Wavelet Correlation of Neural Activity Bursts Generating Spikes

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Abstract: We study neural activity synchronization on the basis of instantaneous wavelet correlation function and simple mathematical model of brain bursts carrying several spikes. The approach allows us to obtain analytical solution for two neurons generating a given number of spikes and estimate the coupled behavior of neurons at different time moments. Neural activity is simulated as a superposition of elementary nonstationary Gaussian signals with some given parameters. Time-frequency properties of neural signals are studied by continuous wavelet transform with adaptive Morlet mother wavelet function.

1 INTRODUCTION

Synchronization of individual neurons and complex neuron ensembles plays an important role in the central nervous system functioning (Hramov et al., 2015). A neuron as a pacemaker can generate rhythms of various duration and frequencies, regular or chaotic. The electric neural activity shows some bursts consisting of short pulses (spikes) and low-frequency oscillations associated with slow changes in the membrane potential. In accordance with the spike model (Izhikevich, 2006, Kislev, 2016, Gerstner et al., 2002) the main carriers of information are the number, duration and the moments of occurrence of spikes. Synchronization of neural activity as a way of information transfer has been considered in numerous experimental and theoretical works (Izhikevich, 2006, Kislev, 2016, Gerstner et al, 2002, Xiaojuan et al., 2011).

A large number of mathematical models of neurons, simulating the dynamics of their electrical activity, can be divided into several classes. The first class includes the models based on kinetic equations simulating the excitation of nerve impulse. Such models use a detailed description of ion channels kinetics. The classical Hodgkin-Huxley model and its various generalizations (Zhou and Kurths, 2003) belong to this class of models. The requirements for these models consist in accurate reproduction of the electrical activity of the mathematical neuron, whose electrical activity must correspond to a single pulse or bursts of pulses of the real biological neuron.

The second class of models includes conceptual models of neurons (Hramov et al., 2015, Izhikevich, 2003). These phenomenological models describe the effect of ion currents with identical characteristic scales by using a single variable. In this case, a few ordinary differential equations are sufficient to describe the electrical activity of a single neuron. The third class includes threshold models of neurons (Nekorkin, 2008, Tuchwell, 1988). In this case, the system accumulates threshold signals. Their combined action results in membrane potential reaching the threshold value. This fixed value is treated as a spike. Thereafter, the value of the membrane potential returns to the initial state. The process of synchronization is described by using mathematical models of synaptic connections (Hramov et al., 2015). It should be noted that both the models of functioning of a neuron ensemble and synapses connecting the neurons require large computing powers.

In this paper, we use the simplest model describing a separate spike in the form of the Gaussian signal, which has a certain duration. In this model, we assume that all spikes produced by neurons have the same shape. The formation of individual bursts both for a single neuron and for two coupled neurons is given phenomenologically in the form of a sequence of individual spikes created by the neurons. Such a simple model has the advantage of allowing us to solve analytically the synchronization problem for two neurons.

It is assumed that the coding of information in the brain is carried out through spike frequencies for a single neuron and a group of several neurons

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(Izhikevich and Gally, 2004). A certain stimulus of electrical activity causes excitation of a specific group of neurons. In this case, the relative times for the production of spikes by different neurons in the group are strictly fixed. The evidence is that temporal coding serves to represent and process information in the cerebral cortex (Lowet et al., 2016). The same set of neurons can encode a large number of different stimuli. Each stimulus is characterized by a unique order of spikes emitted by different neurons. The same is the case with the spacing between the spikes. The activation of neural groups, caused by the presence of any stimulus, assumes the process of creating spikes with strictly fixed delays between them. This procedure of creating spikes is observed for all or almost all participants of the neural groups.

Coherent analysis, instantaneous phase-locking, entropy transfer, and nonlinear dynamics methods have been applied to assess the degree of synchronization of neurons (Lowet et al., 2016, Mizuno-Matsumoto et al., 2005). Spectral coherence method based on the Fourier transform (cross-spectra) and assuming stationarity of signals has long been considered the main method for evaluating the interaction of signals related to rhythmic brain activity. It should be noted that instantaneous phase synchronization methods are recognized as more informative.

The study (Quyen et al., 2001) on the synchronization of neurons at different frequencies compares the efficiency of Hilbert transform and wavelet transform. At present, it is possible to highlight two main directions in the research on the synchronization of neurons and neural networks: the construction of more complex and more realistic models of neurons and their interactions, and the development of methods that take into account the nonstationary and nonlinear nature of neural rhythmic activity.

The purpose of this work is to develop a model of impulse activity of neurons generating spikes; to derive analytical wavelet transform that determines the time-frequency properties of spikes; to calculate wavelet correlation function analytically for comprehensive analysis of the synchronization processes.

2 METHODS

2.1 Mathematical Model of Neural Rhythmic Activity

In contrast to the complicated models (Hramov et al., 2015, Izhikevich, 2003, Nekorkin, 2008, Zhou and Kurths, 2003), which consider in detail the operation of ion channels, we propose a simple mathematical model of the coupling activity of two neurons α and β, and formulate the criteria for their synchronization. Let the signal $Z_\alpha(t)$ of electrical activity of the first α- neuron, be a superposition of N_α elementary Gaussian signals

$$Z_\alpha(t) = \sum_{L=0}^{N_\alpha - 1} z_L(t - t_L), \tag{1}$$

$$z_L(t - t_L) = \frac{b_L}{2\tau_L\sqrt{\pi}} \exp\left[-\frac{(t - t_L)^2}{4\tau_L^2}\right]. \tag{2}$$

The simulation (1) assumes the first α- neuron involving a number of spikes. We determine the time of each spike occurrence either phenomenologically or as a solution of more complex models of neuron functioning. Each spike $L = (b_L; t_L; \tau_L)$ occurs at a time moment $t = t_L$, has its own amplitude b_L and duration τ_L. In addition to the spikes with τ_L much smaller than the time interval between spikes, this model comprises some bursts. Each burst has its own center t_{LB} and its characteristic duration τ_{LB} ($\tau_{LB} >> \tau_L$). Various bursts of α- neuron do not overlap (τ_{LB} is much smaller than the distance between bursts), and the number of spikes in each burst can vary. The proposed model makes it possible to take into account the long-term changes in the work of an individual neuron. Various types of effects on the neuron (medicinal and light effects) can evoke such perturbations. We represent the signal of second neuron $Z_\beta(t)$ as a superposition

$$Z_\beta(t) = \sum_{K=0}^{N_\beta - 1} z_K(t - t_K) \tag{3}$$

of Gaussian peaks $z_K(t - t_K)$ characterized by a set of parameters $K = (b_K; t_K; \tau_K)$.

Let us consider the expression for the correlation function,

$$CCF_{\alpha\beta}(t)=\int_{-\infty}^{\infty} Z_{\alpha}(t')Z_{\beta}(t+t')dt', \tag{4}$$

which shows the coupling between two signals $Z_{\alpha}(t)$ and $Z_{\beta}(t)$ at different time points. We can obtain the analytical expression for the cross-correlation function of two Gaussian signals

$$CCF_{LK}(t)=\frac{b_L b_K}{2\sqrt{\pi\left(\tau_L^2+\tau_K^2\right)}}\exp\left\{-\frac{\left[t-\left(t_K-t_L\right)\right]^2}{4\left(\tau_L^2+\tau_K^2\right)}\right\}. \tag{5}$$

It is convenient to use the normalized cross-correlation function $CCF_{LK}^{(n)}(t)$ with the maximum value of $CCF_{LK}^{(n)}(t)$ equal to one at $t=t_K-t_L$. Taking into account (1), (3), the correlation function (4) takes the form

$$CCF_{\alpha\beta}(t)=\sum_{L=0}^{N_{\alpha}-1}\sum_{K=0}^{N_{\beta}-1} CCF_{LK}^{(n)}(t) \tag{6}$$

We find out that function (6) does not change if we reverse the direction of time, and replace all the times of spikes' and neurons' occurrences by the opposite values $t_L \to -t_L$, $t_K \to -t_K$.

Hereinafter, we assume that all spikes of neurons α and β are equal $\tau_L=\tau_K=\tau$, where τ=0.001*s*, and their maximum amplitudes $b_L=b_K=2\tau\sqrt{\pi}$ are equal to one. Suppose that for α-neuron we have N_{α}=4 of spikes $\alpha_L=(\alpha_0;\alpha_1;\alpha_2;\alpha_3)$ localized at $t_L=\{0.01\,;0.03;0.06;0.1\ s\}$. For β-neuron we have N_{β}=4, $\beta_K=(\beta_0;\beta_1;\beta_2;\beta_3)$ with $t_k=\{0.71;0.73;0.79;0.89\ s\}$. Fig. 1 shows the signal $Z_{\alpha}(t)$ of the first α-neuron. We highlight in bold four spikes of this neuron, given by the Gaussian peaks. Four spikes forming the signal $Z_{\beta}(t)$ associated with β-neuron are not highlighted.

The first peak of $CCF_{\alpha\beta}(t)$ at t=0.61 s is due to the coupling (correlation) of spikes $(\beta_0;\alpha_3)$. The second peak at 0.88 s corresponds to the coupling of spikes $(\beta_3;\alpha_0)$. The peak having a doubled amplitude at t=0.70 s is due to the synchronization of two pairs of spikes $(\beta_0;\alpha_0)$ and $(\beta_1;\alpha_1)$. All other peaks are related to the difference in localization times of other spikes and neurons (Fig. 1).

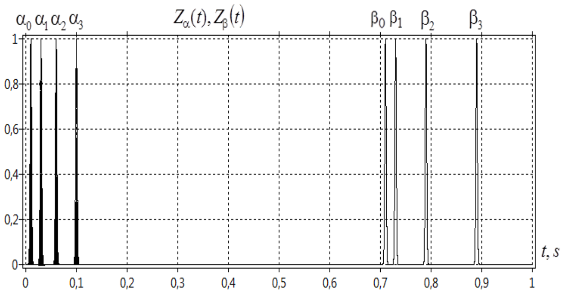

Figure 1: The dependence of time t, s for α-neuron signal $Z_{\alpha}(t)$ (in bold) и β-neuron signal.

Fig.2 shows instantaneous correlation function $CCF_{\alpha}(t)$ (4) for signals $Z_{\alpha}(t)$ and $Z_{\beta}(t)$.

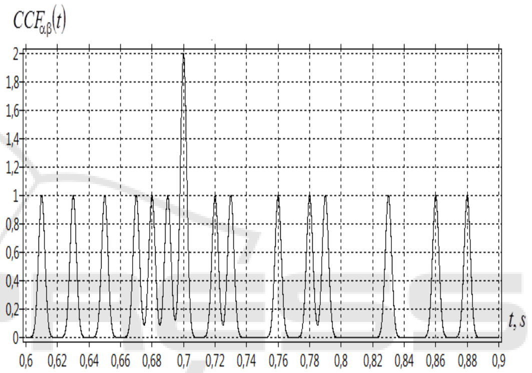

Figure 2: The dependence of time t, s for $CCF_{\alpha\beta}(t)$.

2.2 Continuous Wavelet Transform of Neural Signal

Time-frequency properties of α and β neurons vary with time. We can successfully process such nonstationary signals by Continuous Wavelet Transform – *CWT*. This type of integral transform maps nonstationary signal $Z(t)$ to the plane of time t (*s*) and frequency ν (*Hz*) (Bozhokin, 2010, Bozhokin and Suslova, 2015) by the formula

$$V(\nu,t)=\nu\int_{-\infty}^{\infty} Z(t')\psi^{*}(\nu(t'-t))dt', \tag{7}$$

where $\psi(x)$ is the mother wavelet function, symbol * means complex conjugation. We use here a new adaptive Morlet wavelet function (*AMW*) with the control parameter m (Bozhokin and Suslova, 2016):

$$\psi(x) = D_m \exp\left(-\frac{x^2}{2m^2}\right)\left[\exp(2\pi i x) - \exp\left(-\Omega_m^2\right)\right] \quad (8)$$

In (8) we have the parameter $\Omega_m = m\pi\sqrt{2}$, and constant D_m defined from the condition $\|\psi(x)\|^2 = 1$. The properties of the mother wavelet (8) are given in (Bozhokin and Suslova, 2016). In (Bozhokin and Suslova, 2016) the value of m acts as a control parameter of *AMW*. We can change temporal resolution Δ_x and frequency resolution Δ_F of signals under study by varying m. The characteristic moments of time t', which make the main contribution to the integral (7), satisfy the relation $t - \Delta_x / \nu < t' < t + \Delta_x / \nu$. The adaptive mother wavelet (8) acts as a varying window, which depends on control parameter m. The window width automatically becomes large for small frequencies ν and small for large ones.

To calculate (8), we use the Fourier transform of all functions in (7):

$$V(\nu, t) = \int_{-\infty}^{\infty} \hat{Z}(f)\hat{\psi}^*\left(\frac{f}{\nu}\right)\exp(2\pi i f t)\,df, \quad (9)$$

where $\hat{Z}(f)$ and $\hat{\psi}^*(f/\nu)$ are the Fourier components of $Z(t)$ and $\psi(x)$. The Fourier component $\hat{\psi}(F)$ equals:

$$\hat{\psi}(F) = \frac{D_m \Omega_m}{\sqrt{\pi}} \exp\left[-\Omega_m^2 (F-1)^2\right] \otimes \left[1 - \exp\left(-2\Omega_m^2 F\right)\right]. \quad (10)$$

The application of the *AMW* makes it possible to improve the results for spectral and time resolutions of $Z(t)$ in comparison with the application of the conventional Morlet wavelet. We can illustrate the fact by considering an infinite harmonic signal $Z(t) = \cos(2\pi f_0 t)$ with frequency f_0. We can derive the analytical expression for continuous wavelet transform $V(\nu, t)$ (7) using *AMW* (8). The maximum of $|V(\nu, t)|$ is located at point $\nu = f_0$. The full width at half maximum of $|V(\nu, t)|$ given by $2\Delta_{FWHM} = \sqrt{2\ln 2}\, f_0 / (\pi m)$ decreases with the increase in parameter m.

If we present the signal $Z_\alpha(t)$ as a superposition (1) of elementary signals (2), then $V_\alpha(\nu, t)$ also should be the superposition of wavelet images $V_L(\nu, t)$ corresponding to the signals (2). The wavelet images $V_L(\nu, t)$ for our model of neural signals can be derived analytically:

$$V_L(\nu, t) = \frac{b_L D_m \nu}{a_L} \exp\left[-\frac{x_0^2 + 2m^2\Omega_m^2\left(a_L^2 - 1\right)}{2m^2 a_L^2}\right] \otimes \left\{\exp\left(\frac{2\pi i x_0}{a_L^2}\right) - \exp\left(-\frac{\Omega_m^2}{a_L^2}\right)\right\}, \quad (11)$$

where $x_0 = \nu(t - t_L)$, $a_L = \sqrt{1 + 2\nu^2\tau_L^2 / m^2}$.

3 RESULTS

3.1 Wavelet Analysis of Model Neural Signals

Using the simulation (1), we can calculate analytically the modulus of wavelet transform $|V_\alpha(\nu, t)|$ for signal $Z_\alpha(t)$ with four spikes $t_L = \{0.01\,; 0.03; 0.06; 0.1\ s\}$ presented in Fig.1. Fig. 3 shows the ridges of two-dimensional surface $|V_\alpha(\nu, t)|$.

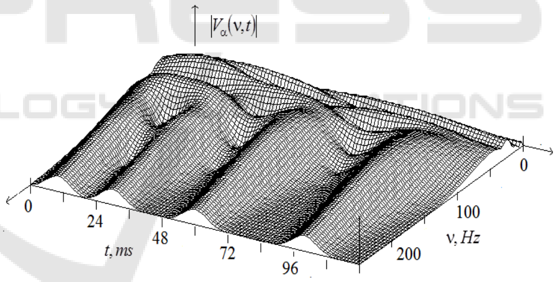

Figure 3: Modulus of wavelet transform $|V_\alpha(\nu, t)|$ depending on frequency ν, *Hz* and time t, s.

Fig. 4 displays the skeleton of the wavelet transform, which shows the location of extremal ridges on time-frequency plane.

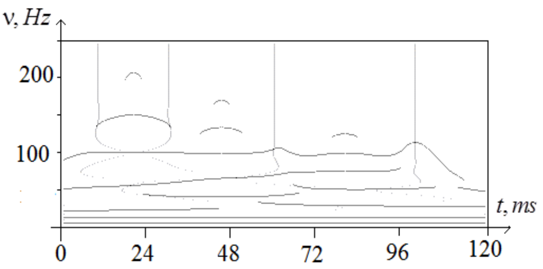

Figure 4: Skeleton of Modulus of wavelet transform $|V_\alpha(\nu, t)|$ depending on frequency ν, *Hz* and time t, s.

3.2 Wavelet Correlation Behavior

We introduce wavelet correlation function $WCF_{\alpha\beta}(\nu,t)$ by the formula

$$WCF_{\alpha\beta}(\nu,t)=\int_{-\infty}^{\infty}V_{\alpha}^{*}(\nu,t')V_{\beta}(\nu,t+t')dt', \tag{12}$$

which, in contrast to (4), shows the correlation between *CWT* of two signals $V_{\alpha}(\nu,t)$ and $V_{\beta}(\nu,t)$ taken at different time moments. According to the principle of superposition wavelet correlation $WCF_{\alpha\beta}(\nu,t)$ (10) can be represented as a double sum, which includes $WCF_{LK}(\nu,t)$ calculated for elementary Gaussian signals. Note that under this approach, we can also derive $WCF_{LK}(\nu,t)$ analytically.

Hereinafter, we will need to know the normalized function

$$WCF_{LK}^{(n)}(\nu,t)=\pi m\sqrt{8e}\,\frac{\sqrt{d^2-1}}{d}\exp\left[-A-2\Omega_m^2\right]\otimes \\ \left\{\exp\left[2iB+\frac{2\Omega_m^2}{d^2}\right]-2\exp\left[iB+\frac{\Omega_m^2}{2d^2}\right]+1\right\}. \tag{13}$$

calculated as $WCF_{LK}^{(n)}(\nu,t)=WCF_{LK}(\nu,t)/WCF_{LK}^{(\max)}$ with maximal value equal to unit. In (13) we have $e\approx$ 2.72 and

$$d=\sqrt{1+\frac{\nu^2\left(\tau_K^2+\tau_L^2\right)}{m^2}}, \tag{14}$$

$$A=\frac{\nu^2\left[t-(t_K-t_L\right]^2}{4m^2d^2}, \tag{15}$$

$$B=\frac{\pi\nu\left[t-\left(t_K-t_L\right)\right]}{d^2}. \tag{16}$$

Function $WCF_{LK}(\nu,t)$ reaches its maximal value $WCF_{LK}^{(\max)}$ at $t=t_K-t_L$. Under the condition $\tau_K=\tau_L=\tau$, the value of $WCF_{LK}^{(\max)}$ has its maximum at the point $\nu_{\max}\approx\left(1+1/(16\pi^2m^2\right)/(4\pi\tau)$, which for $\tau=$ =0.001 *s* approximately equals to 80 *Hz.*

To achieve the best time resolution of spikes, we use here the control parameter $m=1$.

Fig.5 shows $\left|WCF_{\alpha\beta}(\nu,t)\right|$ for two neurons α and β.

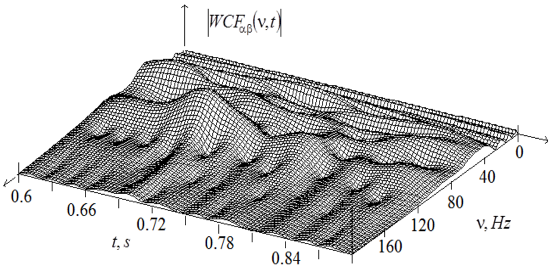

Figure 5: Dependence of $\left|WCF_{\alpha\beta}(\nu,t)\right|$ on frequency ν, Hz and time t, s.

The analysis of Fig. 5 shows that at large frequencies $\nu>>1/(4\pi\tau)$ ($\nu\approx 80$ *Hz*) the time behaviour of wavelet correlation modulus $\left|WCF_{\alpha\beta}(\nu,t)\right|$ corresponds exactly to the classical correlation function $CCF_{\alpha\beta}(t)$. The doubled peak at t=0.70 *s* at these frequencies also appears to be due to the synchronization of two pairs of spikes $(\beta_0;\alpha_0)$ and $(\beta_1;\alpha_1)$. The special features of low-frequency behaviour of $\left|WCF_{\alpha\beta}(\nu,t)\right|$ are associated with the characteristic intervals of peaks sequence in the process of neurons synchronization.

4 CONCLUSION

We propose a simple mathematical model of neural signals, which allows us to obtain analytical expressions for wavelet correlation functions $WCF_{\alpha\beta}(\nu,t)$.The neural signal as a sequence of bursts containing a certain number of spikes is simulated by the superposition of elementary Gaussian signals characterized by several parameters such as amplitude b_L, duration τ_L and time of occurrence $t=t_L$.

The study of the maximal value of $WCF_{\alpha\beta}(\nu,t)$ depending on time gives the opportunity to detect the synchronization of spikes between various neurons at different time moments. The dependence of $WCF_{\alpha\beta}(\nu,t)$ on frequency ν provides additional information on the correlation of spikes. In the limiting case $\nu>>1/(4\pi\tau)$, the time behavior of $WCF_{\alpha\beta}(\nu,t)$ is identical to that of the classical correlation function $CCF_{\alpha\beta}(t)$.

The task of determining neuronal correlations is particularly important in the development of neuro-interfaces, which are multi-electrode arrays that exchange information between the neuronal population and the outside world (Bursáki et al., 2012,). Such neuro-interfaces allow both stimulation and synchronous probing of dozens of neurons at the cellular level. Our method can be used to determine individual spikes of neurons in the patch-clamp method (Suk et al., 2017), as well as in studying the functioning of mirror neurons (Hou et al., 2017).

The wavelet-correlation function introduced in this paper can be used as a tool to study rapidly changing burst processes in radio-physics, plasma physics and astrophysics, as well as the stability of quantum frequency standards.

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