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A Wavelet Analysis to Classify the Interspike Activity of Peptidergic Neurons

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Abstract

Here we propose a statistical approach to characterize interspike signals of the electrical activity of peptidergic neurons from their time-scale similarity. The approach provides a novel way to compare and classify a set of non-stationary time series based on the comparison of their wavelet transforms.

Keywords: Peptidergic neurons, time series clustering, wavelet transform

1 Introduction

Neurosecretory systems are constituted by a set of peptidergic neurons, whose axons arrive at an organized terminal structure that is called the neurohemal organ; at this site the neural terminations release the secreted substances into the circulation. The peptidergic neurons are similar to other neurons with regard to their morphological appearance and electrical activity patterns. Electrical activity in neurons is composed by spikes or spike trains (bursts) and silent segments, called interspike period. The behaviour of the interspike period has been analyzed by linear and non-linear techniques [1], but the interspike voltage fluctuations remain to be explored in full detail [8]. In our case, we analyzed the interspike voltage fluctuations of peptidergic neurons recorded from the X Organ of Cherax quadricarinatus with the current clamp technique. The characterization of spike trains variability is a problem in the study of brain functions [5]. Changes in the spike pattern of a neuron show alterations in physiological dynamics either normal or pathological. The appearance of spontaneous and bursting activity is one of the most obvious.

A neuron in a network receives incoming spike trains from presynaptic neurons. In order to model the summed input a neuron receives from its presynaptic partners it is therefore required to study superpositions of spike trains. Several methods have been proposed for quantitative identification and characterization of interspike intervals, among them the Pause Poisson Surprise method, the Robust Gaussian Surprise method and the Rank Surprise method.

Wavelet analysis is efficient for multi-resolution analysis and local feature analysis of a signal. In other words, wavelet analysis involves decomposing a given signal into its scale and time components, so it is most appropriate to analyse a non-stationary time series. Information can be obtained about both the amplitude of any periodic signal as well as when or where it occurred in time or space.

Similarities or differences among two or more time series can be analyzed either from a spectral or a time approach. If two series are generated by the same stochastic process their second order structures are not different each other, and consequently we can characterize a family of signals or time series from these structures. Accordingly, from a scale-time domain a set of similar non-stationary time series can be characterized depending on their wavelet spectra [3]. In this work we propose a new approach to compare and classify the interspike activity of peptidergic neurons depending on their scale-time similarity.

2 Methods

2.1 The wavelet transform

A wavelet function is a function $\psi \in \mathrm{L}^2(\mathbb{R})$ with zero average (i.e $\int_{\mathbb{R}} \psi = 0$), $||\psi|| = 1$, centered in the neighborhood of $t = 0$, and with a finite number of null moments $\int_{-\infty}^{\infty} t^j \psi(t) dt = 0$ for $j = 0, 1, \ldots, r-1$.

For a wavelet ψ its dilated and translated dyadic version is given by

$$\psi_{j,k}(t) = \frac{1}{\sqrt{2^j}}\psi\left(\frac{t-2^jk}{2^j}\right)$$

where $j,k \in \mathbb{Z}$ [4]. It is important to construct wavelets such that the family $\{\psi_{j,k}(t),\ j,\ k \in \mathbb{Z}\}$ is an orthonormal basis of $\mathrm{L}^2(\mathbb{R})$, i.e.

$$<\psi_{j,k}\,,\,\psi_{l,m}>=\int_{-\infty}^{\infty}\psi_{j,k}(t)\psi_{l,m}(t)\,\mathrm{d}t = \delta_{j,l}\delta_{k,m},$$

where $\delta_{m,n} = 1$ if $m = n$, and $\delta_{m,n} = 0$ if $m \neq n$. Moreover, wavelets can form bases for various spaces of functions. For example, and more technically, $\{\psi_{j,k}(t)\}_{j,k\in\mathbb{Z}}$ can be a complete orthonormal basis for $\mathrm{L}^2(\mathbb{R})$ so that if $X(t) \in \mathrm{L}^2(\mathbb{R})$, it can be descomposed into the following generalized Fourier series as

$$X(t) = \sum_{j=-\infty}^{\infty}\sum_{k=-\infty}^{\infty} d_{j,k}\,\psi_{j,k}(t)$$

and due to the orthogonality of the wavelets, we have

$$d_{j,k} = \int_{-\infty}^{\infty} X(t)\,\psi_{j,k}(t)\mathrm{d}t$$

for integers j,k, where $\{d_{j,k}\}_{j,k\in\mathbb{Z}}$ are called the wavelet coefficients of $X(t)$.

In continuous domine, scaling ψ by a positive quantity s and traslating it by $u \in \mathbb{R}$, we define a family of time-frequency atoms $\psi_{u,s}$ as [4]

$$\psi_{u,s}(t) = \frac{1}{\sqrt{s}}\,\psi\left(\frac{t-u}{s}\right), \qquad u \in \mathbb{R},\ s > 0,$$

such that for all $f \in \mathrm{L}^2(\mathbb{R})$, the continuous wavelet transform (cwt) of f at time u and scale s is defined as

$$Wf(u,s) = \langle f, \psi_{u,s}\rangle = \int_{-\infty}^{+\infty} f(t)\,\frac{1}{\sqrt{s}}\,\psi\left(\frac{t-u}{s}\right)\,dt,$$

and it provides the frequency component (or details) of f corresponding to the scale s and time location t [4]. In general, the wavelet transform of f provides a time-frequency decomposition of f in the so called time-frequency plane. The energy of the continuous wavelet transform of f at scale s is represented by the ***scalogram*** (S) of f defined as

$$S(s) = ||Wf(u,s)|| = \left(\int_{-\infty}^{+\infty} |Wf(u,s)|^2\mathrm{d}u\right)^{1/2},$$

where $S(s) \geq 0$ for all scale s, and if $S(s) > 0$ we will say that the signal f has details at scale s.

2.2 The statistical approach

Let $\{X_t,\, t = 1, ..., T\}$ be a data set of length $T = 2^n,\ n > 0$ integer, the ***wavelet periodogram*** of $\{X_t, t = 1, \ldots, T\}$ is given by

$$\widetilde{I}_{X,jk} = |\widetilde{d}_{X,jk}|^2$$

where

$$\widetilde{d}_{X,jk} = \sum_{t=1}^{T} X_t \psi_{j,k}(t)$$

is the discrete wavelet transform of $\{X(t), t = 1, \ldots, T\}$.
Let consider the two time series $\{X_t, t = 1, ..., T\}$ and $\{Y_s, s = 1, ..., T\}$, we want to test if they were generated by the same locally stationary wavelet process [6], with respect to the same wavelet basis. In other words, we want to test the null hypothesis that there is no difference between the integrated evolutionary wavelet spectra [7] of the two time series at each level j, $j \in \{j_0, ..., J-1\}$, i.e. that the total power of the variance and covariance decomposition at level j are equal for both processes. It does not deal with the case of localized power, since from a practical point of view, it can somewhat limit the type of time series being compared.
The test statistic at each level j is the ratio of the cumulative wavelet periodograms of the series given by

$$R(j) = \frac{\sum_{k=0}^{2^j-1} \widetilde{d}^2_{X,jk}}{\sum_{k=0}^{2^j-1} \widetilde{d}^2_{Y,jk}}.$$

Salcedo et al.(2012) showed that for two independent gaussian locally stationary processes with zero mean, under the null hypothesis and for large T, the statistic

$$R(j) = \frac{\sum_{k=0}^{2^j-1} \widetilde{d}^2_{X,jk}}{\sum_{k=0}^{2^j-1} \widetilde{d}^2_{Y,jk}} \approx \frac{\sum_{k=0}^{2^j-1} \frac{\widetilde{d}^2_{X,jk}}{\sigma^2_{X,j}}}{\sum_{k=0}^{2^j-1} \frac{\widetilde{d}^2_{Y,jk}}{\sigma^2_{Y,j}}} = \frac{\sum_{k=0}^{2^j-1} \frac{\widetilde{d}^2_{X,jk}}{2^j\sigma^2_{X,j}}}{\sum_{k=0}^{2^j-1} \frac{\widetilde{d}^2_{Y,jk}}{2^j\sigma^2_{Y,j}}} \sim F_{2^j,2^j},$$

where $\sigma^2_{X,j} = \sigma^2_{Y,j} + O(T^{-1})$.

For each scale j, the probabilities $P_j = P(R(j) < r_c)$ for the test statistic is calculated, where r_c is the sample value of the statistic. Then, we reject the null hypothesis for a $\alpha\%$ significance level either if $P_j < \alpha/2$ or if $P_j > 1-\alpha/2$, since we are using a two-tail test.

2.3 The clustering procedure

The method of clustering proposed here to classify a set of non-stationary time series of length $T = 2^n,\ n > 0$ integer, follows the next steps: First, for each pair of time series we applied the test of hypothesis described in section 2.2. Since for each resolution level j, the hypothesis testing provides a p-value, we choose the maximum p-value denoted p_{max}. It's well known that the p-value of a test of hypothesis represents a measure of similarity and satisfies the properties of a semimetric [2], so we use the p_{max} as a measure of the spectral similarity between each pair of time series. Finally, we applied an algorithm that incorporates the principles of hierarchical clustering to classify the set of time series. In this step we used the *hclust* function of the R-program.

3 Results

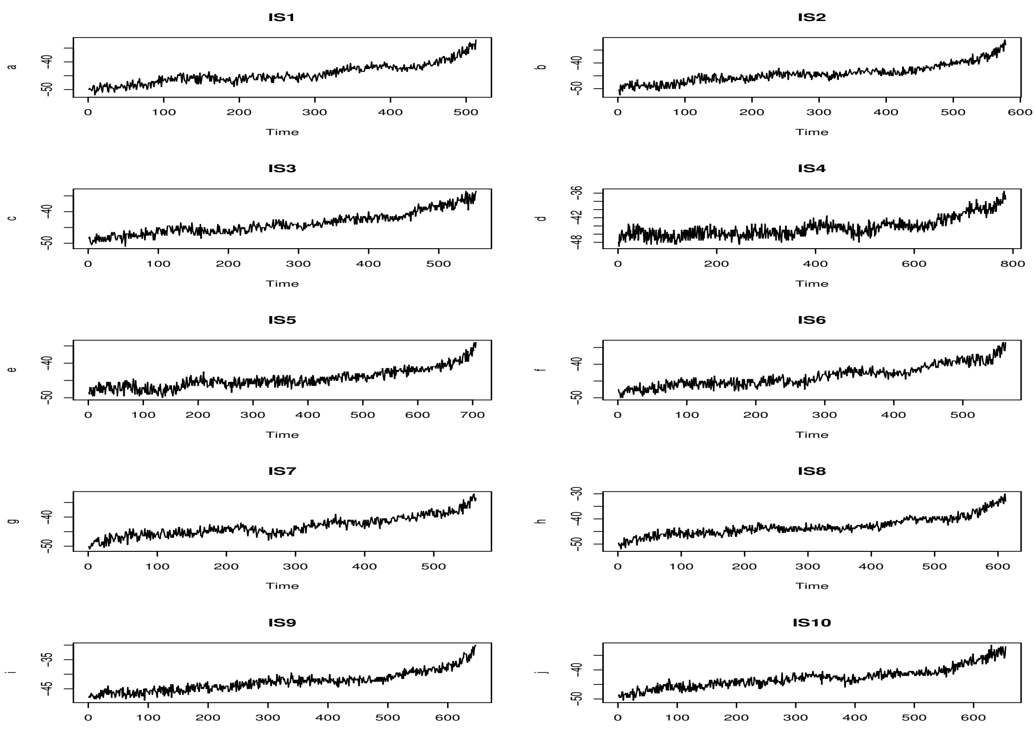

Figure 1: Ten inter-spike signals of a peptidergic neuron

Initially we compare the 10 inter-spike signals of a peptidergic neuron from Figure 1, each inter-spike signal is named $IS_i,\ i = 1, 2, ..., 10$, respectively. Table 1 contains the p-values of all pairwise comparisons at each resolution scale j. Then, from the measure p_{max} and the clustering algorithm, we classified these 10 signals in two well defined clusters: *Cluster1*=$\{IS_4, \{IS_2, \{IS_1, IS_5\}\}\}$ and *Cluster2*=$\{\{IS_8, \{IS_7, IS_{10}\}\}, \{IS_3, \{IS_6, IS_9\}\}\}$. Notice that *Cluster2* can be

Level of resolution	$\frac{IS_1}{IS_2}$	$\frac{IS_1}{IS_3}$	$\frac{IS_1}{IS_4}$	$\frac{IS_1}{IS_5}$	$\frac{IS_1}{IS_6}$	$\frac{IS_1}{IS_7}$	$\frac{IS_1}{IS_8}$	$\frac{IS_1}{IS_9}$	$\frac{IS_1}{IS_{10}}$	$\frac{IS_2}{IS_3}$	$\frac{IS_2}{IS_4}$	$\frac{IS_2}{IS_5}$	$\frac{IS_2}{IS_6}$	$\frac{IS_2}{IS_7}$	$\frac{IS_2}{IS_8}$
8	0.429	0.230	0.449	0.203	0.526	0.395	0.298	0.703	0.197	0.288	0.520	0.257	0.596	0.465	0.362
7	0.172	0.001	0.227	0.066	0.001	0.142	0.094	0.002	0.001	0.017	0.577	0.288	0.019	0.450	0.354
6	0.213	0.181	0.000	0.000	0.039	0.537	0.088	0.000	0.025	0.453	0.005	0.003	0.167	0.812	0.288
5	0.004	0.014	0.000	0.000	0.001	0.000	0.016	0.000	0.000	0.680	0.001	0.000	0.335	0.253	0.700
4	0.017	0.046	0.000	0.000	0.013	0.105	0.026	0.003	0.004	0.676	0.000	0.009	0.455	0.814	0.576
3	0.136	0.273	0.000	0.000	0.103	0.141	0.052	0.002	0.011	0.692	0.003	0.001	0.431	0.508	0.289
2	0.411	0.384	0.003	0.115	0.372	0.354	0.494	0.055	0.297	0.472	0.006	0.160	0.458	0.439	0.582
1	0.251	0.414	0.072	0.095	0.384	0.382	0.233	0.223	0.197	0.678	0.189	0.239	0.650	0.649	0.475
0	0.649	0.523	0.153	0.448	0.509	0.513	0.579	0.677	0.677	0.371	0.095	0.305	0.358	0.362	0.424

Level of resolution	$\frac{IS_2}{IS_9}$	$\frac{IS_2}{IS_{10}}$	$\frac{IS_3}{IS_4}$	$\frac{IS_3}{IS_5}$	$\frac{IS_3}{IS_6}$	$\frac{IS_3}{IS_7}$	$\frac{IS_3}{IS_8}$	$\frac{IS_3}{IS_9}$	$\frac{IS_3}{IS_{10}}$	$\frac{IS_4}{IS_5}$	$\frac{IS_4}{IS_6}$	$\frac{IS_4}{IS_7}$	$\frac{IS_4}{IS_8}$	$\frac{IS_4}{IS_9}$	$\frac{IS_4}{IS_{10}}$
8	0.762	0.250	0.728	0.462	0.788	0.680	0.581	0.898	0.454	0.240	0.576	0.445	0.343	0.746	0.234
7	0.032	0.024	0.989	0.938	0.514	0.976	0.958	0.602	0.556	0.225	0.011	0.374	0.284	0.020	0.015
6	0.005	0.121	0.007	0.004	0.197	0.842	0.329	0.006	0.146	0.432	0.946	0.999	0.977	0.494	0.920
5	0.088	0.075	0.000	0.000	0.186	0.129	0.522	0.035	0.029	0.394	0.996	0.992	0.999	0.962	0.954
4	0.249	0.292	0.000	0.002	0.284	0.669	0.395	0.129	0.158	0.924	0.999	0.999	0.999	0.998	0.999
3	0.028	0.104	0.001	0.000	0.250	0.314	0.147	0.009	0.042	0.394	0.994	0.996	0.986	0.810	0.939
2	0.080	0.378	0.006	0.177	0.486	0.467	0.609	0.090	0.404	0.958	0.992	0.991	0.996	0.910	0.988
1	0.462	0.423	0.099	0.129	0.468	0.466	0.300	0.289	0.257	0.573	0.888	0.887	0.795	0.786	0.758
0	0.531	0.531	0.142	0.424	0.485	0.489	0.555	0.656	0.656	0.820	0.851	0.852	0.879	0.913	0.913

Level of resolution	$\frac{IS_5}{IS_6}$	$\frac{IS_5}{IS_7}$	$\frac{IS_5}{IS_8}$	$\frac{IS_5}{IS_9}$	$\frac{IS_5}{IS_{10}}$	$\frac{IS_6}{IS_7}$	$\frac{IS_6}{IS_8}$	$\frac{IS_6}{IS_9}$	$\frac{IS_6}{IS_{10}}$	$\frac{IS_7}{IS_8}$	$\frac{IS_7}{IS_9}$	$\frac{IS_7}{IS_{10}}$	$\frac{IS_8}{IS_9}$	$\frac{IS_8}{IS_{10}}$	$\frac{IS_9}{IS_{10}}$
8	0.815	0.713	0.618	0.913	0.492	0.369	0.275	0.680	0.179	0.396	0.788	0.279	0.856	0.373	0.082
7	0.065	0.667	0.573	0.099	0.079	0.973	0.954	0.588	0.541	0.401	0.042	0.033	0.070	0.055	0.452
6	0.962	0.999	0.985	0.562	0.942	0.967	0.658	0.052	0.419	0.074	0.000	0.020	0.024	0.270	0.922
5	0.998	0.996	0.999	0.979	0.974	0.404	0.828	0.175	0.154	0.882	0.244	0.218	0.031	0.026	0.465
4	0.987	0.999	0.994	0.956	0.966	0.842	0.619	0.286	0.332	0.241	0.060	0.076	0.193	0.230	0.551
3	0.996	0.998	0.992	0.872	0.963	0.576	0.351	0.039	0.137	0.282	0.027	0.100	0.081	0.236	0.758
2	0.814	0.801	0.881	0.327	0.756	0.480	0.622	0.095	0.417	0.640	0.103	0.436	0.056	0.302	0.868
1	0.855	0.854	0.742	0.732	0.700	0.498	0.327	0.316	0.282	0.329	0.317	0.284	0.486	0.447	0.460
0	0.561	0.565	0.628	0.719	0.719	0.504	0.569	0.669	0.669	0.565	0.666	0.665	0.605	0.605	0.499

Table 1: p-values of the test of equality of wavelet spectra for each pair of inter-spike segments and all resolution levels

divided in two more similar subclusters. Following the results of Table 1, *Cluster1* contains four inter-spike signals with different wavelet spectra in several resolution scales, and *Cluster2* contains all the inter-spike segments that are similar in almost all scales. Obviously, each inter-spike segment of *Cluster1* is different of each inter-spike segment of *Cluster2* in some resolution scale. An exploratory wavelet comparison can be made from the scalograms. For instance, Figures 2 and 3 exhibe the signals IS_4 from *Cluster1* and IS_8 from *Cluster2* with their respective scalograms. Notice that, from $t = 50$ to $t = 350$, apparently signals are not very different among them and the scalograms exhibe a clear similarity between their energy distribution. But after $t = 350$ their trend and variability are clearly different at all resolution levels. To calculate the discrete wavelet transform we used the Daubechies wavelets with 8 null moments, and to calculate the scalograms we used the Morlet wavelet [4].

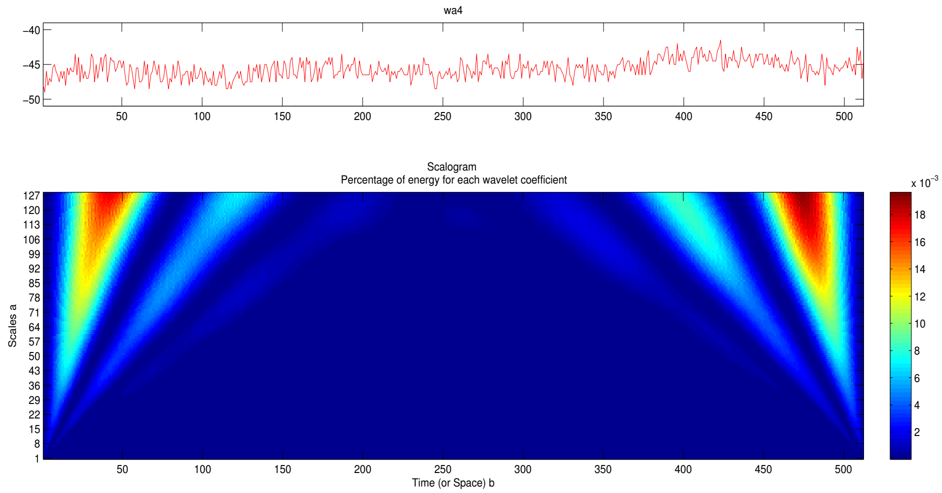

Figure 2: Energy distribution of inter-spike signal IS_4

4 Conclusions

On the basis of hypothesis testing and wavelet analysis we compared and classified a set of 10 non-stationary inter-spike signals of a peptidergic neuron. We could characterize two well defined groups with different patterns of energy distribution of the voltage fluctuations. With this method there is not necessary to consider any probabilistic distribution of burst.

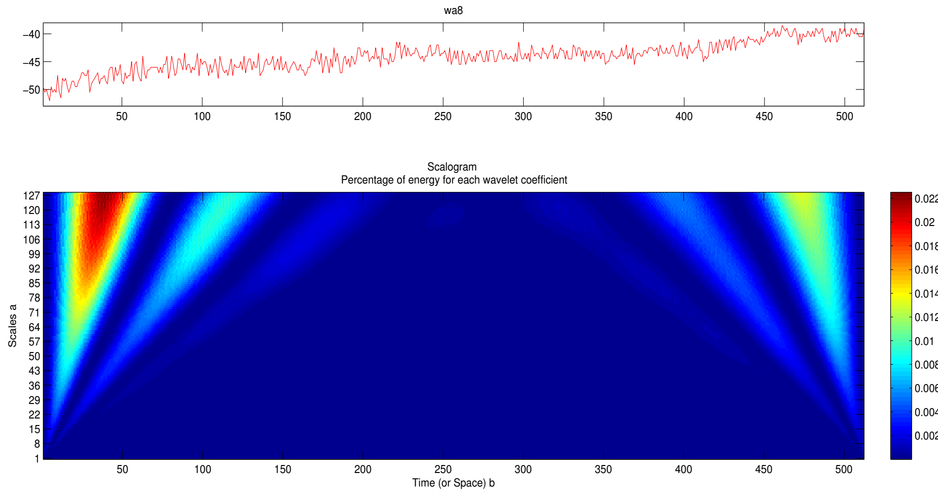

Figure 3: Energy distribution of inter-spike signal IS_8

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