Damage in simulated neural networks: impact of neuronal aggregation

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Abstract: Here, we numerically modelled biologically-realistic neuronal networks. We considered neurons that connected to one another on a Euclidean space and used the Izhikevich model to describe their the activity. Inhibitory and excitatory neurons were considered, and were positioned on the Euclidean space in either a homogeneous or aggregated way. Axons emerging from them were modelled as random walkers. Once the network was built, targeted and random damage were applied, and the dynamic response of the network was quantified, measuring the impact of damage using network analysis. Results show that the simulated networks are most resilient when random attack is applied and nodes are arranged on an aggregated way. The change in dynamics exhibits a non-trivial behaviour, as it is heavily dependent not only on the type of damage applied, but also on the way the network is created and the type of neurons that are deleted.

I. INTRODUCTION

Neuronal networks have come forward as a way to understand the emergence of collective behaviour from an ensemble of interconnected neurons in a controlled environment. Networks do not only allow us to see how an ensemble of synaptically interconnected neurons behave in a dynamic way, but also let us to study the relationship between collective dynamics and the underpinning network connectivity [1].

Collective behaviour is of main importance for these kind of systems, and departure from normal behaviour could be a sign of neurodegeneration. For instance Parkinson's disease patients display an elevated synchronous behavior as compared to the ones in the absence of neurodegeneration [2]. In this context, the brain is a complex system and understanding the robustness of its circuitry is of utter importance to tackle such degenerative diseases. Numerical simulations have emerged as a powerful tool that enables us to explore different network configurations and disease-related aspects, analyzing how the dynamics of the networks changes when the connections are altered, for instance by either deleting neurons or by altering their connections [3].

The main goal of this project is to unveil how synchronization of a network as a whole changes when damage is applied to the *in silico* system, i.e. when we delete connections of the network. For such purpose, we will construct networks that follow plausible biological rules, with two kind of neurons: inhibitory and excitatory. The first ones prevents synchronized behaviour by reducing activity in the network, whereas the second promotes synchronization by fostering the propagation of activity. We will simulate the dynamics of the network, and the emergence of synchronization, using the Izhikevich model, which offers a simple (both mathematically and computationally) yet complete model of spiking neurons, and complement those measures with network analysis. The latter will help us understand the topology changes that will be made in the network upon damage.

II. METHODS

A. Biologically realistic neural networks

Neuronal networks can be thought as a set of nodes and edges, emulating the way in which neurons are displayed in *in vivo* systems, and the connections they form. The cell body (soma) will be modelled as a mathematical point, placed on a bidimensional squared area of lateral size $s = 2$ mm. We will work with densities of around 250 neurons/mm^2, so our systems will be of 1000 neurons.

Depending on how the nodes (neurons) are positioned on this area, we will consider two kinds of networks: homogeneous networks or aggregated networks. On the homogeneous case, they are placed randomly. On the aggregated case, working with 1000 nodes, we will first position 10 nodes randomly (will be the number of modules), and around a circle of 0.2 mm of each one, we will place sets of 10 nodes randomly. An example of network construction can be seen on Figs. 1A-B.

For each soma, an axon will grow following a quasi-straight path. The final length of it, will be given by a Rayleigh distribution, with an average axonal length $\langle \ell \rangle = 1.1$ mm, which will be divided in 100 μm segments. The first segment of the axon will depart from the node following a random direction. Each new segment will be placed immediately after the previous one, and they will be able to change their orientation with an angle that will follow a normal distribution, with $\mu_\theta = 0°$ and $\sigma_\theta = 15°$. If one of these axons is expected to leave the defined area, it will bounce elastically with the wall (Fig. 1A).

Next we will build our networks. We will set up a dendritic tree as a disk around each neuron with diameter R_d, which will follow a normal distribution with $\mu_d =$

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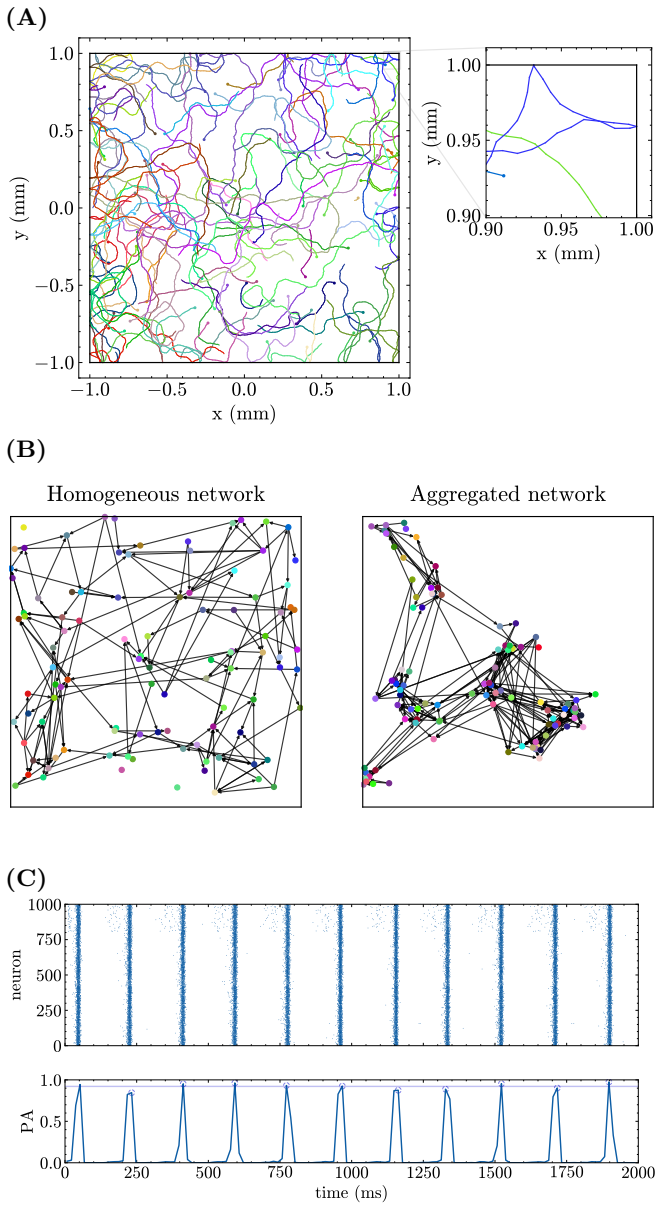

FIG. 1: **Methods.** **(A)** 100 cell bodies with their corresponding axon in the bidimensional squared area. A zoom of the upper-right side of the plot is displayed to showcase how the axons interact elastically with the walls. **(B)** Example of a homogeneous network and aggregate network for 100 neurons. **(C)** Raster plot showing the spiking of 1000 neurons using the Izhikevich model. Below it, the corresponding PA for a 15 ms time window, with the local maxima circled and the mean of those values as a horizontal line.

0.3 mm and $\sigma_d = 0.04$ mm. If an axon from the i-th neuron crosses the dendritic tree of the j-th neuron, there will be a 10% chance of forming a directed connection from $i \to j$. Connections will be stored in an adjacency matrix $A = \{A_{ij}\}$, where $A_{ij} = 1$ if there is a directed connection $i \to j$, and zero otherwise. All the parameters described and used for building the network have been extracted from Ref. [5]. Fig. 1B illustrate final networks.

B. Izhikevich model, Population Activity (PA) and inhibitory and excitatory neurons

The Izhikevich model [4] consist of a two-dimensional system of ordinary differential equations. Depending on four parameters, it successfully reproduces the spiking of individual neurons and bursting behaviour of neural networks of known types of cortical neurons.

$$\frac{dv}{dt} = 0.04v^2 + 5v + 140 - u + I, \tag{1}$$

$$\frac{du}{dt} = a(bv - u), \tag{2}$$

with an after-spike reset given by:

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

The variable v represents the membrane potential of the neuron and u is a membrane recovery variable. I represents synaptic currents, allowing the transmission of activity in the network. The other 4 parameters are:

- a: time scale of the recovery variable u.
- b: sensitivity of the recovery variable u to the subthreshold fluctuations of the membrane potential.
- c: after-spike reset variable of v.
- d: after-spike reset of the recovery variable u.

Initially we will set the potential of all neurons to the one they would have at rest (-65 mV). At each time step, the algorithm will work as follows: we will first introduce a thalamic input through the variable I; if the membrane potential of the i-th neuron is larger than 30 mV, the model will consider it has spiked, according to Eq. 3, and their variables will reset. The ones that have spiked will add a contribution on the membrane potential of the the ones which they are connected (through I), favouring that they spike as well. The original Izhikevich code in Matlab can be found in Ref. [4].

Raster plots will be a representation of the neurons that have spiked at a certain time t (Fig. 1C, top), allowing us to have an idea about the synchronization of the system through the concept Population Activity (PA) [1] (Fig. 1C, bottom). Inside a time window, of 15 ms in our case, we will count the number of neurons that have spiked, and this will be divided by the total number of neurons (1000 neurons in our simulations). High PA values will indicate that a large number of neurons have spiked at the same time window, whereas low PA values will mean that the number of neurons participating in collective events are very few. We will run the simulation for 2000 ms and quantify the synchrony of the network as the mean of local maxima of PA.

To enrich the system, and motivated by the anatomy of mammalian cortex, two types of neurons will be considered: excitatory and inhibitory. The former will favour

the transmission of synaptic signals between neurons, and the latter will difficult this transmission. Their relationship will be 4:1, so in our system, there will be 200 inhibitory neurons and 800 excitatory neurons. No distinction will be made regarding their position to the network. This will be implemented through the addition of positive or negative weights (for excitatory and inhibitory neurons, respectively) to the already refereed adjacency matrix, which will affect the I variable and therefore the membrane potentials of the neurons, and with differences on the variables $\{a, b, c, d\}$.

C. Application of damage

We will measure the change of synchrony, i.e. the mean of the local maxima values of PA, when damage is applied. Deletion of nodes and connections will be applied considering three main actions:

- Highest degree damage: at each step, the deleted node will be the one with the highest number of edges (the sum of both in-degree, edges that go to that node from another, and out-degree, edges that go from that node to another).
- Betweenness centrality damage: at each step, the deleted node will be the one that has the highest betweenness centrality. This parameter gives us an idea of how central a node is in the network, measuring the proportion of shortest paths between all node pairs in the network that pass through it [6].
- Random damage: nodes will be deleted randomly, without taking into account any topological trait.

The simulations will be run as follows: we will apply each type of damage individually, deleting one node at each step, and computing the PA until no nodes are left. These measures will help us understanding how resilient the network is to different damage types.

D. Network topological measures

To further analyse how the different types of damage affect the network, at each step we will compute different topological properties through network analysis [6]:

- Giant component (GC): defined as the number of nodes that the highest sub-graph contains divided by the total number of nodes minus the number of deleted ones (in this way we will be able to see more clearly when the network fragments). It can range between 0 (when there are no edges left) and 1 (when there is a path that links all the nodes).
- Global efficiency: can be understood as how efficient the information is transmitted on the network through the shortest path.

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

with N the total number of nodes and d_{ij} the shortest path between the i-th and j-th node. It ranges from 0 (isolated neurons) to 1 (complete graph).

- Modularity: density of links inside communities as compared to links between communities:

$$Q = \frac{1}{2m} \sum_{i,j} \Big[A_{ij} - \frac{k_i k_j}{2m} \Big] \delta(c_i, c_i), \tag{5}$$

with $m = \sum_{ij} A_{ij}$, A_{ij} being our adjacency matrix, $k_i = \sum_j A_{ij}$ and c_i the community of node i. The communities of the network will be computed using the Louvain algorithm [7], which maximizes the coefficient Q. Technically Q ranges from -1 to 1, but as we are using a method that maximizes Q to find communities, it will only take positive values.

For simplicity, we will only use a directed network to compute G_{eff}. For the other two coefficients, we will use an undirected version, where every directed connection will be transformed to an undirected one. All these measures will use an unweighted version of the adjacency matrix (without making a distinction between inhibitory and excitatory neurons), as we are only interested in the topology of the network itself.

III. RESULTS AND DISCUSSION

A. Damage on homogeneous networks

For a a homogeneous network, the changes in PA and topological measures for different types of damage are shown in Fig. 2. We can see that, as expected, PA decreases with the different types of damage, but the decrease itself depends on the type of damage.

The most resilient scenario, i.e. the one that keeps the highest PA when nodes are deleted, is the random one. When we apply this kind damage there is no specific target, so it is understandable that the synchrony of the network smoothly decreases. Considering the targeted damages, the network is more resilient for the highest degree scenario when damage is mild, but when we have deleted around 30% of the nodes, there is a change in behaviour. This can be understood by looking at the changes in Q. Betweenness centrality damage is more aggressive at the early stages, because it deletes the nodes that are more central to the network, i.e. the nodes in which the most of the shortest paths between all node pairs have to pass through. This is the reason it has the highest increase and decrease in Q and G_{eff}, respectively, as it quickly divides the network into different communities. Once this is done, the network appears more resilient.

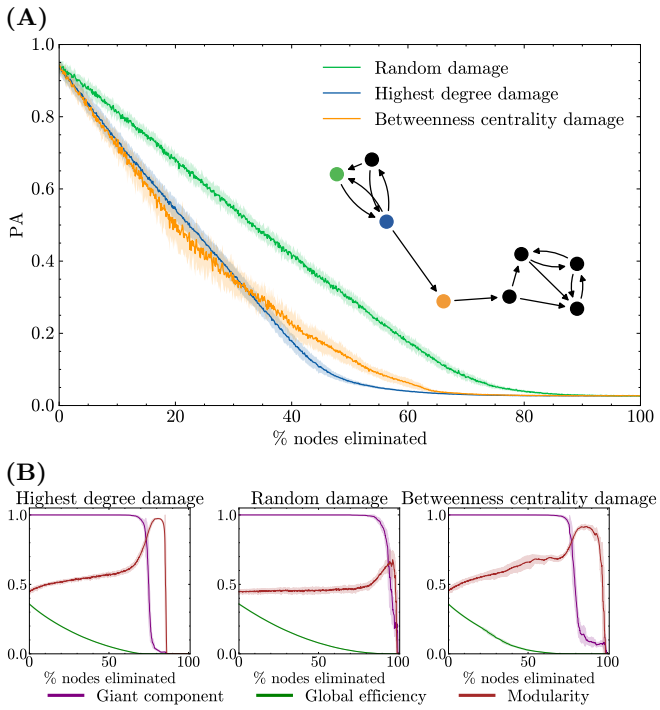

FIG. 2: **Damage on a homogeneous network**. **(A)** Change in PA as a function of the percentage of the nodes deleted for the three different damage types. An example graph is also shown, highlighting the nodes to be deleted for each damage type. **(B)** Change in GC, Q and G_{eff} on the network as a function of the percentage of the nodes deleted for the three different damage types. The lines represent the mean and the shaded area the standard deviation of 10 network realizations.

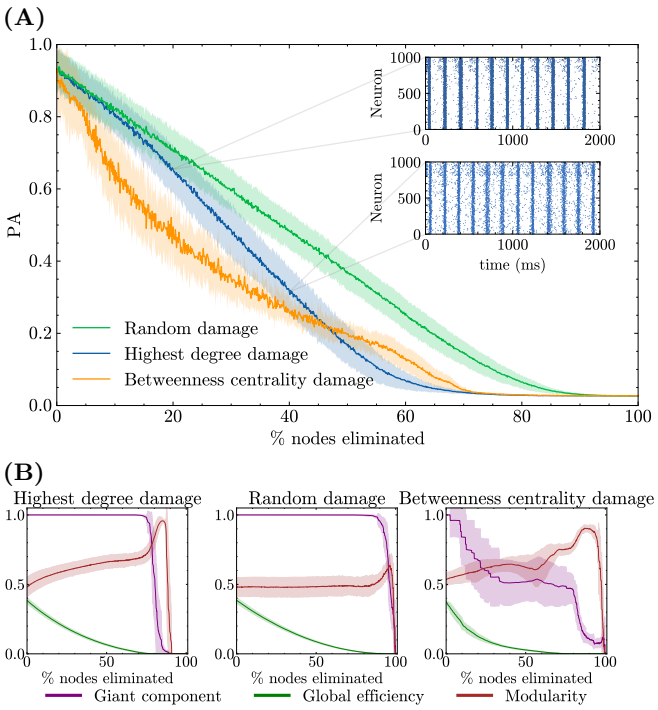

FIG. 3: **Damage on an aggregated network**. **(A)** Change in PA as a function of the percentage of the nodes deleted for the three different damage types. Illustrative raster plots at two different steps are also shown to highlight what the variation in PA implies. **(B)** Change in GC, Q and G_{eff} as a function of the percentage of the nodes deleted for the three different damage types. The lines represent the mean and the shaded area the standard deviation of 10 network realizations.

Highest degree damage, however, has a constant decrease in PA, such as the one we have seen for random damage, but at a much higher rate. This is because this damage will solely be based on the number of edges the nodes have, not the role they play on the network as a whole (so we can expect the behaviour to be similar as the one when random damage is applied). Q increases, because it is indeed a targeted damage, and GC decreases the earliest out of the three types of damage because of the intrinsic nature of this damage.

B. Damage on aggregated networks

The results for aggregated networks are shown in Fig. 3. These types of networks are more resilient to damage, as we have to delete a higher percentage of nodes to effectively remove the collective behaviour (PA).

Random damage and targeted attack on the highest degree behave similarly as before, both in the change in PA and in the measures of the topology, except that now the network is more resilient. However, betweenness centrality damage is much more destructive at the beggining. Because of how the network was created, the nodes are more distributed into modules, so after a few steps, this type of damage creates communities that are not connected between them. This can be captured thought the GC, which already decreases when only a few nodes have been deleted.

We note that this behaviour cannot be seen when highest degree damage is applied, as high degree nodes do not necessarily coincide with those exhibiting highest betweenness centrality (more central).

C. Change on the length of inhibitory axons

To understand how collective behaviour is affected by other simulation variables, we can focus on the role played by excitatory (e) and inhibitory (i) neurons. For this, we will only consider homogeneous networks.

For such purpose we can lengthen, $\langle \ell \rangle_i = 3 \cdot \langle \ell \rangle_e$, or shorten, $\langle \ell \rangle_i = \langle \ell \rangle_e / 3$, the extension of the inhibitory axons and compute the change in PA only for damage on the highest degree. Results are shown in Fig. 4.

We can see that, depending on the relation between the length of the inhibitory and excitatory axons, the

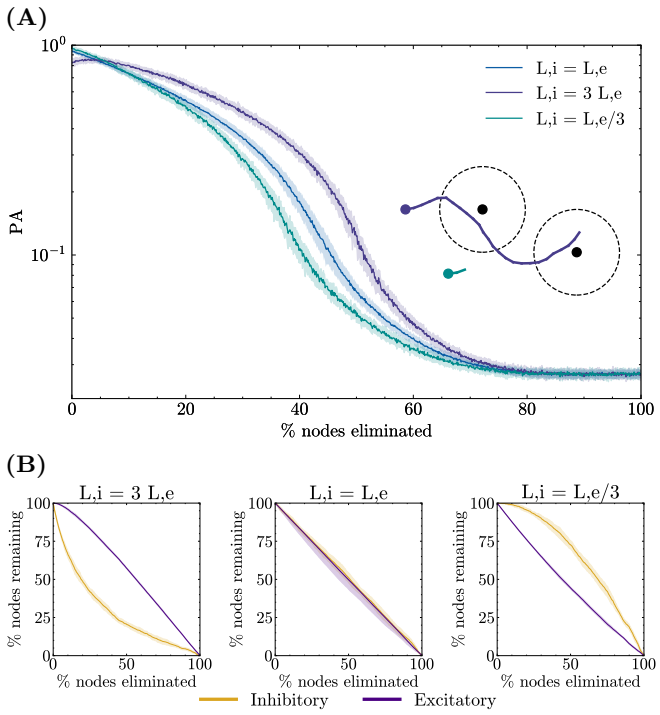

FIG. 4: **Highest degree damage on a homogeneous network for different relations between axonal lengths of inhibitory and excitatory neurons**. (A) Change in PA, with log-y scale, as highest degree damage is applied for different relations between the inhibitory and excitatory axon length. Inset: a sketch of the inhibitory cell body for $\langle \ell \rangle_i = 3 \cdot \langle \ell \rangle_e$ and $\langle \ell \rangle_i = \langle \ell \rangle_e / 3$. (B) Change in the percentage of remaining inhibitory and excitatory neurons as damage is applied for the three cases. The lines represent the mean and the shaded area the standard deviation of 10 network realizations.

behaviour of PA is different: if we lengthen the inhibitory axons, the network is not only more resilient to damage, but even increases PA as nodes are deleted, whereas if we shorten the inhibitory axons, PA is lost earlier.

To understand this behaviour, we can look at Fig. 4B, which represents the percentage of remaining neurons of each type as a function of the percentage of the nodes that have been deleted, bearing in mind the role that excitatory (favours transmission) and inhibitory (oppose transmission) neurons play. If we lengthen the axons of the inhibitory neurons, we are favouring the number of connections they can form, as their axon could cross the interaction circle of more neurons. Therefore, as we are applying damage on the node that has the highest degree, we would first be deleting the inhibitory neurons of the network. So, in this case, as we are first deleting neurons that difficult transmissions, we are favouring the collective events, even though we are deleting connections. On the contrary, if we shorten the axons of the inhibitory neurons, less connections would be able to form, and the neurons that would be deleted first are the excitatory. On a normal case, there would be no distinction.

IV. CONCLUSIONS

We showed that, by exploring different parameters regarding the topology of a neuronal network, one can rationalize why is there a difference in the change of Population Activity, a measure of the synchrony of the network, when nodes of the network are deleted by the different types of damage. However, there is not a direct relationship between dynamics and topology of the network.

Variations on the collective behaviour when damage is applied not only depend on the type of damage we are applying, i.e. the order in which we delete the nodes, but also on the way we have built our network (homogeneous or aggregated) and the type of node we are deleting (inhibitory or excitatory), making it almost impossible to predict the curves presented.

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