

Izhikevich neuron model in networks with topographical obstacles

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Abstract: The aim of this study is to examine the behaviour of a simulated neuronal network in which neurons are located in topographical obstacles shaped as parallel tracks that reduce the capacity of neurons to interconnect. The simulations show that three different scenarios of collective activity are observed, depending on the connectivity between neurons, from few isolated groups of neurons to the entire synchronous activation of the network. We also observed that, when neurons strongly follow the topographical pattern, the activity of the system is highly tied to the structure of the network, indicating that dynamics (functional connectivity) is highly linked to structural one.

I. INTRODUCTION

Neurons are the basic processing unit of the nervous systems, which span from few hundreds in the worm *C. elegans* to the 10^{11} of the human brain. In all cases, the circuits shape complex networks, and where the connectivity details between neurons can shape the overall dynamics and functionality of the neuronal assembly.

Indeed, the complex networks that are the nervous systems are the responsible of much of the functions that we use to interact and understand the world. Thus, by studying these networks, we can understand better the functions of the brain, for instance in the context of processing information or propagating activity. This is important in the context of neurodegenerative diseases, where the loss of neurons and connections affect the capacity of the neuronal circuit to properly operate. For this reason, the study of neuronal networks, and specifically how the wiring among neurons shapes collective dynamics, has become an important field of research.

Of course it would be ideal to study neuronal systems *in vivo*, but this is impossible in practice due to the difficulty involved in accessing systems as large and intricate as the human brain. This causes us to have to use alternative methods to study these systems. A first one of these methods is the *in vitro* preparations of neural cultures, which usually contain on the order of 100 to 1000 neurons, and where the complex behavior and the physical connections can be tuned. Such an idea is normally termed *neuroengineering* and can be implemented by arranging neurons in particular locations, or by guiding them using topographical obstacles or other mechanisms [1]. A second one of these methods is numerical simulations (*silico*), which allows to model in a computer the connectivity among neurons and the corresponding collective dynamics.

In either case, the primary observable for the study of activity in these experiments is the membrane potential, which increases or decreases depending of the inputs from other neurons. When the potential reaches a threshold, it triggers a series of processes that, in the end, shape an *action potential* and that becomes the input of other neurons in form of a pulse. When we have this pulse, we

say that the neuron has fired, it have made a *spike* [2]. These spikes are measured experimentally or observed in the simulations and, by analyzing them, we can extract information and quantify the behavior of the neuronal system.

Ideally, in order to understand how the brain and similar complex systems work, we have to combine the studies of neural networks and the numerical simulations that we can do with everything we know. One of the most accurate simulations is the Hodgkin–Huxley-type model, which is computationally inaccessible because we can only simulate a few neurons in real time. On the other hand, we have the Izhikevich model, which is a simplified model of the previous one, which is capable to simulate on order of 100 to 1000 neurons in real time, in a scale of *ms*, using a desktop PC [3].

In the present study, we want to simulate and compare with experiments a particular case of neuronal connectivity distribution, where inspired by Ref. [1] we add neurons to topographical tracks in which neurons grow, connecting strongly along the track or weakly across neighboring tracks.

II. METHODS

Here we describe the methods used in the numerical study of neuronal networks, which includes the modelling approach, in this case the Izhikevich model [3], and the descriptors to characterize the network.

A. Izhikevich model

This model, presented in 2003, is determined by 4 parameters (a , b , c and d) and two differential equations:

$$\dot{v} = 0.04v^2 + 5v + 140 - u + I, \quad (1)$$

$$\dot{u} = a(bv - u), \quad (2)$$

where u represents the membrane recovery parameter, v represents the membrane potential of the neuron and I represents the synaptic current. When the membrane

potential of the neuron exceeds the 30 mV, the neuron makes a spike and resets the variables u and v , which is described as:

$$\text{if } v \geq 30\text{mV, then } \begin{cases} v \leftarrow c \\ u \leftarrow u + d, \end{cases} \quad (3)$$

and termed ‘auxiliary after-spike resetting’.

The 4 parameters describe the next attributes:

- a : represents the time scale of the recovery of u .
- b : represents the sensitivity of u .
- c : represents the reset value of v .
- d : represents the reset value of u .

In this study, we used the MATLAB code provided in Ref. [3], where we can simulate 1000 neurons in real time, *i.e.*, with a step of 1 ms. The original Izhikevich code named above is the following:

```
% Created by Eugene M. Izhikevich,
%February 25, 2003
% Excitatory neurons      Inhibitory neurons
Ne=800;                   Ni=200;
re=rand(Ne,1);            ri=rand(Ni,1);
a=[0.02*ones(Ne,1);      0.02+0.08*ri];
b=[0.2*ones(Ne,1);       0.25-0.05*ri];
c=[-65+15*re.^2;         -65*ones(Ni,1)];
d=[8-6*re.^2;            2*ones(Ni,1)];
S=[0.5*rand(Ne+Ni,Ne),   -rand(Ne+Ni,Ni)];
v=-65*ones(Ne+Ni,1);     % Initial values of v
u=b.*v;                  % Initial values of u
firings=[];              % spike timings
for t=1:1000              % simulation of 1000 ms
I=[5*randn(Ne,1);2*randn(Ni,1)]; % thalamic input
fired=find(v>=30);       % indices of spikes
firings=[firings; t+0*fired,fired];
v(fired)=c(fired);
u(fired)=u(fired)+d(fired);
I=I+sum(S(:,fired),2);
v=v+0.5*(0.04*v.^2+5*v+140-u+I); % step 0.5 ms
v=v+0.5*(0.04*v.^2+5*v+140-u+I); % for numerical
u=u+a.*(b.*v-u);        % stability
end;
plot(firings(:,1),firings(:,2),'.');
```

Initially we can find a ratio of excitatory to inhibitory neurons of 4 to 1, where the first ones increase the membrane potential while the second ones reduces it, and this activity is controlled by the matrix of synaptic connection weights S , which gives a certain interval of values if the neuron is of one type or the other. The combination of these two types of neurons is what gives the Izhikevich model the biological plausibility and complex behaviour of the mammalian brains [4]. There are other parameters that we can change in order to simulate the model with more precision. We will see that this parameters, like the noise and the maximum weight of the excitatory

neuron connections, can substantially change the simulations’ outcome.

The matrix S will be our observable to simulate the neuronal network with the distribution of topographical tracks that we desire. In our case, we define the connectivity matrix A and then add the weight of every neuron. This matrix A has 1000×1000 binary elements, where every 1 represents a connection between a pair of neurons, and 0 otherwise. This matrix is in general asymmetric, since the connections may not be reciprocal.

B. Network measures

We will use analysis tools from complex systems [5], which will allow us to collect information about the most important characteristics of the simulated networks. These measures are applied to the connectivity matrix A .

A first measure is the *Global efficiency* (G_{eff}), which represents how good the information can travel through the network, and provides values between 0 (inefficient, poorly connected) and 1 (highly efficient, well connected). Its expression is:

$$G_{\text{eff}} = \frac{1}{N(N-1)} \sum_{i \neq j}^N \frac{1}{d_{ij}}, \quad (4)$$

where N is the number of nodes of the network and d_{ij} is the shortest path length between the nodes i and j , *i.e.*, the minimum number of nodes between the i and j node.

A second measure is the *modularity* Q , with values between 0 and 1. It represents the tendency of neurons to form groups of communities, with Q representing the ratio between connections across nodes within the same community and the connections across communities. A network with a high Q indicates many connections between nodes in the same community, and low connections among communities. This is what is named an *segregated network*. In the extreme case we can consider a community for every neuron or node. As a contrary, a network with low Q values is named an *integrated network*.

These measures and other functions, such as the visualization of the network in the *Gephi* program, or the arrangement of the connection matrix by modules, are included in MATLAB programs provided by Dr. Soriano, which I have adapted to my code. Another code that I adapted was used to compute the fraction of neurons that activated collectively in a given time window, a concept that is called ‘global network activity’ (GNA).

III. RESULTS AND DISCUSSION

A. Initial model

First of all, we must determine the criteria to decide if there is a connection between neurons or not. In this

study, we applied a threshold that depended on an exponential whose variable is the Euclidean distance between neurons, given by:

$$th = 1 - e^{-\alpha \cdot dist}, \quad (5)$$

where $dist$ is the Euclidean distance between a given pair of neurons and α is the exponent variable that we will change depending how easy (α low) or difficult (α high) we want the neurons to connect.

Then, we place neurons on a physical space, in this case a square area of lateral size 3 mm. Next we create a connectivity matrix A that is initially filled with random values between 0 and 1. Thereafter, we look at each pair of neurons (i, j) , compute their Euclidean distance, get the threshold value and apply it, so that if $th_{i,j} < A_{i,j}$ then $A_{i,j} = 1$, and 0 otherwise, obtaining finally a binary matrix of connections.

Conceptually, in this model we set a limit for the physical distance at which neurons can connect. If that limit is exceeded, it automatically causes the coefficient to be 0 in the matrix. To be sure of the parameters to use, we have done first a study to know the typical distances and exponents that are interesting. As illustrated in Fig. 1, we used a model of 6 vertical tracks of 0.25 mm wide and 3 mm long, with a space between them of 0.5 mm. In these networks we considered two exponents, one along tracks α_A and one transverse to them α_T . But, first, for clarity, we inspected what happened when a single exponent α was used.

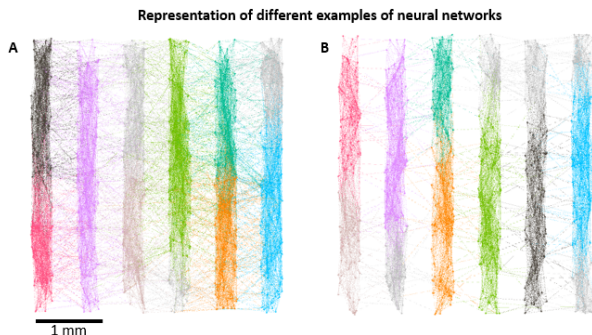


FIG. 1: Representation with Gephi of two extreme neuronal distributions in 2D. Neurons show communities and are colored according to them. **A:** ($\alpha_A = 4.5$, $\alpha_T = 7$). **B:** ($\alpha_A = 5.5$, $\alpha_T = 10.5$)

As shown in Fig. 2, for a single exponent α , we investigated how the modularity of the network changed when we varied the maximum distance between neurons and α . We can see that the typical values for α to obtain an interesting modularity vary between 4 and 9, and a distances of 0.5 mm onwards. This helped us to refine the geometry of the tracks and the density of neurons.

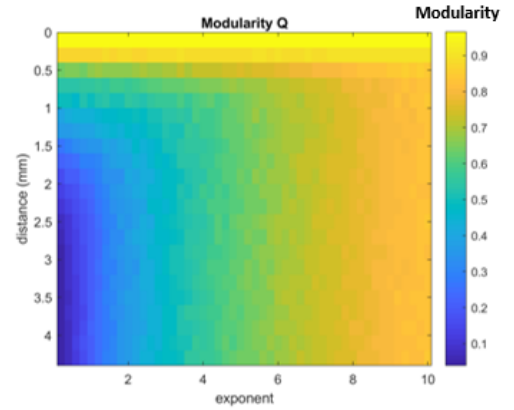


FIG. 2: Behavior of the simulations by calculating the modularity Q as a function of the maximum connection distance and the exponent α .

B. Final model with topographical obstacles

Now, having the parameters delimited in an interval of values, we proceed to explore in detail the effect of the topographical obstacles shaped as tracks in our model. These obstacles limit the capacity of neurons to connect freely in all directions, which we will represent by varying the parameter α of the exponents (Eq. 5) depending on whether we are considering connections that are favored along the same track (low α_A) and/or made difficult across tracks (high α_T). Overall, this causes asymmetry between the same track and the neighboring ones. We can also suggest a reduction of the maximum distance between connections also because of these obstacles, deciding that at most there will be connections between a track and its second neighbor.

Applying now this construction to the dynamical model of 1000 neurons, we can investigate different dynamical regimes. As seen in Fig. 3, three different regimes can be considered, which can be studied by plotting raster plots, *i.e.*, the activation of the neurons along time.

The behavior of the regimes can be understood through the exponents that are used in every example. In the case of Fig. 3A, we have a mostly symmetrical and synchronized activity, where the difference between the two exponents ($\alpha_A = 4.5$ and $\alpha_T = 7$) is not very large and does not cause a great difference from an initial scenario with a unique α . For the case of Fig. 3B, the exponents are more contrasted ($\alpha_A = 5$ and $\alpha_T = 9$), and we can see the beginning of the rupture of the synchronization, which accentuates for the case of Fig. 3C ($\alpha_A = 5.5$ and $\alpha_T = 10.5$), where the dynamics is concentrated at the level of groups that correspond to the tracks themselves. Indeed, we can see that the bursts of neurons within a community are not normally followed by activity in neighboring communities.

All these explorations can be summarized in Fig. 4, where we plot the average fraction of neurons in the network that activate together (*i.e.*, the groups we see in the

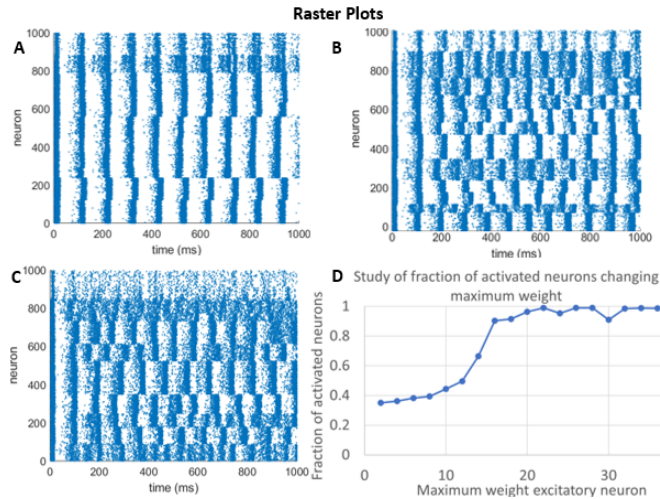


FIG. 3: **A**, **B** and **C**: Raster plots of the different regions of activity in our model, with time in ms on the x-axis and the neuron label on the y-axis. The track and transversal exponents are $(\alpha_A = 4.5, \alpha_T = 7)$, $(5, 9)$ and $(5.5, 10.5)$ respectively. **D**: Study in the variation of the mean of the fraction of neurons activated changing the maximum weight of the excitatory neurons, with the weight in the x-axis and the mean in the y-axis.

raster plots), for all the combinations of exponents. We can clearly see that the dynamic behavior of the neuronal network depends on the exponents we use.

Additionally, to demonstrate the variation of the results by changing parameters, in Fig. 3D we provide a study for the evolution of the average fraction of neurons in the network that activate together as a function of the maximum weight of the excitatory neurons. No other parameters or variables are changed. We can see that the variation of the mean clearly depends on this weight. Therefore, the results obtained in a simulation (Figs. 3 and 4) depend very clearly on the parameters chosen.

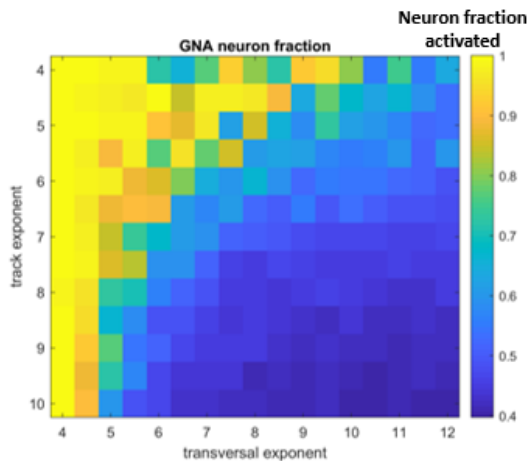


FIG. 4: Dependence of the fraction of activated neurons (GNA) as a function of the two different types of exponents.

C. Functional network

Here we are going to study with more detail the example of Fig. 3B, where we found activity that encompassed neuronal groups. The example corresponds to the exponents $\alpha_A = 5$ and $\alpha_T = 9$. These exponents gives us many connections in the same track and few connections between them. By looking at the connectivity matrix (shown in Fig. 5A) and the spatial representation (Fig. 5B), we can conclude that every collective activation in Fig. 3B is associated to a burst in one or few neuronal communities.

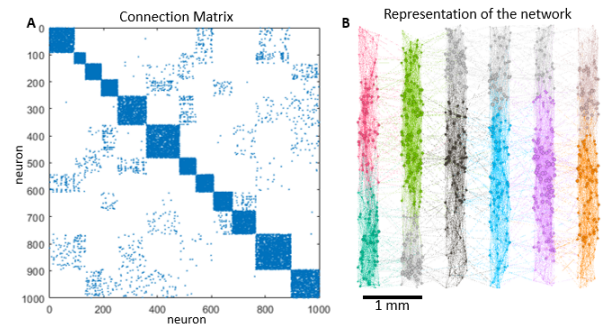


FIG. 5: **A**: Matrix of neuronal connections for the simulation of Fig. 3B, ordered by communities, with the neural label in both axis. Every blue dot represents a connections that goes from the neuron of the row label to the neuron of the column label. **B**: Representation with Gephi of the neuronal model distribution in 2D, with the neurons of communities grouped together by the same color.

We should point out that, in Fig. 5, it is clearly visible the difference among the connections that we have said, as we notice that every line represents a connection between two neurons, and these connections are mostly between neurons in the same vertical track.

As an additional analysis, we calculated the correlation of spikes between the neurons, to achieve what is termed the *functional network*. Conceptually, this functional network let us know how synchronous is the communication among neurons. For that, we compute the cross-correlation among neuronal pairs, which are obtained from the simulation of 1000 ms. Then we represent the correlation values. with 1 indicating that two neurons are very similar in behavior and highly correlated and 0 indicating that they are very different in behavior. We can see the functional network matrix in Fig. 6A.

We are now interested in deleting non-significant functional connections in Fig. 6A in order to achieve a more accurate functional matrix. For that, we will apply a randomness concept called 'surrogates', in which we consider all the spikes from a neuron along the time of the simulation and distribute them randomly along time. Now, with a totally random raster plot, we calculate again the functional network as we have explained before. Once we get the matrix of surrogates, we find the maximum value of correlation between any two neurons that are not the

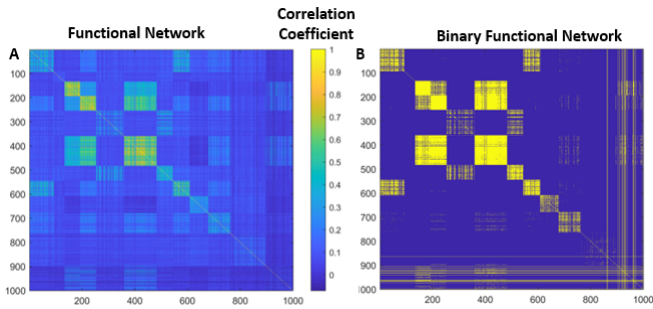


FIG. 6: **A**: Matrix of correlation coefficients for the simulations of Fig. 5. **B**: Binarized matrix according to a threshold.

same, because if it is the same neurons, we will always get a value of 1. The obtained value is 0.38, and we used as a threshold to eliminate non-significant connections. In other words, correlation values in the original matrix that are below 0.38 can appear by chance by having neurons firing randomly, and by doing the surrogate analysis we effectively eliminate those accidental cases, having a final functional network that we can trust. To complete the procedure, for every value of the original matrix, if this value is equal or lower than the threshold we substitute it by a 0, and if it is higher we substitute it by a 1, obtaining the final matrix of Fig. 6B.

The functional matrix indicates the degree of synchrony between neurons and in general is very different from the structural one. Indeed, as we can see if we compare the matrices of Fig. 5A and Fig. 6B, we can observe that the percentage of common entries is 88.69%, a number that we can consider quite high. This result is so powerful that we can get the matrix of connections in experimental cases, as illustrated in Fig. 7 for a neuronal network grown *in vitro*. We note that a strongly or weakly correlated functional networks depend on the structural connectivity and the dynamics of the neurons. In general, the functional network resembles the structural one only when the spatial constraints are very strong.

IV. CONCLUSIONS

We observed that for simulations with topographical obstacles there are different scenarios of activity, with a stronger or weaker synchrony among neurons. Simulations are in general very sensitive to changes of parameters and variables, so a more exhaustive study would

made appear more interesting examples.

When we have a more individual activity of communities, as we have seen in the simulation studied with more detail, we can obtain a functional network that resembles the structural one. This is a strong result that indicates that, when spatial constraints are very strong, one can predict the structure of the network from its dynamics. This could potentially give us information in experimental data with just data analysis of activity.

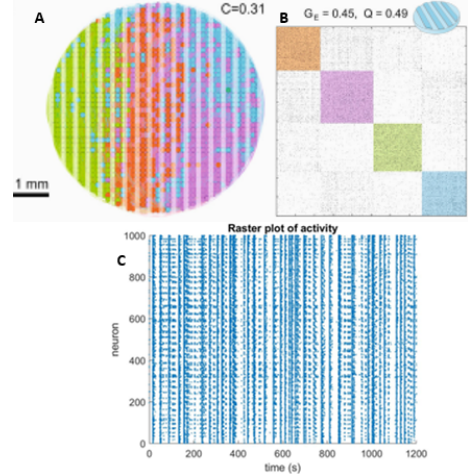


FIG. 7: Experimental case, given by Dr. Jordi Soriano, and that can be found in Ref. [1], conceptually similar to the example made here. **A**: the Gephi representation, **B**: the functional connection matrix and **C**: the raster plot.

Finally, the study of these simulations with more and different topographical obstacles would give us richer information, to take a most complete and improved model and then achieve some new results.

V. ACKNOWLEDGMENTS

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