Active spike transmission in the neuron model with a winding threshold manifold

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Abstract

We analyze spiking responses of excitable neuron model with a winding threshold manifold on a pulse stimulation. The model is stimulated with external pulse stimuli and can generate nonlinear integrate-and-fire and resonant responses typical for excitable neuronal cells (all-or-none). In addition we show that for certain parameter range there is a possibility to trigger a spiking sequence with a finite number of spikes (a spiking message) in the response on a short stimulus pulse. So active transformation of $N$ incoming pulses to $M$ (with $M > N$) outgoing spikes is possible. At the level of single neuron computations such property can provide an active “spike source” compensating “spike dissipation” due to the integrate-and-fire $N$ to $1$ response. We delineate the dynamical mechanism for the $N$ to $M$ transformation based on the winding threshold manifold in the neighborhood of big saddle loop bifurcation. Based on the theoretical predictions, a nonlinear electronic circuit is designed implementing the active transmission in physical conditions.

1. Introduction

The principles of inter-neuron communication, representation of sensory information and its processing in neuronal networks still remain among the key problems in understanding brain dynamics and cognitive functions [1–7]. According to many experimental works and theoretical reviews in modern neuroscience, neuronal networks in the brain form spontaneous and stimulus-induced patterns of spiking activity (spiking patterns). Information and functions are believed to be encoded in the dynamical characteristics of the patterns and their evolution. In time such patterns represent spiking sequences with variable inter-spike intervals (ISI). Sensory signals incoming to the brain act as external stimuli allowing the current configuration to adapt to current environmental conditions. Such processes underly many brain functions, for example associative memory formation, learning, perception, motor control, etc. [3].

It is believed that neurons communicate using excitation pulses (spikes) [1,5,6,8–11]. The information can be encoded in the characteristics of spiking sequences including variable inter-spike interval, modulation of spike frequency or spiking phase relative to an oscillatory drive (rhythm) [12,13]. At the level of a single neuron, the problem of signal processing leads to the analysis of the cell response on different input pulse stimuli. The input pulse can be interpreted either as a single, strong synaptic input or as a packet of synchronously arriving inputs, such as occurs in synfire chains or polychrony. The responses are defined by the dynamics of cell membrane excitability (threshold characteristics, fast and slow time scales, etc.), by the strength and timing of the input. Basic properties of the neuron response include threshold firing by integrating the incoming perturbations (integrate-and-fire) and resonance filtering when the response spikes appear only at favorable frequencies and phases of the incoming signal. Many realistic neuron models have been proposed and explored in detail in a number of previous studies [5,10,11,14–17]. The gallery of the simplest models and their response features compared with electrophysiological recordings from different brain cells has been presented in [5]. When stimulated by periodic pulse signals, the excitable models can generate the response oscillations at a certain level of forcing (integrate-and-fire) and resonance filtering when the response spikes appear only at favorable frequencies and phases of the incoming signal. Many realistic neuron models have been proposed and explored in detail in a number of previous studies [5,10,11,14–17]. The gallery of the simplest models and their response features compared with electrophysiological recordings from different brain cells has been presented in [5]. When stimulated by periodic pulse signals, the excitable models can generate the response oscillations at a certain level of forcing (integrate-and-fire) and resonance filtering when the response spikes appear only at favorable frequencies and phases of the incoming signal.
In this paper we discuss the possibility of active spike transmission when the neuron generates a response with arbitrary large number of output spikes, \( M \geq N \), due to a specific type of excitability with a winding threshold manifold. We consider the complex threshold excitation model (CTE) proposed in [21], implemented with electronic circuits [22] and tested in physical experiments in many configurations [23–26]. The model represents one of the reductions of classical Hodgkin–Huxley equations comprising nonlinear recovery dynamics and three-fixed point kinetics with saddle separatrix accounting for the threshold. Actually, it describes the class of neuronal excitability where the transition from the excitable to oscillatory mode occurs through the big saddle separatrix loop bifurcation. In particular, the properties of the model are similar to the Moris–Lecar [27] one and other models possessing threshold manifolds. We aim to show that CTE property provides active spike transmission with \( M \geq N \) spike locking ratios and investigate the dynamical mechanisms underlying this effect using phase space analysis. In neuroscience, the multi-spike response behavior can be incorporated into a model of synfire activity propagation allowing for iterative transformation of spike sequences [20].

The paper is organized as follows: in Section 2 we briefly describe the model and investigate the dynamical mechanisms underlying the integrating and resonant response of the model to input pulse messages. Section 3 is devoted to the mechanisms of active spike generation in the oscillatory threshold modes. In Section 4 we study the transformation of periodic input spike sequences and illustrate the presence of favorable and unfavorable inter-spike interval range facilitating or depressing the transmission. Section 5 contains brief discussion including the illustration of electronic circuit possessing the active spike transmission effect.

2. Model and integrating response to incoming pulses

Let us consider the CTE equation set in the following form [21]:

\[
\begin{align*}
\dot{u} &= f(u) - v + g_{\text{syn}} I_{\text{syn}}(t), \\
v &= \varepsilon (g(u) - v - \eta).
\end{align*}
\]

Variable \( u \) describes neuron membrane potential and recovery variable \( v \) corresponds to the dynamics of outward ionic current qualitatively describing channel gating dynamics [5]. Nonlinearity \( f \) has the form \( f(u) = u - u^3/3 \) and qualitatively describes \( 1-U \) characteristics of the membrane, parameter \( \eta > 0 \) controls the depolarization level, parameter \( \varepsilon > 0 \) characterizes membrane relaxation time scales. We take the function \( g(u) \) controlling the recovery dynamics in the form

\[
g(u) = \begin{cases} 
au & \text{if } u < 0, \\
\beta u & \text{if } u \geq 0.
\end{cases}
\]

It qualitatively describes the shape of channel activation function. Input signal, \( I_{\text{syn}}(t) \), represents the sequence of pulses of duration \( \tau \) and the period of the stimulation signal \( T \) modeling the synaptic input to the neuron controlled by the strength, \( g_{\text{syn}} \).

If no stimulus has arrived, \( I_{\text{syn}}(t) = 0 \), Eq. (1) have autonomous dynamics, which have been studied in detail in [25]. A rich variety of dynamical modes is found depending on the control parameter values. Treating Eq. (1) as a phenomenological neuron model, we are interested in its excitable dynamics describing spike generation. Typical phase portrait for the excitable mode is depicted in Fig. 1. There are three fixed points with a rest state corresponding to the stable focus, \( O_1(u^{(1)}, v^{(1)}) \), an unstable "excited" state, \( O_2(u^{(2)}, v^{(2)}) \) of unstable focus type and a saddle point, \( O_3(u^{(3)}, v^{(3)}) \) driving the threshold dynamics. Incoming separatrix \( W_i(O_2) \) forms the excitation threshold manifold as shown in Fig. 1. According to the bifurcation analysis [25], the separatrices of the saddle \( O_2 \) can change their mutual arrangement that leads to big separatrix loop bifurcations and appearance of a limit cycle corresponding to periodic spike generation. We fix control parameters \((\varepsilon, \eta)\) for excitable dynamics in the neighborhood of this bifurcation.

Let us analyze first the integrating response, i.e. the conditions of a spike generation in response of the input spike message \((N \rightarrow 1 \text{ transformation})\). The system starts initially with the neuron at rest fixed point \( O_1(u^{(1)}, v^{(1)}) \). Then, for simplicity, we consider only the case of an excitatory stimulus, that is the incoming spikes will be all positive, of equal amplitude, appearing in discrete times \( t_1, \ldots, t_k, \ldots, t_{N} \). That means that \( u(t) = u^{(1)} \) and \( v(t) = v^{(1)} \) for \( t < t_1 \). We consider also the action of these \( N \) incoming spikes as follows [9,21]. By assuming that the amplitude of these stimuli is large enough, each incoming spike causes an instantaneous jump, of value \( u_p \), horizontally in phase space \((u,v)\) as shown in Fig. 1. That means that the membrane potential (variable \( u \)) is instantaneously shifted at instant \( t_k \)

\[
u(t_k) = u(t_k) + u_p = u_k,
\]

\[
t_k = \lim_{t \to t_k^+} (t_k^+ - \delta), \quad \delta > 0,
\]

while the recovery variable \( v \) stays unchanged \( v(t_k^+) = v(t_k^-) = v_k \). During the time interval between two incoming spikes, for \( t_k < t < t_{k+1} \) (\( k = 1, \ldots, N \)), the system evolves autonomously.

Such simplification can be justified for a short input spike (relative to internal time scale), because the recovery variable \( v \) is quite slow \((\Delta v \ll \Delta u)\) comparing to \( u \). The instantaneous shift of \( \nu(t_k^-) \to \nu(t_k^+) \), that we have called \( u_p \), is controlled both by the synapatic strength \( g_{\text{syn}} \) and by the amplitude of the incoming spikes.

The excitation threshold is defined by the saddle separatrix \( W_i(O_2) \) (Fig. 1). To get a response spike at the \( N \)th input pulse, the state \((u_N, v_N)\) should be beyond the threshold. Assuming that there exists function \( W_i(O_2) : v = W(u) \) describing the separatrix shape for \( W_i(O_2) \), the condition to get a spike as a response to \( N \) input pulses, i.e. for \( N \rightarrow 1 \) spike message transformation, can be written as follows:

\[
u(P_{-1}) < u_1 < u_1(P_{1}), \quad v_k-W(u_k) > 0, \quad k = 2, \ldots, N-1,
\]

\[
u_N-W(u_N) < 0,
\]

where \( P_{\pm1} \) are the \( u \)-coordinates of the right threshold separatrix intersections with the line \( v = v^{(1)} \) as shown in Fig. 1.

Simulating Eqs. (1) and (2) with conditions (3), we find the parameter regions, i.e. the strength of the input versus the period of the stimulation signal \( T \), corresponding to the response spike integrating \( N \) input pulses (Fig. 2(a)). Due to the nonlinear character of subthreshold relaxation, the regions have quite complex boundaries. Note, however, that they resemble the integrating property of the response (more pulses are needed to generate a response for increasing the period of the stimulation signal \( T \)) and the resonant scaling corresponding to the presence of damped subthreshold.

![Fig. 1. Qualitative phase portrait of system (1) in its excitable mode.](image-url)
oscillations near the stable focus $O_1$. For example, Fig. 2(b) shows typical response on the message with $N = 3$ incoming spikes.

3. Active response in the case of rolled-up threshold

When the model parameters approach to the bifurcation of saddle separatrix loop the threshold manifold $W_1(O_2)$ tends to the manifold $W_3(O_2)$ and makes a number of oscillations around the three fixed points as shown in Fig. 3(a). Then, there appear several intersection points, $P_i$, of the separatrix, $W_1(O_2)$, with $v = e^{11}$, acting as threshold points. It gives rise to the multi-spike response of model (1) for a single incoming perturbation.

It follows from the phase portrait in Fig. 3(a) that if the condition $u_{th}(P_i) < u^{(1)} + u_p < u_{th}(P_{i+1})$ (4) is satisfied for some particular $i = 1, 2, \ldots, K$, the neuron generates a multi-spike response of $M = i$ sequential excitations. With approaching to the bifurcation point the number of separatrix rotations increases, $K \to \infty$. As shown in Fig. 3(b), the multiple threshold points are located very close to each other. Then, to control the number of response pulses, the input strength, $u_p$, should be tuned very precisely. Note, however, that for $u^{(1)} + u_p > u_{th}(P_K)$, the response is generated with the maximal number of spikes $M = K$. In this case the response is controlled by the parameters of system (1) that can be finely tuned near the bifurcation values even for experimental conditions [22]. The example of active spiking response on a single pulse $1 \to M$ is illustrated in Fig. 4(a). Combining the integrating (Section 2) and active response properties we find that, in the case of the rolled-up threshold manifold, the spike messages in the input can be translated to the sequence with any required number of spikes in
the train (Fig. 4(b)). In other words, active transformation of spike messages \(N \rightarrow M\) (with \(M\) and \(N = 1, 2, \ldots, \infty\)) can be implemented in the CTE model (1). Note that, in the “active” mode, the response spikes, counted from \(M\) to 1, come with increasing ISIs defined by the periods of the threshold separatrix oscillations. Since with each oscillation the trajectories approach to the saddle fixed point the period will be monotonically increasing. Time difference between two sequential oscillations, ISI(i+1,i), can be estimated by the time interval spent by the threshold separatrix in the neighborhood of saddle point \(O_2\), as illustrated in Fig. 5 (we assume that all spikes in the train have equal durations). In linear approximation we can construct local map (Fig. 5(a)) and find that the ISI change is given by the following relation:

\[
\text{ISI}(i,i-1) - \text{ISI}(i+1,i) = \frac{1}{2} \alpha \ln \left( \frac{u_0(P_{i+1}) - u_0(P_i)}{u_0(P_i) - u_0(P_{i-1})} \right), \quad i = 2, 3, \ldots, M - 1,
\]

where the parameter \(\alpha > 0\) is the characteristic eigenvalue for the saddle fixed point \(O_2\). Note that each consequent rotation brings the trajectory closer to the saddle point, hence slowing down its motion. ISI changes in the response spike train can be referred as spike frequency adaptation effect known in many neurobiological examples [5].

4. Active transmission of periodic spike trains

Let us consider now the case when system (1) is stimulated continuously by a periodic spike train through \(I_{syn}(t)\) and analyze possible ISI response modes in function of the period \(T\) of the stimulation signal. For illustration we set the parameters of the model and the strength of the synaptic input, \(E_{syn} = 0.2, T = 50\).

The profile of the signal shows that each input stimulus can activate one or two response spikes. If the stimulation arrives in an unfavorable phase it inhibits the activity and the system evolves toward the rest state until the next stimulus comes. The input and output signals in this case are not synchronized. To analyze the response dynamics we follow the instantaneous ISIs depending on the period of the stimulation pulse \(T\). Observed ISI values are plotted by dots in the bifurcation diagram shown in Fig. 7(a). It shows that there is a variety of periodic and irregular response modes. If the period \(T\) of the input stimulus is large enough, two values of ISIs can be distinguished. Let the first one be denoted by \(e_1\) and the second one by \(e_2\). When \(e_1 = T = 40\), this case corresponds to the interval between the two spikes in the response doublet (see Fig. 4(a)). Note also that this value of \(e_1\) corresponds to the time interval of the trajectory excursion in the phase plane tracked by the threshold separatrix (Fig. 1). In this case, the system is in its excitable mode and does not possess a natural frequency. However, \(e_1\) defines the intrinsic time scale managing timing properties of the system response. The second ISI value, \(e_2\), defines the interval between the consequent doublets linearly decreasing when \(f\) increases until the resonance conditions. Approaching to the resonance conditions at \(T = \sim 3/\Delta = \sim 120\), the ISI curves bifurcate leading to an irregular response which can be quasi-periodic or chaotic (we do not analyze the fine structure of those regions focusing in this study on the effects implementable in a physical conditions). Note that other regions of complex dynamics are localized near another frequencies, \(T \sim 50, 75\). Smaller values of \(T < 40\) correspond to a 1:1 response when the input spikes speed up the second excitation pulse in the doublet. The output ISI linearly decreases with the input frequency increase until the values \(\sim 20\) time units which correspond to the characteristic duration of single excitation cycle, e.g. the spike and the following refractory period. Such linear dependence can be easily explained by the geometry of the excitation trajectories. Their excursions in the phase plane describing the spikes (Fig. 1(a)) are relatively fast in the interval between the two consequent input pulses. Then, evolving in the neighborhood of the rest state, the system can be re-excited by the next incoming pulse since its strength, \(u_{0}\), is taken sufficient to overcome the maximal threshold curve (the part of the separatrix passing the \(P_2\) point).

To investigate input–output spike transmission mode we have computed the quantity:

\[
K_{trans} = \frac{M}{N},
\]

where \(N\) and \(M\) are the total number of input and response spikes, respectively. \(K_{trans}\) can be treated as the spike transmission coefficient accounted for the average number of spikes transmitted within time window \(T\). In simulations we set \(T\) sufficiently large comparing to characteristic ISIs \((T = 10^4\) units of time). Obviously \(K_{trans}\) also accounts the relation of average input–output spike frequencies, \(K_{trans} = f_{in}/f_{out}\) and detects possible synchronization modes between input and output spike trains. If \(K_{trans} < 1\) the neuron operates in its integrate-and-fire (“dis- sipative” or “passive”) filtering mode when the number of output spikes is less than input ones. For \(K_{trans} > 1\) the number of spikes grows in the output and the neuron can be treated as “active” unit.

![Fig. 6. Response of system (1) on a periodic stimulation for the parameters taken in 1−2 response mode. Parameter values: α = 0.5, β = −2, η = 0.21, ε = 0.349, E_{syn} = 0.2, T = 50.](image)
increasing number of spikes in the output. Fig. 7(b) shows the dependence of $K_{\text{trans}}$ on the input period. One can notice the plateaus corresponding to different synchronization modes. The transitions between different spike locking modes occur through the irregular (chaotic) modes with non-integer values of transmission coefficient.

Note that the spike transmission is indeed active since there are input frequencies for which $K_{\text{trans}} > 1$. Note also that for the purpose of our study we have counted only the spike number as the spikes are the main information carriers for the transmission problems motivated by neuron network dynamics [8]. We neglect the true frequency ratios between input and output signals that have to include the subthreshold signal frequency as well. The complete picture characterizing the spike transmission is illustrated in the grey scale plot in Fig. 8 showing the values of $K_{\text{trans}}$ depending on both input frequency and synaptic strength parameters, $T$ and $g_{\text{syn}}$.

One can notice the appearance of generalized Arnold tongues. As expected there are regions with different spike phase locking ratios ending up with the black area of 1:2 response. One can note the appearance of smaller scales near the interfaces between different locking modes. Note that complex profile of the frequency locking diagram shows that the response is quite sensitive and selective to timing properties of the spike messages.

5. Conclusion

In conclusion, we have analyzed the nonlinear mechanisms of spike generation in a reduced neuron model with complex threshold excitability. We have shown that due to the oscillations of the threshold manifold in the neighborhood of big separatrix loop bifurcation the model is capable to generate spike trains in the response on external stimuli. The number of the spikes is controlled by the stimulus intensity. It can be treated as a dynamical encoding mechanism that can transform all the incoming perturbations into spiking sequences with definite number of spikes. Note that such a “code” represents an intrinsic feature of the model as a nonlinear dynamical system with oscillatory separatrix threshold. To generate a spike train, the model needs just a short pulse stimulus, after that it evolves according to its autonomous dynamics. This sensitivity of firing rate to input fluctuations depends on time scale separation between fast and slow variables in single neurons [28].

In case of stimuli containing a certain number of spikes we can theoretically think about a feedfoward network when the output of one neuron is projected to the input of another one. Then, if the parameters are tuned accordingly the propagation of a complex synfire patterns become possible. In other words, spike sequences with $N_1 > N_2 = N_3 > N_4 = \cdots$ with desired values of $M_i$ and $N_i$ can be implemented. Such synfire activation is quite similar to what has been recently proposed for bursting neurons [20]. Here, however, the time scale is important since we deal with spiking trains, e.g. the sequence of localized spikes. In terms of phase space dynamics they are associated with oscillations around big separatrix loop involving the hyperpolarization stage and the refractory period. Thus, the presence of the oscillatory threshold makes possible active transmission of the spike sequence that can be treated as a novel mechanism of communication with spikes in addition to the well-known integrate-and-fire and resonant transmission. The key point is that the number of spikes can be “amplified” by the intrinsic activity of the system. The input and output signals can be synchronized with different ratios and demonstrate an irregular response. There is also a possibility of filtering the input spikes arriving at an unfavorable phase.

The model has been investigated using analog electronic device reproducing differential equations of the model. The CTE model was implemented using analog electronic device, as sketched in Fig. 9 and described in detail in [22]. We tested experimentally the circuit for the active spike response predicted by the theoretical study. Considering the case when the CTE

Fig. 7. Active spike transmission. (a) Bifurcation diagram. Instantaneous ISI distribution in the output signals illustrating the possibility of filtering favorable intervals and irregular responses. (b) Spike transmission coefficient (6) versus $T = 1/f_{\text{input}}$. The regions located above the dashed curve correspond to active transmission. Parameter values: $\alpha = 0.5$, $\beta = 2$, $\eta = 0.21$, $\varepsilon = 0.349$, $g_{\text{syn}} = 0.2$.

Fig. 8. Two-parameter bifurcation diagram of the CTE model showing the regions of spike phase lockings in the active transmission effect. Parameter values: $\alpha = 0.5$, $\beta = 2$, $\eta = 0.21$, $\varepsilon = 0.349$. 
neuron (1) is stimulated continuously by the periodic spike train, the possible response modes for different input parameters (ISI, T) are analyzed. For illustration we set the parameters of the model and the strength of synaptic input to generate 1 → 2 response mode. It is obvious that for sufficiently large values of T, the neuron responds with M = 2 spikes to each input pulse, with a delay. The dynamics becomes much more complex when the input period is of order of the characteristic time scale of the response spike trains, as illustrated in Fig. 10(a). If the stimulation arrives in an unfavorable phase it inhibits the activity and the system evolves toward the rest state until the next stimulus comes. The spike transmission coefficient $K_{trans}$ for CTE model (1) accounted for the average number of spikes transmitted is computed for different values of T of the input spike. The results obtained experimentally are illustrated in Fig. 10(b). One can notice plateaus corresponding to different synchronization modes. The transitions between different spike locking modes occur through the irregular (chaotic) modes with non-integer values of transmission coefficient. It detects possible synchronization modes between input and output spike trains. Finding the property of active spike transmission may be quite important as a milestone to implement biologically realistic neuronal networks to simulate particular neuronal system or functions. By changing the input–output spike ratio due to nonlinear CTE properties the neuron can split and route the output pulse on different signaling pathways [18]. This generally requires external excitatory drive, but with conductance-based synapses, when the network size is large enough the activity can be self-sustained without external drive [19]. There are also bursting neurons responding with many spikes on incoming stimuli [5,20]. These spikes, however, occur at a rather high frequency and are associated with single events. The number of spikes within the burst may be fixed (regular) or variable (chaotic) depending on the neuron parameters. Burst generation is associated with a homoclinic bifurcation in the underlying dynamical system which is typically three-dimensional.

Acknowledgments

This work was supported in part by PICs Russian-French Grant (Nos. 4826 and 09-02-91061), by RFBR grant No. 11-04-12144, by the Russian Scientific-educational Program (Contract no. 652 14.740.11.0075), by the Russian President Grant MD-5096.2011.2, by MCB Program of RAS. V.B.K. acknowledges VIBOT Erasmus Mundus Program and Russian Science Support Foundation for financial support. A.S.T.N. acknowledges VIBOT Erasmus Mundus Program and the Abdus Salam International Centre for Theoretical Physics (ICTP, Trieste, Italy) through the office of external Activities (OEA)-Prj-15 for financial support. The ICMPA is in partnership with the Daniel Iagolnitzer Foundation (DIF), France.

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