

Computational Neuroscience: Inhibitory-Stabilised Networks

B204511

November 2024

1 Introduction

Several brain regions, including the neocortex and hippocampus [1] contain local recurrently connected networks of excitatory and inhibitory neurons. Understanding how those networks function and react to external inputs is important for analysing how the brain operates. This report will introduce the concept of such networks, discuss their biological relevance, present a mathematical model, and provide computer simulations as well as mathematical analysis of the model.

The network is viewed as consisting of 2 pools of neurons: excitatory and inhibitory. Each pool projects to the other, and to itself, forming a recurrent neural network. Excitatory feedback can lead to runaway excitation, which is prevented by the inhibitory feedback. This allows the network to stabilise, earning it the name Inhibitory-Stabilised Network (ISN).

To understand how the system comes together, it is important to get a sense of what the underlying model of each individual neuron is and how the interaction between them integrates.

1.1 Leaky Integrate-and-Fire Neuron

In 1907, Louis Édouard Lapicque [2] introduced the concept of the integrate-and-fire neuron model. Even though the model was developed before scientists had a chance to describe the biophysical mechanics of the neuron, it captured the behaviour of the neuron in a way that was useful for understanding [3].

The neuron is viewed as an electric circuit with a capacitor and a resistor connected in parallel. The membrane has some resistance, which is assumed to be constant and can be described by Ohm's law: $V = IR$, and therefore the

resistor current is $I = \frac{V}{R} = gV$, where g is conductance of the cell. The relationship between the current and the voltage across the capacitor is described by the following equation: $C = \frac{Q}{V}$, where C is the capacitance, Q is the charge stored in the capacitor, and V is the voltage across the capacitor. Knowing this, the current in the circuit:

$$I = \frac{dQ}{dt} = \frac{dCV}{dt} = C \frac{dV}{dt}$$

Real neurons, however, receive current from other neurons via dendrites from synapses, and induce own **ionic** current by letting charged particles in and out of the cell. Therefore, the total current is the sum of the ionic current plus any external input: $I = \sum_i g_i V + I_{ext} = g_m V + I_{ext}$. Neurons are generally **negatively charged** relative to the outside, and therefore the flow outside the cell is treated as positive. Since the size of the cell and its channels is comparable to that of ions, effect of electric attraction is comparable with that of diffusion, and there exists a point, where one balances out the other, resulting in the zero net current flow. This point is called the resting potential V_{rest} of the neuron, and therefore any current should be measured relative to this potential.

$$C \frac{dV}{dt} = -g_m(V - V_{rest}) + I_{ext}$$

Dividing by conductance, we get the following equation:

$$\tau_m \frac{dV}{dt} = -(V - V_{rest}) + \frac{I_{ext}}{g_m}$$

where τ_m is the membrane time constant, describing how quickly it reacts to input.

Now, the external current is the component of interest, by extending this component, we can integrate input from

other neurons. Neurons communicate by sending electrical signals to each other, via the synapse of emitting through the dendrites of the receiving neuron. This interaction can be modelled as a synaptic current, weighted by the strength of connection. Dale’s Law[4] states that a neuron can only be either excitatory or inhibitory, and therefore we can simplify the model, and approximate the synaptic current as a function of emitting neuron’s voltage: $I_{\text{syn},i} = W\phi(V_i)$, where W is the synaptic weight (+ for excitatory, – for inhibitory), and $\phi(V)$ is the transfer function of the neuron. The actual external current collapses into $I_{\text{ext}}/g_m = u_{\text{ext}}$.

Combing all component, we obtain a system of equations:

$$\tau_E \frac{dV_E}{dt} = -(V_E - V_{\text{rest}}) + W_{EE}\phi(V_E) - W_{EI}\phi(V_I) + u_E \quad (1)$$

$$\tau_I \frac{dV_I}{dt} = -(V_I - V_{\text{rest}}) + W_{IE}\phi(V_E) - W_{II}\phi(V_I) + u_I \quad (2)$$

where V_{rest} is the resting potential of the neuron, W_k are the synaptic weights, u_k are the external inputs to neurons, and $\phi(V)$ is the transfer function of a neuron, that acts as a communication channel between the neurons and is defined as a scaled ReLU function:

$$\phi(V) = \beta[V - V_0]_+ \quad (3)$$

Now that we have the model and its origins, it’s important to outline the benefits and limitations of the model.

1.2 Considerations (Q1)

1. The model abstracts away certain biological complexity, such as stochasticity and variability of individual ion channels (both in somas and synapses), described in great detail by the Hodgkin-Huxley model [5], which is a more biologically plausible model of the neuron, but is also significantly more complex.

2. Synaptic weights are a heuristic approximation of synaptic conductances and assumed to be constant, whereas in reality they are subject to plasticity, and can change over time.

3. The input activity from the opposite neural pool is treated as a linear function of its voltage with an activation threshold, which is not realistic as neurons spiking activity varies depending on its structure and intrinsic properties [6].

3. The membrane time constant that comes from conductance is assumed to be constant, and its usage relies on Ohm’s law holding, which is a simplification of the actual behaviour of a neuron. However, it is a good approximation for the passive dynamics of a neuron which makes the model tractable for analysis.

4. The LIF model is a lot more computationally affordable, requires 4 ODEs per neuron in the HH model, instead of 1 in the LIF model, which allows us to run large scale simulations and analyse the network behaviour faster. The model is also more amenable to theoretic analysis, which helps to explain certain activity patterns in the network.

In essence, we trade off biological accuracy for computational efficiency and analytic tractability.

2 Computer Simulations

In this section, simulations of the network are presented, where the network is stimulated with various external inputs for both excitatory and inhibitory pools, and the response of the network is approximated numerically using the Euler method. Python code used for simulations can be found in Appendix A.

In our simulations, we study 2 networks with the following base parameters:

$$V_{\text{rest}} = -70\text{mV}, V_0 = -55\text{mV}, \beta = 1$$

$$\tau = \begin{pmatrix} \tau_E \\ \tau_I \end{pmatrix} = \begin{pmatrix} 20 \\ 10 \end{pmatrix} \text{ms}$$

$$u = \begin{pmatrix} u_E \\ u_I \end{pmatrix} = \begin{pmatrix} 20 \\ 20 \end{pmatrix}$$

$$W = \begin{pmatrix} W_{EE} & W_{EI} \\ W_{IE} & W_{II} \end{pmatrix} = \begin{pmatrix} W_{EE}^n & 0.65 \\ 1.2 & 0.5 \end{pmatrix}$$

where W_{EE}^n is the weight of the excitatory feedback for a given network. The 2 networks differ in the weight of the excitatory feedback, where one is weaker is $W_{EE}^1 = 0.5$ and the other is stronger $W_{EE}^2 = 1.25$.

2.1 Stable External Input (Q2)

We first study both networks subjected to a stable external input of 20mV to both neurons. Both neurons start from

Networks 1 and 2
 $u_E = u_I = 20$

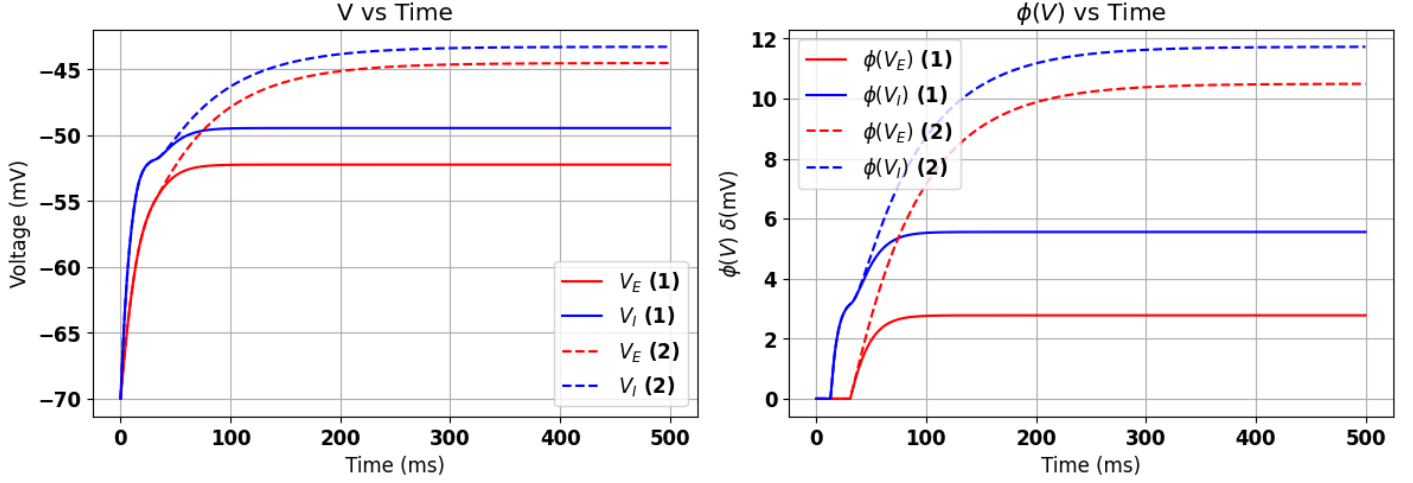


Figure 1: **Stable** external input to both neurons.
Excitatory potentials are red, Inhibitory potentials are blue.
 Network 1 is solid, Network 2 is dashed.

the resting potential. The simulation is ran for 500ms with 1ms time steps. The results are shown in Figure ??.

Looking at the results for Network 1 (solid lines), we can see that both neurons gradually begin responding to the external input. Since $\tau_I < \tau_E$, one might expect the inhibitory neuron to respond faster, which is exactly what is observed. The transfer function $\phi(V)$ is not immediately responding to the increase in voltage as both neurons have to reach the threshold potential, which matches with the timeline of both neurons reaching $V_0 = -55mV$ and begin firing to provide input to the other. After about 5τ , as expected with a capacitor behaviour, the system reaches a stable state and both neurons' activity plateaus. At this point, V_I , however, is about 3mV above V_E , which could be due to a stronger W_{IE} connection relative to W_{EI} , given that the feedback strength to both neurons is equal, excitation of I is stronger than inhibition of E, and therefore less V_E is needed to balance out V_I .

2.2 Inhibitory Input Increase (Q3-4)

Both networks are simulated for further 500ms with an increase in u_I from 20mV to 26mV. The results for this simulation are shown in Figure ??.

Network 1, prior to the u_I increase, is in a stable state, and immediately after inhibitory activity naturally increases. As V_I increases, according to equation (1), V_E decreases, which is expected. 10ms later, inhibitory activity peaks and then drops slightly to stabilise once again, the peak and drop can be explained by equation (2), that tells us that V_I depends on weighted ReLU'd activity of V_E , which has been decreasing previously and therefore at some point decreasing excitatory activity will begin balancing out external inhibitory input and we'd expect the network to begin approaching a stable state. Stable state is eventually reached at about 570ms, where potentials settle once again, however, V_I is above its previous stable value, and V_E is below. This makes sense following the logic from the stable external input simulation - stronger W_{IE} connection tells us that less excitatory activity is needed to balance out the inhibitory.

For Network 2 (dashed lines), the results are similar but with a subtle difference. Both pools are responding to the

Networks 1 and 2
 $u_E = 20, u_I(: 500) = 20, u_I(500 :) = 26$

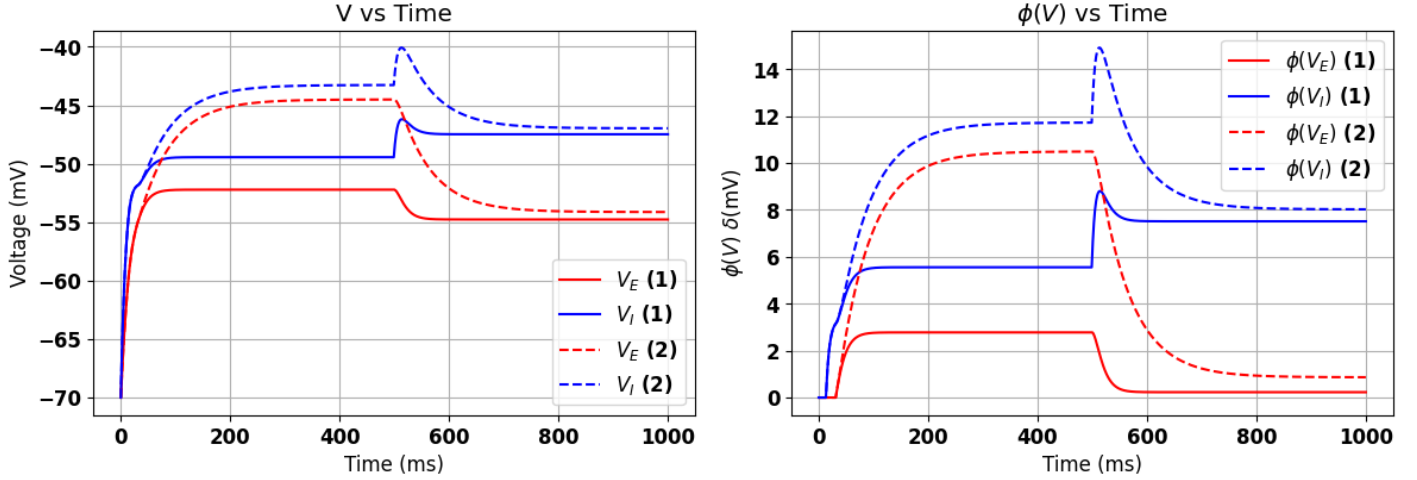


Figure 2: External **inhibitory** input increase after 500ms.
Excitatory potentials are red, **Inhibitory** potentials are blue.
 Network 1 is solid, Network 2 is dashed.

input as described above: inhibitory spike, then excitatory dip, followed by the dip in inhibitory activity and eventual stabilisation. However, this time round, the final stable state is below the original for both neurons, which seems counterintuitive as the increase in inhibitory activity leads to a reduction in the activity of the whole network. The paradox here would be that, for some reason, the activity is not balancing like in Network 1, but decreases overall. Since the only parameter that differs is the W_{EE} synaptic weight, the behaviour can be attributed to it.

2.3 Excitatory Input Increase (Q5)

We will now simulate an increase in external Excitatory input, unlike Inhibitory in the previous section. Similarly, both neurons are reaching a stable state with constant 20mV input to both, when a similar increase to 26mV in u_E occurs. The results can be observed in ??

As before, prior to the change, the system is in a stable state. When the excitatory neuron's external stimulation increases, unsurprising increase in excitatory activity follows, causing the inhibitory activity to rise [Equation (2)], which

inhibits the excitatory neuron itself, flattening the rate of change and eventually stabilising the system. All of the observations are intuitive and follow from the equations describing the system. Both networks behave similarly, but of course, with a subtle difference - before the increase, stable state of both networks has the inhibitory potential above excitatory, in Network 1 that is still the case after the system adapts to the change, however in Network 2, the excitatory stable potential now exceeds that of the inhibitory.

Stronger excitatory feedback combined with a relatively higher external stimulation push the neuron towards an endless excitation, so the inhibitory neuron by extension begins gauging the runaway activity, thus stabilising the network. This behaviour can once again be attributed to a different weight of the synaptic Excitatory feedback.

This experiment kept the network in tact, while stimulating the excitatory neuron and in both cases the system returned to a stable state. There is a very short delay before the inhibitory neuron begins catching up, which according to the Equation 1 and the observations confirms to us that the inhibitory neuron prevents the runaway excitation of E.

In this next experiment, we will stimulate the excitatory

Networks 1 and 2.
 V_I unclamped
 $u_{E(: 500)} = 20, u_{E(500 :)} = 26, u_I = 20$

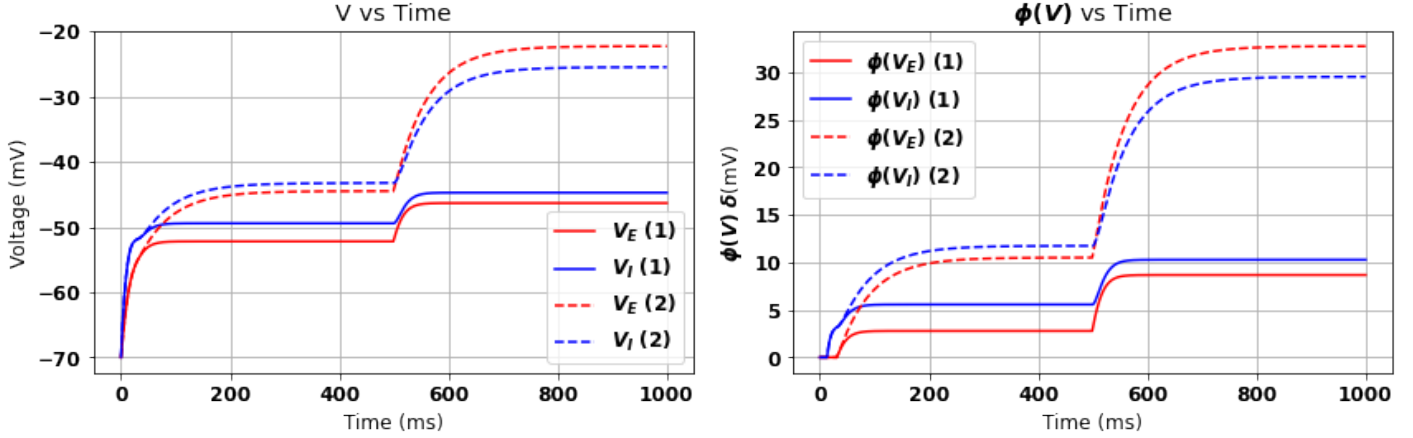


Figure 3: External **excitatory** input increase after 500ms. V_I unclamped
Excitatory potentials are red, **Inhibitory** potentials are blue.
 Network 1 is solid, Network 2 is dashed.

neuron once again, but this time clamp the inhibitory neuron for it to remain at the resting potential. The results of this simulation are shown in ???. With the inhibitory neuron clamped, the excitatory neuron is free to excite indefinitely, however, in network 1, the activity eventually stabilises as the inhibitory neuron still provides feedback to the excitatory neuron. In network 2, on the other hand, the excitatory feedback is much stronger relative to the inhibitory, and the E neuron continues increasing activity indefinitely. To spare the scale of indefinite (biologically unrealistic) simulation, I have limited the max voltage displayed on the graph, but it is clear that the activity explodes in the first 100ms, even before the external input is increased.

2.4 Stabilisation and Paradoxical Inhibition (Q6)

To sum up findings so far: a network is called ISN if the Excitatory component is unstable alone, but combined with the inhibitory it is. The purpose of ISN is to prevent runaway excitation and maintain the balance in a neural network. Paradoxical inhibition is a counterintuitive reaction of

a network, where external inhibitory input causes the overall activity of the network to decrease. Both are most certainly related to the external input, the synaptic weights and the intrinsic properties of each neuron.

Based on the simulations, it looks like it is more affected by the synaptic weights between neurons (including feedback) when the system is adapting to the input to reach a stable state. In particular, on the excitatory feedback strength relative to the inhibitory feedback strength.

Based on the above, it seems reasonable to suppose that low W_{EE} to W_{II} ratio (≤ 1) keeps the network stable and high (> 1) leads to an unstable behaviour, including paradoxical inhibition and runaway excitation.

2.5 Discussion (Q7-8)

The simulations above gave us a glimpse of what the network response is like under different conditions to varying external inputs. However, the simulations are limited in that they only show what it looks like given the input we have manually set, and therefore do not provide a comprehensive understanding of the network behaviour. Given that the

Networks 1 and 2.
 V_I clamped
 $u_{E(: 500)} = 20, u_{E(500 :)} = 26, u_I = 20$

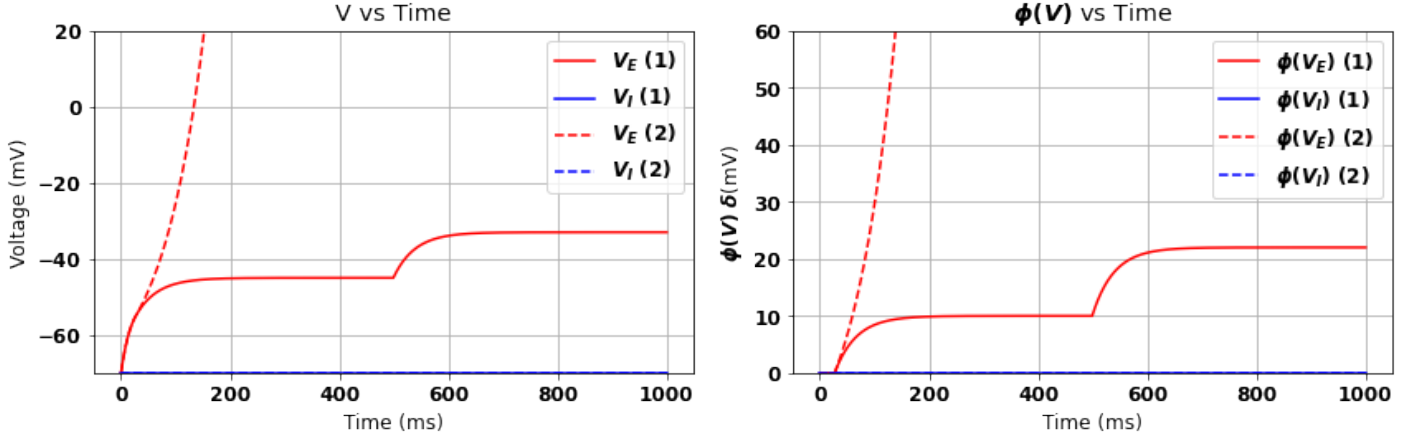


Figure 4: External **excitatory** input increase after 500ms. V_I clamped
Excitatory potentials are red, **Inhibitory** potentials are blue.
Network 1 is solid, Network 2 is dashed.

model has $2 \times 6 = 12$ parameters for 2 neurons, and each can be varied to influence the behaviour. And while the first 10 of them are describing the neurons, the other 2 do external inputs, which can vary in time and shape and running simulations on a specific pattern of external input might not definitively explain the relationship in general. One alternative way to analyse the model to gain more insight into how inhibitory stabilisation relates to the paradoxical inhibition, we might look at a more theoretic approach, including mathematical analysis of the system. Another way would be to try and limit the scope of the problem by limiting parameters we're simulating for based on the biological data. Those can be estimated from data gathered in vitro or in vivo, we could study the brain further to understand what the sources of external input are, and how they vary in time and space, Tsodyks highlights [1] that there are Theta and Gamma oscillations in the brain, which are common sources of external input to the network. Since the model is based on several big assumptions, how can we be sure that the networks in brain are in fact operating in the ISN regime? One way to test this would be to record the activity of the neurons and observe the activity (using EEG or fMRI) given

different stimuli. This is an overly simplistic approach, and the brain has many components, each with its own dynamics and local networks, all of which together interfere with the activity of the network, and it's hard to isolate both the network activity and the inputs to it. Another way would be to use a novel optogenetics approach to embed light-sensitive channels into neural membrane and manipulate the activity with light. This approach allows for high precision and control over the activity of the neurons, but is limited to animal models and is not yet ready for human use [7].

3 Mathematical Analysis

In this section, we will provide a mathematical analysis of the network model and explore the relationship between the inhibitory stabilisation and paradoxical inhibition.

Assuming, $V > V_0$, we can drop the non-linearity of the activation function and expand the expression to do some algebra.

3.1 Reformulation (Q9)

To simplify the analysis, we can reformulate the system of equations describing the network and express it in the matrix-vector form:

$$\frac{d\mathbf{V}}{dt} = A\mathbf{V} + \mathbf{x} = \begin{pmatrix} A_{EE} & A_{EI} \\ A_{IE} & A_{II} \end{pmatrix} \cdot \begin{pmatrix} \mathbf{V}_E \\ \mathbf{V}_I \end{pmatrix} + \begin{pmatrix} \mathbf{x}_E \\ \mathbf{x}_I \end{pmatrix}$$

where A is the matrix of synaptic weights, and \mathbf{x} is the external input. To find the values of each term, Vs are factored out, and constant terms are grouped together based on equations (1) and (2).

$$\begin{aligned} \frac{d\mathbf{V}_E}{dt} &= \mathbf{V}_E \left[\frac{-1 + W_{EE}\beta}{\tau_E} \right] + \mathbf{V}_I \left[\frac{-W_{EI}\beta}{\tau_E} \right] \\ &\quad + \left[\frac{V_{rest} + V_0\beta(W_{EI} - W_{EE}) + u_E}{\tau_E} \right] \\ \frac{d\mathbf{V}_I}{dt} &= \mathbf{V}_E \left[\frac{W_{IE}\beta}{\tau_I} \right] + \mathbf{V}_I \left[\frac{-1 - W_{II}\beta}{\tau_I} \right] \\ &\quad + \left[\frac{V_{rest} + V_0\beta(W_{II} - W_{IE}) + u_I}{\tau_I} \right] \end{aligned}$$

Now the system can be rewritten in the matrix form:

$$\begin{aligned} \frac{d\mathbf{V}}{dt} &= \begin{pmatrix} \frac{-1+W_{EE}\beta}{\tau_E} & \frac{-W_{EI}\beta}{\tau_E} \\ \frac{W_{IE}\beta}{\tau_I} & \frac{-1-W_{II}\beta}{\tau_I} \end{pmatrix} \begin{pmatrix} \mathbf{V}_E \\ \mathbf{V}_I \end{pmatrix} + \\ &\quad + \begin{pmatrix} \frac{V_{rest}+V_0\beta(W_{EI}-W_{EE})+u_E}{\tau_E} \\ \frac{V_{rest}+V_0\beta(W_{II}-W_{IE})+u_I}{\tau_I} \end{pmatrix} \end{aligned}$$

3.2 Steady State (Q10-11)

The steady state of the system $\mathbf{V}_E^*, \mathbf{V}_I^*$ is defined by both derivatives being zero. Since τ are non-zero constant terms, we can drop them from the equation, and solve for the steady state:

$$\begin{pmatrix} 0 \\ 0 \end{pmatrix} = \begin{pmatrix} A_{EE} & A_{EI} \\ A_{IE} & A_{II} \end{pmatrix} \begin{pmatrix} \mathbf{V}_E^* \\ \mathbf{V}_I^* \end{pmatrix} + \begin{pmatrix} \mathbf{x}_E \\ \mathbf{x}_I \end{pmatrix}$$

Rearranging the terms, the solution for steady state voltages:

$$\begin{aligned} \begin{pmatrix} \mathbf{V}_E^* \\ \mathbf{V}_I^* \end{pmatrix} &= - \begin{pmatrix} A_{EE} & A_{EI} \\ A_{IE} & A_{II} \end{pmatrix}^{-1} \begin{pmatrix} \mathbf{x}_E \\ \mathbf{x}_I \end{pmatrix} \\ &= \frac{-1}{\det(A)} \begin{pmatrix} A_{II} & -A_{EI} \\ -A_{IE} & A_{EE} \end{pmatrix} \begin{pmatrix} \mathbf{x}_E \\ \mathbf{x}_I \end{pmatrix} \end{aligned}$$

To compute the determinant:

$$\begin{aligned} \det(\mathbf{A}) &= A_{EE}A_{II} - A_{EI}A_{IE} \\ &= (W_{EE}\beta - 1)(-W_{II}\beta - 1) - W_{EI}\beta(-W_{IE}\beta) \\ &= \boxed{\beta^2(W_{IE}W_{EI} - W_{EE}W_{II}) + \beta(W_{II} + W_{EE}) + 1} \end{aligned}$$

From the solution, we can derive the expression for inhibitory steady state voltage \mathbf{V}_I^* in terms of network parameters:

$$\begin{aligned} \mathbf{V}_I^* &= \frac{-(-A_{IE}\mathbf{x}_E + A_{EE}\mathbf{x}_I)}{\det(A)} = \frac{A_{IE}\mathbf{x}_E - A_{EE}\mathbf{x}_I}{\det(A)} \\ &= \boxed{\frac{W_{IE}\beta\mathbf{x}_E - (W_{EE}\beta - 1)\mathbf{x}_I}{\det(A)}} \end{aligned}$$

To try and understand why the paradoxical inhibition occurs, we can study what happens to the stable state inhibitory voltage when the external inhibitory input is changing. To do so, we can differentiate \mathbf{V}_I^* with respect to \mathbf{u}_I :

$$\begin{aligned} \frac{d\mathbf{V}_I^*}{d\mathbf{u}_I} &= \frac{d}{d\mathbf{u}_I} \left(\frac{W_{IE}\beta\mathbf{x}_E - (W_{EE}\beta - 1)\mathbf{x}_I}{\det(A)} \right) \\ &= \frac{W_{IE}\beta}{\det(A)} \times \frac{d\mathbf{x}_E}{d\mathbf{u}_I} - \frac{W_{EE}\beta - 1}{\det(A)} \times \frac{d\mathbf{x}_I}{d\mathbf{u}_I} \\ &= \frac{W_{IE}\beta}{\det(A)} \times 0 - \frac{W_{EE}\beta - 1}{\det(A)} \times 1 \\ &= \boxed{\frac{-W_{EE}\beta + 1}{\det(A)}} \end{aligned}$$

To spare the complexity of the full expansion, both expressions keep \mathbf{x}_E and \mathbf{x}_I as variables, but they can be substituted with the actual values of the external input derived above. The complete derivation can be found in the Appendix.

In the simulations, we observed that the both neurons' steady state voltage (plateau value) decreased when the external inhibitory input \mathbf{u}_I increased. To understand why this is happening, we can look at the conditions under which

this occurs. That is, when the derivative with respect to external inhibitory input is negative:

$$\frac{d\mathbf{V}_I^*}{d\mathbf{u}_I} = \frac{-W_{EE}\beta + 1}{\det(A)} < 0$$

This gives us 2 cases to consider:

$$\begin{cases} -W_{EE}\beta + 1 > 0 & \text{if } \det(A) < 0 \\ -W_{EE}\beta + 1 < 0 & \text{if } \det(A) > 0 \end{cases}$$

The 2 cases give us the exact conditions under which the paradoxical inhibition occurs.

4 Discussion (Q12)

In the simulations, we observed the behaviour of the 2 networks, reacting to changes in external output and concluded that paradoxical inhibition had something to do with external input and the weight of the synaptic excitatory feedback. To recap, the networks had the following weights: $W_{EE}^1 = 0.5$ and $W_{EE}^2 = 1.25$. And it was Network 2 that exhibited the paradoxical inhibition. Now that we have a mathematical explanation of this behaviour, let us compare the findings. Assuming that the system is not stable when $\det(A) < 0$, the first inequality case can be ignored. The second case tells us that the paradoxical inhibition occurs when $-W_{EE}\beta + 1 < 0$, or when $W_{EE} > \frac{1}{\beta}$. Provided that $\beta = 1$, so the condition becomes $\mathbf{W}_{EE} > \mathbf{1}$. Clearly, Network 2 satisfies the condition and the puzzle is solved.

As mentioned before, the purpose of the ISN is to maintain the balance and prevent endless excitation, while paradoxical inhibition is the overall decrease in network activity due to increased input. Since the parameter of interest here is Excitatory feedback weight, the relationship could be generalised to being a kill switch when the excitatory activity becomes too high and inhibits the network accordingly.

5 Paradoxical Excitation (Q13)

To hypothesize, whether a analogous process - Paradoxical Excitation - could take place, we can define this similarly to Paradoxical Inhibition. That would mean the overall network activity decreases as external excitatory input u_E increases. Similarly, we can look at the derivative of the stable

state voltage \mathbf{V}_E^* with respect to u_E :

$$\begin{aligned} \frac{d\mathbf{V}_E^*}{du_E} &= \frac{d}{du_E} \left(-\frac{(-W_{II}\beta - 1)\mathbf{x}_E + W_{EI}\beta\mathbf{x}_I}{\det(A)} \right) \\ &= \frac{W_{II}\beta + 1}{\det(A)} \times 1 - \frac{W_{EI}\beta}{\det(A)} \times 0 \\ &= \boxed{\frac{W_{II}\beta + 1}{\det(A)}} \end{aligned}$$

Following the same logic as before, the paradoxical excitation occurs when the derivative is negative, or when $W_{II}\beta + 1 < 0$. This gives us the condition under which the paradoxical excitation occurs. Skipping the negative determinant case, we can conclude that for the paradoxical excitation to occur, the condition is $W_{II}\beta < -1$. It is unclear how to interpret negative weights, as technically that violates the Dale's Law, since our model accounts for inhibitory input as negative, and therefore making it act as excitatory. So the paradoxical excitation might is not possible in this model.

6 Conclusion

To conclude, we have introduced the concept of Inhibitory-Stabilised Networks, derived the model, simulated the network and analysed it mathematically, to investigate the dynamics of a neural network with 2 pools of neurons.

The model, based on a leaky integrate-and-fire, captures the essential interactions within neural circuits, in which the excitatory feedback can lead to runaway activity, but inhibitory feedback counters this, stabilizing the network. Over the simulations, the behavior of networks with differing excitatory feedback strengths was examined under varying external inputs, demonstrating the roles of synaptic weights and external stimulation in modulating network activity.

The simulations showed that networks with weaker excitatory feedback (Network 1) stabilize effectively in response to increased external input, exemplifying typical inhibitory-stabilized network behavior. In contrast, networks with stronger excitatory feedback (Network 2) exhibit paradoxical inhibition, where increased inhibitory input paradoxically results in an overall reduction of network activity. Mathematical analysis supports these observations, providing more concrete explanation for how synaptic weights, and in particular the excitatory feedback strength, influence the stability and paradoxical responses of the network.

References

- [1] Misha V Tsodyks et al. “Paradoxical effects of external modulation of inhibitory interneurons”. In: *Journal of neuroscience* 17.11 (1997), pp. 4382–4388.
- [2] Nicolas Brunel et al. “Quantitative investigations of electrical nerve excitation treated as polarization”. In: *Biological Cybernetics* 97.5-6 (2007), pp. 341–349.
- [3] Larry F Abbott. “Lapicque’s introduction of the integrate-and-fire model neuron (1907)”. In: *Brain research bulletin* 50.5-6 (1999), pp. 303–304.
- [4] Daniel H Efron. “Psychopharmacology; a Review of Progress, 1957-1967”. In: (1968).
- [5] A. L. Hodgkin and A. F. Huxley. “A quantitative description of membrane current and its application to conduction and excitation in nerve”. In: *The Journal of Physiology* 117.4 (1952), pp. 500–544. DOI: <https://doi.org/10.1113/jphysiol.1952.sp004764>.
- [6] Eugene M Izhikevich. “Simple model of spiking neurons”. In: *IEEE Transactions on neural networks* 14.6 (2003), pp. 1569–1572.
- [7] Sadra Sadeh and Claudia Clopath. “Inhibitory stabilization and cortical computation”. In: *Nature Reviews Neuroscience* 22.1 (2021), pp. 21–37.

A Appendix

Listing 1: Python code for simulations

```
1 import numpy as np
2 import matplotlib.pyplot as plt
```