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Changes of the Inner Time Structures in the Sequences of Interspike Intervals Produced by the Activity of Excitatory and Inhibitory Synapses: Simulation with Gaussian Input Processes

V. NOVÁK, J. SCHMIDT[1]

Department of Biocybernetics, Institute of Physiology, First Faculty of Medicine, Charles University and [1]LOGICA, Prague, Czech Republic

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Summary

The computer simulation of space-temporal summation of post-synaptic potentials of neurone's membrane demonstrated the outstanding changes in the inner time structures of generated interspike intervals. The output time series of ISIs were studied using non-standard kind of time analysis - recurrence plot method. Using this technique we observed phenomenon of unification in inner time structures of output series. Further we identified such parameters of model which exerted the most considerable influence on this phenomenon.

Key words

Computer simulation of space-temporal summation – Recurrence plot method – RP diagram – Time structures' unification

Introduction

A model of neuronal stochastic activity has been designed according to the results of actual experimental physiology. In principle, it is a discrete polynomic approximation of post-synaptic potentials of excitatory and inhibitory types. With the same approximation, the shape of spikes and the course of changes in threshold during the absolute and relative refractory phase was also modelled.

The space-temporal summation of modelled post-synaptic potentials was evaluated as a weighted sum where the adjustable levels of weights reflect the influence of individual input synapses on the resulting potential. This model thus simulates the electrophysiological actions, which occur on the membrane of a living neurone. At the same time, the activity of individual synapses, either excitatory or inhibitory, as well as the activity of multisynaptic inputs can be modelled. Every simulating experiment has a specific number of degrees of freedom to which correspond the adjustable and physiologically interpretable parameters. These parameters include a number of input synapses and their corresponding excitatory or inhibitory weights (WE, WI respectively). Further variables include the absolute refractory phase (ARP) duration, the threshold level outside the area of the refractory phase (THR) and the properties of input stochastic point processes (Novák and Schmidt 1995, 1996).

In the above mentioned papers some phenomena were described which are related to the dynamic actions of two synapses, one excitatory and the other inhibitory. The different realizations of stochastic point processes with Gaussian distribution of interspike intervals (ISIs) led to the two types of synapses. Their mean values are much shorted than the absolute refractory phase duration. With relation to the analysis of output sequences of ISIs we introduced a special term, the so-called e-curve, which indicates the dependence of the number N ISIs of the output point process upon the size of excitatory weight WE. Other adjustable parameters (WI, ARP, THR, and number of ISIs) of the input process always have the same value (Fig. 1). Every dot of the e-curve corresponds to one experiment, where, depending on the realized space-

temporal summation, both known input point processes are transformed into an output point process that has, in advance, unpredictable properties. It was observed that not only the number N of ISIs of the output point process (e-curve) but also of its statistic properties, had changed. This was described by Novák and Schmidt (1996) who also mentioned characteristic examples of transformation of both input stochastic processes into an output process. These phenomena were evaluated by taking into account only the tests carried out on several known statistic distributions and were found by their corresponding global statistic characteristics. But the obtained output sequences of ISIs had not yet shown their inner time correlations. The aim of the present paper was to describe these relations.

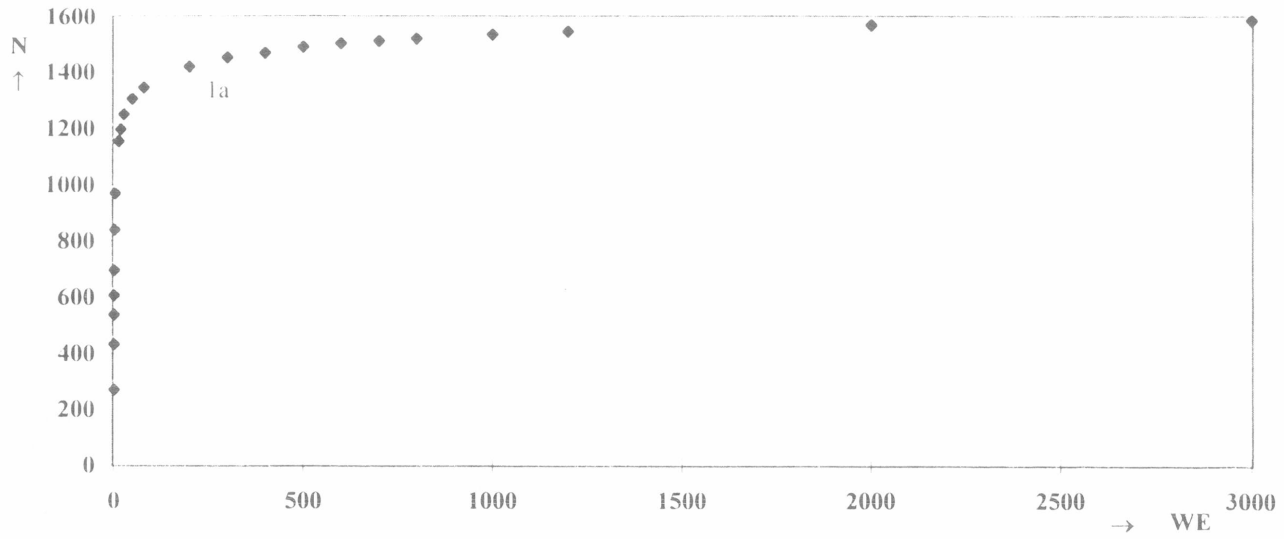


Fig. 1. *The course of the e-curve corresponds to the experiments 1a (WI = 1, ARP = 2.4 ms, THR = −60 mV).*

Table 1. The summary of the analysed series of experiments. Here WI represents the weight of the inhibitory synapse, ARP is the absolute refractory phase duration, THR is the threshold level. Every experimental series includes experiments that differ by values of excitatory weight WE. Quantity N (WE = 3000) gives a number of ISIs of output series for the experiment with the value of excitatory weight WE = 3000.

Series of experiments	WI [1]	ARP [ms]	THR [mV]	N(WE=3000) [1]
1a	1	2,4	-60	1588
2a	15	2,4	-60	1586
3a	25	2,4	-60	1587
1b	1	4,8	-60	883
2b	15	4,8	-60	883
3b	25	4,8	-60	883

Previously, Novák and Schmidt (1996) showed that with the same definition of inputs in the model and with the same value of absolute refractory phase (ARP) and threshold level (THR), a monoparametric system of e-curves can be found. A certain constant inhibitory value WI corresponds to every e-curve of this system. All e-curves of this system have their starting dots at different levels of non-zero weight WE and are asymptotic in character with only one common limiting value. That is dependent on the value of the absolute refractory phase (Fig. 2). The characteristics of these experiments corresponding to the measured e-curves of the system are given it Table 1. There we also indicate the individual series of experiments. In the following

paragraphs we will use simpler reference, e.g. if we talk about the experiment 3a, WE = 400 (Table 1), we mean that the experiment belongs to the series of experiments 3a and that its excitatory weight equals 400 (WE = 400). This experiment corresponds, in curve 3a, to a single point. At this point, the value of independent quantity WE is equal to 400. To quantify the inner time correlations between ISIs of output point processes we used the recurrence plot method (Eckmann *et al.* 1987, Kaluzny and Tarnecki 1993).

Methods

The method of analysis according to Kaluzny and Tarnecki (1993) is based on the time series, realized by N interspike intervals (N+1 spikes). The basic analysed element is the so-called segment of dimension **d**, which represents a grouping of **d** consecutive interspike intervals. The method of analysis can be described as an in-pair comparison of segments that were taken from the tested series. We used the metrics (1.1) to evaluate the similarity between the two segments.

$$\mathrm{dist}(i,j,k)=\left(\sum_{k=0}^{d-1}\left|\tau_{i+k}-\tau_{j+k}\right|\right)\Big/\sum_{k=0}^{d-1}\tau_{i+k} \qquad (1.1)$$

where i,j = 1,2, ..., N-d; d << N

Indexes i and j determine the order of the segment in the time series which is analysed (a time series contains N interspike intervals). Two segments of the dimension **d** are "similar" to each other, if the value of the expression (1.1) conform with condition (1.2).

$$\mathrm{dist}(i,j,d)\le r \qquad (1.2)$$

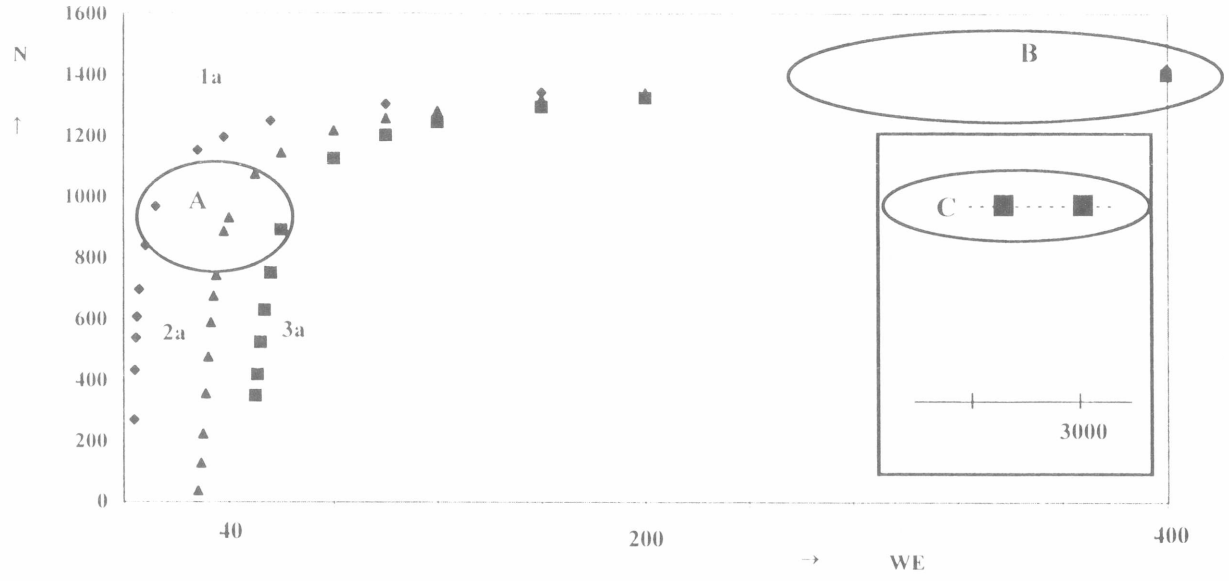


Fig. 2. *The monoparametric system of e-curves corresponds to the experimental series 1a, 2a, 3a (compare with Table 1). Areas A, B, C include the experiments that were analysed by the recurrence plot method (RP).*

In such a case, a dot with i, j co-ordinates is placed on the RP diagram. The resolution **r** is equal to a limiting value of the fraction (1.1) when segment j is still considered to be the same as segment i. If the resolution **r** is, for example, equal to 0.01, it means that we allow a maximum 1 % deviation in the size of the j-th segment (corresponding to the j-th group of d consecutive ISIs) from the size of i-th segment (corresponding to the i-th group of d consecutive ISIs). In this way, the RP diagram represents the square of the dimension NxN with the horizontal (i) and vertical (j) co-ordinate. Displaying such a square for high values of N would be distorted due to its size and would complicate the analysis of the time series. Therefore, only the RP diagram with the size of the edge up to i = j = 400 of dots is shown in this paper. Several of such RP diagrams then correspond to longer time series, which are noted in the referring

commentaries in the figures. Dots that are placed on the diagonal, connecting the lower left corner with the upper right corner of the RP diagram, are the result of comparing the segment of the dimension **d** with itself (i.e. for i = j). According to the expression (1.1) RP diagram is symmetrical with this diagonal.

Let us consider dots on the abscissa which are shifted from the diagonal of the RP diagram to the direction of co-ordinate j with the difference of value p. Its boundary dots have co-ordinates [i, i+p], [i+m, i+m+p], where m = 1, 2, 3, ... Dots appearing on this abscissa correspond to two similar sequences of (m+1) segments in the analysed series. Both sequences are mutually shifted according to the difference of value p of the segments. At the same time, the i-th segment of the first sequence is similar to the (i+p)-th segment of the second sequence etc.

Dots appearing on the vertical abscissa can thus correspond with the set of consecutive segments that are similar to the only "template". The frequent appearance of such forms indicates a small inner variability in the series of ISIs. It may also be caused by an inappropriate selection of the resolution **r** or dimension of segment **d**. Due to the symmetry of a RP diagram and according to its diagonal, dots placed on a certain vertical abscissa correspond with the same number of dots appearing in its opposite half-plane on the horizontal abscissa.

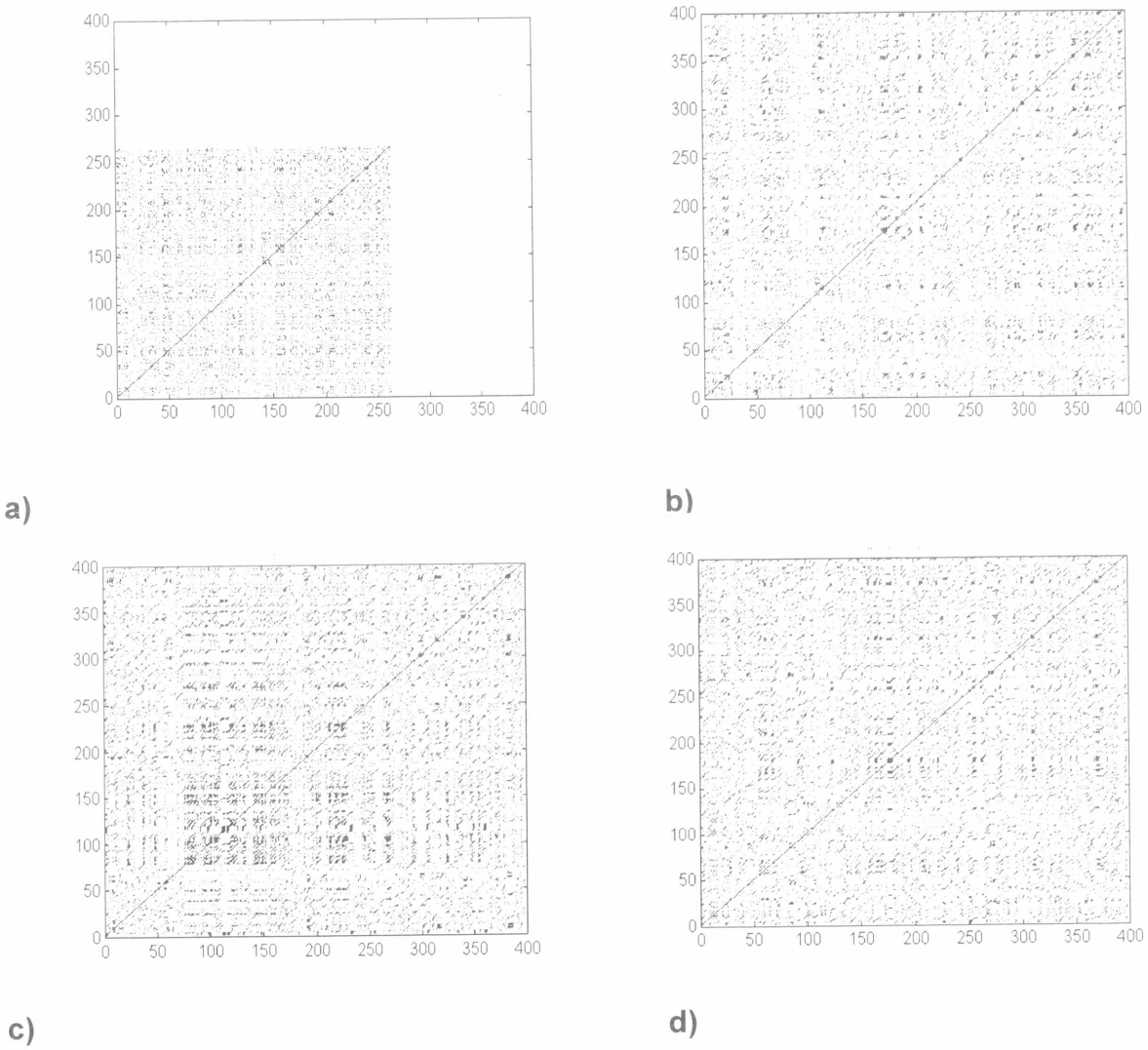


Fig. 3. *RP diagrams of the first 400 segments of output sequences of ISIs corresponding to the experimental series 1a. In part a) analysis of the experiment is shown with the value of excitatory weight WE = 1.85, dimension of segment d = 3 and the resolution r = 0.05. Similarly, part b) corresponds to the experiment with WE = 50, d = 3, r = 0.025. Part c) includes experiments with WE = 400, d = 3, r = 0.025 and part d) includes experiments with WE = 3000, d = 3, r = 0.025.*

The so called "white" vertical strips, which are marked off with the values of segment order (i, i $+\Delta$i), indicate a possible unique character of segments that are placed in the interval of value order (i, i $+\Delta$i) when the resolution **r** is selected. The width Δi of such a strip depends not only upon the number of unique segments in the analysed series of ISIs, but mainly upon the selection of the resolution **r** or dimension of segment **d**. When decreasing the value of both these parameters (**r** or **d**), the speed of computation increases but, at the same time, the RP diagram becomes more empty. The reason for this result is the identification of a small number of segments which are evaluated as "similar". The informative value of such an RP diagram thus becomes useless. On the other hand, when the appropriate combination of the resolution **r** and the dimension of segment **d** is selected, new contours are revealed in the RP diagram.

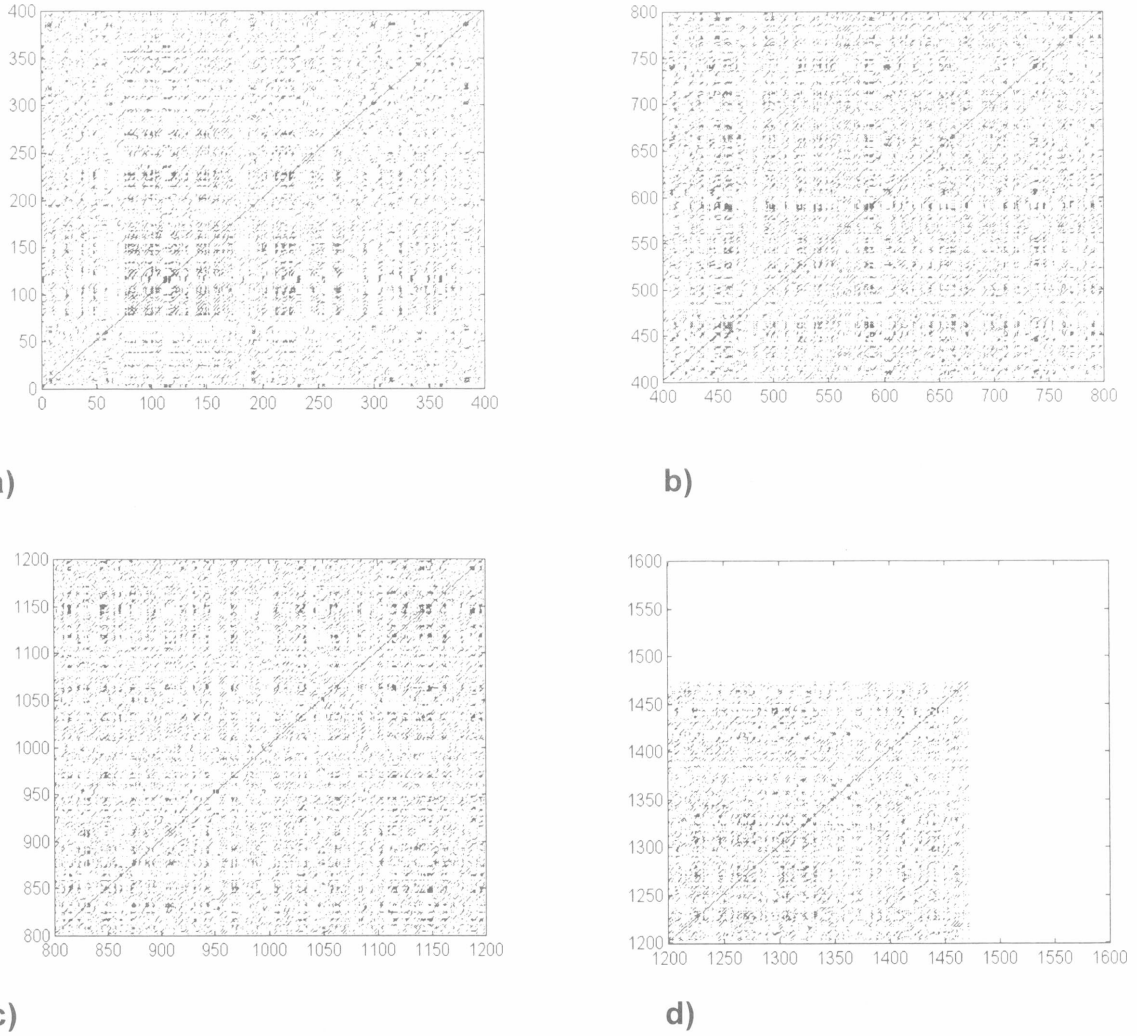


Fig. 4. *RP diagrams of one complete output series of ISIs, corresponding to the series of experiments 1a and to the value of excitatory weight WE = 400. Dimension of segment is d = 3, the resolution is r = 0.025.*

Results

Using the RP method, we concentrated mainly on the three sets of experiments that are given in Fig. 2 and are marked as areas A, B and C. Area A corresponds to the experiments with excitatory weight WE ϵ (10, 50), area B corresponds to excitatory weight WE ϵ (260, 440) and finally area C includes experiments with excitatory weight WE ϵ (2920, 3040). First, let us inspect the experiments appearing on e-curve 1a (see Fig. 2 and Table 1). In all the observed areas A, B, C, the RP diagram shows a "white" strip, either horizontal or vertical, which corresponds to the unique segments of ISIs (Fig. 3). In area A, i.e. in the

region of low WE values, the appearance of strips is not very obvious. With increasing value of the excitatory weight their appearance becomes more marked (Fig. 3a, b). In the experimental area B, which corresponds to higher values of excitatory weight, characteristic sequences of dots placed on short abscissa were found, parallel with the main diagonal of RP diagram (Fig. 3c). In the output time series of these experiments, short sequences with a similar dimension of segments d = 3 began to appear. It is interesting that with the growing size of shift p from the diagonal the segments become less marked. After several repetitions they are disturbed by sharp "white" strips. This means that these sequences of similar segments are separated from each other by short sequences of unique segments. For experiments with a high value of excitatory weight, i.e. in area C, where the e-curve is already asymptotic in character, this phenomenon is less marked (Fig. 3d).

We demonstrated the above mentioned phenomena on RP diagrams starting with 400 segments of the analysed series. But the above described contours are repeated in different modifications during the course of the whole analysed series. Figure 4 shows RP diagrams for the complete analysed series of ISIs corresponding to the experiment of series 1a with excitatory weight WE = 400 (see Table 1). A clear square contour which is obvious in the areas of segments with serial numbers 80–175 again appears in the areas of serial numbers 1275–1325 (see Fig. 4a and 4d). Similarly, the contour looking like a "dark cross", in the area of serial numbers of segments 210–230 (see Fig. 4a) is again repeated in the area of serial numbers 580–590 (see Fig. 4b). But it is missing in the remaining course of the analysed series of ISIs. Even this case is obviously due to the short sequences in similarly evaluated segments of ISIs.

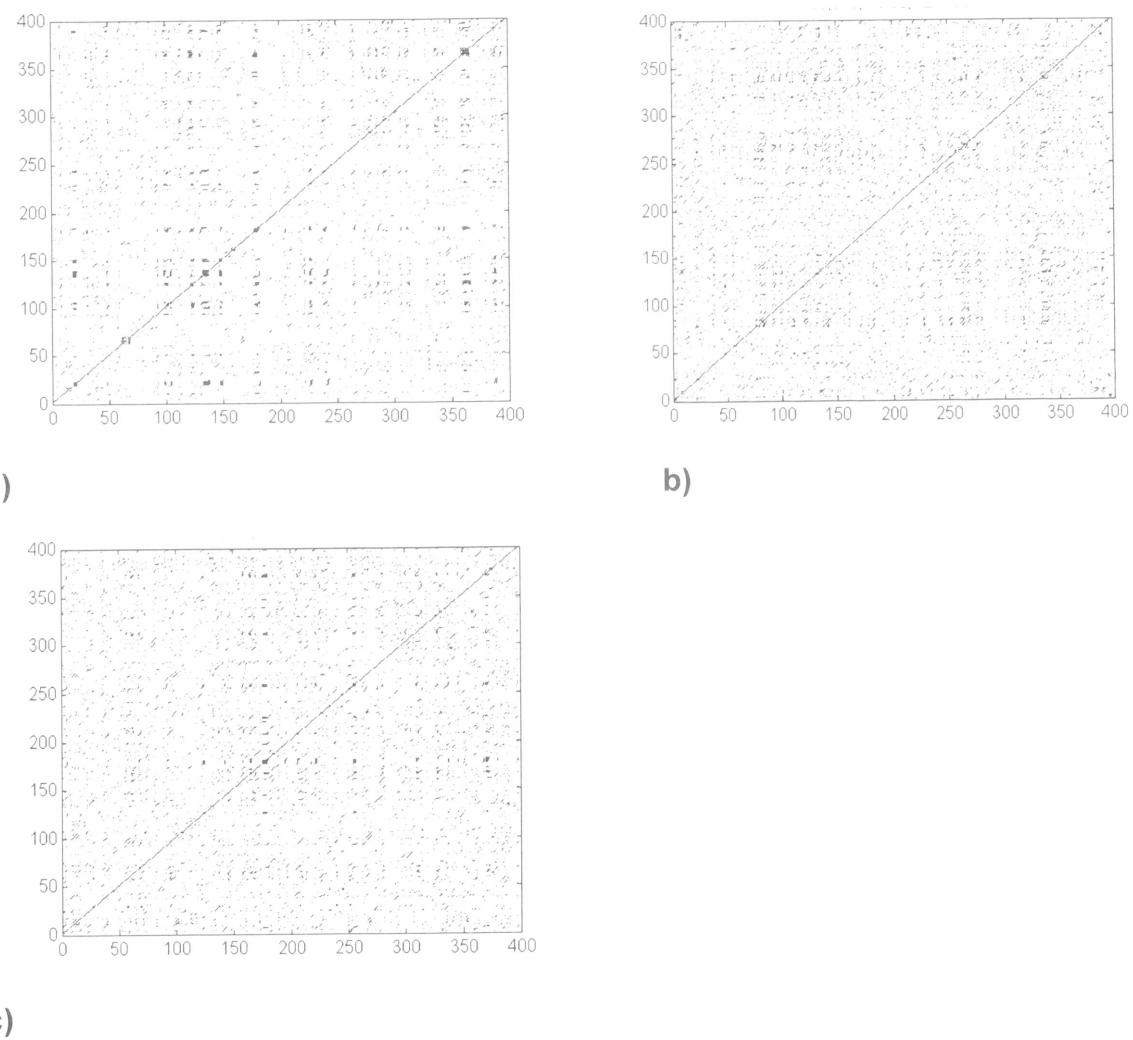


Fig. 5. *RP diagram of the first 400 segments corresponding to the output sequences of ISIs of the experimental series 3a. Fig. a) have WE = 50, d = 3, r = 0.03. Fig. b) have WE = 400, d = 3, r = 0.03. Fig. c) have WE = 3000, d = 3, r = 0.03.*

In the series of experiments 3a, the level of weight of the inhibitory synapse (see Fig. 2 and Table 1) was markedly increased. In Figure 5, the RP diagrams of experiments with the value of excitatory weight WE = 50, 400 and 3000 had the same level of inhibitory weight WI = 25. The characteristic square contour that we found in Figure 4a in the range of serial numbers of segments 80–175, was the same even after increasing the level of inhibitory weight for the series of ISIs experiments with excitatory weights WE = 50. But it is transformed into the range of serial numbers 100–150 and it is not as markedly obvious, however, it is missing in the subsequent analysed time series. For the experimental series 3a and the value of excitatory weight WE = 50 the RP diagrams are emptying. In comparison with the experimental series 1a, an increased level of inhibitory weight gave a much higher number of "white strips" in the series of experiments 3a. This phenomenon proves the presence of a higher number of unique segments of ISIs (see Fig. 5b and 5c). It is thus obvious that the time series of ISIs, corresponding with experiments to higher values of inhibitory weight are in their inner structure more heterogeneous in comparison with the series of ISIs corresponding to lower values of the inhibitory weight.

When increasing the value of absolute refractory phase (ARP) by two the finite RP diagrams displayed an interesting phenomenon. The corresponding series of experiments are marked 1b, 2b, 3b (see Table 1). First, let us compare the 1a and 1b experiments with the value of excitatory weight WE = 400 differing only by the two-fold level of absolute refractory phase ARP. The value of inhibitory weight is the same in both cases. Both analysed series have almost the same value of deviation D from the mean value E (see Table 2). But they are rather different in their inner structure that has become more homogeneous with the two-fold value of ARP (compare Fig. 1c and Fig. 6). We also obtained the same result also in experiments 2b and 3b. With a growing excitatory weight WE in the series of experiments with a two-fold value of ARP, another interesting phenomenon will appear. If we observe the RP diagrams of experiments, realized consecutively with an increasing value of excitatory weight WE, we can find a decreasing influence of the level of inhibitory weight WI on the changes of inner time structure of the finite time series of ISIs. This is supported by the experiments with an excitatory weight value WE = 3000, which were chosen from the series of experiments 1b, 2b and 3b. Their RP diagrams are the same except for a few isolated dots (see Fig. 7a, 7b and 7c). An increased value of the absolute refractory phase for high values of excitatory weight brought a certain "unification" of the inner time structure of the output series of ISIs, which does not vary at certain intervals of inhibitory weight values.

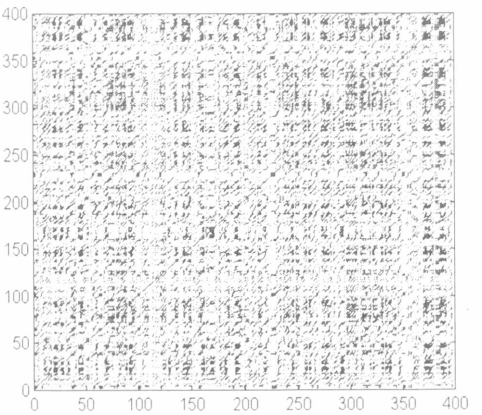


Fig. 6. *RP diagrams of the first 400 segments of output sequence of ISIs for the experiment from series 1b with excitatory weight WE = 400 (dimension of segment d = 3, the resolution r = 0.03).*

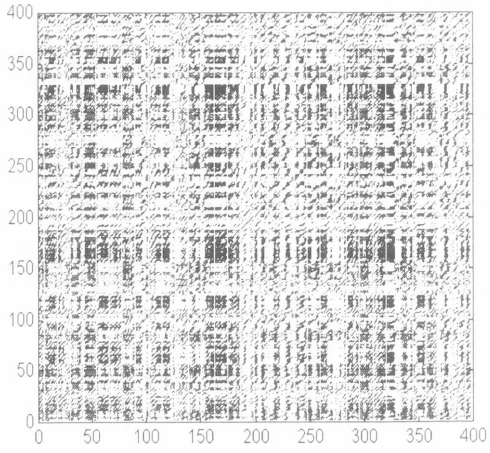
Table 2. The mean values (E) and deviation (D) of output series of ISIs for the series of experiments given in Table 1 and for the value of excitatory weight WE = 400.

	1a	1b	2a	2b	3a	3b
WE	400	400	400	400	400	400
E [ms]	3,258	5,712	3,25	5,717	3,266	5,725
D [ms ^{2}]	0,021	0,025	0,023	0,027	0,026	0,031

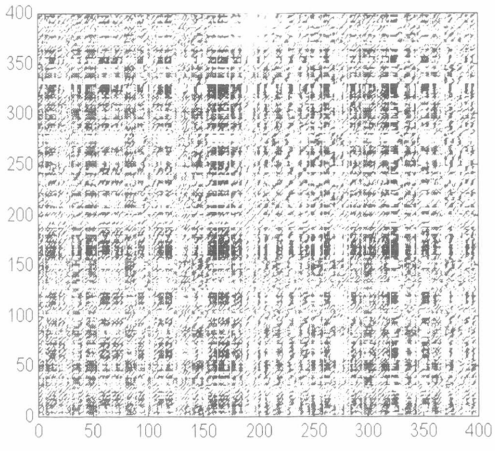
Conclusion

In the present paper, we studied a non-standard kind of time analysis of ISIs series obtained by modelling dynamic processes on the membrane of a neurone. The analysed series correspond to the activity of two input synapses, one excitatory and the other inhibitory. Different realizations of time series with Gaussian distribution of ISIs were led to both input synapses. The output time series of ISIs obtained by simulations were analysed using the recurrence plot method. This method has made it possible to find and to describe the inner time structure of the output series. In many cases it was proved that changes in the obtained inner time structure of output series of ISIs can be definitely modelled by changing the physiologically interpretable parameters of our model. In these modulations, the weight of the excitatory synapse WE and the value of the absolute refractory phase duration ARP exerted a considerable influence. Less marked were the changes in the weight of inhibitory synapse WI.

Some of the described changes of time structure inside the analysed series of ISIs can be compared to so-called "firing patterns" (Sherry and Marczynski 1972, Schmidt and Thews 1977). Their detailed analysis should, moreover, disclose the absolute ordering of interspike intervals inside similar looking segments (Dayhoff and Gerstein 1983a,b, Xiaoying and Zhenming 1991).



a)



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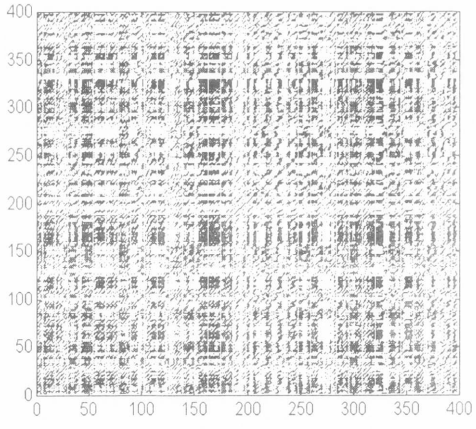

c)

Fig. 7. *RP diagrams of the first 400 segments of output sequences of ISIs for excitatory weight WE = 3000 and the series of experiments 1b (Fig. 7a), 2b (Fig. 7b) and 3b (Fig. 7c). In all the cases, dimension of the segment is d = 3 and the resolution is r = 0.025.*

The described experiments carried out on our model show that even in a simple double-synaptic input when preserving the same input processes, the global statistic properties of the output series of ISIs can be significantly changed. These changes are related to the changes of physiologically interpretable parameters. At the same time, with constant global properties of the ISIs series, we can change even their inner time structures. All these facts experimentally characterize the space-temporal summation of post-synaptic potentials, corresponding to two synapses.

If two or more e-curves converge with an increasing value of WE to one common limit (e.g. Fig. 2), some "outer" statistical characteristics (e.g. mean value, variance etc.) of corresponding ISIs series converge as well. Because of the e-curve character, this behaviour is not so extraordinary. A much more important fact has been discovered by comparing two different ISIs series. From the "inner" time structures point of view even here we can observe the phenomenon of unification when the value of WE is increasing (Schmidt and Novák 1997).

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Reprint requests

Doc. Ing. V. Novák, CSc., Department of Biocybernetics, Institute of Physiology, First Faculty of Medicine, Charles University, Albertov 5, 128 00 Prague 2, Czech Republic.