Inhibition as binding controller at the single neuron level

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Abstract

Natural stimulus for a neuron is a sum of large number of unitary excitatory postsynaptic potentials (EPSP) slightly dispersed in time. We analyze, based on numerical solution of the Hodgkin and Huxley equations, how does the triggering ability of the compound stimulus depend on the relative timing of the EPSPs it comprises. The dependences found suggest that a neuron stimulated from many synaptic inputs can be treated as performing elementary binding function, and that inhibition serves as a controller of that kind of binding. The transient process characterized by EPSP operates in this context as a short-term memory mechanism inherent to a single neuron.

Keywords: Binding, inhibition, EPSP, synaptic integration, memory

> "Although a neuron requires energy, its main function is to receive signals and to send them out — that is, to handle information."
>
> F. Crick, *The Astonishing Hypothesis,* 1994

> "...inhibitory pathways are now known not just to have a general value in keeping down the level of excitation... . In addition, they participate very effectively in neuronal integration, molding and modifying the patterns of neuronal responses."
>
> J. Eccles, *The Understanding of the Brain,* 1972

1 Introduction

One of the main functions of the brain is to process information. It seems relatively well understood how does the brain do this, provided one could be

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satisfied with explanation in terms of very large scale neuronal groups. E. g., it is know which part of brain serves for what (Kupfermann, 1985), and how do the parts interact in order to combine divergent information about an object into coherent image (Damasio, 1989;1996).

At the same time, the brain's most active units are neurons. The physico-chemical mechanisms of neuronal response to various electrical and chemical stimuli are well understood (Noble and Stain, 1966; Fundamentals of Neurophysiology, 1975). Here a natural question arises: either a single neuron should be treated as a plain ions pumping constructive element, and information processing can be performed only by a network of them, or some rudimentary information processing can be found at the single neuron level? If it would be possible to interpret a single neuron functioning in terms of information processing, then one more question arises: what role the inhibition could play in those same terms?

In this paper we analyze a single neuron functioning from the information processing point of view. For this purpose numerical simulation of membrane dynamics is made with stimuli similar to those the neuron receives in natural conditions. As a result for that type of stimuli, a firing criterion is formulated, which allows to interpret single neuron functioning as elementary binding process [1] , and inhibition gets its information processing meaning in this context.

2 Methods

A single nervous system can have many hundreds of types (species) of neurons with their own individualities. Having in mind to obtain conclusions suitable as generic characteristic of any neuron, we should perform simulation by means of a simplified model, comprising only those features, which are generic for neuron of any type. The Hodgkin and Huxley (1952) set of equations is taken for this purpose:

$$\begin{aligned} dV/dt &= (-\bar{g}_K n^4 (V - V_K) - \bar{g}_{Na} m^3 h (V - V_{Na}) - \bar{g}_l (V - V_l))/C_M \\ &+ I(t)/C_M \\ &- \bar{g}_{iK} (V - V_K)/C_M, \end{aligned} \tag{1}$$

$$dn/dt = \alpha_n (1 - n) - \beta_n n, \tag{2}$$

$$dm/dt = \alpha_m (1 - m) - \beta_m m, \tag{3}$$

[1] for definition of binding, or feature linking phenomenon see Damasio (1989;1990)

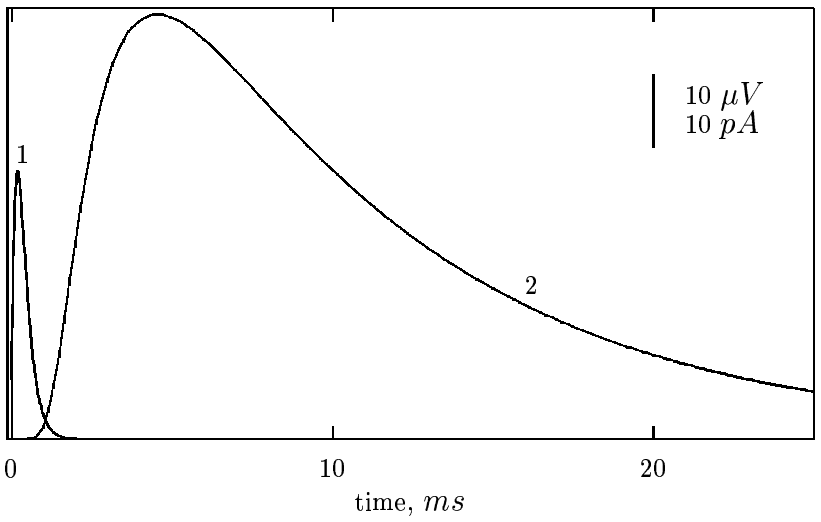

Fig. 1. Synaptic current, 1, and unitary postsynaptic excitatory potential, 2, time courses.

$$dh/dt = \alpha_h(1-h) - \beta_h h, \tag{4}$$

The term with $\bar{g}_{iK}$ is introduced in the Eq. (1) in order to mimic a $GABA_b$ mediated inhibition, which has slow time course (Benardo, 1994), and considered here as time-independent during periods comparable with duration of postsynaptic transients. The stimulating current, I, is constructed as follows. Firstly we find explicit expression for the unitary excitatory postsynaptic potential ($EPSP(t)$):

$$EPSP(t) = \int_0^{t_{max}/\tau_M} f_\delta(t-\theta) f_\alpha(\theta)\, d\theta, \tag{5}$$

where

$$f_\delta(t) = \frac{1}{2\lambda C_{M1}\sqrt{\pi t}} \exp(-\frac{X^2}{4t} - t), \tag{6}$$

is the Hodgkin formula for the function of a unit source in an infinite cable (Fatt and Katz, 1951), and

$$f_\alpha(t) = Q\alpha^2 t \exp(-\alpha t), \tag{7}$$

is the synaptic current time course. Here t is dimensionless, $\tau_M = 10$ ms,

$$\lambda = 100\mu m, \quad X = 1.2\lambda, \tag{8}$$

$\alpha = 50$, $Q = 2.4 \times 10^{-14}$ C, $C_{M1} = 5 \times 10^{-2}$ μF/m, is the capacitance of 1 m long nerve fibre, $t_{max} = 110ms$.

The time course of the EPSP obtained is shown in the Fig. 1.

Then we construct the compound EPSP, resulting from cooperative action of large number of synaptic inputs delivered at random times within time window W:

$$CompEPSP(t) = \sum_{k=1}^{N} EPSP(t - t_k), \tag{9}$$

where $t_k \in [0; W]$, are uniformly distributed independent random numbers.

The stimulus current I is calculated as follows:

$$I(t) = -C_M dCompEPSP(t)/dt. \tag{10}$$

As Eqs. (1)-(4) have no spatial dependence, they could be treated as describing space clamped system, where the membrane is maintained at spatially-uniform electrical and chemical conditions. We choose another interpretation here, considering Eqs. (1)-(4) as describing situation in a small patch of the spike triggering zone, namely, at the place where the action potential usually starts (Moore et al., 1983). In general case, due to lateral mobility of ions and to electrical coupling between adjacent points, one needs information about situation at nearby points, in order to describe what will happen at given point. In our case, the result of lateral mobility before the action potential is triggered is taken into account in Eqs. (5)-(8). The lateral mobility is rather slow before the action potential starts, and its major consequence is the form of EPSP time dependence in the spike-triggering zone[2]. As regards lateral coupling during the action potential development, it is taken into account in Eqs. (1)-(4), because it is namely the lateral coupling between sodium channels that causes positive cooperativity in the population of channels, which results in the triggering behavior. Thus, even if Eqs. (1)-(4), (9) do not include spatial coordinate, they take into account some generic spatial features of neuron by means of specified time course (5) of the EPSP in the spike-triggering zone, and by means of characteristic nonlinearities in the equations.

The compound stimulus (9) could in principal be delivered through a single synapse, but in this case the moments t_k could not be independent (the distance between t_i, t_k cannot be shorter than the refractory time in this case). Therefore, expecting independence we have here multisynaptic situation, thus taking into account another major spatial (morphological) feature of any neuron — to have many synaptic inputs.

3 Results

[2] in this generic model we do not take into account such possibilities as computation in the dendritic tree (Bernander et ai., 1994)

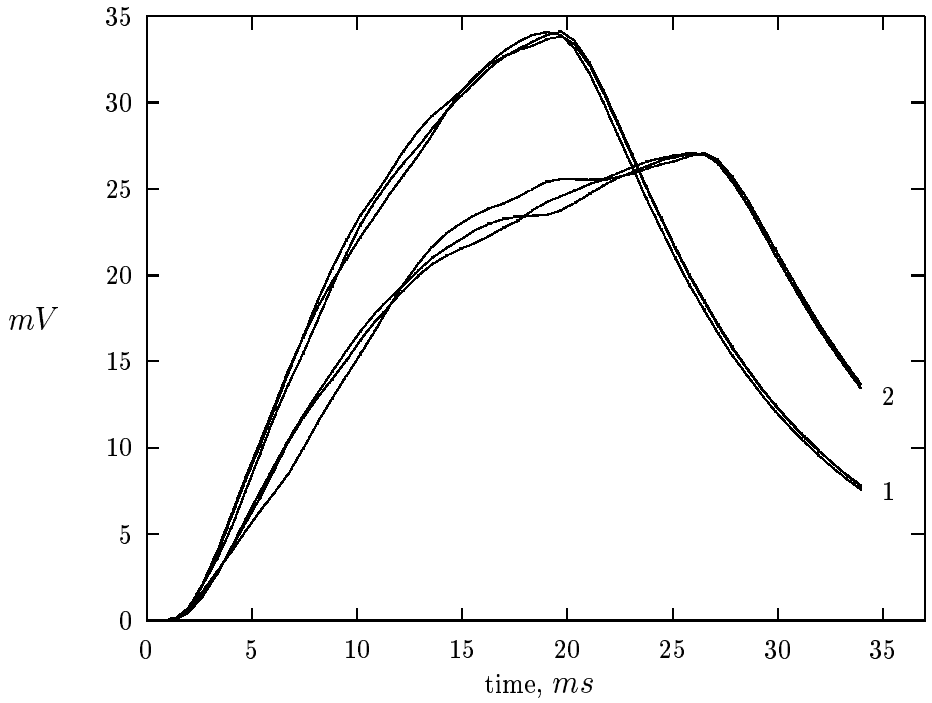

Fig. 2. Examples of $CompEPSP(t)$ curves for $N = 1000$, and $W = 18$ ms, 1, and 25 ms, 2.

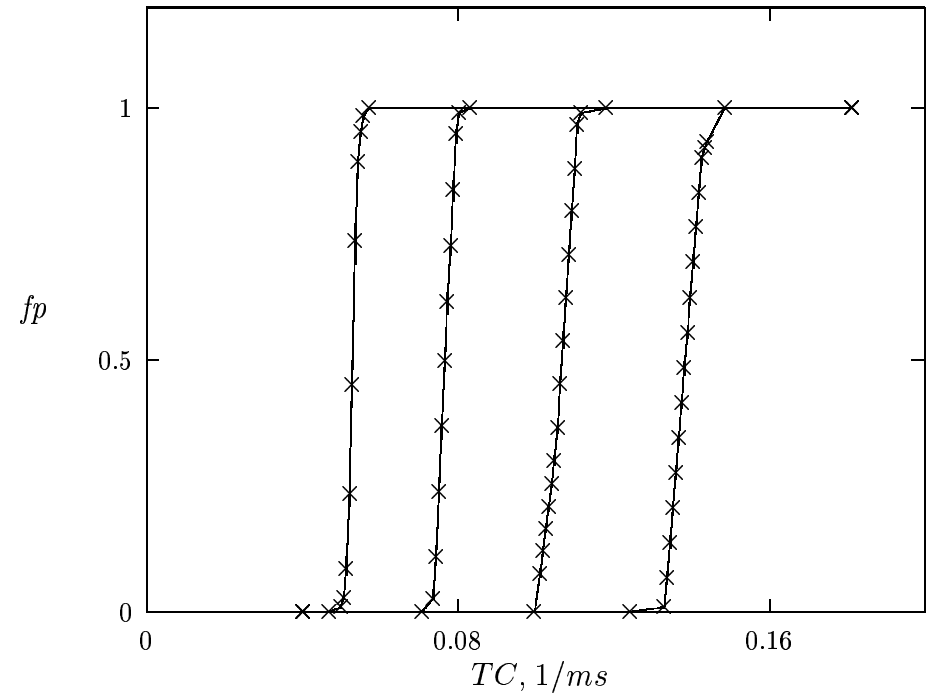

Fig. 3. Firing probability *vs* temporal coherence between the unitary EPSPs within the compound stimulus comprising 1000 EPSPs. The four curves correspond consecutively from the left to the right to the inhibition potentials 0.43, 3.08, 5.02, 6.30 mV.

The numerical simulation of the membrane voltage dynamics by means of Eqs. (1)-(4) with stimulus given in Eq. (10) in combination with the Monte Carlo algorithm was performed in order to estimate the firing probability $fp(W)$ for various values of $\bar{g}_{iK}$ in Eq. (1), and W in Eq. (9). The number of unitary EPSP in a single stimulus, $N = 1000$. Examples of $CompEPSP(t)$ time course are shown in the Fig. 2. By means of consecutive trials the firing probability has been estimated with precision 10% for each window W, and for four distinct inhibition values.

Let us characterize the degree of temporal coherence between the uEPSPs in the stimulus (9) by the inverse window width: $TC = 1/W$. The dependences found for the fp as function of the temporal coherence are shown in the Fig. 3. The results can be formulated in terms of neuronal excitability as follows: 1) The neuron will fire in response to the compound stimulus if and only if the degree of temporal coherence between the elementary synaptic events is above a certain threshold; 2) The degree of temporal coherence, which ensures firing, can be properly adjusted by means of inhibition.

4 Discussion

Based on the results of numerical simulation, we could offer information pro-

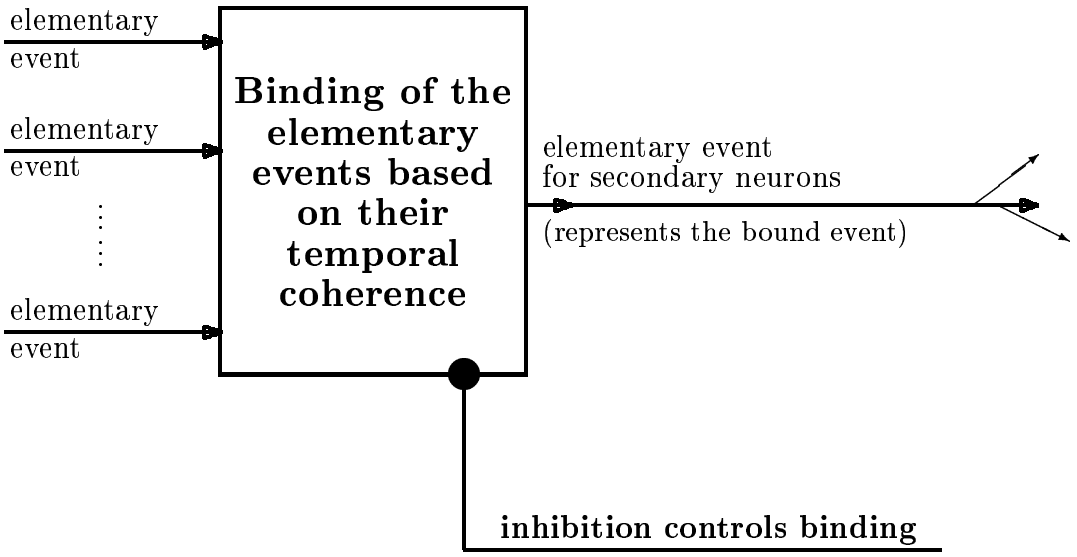

Fig. 4. Proposed scheme of information processing in a single neuron.

cessing interpretation of a single neuron functioning. In this interpretation the short synaptic current pulses could be treated as signals about events outside the neuron. The slow postsynaptic transient (EPSP) looks like a simple memory mechanism, because it keeps for a long time information about the signal received, as compared with the signal duration (see Fig. 1). If many signals come loosely in time, the neuron is able to keep information about them simultaneously due to the EPSP mechanism. If some signals have come coherent in time, they could be treated as belonging to (originated from) a single physically coherent event. In case of neuron, it fires if receives a bundle (volley) of coherent in time synaptic inputs. The action potential sent along the axon may serve as sign (abstract representation) of that (hypothetical) coherent event. The inhibition determines how much tight in time the elementary events must be distributed to be interpreted as signs of a coherent compound event.

In other words, the neuron converts a set of elementary events represented by the set of synaptic inputs into a single event represented by the action potential in the axon. In this sense we could say that elementary binding performance can be attributed to a single generic neuron, and inhibition effectively controls the conditions necessary for this kind of binding to occur (Fig. 4).

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