memories [69]. Therefore, the process of memory consolidation, where an experience is interiorized in our brain to contribute to our knowledge, relies on the ability of the hippocampus (as the first step of the process) to retain episodic memories. Episodic memories will follow further steps of consolidation if they are relevant or not [63](repetition of an event usually makes it more relevant), ultimately becoming more independent of the hippocampus (semantic memory). In support to these, it has been observed that patients with hippocampal damage could remember events that happened years before but could not remember what they ate for breakfast [69].

The process of how memories gradually get independent from the hippocampus is not fully comprised. It is widely believed that the memory storage framework used by the mammalian brain is based on the synaptic weights and connections that neurons have between them. Connections and weights encoding for episodic memories are built during events. Some oscillation and firing patterns originating from neuronal ensembles[[10]](#footnote-10) are thought to be involved in the process of transferring those connections and weights to the neocortex, where they will be available for a long period of time. Then, the hippocampus will leave those connections free to new incoming events.

### Sharp Wave Ripples (SWR)

SWRs are distinctive patterns of neural activity observed in the hippocampus. These patterns consist of high-frequency oscillations (ripples) superimposed on sharp-wave complexes, which are characterized by brief, high-amplitude deflections in the local field potential (LFP)[[11]](#footnote-11). They represent the most synchronous population pattern in the mammalian brain [70]. In the ~100 ms time window of a hippocampal SWR, 10-20% of the total neural population in the rat hippocampus discharge simultaneously in the CA3-CA1 subregions [71].

Un dibujo de una persona

Descripción generada automáticamente con confianza baja

**Figure 3.** SWR recorded from different mammal hippocampus. They all have a similar pattern: 3-9 high amplitude waves in a frequency ranging from 100-250 Hz (Figure from [70] )

They arise from neuronal ensembles in the hippocampus. Their excitatory output stimulates a wide area of the cortex and several subcortical nuclei. SWRs occur during “off-line” states of the brain, associated with consummatory behaviours[[12]](#footnote-12) and non-REM sleep, and are inﬂuenced by numerous neurotransmitters and neuromodulators. Numerous studies unveil their relevance in the process of episodic memory encoding [70], [72], [73]. The memory traces are encoded via weak synaptic potentiation[[13]](#footnote-13) in the CA3 network induced by theta oscillations during consummatory behaviours. Then, synapses strengthened during the process contribute to the generation of SWRs, which target, through entorhinal cortex, neocortical regions. Therefore, SWRs stablish a bidirectional communication between hippocampus and neocortex, being able to gradually transfer memories outside the hippocampus and playing a pivotal role in the process of knowledge and memory consolidation.

**SWRs related terms and definitions** [74]

*Sharp waves* are characterized by brief, high-amplitude deflections in the LFP recorded in the hippocampus. They typically have a frequency range of around 0.1 to 4 Hz. These sharp waves represent synchronous depolarization of populations of neurons, often associated with the reactivation of neuronal ensembles involved in memory consolidation.

*Ripples* refer to high-frequency oscillations superimposed on the sharp waves. They are fast oscillations in the frequency range of approximately 100 to 250 Hz. Ripples are thought to reflect synchronized activity within local neuronal circuits, particularly involving the coordinated firing of interneuron[[14]](#footnote-14) populations.

*Fast Ripples* are ripples occurring at higher frequencies, typically above 250 Hz. They are often observed in pathological conditions such as epilepsy and are believed to be related to abnormal neural firing patterns associated with seizure generation.

Muy bonito.
**Pathological SWRs**

**Figure 4.** Ripples refer to highamplitude oscillatory activity in frequencies ranging from 100-250 Hz. Sharp Waves show a deeper low frequency wave sharply decreasing at the beggining.

In rat brains, SWRs duration range from 30 to 150ms, and its amplitude should never exceed 3mV [70]. Alteration of the physiological mechanisms supporting SWRs leads to a pathological signal morphology, which is a marker of epileptogenic tissue and can be observed in Schizophrenia and AD. In addition, dysfunctional SWRs could be an important cue for early-stage detection of AD, as these signals show different morphological features in the affected host and start appearing near the start of the disease, when there are no symptoms and no damage is yet done to brain tissue. It is true that genetic and environmental risk factors can be used to predict future AD, however, the confidence of these predictions and temporal prediction for the appearance of symptoms remains poor. Alternatively, these factors could be combined with an analysis of SWRs to detect the disease and treat it at an early stage.

Being these signals a promising biomarker for future neurodegenerative diseases affecting memory and cognition, it is of valuable interest to learn to correctly assess and detect them.

## Overview

The human brain, with its intricate web of neurons and synapses, remains one of the most complex and enigmatic systems in nature. Understanding its fundamental workings holds the key to unraveling mysteries such as cognition and memory formation, which represent one of the main downsides of Neurodegenerative Disorders. Among the brain's many regions, the hippocampus stands out as a focal point for memory encoding and retrieval, spatial navigation, and emotional processing [71], [74], [75].

Within the hippocampus, high-frequency oscillations (HFOs), such as sharp wave ripples (SWRs) have emerged as crucial neural events implicated in various cognitive functions and dysfunctions [63]. These oscillations, often ranging from 100 to 500 Hz, play a pivotal role in information processing and communication within neural circuits. Detecting and deciphering these HFOs provide invaluable insights into the underlying mechanisms of learning, memory, and pathologies such as epilepsy and Altheimer’s Disease (AD) [70], [72], [73].

However, capturing and analysing HFOs pose significant challenges, particularly concerning power consumption and computational efficiency [6]. Traditional computing approaches struggle to cope with the complexity and real-time demands of neural data processing, especially when targeting low-power applications [76]. These applications, among others, include closed-loop systems [77], which typically involve the integration of sensing and stimulation components that can monitor neural activity in real-time and deliver therapeutic interventions accordingly, therefore becoming independent from outer machines and more comfortable for the patient. In Parkinson’s Disease (PD) closed loop deep brain stimulation (DBS) systems are being developed willing to monitor neural activity and adjust stimulation parameters in response to variations in neural activity [57], [60], [61]. Of course, these systems require minimum energy consumption to minimize the number of recharging interventions.

Neuromorphic computing (NC), a groundbreaking approach inspired by the brain's own architecture and functionality, emulate the parallelism, plasticity, and energy efficiency of biological brains, offering promising opportunities for real-time and low-power neural data analysis [10], [78]. By harnessing the principles of SNNs and event-driven computation[[15]](#footnote-15), neuromorphic platforms hold immense promise for revolutionizing the way we study and understand brain dynamics [8], [9].

Artificial intelligence has supposed a technological explosion in the last ten years. Current AI are performing better than humans, and the development possibilities it offers are uncountable. The relentless improvement of algorithms has been accompanied by a notable increase in energy consumption, which at first was overlooked. However, its widespread implementation is starting to raise concerns about sustainability and environmental impact[79]. Efforts underway to develop energy-efficient AI algorithms and hardware, are one of the causes pushing the advances of NC. Other pushing force of this research branch includes advancements in brain computer interfaces due to its further resemblance in the way of processing information [9] (which is more similar to neurons). Furthermore, these platforms are facilitating breakthroughs in understanding the complex dynamics of neural systems. By simulating the behaviour of biological neurons and synapses, fundamental principles of brain function, such as learning and memory can be studied[9][80].

In light of all benefits offered by NC among other computation systems, this work is commited to implement it in a neuroengineering framework. SNNs and neuromorphic computing have their origins many years ago, but it was near 2000 when it got accelerated due to the explosion of semiconductors industry and due to notable contributions from researchers such as Eugene Izhikevich, who introduced a revolutionary concept of neuron model in 2003. Up to date, NC have a solid background and implementation in diverse low-power engineering tasks, such as image classification systems [10]. Namely embedded cameras in cars, street traffic, security systems…[17]. Nonetheless, very few works about closed loop systems for brain applications have been reported [81]. Enabling low power and faster computation on implanted systems in the brain holds immense promise for revolutionizing health care, human-machine interaction, and seamless integration of advanced technologies within the human brain[77], [82].

This final degree project aims to explore the use of neuromorphic computing for the detection of Sharp Wave Ripples (SWRs), which is a kind of HFO, in the hippocampus. By leveraging state-of-the-art neuromorphic hardware and algorithms, a competent “*SNN-based*” signal detector can be built and trained. Cutting edge neuromorphic hardware device may be used to run the model instead of using a neuromorphic simulator. Different neuron models and neuromorphic computation paradigms from the literature [18] and network architectures will be explored aiming to find the better performant appropriate combination. Furthermore, the frameworks used in these areas will be learnt from online documentation. Naturally, state-of-the-art knowledge from different areas involved in the project will be learnt and embraced.

Lastly, once achieved data preparation and training of the model, the performance and computation time will be compared with state-of-the-art ANN models [83] and SNN models [27], [28] designed to detect same or similar oscillation patterns.

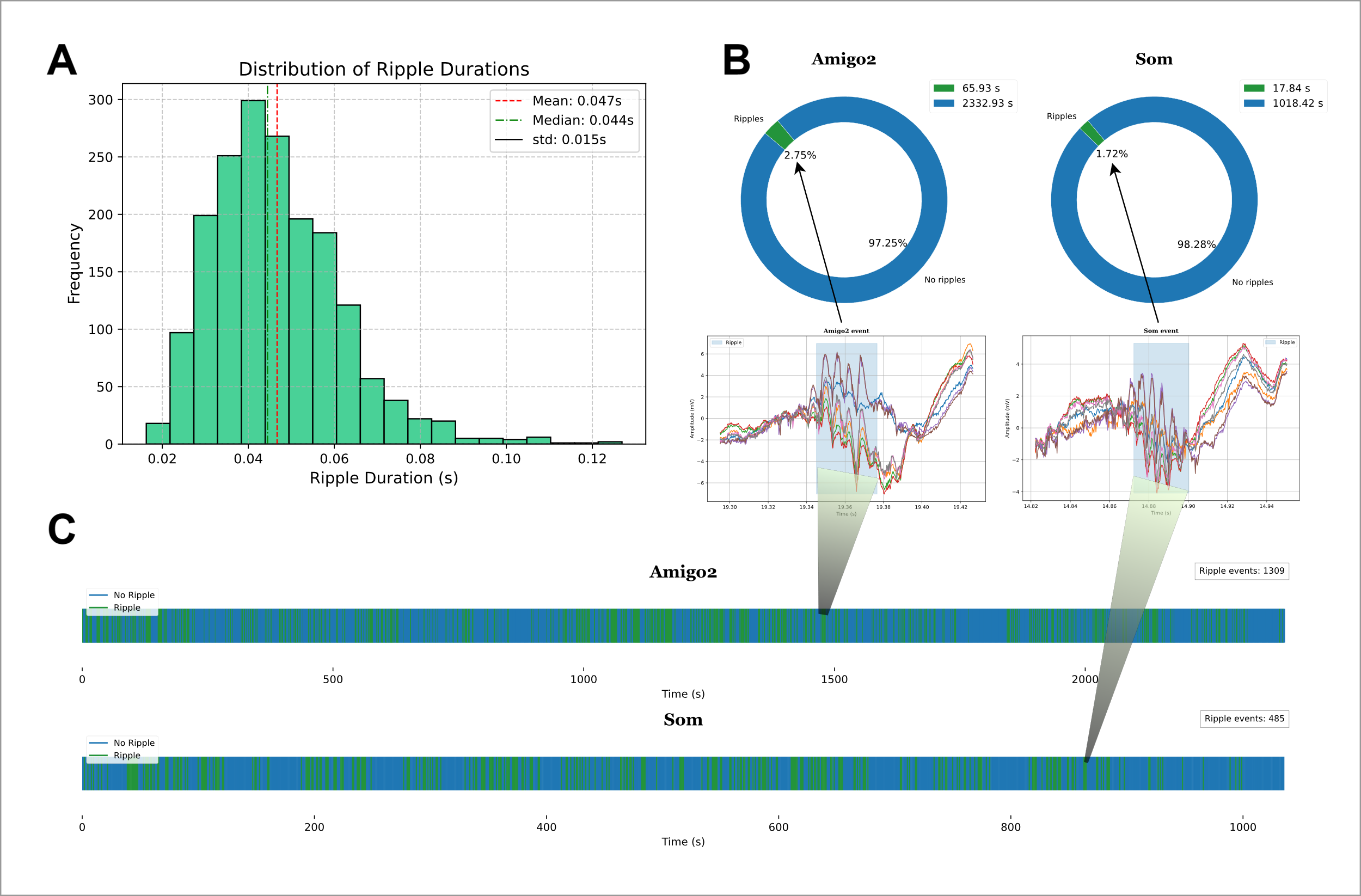
Neuromorphic computing, utilizing SNNs and state-of-the-art neuromorphic hardware, will achieve higher, or similar performance and efficiency in detecting Sharp Wave Ripples (SWRs) recorded from the rat hippocampus compared to traditional Artificial Neural Networks (ANNs) and existing SNN models.

The hypothesis is based on the premise that neuromorphic hardware and algorithms, which mimic the neural mechanisms of the brain, can offer improved performance and reduced computation time compared to conventional ANNs and current SNN models. This premise aligns with the goal of exploring the potential advantages of neuromorphic computing in detecting specific neural oscillation patterns, aiming to demonstrate its efficacy and efficiency in this domain.

# Materials

## Dataset

The dataset was recorded by Neural Circuits Lab from CSIC, Instituto Cajal, Madrid guided by Liset M. de la prida[[16]](#footnote-16). **μ**-LED optoelectrodes (32 channels, 4 shanks of 8-channels) where used in head-fixed awake transgenic Thy1-GCaMP7 mice[[17]](#footnote-17) to record local field potentials (LFPs) at 30 KHz in the dorsal hippocampus [83]. Recordings were done several days before the implantation to let them habituate.

****The dataset used for this study consisted on two recording sessions in different rats “Amigo2\_1\_hippo” and “ Som\_2\_hippo”. Each session contained ripples and SWR events tagged altogether as ground truth ripples. The times when ripples occurred were tagged by an expert in a postprocess phase. The expert would tag the start and the end of the event. This is because ripples have a range of durations and can include to 3-9 ripple oscillations. Therefore, it would not be correct to set a fixed window for all of them. In other studies, the events are tagged by setting an only marker in the centre of the ripple [84]**.** However, more information can be extracted by tagging the precise full window.

**Figure 5.** **Overview of the two recording sessions: Ripple events, durations, and features.** Both datasets have very similar events. Amigo2 represents a major part of the data. Both sessions contain altogether 1794 ripple events. **A)** Normal distribution of the duration of the hand-tagged ripples. Most of them are in the range of 30-60 ms, however there is a non-small part of the population with longer durations ranging from 80-120 ms. **B)** Ripple events represent a ~2% of the recording and are **C)** uniformly distributed through it. Each vertical green line represent a second of the recording which contained at least one event.

Each session had a binary raw file with the recorded LFPs, and an info file containing all the tagged events.

# Methods

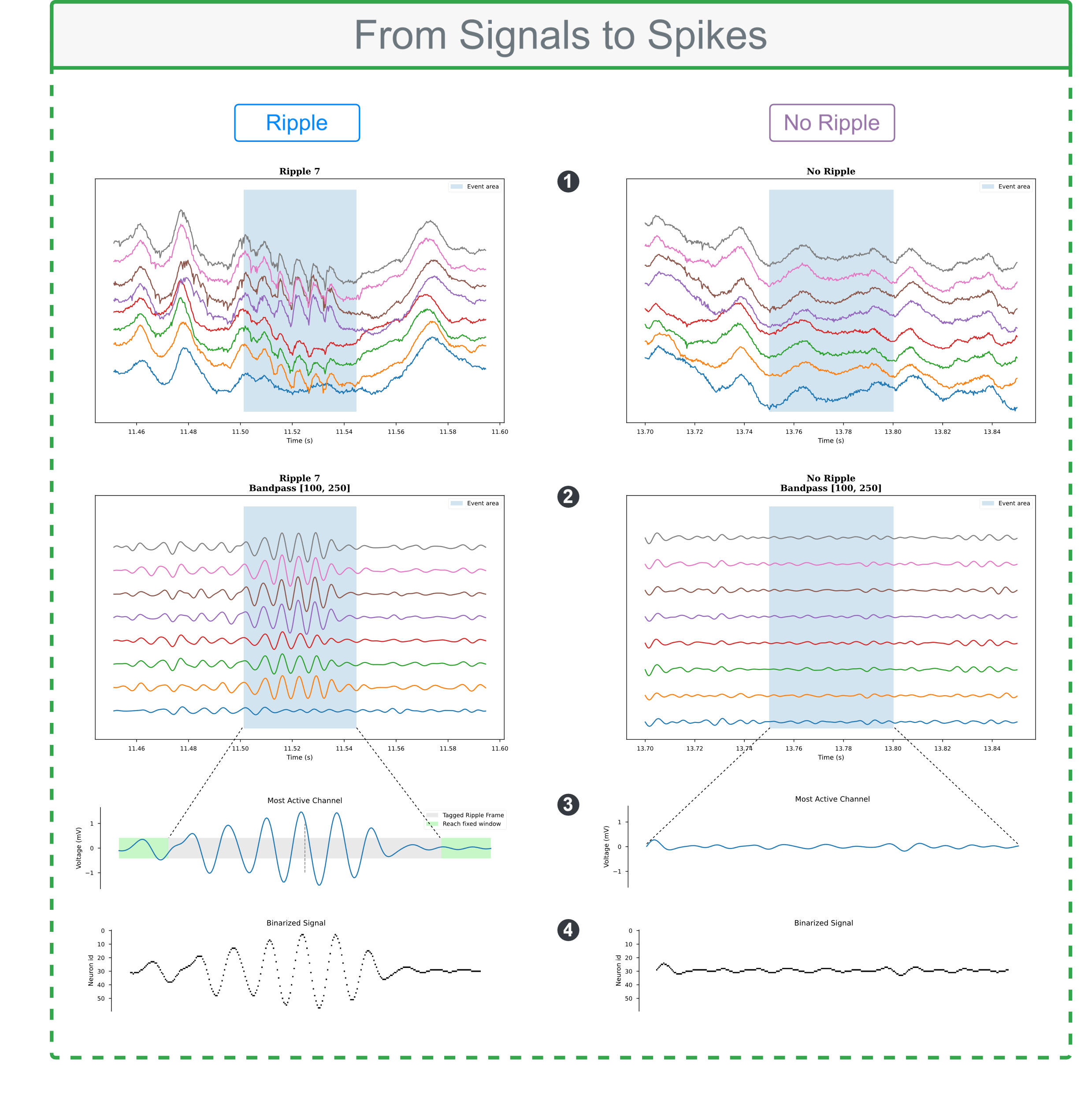
## Signal visualization

## Deciding the approach

## Data preparation

## Network training







# Results



# References

[1] R. Yang, H. M. Huang, and X. Guo, ‘Memristive Synapses and Neurons for Bioinspired Computing’, *Advanced Electronic Materials*, vol. 5, no. 9. Blackwell Publishing Ltd, Sep. 01, 2019. doi: 10.1002/aelm.201900287.

[2] N. Zins, Y. Zhang, C. Yu, and H. An, ‘Neuromorphic Computing: A Path to Artificial Intelligence Through Emulating Human Brains’, in *Frontiers of Quality Electronic Design (QED): AI, IoT and Hardware Security*, Springer International Publishing, 2023, pp. 259–296. doi: 10.1007/978-3-031-16344-9\_7.

[3] CARVER MEAD, ‘Neuromorphic Electronic Systems’, *IEE Invited paper*, vol. 78, 1990.

[4] K. Aboumerhi, A. Güemes, H. Liu, F. Tenore, and R. Etienne-Cummings, ‘Neuromorphic applications in medicine’, *Journal of Neural Engineering*, vol. 20, no. 4. Institute of Physics, Aug. 01, 2023. doi: 10.1088/1741-2552/aceca3.

[5] P. S. Zarrin, R. Zimmer, C. Wenger, and T. Masquelier, ‘Epileptic Seizure Detection Using a Neuromorphic-Compatible Deep Spiking Neural Network’, in *Lecture Notes in Computer Science (including subseries Lecture Notes in Artificial Intelligence and Lecture Notes in Bioinformatics)*, Springer, 2020, pp. 389–394. doi: 10.1007/978-3-030-45385-5\_34.

[6] K. Burelo, M. Sharifshazileh, N. Krayenbühl, G. Ramantani, G. Indiveri, and J. Sarnthein, ‘A spiking neural network (SNN) for detecting high frequency oscillations (HFOs) in the intraoperative ECoG’, *Sci Rep*, vol. 11, no. 1, Dec. 2021, doi: 10.1038/s41598-021-85827-w.

[7] P. S. Zarrin, R. Zimmer, C. Wenger, and T. Masquelier, ‘Epileptic Seizure Detection Using a Neuromorphic-Compatible Deep Spiking Neural Network’, in *Lecture Notes in Computer Science (including subseries Lecture Notes in Artificial Intelligence and Lecture Notes in Bioinformatics)*, Springer, 2020, pp. 389–394. doi: 10.1007/978-3-030-45385-5\_34.

[8] M. Ziegler, C. Wenger, E. Chicca, and H. Kohlstedt, ‘Tutorial: Concepts for closely mimicking biological learning with memristive devices: Principles to emulate cellular forms of learning’, *J Appl Phys*, vol. 124, no. 15, Oct. 2018, doi: 10.1063/1.5042040.

[9] F. D. Broccard, S. Joshi, J. Wang, and G. Cauwenberghs, ‘Neuromorphic neural interfaces: From neurophysiological inspiration to biohybrid coupling with nervous systems’, *Journal of Neural Engineering*, vol. 14, no. 4. Institute of Physics Publishing, Jun. 02, 2017. doi: 10.1088/1741-2552/aa67a9.

[10] K. Roy, A. Jaiswal, and P. Panda, ‘Towards spike-based machine intelligence with neuromorphic computing’, *Nature*, vol. 575, no. 7784, pp. 607–617, Nov. 2019, doi: 10.1038/s41586-019-1677-2.

[11] D. B. Strukov, G. S. Snider, D. R. Stewart, and R. S. Williams, ‘The missing memristor found’, *Nature*, vol. 453, no. 7191, pp. 80–83, May 2008, doi: 10.1038/nature06932.

[12] H. Li *et al.*, ‘Memristive Crossbar Arrays for Storage and Computing Applications’, *Advanced Intelligent Systems*, vol. 3, no. 9, Sep. 2021, doi: 10.1002/aisy.202100017.

[13] R. Brette, ‘Philosophy of the spike: Rate-based vs. Spike-based theories of the brain’, *Frontiers in Systems Neuroscience*, vol. 9, no. November. Frontiers Research Foundation, Nov. 10, 2015. doi: 10.3389/fnsys.2015.00151.

[14] F. Zeldenrust, W. J. Wadman, and B. Englitz, ‘Neural coding with bursts—Current state and future perspectives’, *Frontiers in Computational Neuroscience*, vol. 12. Frontiers Media S.A., Jul. 06, 2018. doi: 10.3389/fncom.2018.00048.

[15] B. Gardner and A. Grüning, ‘Supervised learning in spiking neural networks for precise temporal encoding’, *PLoS One*, vol. 11, no. 8, Aug. 2016, doi: 10.1371/journal.pone.0161335.

[16] R. V. Florian, ‘The chronotron: A neuron that learns to fire temporally precise spike patterns’, *PLoS One*, vol. 7, no. 8, Aug. 2012, doi: 10.1371/journal.pone.0040233.

[17] K. Yamazaki, V. K. Vo-Ho, D. Bulsara, and N. Le, ‘Spiking Neural Networks and Their Applications: A Review’, *Brain Sciences*, vol. 12, no. 7. MDPI, Jul. 01, 2022. doi: 10.3390/brainsci12070863.

[18] D. Sterratt, *Principles of computational modelling in neuroscience*. Cambridge University Press, 2011.

[19] L. Deng *et al.*, ‘Rethinking the performance comparison between SNNS and ANNS’, *Neural Networks*, vol. 121, pp. 294–307, Jan. 2020, doi: 10.1016/J.NEUNET.2019.09.005.

[20] A. Tavanaei, M. Ghodrati, S. R. Kheradpisheh, T. Masquelier, and A. Maida, ‘Deep learning in spiking neural networks’, *Neural Networks*, vol. 111, pp. 47–63, Mar. 2019, doi: 10.1016/J.NEUNET.2018.12.002.

[21] S. B. Shrestha and G. Orchard, ‘SLAYER: Spike Layer Error Reassignment in Time’, Sep. 2018, [Online]. Available: http://arxiv.org/abs/1810.08646

[22] F. Zeldenrust, W. J. Wadman, and B. Englitz, ‘Neural coding with bursts—Current state and future perspectives’, *Frontiers in Computational Neuroscience*, vol. 12. Frontiers Media S.A., Jul. 06, 2018. doi: 10.3389/fncom.2018.00048.

[23] T. Iakymchuk, A. Rosado-Muñoz, J. F. Guerrero-Martínez, M. Bataller-Mompeán, and J. V. Francés-Víllora, ‘Simplified spiking neural network architecture and STDP learning algorithm applied to image classification’, *EURASIP J Image Video Process*, vol. 2015, no. 1, 2015, doi: 10.1186/s13640-015-0059-4.

[24] Y. Guo, X. Huang, and Z. Ma, ‘Direct learning-based deep spiking neural networks: a review’, *Frontiers in Neuroscience*, vol. 17. Frontiers Media SA, 2023. doi: 10.3389/fnins.2023.1209795.

[25] J. Ding, Z. Yu, Y. Tian, and T. Huang, ‘Optimal ANN-SNN Conversion for Fast and Accurate Inference in Deep Spiking Neural Networks’, May 2021, [Online]. Available: http://arxiv.org/abs/2105.11654

[26] C. H. Thompson, T. E. Riggins, P. R. Patel, C. A. Chestek, W. Li, and E. Purcell, ‘Toward guiding principles for the design of biologically-integrated electrodes for the central nervous system’, *Journal of Neural Engineering*, vol. 17, no. 2. Institute of Physics Publishing, 2020. doi: 10.1088/1741-2552/ab7030.

[27] K. Burelo, M. Sharifshazileh, N. Krayenbühl, G. Ramantani, G. Indiveri, and J. Sarnthein, ‘A spiking neural network (SNN) for detecting high frequency oscillations (HFOs) in the intraoperative ECoG’, *Sci Rep*, vol. 11, no. 1, Dec. 2021, doi: 10.1038/s41598-021-85827-w.

[28] M. Sharifshazileh, K. Burelo, J. Sarnthein, and G. Indiveri, ‘An electronic neuromorphic system for real-time detection of high frequency oscillations (HFO) in intracranial EEG’, *Nat Commun*, vol. 12, no. 1, Dec. 2021, doi: 10.1038/s41467-021-23342-2.

[29] M. E. J. Obien, K. Deligkaris, T. Bullmann, D. J. Bakkum, and U. Frey, ‘Revealing neuronal function through microelectrode array recordings’, *Frontiers in Neuroscience*, vol. 9, no. JAN. Frontiers Media S.A., p. 423, 2015. doi: 10.3389/fnins.2014.00423.

[30] J. W. Salatino, K. A. Ludwig, T. D. Y. Kozai, and E. K. Purcell, ‘Erratum: Publisher Correction: Glial responses to implanted electrodes in the brain (Nature biomedical engineering (2017) 1 11 (862-877))’, *Nature biomedical engineering*, vol. 2, no. 1. NLM (Medline), p. 52, Jan. 01, 2018. doi: 10.1038/s41551-017-0177-7.

[31] R. Biran, D. C. Martin, and P. A. Tresco, ‘Neuronal cell loss accompanies the brain tissue response to chronically implanted silicon microelectrode arrays’, *Exp Neurol*, vol. 195, no. 1, pp. 115–126, Sep. 2005, doi: 10.1016/J.EXPNEUROL.2005.04.020.

[32] K. L. Drake, K. D. Wise, J. Farraye, D. J. Anderson, and S. L. Bement, ‘Performance of Planar Multisite Microprobes in Recording Extracellular Single-Unit Intracortical Activity’, 1988.

[33] R. J. Vetter, J. C. Williams, J. F. Hetke, E. A. Nunamaker, and D. R. Kipke, ‘Chronic neural recording using silicon-substrate microelectrode arrays implanted in cerebral cortex’, *IEEE Trans Biomed Eng*, vol. 51, no. 6, pp. 896–904, Jun. 2004, doi: 10.1109/TBME.2004.826680.

[34] I. H. Stevenson and K. P. Kording, ‘How advances in neural recording affect data analysis’, in *Nature Neuroscience*, Feb. 2011, pp. 139–142. doi: 10.1038/nn.2731.

[35] G. Hong and C. M. Lieber, ‘Novel electrode technologies for neural recordings’, *Nature Reviews Neuroscience*, vol. 20, no. 6. Nature Publishing Group, pp. 330–345, Jun. 01, 2019. doi: 10.1038/s41583-019-0140-6.

[36] K. Woeppel, Q. Yang, and X. T. Cui, ‘Recent advances in neural electrode–tissue interfaces’, *Curr Opin Biomed Eng*, vol. 4, pp. 21–31, Dec. 2017, doi: 10.1016/J.COBME.2017.09.003.

[37] S. M. Won, E. Song, J. Zhao, J. Li, J. Rivnay, and J. A. Rogers, ‘Recent Advances in Materials, Devices, and Systems for Neural Interfaces’, *Advanced Materials*, vol. 30, no. 30. Wiley-VCH Verlag, Jul. 26, 2018. doi: 10.1002/adma.201800534.

[38] D. Khodagholy, J. N. Gelinas, and G. Buzsáki, ‘Learning-enhanced coupling between ripple oscillations in association cortices and hippocampus’. [Online]. Available: https://www.science.org

[39] C. Stringer, M. Pachitariu, N. Steinmetz, C. B. Reddy, M. Carandini, and K. D. Harris, ‘Spontaneous behaviors drive multidimensional, brain-wide activity’.

[40] J. J. Jun *et al.*, ‘Fully integrated silicon probes for high-density recording of neural activity’, *Nature*, vol. 551, no. 7679, pp. 232–236, Nov. 2017, doi: 10.1038/nature24636.

[41] G. Livingston *et al.*, ‘Dementia prevention, intervention, and care: 2020 report of the Lancet Commission’, *The Lancet*, vol. 396, no. 10248. Lancet Publishing Group, pp. 413–446, Aug. 08, 2020. doi: 10.1016/S0140-6736(20)30367-6.

[42] A. Chudzik, A. Śledzianowski, and A. W. Przybyszewski, ‘Machine Learning and Digital Biomarkers Can Detect Early Stages of Neurodegenerative Diseases’, *Sensors*, vol. 24, no. 5. Multidisciplinary Digital Publishing Institute (MDPI), Mar. 01, 2024. doi: 10.3390/s24051572.

[43] E. Passeri *et al.*, ‘Alzheimer’s Disease: Treatment Strategies and Their Limitations’, *International Journal of Molecular Sciences*, vol. 23, no. 22. MDPI, Nov. 01, 2022. doi: 10.3390/ijms232213954.

[44] A. M. Cardoso *et al.*, ‘Recent Trends in Nanotechnology Toward CNS Diseases: Lipid-Based Nanoparticles and Exosomes for Targeted Therapeutic Delivery’, *Int Rev Neurobiol*, vol. 130, pp. 1–40, Jan. 2016, doi: 10.1016/BS.IRN.2016.05.002.

[45] H. Choi *et al.*, ‘Strategies for Targeted Delivery of Exosomes to the Brain: Advantages and Challenges’, *Pharmaceutics*, vol. 14, no. 3. MDPI, Mar. 01, 2022. doi: 10.3390/pharmaceutics14030672.

[46] ‘Figure 1: Different methods of drug administration to the CNS’. [Online]. Available: http://journals.lww.com/iphr

[47] L. R. Hanson and W. H. Frey, ‘Intranasal delivery bypasses the blood-brain barrier to target therapeutic agents to the central nervous system and treat neurodegenerative disease’, *BMC Neurosci*, vol. 9, no. S3, Dec. 2008, doi: 10.1186/1471-2202-9-s3-s5.

[48] J. Cummings, A. Ritter, and K. Zhong, ‘Clinical Trials for Disease-Modifying Therapies in Alzheimer’s Disease: A Primer, Lessons Learned, and a Blueprint for the Future’, *Journal of Alzheimer’s Disease*, vol. 64, no. s1. IOS Press, pp. S3–S22, 2018. doi: 10.3233/JAD-179901.

[49] A. Majdi, Z. Deng, S. Sadigh-Eteghad, P. De Vloo, B. Nuttin, and M. Mc Laughlin, ‘Deep brain stimulation for the treatment of Alzheimer’s disease: A systematic review and meta-analysis’, *Frontiers in Neuroscience*, vol. 17. Frontiers Media S.A., 2023. doi: 10.3389/fnins.2023.1154180.

[50] D. C. Mcintyre and C. K. Leech, ‘A Permanent Change in Brain Function Resulting from Daily Electrical Stimulation’, 1969.

[51] J. Olds and P. Milnkr, ‘POSITIVE REINFORCEMENT PRODUCED BY ELECTRICAL STIMULATION OF SEPTAL AREA AND OTHER REGIONS OF RAT BRAIN’’.

[52] D. C. Mcintyre and C. K. Leech, ‘A Permanent Change in Brain Function Resulting from Daily Electrical Stimulation’, 1969.

[53] T. F. Yuan *et al.*, ‘Targeting neuroplasticity in patients with neurodegenerative diseases using brain stimulation techniques’, *Translational Neurodegeneration*, vol. 9, no. 1. BioMed Central Ltd, Dec. 01, 2020. doi: 10.1186/s40035-020-00224-z.

[54] J. P. Lefaucheur, ‘Transcranial magnetic stimulation’, *Handb Clin Neurol*, vol. 160, pp. 559–580, Jan. 2019, doi: 10.1016/B978-0-444-64032-1.00037-0.

[55] A. M. Lozano *et al.*, ‘Deep brain stimulation: current challenges and future directions’, *Nature Reviews Neurology*, vol. 15, no. 3. Nature Publishing Group, pp. 148–160, Mar. 01, 2019. doi: 10.1038/s41582-018-0128-2.

[56] R. S. Fisher and A. L. Velasco, ‘Electrical brain stimulation for epilepsy’, *Nature Reviews Neurology*, vol. 10, no. 5. Nature Publishing Group, pp. 261–270, 2014. doi: 10.1038/nrneurol.2014.59.

[57] D. L. Castro, M. Aroso, A. P. Aguiar, D. B. Grayden, and P. Aguiar, ‘Disrupting abnormal neuronal oscillations with adaptive delayed feedback control’, *Elife*, vol. 13, Mar. 2024, doi: 10.7554/elife.89151.

[58] T. F. Yuan *et al.*, ‘Targeting neuroplasticity in patients with neurodegenerative diseases using brain stimulation techniques’, *Translational Neurodegeneration*, vol. 9, no. 1. BioMed Central Ltd, Dec. 01, 2020. doi: 10.1186/s40035-020-00224-z.

[59] J. Kricheldorff *et al.*, ‘Evidence of Neuroplastic Changes after Transcranial Magnetic, Electric, and Deep Brain Stimulation’, *Brain Sciences*, vol. 12, no. 7. MDPI, Jul. 01, 2022. doi: 10.3390/brainsci12070929.

[60] J. E. Fleming, E. Dunn, and M. M. Lowery, ‘Simulation of Closed-Loop Deep Brain Stimulation Control Schemes for Suppression of Pathological Beta Oscillations in Parkinson’s Disease’, *Front Neurosci*, vol. 14, Mar. 2020, doi: 10.3389/fnins.2020.00166.

[61] S. Wang *et al.*, ‘Closed-Loop Adaptive Deep Brain Stimulation in Parkinson’s Disease: Procedures to Achieve It and Future Perspectives’, *Journal of Parkinson’s Disease*, vol. 13, no. 4. IOS Press BV, pp. 453–471, Jun. 13, 2023. doi: 10.3233/JPD-225053.

[62] G. Buzsáki, ‘Hippocampal sharp wave-ripple: A cognitive biomarker for episodic memory and planning’, *Hippocampus*, vol. 25, no. 10, pp. 1073–1188, Oct. 2015, doi: 10.1002/hipo.22488.

[63] L. R. Squire, L. Genzel, J. T. Wixted, and R. G. Morris, ‘Memory consolidation’, *Cold Spring Harb Perspect Biol*, vol. 7, no. 8, Aug. 2015, doi: 10.1101/cshperspect.a021766.

[64] A. Ecker *et al.*, ‘Hippocampal sharp wave-ripples and the associated sequence replay emerge from structured synaptic interactions in a network model of area CA3’, *Elife*, vol. 11, Jan. 2022, doi: 10.7554/eLife.71850.

[65] L. R. Squire, ‘The Legacy of Patient H.M. for Neuroscience’, *Neuron*, vol. 61, no. 1. pp. 6–9, Jan. 15, 2009. doi: 10.1016/j.neuron.2008.12.023.

[66] György Buzsáki & James J Chrobak, ‘Synaptic plasticity and self-organization in the hippocampus’, 2005. [Online]. Available: http://www.nature.com/natureneuroscience

[67] C. Wang, M. A. Grohme, B. Mali, R. O. Schil, and M. Frohme, ‘Towards decrypting cryptobiosis - Analyzing anhydrobiosis in the tardigrade Milnesium tardigradum using transcriptome sequencing’, *PLoS One*, vol. 9, no. 3, Mar. 2014, doi: 10.1371/journal.pone.0092663.

[68] A. Oliva, A. Fernández-Ruiz, G. Buzsáki, and A. Berényi, ‘Spatial coding and physiological properties of hippocampal neurons in the Cornu Ammonis subregions’, *Hippocampus*, vol. 26, no. 12, pp. 1593–1607, Dec. 2016, doi: 10.1002/hipo.22659.

[69] C. Wang, M. A. Grohme, B. Mali, R. O. Schil, and M. Frohme, ‘Towards decrypting cryptobiosis - Analyzing anhydrobiosis in the tardigrade Milnesium tardigradum using transcriptome sequencing’, *PLoS One*, vol. 9, no. 3, Mar. 2014, doi: 10.1371/journal.pone.0092663.

[70] G. Buzsáki, ‘Hippocampal sharp wave-ripple: A cognitive biomarker for episodic memory and planning’, *Hippocampus*, vol. 25, no. 10, pp. 1073–1188, Oct. 2015, doi: 10.1002/hipo.22488.

[71] György Buzsáki & James J Chrobak, ‘Synaptic plasticity and self-organization in the hippocampus’, 2005. [Online]. Available: http://www.nature.com/natureneuroscience

[72] E. A. Jones, A. K. Gillespie, S. Y. Yoon, L. M. Frank, and Y. Huang, ‘Early Hippocampal Sharp-Wave Ripple Deficits Predict Later Learning and Memory Impairments in an Alzheimer’s Disease Mouse Model’, *Cell Rep*, vol. 29, no. 8, pp. 2123-2133.e4, Nov. 2019, doi: 10.1016/j.celrep.2019.10.056.

[73] Z. H. Zhen *et al.*, ‘Normal and Abnormal Sharp Wave Ripples in the Hippocampal-Entorhinal Cortex System: Implications for Memory Consolidation, Alzheimer’s Disease, and Temporal Lobe Epilepsy’, *Frontiers in Aging Neuroscience*, vol. 13. Frontiers Media S.A., Jun. 28, 2021. doi: 10.3389/fnagi.2021.683483.

[74] G. Buzsáki, ‘Hippocampal sharp wave-ripple: A cognitive biomarker for episodic memory and planning’, *Hippocampus*, vol. 25, no. 10, pp. 1073–1188, Oct. 2015, doi: 10.1002/hipo.22488.

[75] L. R. Squire, L. Genzel, J. T. Wixted, and R. G. Morris, ‘Memory consolidation’, *Cold Spring Harb Perspect Biol*, vol. 7, no. 8, Aug. 2015, doi: 10.1101/cshperspect.a021766.

[76] A. Sanaullah, C. Yang, Y. Alexeev, K. Yoshii, and M. C. Herbordt, ‘Real-time data analysis for medical diagnosis using FPGA-accelerated neural networks’, *BMC Bioinformatics*, vol. 19, Dec. 2018, doi: 10.1186/s12859-018-2505-7.

[77] T. C. Stewart, T. DeWolf, A. Kleinhans, and C. Eliasmith, ‘Closed-loop neuromorphic benchmarks’, *Front Neurosci*, vol. 9, no. DEC, 2015, doi: 10.3389/fnins.2015.00464.

[78] ‘MeadNeuro1990’.

[79] S. E. Bibri, A. Alexandre, A. Sharifi, and J. Krogstie, ‘Environmentally sustainable smart cities and their converging AI, IoT, and big data technologies and solutions: an integrated approach to an extensive literature review’, *Energy Informatics*, vol. 6, no. 1. Springer Nature, Dec. 01, 2023. doi: 10.1186/s42162-023-00259-2.

[80] N. Winter-Hjelm, Å. Brune Tomren, P. Sikorski, A. Sandvig, and I. Sandvig, ‘Structure-function dynamics of engineered, modular neuronal networks with controllable afferent-efferent connectivity’, *J Neural Eng*, vol. 20, no. 4, Aug. 2023, doi: 10.1088/1741-2552/ace37f.

[81] M. B. Milde *et al.*, ‘Neuromorphic Engineering Needs Closed-Loop Benchmarks’, *Frontiers in Neuroscience*, vol. 16. Frontiers Media S.A., Feb. 14, 2022. doi: 10.3389/fnins.2022.813555.

[82] K. Aboumerhi, A. Güemes, H. Liu, F. Tenore, and R. Etienne-Cummings, ‘Neuromorphic applications in medicine’, *Journal of Neural Engineering*, vol. 20, no. 4. Institute of Physics, Aug. 01, 2023. doi: 10.1088/1741-2552/aceca3.

[83] A. Navas-Olive, R. Amaducci, M.-T. Jurado-Parras, E. R. Sebastian, and L. M. de la Prida, ‘Deep learning-based feature extraction for prediction and interpretation of sharp-wave ripples in the rodent hippocampus’, vol. 11, p. 77772, 2022, doi: 10.7554/eLife.

[84] A. Ecker *et al.*, ‘Hippocampal sharp wave-ripples and the associated sequence replay emerge from structured synaptic interactions in a network model of area CA3’, *Elife*, vol. 11, Jan. 2022, doi: 10.7554/eLife.71850.

1. Arithmetic circuits are components in computers that perform mathematical operations, like addition or multiplication, using binary logic and electrical circuits. They're the building blocks for calculations in digital systems. [↑](#footnote-ref-1)
2. **A Spiking Neural Network (SNN)** is a type of artificial neural network that mimics the way biological neurons communicate. Unlike traditional neural networks that use continuous values for neuron activations, SNNs use discrete events called "spikes" to transmit information. These spikes are sent only when a neuron's membrane potential reaches a certain threshold, making SNNs more energy-efficient and capable of capturing temporal dynamics of neural activity, similar to the brain. [↑](#footnote-ref-2)
3. **Spike** refers to an action potential, which is a rapid and temporary electrical signal that travels along the membrane of a neuron. [↑](#footnote-ref-3)
4. **Backpropagation**, short for "backward propagation of errors", is an algorithm for supervised learning of artificial neural networks using gradient descent. Given an artificial neural network and an error function, the method calculates the gradient of the error function with respect to the neural network's weights. [↑](#footnote-ref-4)
5. Documentation: <https://lava-nc.org/>

   Github: <https://github.com/lava-nc> [↑](#footnote-ref-5)
6. The challenge of **non-differentiability in spike generation** refers to the difficulty in calculating the precise changes needed to improve the network's performance because the spiking function is not smooth and doesn't have a straightforward derivative. [↑](#footnote-ref-6)
7. A **shank** is typically a slender, elongated structure that houses multiple electrode sites along its length, allowing for the recording of electrical activity from different depths within the brain or other neural tissues. [↑](#footnote-ref-7)
8. **Multiplexing** refers to combining multiple signals from various electrodes into a single data stream for transmission or processing. [↑](#footnote-ref-8)
9. **H.M.,** whose full name was Henry Molaison, was a patient who became one of the most famous cases in the history of neuroscience. In 1953, when he was 27 years old, Molaison underwent experimental brain surgery to alleviate severe epileptic seizures. The surgery, performed by Dr. William Scoville, involved the removal of large portions of his medial temporal lobes, including most of his hippocampus [65]. [↑](#footnote-ref-9)
10. A neuronal **ensemble** refers to a group of neurons that function collectively to perform specific tasks or processes. [↑](#footnote-ref-10)
11. **LFPs** reflects the synchronized activity of a group of neurons in the vicinity of the recording electrode. [↑](#footnote-ref-11)
12. **Consummatory behaviours** are actions or activities that fulfil a biological or psychological need, typically associated with the satisfaction of a primary drive or motivation. (i.e. Eating, resting …) [↑](#footnote-ref-12)
13. **Weak synaptic potentiation** typically involves a moderate increase in the efficiency of neurotransmission at the synapse, leading to a relatively modest enhancement in the postsynaptic neuron's excitability or responsiveness. [↑](#footnote-ref-13)
14. Interneurons also known as association neurons, are a type of neuron that serves as a mediator or connector within the nervous system. [↑](#footnote-ref-14)
15. **Event-driven computation** is a computational paradigm where the execution of tasks or processes is triggered by events rather than being based on a fixed, predetermined schedule. In this approach, tasks are initiated in response to specific occurrences or stimuli, referred to as events. [↑](#footnote-ref-15)
16. https://cajal.csic.es/laboratorios/circuitos-neuronales/ [↑](#footnote-ref-16)
17. These mice express GCaMP7 in their neurons, allowing researchers to monitor neuronal activity in real-time by measuring changes in fluorescence. This provides insights into the dynamics of neural circuits during different behaviors or conditions. [↑](#footnote-ref-17)