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Is the Action Potential Waveform Constant?

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1. Introduction

Neurons perform multiple operations. These operations include the receiving of information, processing, coding and transmitting it to other neurons. These involve synapses, membrane ionic channels and changes in membrane potential. The operations are thought of as steps in an algorithm or as computations. The concept of a neuron as a simple integrator unit is antiquated. A neuron could be regarded as complex processor with mixed analogue-digital logic and highly adaptive synaptic elements. Individual nerve cells convert the incoming streams of binary pulses into analogue, spatially distributed variables, such as postsynaptic membrane potential and calcium distribution throughout the dendritic tree and cell body. A number of transformations are applied to these variables which might be understood as subtraction and addition, low- and band-pass filtering, normalization, etc. (Koch, 1999).

"The mammalian brain contains more than 10^{10} densely packed neurons that are connected to an intricate network. In every small volume of the cortex, thousands of spikes are emitted each millisecond. For a long time it has been thought that most of the relevant information was contained in the mean firing rate of the neuron. The firing rate was defined by a temporal average. The concept of mean firing rates has been successfully applied during the last 80 years. It is clear, however, that an approach based on a temporal average neglects all of the information that might be contained in the exact timing of the spikes. From behavioural experiments, it is known that reaction times are often short. Temporal averaging can work well in cases where the stimulus is constant or slowly varying and does not require a fast reaction from the organism. Real inputs change on a fast time-scale. A fly can react to new stimuli and change the direction of flight within 30-40 ms; it has to respond after a postsynaptic neuron has received one or two spikes. Humans can recognize visual scenes in just a few hundred milliseconds. This does not leave enough time to perform temporal averages on each level. In fact, humans can detect images in a sequence of unrelated pictures even if each image is shown for only 14-100 milliseconds. In some cases, a neuron might be driven by an external stimulus which is suddenly switched. For example, when we look at a picture, our gaze jumps from one point to the next. After each saccade, the photo receptors in the retina receive a new visual input. Information about the onset of a saccade would easily be available in the brain and it could serve as an internal reference signal. In such a scenario, it is possible that there exists a code where, for each neuron, the timing of the *first* spike after the reference signal contains all of the information about the

new stimulus. In such cases, each neuron transmits exactly one spike per stimulus and it is clear that only the timing conveys information rather than the number of spikes. In the hippocampus, in the olfactory system, and also in other areas of the brain, oscillations of some global variable (e.g., the population activity) are quite common. These oscillations could serve as an internal reference signal. Neuronal spike trains could then encode information in the phase of a pulse with respect to the background oscillation. There is, for example, evidence that the phase of a spike during an oscillation in the hippocampus of rats conveys information on the spatial location of the animal which is not fully accounted for by the firing rate of the neuron" (Gerstner & Kistler, 2002).

The next step in information coding was "rate codes" (Tateno & Robinson, 2006). In fact, there are three different notions of rate, the three definitions of which refer to three different averaging procedures: either an average over time, an average over several repetitions of the experiment, or an average over a population of neurons.

In the view of the above mentioned codes, an action potential (AP) is normalized into a stereotypical form. However, recently we have witnessed another approach to information processing in the single neuron. An ongoing debate surrounds the question of the temporal resolution at which information is represented by individual APs. The longstanding view that an AP is an unchangeable thing has now been challenged.

There is a method of neuron stimulation called "conductance injection" (or "dynamic clamp") (Robinson, 1994). Conductance - representing the response to patterns of presynaptic firing - is applied to the neuron such that current is injected according to the instantaneous value of this conductance and the neuron's membrane potential. Conductance injection reproduces the current-limiting and shunting behaviour and the other dynamical aspects of real synaptic inputs. If experiments are done using conductance injection, the shapes of the resulting APs follow a characteristic width–height distribution. With this method it is possible to look up its immediate conductance history for each spike. The conductance histories leading to different AP waveforms are different: higher background conductance results in broader spikes.

In a study by de Polavieja et al. (2005), dynamic conductance stimulus patterns were used to investigate whether spike shapes reliably depend on the previous stimulus history. They show that in cortical neurons AP waveforms depend on the previous 50 ms of the conductance stimulus history. The authors concluded that this relationship is low in noise, carrying three to four times more information than spike times alone. Although spike frequency and spike shape are related, in general, it is only the spike shape which reliably depends on the different features of the stimulus history on a trial-by-trial basis.

It was shown by Koch & Segev (2000) that for a spike rate of 10 AP/sec, a code based on AP waveforms can transmit 200 bits/sec, compared to the 50 bits/sec of a code based on spike times. It becomes clear that the interaction between incoming postsynaptic potentials and a back propagating AP - as well as, therefore, the probability of producing the next spike - depends upon the AP waveform.

In a recent work, Juusola et al. (2007) have shown that the different AP shapes produced by the same pyramidal cortical neuron are not random but correspond to the level of the

previous conductance. The authors named this phenomenon the "AP waveform code". It is proposed that the code influences postsynaptic targets in different ways. One of these ways sees APs of different shapes interacting with incoming excitatory postsynaptic potentials (EPSPs) and influencing synaptic integration differently. Another way could be that the variability of AP waveforms might be saved in the synaptic terminal until a different calcium influx translates these variables into different EPSP sizes in the postsynaptic cell.

Shu et al. (2006) have shown that the somatic AP waveforms survive axonal conduction. It was also shown that the differences in the somatic AP waveforms are further augmented by axonal conduction. This result was obtained using simultaneous somatic and axonal recordings. Furthermore, the EPSPs that they recorded were larger when the presynaptic somatic and axonal spikes were broader.

Häusser et al. (2001) have shown that because the cortical APs of different waveforms differentially shunt incoming synaptic events, they participate in the synaptic integration and the generation of succeeding APs. Therefore, at least 50 ms of the stimulus history can affect the state of the synaptic integration of the neuron and the generation of spikes, through the modulation of the waveform. This is a form of local encoding at the single-neuron level with a 50-ms-long memory, which affects neuronal communication by influencing the production of future spikes.

In summary, for a long time it was thought that the waveform of the AP was constant. However, new evidence continues to show the opposite: it has become clear that the waveform of an AP carries information.

The question arises: Is it possible that the AP waveform contains information about habituation when a single neuron is stimulated with intracellular current impulses and habituates to the stimulation?

The most desirable experiment for answering this question might consider conductance injection into the single neuron. However, there are major limitations to conductance injection. It has to be fast and temporally consistent. For this reason, we decided to stimulate a single neuron with the injection of short current impulses and investigate habituation to the stimulation. We investigated the possible relation of changes of the AP's parameters (and consequently the AP waveform) with the process of habituation.

2. Materials and methods

The isolated nervous system of the mollusc *Helix pomatia* was used in the experiments. Each snail was anesthetized by the injection of isotonic $MgCl_2$, described elsewhere (Patsvania et al., 2008). Then the nervous system was separated from the body. Ganglia were treated with 0.5% Pronaze solution (Protease from Streptomyces griseus - "Sigma-Aldrich") for 30 minutes at room temperature. After proteolytic treatment, the conjunctive tissue was carefully removed using fine micro scissors. Then, the ganglia were washed several times with Ringer solution. This solution consists of: NaCl - 80 mmol, KCl - 4 mmol, $CaCl_2$ - 35 mmol, $MgCl_2$ .6 H_2O - 5 mmol, Tris -7 mmol at pH=7.5. The nervous system was placed in a Petri dish and positioned in a Faraday cage to filter out any environmental electromagnetic noise. The identified giant

neuron #3 of the Left Parietal Ganglion was selected for the investigation. The average diameter of this neuron was 150-200 μm. Identifications were made according to Arakelov et al. (1991). The most naturalistic means of stimulating the neuron is through synaptic input. Antidromic excitation of the nerve with direct current (DC) or pulsed voltage causes AP firing in the inter-neurons, which in turn excites the investigated neuron synaptically. However, if voltage is applied at different locations, the nerve reactions will differ from each other. For this reason, with nerve stimulation it is impossible to maintain any invariance of stimulation. This was the reason for which we chose neuron stimulation with intracellular short current impulses. In this case, it is easy to obtain a condition where the neuron reacts with one AP to one intracellular stimulating impulse. On the other hand, the current stimulating impulse has to be much shorter than the latency period in order to avoid the blending of the AP with the stimulating impulse. The reaction of the neuron depends on the amplitude of the intracellular stimulating impulses. Stimulation was always begun with impulses of a very low amplitude. At the beginning of each recording, the critical value of the intracellular stimulating impulse was established which depolarized the neuron to the threshold and caused the firing of an AP. The experiments showed that this value was always above 0.05 nA and varied from neuron to neuron. Each stimulus triggered only one AP. As such, the reaction pattern consisted of one AP as a reaction to one intracellular stimulating impulse. First, we established the value of the threshold (i.e. we found the critical value of the stimulus that depolarised a neuron to the threshold and caused the firing of only one AP). Next, we increased the amplitude of the stimulus to slightly higher than this critical value.

Figure 1 illustrates a neuron reaction to stimulation with intracellular impulses of an increasing amplitude.

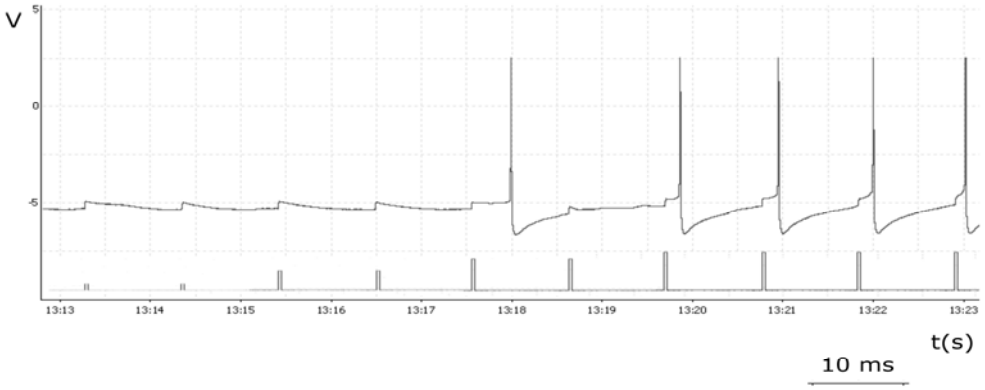


Fig. 1. Neuron reaction to stimulation with increased intracellular current impulses. Current stimulating impulses are shown schematically under the recording. The first four impulses evoke only small shift of membrane potential towards depolarization. The fifth stimulating impulse, with an amplitude 0.5 nA evoked the AP firing of the neuron. The sixth stimulating impulse and those following it have an amplitude of 0.6 nA. The duration of each intracellular impulse is 0.4 ms. It is obvious that this duration is much shorter than the latency period (the latency period is defined as the time interval between the front edge of stimulating impulse and the time moment when membrane potential crosses the threshold value).

For intracellular stimulation, the neuron was impaled with two glass microelectrodes (ME) filled with 2.5 mol KCl. For this purpose, "Piezo Mikromanipulators - PM 20" (Märzhäuser, Wetzlar, Germany) were used. The ME were prepared from capillaries - Borosilicate Tubing (PYREX©) BF 150 75 10 - with filaments (Sutter Instrument Company, Novato, CA, USA). The size of the microelectrode tip was less than 1 μm. The resistance of each microelectrode did not exceed 15 mOhm. Microelectrodes were connected to the "intracellular electrometer IE 251A" (Warner Instruments). One microelectrode served for registration and the other for intracellular stimulation. "Picoamper source K 261" (Keithley Instruments Inc., Cleveland, OH, USA) was used for intracellular stimulation. The output of this device was controlled by a specially designed pulse breaker guaranteeing the application of depolarizing current impulses to the neuron. The intracellular stimuli consisted of a train of depolarizing current impulses, each with a 4 ms width. The frequency of these impulses was 0.9 Hz. This value is close to the frequency of the AP firing of many of the pacemaker neurons of the mollusc ganglion which are synaptically connected to the investigated LPG#3. The PowerLab ML866 data acquisition unit (ADInstruments Co., Castle Hill, NSW, Australia) was used for the registration of experimental data. In Table 1, the variables measured in our experiments are given. All of these variables were measured for each AP. Consequently, sets of numbers were obtained for each experiment. The sets contain data about latent periods, W20s, Tr and Areas. Measurements were performed using the "peak analysis module" for the software "Chart-5".

Parameter description.	Notation
The time interval between the leading edge of the intracellular stimulating impulse and the appearance of AP triggering.	Latency Period
Width of the AP at the level of 20% from the baseline. The baseline corresponds to the neuron resting potential.	W20
Increasing time between two levels (10% and 90 % from the baseline) on the leading edge of the AP.	Tr
Area between the waveform and the baseline.	Area

Table 1. Designations used in the text.

3. Results

Neuron reactions to the intracellular current impulses depend on the amplitude and width of the stimulating impulses. The neuron reacted to the intracellular stimulating impulses with an AP several times, and then habituation arose. Habituation was expressed as a decline of the stimulus-induced AP. The time necessary for habituation varied from several seconds to 1-2 minutes. This time span covers the period between the first intracellular stimulating impulse and the last intracellular impulse after which no more AP was evoked. There is a one-to-one relationship between the time of habituation and the number of APs (or stimulating impulses). For this reason, we define the time of habituation as the amount of stimulating impulses necessary to give rise to habituation. For the purposes of illustration, a sample of the habituation dynamics for one of the neurons is shown in Figure 2.

After habituation, the recovery of the neuron required 15-20 minutes and a new series of stimulation might trigger APs. However, the new response was shorter and habituation was established sooner. For this reason, each neuron was stimulated with the train of intracellular impulses only once.

The parameters of AP, latent period (and consequently AP waveform) were not constant and varied during stimulation. Figure 3 shows a typical change of AP parameters and latent period evoked by the application of the recurrent intracellular current impulses.

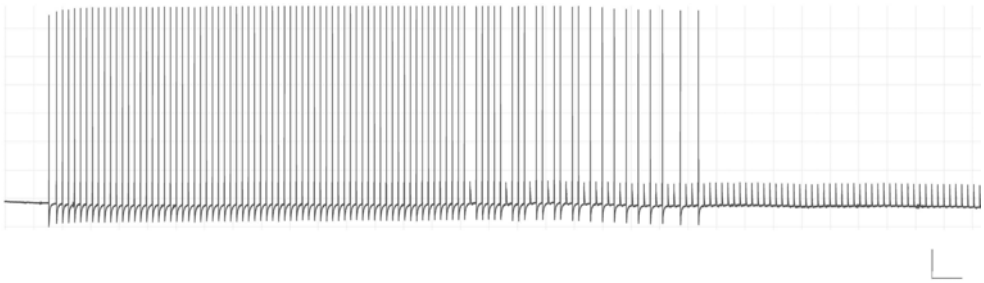


Fig. 2. Neuronal response to stimulation with intracellular current impulses. The neuron responded to stimulation with 93 AP after which all of the stimuli ceased to evoke an AP, Complete habituation was established and small depolarizing artefacts were present in recordings instead of the AP. The amplitude of the stimulus pulses was 0.7 nA. the width of the intracellular stimulating impulses was 4 msec. Current stimulating impulses are not shown because each of these impulses causes the firing of one AP or the appearance of one artefact on the recordings. The calibration is 10 mV, 5 s.

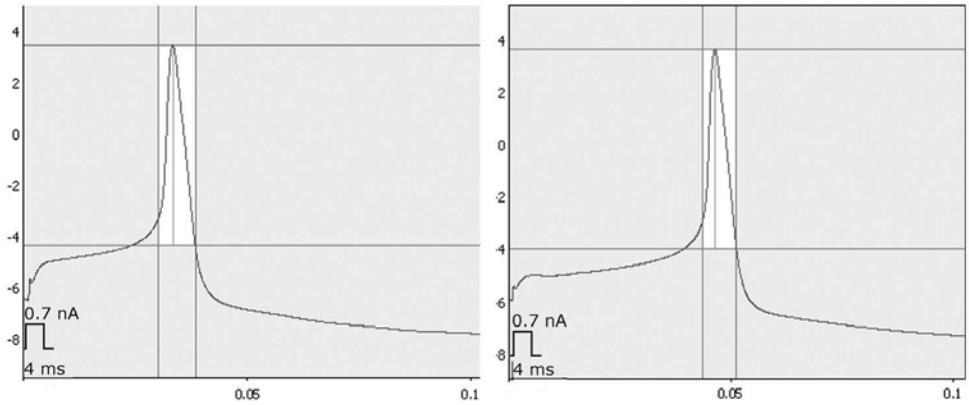


Fig. 3. The different AP parameters correspond to a different stimulus number:
a) AP fired by the neuron in response to the 1st intracellular current impulse. The parameters are: Latent period = 20.8 ms; W20 = 25.6 ms; Tr = 1.92 ms; Area = 0.106 V.s.
b) AP fired by the neuron in response to the 10th intracellular current impulse. The parameters are: Latent period = 33.6 ms; W20 = 33.6 ms; Tr = 2.56 ms; Area = 0.135 V.s. The broadening of the AP is evident. The intracellular stimulating impulses are schematically shown at the left lower corner of the recordings.

The parameters of the AP and the latent period varied irregularly during an increase of the number of the applied intracellular current impulses. The numerical values of AP parameters and the latent period trended to increase during an increase of the number of stimulating impulses (i.e. with an increase of the AP number, since the stimulus number coincides with the AP number). The typical dependence of the latent period, W20, Tr and Area on the stimulating impulse number (consequently on AP number) for one of the neurons is shown, respectively, in the Figures 4-7.

We determined the amount of information about habituation contained in the AP parameters (W20, Tr, Area) and the latent period. For this purpose, a mathematical model was selected for each parameter of the AP and the latent period. It was shown that this amount of information changes during an increase of the AP number. We deal with experimentally measured data. Consequently, it is essential that corresponding mathematical models have a stochastic character. In particular, sequences of latent periods and AP parameters (W20, Tr, Area) create a time series with a linear trend. According to the statistical investigations (the appendix), a time series with a linear trend represents a sufficiently good mathematical model. Concerning the time necessary for establishing habituation - it was not constant and it varied from neuron to neuron. Consequently, we obtained a numerical sequence containing 32 observed values of the time of habituation. The time of habituation might be regarded as a random variable. The theoretical mean value (mathematical expectation) of this random variable is unknown. A 99% confidence interval of this unknown mean value is 22, 45 -- 57, 49. The amount of information was experimentally calculated. The dynamics of the calculated information for the latent period are given in Figure 8. The information amount reaches its maximum value and then begins

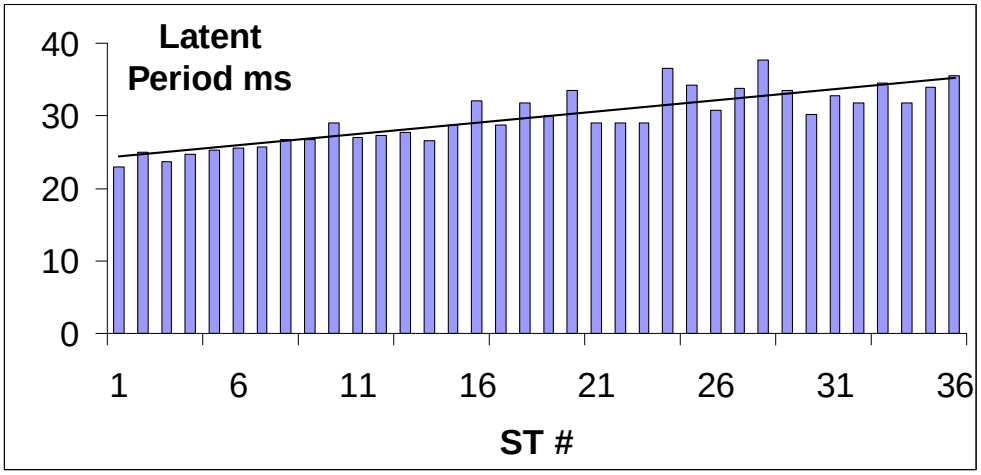


Fig. 4. An example of the latent period dependence on the stimulating impulse number for one neuron. On the abscissa, the number of intracellular stimulating impulses is plotted, while on the ordinate the latent period in milliseconds is plotted. Mean values of the measured latent period vary irregularly; however, the trend increases steadily. The amplitude of the applied intracellular current impulses was 0.1 nA and the duration of each of these impulse was 4 ms.

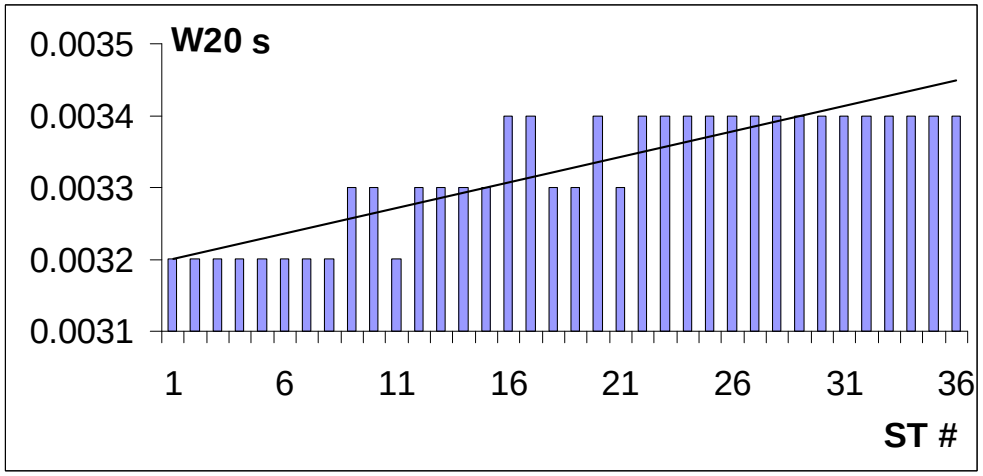


Fig. 5. An example of W20 dependence on the stimulating impulse number. On the abscissa is plotted the number of intracellular stimulating impulses, while on the ordinate is plotted W20 in seconds. The increase of the W20 is evident. The character of the trend is towards an increase. The amplitude of the applied intracellular current impulses was 0.1 nA, while the duration of each of these impulses was 4 ms.

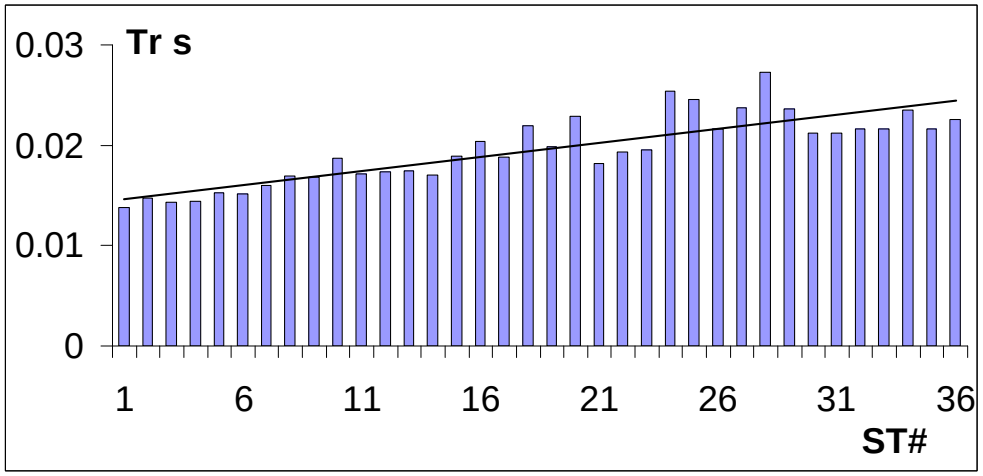


Fig. 6. Tr dependence on the stimulating impulse number. On the abscissa is plotted the number of intracellular stimulating impulses, while on the ordinate is plotted Tr in seconds. Tr varies irregularly, like the latent period. The trend also increases. The amplitude of the applied intracellular current impulses was 0.1 nA and the duration of each these was 4 ms.

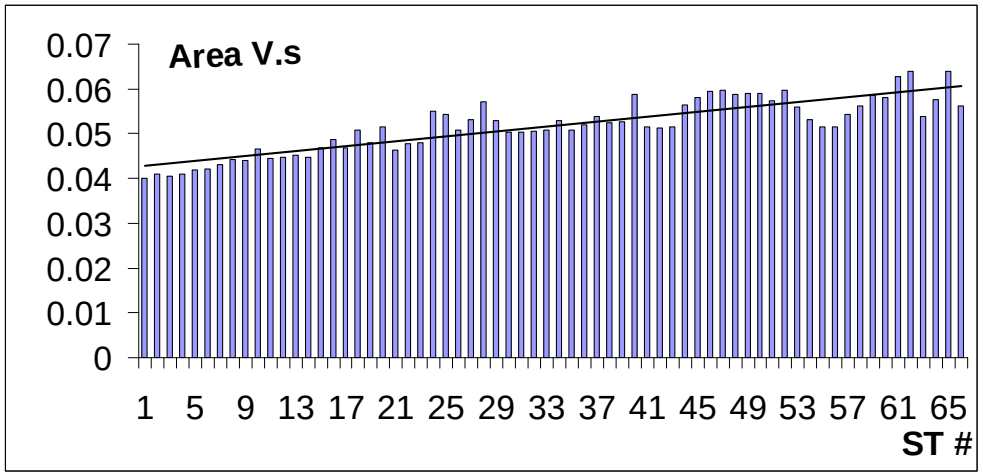


Fig. 7. Area dependence on the stimulating impulse number. On the abscissa is plotted the number of intracellular stimulating impulses, while on the ordinate is plotted the Area in Volt•seconds. The variations and trends are similar to the other parameters. The amplitude of the applied intracellular current impulses was 0.1 nA, while the duration of each of these pulses was 4 ms.

to decrease during the above mentioned 99% confidence interval. The dynamics of the calculated information for the other AP parameters were similar and, for this reason, are not shown here.

For more detailed consideration, let us consider the case of the latent period and then generalize it for the AP parameters. As is known (Yaglom & Yaglom, 1983), one random experiment contains some information about another random experiment. It is obvious that experiments must be interconnected. In our case, the first random experiment is the latent period's variation relative to its own trend. Let us denote this random experiment as experiment α. The second random experiment shows whether habituation is established. Let us denote this experiment as β.

The stimulating impulse numbers are plotted on the X axis. The amount of information contained in the α experiment in respect of the β experiment (i.e., about habituation) is plotted on the Y axis (Figure 8).

The number of the AP (which coincides with the stimulating impulse number) is plotted on the X axis. The calculated amount of information is plotted on the Y axis. As is noticeable, the amount of information firstly increases very quickly with an increase of the AP number. Then, the amount of information reaches a maximum value, after which it decreases. The 99% confidence interval is 22, 45 -- 57, 49. This confidence interval is shown through the lighter colouration.

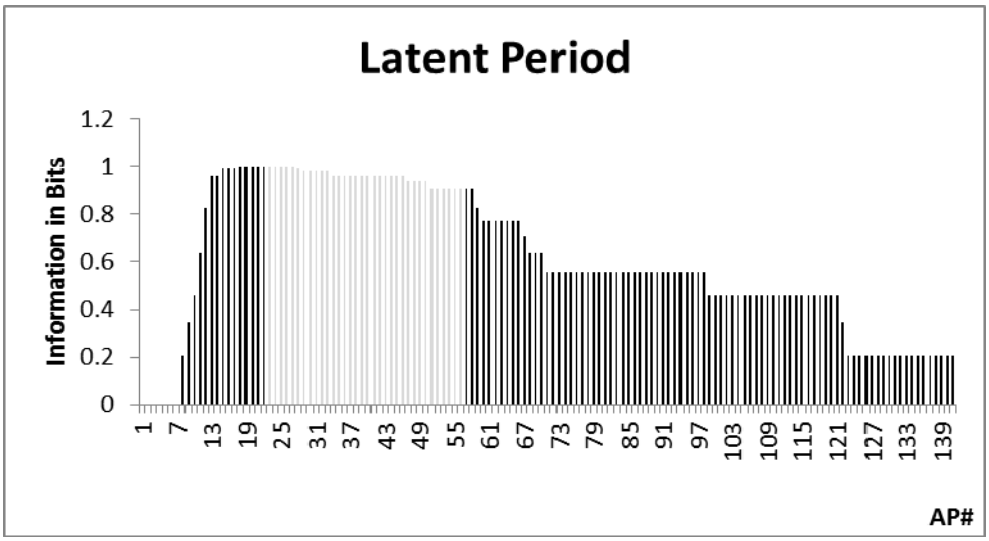


Fig. 8. Dependence of the amount of information on the AP number.

4. Discussion

Habituation is regarded as one form of learning (Kandel, 1976). Consequently, habituation might be understood as a result of the processing and saving of information. This phenomenon appears at different levels of the organism. Habituation also appears at the level of the individual neuron. Therefore, it could be stated that the observed effect of neuronal habituation in response to intracellular stimulation with current impulses might be thought of as a result of information processing at the level of the individual neuron.

We measured the defined quantities in our experiments. These quantities represent interconnected random variables. The variation of one of them inevitably causes the variation of the corresponding probability of the other random variable. Consequently, it is possible to speak about the amount of information which is contained in one random variable (random experiment) about another random variable.

As the parameters of the AP and the latent period are interconnected random variables, it is possible to calculate, experimentally, the amount of information with respect to the habituation contained in these variables.

The calculations show that an amount of information contained in each of the separate AP parameters or in the latent period differs from zero. Their behaviour is given by Figure 8. This enables one to discuss and analyse the semantics of the information; however, this is an issue for a separate study. In the present study, we are concerned only with changes of the

amount of information and so we emphasise that the AP parameters contain certain information about habituation (habituation time).

Results similar to each other were observed for all variables. Particularly, at the beginning of stimulation up to the 7th - 10th application of intracellular current pulses the amount of information contained in the AP parameters or in the latent period is equal to zero- see figure 8. This means that 7-10 stimuli are not "understood" by the neuron as a signal that has to be learnt, i.e., to be habituated. With continuing stimulation, the amount of information begins to rapidly increase and reaches a value of approximately 1 bit. Although the absolutely value 1 bit is not high, nevertheless it shows that AP parameters and latent period are sensitive to information processing. Then the information begins to decline. This is also essential- apparently signals become "common" to the neuron and the amount of information begins to decrease. It might be speculated that a neuron does not receive more "new" information and "makes decision" to stop AP firing as a response to the stimulation (see the appendix).

As was mentioned above, the experiments revealed that the AP parameters and the latent period vary irregularly. Variation of any of these variables in time is well-described by the time series with a linear trend:

$$Y(t) = a + bt + \varepsilon(t),$$

where a and b are constant parameters, $t-$ is a time variable (the number of applied stimuli), $\varepsilon(t)$ is a random component with zero mathematical expectation. $Y(t)$ may be the latent period, W20, Tr, or Area. As the corresponding statistical procedures of hypothesis-testing confirm, all of the above mentioned variables display an increasing trend (see appendix).

It can be stated that the mechanisms producing the W20, Tr, Area and latent period are responsible for the process of information processing. The speculative explanation of the variation of the AP parameters and the latent period can be described as follows: the recurrent application of current stimulating impulses might increase the resistance of the membrane around the tip of the stimulus microelectrode. This, in turn, might reduce the amplitude of the perturbation of the membrane potential and slow down the electro-tonic propagation of the depolarization to the AP triggering zone. The result is an increase of the latent period and a broadening of the AP parameters. This, in turn, leads to habituation to intracellular stimulation.

5. Conclusion

A neuron habituates to repeated stimulation with intracellular current impulses. The parameters of an AP and the latency period vary during habituation (i.e., the waveform of the AP changes). These variations contain information about habituation. Therefore, the question "Is it possible that the AP waveform contains some information about habituation when a single neuron is stimulated intracellularly?" has to be answered positively.

6. Appendix

One and the same type of mathematical model is used for all of the variables - W20, Tr, Area and the latent period. The model is called a "time series with linear trend". Consequently, for the purpose of notational simplification, let us first consider the mathematical model of latent period variation and then generalize it for the AP parameters.

$$Y(t) = a + bt + \varepsilon(t), \tag{1}$$

Here: $Y(t)$ is the latent period, $t-$ is the number of intracellular impulses (its time variable), a and b are constant parameters and $\varepsilon(t)$ represents a random component with zero mathematical expectation. Experiments were performed on 32 neurons. Consequently, the latent period was measured in a series of 32 experiments. From formula (1), it is derived that the result of measurements for an ith series (i.e., for ith neuron) could be written as follows:

$$Y_i(t) = a_i^* + b_i^* t + \varepsilon_i(t),\ i = 1,2,...,32$$

where a_i^* and b_i^* represent statistical estimations of unknown a and b coefficients.

As is well known (Cramer, 1945), a_i^* and b_i^* are given by the following formulae:

$$b_i^* = \frac{\sum_{t=1}^{m_i} tY_i(t) - m_i\left(\frac{1+m_i}{2}\right)\overline{Y_i}}{\sum_{t=1}^{m_i} t^2 - m_i\left(\frac{1+m_i}{2}\right)^2}, \tag{2}$$

$$a_i^* = \overline{Y_i} - \frac{1+m_i}{2} b_i^*, \tag{3}$$

$$\overline{Y_i} = \frac{1}{m_i}\sum_{t=1}^{m_i} Y_i(t). \tag{4}$$

where m_i is the time of habituation for the i^{th} neuron.

The adequacy of the selected model (1) must first be tested with statistical methods.

Let us introduce the notation $X(t) = a + bt$ for the linear trend. Consequently, we will have notations for observed data of the ith neuron, such that:

$$X_i^*(t) = a_i^* + b_i^* t, \quad i = 1,2,...,32$$

Let us consider the difference $\varepsilon(t) = Y(t) - X(t)$ for the testing of the adequacy of the model (1) and let us set the following task for hypothesis testing:

H_0: $E\varepsilon(t)=0$ (main hypothesis),

H_1: $E\varepsilon(t)\neq 0$ (alternative hypothesis).

Here, $E\varepsilon(t)$ is the mathematical expectation for the fixed t.

Let us consider the differences $\varepsilon_i^*(t)=Y_i(t)-X_i^*(t)$, $t=1,2,...,m_i$ and the arithmetical mean comprised by these differences $\overline{\varepsilon_i^*}=\frac{1}{m_i}\sum_{t=1}^{m_i}\varepsilon_i^*(t)$ for each i[th] neuron for the purpose of conducting the hypothesis testing procedures (the so-called t test). Statistics $\overline{\varepsilon_1^*},\overline{\varepsilon_2^*},...,\overline{\varepsilon_{32}^*}$ will then be obtained. Let us take the statistics $T=\frac{\overline{\varepsilon^*}}{s}\sqrt{32}$ as criteria statistics – so-called t statistics.

Here, $\overline{\varepsilon^*}=\frac{1}{32}\sum_{i=1}^{32}\overline{\varepsilon_i^*}$ and $s=\left(\frac{1}{31}\sum_{i=1}^{32}\left(\overline{\varepsilon_i^*}\right)^2-\frac{32}{31}\left(\overline{\varepsilon^*}\right)^2\right)^{1/2}$.

We use standard normal distribution tables because the statistical sample consists of the 32 terms and the corresponding tables of the t-statistics is comprised by not more than 30 terms from the sample. The corresponding calculation for the latent periods shows that the numerical value of the $t-$ statistics is approximately equal to -0.199, and the P value is approximately equal to 0.846. The above mentioned mathematical model was applied to the AP parameters also. The corresponding calculations show that:

1. Numerical value of t - statistics is -0.474 and P value is 0.64 for W20.
2. Numerical value of t - statistics is -0.531 and P value is 0.6 for Tr.
3. Numerical value of t - statistics is -0.232 and P value is 0.82 for Area.

It is obvious that the P values are sufficiently large in all cases. Consequently, it could be stated that there is no basis for discarding H_0 hypothesizes. This means, in turn, that the application of the mathematical model (1) of the time sequence is relevant for all AP parameters and the latent period. Now, let us consider the statistical hypothesis test for proving that there are increasing trends for the latent period and the AP parameters before establishing habituation. To avoid overloading the corresponding formulas with too much notation, let us provide a procedure of statistical hypothesis testing for the latent period (the so-called $t-$test). Then, generalize this t test for all of the AP parameters. Let us calculate statistical estimations b_i^* of the unknown b coefficients included in formula (1) by means of formula (2) for each i[th] neuron.

Statistics $b_1^*,b_2^*,...,b_{32}^*$ will be obtained as a result. The statistical hypotheses

$H_0: b=0$ (main hypothesis)

$H_1: b > 0$ (alternative hypothesis)

must be tested based on these statistics. The alternative hypothesis obviously implies that the line of the trend is rising.

The numerical value of the so-called t statistics $T = \frac{\overline{b^*}}{s}\sqrt{32}$ has to be calculated for the use of the $t-$test. Here, $\overline{b^*} = \frac{1}{32}\sum_{i=1}^{32} b_i^*$ and $s = \left(\frac{1}{31}\sum_{i=1}^{32}\left(\overline{b_i^*}\right)^2 - \frac{32}{31}\left(\overline{b^*}\right)^2\right)^{1/2}$. The calculations show that the numerical value of the $t-$statistics for the latent period is approximately equal to 2.77. The P value is approximately equal to 0.003.

For the AP parameters, similar calculations show that:

1. The numerical value of the t -statistics is 3.254. The P value is approximately equal to 0.0001 for the W20
2. The numerical value of the t -statistics is 2.498. The P value is approximately equal to 0.007 for the Tr.
3. The numerical value of the t -statistics is 3.07. The P value is approximately equal to 0.002 for the Area.

It is obvious that the P values are such small numbers that H_0 hypothesis must be discarded for the AP parameters and the latent period. Correspondingly, H_1 must be accepted. Therefore, it could be stated that the AP parameters and latent periods have an increasing trend. Let us calculate the amount of information. We take "α experiment" for the determination of the variable's location relative to its own trend (above or under) and "β experiment" for the determination of the habituation. Under the term "α experiment" we imply the results of measurements of the variables. Under the term "variables", values of the latent period, W20, Tr and Area are implied. Under the term "β experiment", we imply the determination of whether habituation is established. $I(\alpha,\beta) = H(\beta) - H_\alpha(\beta)$ is the amount of information retained in the "α experiment" regarding the "β experiment" – (Yaglom & Yaglom, 1983). Here, $H(\beta)$ is the entropy of the "β experiment" and $H_\alpha(\beta)$ is the conditional entropy of the "β experiment" in relation to the "α experiment". It is known that $H(\beta) = -P(B_1)\log_2 P(B_1) - P(B_2)\log_2 P(B_2)$. Here, B_1 is the state of affairs where habituation exists, while B_2 is the state of affairs where habituation is absent.

Correspondingly:

$$H_\alpha(\beta) = P(A_1)H_{A_1}(\beta) + P(A_2)H_{A_2}(\beta)$$

$$H_{A_i}(\beta) = -P_{A_i}(B_1)\log_2 P_{A_i}(B_1) - P_{A_i}(B_2)\log_2 P_{A_i}(B_2),\ i = 1,2$$

Here A_1 is state of affairs where the numerical value is over the trend line, while A_2 is the state of affairs where the numerical value is under the trend line. In our experiments,

the amount of information depends upon the stimulating impulse number n. For this reason, $I_n(\alpha,\beta)$ will be written instead of $I(\alpha,\beta)$. We are interested in the amount of information's behaviour during increase of n. The charts of the amount of information $I_n(\alpha,\beta)$ are obtained as a result of experimental calculations of the above given probabilities $P(A_i), P(B_i), P_{A_i}(B_j), i,j=1,2$. The stimulating impulse numbers are plotted on the abscissa axis, while the numerical values of the amount of information $I_n(\alpha,\beta)$ are plotted on the ordinate axis in these charts. As these charts show, the amount of information increases up to certain value, and then it decreases and habituation increases. It might be stated that after a certain number of stimulating impulses no "novelty" occurs for the neuron, and so the amount of information decreases and habituation increases.

7. References

Arakelov, G. Marakujieva, I. & Palikhova, T. (1991). Structural and functional analysis of monosynaptic connections between identified neurons of Helix lucorum. *Simpler nervous systems* (Eds. D.A. Sakharov and W. Winlow), pp. 258-269, University Press, Manchester.

Cramer, H. (1945). *Mathematical methods of statistics*. Almqvist & Wiksells, Uppsala.

De Polavieja, G. Harsch, A. Kleppe, I. Robinson, H. & Juusola, M. (2005). Stimulus History Reliably Shapes Waveforms of Cortical Neurons. *J. Neurosci.* Vol. 25, No. 23 , pp. 5657–5665.

Gerstner, W. & Kistler, W. (2002). *Spiking Neuron Models. Single Neurons, Populations, Plasticity, 2002.* Available from:
http://icwww.epfl.ch/~gerstner/SPNM/node8.html

Häusser, M. Major, G. & Stuart, G. (2001). Differential shunting of EPSPs by Action Potentials. *Science* Vol. 291, No. 5501 pp. 138-141.

Juusola, M. Robinson, H. & de Polavieja, G. (2007). Coding with spike shapes and graded potentials in cortical networks. *Bioessays* Vol. 29, No. 2, pp. 178-187.

Kandel, E. (1976). *Cellular Basis of Behavior*, W.H. Freeman & Company, San Francisco.

Koch, C. (1999). *Biophysics of Computation,* Oxford Univ. Press, ISBN, New York.

Koch, C. & Segev, I. (2000). The role of single neurons in information processing, Nature Neurosience, Vol. 3, No. Supp, pp. 1171-1177.

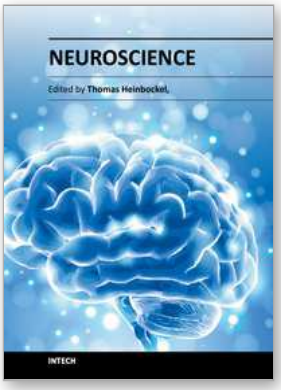
Partsvania, B. Shoshiashvili, L. Sulaberidze T. & Modebadze, Z. (2008). Extremely Low Frequency Magnetic Fields effects on the Snail Single Neurons. *Electromagnetic biology and Medicine*. Vol. 27, No. 4, pp. 409-418.

Robinson, H. (1994). Conductance injection. *Trends Neurosci.* Vol. 17, No. 4, pp. 147-148.

Shu, Y. Hasenstaub, A. Duque A. Yu, Y. & McCormick, D. (2006). Modulation of intracortical synaptic potentials by presynaptic somatic membrane potential. *Nature.* Vol. 441, No. 7094, pp. 761-765.

Tateno, T. & Robinson, H. (2006). Rate Coding and Spike-Time Variability in Cortical Neurons with Two Types of Threshold Dynamics. *J. Neurophysiol*. Vol. 95, No. 4, pp. 2650-2663.

Yaglom, A. & Yaglom, I. (1983). *Probability and Information*. Reidel Publishing Co., Delhi.



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If one asks what neuroscience is, the answer can be found in this book. Neuroscience embraces not only anatomical and physiological studies but also cell biology, computer science, and biochemistry. Equally important for neuroscientific research are other disciplines, such as psychology, psychiatry, neurology and additional recent ones, such as neuroeconomics and social neuroscience. This book comprises chapters on diverse topics in neuroscience ranging from cellular, computational, cognitive, and clinical neuroscience. Individual chapters focus on recent advances in specific areas including social neuroscience, which is a relatively new field that studies the neural basis of social interactions. Other chapters focus on technological developments such as optical tools to study the function of the brain. All chapters represent recent contributions to the rapidly developing field of neuroscience and illustrate the range of research conducted under the umbrella of the truly interdisciplinary neurosciences.