Università degli studi di Padova

Physical Models of Living Systems

Master Degree in Physics of Data, 2022-2023

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Contents

1 Homework Week 01

Tasks:

1. Solve the Quasi Stationary Approximation of the Consumer Resource Model with 1 species and 1 abiotic resource and compare it numerically with the full solution. Optional: find a regime of parameters where the QSA is good. Remember to check that parameters you choose and initial condition for R and N should be so that R* in the QSA is not negative.
2. Write the Fokker Plank Equation associated to the stochastic logistic equation with environmental noise and solve for the stationary solution P*. Optional: compare analytical and numerical simulation of the SDE.

1.1 Exercise 1

Let $N(t)$ be the size of the population and $R(t)$ the amount of resources available. The Consumer Resource Model with 1 species and 1 abiotic resource is described by the following system of differential equations:

$$\frac{dR}{dt} = \mu(R) - cRN \tag{1}$$

$$\frac{dN}{dt} = (\gamma cR - d)N \tag{2}$$

For abiotic resources, $\mu(R)$ is given by the Monod function:

$$\mu(R) = \frac{R}{k_s + R} \tag{3}$$

In order to solve the system using the QSA, first we need to find the stationary solution of equation (1), which corresponds to assuming R is fixed at equilibrium.

$$0 \stackrel{!}{=} \frac{dR}{dt} = \frac{R}{k_s + R} - cRN\Big|_{R=R^*} \tag{4}$$

Using the fact that $R^* = \text{const} \neq 0$ we can solve it for R^*:

$$(1 - cNk_s)R - cNR^2|_{R=R^*} = 0 \Longrightarrow R^* = \frac{1 - cNk_s}{cN} \tag{5}$$

This solution can be substituted in equation (2), leading to a linear ordinary differential equation for the population $N(t)$:

$$\frac{dN}{dt} = \left[\frac{\gamma(1 - cNk_s)}{N} - d\right] N \tag{6}$$

If we define $\tilde{a} = \gamma$ and $\tilde{b} = \gamma c k_s + d$ we can rewrite the equation as:

$$\frac{dN}{dt} = \tilde{a} - \tilde{b}N \tag{7}$$

The general solution can be found solving the corresponding homogeneous equation and adding a particular solution, which can be found for example by looking at the stationary state.

$$\text{Homogeneous: } \dot{N} = -\tilde{b}N \Rightarrow N(t) = Ce^{-\tilde{b}t}$$

$$\text{Stationary state: } 0 \stackrel{!}{=} \dot{N} = \tilde{a} - \tilde{b}N \Rightarrow N(t) = \frac{\tilde{a}}{\tilde{b}}$$

So the full solution of the QSA of the Consumer Resource Model with 1 species and 1 abiotic resource is given by:

$$N(t) = Ce^{-\tilde{b}t} + \frac{\tilde{a}}{\tilde{b}} \tag{8}$$

and the multiplicative constant C can be determined imposing the initial condition $N(t = 0) = N_0$, which leads to:

$$C = N_0 - \frac{\tilde{a}}{\tilde{b}} \tag{9}$$

1.1.1 Numerical comparison

Let's consider the following set of parameters:

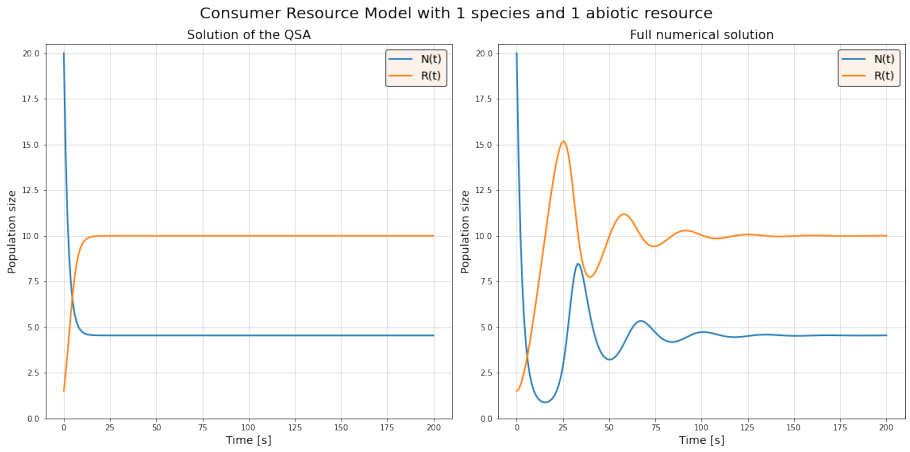
$$k_s = 1, \quad c = 0.02, \quad d = 0.4, \quad \gamma = 2 \tag{10}$$

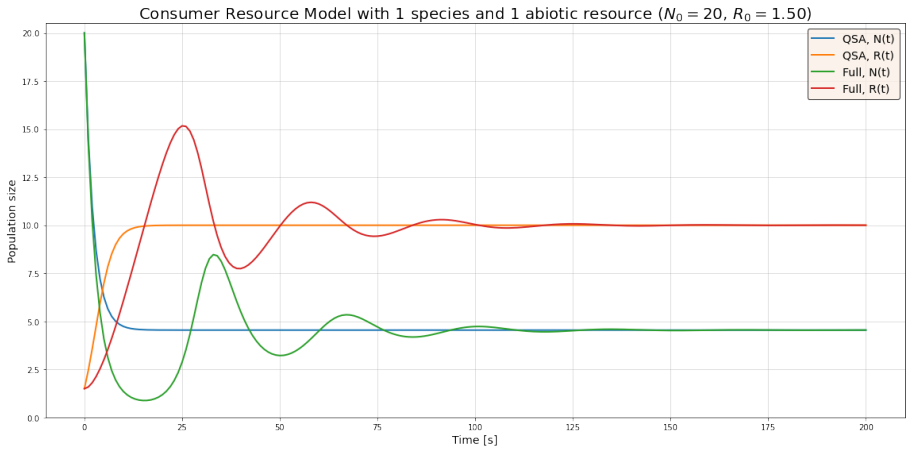
and the initial condition:

$$N(t=0) = N_0 = 20 \tag{11}$$

$$R(t=0) = \frac{1 - cN_0k_s}{cN_0} = 1.5 \tag{12}$$

The following plots are obtained by simulating the evolution of $N(t)$ and $R(t)$ for $t \in [0, 200]$ with the above set of parameters and initial condition. Through them it is possible to compare numerically the QSA solution with the full one.





For more details, see the corresponding notebook: hw01_Dynamics_of_Single_Species.ipynb.

1.2 Exercise 2

Given the stochastic logistic equation with environmental noise:

$$\frac{dx}{dt} = \frac{x}{\tau}\left(1 - \frac{x}{K}\right) + \sqrt{\frac{\sigma}{\tau}}x\xi(t) \tag{13}$$

where $\xi(t)$ is Gaussian white noise, it is possible to identify $A(x)$ and $B(x)$ such that the previous equation can be reformulated as:

$$\frac{dx}{dt} = A(x) + \sqrt{B(x)}\xi(t) \tag{14}$$

In this case, we have that:

$$A(x) = \frac{x}{\tau}\left(1 - \frac{x}{K}\right) \tag{15}$$

$$B(x) = \frac{\sigma}{\tau}x^2 \tag{16}$$

At this point it is possible to write the associated Fokker Plank equation:

$$\begin{aligned}\frac{\partial P}{\partial t} &= -\frac{\partial}{\partial x}[A(x)P(x)] + \frac{1}{2}\frac{\partial^2}{\partial^2 x}[B(x)P(x)] = \\ &= -\frac{\partial}{\partial x}\left[\frac{x}{\tau}\left(1 - \frac{x}{K}\right)P(x)\right] + \frac{1}{2}\frac{\partial^2}{\partial^2 x}\left[\frac{\sigma}{\tau}x^2 P(x)\right]\end{aligned} \tag{17}$$

To find the stationary solution P^* we have to impose that $\frac{\partial P}{\partial t} \stackrel{!}{=} 0$. Defining the flux:

$$J(x) = -\frac{x}{\tau}\left(1 - \frac{x}{K}\right)P(x) + \frac{1}{2}\frac{\partial}{\partial x}\left[\frac{\sigma}{\tau}x^2 P(x)\right] \tag{18}$$

we have that $\frac{\partial P}{\partial t} = 0 \iff \frac{\partial J(x)}{\partial x} = 0 \iff J(x) = \text{const.} = 0$, where the last equal is achieved by imposing the boundary condition $J(0) = 0$. We are left with a first order differential equation, $J(x)|_{P(x)=P^*} = 0$, which can be solved by separation of variables.

$$\begin{aligned}&J(x) = 0 \\ &\Rightarrow -\frac{x}{\tau}\left(1 - \frac{x}{K}\right)P(x) + \frac{\sigma}{\tau}xP(x) + \frac{1}{2}\frac{\sigma}{\tau}x^2\frac{dP(x)}{dx} = 0 \\ &\Rightarrow \frac{1}{P(x)}\frac{dP(x)}{dx} = \frac{2}{x}\left(\frac{1}{\sigma} - 1\right) - \frac{2}{\sigma K}\end{aligned}$$

Integrating on both sides we obtain:

$$\ln P(x) = 2\left(\frac{1}{\sigma} - 1\right)\ln x - \frac{2}{\sigma K}x + C \tag{19}$$

and, finally, taking the exponential and redefining the constant C we have the stationary solution:

$$P^*(x) = C\exp\left\{\left\{2\left(\frac{1}{\sigma} - 1\right)\ln x - \frac{2}{\sigma K}x\right\}\right\} \tag{20}$$

To find C we have to impose the normalization condition on $P^*(x)$ and solve the corresponding equation:

$$\int P^*(x)dx = 1 \tag{21}$$

The integral can be solved using the Gamma function and the final expression of the stationary distribution is:

$$P^*(x) = \frac{1}{\Gamma\left(\frac{2}{\sigma}\right)}\exp\left\{\left\{2\left(\frac{1}{\sigma} - 1\right)\ln x - \frac{2}{\sigma K}x\right\}\right\} \tag{22}$$

2 Homework Week 02

Infer the number of species from data of a forest sampled in 1% of the total area. Each row of the file represent a different species, and the number indicates the species abundance (i.e., the number of individuals). Perform the analysis to infer the number of species at the whole scale (p=1). You can work in small group of 2/3 people.

2.1 Solution

The solution can be found in the repository of the course[2]. The notebook is developed together with Tommaso Amico and Andrea Lazzari, and it can be accessed via the following link: hw02_Spatial_Scaling_RSA.ipynb.

3 Homework Week 03

Consider the Lotka-Volterra equations:

$$\frac{dx}{dt} = ax - pxy \tag{23}$$

$$\frac{dy}{dt} = -cy + pxy \tag{24}$$

Tasks:

1. Find the stationary solutions.
2. Do the stability analysis of the stationary solutions. Is there any stable solution?
3. (optional) Simulate Eqs.(23)-(24) with different parameters. Is there a range of parameters where do you observe sustained oscillations?

3.1 Stationary solutions

Stationary solutions are characterized by:

$$\begin{cases} \frac{dx}{dt} \stackrel{!}{=} 0 \\ \frac{dy}{dt} \stackrel{!}{=} 0 \end{cases} \quad \Longrightarrow \quad \begin{cases} 0 = ax - pxy \\ 0 = -cy + pxy \end{cases} \tag{25}$$

The solutions of this system are:

- $x_0^* = y_0^* = 0$
- $x_1^* = \frac{c}{p}$, $y_1^* = \frac{a}{p}$

so we found 2 stationary points, $(x_0^*, y_0^*) = (0, 0)$ and $(x_1^*, y_1^*) = (\frac{c}{p}, \frac{a}{p})$. Notice that the first solution corresponds to the extinction of both species.

3.2 Stability analysis

For each stationary point, we have to compute the Jacobian of the system in it:

$$J_i = \begin{pmatrix} \partial_x f_1 & \partial_y f_1 \\ \partial_x f_2 & \partial_y f_2 \end{pmatrix} \Bigg|_{x_i^*} = \begin{pmatrix} a - py & -px \\ py & px - c \end{pmatrix} \Bigg|_{x_i^*} \tag{26}$$

We obtain:

$$J_0 = \begin{pmatrix} a & 0 \\ 0 & -c \end{pmatrix} \qquad J_1 = \begin{pmatrix} 0 & -c \\ a & 0 \end{pmatrix} \tag{27}$$

Writing the linearized equations around the stationary point, we know that stability is determined by the largest real part of the Jacobian's eigenvalues. The eigenvalues corresponding to J_0 and J_1 are, respectively:

$$\lambda_1^0 = a \qquad \lambda_2^0 = -c \tag{28}$$

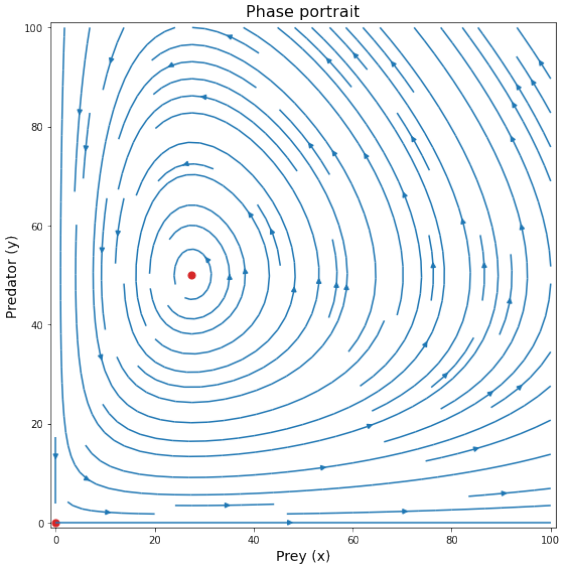
$$\lambda_1^1 = -i\sqrt{ac} \qquad \lambda_2^1 = i\sqrt{ac} \tag{29}$$

where we used the fact that $a, c > 0$.

As $\lambda_1^0 = a > 0$, the first stationary point x_0^* is unstable. Moreover, since the eigenvalues are one positive and one negative, the stationary point in $(0, 0)$ is a saddle point. This is a very important result. Indeed, if it were stable, both species populations could be attracted to it. This would result in an extinction process for different non-zero initial condition. However, this does not happen because this fixed point is unstable, which means that according to the model it is difficult for the extinction of both species to occur.

On the other side, in the second stationary point we have that $\mathrm{Re}(\lambda_1^1) = \mathrm{Re}(\lambda_2^1) = 0$, which corresponds to a neutral or critical situation. In general, all typical behaviours are possible in this case (unstable focus, stable focus, saddle point, etc.), together with another one, namely a centre, which is a closed orbit that is neutrally stable. Since the imaginary part of x_1^* is nonzero, or in other words x_1^* is complex, and the system is conservative, there exist closed orbits about the fixed point, and we expect an oscillatory, periodic behaviour around the it.

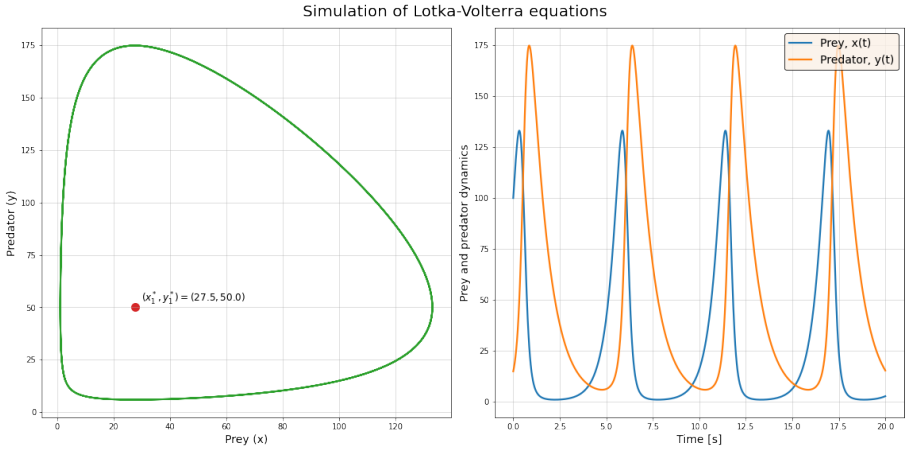
This results can be understood also by looking at the phase portrait corresponding to the Lotka-Volterra equations we are studying:



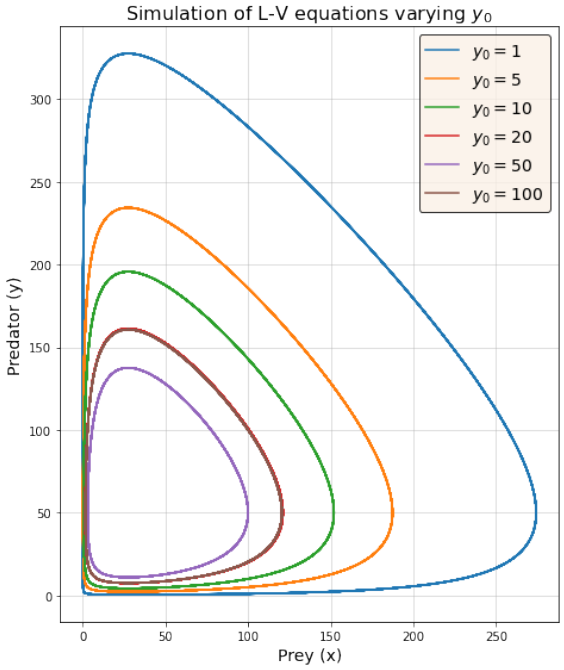
3.3 Simulation results

This section shows some simulation results. The corresponding notebook is available at the following link: hw03_Lotka_Volterra.ipynb. First, a simulation is performed setting $x(0) = 100$, $y(0) = 15$ as initial conditions and using the following set of parameters:

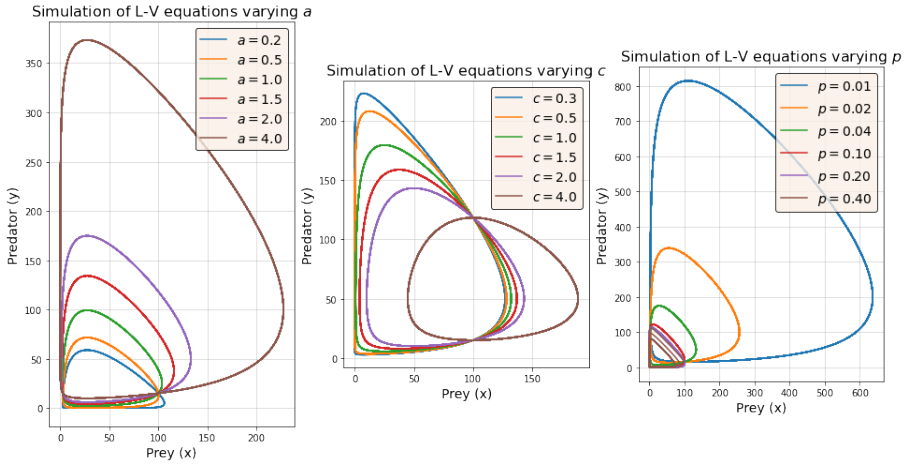
- $a = 2$
- $c = 1.1$
- $p = 0.04$



Then, to better visualize the oscillatory and periodic behaviour we simulate the dynamics with the same set of parameters, varying the initial size of the predator's population.



Finally, the same plot is obtained by varying a, c or p, respectively. In all cases reported the graphs show the presence of sustained oscillations. The resulting plots are shown here:



4 Homework Week 04

Assignment:

1. Generate a random a SxS matrix with C non zero entries and 1-C zeros (C is between zero and one). Set the diagonal to -d. The non-zero elements are drawn from a given distributions. Calculate the eigenvalues. Repeat different realizations and plot all the eigenvalues in the complex plane [Real part (x-axis) and imaginary part (y-axis)]. Compare this result with the expectations from the circular law.

2. Generate the same as above but for mutualistic structure and find how the maximum real eigenvalues scales with S (use S=20,30,40,..100) and compares your numerical finding with the analytical expectations (we did not explicitly have calculated this in class).

3. Analyse the food web using the metrics we have seen in class. The file represent the weighted adjacency matrix of the food web. For the analysis you can binarize (zero and one) the matrix. You find the file in the google drive.

4. (optional) Calculate the same as 1) but with for the cascade model or for the nested mutualistic network.

4.1 Solution

The solution is fully developed in a Jupyter Notebook: hw04_Ecological_Interactions.ipynb [2].

5 Homework Week 05

Consider a consumer resource model where the supply rate is $s(c) = \omega c(1 - c/K)$ and the resource concentration $r(c) = c$ is linear, for $S = 5$ species and $R = 5$ resources. Assign the metabolic strategies at random from a Uniform Distribution between $[0, 0.2]$, while set all other parameters to 1 and choose the death rate small enough as you prefer.

1. Perform the simulations of the full CRM model and compare the stationary solution you find numerically with those obtained analytically.
2. Set $w = 10$ and do the simulation of the quasi stationary approximation (finding first c^* and then simulating $n(t, c^*)$) and compare it with the simulations of the full CRM (keeping fix the metabolic strategies in the two cases for a given realization). Do several (e.g. >20) realizations of the dynamics to obtain a statistics of the species population stationary states in the two cases, represent each population through a Box-Whisker Plot both for the full CRM and the GLV and compare the two.
3. Does the quasi-stationary approximation works if $w = 0.1$? Why?

5.1 Solution

The solution is carried out in the following Jupyter Notebook, which is publicly accessible from the course repository[2]: hw05_Generalized_Consumer_Resource_Model.ipynb.

6 Homework Week 06

No homework! Just continue and wrap up last week's homework.

7 Homework Week 07

Calculate the avalanche duration probability $P_>(t)$ if $\lambda_i = \lambda$ for all t and all neurons. This leads, as only sketched in class, to the following integral:

$$\gamma \int_0^\infty d\lambda \cdot \exp(-\gamma\lambda) \cdot (1 - \exp(-\delta\lambda))^n \tag{30}$$

which can be solved through the saddle point approximation.

Optional. Create a time series $\lambda(t)$, with $t = 1, 2, ..., T$ where at each time t, the value of λ is extracted from an exponential distribution. Then simulate $N = 100$ independent heterogeneous Poisson processes, where each one describes the spikes events of a single neuron, but all have the same time dependent rate parameter $\lambda(t)$.

7.1 Calculation of the avalanche duration probability

Introduction

A neuronal avalanche is a cascade of synchronized activity in a neuronal network. In practice, it can be defined as a sequence of time bins characterized by the spiking of at least one neuron in each bin. We define the size and the duration of the avalanche as, respectively, the number of neurons firing simultaneously and the time between the first and the last neural activity. Experimentally, both size and duration distributions are approximated by a power law.

We denote with $P_>(t|\lambda_1, \lambda_2, ..., \lambda_n)$ the probability of having an avalanche of duration longer than $t = n \cdot dt$, given the sequence of firing rates λ_i. In this case, we are considering correlated and time-independent firing rates, such that $\lambda_i = \lambda$ for all t and for all neurons.

Moreover, we consider a population of N neurons and we define $dt \equiv \delta/N$, such that in the continuum limit $N \to \infty$ and $dt \to 0$, while δ is fixed. Notice that this implies that the number of time intervals $n \equiv t/dt$ can be written as $n = Nt/\delta$.

The avalanche duration probability

We saw in class that the probability that at least one neuron spikes in $[t_i, t_i + dt]$ is given by:

$$1 - (1 - \lambda_i dt)^N \tag{31}$$

Then, $P_>$ can be computed recursively, assuming as boundary condition $P_>(0|\vec{\lambda}) = 1$:

$$P_>(t|\vec{\lambda}) = \prod_{i=1}^{n} \left[1 - (1 - \lambda_i dt)^N\right] \tag{32}$$

Given the assumption that all $\lambda_i = \lambda$ are the same, we can rewrite this as:

$$P_>(t|\vec{\lambda}) = P_>(t|\lambda) = \left[1 - (1 - \lambda dt)^N\right]^n \tag{33}$$

The value of λ is sampled from a generic distribution $\lambda \sim Q(\lambda)$. Then, we can marginalize over it to obtain the avalanche duration probability $P_>(t)$:

$$\begin{aligned} P_>(t) &= \int_0^\infty d\lambda P(\lambda) P_>(t|\lambda) = \\ &\Big| \\ &= \int_0^\infty d\lambda Q(\lambda) \left[1 - (1 - \lambda dt)^N\right]^n \end{aligned}$$

In the continuum limit we have that:

$$\lim_{\substack{N\to\infty \\ dt\to 0 \\ \delta \text{ const}}} (1 - \lambda_i dt)^N = \lim_{\substack{N\to\infty \\ dt\to 0 \\ \delta \text{ const}}} \left(1 - \lambda_i \frac{\delta}{N}\right)^N = e^{-\delta\lambda} \tag{34}$$

Finally, putting all together and imposing that the firing rates are exponentially distributed $Q(\lambda) = \gamma e^{-\gamma\lambda}$ we get the integral presented in equation (30), to be solved using the Saddle Point approximation:

$$P_>(t) = \gamma \int_0^\infty d\lambda \cdot \exp(-\gamma\lambda) \cdot [1 - \exp(-\delta\lambda)]^n \tag{35}$$

The Saddle Point approximation

In a general setting, the Saddle Point approximation is a method that can be used to approximate a function near a particular critical point, i.e. a saddle point. A saddle point is characterized by the fact that the derivatives in orthogonal directions are all zero (indeed it is a critical point), but it is not a local extrema of the function.

The idea behind the Saddle Point approximation is that, near a saddle point, a function can be approximated by a quadratic function. This can be used for approximating an integral, as we will do here.

Theorem 7.1 (*Saddle Point approximation*)

Let $f(\mathbf{x})$ be a function with a single minimum at $\mathbf{x_0}$ and such that:

$$I_f = \int_D e^{-Nf(\mathbf{x})}\, \mathrm{d}^d\mathbf{x} \qquad D \subset \mathbb{R}^d \tag{36}$$

Suppose that $\mathbf{x_0}$ is not on the boundary of D, meaning that there exists some $r > 0$ so that the sphere centred on $\mathbf{x_0}$ of radius r is entirely inside D:

$$\exists r > 0 \text{ s.t. } \{\mathbf{x} \in \mathbb{R}^d \colon |\mathbf{x} - \mathbf{x_0}| < r\} \subset D$$

Then, it is possible to prove that:

$$I_f \equiv \int_D e^{-Nf(\mathbf{x})}\, \mathrm{d}^d\mathbf{x} = e^{-Nf(\mathbf{x_0})} \left(\frac{2\pi}{N}\right)^{d/2} [\det(\partial_\alpha\partial_\beta f(\mathbf{x_0}))]^{-1/2} \cdot \left[1 + O\left(\frac{1}{N}\right)\right] \quad N \gg 1 \tag{37}$$

where $\partial_\alpha\partial_\beta f(\mathbf{x_0})$ is the Hessian of $f(\mathbf{x})$ evaluated at $\mathbf{x} = \mathbf{x_0}$.

In the 1-dimensional case, equation (37) becomes:

$$I_f \equiv \int_{D\subset\mathbb{R}} e^{-Nf(x)}\mathrm{d}x = e^{-Nf(x_0)} \sqrt{\frac{2\pi}{N|f''(x_0)|}} \cdot \left[1 + O\left(\frac{1}{N}\right)\right] \quad N \gg 1 \tag{38}$$

Essentially, the Saddle Point approximation states that an integral of the form presented in (36) can be approximated, provided that N is large, with the value of the integrand calculated at its maximum (up to a multiplicative Gaussian factor).

Solution of the integral

At this point, we can apply this approximation to solve the integral (30). We define:

$$I_n \equiv \frac{1}{\gamma} P_>(t) = \int_0^\infty d\lambda \cdot \exp(-\gamma\lambda) \cdot (1 - \exp(-\delta\lambda))^n = \int_0^\infty e^{-nf(\lambda)} \tag{39}$$

where

$$f(\lambda) \equiv \frac{\gamma\lambda}{n} - \log[1 - \exp(-\delta\lambda)] \tag{40}$$

In order to use the Saddle Point approximation, first we have to find the critical point of $f(\lambda)$ by setting its first derivative to zero.

$$f'(\lambda) = \frac{\gamma}{n} - \frac{\delta}{e^{\delta\lambda} - 1} \stackrel{!}{=} 0 \quad \Rightarrow \quad \lambda_0 = \frac{1}{\delta} \log\left(1 + \frac{\delta n}{\gamma}\right) \tag{41}$$

Then, we need to evaluate $f''(\lambda)$ in λ_0 to find the curvature of f at the critical point:

$$f''(\lambda) = \frac{\delta^2 e^{\delta\lambda}}{(e^{\delta\lambda}-1)^2} \quad \Rightarrow \quad f''(\lambda_0) = \left(\frac{\gamma}{n}\right)^2 \left(1+\frac{\delta n}{\gamma}\right) > 0 \tag{42}$$

Notice that $f(\lambda)$ has a single minimum at λ_0 and λ_0 is not on the boundary of $D = [0, \infty)$. Indeed, $\delta, n, \gamma > 0$ so also $\lambda_0 > 0$, plus we can compute the limits at the extrema of the domain. The conditions of the theorem (7.1) are therefore satisfied.

Next, using the Saddle Point approximation, for large n, we have that:

$$I_n = e^{-nf(\lambda_0)}\sqrt{\frac{2\pi}{n|f''(\lambda_0)|}} = \frac{1}{\gamma}(1+\theta)^{-\frac{n}{\theta}}\left[\frac{\theta}{1+\theta}\right]^n \sqrt{\frac{2\pi n}{1+\theta}} \quad , \quad \theta \equiv \frac{\delta n}{\gamma} \tag{43}$$

Where we used the fact that at the critical point the value of f is:

$$\begin{aligned} f(\lambda_0) &= \left\{\frac{\gamma\lambda}{n} - \log[1-\exp(-\delta\lambda)]\right\}\Big|_{\lambda=\lambda_0} = \\ &= \log\left[1+\frac{\delta n}{\gamma}\right]^{\frac{\gamma}{\delta n}} - \log\left[\frac{\frac{\gamma}{\delta n}}{1+\frac{\gamma}{\delta n}}\right] \end{aligned}$$

The avalanche duration probability is simply obtained by multiplying I_n by γ. Finally, we can rewrite $P_>(t)$ in terms of t using the definition θ and the relation between (δ, n, N, t):

$$\left.\begin{aligned} n &= \tfrac{Nt}{\delta} \\ \theta &= \tfrac{\delta n}{\gamma} \end{aligned}\right\} \quad \Rightarrow \quad \theta = \frac{Nt}{\gamma} \tag{44}$$

Notice also that $n/\theta = \gamma/\delta$. We obtain:

$$\boxed{P_>(t) = \sqrt{\frac{2\pi\gamma}{\delta}}\left(1+\frac{Nt}{\gamma}\right)^{-\frac{\gamma}{\delta}}\left[\frac{Nt}{Nt+\gamma}\right]^{\frac{Nt}{\delta}+\frac{1}{2}}} \tag{45}$$

In the limit $t \to \infty \iff n \to \infty$ we have that $\left[\frac{Nt}{Nt+\gamma}\right]^{\frac{Nt}{\delta}+\frac{1}{2}} \to e^{-\frac{\gamma}{\delta}}$ which is constant, so the behaviour of avalanche duration probability $P_>(t)$ is a power law with exponent $-\frac{\gamma}{\delta}$.

7.2 Simulation of independent heterogeneous Poisson processes

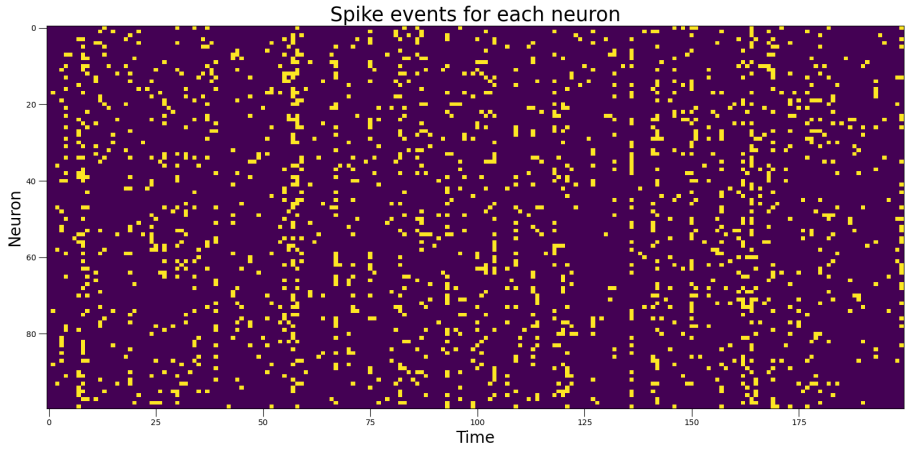
After extracting the values of λ from an exponential distribution, we simulate such process following 3 steps:

1. Select the maximum firing rate in the interval $[0, T]$:
$$\lambda_{max} = \max_{t\in[0,T]} \lambda(t)$$
2. Generate a spike train with constant frequency λ_{max}. This corresponds to simulating an Homogeneous Poisson Process with rate λ_{max}.
3. **Thinning**: some sample are discarded to reduce the spike rate. For each spike i, generate a random number from a uniform distribution, $x^i_{rand} \sim \mathcal{U}(0,1)$. The spike is removed if:
$$\frac{\lambda_i}{\lambda_{max}} < x^i_{rand}$$

About step 2, the simulation of the HPP is performed by sampling interarrival times τ_i from the corresponding exponential distribution $\tau_i \sim Exp(\lambda_{max})$, such that $\sum_i \tau_i \leq T$. As we are dealing integer times, we convert τ_i to `int`. The cumulative sum of τ_i gives us the times at which the considered neuron spikes. After creating an $N \times T$ matrix, we set to 1 the elements (i, j) that correspond to the activation of neuron i at time j.

Simulation results

The simulation is performed for $N = 100$ neurons and a total time of $T = 200$, using a value of $\gamma = 10$. The resulting activation map is presented here, for further details see the corresponding notebook: hw07_Avalanche_Duration_Probability.ipynb.



8 Homework Week 08

Study the stability of the excitatory-inhibitory two neurons system (Eq. 7.5 in the notes) for the parameters:

- $M_{EE} = 1.25$, $M_{IE} = 1$, $M_{EI} = -1$, $M_{II} = 0$;
- $h_E = 10\,Hz$, $h_I = -h_E$;
- $\tau_E = 10\,ms$

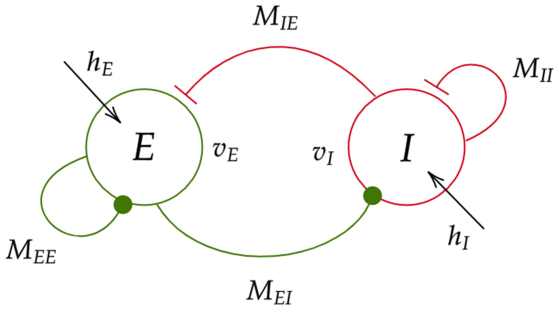
as a function of the free parameter τ_I. Simulate a trajectory in the stable regime and one in the limit cycle regime (different τ_I).

8.1 Stability study

In the *excitatory-inhibitory two neuron system* we study the interaction between an excitatory and an inhibitory neuron, using equations similar to the Lotka-Volterra model. This is motivated by the Dale's law, according to which a neuron cannot exert both actions on its post-synaptic neurons. The neurons output are called, respectively, v_E and v_I and their interaction is described by the weights matrix:

$$\begin{pmatrix} M_{EE} & M_{EI} \\ M_{IE} & M_{II} \end{pmatrix} \tag{46}$$

Calling h_E and h_I the external stimuli, we can represent the interaction between excitatory and inhibitory neurons as follows.



The dynamics of the system is described by:

$$\begin{cases} \tau_E \frac{dv_E}{dt} & = -v_E + \psi(h_E + M_{EE}v_E + M_{EI}v_I) \\ \tau_I \frac{dv_I}{dt} & = -v_I + \psi(h_I + M_{IE}v_E + M_{II}v_I) \end{cases} \tag{47}$$

where τ_E and τ_I are time constants and ψ is the activation function, in this case a ReLu:

$$\psi(x) = \max(0, x) \equiv [x]_+$$

First, we can find the fixed points of the system by setting:

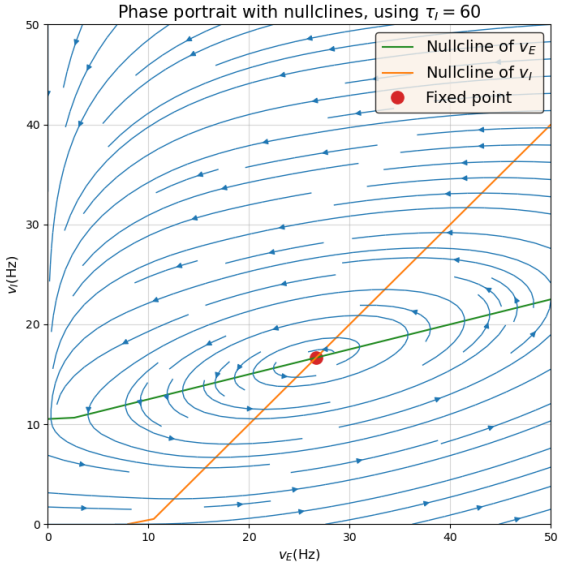
$$\begin{cases} \frac{dv_E}{dt} & \stackrel{!}{=} 0 \\ \frac{dv_I}{dt} & \stackrel{!}{=} 0 \end{cases} \implies \begin{pmatrix} 1 - M_{EE} & -M_{EI} \\ -M_{IE} & 1 - M_{II} \end{pmatrix} \begin{pmatrix} v_E^* \\ v_I^* \end{pmatrix} = \begin{pmatrix} h_E \\ h_I \end{pmatrix} \tag{48}$$

In eq.(48) we considered only solutions characterized by $\psi(x) = x$, which is equivalent to imposing x to be positive. In order to satisfy this condition we must have:

$$\begin{cases} h_E + M_{EE}v_E^* + M_{EI}v_I^* & \geq 0 \\ h_I + M_{IE}v_E^* + M_{II}v_I^* & \geq 0 \end{cases} \iff \begin{cases} v_E^* & \geq 10 \\ v_I^* & \geq 10 + 1.25v_E^* \end{cases}$$

This is motivated by the fact that only in this case is the dynamics interesting, otherwise it is trivial. However, it can be proven that the solution we find in this way is unique. Here we give

only a graphical interpretation of this, plotting the *nullclines*, i.e. the curves where $\dot{v}_E = 0$ or $\dot{v}_I = 0$, which intersect at a single point. The analytical proof is left to the reader.



Going back to eq. (48), the solution of the system can be found inverting the matrix:

$$\begin{pmatrix} v_E^* \\ v_I^* \end{pmatrix} = \frac{1}{(1-M_{EE})(1-M_{II}) - M_{EI}M_{IE}} \begin{pmatrix} 1-M_{II} & M_{EI} \\ M_{IE} & 1-M_{EE} \end{pmatrix} \begin{pmatrix} h_E \\ h_I \end{pmatrix}$$

Substituting the numerical values we get:

$$\begin{pmatrix} v_E^* \\ v_I^* \end{pmatrix} = \frac{10}{3} \begin{pmatrix} 8 \\ 5 \end{pmatrix} \approx \begin{pmatrix} 26.67 \\ 16.67 \end{pmatrix} \tag{49}$$

At this point, we can perform a linear stability analysis by computing the Jacobian of the system and evaluating it at this point:

$$J = \begin{pmatrix} -\frac{1-M_{EE}}{\tau_E} & \frac{M_{EI}}{\tau_E} \\ \frac{M_{IE}}{\tau_I} & -\frac{1-M_{II}}{\tau_I} \end{pmatrix}$$

To study the stability and write the linearized equations around the stationary point we have to compute the eigenvalues of the Jacobian of the system. The characteristic polynomial of J is:

$$\begin{aligned} &\left(\frac{1-M_{EE}}{\tau_E} + \lambda\right)\left(\frac{1-M_{II}}{\tau_I} + \lambda\right) - \frac{M_{EI}M_{IE}}{\tau_E\tau_I} = \\ &= \lambda^2 + \left(\frac{1-M_{EE}}{\tau_E} + \frac{1-M_{II}}{\tau_I}\right)\lambda + \frac{(1-M_{EE})(1-M_{II})}{\tau_E\tau_I} - \frac{M_{EI}M_{IE}}{\tau_E\tau_I} \stackrel{!}{=} 0 \end{aligned}$$

Finally, we can solve the second order equation to get the eigenvalues in the general case:

$$\lambda_\pm = -\left(\tfrac{1-M_{EE}}{\tau_E} + \tfrac{1-M_{II}}{\tau_I}\right) \pm \sqrt{\left(\tfrac{1-M_{EE}}{\tau_E} + \tfrac{1-M_{II}}{\tau_I}\right)^2 + 4 \cdot \tfrac{M_{EI}M_{IE} - (1-M_{EE})(1-M_{II})}{\tau_E\tau_I}}$$

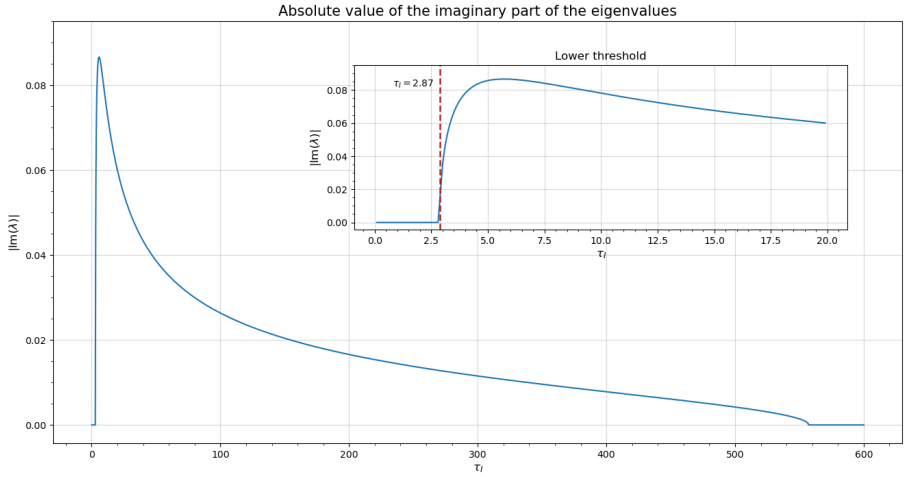
Substituting the numerical values we obtain:

$$\lambda_\pm = -\left(\frac{1}{\tau_I} - \frac{1}{40}\right) \pm \sqrt{\left(\frac{1}{\tau_I} - \frac{1}{40}\right)^2 - \frac{3}{10\tau_I}} \tag{50}$$

To perform the stability analysis we first study the sign of the argument of the square root, to determine whether the eigenvalues are complex conjugate or real.

$$\left(\frac{1}{\tau_I} - \frac{1}{40}\right)^2 - \frac{3}{10\tau_I} > 0 \quad \Rightarrow \quad \frac{\tau_I^2 - 560\tau_I + 1600}{\tau_I^2} > 0$$

The solutions of the associated equation are $\tau_{I,-} \simeq 2.87$ and $\tau_{I,+} \simeq 557.13$. Thus we have that the eigenvalues are complex conjugate only if $2.87 \lesssim \tau_I \lesssim 557.13$, and they are real otherwise. We can see this also by computing numerically the eigenvalues of the Jacobian and plotting the absolute value of their imaginary part:



8.2 Complex conjugate eigenvalues

If we consider the case where $2.87 \lesssim \tau_I \lesssim 557.13$, the argument of the square root is negative and the eigenvalues are complex conjugate. This implies that the behaviour around the fixed point is oscillatory. The stability is determined by the $\mathrm{Re}(\lambda_\pm)$:

- If $\mathrm{Re}(\lambda_\pm) < 0$ the fixed point is stable and the trajectory spirals into it.
- If $\mathrm{Re}(\lambda_\pm) < 0$ the fixed point is unstable and the system spirals out of it.
- If $\mathrm{Re}(\lambda_\pm) = 0$ the fixed point is a center and the solution is a closed orbit which is neutrally stable.

Notice that in the second case, because of the non-linearity introduced by the activation function, the unstable trajectory does not expand indefinitely but converges towards a so-called *limit cycle*.

Which of these behaviors the system underlies depends on the value of the parameter τ_I. We can find the *bifurcation point*, i.e. the point that separates these regimes, by setting $\mathrm{Re}(\lambda_\pm) = 0$:

$$\mathrm{Re}(\lambda_\pm) = 0 \quad \Longleftrightarrow \quad \tau_I = 40$$

8.2.1 Simulations

Below we report the results of the simulations carried out respectively with $\tau_I = 20$, $\tau_I = 40$ and $\tau_I = 60$. The results reflect what the theory predicts.

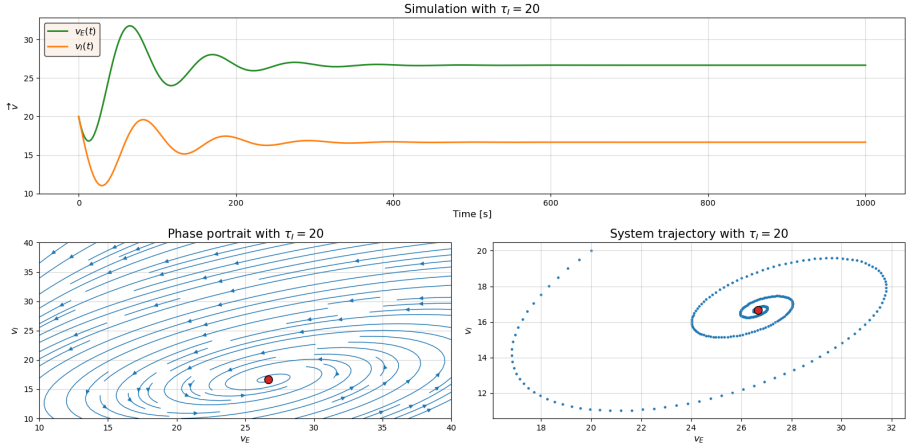


Figure 1: Simulation in the stable regime. Typical trajectory of the model when $\tau_I < 40\,ms$. The real part of the eigenvalues is negative and the fixed point is stable.

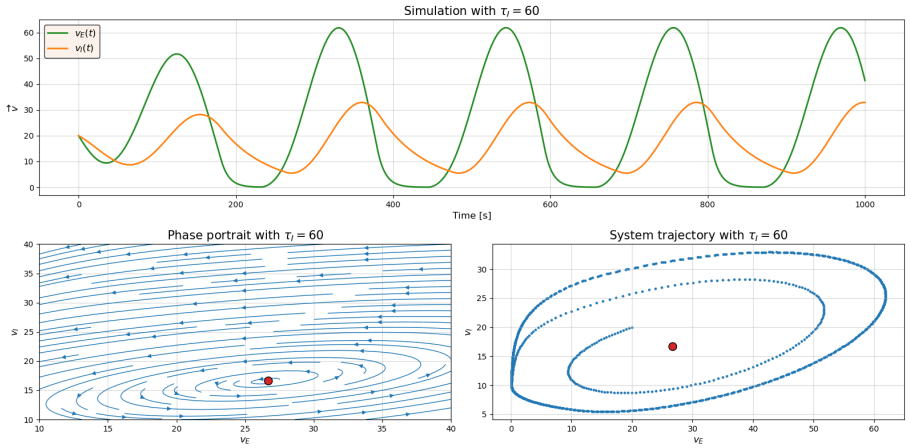


Figure 2: Simulation in the limit cycle regime. Typical trajectory of the model when $\tau_I > 40\,ms$. The real part of the eigenvalues is positive and the fixed point is unstable.

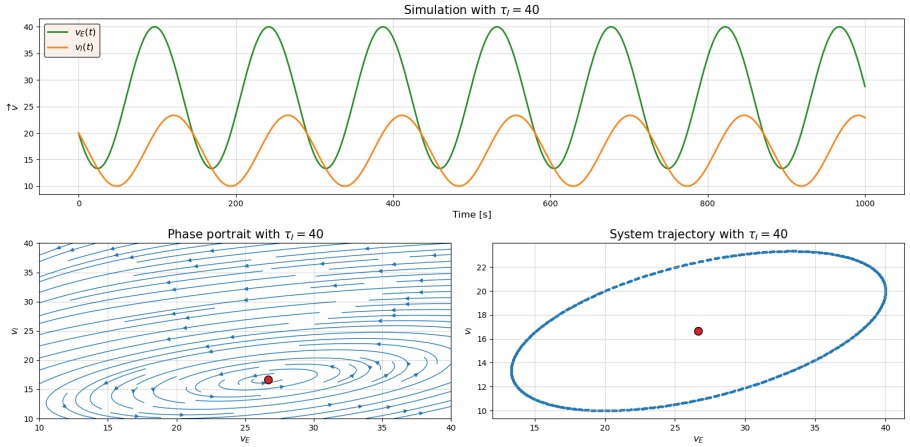


Figure 3: Simulation in the critical case. Trajectory of the model when $\tau_I = 40\,ms$. The real part of the eigenvalues is zero and the fixed point is a center.

8.3 Real-valued eigenvalues

We saw that if $0 < \tau_I \lesssim 2.87$ or $\tau_I \gtrsim 557.13$ the eigenvalues of the Jacobian are real. The stability of the fixed point is determined by the sign of the largest eigenvalue, so λ_+. Thus, from eq. (50) we have that:

$$\lambda_+ > 0 \iff \left(\frac{1}{\tau_I} - \frac{1}{40}\right) < \sqrt{\left(\frac{1}{\tau_I} - \frac{1}{40}\right)^2 - \frac{3}{10\tau_I}}$$

Distinguishing the cases in which $\left(\frac{1}{\tau_I} - \frac{1}{40}\right)$ is positive and negative, and taking the square of both sides in the first, the solution of this inequality is:

$$\tau_I > 40 \quad \cup \quad \begin{cases} \tau_I < 40 \\ -\frac{3}{10\tau_I} > 0 \iff \tau_I < 0 \end{cases}$$

Considering only the physical values of τ_I and restricting it to the interval where the eigenvalues are real, finally we get that:

$$\lambda_+ \in \mathbb{R} \text{ and } \lambda_+ < 0 \iff 0 < \tau_I \lesssim 2.87 \tag{51}$$

$$\lambda_+ \in \mathbb{R} \text{ and } \lambda_+ > 0 \iff \tau_I \gtrsim 557.13 \tag{52}$$

In the first case the 2 eigenvalues are both negative and the fixed point is stable. In the second case, instead, at least one of them is positive and the fixed point is unstable. Actually, it can be easily proven that in this range also $\lambda_- > 0$, so the eigenvalues are both positive.

Notice that when the argument of the square root is zero, the 2 eigenvalues are not distinct and there is a so-called *degenerate node*. This happens for $\tau_I \simeq 2.78$ and $\tau_I \simeq 557.13$.

8.3.1 Simulations

Below we present the simulations carried out respectively with $\tau_I = 2$ and $\tau_I = 600$. The dynamics of the systems thus obtained is in agreement with the theoretical results just discussed.

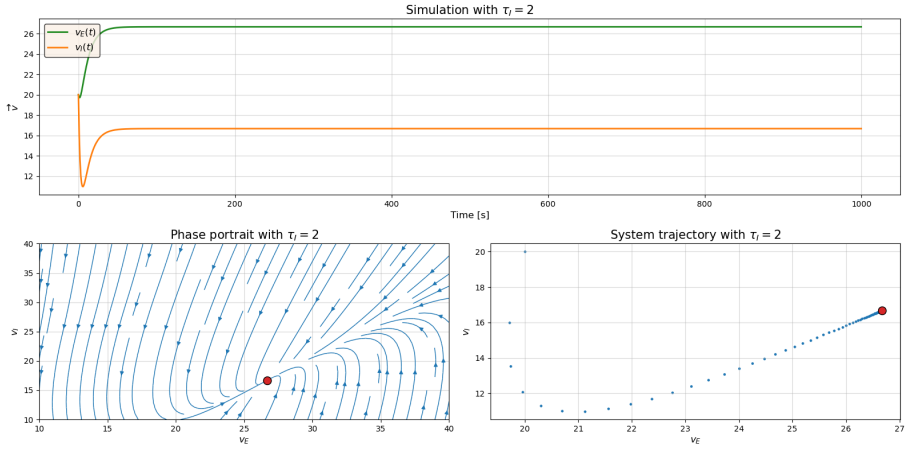


Figure 4: Simulation in the case of real eigenvalues, for $\tau_I = 2$. Both eigenvalues are negative and the fixed point is stable.

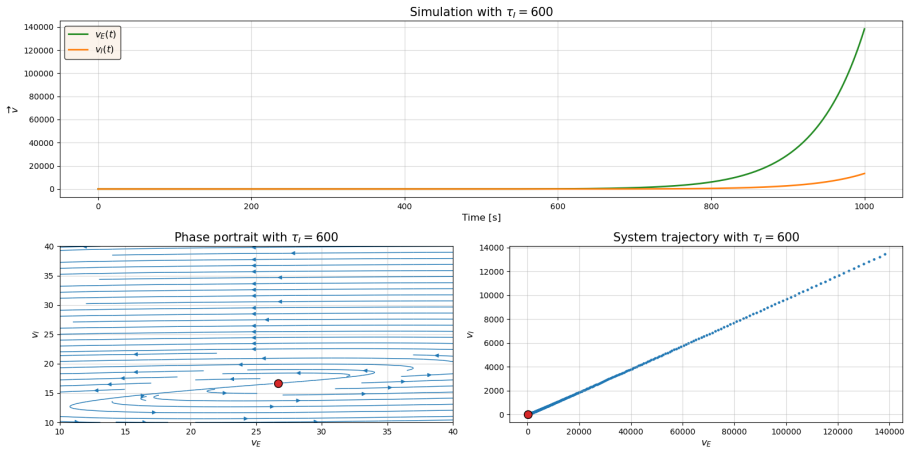


Figure 5: Simulation in the case of real eigenvalues, for $\tau_I = 600$. Both eigenvalues are positive and the fixed point is unstable.

8.4 Summary of the nature of the fixed point

We can sum up the stability of the excitatory-inhibitory two neurons system presented in the assignment as follows:

- $0 < \tau_I < 2.87 \Rightarrow$ stable point
- $\tau_I \simeq 2.78 \Rightarrow$ degenerate node
- $2.87 < \tau_I < 40 \Rightarrow$ stable spiral
- $\tau_I = 40 \Rightarrow$ closed orbit, neutral stability, the fixed point is a center
- $40 < \tau_I < 557.13 \Rightarrow$ unstable spiral, limit cycle regime
- $\tau_I \simeq 557.13 \Rightarrow$ degenerate node
- $\tau_I > 557.13$ unstable point

9 Homework Week 09

Understand and run the code `hopfield.py`. Use stored images as memory patterns, and input images as initial conditions to retrieve the patterns. What pattern do you retrieve if you use *samir.jpg* as input? And if you use superman?

9.1 Solution

The code and images are available in the course repository[2], see hw09_Hopfield. The solution is carried out without making a presentation of the results.

10 Homework Week 10

Simulate the stochastic dynamics of the two stage model using the Gillespie algorithm.

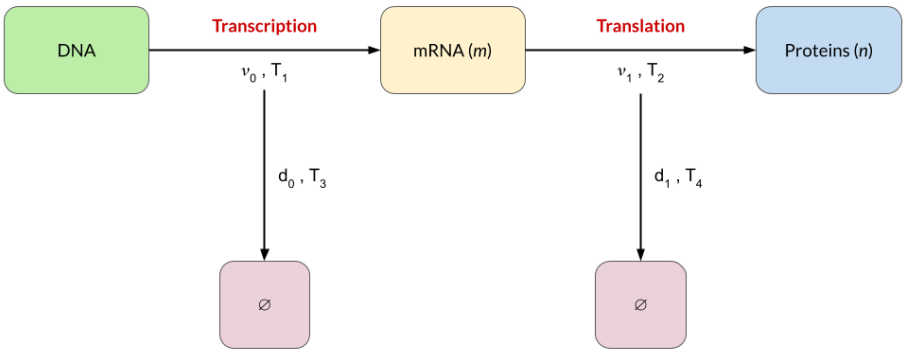
10.1 Two-stage model for gene expression

Assuming the cell is a well-stirred chemical reactor, in the language of reaction kinetics we have the following elementary reactions:

$$\begin{aligned} \emptyset &\xrightarrow{\nu_0} \text{mRNA} \\ \text{mRNA} &\xrightarrow{d_0} \emptyset \\ \text{mRNA} &\xrightarrow{\nu_1} \text{mRNA} + \text{Protein} \\ \text{Protein} &\xrightarrow{d_1} \emptyset \end{aligned}$$

The first reaction is a zeroth-order reaction, while the others are first-order (linear and non-autocatalitic reactions). Rate constants (ν_0, d_0, ν_1, d_1) depend on many factors, but we assume they do not vary in time. This implies that we are modelling intrinsic fluctuations only and neglecting environmental/extrinsic noise.

Between the experimental data we have, it is worth it to mention that gene expression is intrinsically stochastic. This is because the number of molecules is small and the timing of individual chemical reactions is random. However, the **one-stage model** produces no fluctuations at all and describes average values only. To include fluctuations and describe the experimental phenomena we have, a fully stochastic description is needed. This is why we introduce the **two-stage model**, which considers both mRNAs and proteins. This is motivated by the fact that the presence of mRNA is crucial for the production of proteins and cannot be neglected, so that they cannot be disentangled. The 2 stages of the model, *transcription* and *translation*, are described in the following figure:



where the rates that describe the model of gene expression are:

- $T_1(m+1, n|m, n) = \nu_0$
- $T_2(m, n+1|m, n) = m\nu_1$
- $T_3(m-1, n|m, n) = md_0$
- $T_4(m, n-1|m, n) = nd_1$

They, respectively, describe transcription, translation, mRNA degradation and protein degradation. Finally, these rates allow us to write the Master Equation of the two-stage model:

$$\frac{\partial P_{m,n}(t)}{\partial t} = \nu_0 \Big[P_{m-1,n}(t) - P_{m,n}(t) \Big] + \nu_1 m \Big[P_{m,n-1}(t) - P_{m,n}(t) \Big] + \\ + d_0 \Big[(m+1) P_{m+1,n}(t) - m P_{m,n}(t) \Big] + d_1 \Big[(n+1) P_{m,n+1}(t) - n P_{m,n}(t) \Big]$$

We simulate it via the **Gillespie algorithm**.

10.2 Gillespie algorithm

The Gillespie algorithm was build to obtain a stochastic simulation of chemical kinetics (see [1]). However, it is applied in many different contexts (e.g. ecology and sociology) and it constitutes a powerful tool for simulating complex stochastic dynamics. The algorithm works by specifying a set of possible reaction events, along with their associated rates, and then using probability to determine which reaction will occur next and when. Its strong efficiency comes, indeed, from the fact that it directly provides the time and nature of the next reaction event.
The algorithm can be summarized by the following steps:

1. Initialize the system state $x(0) = x(t = 0)$
2. Calculate the propensity function $a_j(x)\, \forall j$ reaction events, i.e. the rate of each reaction event
3. Compute the total propensity $a_0(x) = \sum_{j=1}^{n} a_j(x)$
4. Compute the occurrence time τ of the next reaction, sampling it form an exponential distribution with parameter $a_0(x)$:
$$P(\tau | x(t)) = \gamma e^{-\gamma \tau} \quad , \quad \gamma = a_0(x(t))$$
5. Determine which is the next reaction by extracting a uniform number u from $\mathcal{U}[0, 1]$. The index $i \in \{1, \dots, n\}$ of such reaction is the smallest index such that $\sum_{j=1}^{i} a_j(x) \geq u a_0(x)$.
6. Update the state of the system $x(t + \tau)$ by appling the reaction $a_i(x)$; update the time t
7. Reiterate from step 2 to 6 until the total time is reached

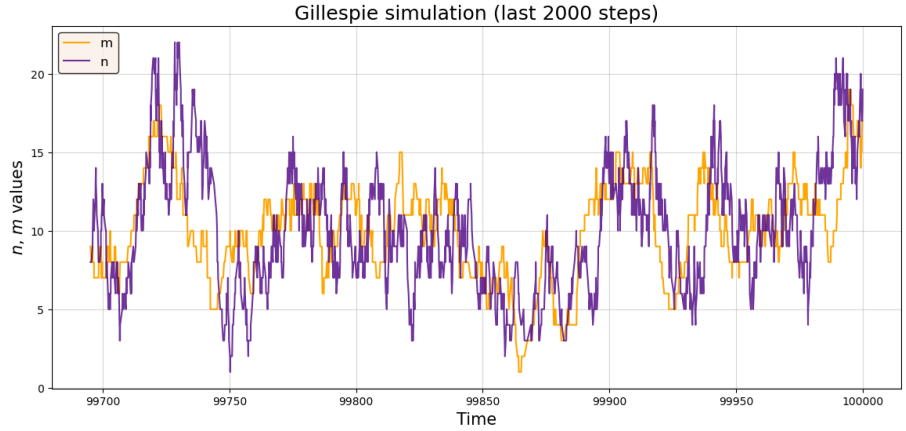
By construction we are guaranteed that $x(t)$ satisfies the corresponding M.E. as $P(x(t))$ is a solution of it.

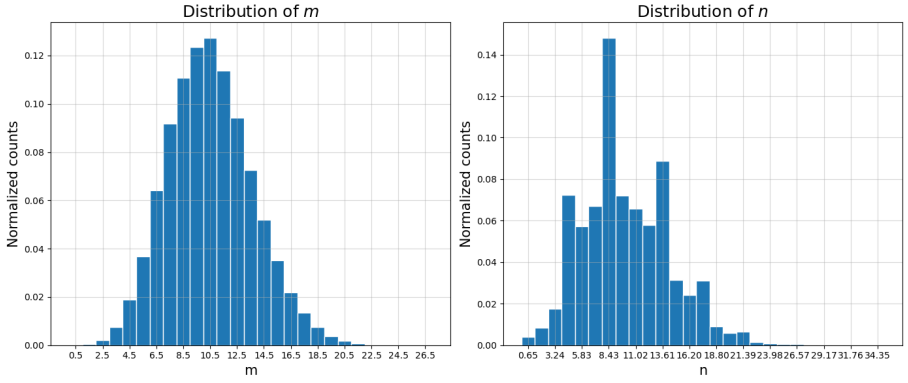
10.3 Simulation results

This section shows an example of a simulation of the two-stage model done with the Gillespie algorithm. The corresponding notebook, where the algorithm is actually implemented, is available at the following link: hw10_Two_Stage_Model.ipynb. The simulation is performed with the following rate values:

- $\nu_0 = 0.8$
- $\nu_1 = 0.25$
- $d_0 = 0.08$
- $d_1 = 0.25$

starting from an empty initial state, $m(t = 0) = n(t = 0) = 0$.


Gillespie simulation (last 2000 steps)
m
n
n, m values
Time
0
5
10
15
20
99700
99750
99800
99850
99900
99950
100000


Distribution of m
Normalized counts
m
Distribution of n
Normalized counts
n

References

[1] Daniel T. Gillespie. "Stochastic Simulation of Chemical Kinetics". In: *Annual Review of Physical Chemistry* 58.1 (2007). PMID: 17037977, pp. 35–55. DOI: 10.1146/annurev.physchem.58.032806.104637.

[2] Nicola Zomer. *Github Repository of Physical Models of Living Systems*. Nov. 2, 2022. URL: https://github.com/NicolaZomer/Physical_Models_of_Living_Systems.