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Activity of Excitatory Neuron with Delayed Feedback Stimulated with Poisson Stream is Non-Markov

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Abstract For a class of excitatory spiking neuron models with delayed feedback fed with a Poisson stochastic process, it is proven that the stream of output interspike intervals cannot be presented as a Markov process of any order.

Keywords Spiking neuron · Poisson stochastic process · Probability density function · Delayed feedback · Non-Markov stochastic process

Mathematics Subject Classification 60G55 · 60G10 · 60K99 · 92B20

1 Introduction

Statistics of neuronal activity is often described as a renewal point process, or even a Poisson process, see [2] and references therein. On the other hand, in some sets of experimental data correlations are observed between consecutive interspike intervals (ISI) [20, 21, 23, 25], which does not conform with the renewal hypothesis. What could be the reason of such correlations? In principle, any sort of memory in the neuronal firing mechanism could bring about memory into the sequence of ISIs, thus disrupting a possibility for it to be renewal. Memory in the firing mechanism can appear due to partial reset of the membrane potential after firing [7, 19, 26], or due to threshold fatigue [10], or for other reasons, see [3] for a review.

Biologically, non-renewal statistics of neuronal activity can improve discrimination of weak signals [3, 25], and therefore is essential feature of functioning of a nervous system. In this context, it was checked in [25] if it is possible to represent activity of electrosensory neuron as a Markov chain of some finite order. Conclusion made in [25] is that the corresponding order, if any, cannot be lower than 7.

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Normally, any neuron is embedded into a network. Inter-neuronal communication in the network is delayed due to finite speed of nervous impulses. In a reverberating network, this brings about one more reason for non-renewal firing statistics—the delayed feedback. We study here the simplest possible case of a network—a single neuron with delayed feedback. In the previous paper [32], it was proven for a concrete neuronal model—the binding neuron¹ with threshold 2—stimulated with Poisson stream of input impulses, that statistics of its ISIs is essentially non-Markov. In this paper, we refine and extend methods of [32] making those applicable to any neuron, which satisfies a number of very simple and natural conditions (see Cond0–Cond4 in n. 2.1). Under those conditions, we prove rigorously that ISI statistics of a neuron with delayed feedback cannot be represented as a Markov chain of any finite order.

2 Definitions and Assumptions

2.1 Neuron Without Feedback

We do not specify any concrete neuronal model, only expect that a neuron satisfies the following conditions:

- Cond0: Neuron is deterministic: Identical stimuli elicit identical spike trains from the same neuron.
- Cond1: Neuron is stimulated with input Poisson stream of excitatory impulses. The input stream has intensity λ .
- Cond2: Neuron may fire a spike only at a moment when it receives an input impulse.
- Cond3: Just after firing, neuron appears in its standard state, which is always the same.
- Cond4: The output interspike interval (ISI) distribution is characterized with a probability density function (pdf) $p^0(t)$, which is positive: $t > 0 \Rightarrow p^0(t) > 0$, and bounded: $\sup_{t>0} p^0(t) < \infty$.

2.2 Feedback Line Action

We expect that output impulses fired by neuron are fed back to the neuron's input through a feedback line. The feedback line has the following properties:

- Prop1: The time delay in the line is $\Delta > 0$.
- Prop2: The line is able to convey no more than one impulse.²
- Prop3: The impulse conveyed to the neuronal input is identical to that from the input Poisson stream.

The important for us consequence of Prop2 is that at any moment of time the feedback line is either empty, or conveys a single impulse. If it does convey an impulse, then its state can be described with a stochastic variable s , which we call further “time to live”. The variable s denotes the exact time required by the impulse to reach the output end of the line, which is the neuron's input, and to leave the line. It is clear that $0 < s \leq \Delta$. In what follows, we use the time to live s only at moments when an ISI starts (just after triggering).

Now it is worth noticing that each triggering starts a new ISI. And at the beginning of any ISI the line is never empty, but holds an impulse. This happens for the following reasons:

¹ Detailed description of the binding neuron model can be found in [31]. See also http://en.wikipedia.org/wiki/Binding_neuron.

² This means that if the line already conveys an impulse at the firing moment, then the just fired impulse is ignored by the line.

- a) If neuron is triggered by an impulse from the Poisson input stream, and the line was empty just before that moment, then the emitted impulse enters the line. At that moment the line is characterized with $s = \Delta$.
- b) If neuron is triggered by an impulse from the Poisson input stream, and the line already conveys an impulse at that moment with time to live s , then that same impulse with that same time to live is retained at the beginning of the ISI that starts after that triggering, and the line is characterized with that same s .
- c) If neuron is triggered by an impulse from the line, then the line is empty at the firing moment and the emitted impulse enters the line. After that moment the line is characterized with $s = \Delta$.

2.3 Biological Motivation

In the natural conditions, neurons are embedded into a reverberating networks. As a result, most neurons can “feel” their own activity produced some time earlier. Such a self-influence is possible because output activity of a neuron can be fed back transformed and transmitted by other neurons. This justifies consideration of a feedback in neural systems.

At the same time, it is known that some neurons can form synapses (autapses) on its own body, or dendritic tree. This feature has been observed both for excitatory [1, 24], and inhibitory [4–6, 28] neurons. This substantiates consideration of a single neuron with excitatory feedback not only as the simplest reverberating “network” possible, but also as an independent biologically relevant case. The delay Δ comprises the time required by the output spike to pass the distance from axonal hillock, where it is generated, to the autapse and the synaptic delay. The Prop2 is somehow related to the refractoriness even if we do not introduce here the refractoriness to its full extent. The Prop3 means that we consider here an excitatory neuron.

The Cond0, above, is imposed on a neuron without feedback in accordance with experimental observations, see e.g. [8, 22]. As regards the Cond1, Poisson stream is a standard stimulation when neuronal random activity is studied. Actually, the Cond1 is not fully justified by the result of this paper, since neurons in a network receive stimulation from other neurons, and that stimulation is barely Poisson. In the case it is not Poisson, the output of this way stimulated neuron will be naturally more complicated than Poisson. The essence of this paper is that even if stimulation is Poisson, the evoked output will be more complicated than Poisson (actually, non-Markov) due to delayed feedback presence.

The question of whether some biological neurons with autapses receive a Poisson stimulation might be addressed by experimenters. As to my knowledge, olfactory receptor neurons (ORN) receive odor stimulation, which is close to Poisson one. This is because the odor molecules are absorbed by the ORN from the air in a random manner and then degrade in the process of odor perception, see more about this in [15–17].

The Cond2, above, is satisfied for most threshold-type neuronal models, starting from standard leaky integrate and fire (LIF) neuron [29] and its modifications [9]. In order the Cond2 to be valid, it is enough that the following three conditions are satisfied: (i) neuronal excitation³ gets abrupt increase at the moment of receiving input impulse⁴, (ii) after that moment, the degree of excitation does not increase (it decreases for most neuronal models) until the next input impulse. (iii) the neuron fires when its degree of excitation exceeds a

³ We use here term “excitation” instead of “depolarization voltage” because we do not specify any triggering mechanism. Our consideration as regards feedback shaping of firing statistics could be valid also for essentially artificial neurons, where excitation not necessarily has a voltaic nature.

⁴ If considering an input impulse as a current impulse, then it has a δ -function form.

threshold level. The threshold can be either static, as in the basic LIF model, or dynamic [27]. These conditions seem to be standard for many threshold-type neuronal models used, see [10, 13, 14] and citations therein. The biological justification of the Cond2 thus reduces to that of those models.

Cond3 means that any kind of memory about previous input/output activity, which can be present in a neuron, is cleared after each triggering. This excludes adaptation. Due to Cond3, output stream of neuron without feedback will be a renewal stochastic process, and this fact will be used later.

Cond4 is a mathematical assumption. It seems to be natural for any neuronal model stimulated with Poisson stream. At least, all the five conditions are satisfied for the binding neuron model and for the basic LIF model, see [33, 34], where $p^0(t)$ is calculated exactly for each model, respectively.

Finally, it should be mentioned that our result can also be applied to abstract mathematical neurons and also to hardware implemented artificial neurons.

3 Results

We expect that defined in nn. 2.1, 2.2 system of neuron with delayed feedback line fed with Poisson stream is in its stationary regime. This can be achieved if the system functions long enough that its initial state is forgotten.

In the stationary regime, let $p(t_n, \dots, t_1)$ denotes the joint probability density function of neuron with delayed feedback. The probability to get, in the output, starting from the beginning, n consecutive ISIs t'_1, \dots, t'_n such that $t'_i \in [t_i; t_i + dt_i[$, $i = 1, \dots, n$ with infinitesimal dt_i is given by $p(t_n, \dots, t_1)dt_1 \dots dt_n$.

Let $p(t_{n+1} | t_n, \dots, t_0)dt_{n+1}$ denotes the conditional probability to get the duration of $(n + 2)$ th ISI in $[t_{n+1}; t_{n+1} + dt_{n+1}[$ provided that previous $n + 1$ ISIs had duration t_n, \dots, t_0 , respectively. The conditional probability density function can be calculated as follows:

$$p(t_{n+1} | t_n, \dots, t_0) = \frac{p(t_{n+1}, t_n, \dots, t_0)}{p(t_n, \dots, t_0)}. \tag{1}$$

Now we reformulate in terms of probability density functions the definition from [11, Ch. 2 Sect. 6]:

Definition 1 The sequence of random variables $\{t_j\}$, taking values in Ω , is called the Markov chain of the order $n \geq 0$, if

$$\forall_{m>n} \forall_{t_0 \in \Omega} \dots \forall_{t_m \in \Omega} p(t_m | t_{m-1}, \dots, t_0) = p(t_m | t_{m-1}, \dots, t_{m-n}), \tag{2}$$

and this equation does not hold for any $n' < n$.

In this section we prove the following Theorem:

Theorem 1 *Let a neuronal model satisfies conditions Cond0–Cond4, above. Expect that the model is extended by introducing an excitatory delayed feedback line, which satisfies Prop1–Prop3, above. Then, in the stationary regime, the output stream of ISIs of the neuron cannot be presented as a Markov chain of any finite order.*

3.1 Proof Outline

By taking $m = n + 1$ in Eq. (2), we have the necessary condition

$$p(t_{n+1} | t_n, \dots, t_1, t_0) = p(t_{n+1} | t_n, \dots, t_1), \quad t_i \in \Omega, \quad i = 0, \dots, n + 1, \tag{3}$$

required for the stochastic process $\{t_j\}$ to be n -order Markov chain. In the case of ISIs one reads $\Omega = \mathbb{R}^+$.

We intend to prove that the relation (3) does not hold for any n . For this purpose we calculate exact expression for $p(t_{n+1} | t_n, \dots, t_0)$ as defined in Eq. (1), from which it will be clearly seen that the t_0 -dependence in $p(t_{n+1} | t_n, \dots, t_0)$ cannot be eliminated whatever large the n is.

As it is seen from (1), we need initially to calculate exact expressions for $p(t_n, \dots, t_0)$ with arbitrary n . In [32], for the binding neuron model with threshold 2, this is done by introducing an auxiliary stochastic process $\{(t_0, s_0), (t_1, s_1), \dots\}$ in which a single event (t_i, s_i) is composed of t_i , which is the i th ISI duration, and s_i , which is the time to live at the beginning of that ISI. It was proven in [32] that the sequence of events $(t_i, s_i), i = 0, 1, \dots$, is a Markov chain, which helps to calculate the joint probability density $p((t_n, s_n), \dots, (t_0, s_0))$ and then $p(t_n, \dots, t_0)$ as marginal probability by integrating it over $]0; \Delta]$ with respect to each s_i . To simplify this approach, it is worth noticing that in the sequence of consecutive random events $(t_n, s_n), \dots, (t_0, s_0)$ only the values of variables $t_n, \dots, t_1, t_0, s_0$ are fairly random. Indeed, with t_0, s_0 given, one can figure out exact value for the s_1 : if $t_0 < s_0$ then $s_1 = s_0 - t_0$, and $s_1 = \Delta$ otherwise. Now, with t_1, s_1 known, it is possible to find the same way the exact value of s_2 and so on. This allows one to reconstruct unambiguously all the values s_1, \dots, s_n from the given sequence of values of $t_n, \dots, t_1, t_0, s_0$. Having this in mind, we introduce here the conditional joint probability density $p(t_{n+1}, \dots, t_0 | s)$, which we use to calculate the required joint pdfs as follows

$$p(t_{n+1}, \dots, t_0) = \int_0^\Delta p(t_{n+1}, \dots, t_0 | s) f(s) ds, \tag{4}$$

where s (denoted previously as s_0) is the time to live at the beginning of ISI t_0 , $f(s)$ is the stationary pdf which describes distribution of times to live at the beginning of any ISI in the stationary regime. In what follows we analyze the structure of functions $f(s)$ and $p(t_{n+1}, \dots, t_0 | s)$. It appears that $f(s)$ has a singular component $a\delta(s - \Delta)$ with $a > 0$, and $p(t_{n+1}, \dots, t_0 | s)$ has a δ -function-type singularities at definite hyper-planes in the $(n + 3)$ -dimensional space of its variables (t_{n+1}, \dots, t_0, s) . After integration in (4), some of those δ -functions will survive, and exactly one of those survived has its argument depending on t_0 . The latter statement depends on exact value of ISIs in the sequence t_{n+1}, \dots, t_0 . Here, we limit our consideration to the domain in the $(n + 2)$ -dimensional space of variables (t_{n+1}, \dots, t_0) , which is defined as follows

$$\sum_{i=0}^n t_i < \Delta. \tag{5}$$

Notice that t_{n+1} is not involved in (5).

The t_0 -depending δ -function will as well survive in the $p(t_{n+1} | t_n, \dots, t_0)$ for any n , which will complete the proof that the condition (3) cannot be satisfied for any n .

A question remains of whether the domain (5) has a strictly positive probability. This indeed takes place due to positiveness of pdfs $p(t_{n+1}, \dots, t_0)$ for any positive values of (t_{n+1}, \dots, t_0) . The latter follows from the exact expressions for $p(t_{n+1}, \dots, t_0)$ given in n. 3.2.5, Eq. (20).

3.2 The Proof

3.2.1 Structure of Functions $p(t_{n+1}, \dots, t_0 | s)$

Expect that the inequality (5) holds. In order to perform integration in (4), we split the integration domain into the following $n + 2$ disjoint sub-domains:

$$D_k = \left[\sum_{i=0}^{k-1} t_i ; \sum_{i=0}^k t_i \right], k = 0, \dots, n, D_{n+1} = \left[\sum_{i=0}^n t_i ; \Delta \right].$$

It is clear that $\bigcup_{k=0}^{n+1} D_k =]0; \Delta]$, and that any $D_k, k = 0, \dots, n$, coincides with the area covered by the ISI t_k at the time axis. The conditional pdf $p(t_{n+1}, \dots, t_0 | s)$ has different structure at different domains. If $s \in D_k$, then a relation between s and t_i is as shown in Fig. 1. As it could be suggested by the Fig. 1, the first $k - 1$ ISIs are produced with the delay line not involved, the corresponding stochastic process is renewal. The k th ISI is generated with the line involved. The corresponding time to live is $s_k = s - \sum_{i=0}^{k-1} t_i \leq t_k$, the next time to live is $s_{k+1} = \Delta$. Therefore, the structure of $p(t_{n+1}, \dots, t_0 | s)$ at D_k is as follows

$$p(t_{n+1}, \dots, t_0 | s) = p(t_{n+1}, \dots, t_{k+1} | \Delta) p\left(t_k | s - \sum_{i=0}^{k-1} t_i\right) \prod_{i=0}^{k-1} p^0(t_i), \quad (6)$$

where $k = 0, 1, \dots, n$. And if $s \in D_{n+1}$, then relation between s and t_i is as shown in Fig. 2. This suggests the following structure for $p(t_{n+1}, \dots, t_0 | s)$

$$p(t_{n+1}, \dots, t_0 | s) = p\left(t_{n+1} | s - \sum_{i=0}^n t_i\right) \prod_{i=0}^n p^0(t_i), \quad s \in D_{n+1}. \quad (7)$$

Here $p(t | s)$ denotes the conditional pdf to get ISI of duration t if at its beginning, time to live of impulse in the feedback line is s .

By utilizing the same reasoning with (5) taken into account, one can represent the first factor in (6) as follows

$$p(t_{n+1}, \dots, t_{k+1} | \Delta) = p\left(t_{n+1} | \Delta - \sum_{i=k+1}^n t_i\right) \prod_{i=k+1}^n p^0(t_i). \quad (8)$$

Representation of $p(t_{n+1}, \dots, t_0 | s)$ by means of $p^0(t)$ and $p(t | s)$, similar to that displayed in (6), (7), (8), can be as well constructed if (5) does not hold. For our purpose it is enough to have (6), (7) and (8).

Fig. 1 Mutual disposition in time of s and t_0, \dots, t_n if $s \in D_k$

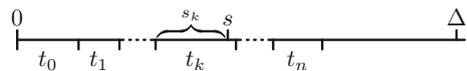
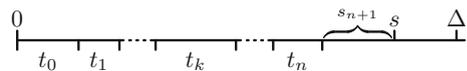


Fig. 2 Mutual disposition in time of s and t_0, \dots, t_n if $s \in D_{n+1}$



3.2.2 Structure of Function $p(t | s)$

Expect that at the beginning of an ISI, there is an impulse in the feedback line with time to live s . Then the probability that this ISI will have its duration $t < s$ is not influenced by the feedback line presence. Therefore,

$$t < s \Rightarrow p(t | s) = p^0(t).$$

The probability to get exactly $t = s$ is not zero, because in this case the impulse, which triggers the neuron and completes the ISI under consideration comes from the delay line. In order this to happen, it is necessary and sufficient that the following two events take place: (i) the neuron does not fire at the interval $]0; s[$; (ii) at the moment s , the neuron, due to previous stimulation from the Poisson stream, achieves such a state that adding one more input impulse will trigger it. The probability of (i) and (ii) is $\frac{p^0(s)}{\lambda}$, which can be easily concluded from the definition of $p^0(t)$. Thus,

$$t \in]s - \epsilon; s + \epsilon[\Rightarrow p(t | s) = \frac{p^0(t)}{\lambda} \delta(s - t)$$

with infinitesimal $\epsilon > 0$. If the neuron still not triggered at the moment s , then it is triggered by an input impulse from the Poisson stream at $t > s$. The probability to get such an impulse in $[t; t + dt[$ is λdt . Therefore, one can expect that for $t > s$, $p(t | s) \leq \lambda$.

Based on the above reasoning we represent $p(t | s)$ in the following form

$$p(t | s) = p^b(t | s) + \frac{p^0(t)}{\lambda} \delta(s - t), \tag{9}$$

where $p^b(t | s)$ is a bounded function⁵.

3.2.3 Structure of Probability Density Function $f(s)$

In the stationary regime, the pdf $f(s)$ must satisfy the following equation

$$f(s) = \int_0^\Delta \mathbf{P}(s | s') f(s') ds', \tag{10}$$

where the transition function $\mathbf{P}(s | s')$ gives the probability density to find at the beginning of an ISI an impulse in the line with time to live s provided at the beginning of the previous ISI, there was an impulse with time to live s' .

To determine exact expression for $\mathbf{P}(s | s')$ we take into account that after single firing, time to live can either decrease, or become equal Δ . Therefore,

$$s' \leq s < \Delta \Rightarrow \mathbf{P}(s | s') = 0. \tag{11}$$

If $s < s'$, then the firing, which causes transition from s' to s , happens without the line involved. Therefore,

$$0 < s < s' \Rightarrow \mathbf{P}(s | s') ds = p^0(s' - s) ds. \tag{12}$$

⁵ Compare this with [30, Eq.(7)], where $p(t | s)$ is calculated exactly for the binding neuron model.

Finally, it is possible that starting from s' one obtains $s = \Delta$ after the next firing. In order this to happen, it is necessary and sufficient that no firing happens during s' units of time. And this happens with probability

$$\mathbf{P}^0(s') = 1 - \int_0^{s'} p^0(t) dt.$$

Having this in mind, one could conclude that in the plane (s, s') , at the straight line $(s = \Delta, s' \text{—any})$, the $\mathbf{P}(s | s')$ has singularity of the following form:

$$\mathbf{P}^0(s')\delta(s - \Delta). \tag{13}$$

Now, with (11)–(13) taken into account, Eq. (10) can be rewritten as follows

$$f(s) = \int_s^\Delta p^0(s' - s) f(s') ds' + \delta(s - \Delta) \int_0^\Delta \mathbf{P}^0(s') f(s') ds'.$$

It is clear from this equation that $f(s)$ has the following form⁶

$$f(s) = g(s) + a\delta(s - \Delta), \tag{14}$$

where $a > 0$ and $g(s)$ is bounded and vanishes out of interval $]0; \Delta]$.

3.2.4 Form of $p(t_{n+1}, \dots, t_0)$ After Integration in (4)

Let $D = \bigcup_{k=0}^n D_k$. At D , representations (6) and (8) are valid. Also at D , $f(s)$ reduces to $g(s)$. Therefore,

$$\begin{aligned} & \int_D p(t_{n+1}, \dots, t_0 | s) f(s) ds \\ &= \sum_{k=0}^n p\left(t_{n+1} | \Delta - \sum_{i=k+1}^n t_i\right) \prod_{\substack{i=0 \\ i \neq k}}^n p^0(t_i) \int_{D_k} p\left(t_k | s - \sum_{i=0}^{k-1} t_i\right) g(s) ds. \end{aligned} \tag{15}$$

Taking into account (9) it can be concluded that expression (15), after performing integration, does not have any term with δ -function depending on t_0 .

Consider now the remaining part of integral in (4). With (7) taken into account one has:

$$\int_{D_{n+1}} p(t_{n+1}, \dots, t_0 | s) f(s) ds = \prod_{i=0}^n p^0(t_i) \int_{D_{n+1}} p\left(t_{n+1} | s - \sum_{i=0}^n t_i\right) f(s) ds.$$

⁶ Compare this with [30, Eqs. (14)–(16)], where $f(s)$ is calculated exactly for the binding neuron model.

After substituting here expressions (9), (14) one obtains four terms:

$$\begin{aligned}
 & \int_{D_{n+1}} p(t_{n+1}, \dots, t_0 | s) f(s) ds \\
 &= \prod_{i=0}^n p^0(t_i) \int_{D_{n+1}} p\left(t_{n+1} | s - \sum_{i=0}^n t_i\right) f(s) ds \\
 &= \prod_{i=0}^n p^0(t_i) \int_{D_{n+1}} p^b\left(t_{n+1} | s - \sum_{i=0}^n t_i\right) g(s) ds \\
 &\quad + a \prod_{i=0}^n p^0(t_i) p^b\left(t_{n+1} | \Delta - \sum_{i=0}^n t_i\right) \\
 &\quad + \frac{1}{\lambda} \prod_{i=0}^{n+1} p^0(t_i) g\left(\sum_{i=0}^{n+1} t_i\right) + \frac{a}{\lambda} \prod_{i=0}^{n+1} p^0(t_i) \delta\left(\Delta - \sum_{i=0}^{n+1} t_i\right). \tag{16}
 \end{aligned}$$

After performing integration, only the fourth term here includes a δ -function. And argument of this δ -function does depend on t_0 .

After taking (15) and (16) together we conclude that the required joint probability density has the following form

$$p(t_{n+1}, \dots, t_0) = p^w(t_{n+1}, \dots, t_0) + \frac{a}{\lambda} \prod_{i=0}^{n+1} p^0(t_i) \delta\left(\Delta - \sum_{i=0}^{n+1} t_i\right), \tag{17}$$

where function $p^w(t_{n+1}, \dots, t_0)$ does not have singularities depending on t_0 .

3.2.5 Form of $p(t_n, \dots, t_0)$ After Integration

If (5) is satisfied, then we have similarly to (6), (7)

$$\begin{aligned}
 p(t_n, \dots, t_0 | s) &= p(t_n, \dots, t_{k+1} | \Delta) p\left(t_k | s - \sum_{i=0}^{k-1} t_i\right) \prod_{i=0}^{k-1} p^0(t_i), \\
 s &\in D_k, \quad k = 0, \dots, n-1,
 \end{aligned}$$

$$p(t_n, \dots, t_0 | s) = p\left(t_n | s - \sum_{i=0}^{n-1} t_i\right) \prod_{i=0}^{n-1} p^0(t_i), \quad s \in D_n.$$

Again due to (5), and in analogy with (8) we have instead of the last two equations the following one:

$$p(t_n, \dots, t_0 | s) = p\left(t_k | s - \sum_{i=0}^{k-1} t_i\right) \prod_{\substack{i=0 \\ i \neq k}}^n p^0(t_i), \quad s \in D_k, \quad k = 0, \dots, n. \tag{18}$$

It is clear that expression similar to (7) turns here into the following

$$p(t_n, \dots, t_0 | s) = \prod_{i=0}^n p^0(t_i), \quad s \in D_{n+1}. \tag{19}$$

Now, due to (18), (19) we have

$$\begin{aligned}
 p(t_n, \dots, t_0) &= \int_0^\Delta p(t_n, \dots, t_0 | s) f(s) ds \\
 &= \sum_{k=0}^n \prod_{\substack{i=0 \\ i \neq k}}^n p^0(t_i) \int_{D_k} p\left(t_k | s - \sum_{i=0}^{k-1} t_i\right) g(s) ds \\
 &\quad + \prod_{i=0}^n p^0(t_i) \int_{D_{n+1}} f(s) ds.
 \end{aligned} \tag{20}$$

3.2.6 t_0 -Dependence Cannot be Eliminated in $p(t_{n+1} | t_n, \dots, t_0)$

Now, with representations (17) for $p(t_{n+1}, \dots, t_0)$ and (20) for $p(t_n, \dots, t_0)$ we can pose a question about the form of $p(t_{n+1} | t_n, \dots, t_0)$. The latter can be found as defined in (1). First of all notice that due to (20) and Cond4, $p(t_n, \dots, t_0)$ is strictly positive for positive ISIs. This allows us to use it safely as denominator in the definition (1). Second, it can be further concluded from (20) and Cond4, that $p(t_n, \dots, t_0)$ is bounded, and therefore does not include any singularity of δ -function type. The latter means that any singularity contained in the $p(t_{n+1}, \dots, t_0)$ appears as well in the $p(t_{n+1} | t_n, \dots, t_0)$. It follows from the above that the conditional pdf $p(t_{n+1} | t_n, \dots, t_0)$ can be represented in the following form:

$$p(t_{n+1} | t_n, \dots, t_0) = p^w(t_{n+1} | t_n, \dots, t_0) + Q(t_{n+1}, \dots, t_0) \delta\left(\Delta - \sum_{i=0}^{n+1} t_i\right), \tag{21}$$

where $p^w(t_{n+1} | t_n, \dots, t_0)$ does not contain any δ -function depending on t_0 , and $Q(t_{n+1}, \dots, t_0)$ is strictly positive bounded function:

$$Q(t_{n+1}, \dots, t_0) = \frac{a \prod_{i=0}^{n+1} p^0(t_i)}{\lambda p(t_n, \dots, t_0)}.$$

The representation (21) thus proves unequivocally that for any n , conditional pdf $p(t_{n+1} | t_n, \dots, t_0)$ does depend on t_0 (the second term in (21)) and this dependence cannot be eliminated. □

4 Conclusions and Discussion

We have proven here that any model of excitatory neuron, which satisfies Cond0-Cond4, above, and is equipped with a delayed feedback, will display essentially non-Markov activity expressed in terms of output ISIs, when stimulated with Poisson stream. This has a consequence for admissible approaches while modeling activity of reverberating neuronal networks with stochastic behavior. Indeed, in a reverberating network, a delayed feedback mediated by other neurons is always present. Our result suggests that in this case, activity of individual neurons in the network should be essentially non-Markov. Another situation takes place in networks with instantaneous interneuronal communication. In the case of no delay communications, the neuronal activity can well be Markov, or even Poisson, see example in [12].

We used here a single neuron with delayed feedback as the simplest case of reverberating “network”. At the same time, neurons which send to themselves their output impulses are known in real nervous systems [6, 24]. Therefore, our conclusions about essentially non-Markov behavior should be valid for those neurons even without taking into account their involvement in a wider network activity.

The set of conditions Cond0-Cond4, while being rather natural and wide enough, leaves out of our consideration many neuronal models known in neuroscience. E.g., Cond2 excludes models with spike latency. Cond3 excludes models with internal memory extending beyond a single ISI duration. Thus, we do not consider here partial afterspike resetting [19, 26], threshold fatigue [10], another types of adaptation, like multi-timescale adaptive threshold [18]. Any kind of adaptation in individual neuron is by itself able to bring about a kind of memory in the neuronal output stream. The same is valid for neuronal models, which retain some memory about previous activity, as it is shown in [7] for two compartmental model with only partial reset in the first (input) compartment. Therefore, considering here neurons without adaptation and partial reset we demonstrate, that delayed feedback itself, without additional memory-like mechanisms, makes neuronal output essentially non-Markov.

Another limitation is Cond1—we use a Poisson process as a stimulus. It seems that the proof given here can be extended to a wide class of renewal processes taken as stimuli. This will be checked in further work.

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