# Impact of neuronal aggregation: burst-originating neurons

Author: Àlex Vilchez Costa
*Facultat de Física, Universitat de Barcelona, Diagonal 645, 08028 Barcelona, Spain.*

Advisors : Dr. Jaume Casademunt Viader, Dr. Jordi Soriano Fradera
*Departament de Física de la Matèria Condensada.*

**Abstract:** This study explores the spatial distribution of burst-initiating neurons in simulated 2D neuronal cultures with a toroidal topology, in relation to the global network structure and its activity dynamics. A total of 25 simulations were conducted with varying levels of spatial aggregation, using the Izhikevich model, which is inspired by real neurons. The results show that, as the overall population becomes more spatially aggregated, the burst-initiating neurons also tend to cluster, reaching a plateau for population Gini coefficients above 0.5. *In vivo* results for the homogeneous case are consistent with this study, lending support to the non-experimentally tested scenarios. Moreover, more aggregated networks tend to exhibit higher burst frequencies, although a stable frequency of approximately 3.9 bursts per second is maintained.
**Keywords:** neurons, network, bursts, burst-originating, aggregation, Izhikevich
**SDGs:** 3: Good Health and Well-being, 9: Industry, Innovation and Infrastructure, 17:Partnerships for the Goals

## I. INTRODUCTION

Neuronal simulated networks are essential for understanding the complexity of brain function, since they provide a controlled framework to test hypotheses and reveal principles that are difficult to investigate in vivo. In these simulations, the presence of bursts – short time intervals of high-frequency spiking – is a characteristic feature of coordinated neural activity and is crucial for functions including signal amplification, memory encoding and synchronization. It is particularly interesting to study the neurons that trigger these bursts in 2D neuronal models, as they typically act as pacemakers in the network. By profiling and characterizing these burst-generating neurons, we may gain insight into factors contributing to network scale dynamics and set the ground for relations between structure and function, designing future therapeutic interventions and neuromorphic systems.

The aim of this project is to shed new light on these burst-originating neurons, focusing our investigation on the relation between their level of spacial aggregation and the degree of aggregation that have the total population of neurons. Furthermore, we will study the connection between the frequency of bursting and the aggregation of burst-originating neurons.

To this end, a series of simulations are performed in which the level of spatial aggregation is systematically varied. These networks are endowed with dynamics following the realistic Izhikevich model. Furthermore, the analysis is focused on the Gini coefficient of overall neuronal density, the Gini coefficient specific to burst-originating neurons, and the frequency of bursts for all distinct simulations.

Moreover, to identify these burst-generating neurons, we will consider them as the first neuron to fire in the burst due to the fact that they are reliables indicators of burst initiation, as shown in the Reference [1]. These first-to-fire neurons were impossible to determine with the code given in the reference [2] as the time resolution was not sufficient to discriminate the very first neuron to spike, leaving many candidates with the exactly same spike time. To deal with this problem, we could simply take one of the neurons that the code considered first to fire randomly, but we modified a little the code in [2] to give a more rich temporal resolution of the spikes. With this variation, we obtained a more accurate ordered list of spikes of our burst, being able to consider the first of them, our burst initiating neuron.

## II. METHODS

### A. Realistic neuronal culture model using toroidal boundaries

In order to recreate a biologically realistic 2-dimensional neural network model, we developed a MATLAB code that generates an artificial 2D neuronal culture in a square area of 4mmx4mm; within this space, 2000 neurons are distributed across $X$ modules, each containing $Y = 2000/X$ neurons. This yields an overall neuronal density of 125 neurons/mm$^2$, which is inside the range observed in various mammalian cortical layers [3].

In first place, the centres of the modules are randomly distributed inside the 16 mm$^2$ square grid map. Next, each soma neuron is placed around the centre of its corresponding module following a normal distribution of 0.5 mm radius.

The purpose of dividing the population in modules allows us to directly affect the spatial aggregation of the simulated neuronal culture. Increasing the number of modules while reducing neurons per module leads to a more homogeneous distribution, as the centres are placed totally randomly. In contrast, decreasing the number of modules and increasing the quantity of neurons per module results in a highly aggregated culture. For the

purpose of this study we will consider 15 different combinations, ranging from the most homogeneous network – 4 neurons in each 500 module – to a very aggregated example:125 neurons for 16 modules (see Figure 1A).

Each neuron, in turn, is also given an individualized axon of length that is drawn from a Rayleigh distribution with mean 1.1 mm [4], with each of these divided into 0.02 mm segments. The axons extend from the soma positioning these pieces with changes in direction based on a 15° standard deviation of a Gaussian distribution, adding realistic curvature and variation.

Finally, dendritic fields are represented as round regions around each soma with radii that are drawn from normal distribution with mean 0.2 mm.

The placement follows toroidal –periodic– boundary conditions such that neurons and axons extending beyond the boundary of the simulation grid are wrapped to the opposite side of the grid. (see Figure 1A)This is an approximation to recreate an uninterrupted, boundaryless surface without privileged regions.

Beyond the physical representation of neurons, its connectivity is based on geometric proximity: if any piece of one neuron's axon falls within the dendritic radius of any other neuron, there is a bidirectional connection between them. This is modelled in a 2000×2000 binary adjacency matrix for the existence of synaptic connections between pairs of neurons.

The program's design is biologically inspired with toroidal geometry, stochastic outgrowth of the axons, and distance-based synaptogenesis that imitate the important structural details of realistic neural tissue.

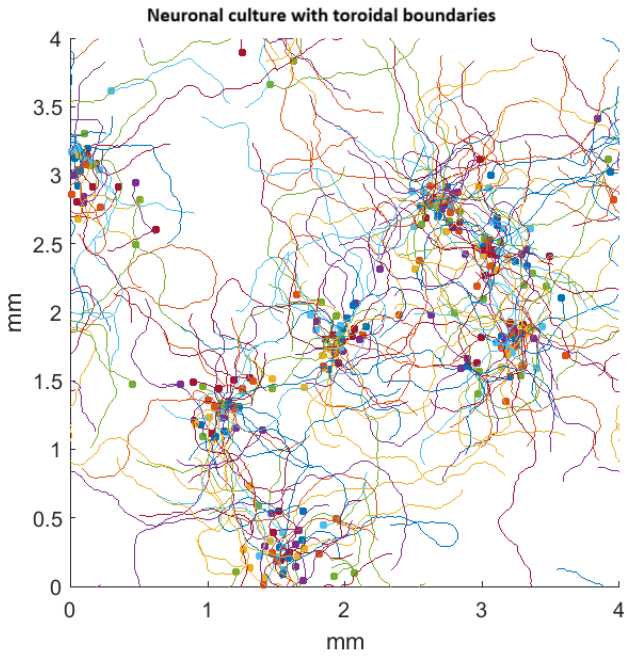


FIG. 1: **A neuronal aggregated culture with toroidal boundaries.**
Sample with 7 modules, each one containing 40 neurons. We can appreciate the toroidal topology, where axons leaving a boundary continue their path in the opposite side. For the same reason, part of one single module can be at one end, whereas the other part at the opposite boundary.

### B. Izhikevich model and variation

The dynamics of the culture is created following the Izhikevich neuron model. With a default 80% *excitatory*, 20% *inhibitory* neurons for 5000 ms of total simulation time, the simulation captures spiking dynamics with biologically plausible differential equations. Connectivity of the network is read from the code previously mentioned and then sparsified such that 85% of the connections are set to zero to recreate a more realistic model.

Each of these synapses is assigned a synaptic weight: the excitatory ones receive between *0* and 6, the inhibitory ones between *0* and 0.5, in a weight matrix `W`. There is noise in the form of random thalamic inputs with maximum amplitude of 4 for the excitatory ones but **2** for the inhibitory ones to support constant firing regardless of the absence of input stimulation.

During the simulation of the code that can be found in the reference [4], neurons change over time with a 2-step numerical integration of 0.5 ms per half-step of both their voltage and recovery variables.

Finally, the spikes are captured in a firings matrix that is then plotted in a raster plot.

A raster plot is an essential tool in the field of neuroscience for displaying the temporal firing of neurons in a network. In the case of neuronal cultures, it offers a clear and compact way to show the timing of spikes across multiple neurons simultaneously. Each line in the plot represents a single neuron, and each vertical tick marks a spike at a given moment in time. When applied to data from neuronal cultures, raster plots help researchers identify patterns of synchronized activity, such as network bursts, and explore the spatiotemporal nature of firing.

Our code new model is an extension of the basic Izhikevich spiking neuron network but adds an important refinement in the numerical integration scheme that is used in simulation. Both variants simulate an 80% excitatory, 20% inhibitory network of neurons for 5,000 ms with identical parameters of the Izhikevich neuron and with an Erdős–Rényi-style sparsified directed connectivity matrix (frac_delete = 0.85), but our new variant enhances temporal resolution by breaking each millisecond into four 0.25 ms integration steps. This higher-resolution integration resolves faster synaptic dynamics better and more realistically captures spike timing that can be essential for synchrony, oscillations, or temporal coding investigations.

Other essential features are maintained in both versions such as those using synaptic weights (MAX_EXC_WEIGHT = 6, MAX_INH_WEIGHT = 0.5), noise-induced spontaneous activity (NOISE_MAX = 4), and an end synchrony measure based on the

ratio of active neurons within 10 100-ms windows. The increased sub-steps per iteration in the new version offer higher-granularity precision without changing the qualitative dynamics of the model but render it stronger for subsequent analyses based on exact timing like the detection of bursts or spike-time correlations.

### C. Spacial origin of bursts

In order to study the dynamics of the burst in greater depth, we made a MATLAB code to find out the neurons that origin each of the analysed burst. For such purpose, we will consider them as the first neuron to fire in the burst, as mentioned before.

The analysis begins by dividing the raster plot created with the Izhikevich model into temporal windows of $10ms$ and computing the proportion of active neurons within each window. We considered bursts those temporal windows with more than 30% neurons activated to identify the occurrence of bursts. For each detected burst, the first neuron to fire is identified, excluding neurons with abnormally high activity levels, that is those neurons that are activated more than 85% of the total time.

For this task it is used the Izhikevich code model modified to have more clear identification of first-to-fire neurons.

The results are visualized using a raster plot that highlights burst-initiating neurons, as well as a 2D spatial maps that depict their locations and activation times. Finally, bursting frequency is calculated, and relevant data—including burst intervals and initiating neurons—are saved for further analysis.

### D. Lorenz curve and Gini's coefficient

The Lorenz curve is a graphical tool used to describe the cumulative distribution of a quantity across a population. In this study, it is employed to examine the spatial aggregation of both the entire neuronal population and the subset of neurons that are origins of bursts. To this end, our map is divided into discrete cells, each measuring 0.2x0.2mm$^2$ for study of the total population of neurons, and 1x1mm$^2$ for the neurons that act as burst's origins. These cells are then sorted by the number of neurons they contain, and their cumulative sum form the Lorenz curve.

The Gini coefficient, in turn, is a scalar value derived from the Lorenz curve that quantifies the degree of inequality in a distribution. It is calculated as twice the area between the Lorenz curve and the straight line $x = y$. In our context, the closer the Gini coefficient is to 0, the more homogeneous spatial distribution of neurons; conversely, values closer to 1 indicate a higher degree of spatial aggregation.

## III. RESULTS AND DISCUSSION

### A. Contrasting homogeneous and aggregated cultures

Although we used 25 distinct cultures with variations on the number of modules and neurons per module for the forthcoming study, we now expose only the figures of the two extreme cases. For the homogeneous condition, we consider the sample composed of 500 modules randomly distributed with 4 neurons each; and for the most aggregated condition, we use the culture consisting of 125 neurons distributed across 16 modules.

With the computation of the Lorenz curve for every culture and its corresponding Gini coefficient, the varying degrees of aggregation becomes clear. In Figures 2A and 2B we can observe the Lorenz curve for both $4 \times 500$ and $125 \times 16$ networks, resulting in a Gini coefficient of 0.31 and 0.76 respectively. For all intermediate scenarios, the Gini coefficient takes values between these two extremes in an approximately linear trend, creating an illustrative sample of cultures with different levels of aggregation.

As we simulate the dynamics of the cultures, we can observe the burst-originating neurons both in spatial culture maps and in raster plots.

On the one hand, burst-originating neurons can be seen highlighted with colour in the spatial map (Figure 2C and 2D), contrasting with the remaining neurons of the total population coloured in grey. For the homogeneous case (Figure 2C), it is not easy to recognize any spacial patron given that the population is uniform grown without any privileged region. By contrast, in the aggregated network (Figure 2D), we can appreciate the intuitive fact that burst initiators are usually located close to the centres of the modules but not necessarily.

On the other hand, the representation of raster plots (Figure 2E and 2F) provide a closer look at the time that neurons spike. These graphics bring a very clear visualization of bursts, and with them, the burst-initiators. Interestingly, can observe, that in the homogeneous case (Figure 2E) the neurons that start the bursts do not follow any visual order, having different initiators for different bursts. Nevertheless, there is a drastic change of scenario when the aggregated culture is considered (Figure 2F). In it, we can appreciate a layout pattern: some neurons seem to repeat as bursts initiators over time passed. The quantity of burst-originating neurons for cultures that have a Gini coefficient above 0.6 is typically around 2 and 3 same neurons, with the parameters of our study.

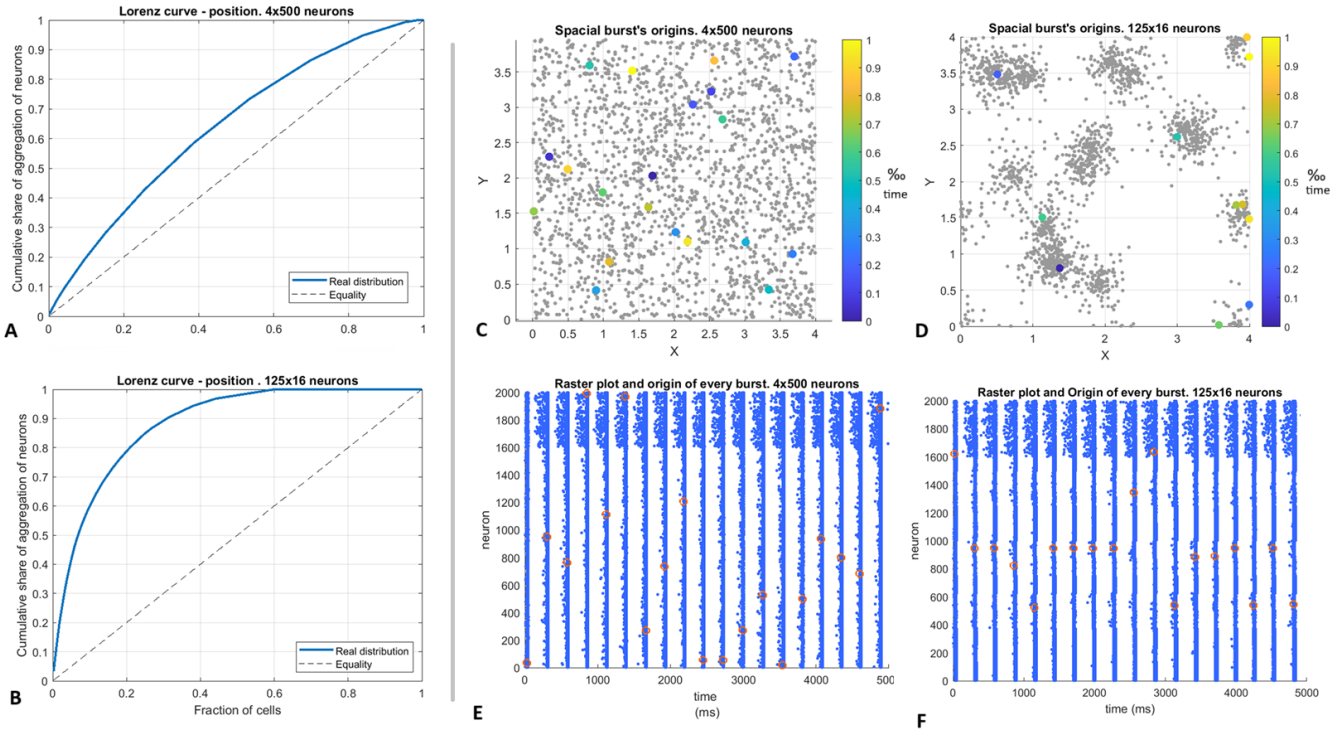


FIG. 2: **Aggregation study and identification of burst-originating neurons.**
In the Figure A we can see the Lorenz curve of a culture of neurons with a Gini coefficient of 0.31, as the homogeneous case. In contrast, Figure B is the aggregated culture with a Gini coefficient of 0.76. For Figure C and D we can examine the spacial distribution of neurons with the bursts originating neurons highlighted in colour: Those with a more vivid colour are the last ones and the more blue are, the earlier their burst spiked. For Figures E and F a raster plots are shown with orange marks in the burst-originating neurons.

### B. Spatial correspondence between population aggregation and burst origins aggregation

As previously discussed, the Lorenz curve and Gini coefficient are measures that provide insight into the degree of aggregation within the entire neuronal population. Nonetheless, these metrics can also be applied to analyse the aggregation of the subset of burst-originating neurons. By considering all 25 cultures with varying levels of aggregation, we can compute a representation of the relationship between the two levels of aggregation: the one of the total population and that of the subset responsible for initiating bursts.

This is shown in the Figure 3A, where every dot represents a different sample. In here we can appreciate a certain dependence between both magnitudes: The more aggregated the system is, the more aggregated the subset of burst-originating neurons also appears to be – up to a certain limit. Based on the observations, once the Gini coefficient of the total population exceeds 0.5, the level of aggregation among burst-initiating neurons stops increasing and stabilizes without surpassing 0.9 Gini coefficient.

### C. Relation between population aggregation and bursting frequency

Furthermore, it is of interest to examine the relationship between burst frequency and the degree of aggregation among burst-originating neurons. Figure 3B presents the burst frequency plotted against the Gini coefficient of the total population across all 25 cultures. A clear increasing trend can be observed, which appears to follow a pattern similar to the function $x^{1/3}$. Following this observation, it can be noted that the minimum burst frequency tends to stabilize around 3.9 bursts per second, regardless of the degree of aggregation.

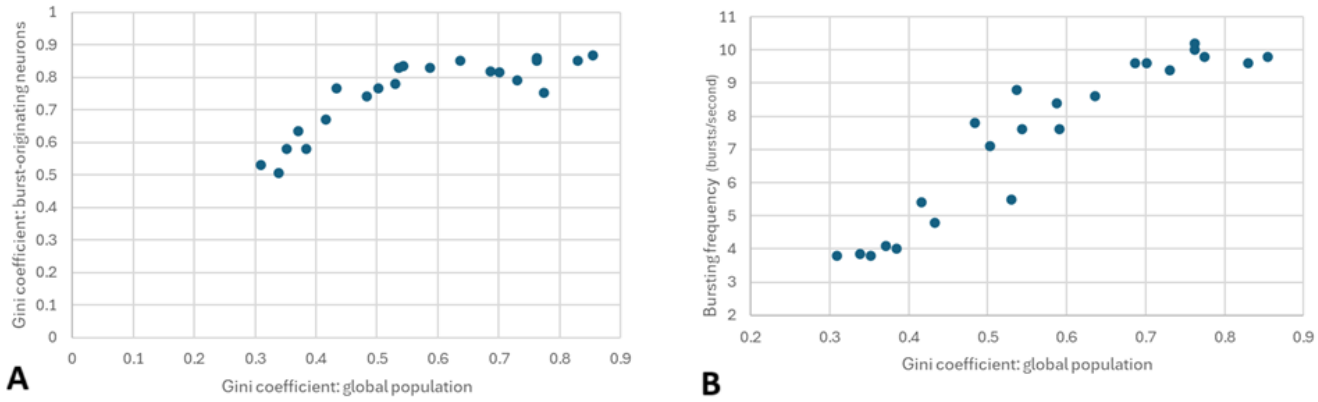


FIG. 3: **Statistical final results**
Spatial correspondence between population aggregation and burst origins aggregation and relation between population aggregation and bursting frequency

## IV. CONCLUSIONS

In this work, we conducted a systematic examination of the spatial patterning of neurons that initiate bursts in biologically inspired simulated neural cultures. By adjusting the level of aggregation across 25 different configurations and applying tools like the Lorenz curve and Gini coefficient, we found a certain correlation between the spatial aggregation of the full neuronal population and the one of the specific neurons responsible for triggering bursts. Specifically, we observed that as the overall aggregation increased, burst-originating neurons also tended to cluster spatially—though this relationship saturated beyond a Gini coefficient of 0.5, suggesting a structural limit in how concentrated burst initiators can become. Additionally, comparing with experiments *in vivo* like the reference [5] we can check that the fact that in homogeneous networks, the Gini coefficient is around 0.5.

Moreover, our results reveal another interesting link between network dynamics and spatial organization: cultures with higher aggregation levels tended to produce bursts more frequently. Even in highly homogeneous cultures, we observed a consistent baseline bursting rate of around 3.9 bursts per second, indicating that spontaneous activity is preserved regardless of the spatial arrangement. Taken together, these results highlight the significant role of spatial structure in shaping the functional behaviour of neural networks, offering valuable insights for understanding biological systems and designing neuromorphic models that rely on coordinated patterns of activity.

### Acknowledgments

I want to specially thank my advisors, Dr. Jaume Casademunt and Dr. Jordi Soriano, for being there every week even until the very last day. By all means, my family deserves to be represented here for being there, always.

[1] Pan, L., et al. First-spike rank order as a reliable indicator of burst initiation and its relation with early-to-fire neurons. *IEEE Trans. Biomed. Eng.* **56**, 1673-1682 (2009).
[2] E. M. Izhikevich. Simple model for Spiking Neurons, *IEEE Transactions on Neural Networks*, **14**, 1569-1572 (2003)
[3] Mota, B. & Herculano-Houzel, S. Cortical folding scales universally with surface area and thickness, not number of neurons. *Science*. **349**: 74–77 (2015).
[4] Spitkó, A., Káli, S., Farkas, D. & Gros, C. Noise-driven amplification mechanisms governing the emergence of coherent extreme events in excitable systems. *Physical Review Research*. **3**, 023133 (2021)
[5] Montalà-Flaquer, M., López-León, C. F., Tornero, D., Houben, A. M., Fardet, T., Monceau, P., Bottani, S., i Soriano, J. *Rich dynamics and functional organization on topographically designed neuronal networks in vitro*. *iScience* **25**, 105680 (2022)

## Impacte de l'agregació neuronal: neurones iniciadores d'esclats síncrons

Author: Àlex Vilchez Costa
*Facultat de Física, Universitat de Barcelona, Diagonal 645, 08028 Barcelona, Spain.*

Advisors : Dr. Jaume Casademunt Viader, Dr. Jordi Soriano Fradera
*Departament de Física de la Matèria Condensada.*

**Resum:** En aquest estudi s'explora la distribució espacial de les neurones que inicien esclats (bursts) en cultius neuronals simulats en 2D seguint una topologia toroidal, en relació amb l'estructura global de la xarxa i la seva dinàmica d'activitat. S'han realitzat 25 simulacions amb diferents nivells d'agregació espacial, utilitzant el model Izhikevich, inspirat en neurones reals. Els resultats mostren que, a mesura que la població total esdevé més agregada, les neurones iniciadores dels esclats també tendeixen a agrupar-se, assolint un màxim d'agregació per a coeficients de Gini de la població superiors 0,5. Resultats realitzats *in vivo* pel cas homogeni coincideixen amb el meu estudi, aportant valor als casos no realitzats experimentalment. A més, les xarxes més agregades tendeixen a mostrar una freqüència d'esclats més elevada, tot i que es manté una freqüència d'aproximadament 3,9 esclats per segon.
**Paraules clau:** neurones, esclats, xarxa, Izhikevich, agregació, toroidal
**ODGs:** 3: Salut i benestar, 9: Indústria, innovació, infraestructures, 17:Aliança pels objectius