## Pattern Recognition in a 2D/3D Spiking Neuron Culture Using STDP and Implications for Brain Organoid Studies

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#### **Abstract**

This project explores the pattern recognition capabilities of a 2D spiking neuron culture and its ability to react to noise and overcome it. Utilizing a simple Leaky Integrate-and-Fire (LIF) model and the Spike-Timing-Dependent Plasticity (STDP) learning mechanism, a group of excitatory and inhibitory are randomly arranged in a 2D grid and trained to learn distinct visual patterns. The synaptic connectivity was based on neurons' distance from each other, and input patterns were processed into spike times. Unlike traditional neural network implementations that involve multiple layers, including hidden and output layers, this study focuses solely on a single-layer 2D culture of neurons. Our findings demonstrate the fundamental mechanisms of neural learning and plasticity in a new form while covering its similarities and differences with brain organoids. Our results help us conclude that this approach of 2D neuron cultures is a viable method for pattern recognition in various forms which also excels in terms of robustness even with a limited number of neurons.

#### Introduction

Spiking Neural Networks (SNNs) will always stand out as a biologically inspired approach to neural networks and are noteworthy for providing a better understanding of brain activity and designing artificially intelligent systems. This project takes a closer look at how an SNN consisting of a 2D culture of spiking neurons with only a single layer can be utilized to perform pattern recognition tasks while also creating a robust environment.

#### **Spiking Neural Networks**

SNNs are a class of neural networks that aim to mimic the natural processes and mechanisms that take place in our brains in a closer and more accurate manner than traditional neural networks. Just like in our brain, SNNs make use of neurons, connections between them known as synapses to "learn" and utilize spikes as means to send and receive information between its building blocks. This spiking behavior

allows them to harness the computing power and neural processing capabilities of the brain, or at least try to do so.

#### The Leaky Integrate-and-Fire (LIF) Model

The Leaky Integrate-and-Fire neuron model is a widely used representation of neuronal behavior in SNNs. This model uses a simplified model of biological neurons while retaining key characteristics such as membrane potential, threshold for firing, and refractory periods. In this model, the neuron's membrane potential integrates spikes over time and "leaks" due to resistance. When the membrane potential reaches its defined threshold, the neuron fires a spike and then resets, simulating the process of action potential generation in biological neurons.

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

Spike-timing-dependent plasticity is a biologically inspired learning mechanism that adjusts the strength of synapses based on the precise timing of pre-synaptic and post-synaptic spikes. If a presynaptic spike precedes a postsynaptic spike within a short time window, the synapse is strengthened (Long-Term Potentiation). Conversely, if the postsynaptic spike occurs before the presynaptic spike, the synapse is weakened (Long-Term Depression). STDP captures the temporal aspect of synaptic plasticity observed in the brain, playing a crucial role in learning and memory.

#### **Objectives**

The specific objectives to test the limits of a 2D spiking neuron culture are:

- To model a network of excitatory and inhibitory neurons arranged in a 2D grid.
- To implement distance-based synaptic connectivity and apply the LIF neuron model.
- To preprocess input patterns into spike times and train the network using STDP.
- To analyze the network's ability to distinguish between different visual patterns through synaptic weight changes and spiking activity.
- To draw parallels between the 2D culture model and the 3D complex brain organoid model, highlighting the relevance of this simplified model to understanding neural development and function.

#### **2D Neuron Culture**

First proceed with a neuron group consisting of 8 excitatory neurons and 2 inhibitory neurons and later expand to larger models. These neurons are placed randomly in a 2D space and do not follow a full connectivity scheme. Instead, their connectivity depends on a probability function based on the distance between them. The closer two neurons are, the more likely they are to form a synaptic connection. The nature of this synapse, whether inhibitory or excitatory, depends on the type of neuron sending the incoming spikes. The neurons all conform to the LIF model, and have the following attributes:

Membrane Time Constant (Tau)	Volt
Current (I)	$Volt^{1}$
Horizontal Position (X)	Metre
Vertical Position (Y)	Metre

The equation used for this model is also the standard LIF equation used throughout all SNNs and the fluctuations and changes in each neuron follow this equation, unless in a refractory period:

$$\frac{dv}{dt} = \frac{v_{rest} - v + I}{\tau}$$

There are also other parameters involved in this simulation, such as normal parameters for neuron simulation, and additional parameters that come into play when the STDP learning mechanism is utilized in our simulation and training process. These parameters have been experimented with and tuned in order to find their optimal value to a feasible extent and they are as follows:

Membrane Time Constant (Tau)	<b>60</b> ms
Resting Potential ( $V_{rest}$ )	-65 mv
Reset Potential ( $V_{reset}$ )	-65 mv
Membrane Potential Threshold ( $V_{threshold}$ )	-55 mv

<sup>&</sup>lt;sup>1</sup> Although using volts (V) for current (I) instead of amperes (A) may seem unconventional, it simplifies the modeling process and maintains dimensional consistency within the simulation framework.

Refractory Period	5 ms
STDP Time Constant ( $Tau_{STDP}$ )	<b>15</b> ms
Potentiation Factor ( $A_{Plus}$ )	0.1
Depression Factor ( $A_{Minus}$ )	-0.1

Another parameter used for neuron placement in the 2D plane is "neuron spacing," which is crucial in the initialization of each neuron. During this phase, two random numbers are generated for each neuron multiplied by the neuron spacing, determining its X and Y coordinates in the 2D space.

The height and width of our space are also determined by the maximum value of X and Y available in our neuron group.

Before moving on to how neurons are connected and the corresponding probability function that is involved, we will first dive into the mechanisms behind the synapse, which are the STDP rule and the excitatory/inhibitory concepts that are tied together in this implementation. The STDP synapse model is defined using a set of equations that describe the dynamics of synaptic weight changes. The normal STDP equation simply states that changes in the pre- and post-synaptic variables, depicted by  $A_{Plus}$  and  $A_{Minus}$  symbols, decay over time depending on the  $Tau_{STDP}$  parameter.

However, the updates to the synaptic weights and variables  $A_{Pre}$  and  $A_{Post}$  are defined separately for excitatory and inhibitory synapses.

#### For excitatory synapses:

- When a pre-synaptic neuron fires, the post-synaptic current is increased by w. The  $A_{Pre}$  variable is incremented by  $A_{Plus}$ , and the synaptic weight w is updated by adding  $A_{Post}$  to it. The updated weight is clipped to ensure it remains within the range [0, 1].
- When a post-synaptic neuron fires, the  $A_{Post}$  variable is incremented by  $A_{Minus}$ , and the synaptic weight w is updated by adding  $A_{Pre}$  to it. The updated weight is again clipped to stay within the range [0, 1].

#### For inhibitory synapses:

- When a pre-synaptic neuron fires, the post-synaptic current is decreased by w. The  $A_{Pre}$  variable is incremented by  $A_{Plus}$ , and the synaptic weight w is updated by adding  $A_{Post}$  to it. The updated weight is clipped to the range [0, 1].

- When a post-synaptic neuron fires, the  $A_{Post}$  variable is incremented by  $A_{Minus}$ , and the synaptic weight w is updated by adding  $A_{Pre}$  to it. The updated weight is once again clipped to stay within the range [0, 1].

Now that we are familiar with the synapses themselves, we can take a look into what approach will be used to form them. As stated before, we will implement the connection probabilities between neurons based on their distances in 2D space. This ensures that neurons are more likely to connect with closer neurons, thus creating a more biologically plausible neural network.

The connection probability between two neurons is computed using a Gaussian function that depends on the Euclidean distance between the neurons:

$$exp(-4\frac{(x_{pre}-x_{post})^2+(y_{pre}-y_{post})^2}{width^2})$$

Where  $x_{pre}$  and  $y_{pre}$  are the coordinates of the pre-synaptic neuron,  $x_{post}$  and  $y_{post}$  are the coordinates of the post-synaptic neuron, and the width parameter that controls the spread of the Gaussian function. A smaller width results in higher connectivity between closer neurons and lower connectivity between distant neurons.

We then compute the connection probabilities for both excitatory and inhibitory synapses separately and store them in their corresponding connectivity matrix which will be used later.

First, a connection probability matrix for excitatory synapses is computed. Each element in this matrix represents the probability of a synapse forming between an excitatory neuron and another neuron, based on their distances. Following the calculation of connection probabilities, excitatory synapses are created. For each potential connection, a random number is generated and compared to the precomputed connection probability. If the random number is smaller and the neurons are not the same, a synapse is created between them. The weights of these synapses are initialized randomly between 0 and 0.5. A similar process is followed for inhibitory synapses. The probabilistic nature of our synapse creation introduces variability and randomness, making the network more robust and capable of complex pattern recognition.

#### **Input Processing**

As the input patterns for this project, we will be using images from <a href="mailto:the MNIST">the MNIST</a> dataset, specifically the digits "3" and "7". The use of visual inputs offers several advantages. Firstly, visual data is high-dimensional and complex, which provides a rich source of information for training neural networks. This complexity allows for more effective testing and validation of the network's pattern recognition capabilities. Additionally, using standardized datasets like MNIST ensures reproducibility and comparability of results with other studies. Visual patterns are also more intuitive for humans to interpret, making it easier to understand and analyze the network's performance and learning process.

These images will go through a preprocessing stage, where the images are loaded and converted to grayscale, then are resized to a 10x10 pixel array to both do not overwhelm the SNN with high dimensions especially due to the limited number of neurons, and also due to the fact that the input arrays must be of the same size and format.

After preprocessing, the images are aggregated. This involves averaging the pixel values along one dimension, resulting in 10 values for each image. These aggregated values represent the intensity of the image across different rows. The aggregated image data is then converted into spike times for the neurons. Each value in the aggregated data is mapped to a number of spikes that a neuron will generate within a specified duration. The spike times are generated randomly but uniformly within the given duration.

Finally, A *SpikeGeneratorGroup* is created using the combined spike times and indices of both images. This group serves as the input to the neuron network, providing a sequence of spikes that mimic the input patterns derived from the images.

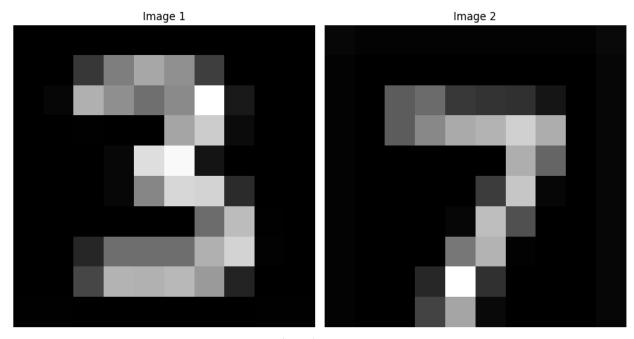
This input group is fed into our network using a new synapse group that is created only for input purposes and is connected to each and every neuron in our group.

#### **Training and Pattern Recognition**

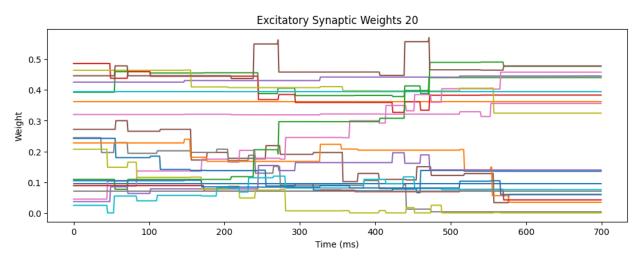
To understand how input patterns influence neuron activity in the 2D spiking neuron culture, we connected the input group to the neurons network and monitored various parameters. Specifically, we observed synaptic weights, neuron spikes and membrane voltages to analyze the network's response to input patterns.

#### **Initial Simulation (700 ms)**

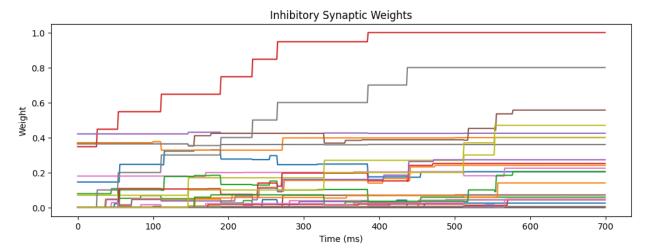
In the initial simulation phase, run the network for 700 ms. During the period, inject spikes into the network from the input group and monitor the changes.



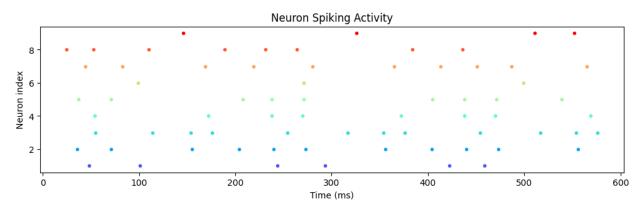
1. Input Images



2. The synaptic weights of excitatory connections indicating that the network was learning the presented pattern.

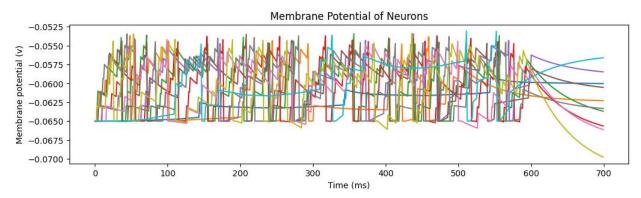


3. The inhibitory synaptic weights, which are consistent with their role in stabilizing network activity.



4. This plot illustrates the Spiking activity of neurons in the network following the input of patterns. Each 100 ms interval represents the presentation of a distinct pattern across three epochs.

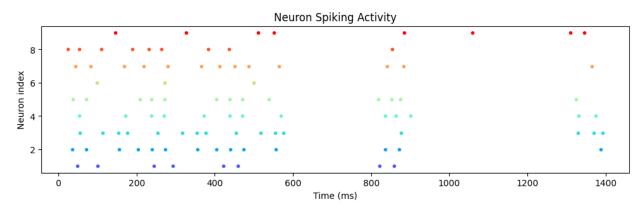
The plot highlights the variations in neuron firing rates in response to different input patterns, demonstrating the network's ability to recognize and react to the presented visual stimuli.



5. The voltage monitor tracked membrane of neurons. Neurons displayed characteristic leaky integrate-and-fire behavior with membrane potentials increasing due to input spikes and decaying in the absence of spikes.

#### **Extended Simulation with Delayed Inputs (1400 ms)**

To further investigate the network's behavior over a longer period and assess its response to delayed inputs, we extended the simulation time to  $1400 \, \underline{ms}$ .



Each time an input pattern was presented, the spiking activity plot showed significant activity, indicating that the network recognized and responded to the patterns.

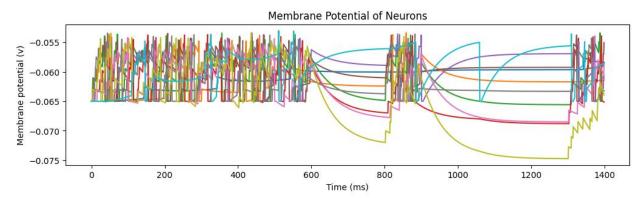
#### 1. Learning Phase (0-600 ms):

The network underwent three epochs of learning during the first 600  $\mathrm{ms}$ . During this phase, synaptic weights were adjusted as the network learned to recognize the input patterns.

2. Pattern Presentation and Response (600-1400 ms):

At 800  $\mathrm{ms}$ , Pattern 1 was presented to the network. The network's response was recorded.

At 1200  $\mathrm{ms}$ , Pattern 2 was presented. The network's reaction to Pattern 2 was observed.

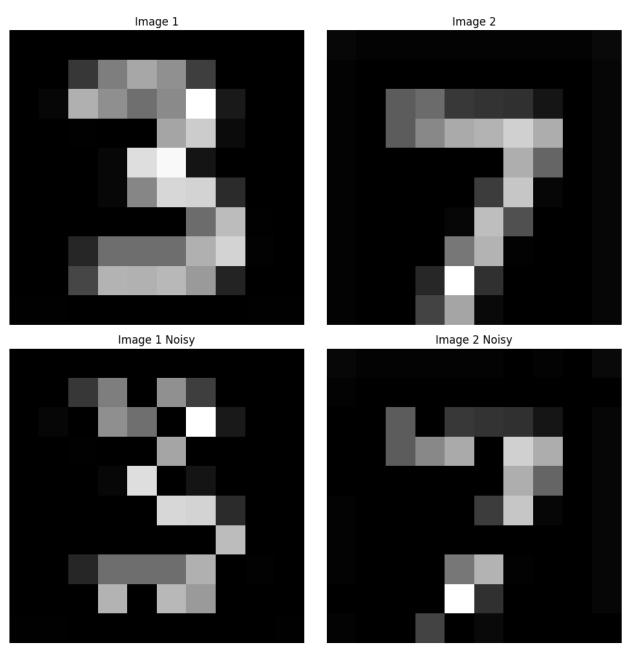


7. The membrane potential plots showed noticeable changes and spikes in response to input patterns. Each time an image was input the potential started reacting significantly, indicating pattern recognition.

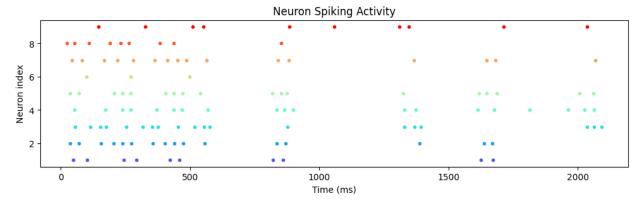
#### **Effect of Noisy Input Pattern**

To test the network's robustness, we introduced noisy versions of the patterns. Extended Simulation with Noisy Inputs (2100  ${
m ms}$ )

In this extended simulation, the network was run for 2100  $\,\mathrm{ms}$  to observe its response to noisy inputs.



8. Images and this noisy one (30% noise)



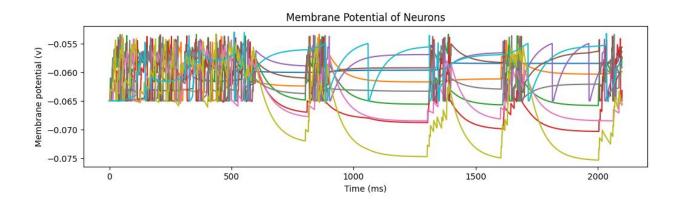
9. The spiking activity pilots demonstrated that the network could still recognize the noisy patterns, although the response was less pronounced compared to noise-free patterns.

- Learning Phase (0-600 ms)
   Like the previous phase, the network learned the patterns over three epochs.
- 2. Pattern Presentation and Response: At 800  $\rm ms$ , Pattern 1 was presented to observe the network's response.

At 1600  $\mathrm{ms}$ , Pattern 1 with 30% noise was presented to the network's robustness to noise.

At 2000  $\mathrm{ms}$ , Pattern 2 with 30% noise was presented.

At 1200 ms, Pattern 2 was presented.



Despite the introduction of noise, the network maintained a high level of recognition accuracy. The membrane potentials and spiking activity showed that the network could differentiate between the noisy patterns, indicating its robustness and reliability.

#### **Extended Neurons Network Simulation**

In this section, we extend the size of the neuron network to 40 neurons, consisting of 80% excitatory neurons and 20% inhibitory neurons. We also implement several parameter changes:

#### 1. Membrane Potential Parameters

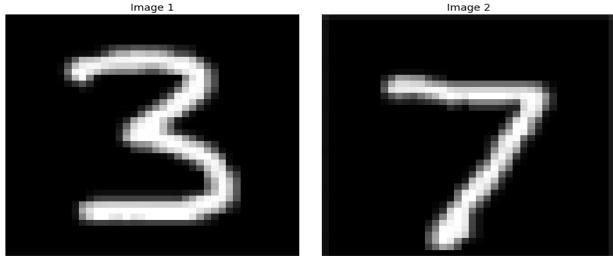
Reset Potential ( $V_{reset}$ )	-70 mv
Threshold Potential ( $V_{ m threshold}$ )	<b>-48</b> mv
Membrane Time constant ( $ au$ )	<b>70</b> ms

#### 2. STDP Parameters

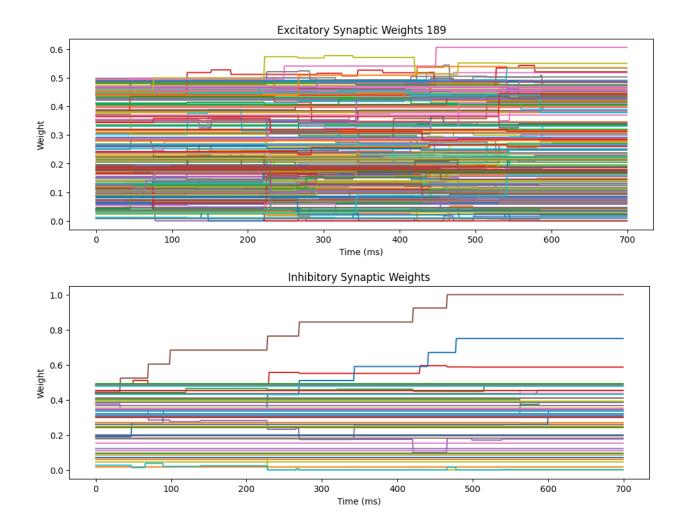
Potentiation Factor ( $A_{plus}$ )	0.08
Depression Factor ( $A_{minus}$ )	-0.08

#### Initial Simulation (700 ms):

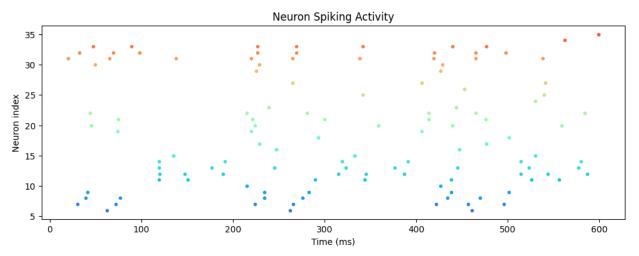
The network is simulated for 700  ${
m ms}$  with the new parameters to observe the initial learning phase and neuronal responses to input patterns.



10. Input image in size of 40\*40

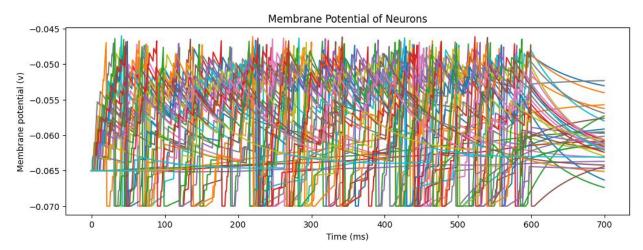


Both excitatory and inhibitory synapses showed updates, reflecting the learning process. Excitatory synapses demonstrated significant potentiation due to the increased  $A_{Plus}$  value.



11. This plot illustrates the spiking activity of neurons in the network following the input of patterns. Each 100 ms interval represents the presentation of a distinct pattern across three epochs.

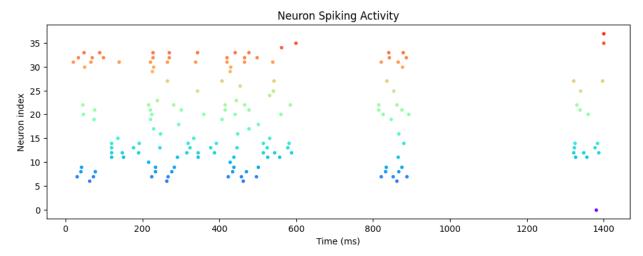
The plot highlights the variations in neuron firing rates in response to different input patterns, demonstrating the network's ability to recognize and react to the presented visual stimuli.



The voltage monitor tracked the membrane of neurons. Neurons displayed characteristic leaky integrate-and-fire behavior with membrane potentials increasing due to input spikes and decaying in the absence of spikes.

#### Extended Simulation with Delayed Inputs (1400 ms)

To further investigate the network's behavior over a longer period and assess its response to delayed inputs, we extended the simulation time to 1400 ms.



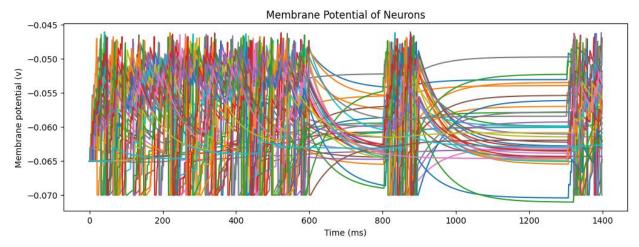
#### 1. Learning Phase (0-600 ms):

The network underwent three epochs of learning during the first 600  $\mathrm{ms}$ . During this phase, synaptic weights were adjusted as the network learned to recognize the input patterns.

2. Pattern Presentation and Response (600-1400  $\mathrm{ms}$ ): At 800  $\mathrm{ms}$ , Pattern 1 was presented to the network. The network's response was recorded.

At 1200 ms, Pattern 2 was presented. The network's reaction to Pattern 2 was observed.

Each time an input pattern was presented, the spiking activity plot showed significant activity, indicating that the network recognized and responded to the patterns.

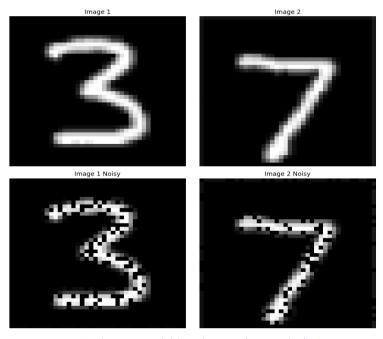


12. The membrane potential plots showed noticeable changes and spikes in response to input patterns. Each time an image was input the potential started reacting significantly, indicating pattern recognition.

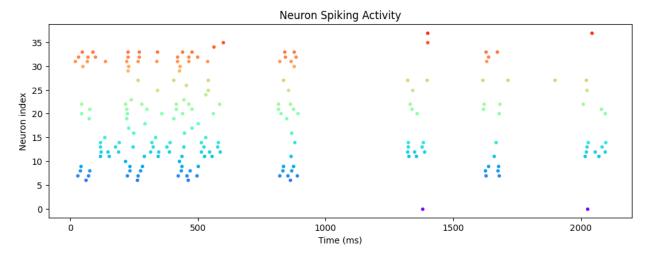
#### **Effect of Noisy Input Pattern**

To test the network's robustness, we introduced noisy versions of the patterns. Extended Simulation with Noisy Inputs (2100  ${
m ms}$ )

In this extended simulation, the network was run for 2100  $\mathrm{ms}$  to observe its response to noisy inputs.



13. Images and this noisy one (30% noise)



14. The spiking activity pilots demonstrated that the network could still recognize the noisy patterns, although the response was less pronounced compared to noise-free patterns.

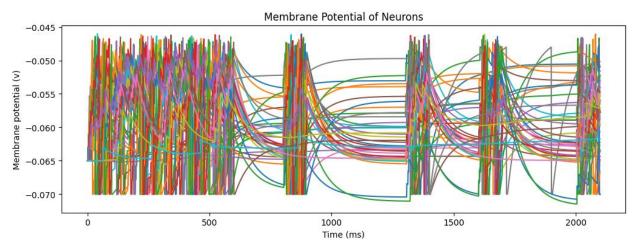
# Learning Phase (0-600 ms): Like the previous phase, the network learned the patterns over three epochs.

4. Pattern Presentation and Response:

At 800 ms, Pattern 1 was presented to observe the network's response. At 1200 ms, Pattern 2 was presented.

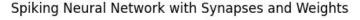
At 1600 ms, Pattern 1 with 30% noise was presented to the network's robustness to noise.

At 2000 ms, Pattern 2 with 30% noise was presented.

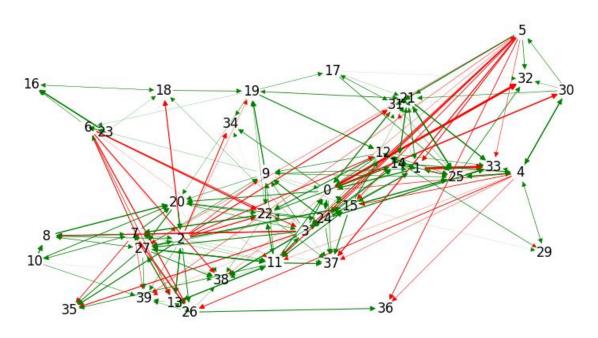


Despite the introduction of noise, the network maintained a high level of recognition accuracy. The membrane potentials and spiking activity showed that the network could differentiate between the noisy patterns, indicating its robustness and reliability.

As seen, the extended 2D spiking neuron culture effectively distinguished between different visual patterns, even with increased network size and parameter changes. The network responded appropriately to delayed inputs, showcasing its temporal processing capabilities. The network demonstrated resilience by recognizing noisy patterns, highlighting its robustness and potential for practical applications.



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15. This plot illustrates the synaptic connectivity within the spiking neural network, where each Neuron represented as points in the network diagram, each with a corresponding position in the 2D space and each synapse is represented by a line connecting pairs of neurons. The width of each line corresponds to the weight of the synapse, providing a visual representation of the synaptic strength. The color coding distinguishes the type of synapses: Red Lines -> Inhibitory Synapses, Green Lines -> Excitatory Synapses.

#### **3D Neuron Culture**

To approximate the complex structure of a brain organoid, the neurons in our spiking neural network are positioned on the surface of a sphere. This 3D arrangement is more biologically realistic compared to a 2D layout. The spherical coordinates are randomly generated to simulate the distribution of neurons in a brain-like structure.

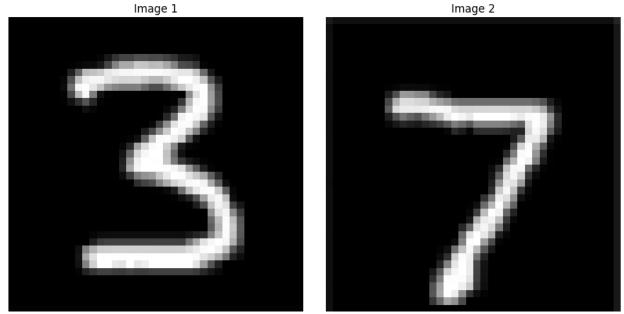
The spherical coordinates are then converted to Cartesian coordinates (x, y, z) to place the neurons in a 3D space.

#### Simulation:

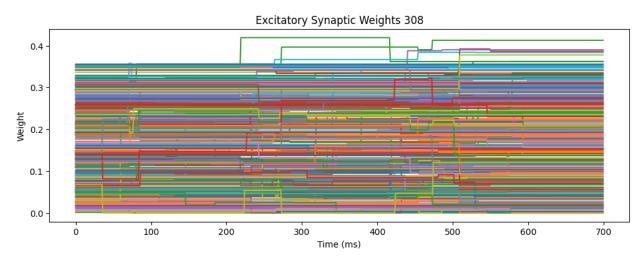
Continue with the previous simulation setup, monitoring synaptic weights and neuron spikes, but with the neurons now placed on a spherical surface.

#### Initial Simulation (700 ms):

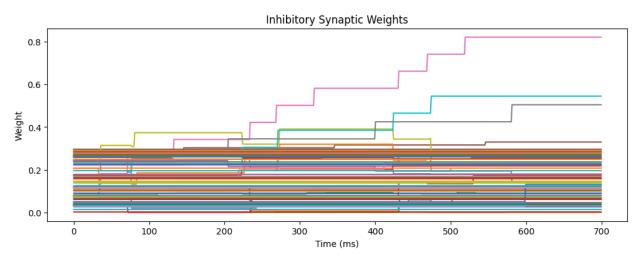
In the initial simulation phase, run the network for 700 ms. During the period, inject spikes into the network from the input group and monitor the changes.



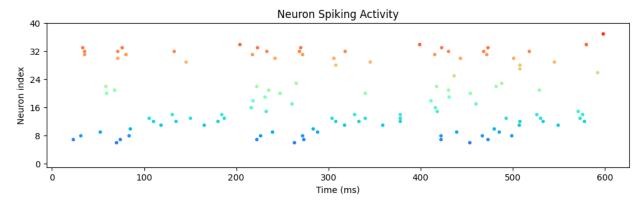
16. Input Images



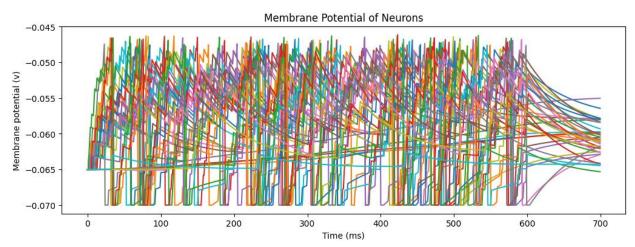
17. The synaptic weights of excitatory connections indicating that the network was learning the presented pattern.



18. The inhibitory synaptic weights, which is consistent with their role in stabilizing network activity.



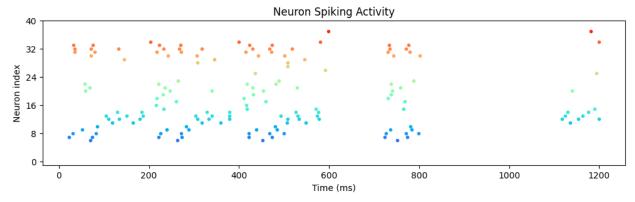
19. This plot illustrates the Spiking activity of neurons in the network following the input of patterns. Each 100 ms interval represents the presentation of a distinct pattern across three epochs. The plot highlights the variations in neuron firing rates in response to different input patterns, demonstrating the network's ability to recognize and react to the presented visual stimuli.



20. The voltage monitor tracked membrane of neurons. Neurons displayed characteristic leaky integrate-and-fire behavior with membrane potentials increasing due to input spikes and decaying in the absence of spikes.

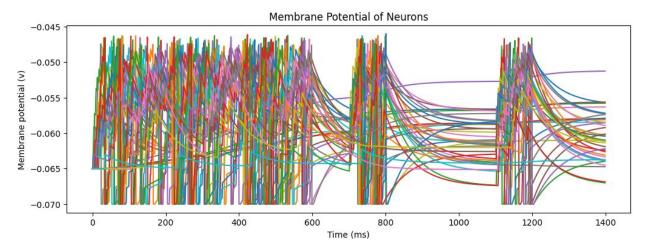
#### **Extended Simulation with Delayed Inputs (1400 ms)**

To further investigate the network's behavior over a longer period and assess its response to delayed inputs, we extended the simulation time to 1400 ms.



21. Each time an input pattern was presented, the spiking activity plot showed significant activity, indicating that the network recognized and responded to the patterns.

- 5. Learning Phase (0-600 ms):
  - The network underwent three epochs of learning during the first 600 ms. During this phase, synaptic weights were adjusted as the network learned to recognize the input patterns.
- 6. Pattern Presentation and Response (600-1400 ms):
  - At 800 ms, Pattern 1 was presented to the network. The network's response was recorded.
  - At 1200 ms, Pattern 2 was presented. The network's reaction to Pattern 2 was observed.

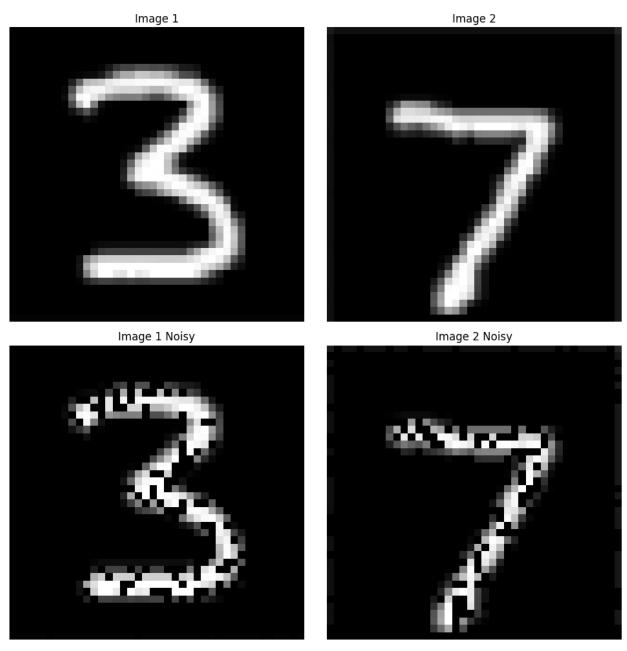


22. The membrane potential plots showed noticeable changes and spikes in response to input patterns. Each time an image was input the potential started reacting significantly, indicating pattern recognition

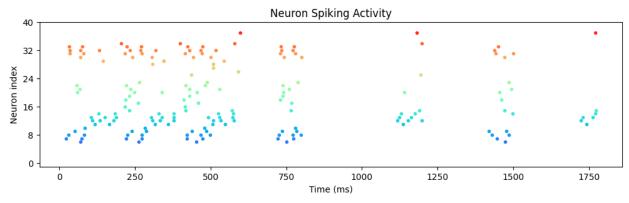
#### **Effect of Noisy Input Pattern**

To test the network's robustness, we introduced noisy versions of the patterns. Extended Simulation with Noisy Inputs (2100 ms)

In this extended simulation, the network was run for 2100 ms to observe its response to noisy inputs.



23. Images and this noisy one (30% noise)



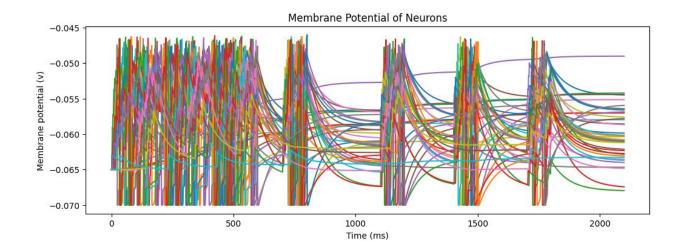
24. The spiking activity pilots demonstrated that the network could still recognize the noisy patterns, although the response was less pronounced compared to noise-free patterns.

- 7. Learning Phase (0-600 ms):
  Like the previous phase, the network learned the patterns over three epochs.
- 8. Pattern Presentation and Response:

At 800 ms, Pattern 1 was presented to observe the network's response. At 1200 ms, Pattern 2 was presented.

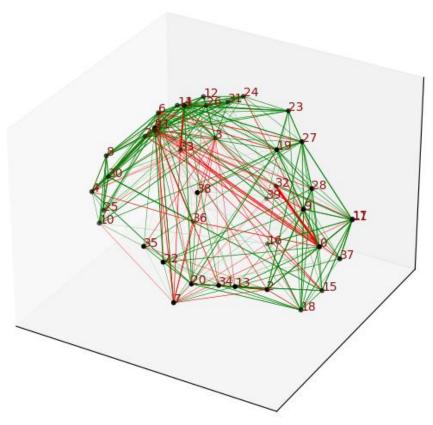
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At 2000 ms, Pattern 2 with 30% noise was presented.



Despite the introduction of noise, the network maintained a high level of recognition accuracy. The membrane potentials and spiking activity showed that the network could differentiate between the noisy patterns, indicating its robustness and reliability.

#### Spiking Neural Network with Synapses and Weights



25. The synaptic connectivity within the network was visualized, with line thickness representing synaptic strength and color indicating synapse type (red for inhibitory and green for excitatory). This visualization provides insights into the connectivity structure and synaptic weight distributions across the network.

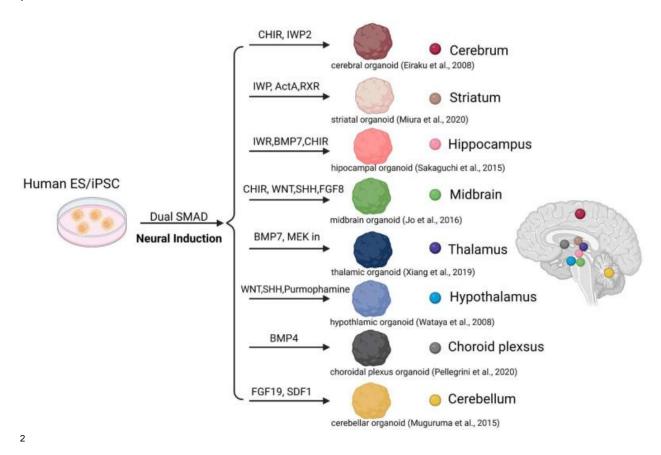
This experiment demonstrates the potential of using a spiking neural network with neurons positioned on a spherical surface to approximate the structure of a brain organoid. The network's ability to recognize patterns and its robustness to noise suggests that such a configuration can be useful for modeling and studying brain-like structures. Future work will involve developing a system for neuro reproduction and designing adaptable neuron types to future enhance the network's biological realism and functionality.

#### **Implications on Brain Organoids**

Brain organoids, also known as cerebral organoids, are three-dimensional cellular structures grown in vitro that mimic aspects of the human brain's architecture and function. These miniature, self-organized tissues are derived from pluripotent stem cells (PCSs), which can differentiate into various cell types, including neurons and glial cells. Brain organoids have gained significant attention in neuroscience research due to their potential to model

brain development, disease, and function in ways that were previously out of our reach.

The process of creating brain organoids begins with the differentiation of PSCs into neural progenitor cells. These progenitor cells then self-organize into structures that resemble the early stages of brain development. Over time, these structures form distinct brain regions, such as the cerebral cortex, and exhibit cellular diversity similar to that found in the human brain. Although brain organoids do not fully replicate the complexity of an actual brain, they provide a valuable approximation for studying neurodevelopmental processes and diseases.



26. The production of brain region-specific organoids from PSCs

#### **Applications**

- **Modeling Brain Development**: Brain organoids are used to study the intricate processes of brain development, including neural differentiation, migration, and synaptogenesis. They provide insights into the molecular and cellular mechanisms that guide brain formation.

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<sup>&</sup>lt;sup>2</sup> https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10420018/

- **Disease Modeling**: By using patient-derived induced pluripotent stem cells (iPSCs), researchers can create brain organoids that model specific genetic disorders. This approach has been instrumental in understanding diseases like microcephaly, autism spectrum disorders, and neurodegenerative conditions such as Alzheimer's and Parkinson's diseases.
- **Drug Testing and Toxicology**: Brain organoids serve as platforms for testing the efficacy and safety of new drugs. They offer a more accurate representation of how drugs interact with human brain tissue compared to traditional cell cultures or animal models.
- **Neurogenesis and Regeneration**: Researchers are exploring the potential of brain organoids to understand the processes of neurogenesis and brain tissue regeneration. This research could lead to breakthroughs in treating brain injuries and degenerative diseases.

#### **Relevance and Similarities**

Our research focuses on creating spiking neuron cultures in both 2D and 3D spaces to model neural network behavior and plasticity which is relevant to brain organoids in several aspects.

First, by studying SNNs and their interactions with each other such as we did in this project, we can gain insights into how neurons in brain organoids might communicate and adapt. Second, the way our project focuses on pattern recognition and learning is fundamental for understanding brain sensory information processing and allows us to study how these mini brains might learn and respond to different stimuli. Most importantly, by extending our research to 3D neuron cultures, we better mimic the structural and functional complexities of brain organoids, allowing us to study how neurons organize and interact in a more physiologically relevant environment, and providing deeper insights into brain development and disease. The ties between these cultures and brain organoids have been researched in <u>several studies</u>. Their differences and similarities are also an important debating point.



1	ZD Culture
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1	
1	(2)
	hamaganaalii

Cell types

Cellular interactions

Modeling cellular/

mechanical communications

Human specific genes

Manipulation

Biobanking

Reproducibility

Neurodevelopmental

disease modeling

Neurodegenerative

disease modeling

homogeneous /heterogeneous

feasible

conserved

feasible feasible

moderate

moderate (limited phenotype, limited circuit)

moderate (limited phenotype, limited circuit)



#### brain organoid

heterogeneous (limited)

conserved

feasible

conserved

feasible

feasible

low

good

low (immature cell circuit, limited

glia, no vascularization)



#### animal model

heterogeneous (rodent-specific)

conserved

limited

introduced by genetic tools (but in rodent context)

limited

feasible (only at the cellular level)

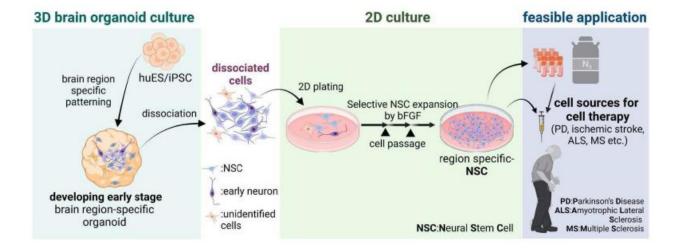
high

moderate

moderate (no sporadic pathology, accelerated phenotype)

27. Comparison of characteristics among two-dimensional (2D) cell culture, three-dimensional (3D) brain organoid models, and animal models. Organoids have advantages compared to 2D cultures and animal models and can be a practical platform for modeling diseases.

3D brain organoids and 2D cultures can be used in parallel to harness their unique strengths. The image illustrates the development of brain region-specific organoids from human embryonic stem cells (huES) or induced pluripotent stem cells (iPSCs). These organoids mimic early brain development. They can be dissociated into single cells and plated onto a 2D surface for selective expansion of neural stem cells (NSCs). Both 3D and 2D cultures are valuable for cell therapy applications, offering potential treatments for neurological conditions like Parkinson's Disease, ischemic stroke, ALS, and Multiple Sclerosis. This complementary approach enhances research and therapeutic possibilities for neurological disorders.



#### Conclusion

In this project, we explored the capabilities and dynamics of spiking neural networks (SNNs) within a 2D neuron culture, making use of spike-timing-dependent plasticity (STDP) to facilitate learning and adaptation. Our primary goal was to investigate how these networks can recognize and distinguish between patterns, using images from the MNIST database as a test case.

We began by establishing a 2D culture of excitatory and inhibitory neurons, randomly distributed across a plane, with synaptic connections determined probabilistically based on inter-neuronal distance. This setup emulates the spatial constraints and connectivity patterns observed in biological neural networks. Through the implementation of the Leaky Integrate-and-Fire (LIF) model and STDP rules, we enabled our network to undergo synaptic changes in response to neuronal activity, thereby recreating the plasticity seen in the brain.

Our findings indicate that even in the absence of a conventional layered architecture, such as input, hidden, and output layers, a single-layer network of spiking neurons is capable of learning and differentiating patterns. This demonstrates the inherent potential of 2D cultures to perform complex computational tasks through local synaptic modifications.

Additionally, the methodology of integrating noisy inputs and observing the network's response provides a robust framework for examining the resilience and adaptability of neural networks. This aspect is particularly relevant for understanding how real-world sensory inputs, often riddled with noise, are processed by biological systems.

The relevance of our work extends to the study of brain organoids, which are 3D cultures that mimic the structural and functional properties of the brain. By understanding the principles of network dynamics, pattern recognition, and

synaptic plasticity in 2D cultures, we can draw parallels and gain insights into the behavior of neurons in brain organoids. The concept of brain organoids holds significant implications for studying brain development, disease modeling, drug testing, and the potential for neurogenesis and brain tissue regeneration.

Our 3D model is the closest we can get to brain organoids with our simple framework. To get closer to the model of brain organoids in real life, we will need to make neurons adaptable and able to act like stem cells, recreating and changing forms based on the specific brain region they want to emulate and the tasks they want to accomplish. We tried to approximate this model as much as possible using our 3D model.

In conclusion, our project showcases the viability of using 2D spiking neuron cultures as a simplified yet powerful model for studying neural dynamics. By bridging the gap between simplified neural models and complex brain-like structures, we move closer to implementing and utilizing brain organoids using our current resources.

### **References**

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