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

**Bachelors of Bioengineering**

Histograma

Descripción generada automáticamente con confianza media

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# Abstract

Hola me

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# Introduction

## Motivation

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.

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. 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).

However, capturing and analysing HFOs pose significant challenges, particularly concerning power consumption and computational efficiency. Traditional computing approaches struggle to cope with the complexity and real-time demands of neural data processing, especially when targeting low-power applications. These applications, among others, include closed-loop systems, 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. We see this closed loop systems in patients with Parkinson’s disease (PD). In PD closed loop deep brain stimulation (DBS) systems have been developed to continuously monitor neural activity and adjust stimulation parameters in response to variations in neural activity. 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. By harnessing the principles of spiking neural networks[[1]](#footnote-1) and event-driven computation[[2]](#footnote-2), neuromorphic platforms hold immense promise for revolutionizing the way we study and understand brain dynamics.

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. Efforts underway to develop energy-efficient AI algorithms and hardware, are one of the causes pushing the advances of NC. Other promise of this research branch includes advancements in brain computer interfaces due to their further resemblance in the way they process information (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.

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 low-power image classification systems where it is mainly performed object detection and navigation. Namely embedded cameras in cars, street traffic, security systems…[1]. Nonetheless, very few works about closed loop systems for brain applications have been reported. 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.

## Objective

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 [2] and network architectures will be explored aiming to find the most higher performance 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.

Ultimately, once achieved data preparation and training of the model, the performance and computation time will be compared with state-of-the-art ANN models [3] and SNN models [4], [5] designed to detect same or similar oscillation patterns.

## Hypothesis

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.

# State of the art

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 [6], 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[7]. 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[6].

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.

## Current stage of research in neurological diseases

### 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 [8].

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 1.** Schematic representation of BBB complex interaction with inorganic and polymeric nanoparticles [8].

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. Moreover, other delivery routes were explored to overcome traditional ones. Intranasal delivery (IN) administration provides an alternative to intravenous administration. 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.

With all the proposed techniques significant advances with improving results were obtained. However, any of them was able to revert the progress 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 [8]. *Cummings J. et al.* claim the need of better diagnosis in the early stages of AD using additional biomarkers to improve their prospects [9].

### 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 [10].

There are several types of electrical stimuli applied to brain tissue. 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 [11], Mcintyre et al (1969) reported changes in rats behaviour as a result of daily brain electrical simulation [12]. This opened a new realm in the context of therapies for neurological diseases. Since then, many electrical stimulations methods have been explored.

**Most popular**

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.

*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.

*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 [13].

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. It may disrupt pathological oscillations, synchronize neuronal activity, or induce plastic changes in neural circuits, ultimately leading to therapeutic effects. *Castro D et al* proposed a closed-loop system to detect abnormal high frequency oscillations in the hippocampus and perform local electrical stimulation to restore normal firing activity [14].

Dysfunctional neuronal firing patterns are one target for DBS regarding PD and epilepsy. 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 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 [13], [15], [16]. 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 current

Diagrama

Descripción generada automáticamente

**Figure 2.** Overview of DBS on neuroplasticity. Neurotransmitters (inset) are released in response to stimulation, leading to calcium waves and subsequent release of gliotransmitters. This release influences synaptic plasticity, leading to arteriole dilation and increased regional blood flow ultimately leading to tissue regeneration [13].

same can be achieved with an electrode to measure instead of stimulating. So, with the development of DBS, local invasive electrodes have also gone through a process of tailoring. 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.

## The hippocampus

The hippocampus is one of the most thoroughly investigated parts of the brain. Since the famous report of the case study H.M., 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. The intense research has given rise to 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 (as shown in ***Figure 3***), thus providing the brain with a spatiotemporal framework where memories can be stored and consolidated.

### Hippocampal subregions

Entorhinal Cortex (EC) provides the major cortical input source to the hippocampus and primarily targets Dentrite Girus (DG), which then targets Cornu Ammonis 3 (CA3), finally leading to CA1, which will project back to EC to complete the loop. However, later it was found that the complex was not so stratified into separate regions, where each part was as a closed box receiving an input and generating an output. Simultaneous activity, parallel processing and widespread connectivity was revealed in further studies.



**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".

### 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. In the literature it have been reported two types of declarative memory:

***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 are more critical for semantic memories [17]. 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 in the medial temporal lobe if they are relevant or not (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 [17].

The process of how memories gradually get independent from the hippocampus is not fully understood. It is widely believed that the memory storage framework used by the mammalian brain is based on the 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[[3]](#footnote-3) 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)[[4]](#footnote-4). They represent the most synchronous population pattern in the mammalian brain [18]. 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 [19].

Un dibujo de una persona

Descripción generada automáticamente con confianza baja

**Figure 4.** 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 [18] )

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[[5]](#footnote-5) and non-REM sleep, and are inﬂuenced by numerous neurotransmitters and neuromodulators. Numerous studies unveil their relevance in the process of episodic memory encoding [18], [20], [21]. The memory traces are encoded via weak synaptic potentiation 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**

*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[[6]](#footnote-6) 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.


**Figure 5.** Ripples only show high frequency oscillatory pattern whereas sharp waves have a sudden decrease (sharp) in amplitude[21]

**Pathological SWRs**

In rat brains, SWRs duration range from 30 to 150ms, and its amplitude should never exceed 3mV [18]. 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 when symptoms will arise 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.

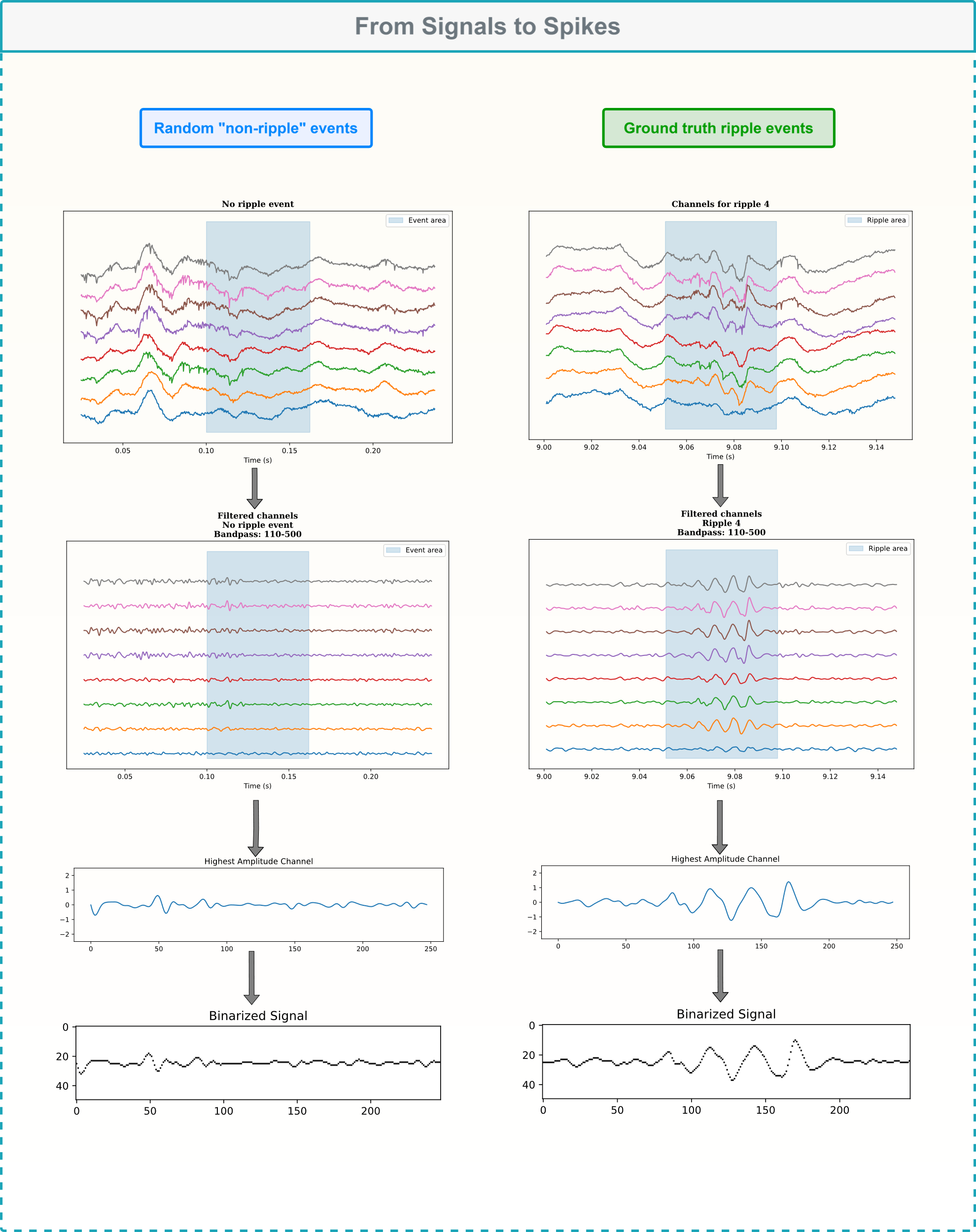
## Neuromorphic Computation

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. 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 learning patterns. Following inspiration by nature, NC raised as another approach to recreate intelligence through a deeper emulation of the biological neural system [22]. At all ends, ANNs achieve intelligence by simulating the inputs and outputs of the nodes. In contrast, human brain has physical nodes with real connections and weights. 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 size which are connected as a circuit recreating a neural network.

# Empirical Study







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1. Spiking neural networks (SNN) are artificial neural networks which communicate through discrete spikes or pulses of activity, similar to the firing of action potentials in real neurons.Principio del formulario [↑](#footnote-ref-1)
2. 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-2)
3. A neuronal ensemble refers to a group of neurons that function collectively to perform specific tasks or processes. [↑](#footnote-ref-3)
4. LFPs reflects the synchronized activity of a group of neurons in the vicinity of the recording electrode. [↑](#footnote-ref-4)
5. 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-5)
6. Interneurons also known as association neurons, are a type of neuron that serves as a mediator or connector within the nervous system. [↑](#footnote-ref-6)