

Simulation of large scale cortical networks by use of individual neuron dynamics

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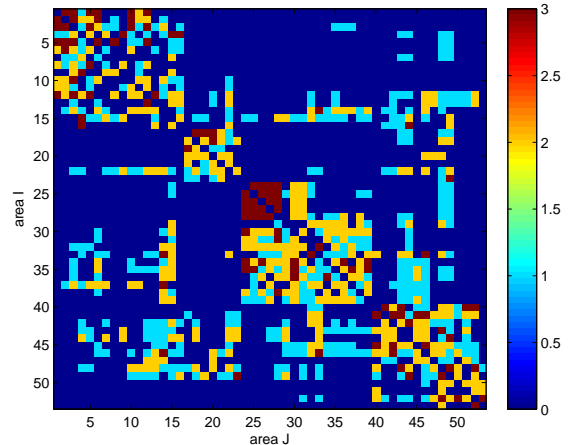
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I. INTRODUCTION

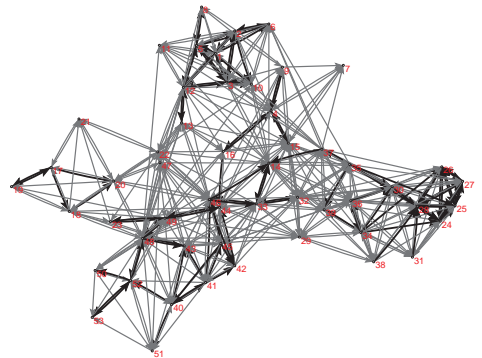
Understanding the dynamics of the mammalian brain is one of the central aims of modern neuroscience. Besides of developing and improving imaging methods like EEG, fMRI, PET, mathematical modelling i.e. computational simulation of neural networks, can help to understand the dynamical behaviour of the brain. While the dynamics of single neurons is quite well conceived and their dynamical behaviour can be reproduced by differential equations e.g. Hodgkin-Huxley [7] or iterated maps e.g. Rulkov [4], systematic exploration of the impact of connection topology on the dynamical organisation in neuronal networks is barely beginning.

In [1–3] the authors made an attempt by comparing two models to simulate the mammalian cortex of the cat. Both models consisted of a network of 53 cortical areas with a realistic connectivity topology (shown in Fig. 1) as given in [5]. Their first approach was to model areas using a neural mass model [8], which represents a population of neurons and is capable of reproducing EEG-like oscillations, hence it promises to be a biologically plausible approach to model a brain area. Synchronisation in this model did not follow the patterns of anatomical connectivity, hence it was considered to be not suitable to reflect the relationship between the intricate structural and functional connectivities of cortical networks. The second approach was a multilevel model in which each area was represented by a subnetwork of 200 neurons. While the connectivity between cortical areas remained the same, the internal 200 neurons were connected by a small-world topology. This model showed biologically plausible behaviour, meaning that synchronisation and dynamical clustering followed the biological topology. Additionally, the mean field signals of the areas showed strong similarities to real EEG data. The drawback of this model is its computational cost that is necessary for running simulations.

The goal of the present work is to investigate how much of the dynamical behaviour of the multilevel model can be reproduced by a simplified model, which is computationally competitive.



a)



b)

FIG. 1: a) Plot of the adjacency matrix, b) Visualisation of the network using the Kamada-Kawai lay-outing algorithm

A. Data

As in [1–3] we simulated the cortico cortical connectivity based on an adjacency matrix of the mammalian cortex of a cat, holding the connection strengths of 53 areas linked by about 830 fibres of different densities taken from [5].

The raw data was obtained from various studies of the cortex of cats and was gathered in a database of the thalamo-cortico-cortical connections [5]. In physiologi-

System	Areas
Visual(V)	0-15
Auditory(A)	16-22
Somato-motoric(SM)	23-38
Fronto-limbic(FL)	39-52

cal studies where connections between one area and another were referenced as “dense” or “strong”, the connection weight was set to 3, weak or sparse connection were weighted as 1 and intermediate weights as 2. The cases “explicitly reported as absent” and “no information available” were treated the same and were weighted with 0. Hence, it is possible, that some existent connections in the biological brain do not appear in the adjacency matrix because they were not reported.

The brain network of a cat reported in [5] has a high clustering coefficient and short average path length which are typical small-world properties. The degree of the nodes is very heterogeneous and ranges from 2 to 35 connections [2]. Fig. 1 shows a plot of the adjacency matrix M_{ij} , that holds the connection strengths of the areas. In the plot one can see four main “blocks” or communities which have high connectivity inside themselves. These communities correspond to the biological functional subsystems *visual (V)*, *auditory (A)*, *somato-motoric (SM)* and *fronto-limbic (FL)*.

II. METHODS

In order to achieve our goal of developing a model that reproduces the dynamical behaviour of the multi level model in [1–3] and is computationally competitive, we chose to turn back from the multi level approach and searched for alternative dynamics for modelling areas.

The dynamical behaviour of a single area was now modelled in two different ways. One approach was to use an iterated map, developed by N.F. Rulkov [4], the other was to use a system of two first order ODEs developed by E. Izhikevich [6].

Rulkov introduced a model that replicates the spiking and spike-bursting behaviour of real neurons. The model is represented by a two dimensional map, which is capable of producing spiking and spike bursting signals. It has a fast variable (x), which represents the membrane potential of the neuron and a slow one (y). The main idea behind this is to enable the possibility to operate on different time scales. For the fast dynamics of x , one can regard y as a control parameter. For some regions of y there exists a stable cycle in the fast dynamics of x , which generates periodic spiking. As y slowly changes, the system will undergo a bifurcation that destroys the stable cycle in the fast dynamics and x will converge to a fixed point. After some time y returns to the regime, where a stable cycle in x exists and everything starts

TABLE I: Parameter values of the Rulkov map

constant	value
α	6
β	1
μ	0.001
σ	0.3

over again.

$$x_{i,n+1} = f(x_i, y_i + \beta) \quad (1)$$

$$y_{i,n+1} = y_{i,n} - \mu(x_{i,n+1}) + \mu\sigma \quad (2)$$

$$f(x_i, y_i) = \begin{cases} \alpha/(1-x_i) + y_i, & x_i \leq 0 \\ \alpha + y_i, & 0 \leq x_i \leq \alpha + y_i \\ -1 & x_i \geq \alpha + y_i \end{cases} \quad (3)$$

To couple the neurons, we modified equations as in [4] and added a noise term:

$$x_{i,n+1} = f(x_i, y_i + \beta) + \xi \quad (4)$$

$$y_{i,n+1} = y_{i,n} - \mu(x_{i,n+1}) + \mu\sigma \frac{C}{N} \sum_{j=1}^N M_{ij}(x_i - x_j) + \xi \quad (5)$$

where, x_i , y_i corresponds to the i th area and M_{ij} is the adjacency matrix. The constants α , β , σ , μ are model parameters and are all the same for every area, while $\xi = D\Xi_{0,1}(t)$ stands for Gaussian distributed white noise with zero average and variance 1 multiplied by a constant (D) to adjust the noise level. The coupling strength is denoted as C . Note, that one could leave C and take σ as correlation coefficient in this case, but we wanted to gain the option to assign each neuron different parameters for future investigations.

In [4], Rulkov also used coupling in the fast variable which we omitted. For our purpose, the coupling showed in Eq.(5) is totally sufficient. Experiments with (linear) $x - x$ and $y - y$ coupling showed, that they do not lead to the dynamical clustering behaviour.

Based on suggestions in [4], we set up the constants, such that the non coupled model produces a kind of “chattering” signal, which means it generates bursts of short length, followed by breaks of roughly the same length.

Note, that this choice is not arbitrary. Rulkov mentions in [4] that only the onset of burstings will synchronise while single spikes remain unsynchronised. Since we are interested in synchronisation, we have to choose the parameters in the bursting regime.

Additionally, we used another dynamic, consisting of a system of two first order ordinary differential equations by E. M. Izhikevich [6].

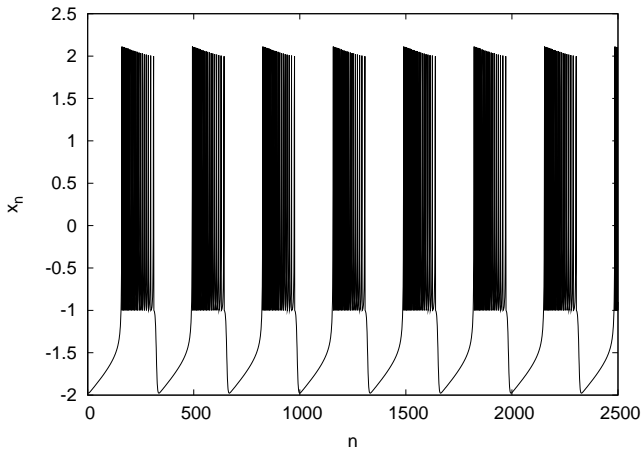


FIG. 2: Signal of an area without coupling and noise using the Rulkov map

TABLE II: Parameter values for the Izhikevich ODE

constant	value
a	0.02
b	0.2
c	-50.0
d	2
I_0	10

$$\frac{d}{dt}v = 0.04v^2 + 5v + 140 - u + I \quad (6)$$

$$\frac{d}{dt}u = a(bv - u) + \xi \quad (7)$$

with an after spike resetting

$$\text{if } v \geq 30, \text{ then } v := c \text{ and } u := u + d \quad (8)$$

In our simulations, we integrated the equations, using the classical fourth-order Runge-Kutta method with a step size of $dt = 0.1$.

This model is also capable of generating spiking and spike-bursting signals, but, as it consists of a system of two first order ODEs, it is not chaotic in the uncoupled case.

We investigated the kind of coupling which Izhikevich introduces in [6]. Coupling is done by replacing I by

$$I = I_0 \left(1 + \frac{C}{N} \sum_{j=1}^N M_{ij} \Theta(v_j - 20) \right) + \xi \quad (9)$$

while M_{ij} is the adjacency matrix as above, C is the coupling parameter and $\xi = D\Xi_{0,1}(t)$ stands for Gaussian distributed white noise with zero average and variance 1 multiplied with a constant (D) to adjust the noise level.

We chose the control parameters such that the model generates a “chattering” signal as they were proposed by

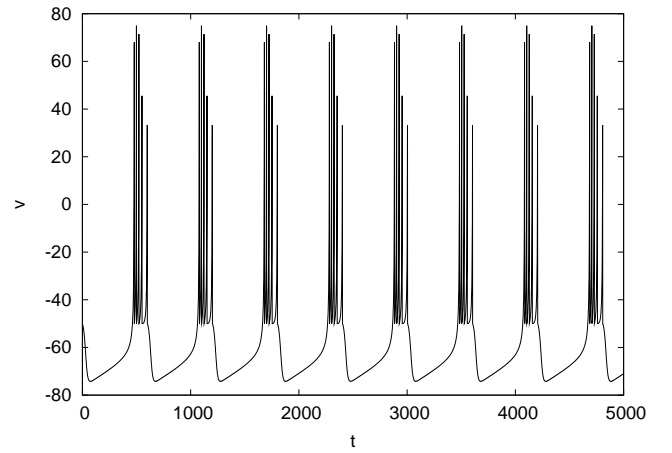


FIG. 3: Signal of an area without coupling and noise using the Izhikevich model

Izhikevich in [6]. The signal $v(t)$, shown in Fig. 3 appears to be similar to the Rulkov signal, exhibited in Fig. 2.

All test runs started with random initial conditions and had a transient of 10000 iterations, which were not saved and 50000 iterations which were saved for further calculations. Our exhibited correlation matrices are an average of the correlations of 10 realisations for the Rulkov model and 50 for the Izhikevich model. Calculations for the Rulkov model take about two minutes per run.

We are interested in the synchronisation behaviour of the model i.e. if synchronicity and clustering follows the biological topology. As a measure for synchronicity of the outputs $x_{i,n}$ we use the linear, zero-lag correlation coefficient.

$$r(i, j) = \frac{\langle x_i x_j \rangle - \langle x_i \rangle \langle x_j \rangle}{\sigma(x_i) \sigma(x_j)} \quad (10)$$

Unlike the authors in [1–3], we do not have a sub-network for each area and hence, we have no mean-field of the sub-network. After averaging the output of the sub-neuron network, the spiking patterns of the individual neurons are lost and result in an EEG like signal, while in our dynamics, we still have spiking and spike-bursting patterns in both cases (Rulkov and Izhikevich).

In our signal, we have two main frequencies as there is a (fast) occurrence of spikes and a (slow) occurrence of bursts. As we are interested in the correlation of neural activity, by which we do not mean single spikes, but bursts of spikes, we have filtered the signal to eliminate the high frequencies. Furthermore, coupling between Rulkov maps yields synchronous bursts, while the single spikes do not synchronise. To eliminate the high frequent spikes, while conserving low frequent occurrence of bursts, we filter our data by applying a low pass filter. We chose a recursive filter of the type

$$z_n = (a - 1)x_n + az_{n-1} \quad (11)$$

which we applied in both directions (forward and backward) to remove the phase shift, that the filter generates

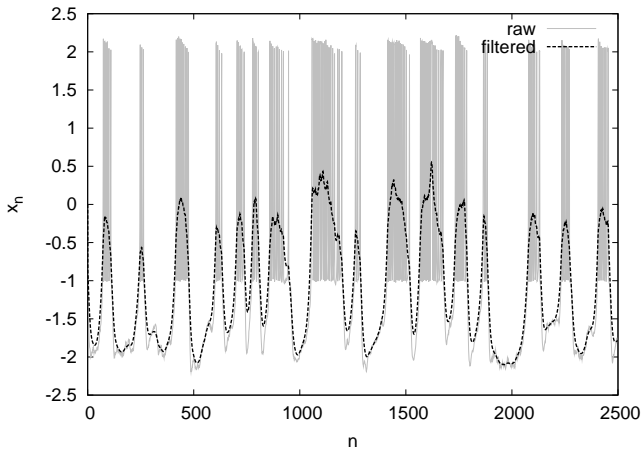


FIG. 4: Comparison between the filtered and the unfiltered signal

if applied only once. We found 0.9 a suitable value for a . Fig. 4 shows the effect of the filter on our data.

III. RESULTS

Fig. 5 shows a gallery of correlation matrices $r(i, j)$ for the Rulkov map and the corresponding cluster trees (dendrograms). The noise level was $D = 0.01$ and the shown correlation matrices are an average of the correlations of 10 realisations for each coupling strength. We computed correlation matrices and dendrograms for realisations with coupling strengths ranging from 0 to 1000. The plots in Fig. 5 correspond to coupling strengths of $C = 10$ (a), 75 (b), 120 (c) and 525 (d)

In the correlation matrix a), the dynamical clusters are visible although the correlations are very weak and noisy. The dynamical clusters in b) raise from the background with high contrast, while in c), inter cluster correlation becomes more dominant and finally leads to global correlation (d).

The dendrograms were done using the Statistics Toolbox in Matlab, version 7.6.0. A dendrogram is a graph of many U-shaped lines, which connect hierarchical nodes in a binary tree. The height of each line stands for the distance between two nodes. The distances are obtained from the correlation matrix. The (euclidean) distance between two areas is defined as $d_{ij} = \sqrt{\sum_m (r_{i,m} - r_{j,m})^2}$. The linkage function in Matlab then takes the distance information and links pairs of objects that are close together into binary clusters. After that, the algorithm links these newly formed clusters to each other and to other objects to create bigger clusters until all the objects in the original data set are linked together in a hierarchical tree, which is visualised in the dendrograms. This technique enables us to see which areas are closely connected and how they build up dynamical clusters.

As we are concerned about the anatomical clusters, we

concentrate on the hierarchy level where the correlation matrix decomposes to four clusters corresponding to the biological communities. Apparently, the stability of hierarchical levels is a function of correlation. By stability, we mean the height of the hierarchical level where there are four clusters in the dendrogram. With low correlation, the stability of our region of interest is very weak. Here, the correlation between single nodes is dominating the synchronisation behaviour, while an intermediate correlation leads to the desired synchronisation of four stable clusters where each cluster has its own dynamics and is only weakly coupled to other clusters. Very high coupling strengths destabilise the four clusters and “melt” them together, which means that individual dynamics is getting lost, while synchronisation of all clusters becomes dominant, as is shown in case c) and d) in Fig. 5.

Note, that in these dendrograms, areas are generally not ordered by their number. To see, which areas form a cluster, we provide another graph (Fig. 6). The dynamical clusters correspond to the functional communities, although some of the areas seem to be assigned to the “wrong” cluster. These areas belong to a community, but have a very close connection to another, such that they get synchronised with other communities and therefore, the clustering algorithm assigns it to the “wrong” area. These particular areas can be denoted as hubs, or inter community links [2].

As we saw in Fig. 5, the coupling strength determines the regime of synchronisation, i.e. intra community vs. global synchronisation.

Fig. 7 shows the dependency of the correlation coefficient $\langle r \rangle$ on the coupling strength C . One can see that the transition function is almost linear until a coupling of $C = 100$ and then monotonously grows. In the multi-level model of [1–3], the average correlation $\langle r \rangle$ displayed a sigmoidal function of coupling strength C , showing a transition in the network dynamics (see inset in Fig. 7) Using the Izhikevich dynamics also yields synchronisation, but as we can see in Fig. 8 the clustering behaviour is very different. Clusters are not concordant with the biological communities, regardless of the coupling strength. This observation is very similar to the neural mass model, discussed in [2].

IV. CONCLUSION AND OUTLOOK

Our goal was to find and examine an alternative to the multi level approach of [1–3], which can be computed faster and hence, is suitable for computer experiments. The comparison of our results using the Rulkov map (Fig. 5) with [1–3] shows, that our model reproduces the biologically plausible synchronisation and clustering behaviour, displayed in Fig. 9, which exhibits the correlation matrix, dendrogram and clustering map of the multi-level model in weak coupling regime. This means that

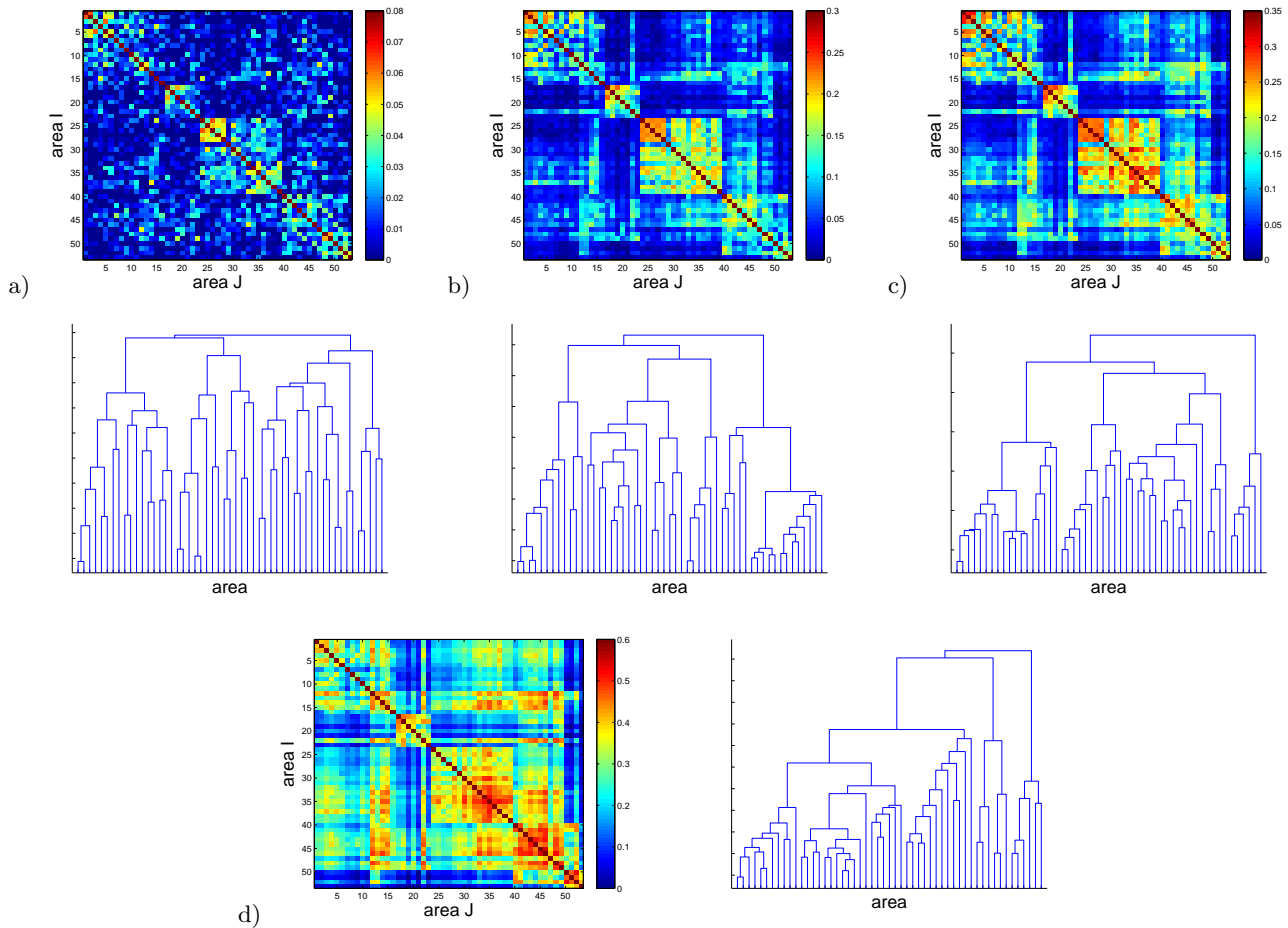


FIG. 5: Correlation matrices and dendrograms for the Rulkov map with different coupling strengths. a) $C=10$, b) $C=75$, c) $C=120$, d) $C=525$

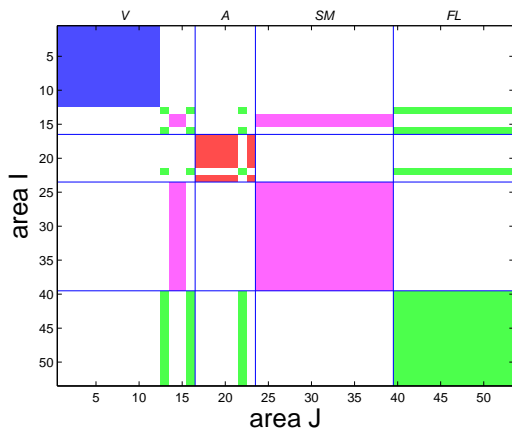


FIG. 6: The four dynamical clusters of the Rulkov model at an intermediate coupling strength of 75, result of the clustering algorithm described in section III

the global dynamics follows the topological connectivity depending on the coupling strength in a way that dynamical clusters correspond to the biological functional com-

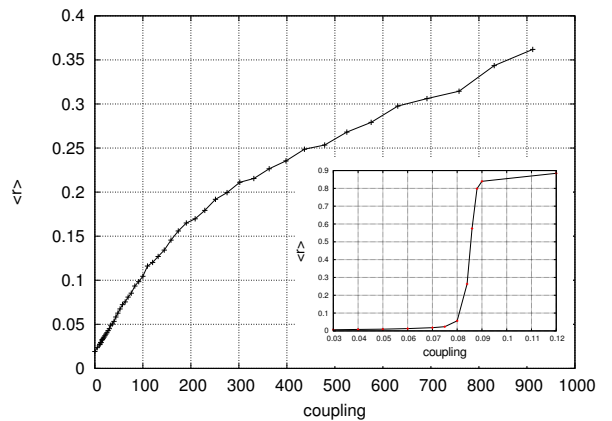


FIG. 7: coupling strength dependency of $\langle r \rangle$ at a noise level of 0.01 with Rulkov map dynamics (large picture), coupling strength dependency of $\langle r \rangle$ of the multi level model (small picture)

munities *Visual*, *Auditory*, *Somato motoric* and *Fronto Limbic* (see Fig. 6).

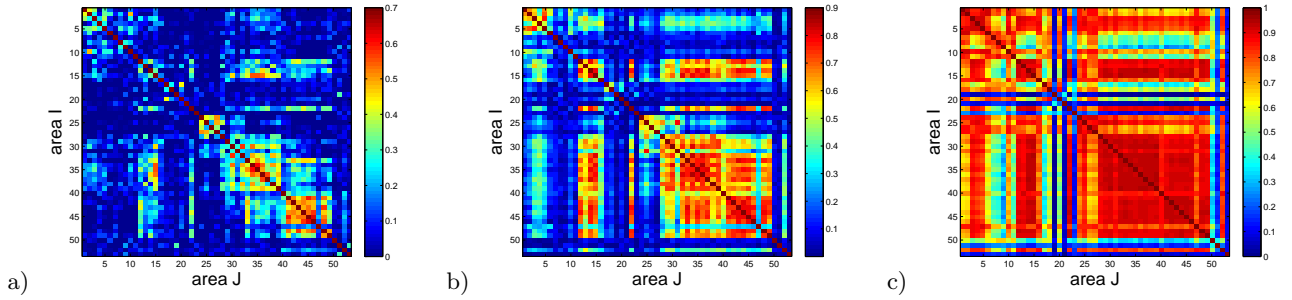


FIG. 8: Correlation matrices for the Izhikevich map with different coupling strengths. a) $C=3$, b) $C=5$, c) $C=10$

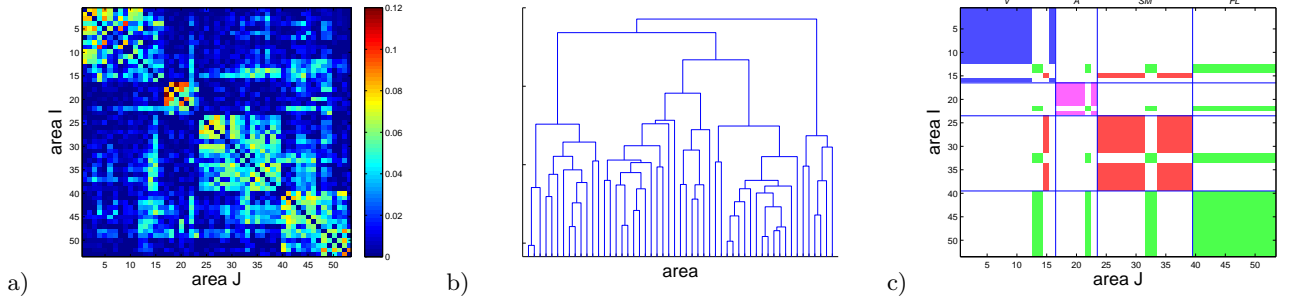


FIG. 9: Multilevel model of [1–3] a) correlation matrix, b) dendrogram, c) clustering map in a weak coupling regime

Unlike in [1–3], the signal of an area in our model, regardless of which dynamic we use, is a spiking - spike bursting pattern, hence interpreting it as EEG data is implausible. The authors of [1–3] found it biologically plausible to interpret their signal of an area as a typical EEG pattern because they modelled an area using a sub network build up of 200 neurons with random connections and took the mean field of that sub network as signal. In our case, an area is modelled using a dynamics, which has been designed to model a single neuron. If we regard the low pass filtered output as the signal, which has some similarities with biological EEGs, interpretation of our signal as EEG might be possible, but would require some additional explanation.

The multilevel approach of [1–3] is assumed to be biologically plausible because it maps the small world topology of a natural brain, using the FitzHugh-Nagumo model for individual neurons. It might be worth to investigate how substituting the neural dynamics in [1–3] by the Rulkov map while retaining the multilevel approach, would affect the model dynamics. Furthermore, a discussion of the reasons *why* the dynamics of a single neuron is suit-

able to simulate a whole area could be fruitful to obtain a general understanding of brain dynamics.

Another interesting topic would be a general examination of why the Izhikevich model failed in reproducing the functional topology of the network, while the Rulkov map succeeded, although both intend to model neurons. A speculative answer could lie in the fact, that even one-dimensional maps are capable of showing much richer, even chaotic behaviour, while differential equations such as the Izhikevich ODE show chaotic behaviour not until they are at least three-dimensional. As brain areas consist of a large number of neurons, which altogether have a very high-dimensional phase space, in which chaotic behaviour is likely, iterated maps could be interpreted as Poincaré-map of such a high dimensional system and hence, are more suitable to represent them as two-dimensional ODEs like the Izhikevich ODE.

However, since our model promises to be plausible and computes very fast, it is eligible for applications that investigate properties of the brain e.g. information processing and flow.

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