Dynamical systems in neurosciences
Hands-on session

1 Introduction

During this session, you will have to choose from three projects that will be presented here. To start, we suggest you read them carefully, familiarize yourself with the related codes, and ask us questions whenever something is unclear to you. The main objective is for you to familiarize with simulations and methods of dynamical systems in neuroscience but also to eventually come up with your own interrogations and propose a way to address them.

But before let us start with a few reminders on the model and theoretical framework we are using here: the Adaptative Exponential integrate and fire model (AdEx) and the networks built from it.

1.1 The AdEx model

In the historical development of neuroscience, the time evolution of the membrane potential observed in single biological neurons has been considered as a relevant observable to explain their functions in neural tissues. The main goal for neuron models is thus to reproduce the dynamics the membrane potential.

The AdEx model is built from the integrate-and-fire model:

$$C\frac{dV}{dt} = I_{inputs} \tag{1}$$

where C is the membrane capacitance, V the membrane potential, and I_{input} is the input current. A "leak current" is then added to reproduce the value of the resting membrane potential:

$$C\frac{dV}{dt} = g_L(E_L - V) + I_{inputs} \tag{2}$$

g_L is the leak capacitance and E_L the leak reversal potential. An exponential term permits to create a dynamics similar to the opening of fast sodium channels:

$$C\frac{dV}{dt} = g_L(E_L - V) + g_L\Delta_T \exp\left(\frac{V - V_T}{\Delta_T}\right) + I_{inputs} \tag{3}$$

where V_T is a threshold that defines when the exponential kicks in, and Δ_T is a slope factor. Finally a second variable, w, permits frequency adaptation and larger repertoire of patterns [4]

$$\begin{aligned} C\frac{dV}{dt} &= g_L(E_L - V) + g_L\Delta_T \exp\left(\frac{V - V_T}{\Delta_T}\right) - w + I_{inputs} \\ \tau_w\frac{dw}{dt} &= a(V - E_L) - w, \end{aligned}$$

where a is adaptation coupling parameter, and τ_w is the adaptation time constant. After a spike is detected at a fixed threshold V_D, the system is reset as follows:

$$\text{if } V \geq V_D \quad \text{then} \quad \begin{cases} V \to V_R \\ w \to w + b. \end{cases} \tag{4}$$

In other words, the membrane potential is reset to V_R while the adaptation current is incremented by b. More details can be found on the scholarpedia page.

1.2 Network of AdEx

From single-cell models it is possible to build models of neuronal networks. The connection between neurons can be implemented through a model of synaptic activity. In the model considered here, the connection between neurons is "conductance-based", meaning that each pre-synaptic spike generate an increase of a channel conductance, then creating currents through the membrane (nonlinear terms) of the following form:

$$I_{syn} = g_E(E_E - V) + g_I(E_I - V), \tag{5}$$

where E_E is the reversal potential of excitatory synapses and E_I is the reversal potential of inhibitory synapses. g_E and g_I are respectively the excitatory and inhibitory conductances, which increase by quantity Q_E and Q_I for each incoming spike. The increment of conductance is followed by an exponential decrease, with time constant τ_{syn}, according to the equation:

$$\frac{dg_{E/I}}{dt} = -\frac{g_{E/I}}{\tau_{syn}}. \tag{6}$$

In the network, models interact *only* through spiking events, which is the reason why we speak of *spiking networks*, even if models also have (continuous) internal variables like membrane potential.

Based on such (synaptic) interactions, it is possible to build networks by interconnecting neurons either with a given structured connectivity or randomly with a given probability of connection. The obtained system may be of very high dimension, in which case classical tools from low-dimensional dynamical systems, such as phase portrait studies, are not possible anymore. However we can still learn interesting aspects of dynamics with such models, it depends on what we chose to measure, and how. This will be the focus of the second project.

1.3 Mean-field models

One way to study the activity of a large network of neurons is with the use of mean-field models. Mean-field models use statistical techniques to estimate the activity of large neuronal populations (from hundreds to thousands of neurons), which allows to reduce high-dimensional systems into low dimensions based on

the first few statistical moments (in particular mean firing rates and their standard deviations). Thus, the activity of local brain circuits can be described in terms of a few differential equations. These models have proven to be extremely useful to understand the dynamics of large networks and characterize the global states of these system (from asynchronous irregular activity to slow-waves oscillations). For the particular case of the AdEx model described above, a mean-field model has been developed that allows to estimate the mean-firing rate and mean level of adaptation of the network. This model is described by the following set of differential equations [2, 5, 1]:

$$T\frac{d\nu_j}{dt} = F_j(W, \bar{\nu}_e, \nu_{SPN}, \nu_{FS}) - \nu_j \tag{7}$$

$$\frac{dW_j}{dt} = -\frac{W_j}{\tau_w} + b\nu_j + a(\mu_V(\bar{\nu}_e, \nu_{SPN}, \nu_{FS}, W_j) - E_L) \tag{8}$$

where ν_j is the mean neuronal firing rate of the population j (j =RS, FS), W_j is the mean value of the adaptation variable for population j, F is the neuron transfer function (i.e. output firing rate of a neuron when receiving the corresponding excitatory and inhibitory inputs with mean rates $\nu_j's$ and with a level of adaptation W), a and b are the sub-threshold and spiking adaptation constants, t_w is the characteristic time of the adaptation variable and T is a characteristic time for neuronal response (we adopt $T = 5$ ms).

Following Zerlaut et al (2018) [5] we write the transfer function for each neuronal type as:

$$F_\nu = \frac{1}{2\tau_V} erfc\left(\frac{V_{\text{thre}}^{\text{eff}} - \mu_V}{\sqrt{2}\sigma_V}\right), \tag{9}$$

where $erfc$ is the error function, $V_{\text{thre}}^{\text{eff}}$ is an effective neuronal threshold, μ_V, σ_V and τ_V are the mean, standard deviation and correlation decay time of the neuronal membrane potential. The effective threshold can be written as a second order polynomial expansion:

$$\begin{aligned} V_{\text{thre}}^{\text{eff}}(\mu_V, \sigma_V, \tau_V^N) = P_0 + \sum_{x \in \{\mu_V, \sigma_V, \tau_V^N\}} P_x \cdot \left(\frac{x - x^0}{\delta x^0}\right) + \\ \sum_{x,y \in \{\mu_V, \sigma_V, \tau_V^N\}^2} P_{xy} \cdot \left(\frac{x - x^0}{\delta x^0}\right)\left(\frac{y - y^0}{\delta y^0}\right), \end{aligned} \tag{10}$$

where $x^0, y^0, \delta x^0, \delta y^0$ are constants, and where the coefficients P_{xy} are to be determined by a fit over the numerical transfer function obtained from single-cell spiking simulations for each specific cell-type.

The mean membrane potential and standard deviation as can be written as [5]:

$$\mu_V = \frac{\sum_j \mu_{Gj} E_j + g_L E_L - w + I}{\sum_j \mu_{Gj} + g_L} \tag{11}$$

where $\mu_{Gj} = Q_j \tau_j \nu_j K_j$ is the mean synaptic conductance and K_j is the mean synaptic convergence of type j.

Finally, we can write the standard deviation and correlation decay time of the neuronal membrane potential as [5]:

$$\sigma_V = \sqrt{\sum_j \frac{K_j \nu_j (U_j \tau_j)^2}{2(\tau_m^{eff} + \tau_j)}} \tag{12}$$

$$\tau_V = \frac{\sum_j K_j \nu_j (U_j \tau_j)^2}{\sum_j \frac{K_j \nu_j (U_j \tau_j)^2}{2(\tau_m^{eff} + \tau_j)}} \tag{13}$$

with $\tau_m^{eff} = \frac{C}{\sum_j \mu_{Gj} + g_L}$ and $U_j = \frac{Q_j}{\sum_j \mu_{Gj} + g_L}(E_j - \mu_V)$

The detailed derivation of the mean field equations can be found in Refs. [5, 1].

2 Evaluation

Note that if you are not comfortable with numerical methods and integration of differential equations, we would suggest going for the first project, as it starts from a simpler system.

For the evaluation, we ask you to send a report by email **before 06/01/2025**. The mark (for the group) will not depend on the choice of the project but on the quality and clarity of the presentation of the results and, above all, on the relevance of the discussion. We are aware that this work can be challenging, as there are no evident right answers, but this gives you the opportunity to explore and pose your own questions, closer to the everyday life of scientific research.

We expect the report to be **around 3-5 pages** (figures included, and if really needed you can add annexes), to explain the problem clearly in your own words, then to present methods and results and, finally, to propose a detailed discussion.

3 First project

3.1 Characterization of the single model

As said before, the main goal of a reduced model is to reproduce the time evolution of the membrane potential observed in single biological neurons. The fewer variables there are, the less computer resources it consumes, but a single variable is not sufficient to reproduce certain patterns such as bursts for example. This is why the AdEx model has two variables, which also conserves the advantage of allowing to visualize the phase space in two dimensions.

You can use the *AdEx_NC.py* code to visualize it, with the nullclines for each variable and the trajectory of a simulation. You can see the influence of the parameters on the dynamics by changing for example I_s, V_{reset}, E_L, etc

... It's a way to intuitively understand how the model works. By adjusting the parameters and modifying the topology of the phase space it is possible to obtain the desired patterns. But without many precautions, this type of approach of "fine-tuning", can take us even further away from biological realities.

3.2 Relation to experiments (Should I burst?)

Keeping a close relation to experiments is a good recipe to avoid "fine-tuning". For example, if the interest lies in understanding the transition from one dynamical regime to another, biological systems are known to support several.

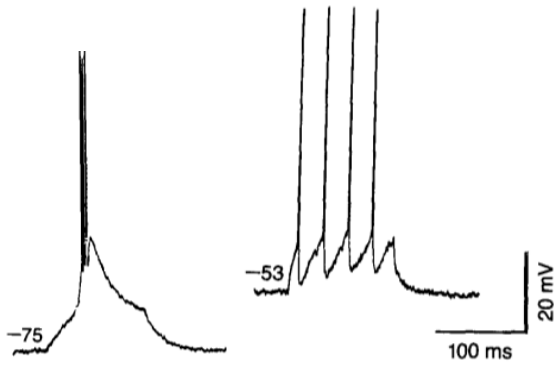

Figure 1: A thalamic cell response to current injection in the absence (left) and presence (right) of Acetylcholine (ACh).

For example, let's look at figure 1 (taken from [3]). Here, a neuron was stimulated with a current injection while being in one of two condition (linked to the absence or presence of the neuromodulator Acetylcholine). In one condition (left), the membrane potential resting state is very negative (around -75 mV), and responds to a brief stimulus with a burst. In the other condition (right), the membrane potential resting state is less negative (-53 mV), and responds to a brief stimulus with a regular series of spikes.

We provide two python scripts, *ADEX_TC_Ctl.py* and *ADEX_TC_ACh.py*, modeling these two conditions. Just three parameters of the AdEx model change between the two scripts, but the results are quite different.

- What are the main differences in the phase space?
- Are the model parameters for the resting state (El) similar to those in the figure? What happens if you change them?
- How is the bursting behavior achieved in *ADEX_TC_Ctl.py*?
- Why is the model in *ADEX_TC_ACh.py* spiking regularly?

3.3 Effects of interactions between neurons

As the single AdEx model no longer has any secret for you, we can then focus on the interaction between many models. Let's start with two. To do so, you can use the code called *AdEx_interact.py*. You can change the number of neurons with inhibitory or excitatory effects. You can try to vary parameters related to the strength of the coupling like Q_e, Q_i. It is thus possible to see that the overall system can evolve with different types of dynamical regimes. From these observations several questions can arise, here is a non-exhaustive list, others are of course very welcome:

- What can we say about the coupled system from the single model phase portrait?
- Are there levels of input (or interaction) for which such description is relevant to understand the global dynamics ?
- How to characterize the behavior of the global system?
- What if we increase the number of neurons in the network?

4 Second project: Network, scales and measures (on the nature of complexity)

In this project you directly jump to the network scale. The general idea of this project is that you propose a possible description and characterization of the activity of the network. To help you with that, here is a little introduction to possible measures (more are welcome! do not hesite to propose !), and also some questions to feed your thinking.

In the code proposed *Network_Brian2.py*, the network is made of two populations: 80% Regular Spiking (RS) and 20% Fast Spiking (FS) models, describing respectively excitatory and inhibitory neurons, for a total of 10000 neurons. It receives a Poissonian external input of incoming spikes. By changing parameters, such as connectivity between population, b value or external input, you may observe different regimes.

Each neurons being describe by 4 variables (2 from AdEx and 2 for the synaptic conductance), the system is now composed of 40000 equations. It is then very difficult to look at each variables or to represent the phase space in 40000 dimensions. We therefore need to find another way to represent, understand, and analyze the dynamics, through measures for example.

4.1 Global measurements of the network activities

From the network simulation it is possible to record the evolution of the variables, or the evolution of the mean and standard deviation of the variables. But we can also record elements of interest such as spikes, to obtain the raster plot,

but also, to calculate an average firing rate through a time window. We then have also the question of time averaging in this case. The effect of "averaging" can make us lose important information, it depends on the dynamical regimes and the question asked (i.e. why are we using this model of network). We can therefore be interested in underlying scales.

4.2 From one to the whole

If we are interested in the activity of spike and the different possible regimes, measuring the coefficient of variation for each model and looking at the statistics maybe be interesting. However, it may not be enough to characterize the contribution of individual to the whole. Then a possibility is to look at the correlations between individual and global measures. But you can think in many other ways of characterizing the network activity.

4.3 General questions

- What can we call the network "behavior"? What can we measure in the network? How?
- Can we see correlations between the measures?
- What information do we lose, what information do we want to keep?
- How does the activity of a single model relate to the global behavior of the network?
- Does it depend on the global dynamical regime?

5 Mean-field models

As explained in the introduction, mean-field models (MF) provide a powerful tool to study large populations of neurons based on statistical techniques. To test the validity of such models a comparison has to be done with the corresponding spiking network that they describe. We propose here to test the predictions obtained from the AdEx mean-field model by performing a comparison with the results of the corresponding network. A code to run this mean-field model is provided in the file MF_script.py from where the mean firing rates and mean adaptation can be calculated. A first direct test would imply to compare the output of the MF with the network under different stimuli (either a constant stimulus of different strength or a time-varying stimulus). In addition, it's possible to explore the parameter space to analyze the extent of validity of the MF. Taking into account that the mean-field is based on statistical methods, the size of the network can be an important parameter to analyze.

5.1 General questions

- What are the advantages of using mean-field models? What type of information can we extract from them?
- What are the limitations of the mean-field model?
- Does the MF model correctly capture the behaviour of the spiking network? Under what conditions? How do you test the robustness of the model?

References

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