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MODULATION OF SYNCHRONOUS GAMMA RHYTHM CLUSTERS

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Abstract
Gamma rhythm plays a key role in a number of cognitive tasks: working memory, sensory processing and routing of information across neural circuits. In comparison with other (lower frequency) oscillations it is sparser and heterogeneous in space. One way to model such properties of gamma rhythm is to describe it through a neural network consisting of interacting populations of pyramidal cells (excitatory neurons) and interneurons (inhibitory neurons), demonstrating cluster synchronization. The structure of such clusters can be modulated by endogenous neuromodulators: dopamine, acetylcholine, adrenaline, etc. In this article we consider the reconfiguring of synchronous clusters of pyramidal interneuron gamma rhythm (pyramidal interneuron gamma, PING) due to the variation of the frequency adaptation parameter of pyramidal cells and the strength of excitatory synaptic connections. We have shown that the variation of the frequency adaptation parameter has the strongest impact on the strongest influence on the cluster structure and can lead to either an increase or a decrease of the number of synchronous clusters.

Key words
Gamma rhythm, PING network, cluster formation, dopamine modulation.

1 Introduction

Gamma rhythm (30-100 Hz) plays a key role in numerous cognitive tasks [Buzsáki 2006]: working memory, sensory processing and routing of information across neural circuits [Akam and Kullmann 2014]. Gamma oscillations have also been implicated in navigational coding and attentional modulation apported to cognitive constructs [Tallon-Baudry et al. 2004]. Several lines of evidence indicate that gamma oscillation in the cortex are locally generated [Strüber, Sauer, Jonas and Bartos 2017], yet may have non-trivial structure with emergent coherence between local oscillatory populations across multiple cortical areas [Roberts 2013] and with non-trivial phase relationships [Fries 2009]. One way we may conceptualize this structure is the emergence of multiple mutually synchronized clusters of gamma oscillations. How such spatially clustered structure emerges from interactions of intrinsic cellular properties and synaptic connectivity is one of the key computational questions is cortical neuroscience. Further of interest is how may the structure of gamma oscillations is affected by the endogenous neuromodulators of the central nervous system.

Typically, gamma rhythm that is observed in the cortex is generated by local interacting populations of pyramidal (PY) cells and interneurons (IN) [Bartos 2007]. This is the so-called Pyramidal Interneuron Gamma (PING) mechanism [Whittington et al. 2000]. It is possible conditionally to divide the gamma into two types. The first type is a strong gamma rhythm. Usually it is observed in the globally synchronized population of the PY cells. Note that in this case the IN and PY neurons fire with the same frequency. The second type is a weak gamma. It differs from the strong gamma by existing of two or more synchronous clusters of the PY cells which fire alternately. Actually, it means that the PY cells frequency is much smaller than the IN neurons frequency the gamma oscillations are formed not in the PY cells clusters but only in the PY cells populations. Within this paper we consider the second type of the gamma oscillations – the weak gamma. It is important to note that experimental data shows that typically the gamma is not global – it is sparser and more locally distributed in the cortex than the other lower frequency

oscillations [Dickson, Biella and de Curtis 2000]. One of the possibilities to describe gamma features is to suggest that gamma is generated within local synchronous neuronal clusters [Krupa, Gielen and Gutkin 2014; Kilpatrick and Ermetrout 2011].

The cluster patterns are dependent on the intrinsic properties of the constituent neurons (e.g. spike frequency adaptation) and this may be returned by processes in the cortex that affect these properties. In particular brain neuromodulators such as dopamine, acetylcholine and adrenaline may be key to this tuning. Dopamine modulates adaptation of the PY cells [Pedarzani and Storm 1995] and synaptic connections between the populations [Wang and O'Donnell 2001; Seamans, Gorelova, Durstewitz and Yang 2001]. In [Krupa, Gielen and Gutkin 2014] it was shown that shunting inhibition and adaptation determine the maximal number of synchronous cluster in the PING networks. Within this paper we consider influence of neuromodulatory modification of PY cells adaptation and interpopulation synaptic connections on the cluster synchronization processes.

2 Model

As a basis the network model of clustered gamma we took one from [Krupa, Gielen and Gutkin 2014] consisting of (PY) cells and interneurons (IN). Within this network the IN neurons modeled by the quadratic integrate-and-fire model and the PY cells modeled by the modified Miles-Traub model:

$$\dot{v}_{e,j} = I_{app} - I_L(v_{e,j}) - I_K(v_{e,j}) - I_{Na}(v_{e,j}, n_j) - I_{Ca}(v_{e,j}) - I_{AHP}(v_{e,j}, [Ca]_j) - g_{ei}\left(\frac{1}{N_i}\sum_{k=1}^{N_i} s_{e,k}\right)(v_{e,j} - E_{rev}^{ei}),$$

$$[Ca]_j = -\varepsilon_{Ca} I_{Ca,j} - \frac{[Ca]_j}{\tau_{Ca}},$$

$$n_j = -\alpha_n(v_{e,j})(1 - n_j) - \beta_n(v_{e,j}) n_j, j = \overline{1, N_e}.$$

$$\dot{v}_{i,l} - I_{int} - 2v_{i,l}(v_{i,l} - 1) - g_{ie}\left(\frac{1}{N_e}\sum_{k=1}^{N_e} s_{e,k}\right)(v_{i,l} - E_{rev}^{ie}) - g_{ii}\left(\frac{1}{N_i}\sum_{k=1}^{N_i} s_{i,k}\right)(v_{i,l} - E_{rev}^{ii}),$$

$$with\ reset: if\ v_{i,l} \geq 1, v_{i,l} \to 0, l = \overline{1, N_i}.$$

Here $v_{e,j}$ is a membrane potential of the j-th PY cell, $[Ca]_j$ is its Calcium concentration, and n_j is a gate variable of the Sodium current. The variable $\dot{v}_{i,l}$ is a membrane potential of the l-th IN neuron. The number of the PY cells N_e=200 and the number of the IN neurons is N_i=20. In the right part of the PY cell membrane potential there are some ionic currents: I_{app} is an applied current, $I_L = g_L(v_e - E_K)$ is a leak current, $I_{AHP} = g_{AHP}(v_e - E_{Ca})[Ca]/(1 + [Ca])$ is an afterhyperpolarization current, and also there are a sodium (I_{Na}), potassium (I_K) and calcium (I_{Ca}) currents. Additionally, we introduce to the model the uniform distribution of the parameter $g_l \in [0.075, 0.125]$ that controls intrinsic frequency of the PY cells. All IN neurons are coupled with each other (all-to-all topology) whereas a PY cell can interact with the other PY cells only indirectly through the IN neurons. Interpopulation connections have an all-to-all topology and are inhibitory if these are connections from the IN neurons to the PY cells and are excitatory in the opposite direction. One can find more detailed description of the model and parameter set in [Krupa, Gielen and Gutkin 2014].

The maximal number of the clusters, which can immediately exist in such network, depends, in particular, on the parameter g_{AHP} which is responsible for adaptation of intrinsic PY cells period and changes their PRC shape, and g_{ie}, g_{ei} determining the strength of the inhibitory and excitatory chemical connections between the populations. Taking into account that dopamine is able to modulate these parameters we consider an issue how number of clusters depends on them. To get effective modulation process (possibility either to increase or decrease the intrinsic frequency of the PY cells) we set the control parameters of the model (g_{ie}, g_{ei} and g_{AHP}) to have a 3 cluster regime (other parameter values are as in [Krupa, Gielen and Gutkin 2014]) and estimate parameter regions with different cluster numbers occurred by the immediate reset of the control parameters. In other words, we examine the stability region of a 3 cluster regime in the control parameter space. It is important because if such parameter reset is able to change the cluster number of cluster it also changes the frequency of the PY cells and properties of the gamma oscillations formed by the alternately firing clusters. And that is more important, due to multistability these changes may remain after the parameter returns to their initial value.

3 Results

Our study shows that each control parameter makes an important contribution to the formation of the cluster structure. In our model (PING mechanism) as well as the models with ING (interneuronal gamma) mechanism [Whittington, Traub and Jefferys 1995] the key role in rhythmic activity are played by the IN neurons. In fact, difference between these mechanisms is existence of the excitatory connections (g_{ei}) from the PY cells to the IN neurons in addition to inhibitory couplings (g_{ie}) from the IN neurons to the PY cells, both of which are provided bidirectional interaction between the populations. The last control parameter (g_{AHP}) determines the intrinsic period of the PY cells and changes their PRC [Krupa, Gielen and Gutkin 2014]. In fig. 1 there shows dependence of number of clusters on the parameter plane (g_{AHP}, g_{ei}) for two different values of g_{ie}. The variation of the parameter of PY cells frequency adaptation provides the strongest influence on the cluster structure. To vary this parameter, it is possible to obtain transitions (from a 3 cluster regime) to the structure with the other number of clusters (fig. 2): to relatively simple structures consisting of one, two (fig. 2B), three (fig. 2C), four (fig. 2D) or, for example, to a more complex three cluster regime with skipping of firing of one (of four) period of the PY cells (fig. 3E). It seems that such regimes with skipping a period appear due to the need for accurate matching of oscillation periods. If the tuning of IN and PY frequencies is not able to archive the desired ratio, an arbitrary pause in generation (skipping a period of oscillation) looks as an optimal solution of the problem.

The influence of the strength of the excitatory interpopulation connections, in comparison with the parameter of PY frequency adaptation, is weaker (fig. 1). It takes place either in the low value interval of g_{ie}, where there is a "transition" from ING mechanism to PING one, or in the interval of larger values of g_{AHP}, where there is an increase of "intermittent" region of cluster regimes.

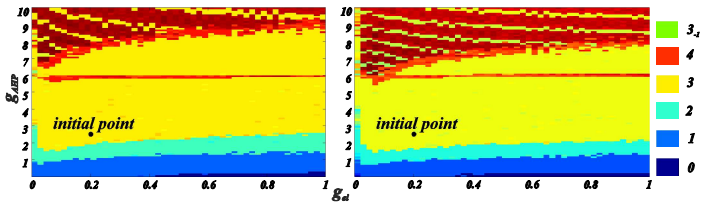

Figure 1. The color plots showing dependences of the cluster number on the control parameters determining PY cells adaptation (g_{AHP}) and excitatory synapses strength (g_{ei}) for different values of the interpopulation inhibitory connections: $g_{ie}=2$ (A) and $g_{ie}=0.9$ (B). Each point of the diagrams corresponds to a cluster number demonstrated by the network model after the reset of the control parameters to the values determines the point on the parameter plane. 0 corresponds to the oscillations death at least in one of the populations, 1, 2, 3 and 4 corresponds to the number of clusters and 3_{-1} corresponds to the 3 cluster regime but with the skipping of one period oscillation of the PY cells (see fig. 2E). Marker "initial point" corresponds to the initial parameter set.

To compare the two diagrams in fig. 1, you can see that the growth of inhibitory couplings leads to an increase of the region where the 3 cluster regime exists. We want to draw your attention that this is a crucially important parameter for the generation of the gamma rhythm. It may not be sufficiently small because the IN population cannot effectively influence to the (directly uncoupled with each other) PY cells. It results to loss of a rhythmic activity of the network model. From the other hand, sufficiently large values of the parameter lead to ING mechanism of gamma oscillations.

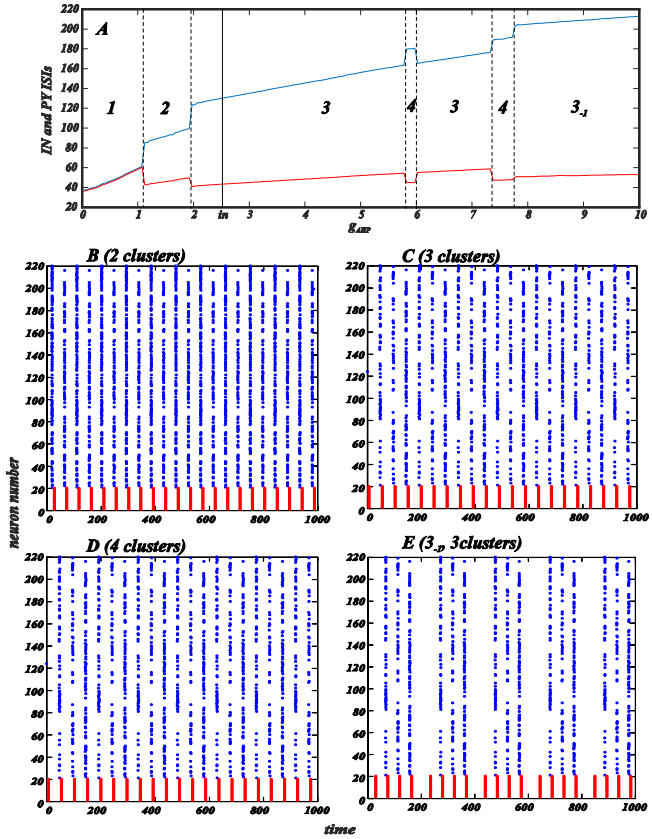

Figure 2. Dependence (A) of the PY cells (blue line) and the IN neurons (black line) Interspike Intervals (ISIs) on the g_{AHP} for $g_{ie}=2$ and $g_{ei}=0.2$. The line marked "in" correspond to the initial value of the parameter g_{AHP}. The diagram is split into the regions of the different number of clusters (1,2,3, etc). In panels B-E there are raster plots (red points correspond to IN spikes, blue points correspond to PY spikes) for $g_{AHP}=1.5$ (two clusters, 2), $g_{AHP}=4$ (three clusters, 3), $g_{AHP}=5.9$ (four clusters, 4), $g_{AHP}=8$ (three clusters, 3_{-1}) respectively.

Separately, it is necessary to raise the question how the reconfiguring process depends on the phase of PY cells at the beginning of the parameter change. It seems that it is possible to speak about an analogue of PRC for synchronous clusters of pyramidal cells. We consider this dependence on the example of the variation of the frequency adaptation parameter, since it has the greatest impact on the restructuring of the cluster structure. The corresponding diagram shown in fig. 3 shows that the moment, the modulation starts, can affect the cluster structure only in a small area with a sufficiently large value of the parameter g_{AHP}.

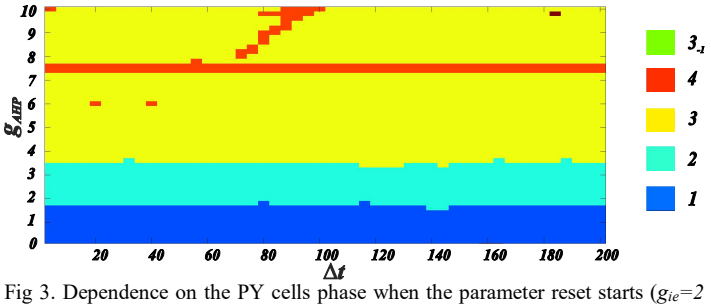

Fig 3. Dependence on the PY cells phase when the parameter reset starts ($g_{ie}=2$ and $g_{ei}=0.2$). The initial conditions is on the 3 cluster regime/ Numerical markers of the cluster regimes are the same as in fig. 1.

4. Conclusion

In this paper, within the PING model (1) we examined the influence of instantaneous parameter changes on the number of clusters in the PY population in the case of the weak (cluster) gamma rhythm. Since, in this case, the PY cells do not generate action potentials every cycle of gamma rhythm, the increase in the number of clusters leads to a decrease in the coherence of the rhythm and its power, which, in turn, can significantly change the cognitive processes occurring in the cortex. In particular, it was shown that the frequency adaptation parameter of PY cells has the strongest impact on the reconfiguring of the cluster structure. It can cause a significant change in the number of synchronous clusters. At the same time, this phenomenon was almost insensitive to the phase of the PY cells at the time of beginning of the parameter resetting. The change in the number of clusters was observed only in a small area for large values of the frequency adaptation parameter. This result allows for a biological interpretation. For example, during the reinforcement learning [Schultz 1998], the activity of dopaminergic neurons changes. It results in changing of the concentration of dopamine. In the case of positive reinforcement, the concentration of dopamine increases, which causes a decrease of the parameter of frequency adaptation of the PY cells, which, in turn, leads to a decrease in the number of clusters and an increase of the coherence of the gamma rhythm. In the case of negative reinforcement, the concentration of dopamine is significantly lower than the background level. It leads to an increase of either the frequency adaptation parameter or the number of

clusters in the population of pyramidal cells. Note that the transition from the ING mechanism to the PING mechanism of gamma rhythm generation significantly increases the possibility of reconfiguring the cluster structure and, in a certain range of control parameters, makes this process more efficient. This is primarily due to the excitatory connections from the population of PY cells to the IN neurons, which allows adjusting the frequency of generation of interneurons (see, for example, Fig. 2A).

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