A Model for Electro-Chemical Neural Communication

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A model for electro-chemical neural communication

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Abstract. The neuro-spike communication is conducted using electro-chemical nervous signal transmissions between neurons and synapses. The nervous signal is composed of a sequence of electrically charged ions exchange in the neurons. It passes to other from one neuron to another one through the process of release and a combination of chemical substances in synapses. The neuro-spike communication is subject to disruptions due to different biological factors that impact the permanence of neural communications. In this paper, we investigate the performance of a neuro-spike communication between two neighboring neurons. We first present a mathematical model to capture the inherent biological characteristics of the nervous system. Next, the error probability of signal detection as a function of biological parameters has been characterized. Finally, we study the impacts of some specific medicines on the parameters of neuro-spike communication in the diseases of Multiple Sclerosis and Alzheimer's.

Keywords: Neural communication · axonal noise · cooperative communication synapses · synaptic channel · neuro-spike communication.

1 Introduction

Neuro-spike communication in biological nervous systems is a promising research field that is expected to have impacts on brain-machine communication system design and medical science. The neuro-spike communication is a heterogeneous communication process comprising electrical and chemical communications. In the nervous transmission, a signal may be blocked, may be changed into several spikes, or maybe added to other spikes and makes complex or wrong patterns of spikes. In addition, because of certain types of nervous system diseases or using specific types of medicines, a fault signal may be generated while there has been no nervous signal to transmit. It is a challenging task to model the biological nervous system as a mathematical model.

Several statistical approaches have been investigated in [1], [2], and [3] to

model nervous systems. Signal estimation and signal detection in a nervous communication system subjected to noise and several random disturbances have been investigated in [1]. In this work, a mathematical model for a neuro-spike communication link has been developed for the cases of a synapse and multiple cooperative synapses. In [2], the binary stochastic channels are used to model nervous processes. Also, the detection error at the receiver is computed. In [4] the axonal-synaptic channel is modeled as a multiple-input-single-output (MISO) communication link and the error probability of an optimum detector for the axonal-synaptic channel is computed. In [3], several sources of randomness have considered in the model of a neuro-spike communication link, and the bit error rate for signal detection is computed. Also, an optimum receiver is designed in [3] to enhance the bit error rate. The authors have derived the closed form equation for the signal detection threshold and the optimum input spike rate. The results depicted a high efficiency in achievable bit rate with the proposed system design. In [5], a model is presented for signal propagation in nanomachine to neuron communications based on molecular communications, where the behavior of such a system as a function of the frequency is characterized. It is shown that in a frequencies range of about 3-84 Hz, a nanomachine is able to successfully communicate with a biological neuron with an acceptable time delay of about 13.5-43 ms.

In this work, we consider a neuro-spike communication link between two successive neurons with several synapses between them. We describe the transmission of action potentials along the axon as an additive white Gaussian noise (AWGN) and consider the axon in the presynaptic neuron as an AWGN channel. Next, we use a stochastic binary Z-channel to model the release of neurotransmitters. Because the communication in the synaptic cleft has a molecular nature, we use a binary stochastic X-channel to model this process. Also, we model the aggregation of synaptic channels effects as a binary Z-channel with an aggregation crossover probability. Finally, We compute the error probability of signal detection using the developed model. The model and the underlying analysis can be used to investigate the impact of different biological parameters on the performance of the neuro-spike communication link. This study could serve as an initial step in the analysis of the impacts of specific medicines or experimental treatments on special nervous system diseases such as Multiple Sclerosis and Alzheimer. Since the access to real data regarding the communication in the neocortex is difficult, similar to most related works in this field, our assumption and findings are based on the insights from the physilogy of the brain.

The remainder of this paper is organized as follows. In Section 2, a physiological background of the central nervous system is presented. A mathematical system model for a neuro-spike communication link is described in Section 3. In Section 4, the error probability of nervous signal detection using the developed model is evaluated. The nervous communication performance subject to some nervous system diseases using the developed model is discussed in Section 5. Simulation and numerical results are presented in Section 6. Finally, concluding remarks are drawn in Section 7.

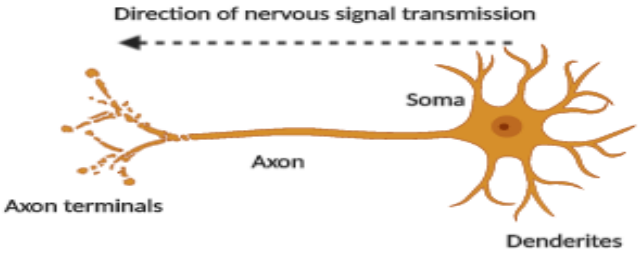

Fig. 1. Structure of a neuron in the central nervous system representing its main functional parts.

2 Biological background of neuro-spike communication

The human central nervous system consists of billions of interconnected neurons that are connected successively together by synaptic clefts that are named synapse [6]. A typical neuron, shown depicted in Fig. 1, mainly is made of several segments that are named as dendrites, cell body (soma), and axon. The outer layer of neuron is called a membrane. The axon is covered by myelin sheath with periodic gaps that nodes of Ranvier are located on them. The myelin sheath with insulating the axon speeds up signal propagation along the axon. A nervous signal first, enters the neuron through dendrites which are located on the top of soma, next, passes through the axon pathway and then, leaves neuron by axon terminals. The synapse is a small gap that passes a nervous signal only in one direction, from the presynaptic neuron to the postsynaptic neuron, see Fig. 2.

When there is no signal to transmit via the nervous system, the neuron is in a resting manner and is polarized with an intracellular potential about -95 to -65 mV. Electrically charged ion flows of potassium (K+), sodium (Na+), chloride (Cl-), cause the transmitting signal throughout the nervous system. These ions enter the neuron or exit from that via the ion channels located on the soma and dendrites (cation and anion channels) and, on the nodes of Ranvier (Sodium and potassium channels). The ion exchanges between inside and outside of the neuron, change the membrane potential of the neuron to either a higher level or lower than the resting manner potential. With a potential increasing high enough about 20 mV to reaches a firing threshold level, the neuron will be excited, the membrane will be depolarized, and the firing will happen. When a neuron fires, an action potential (spike) about 90 mV at a time period of 1 ms will be generated in the neuron. The potential increase is called the excitatory-postsynaptic-potential (EPSP). Conversely, a potential decrease to a lower value than the resting manner potential causes the hyperpolarization of the neuron membrane that is called inhibitory-postsynaptic-potential (IPSP). As firing happens, a spike passes along the axon. The spike jumps along the axon, from a node to the next node, and reaches the axon terminals. It requires to pass through the synapses to excite the next neuron [7]. When a spike reaches

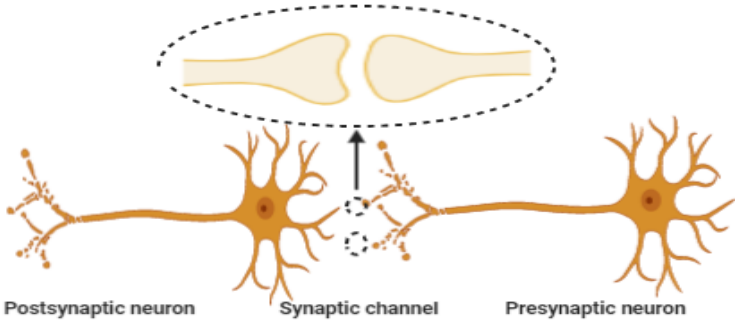

Fig. 2. Two successive neurons which are connected by chemical synaptic clefts; the nervous signal passes from presynaptic neuron to the postsynaptic neuron via multiple synapses.

an axon terminal, the depolarization leads to opening the calcium channels and causes an influx of calcium ions (Ca++) into the presynaptic neuron [8]. An increase in calcium ions causes the release of chemical substances called neurotransmitters into the synapse cleft. Neurotransmitters, in turn, bind to the receptor of the postsynaptic neuron, and by changing of permeability features of the neuron, making the cation or anion channel open. Opening cation channels conduct positively charged ions into the neuron, and thus, increases its potential to a value larger than the threshold and leads to a spike firing. Inversely, with opening anion channels, negatively charged ions conduct into the neuron, and due to a decrease of potential to a smaller value of resting potential, the neuron will be inhibited or in another point of view, its sensitivity to the next nervous signal will be reduced.

3 Neuro-spike communication model

Fig. 3 depicts the mathematical model for a neuro-spike communication link consisting of two successive neurons and multiple synapses between them, which is shown in Fig. 2. This model is complex and heterogeneous and thus, it is split to several blocks which are investigated separately in the following.

3.1 Transmitter (presynaptic neuron)

A presynaptic neuron as a transmitter should pass the nervous signal through the axon and then, releases neurotransmitter into synapses. The nervous signal, as the input of the neuro-spike communication model, could be modeled as a sequence of delta functions that is so-called spike train and is defined as follows [1]:

$$x(t) = \sum_i \delta(t - t_i), \tag{1}$$

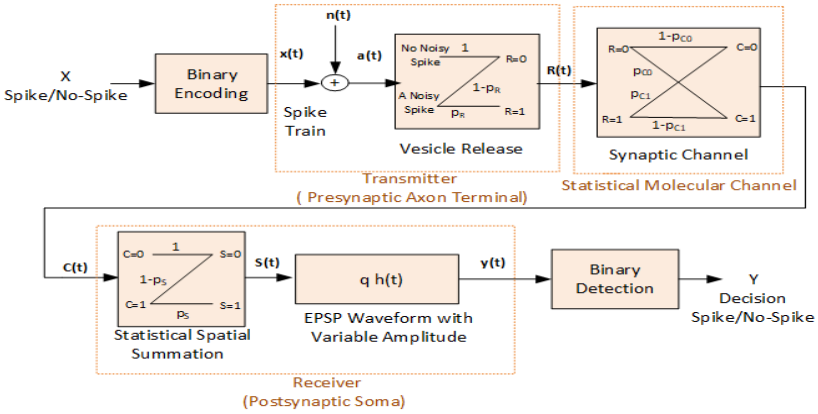

Fig. 3. Representation of the mathematical model for a neuro-spike communication link.

where $\delta(t)$ expresses the delta function, and t_i is the time duration in which the i-th spike occurs. The achieved signal at the axon terminal is obtained as

$$a(t) = x(t) + n(t), \tag{2}$$

where $n(t)$ implies the axonal noise that is assumed to have Gaussian distribution over a bandwidth BW_n with the variance σ_n^2. The power-spectral-density of $n(t)$ is [3]

$$S_n(f) = \begin{cases} \frac{\sigma_n^2}{2BW_n} & , -BW_n \leq f \leq BW_n \\ 0 & ,\text{o.w.} \end{cases} \tag{3}$$

therefore, the axon signal to noise ratio (SNR) can be obtained as follows:

$$SNR_{ax} = \frac{1}{S_n(f)} \int_0^\infty x^2(t)dt = \frac{2BW_n}{\sigma_n^2} \int_0^\infty x^2(t)dt. \tag{4}$$

The axon SNR depends on the characteristics of the axon. Therefore, the higher value of SNR implies the enhancement of the axon health and leads to the more smoothing pathway of the nervous signal transmission throughout the axon. The main reason for some nervous system diseases such as multiple sclerosis (MS) [9] is the weak passing of signals through the axon. Therefore, the value of axon SNR in these nervous diseases is small. It is expected that specific nervous medicines and treatments be effective to smooth the pathway of transmitting nervous spikes in the axon and thereby increase the value of SNR_{ax}.

The process of releasing neurotransmitters into the synapse can be modeled as a stochastic binary Z-channel, with a crossover probability of p_R. The binary input of this channel is equal to 1 when there is 'a spike' or is equal to 0 when there is'no spike'. Also, the binary output $R(t)$ is 1 or 0, respectively when

neurotransmitters release happens or not. The probabilities p_R and $1-p_R$ imply the cases of a noisy spike leads to the release and a noisy spike is failed to leading to the release. The proper synthesis of neurotransmitters, the on-time opening of calcium channels, and the influx of sufficient calcium ions into the neuron, and the perfect chemical combination in the axon terminals increase the value of p_R [10].

3.2 Synaptic channel

Communication in the synaptic channel is mainly due to the activity of released chemical substances by the presynaptic neuron, and the opening and closing of ion channels on the postsynaptic neuron. Therefore, the synaptic channel has a molecular nature and we model it by a Z-binary channel with synaptic error probabilities p_{c0} and p_{c1}. The binary input of this channel is $R(t)$, that represents the release or not release of neurotransmitter into the synapse. Besides that, the binary output is $C(t)$ which is equal to 1 and deals to the opening of cation channels, otherwise is 0. Probabilities $1-p_{c1}$ and $1-p_{c0}$, respectively are equivalent to cases that neurotransmitters are released and cation channels open, and there is no release and cation channels remain closed. Somewhere in this paper, all these stochastic parameters are called synaptic parameters.

The values of synaptic parameters mainly dependent on the synaptic channel characteristics. Therefore, in some special nervous system diseases due to synaptic disruptions, the values of p_{c0} and p_{c1} are considerably high, while with the appropriate performance of synaptic channel the values of these parameters are negligible. To facilitate the describing of the synaptic channel performance we use a new concept as synapse operation probability which is obtained as

$$p_{Ch} = 1 - p_{Ch_e}, \tag{5}$$

where p_{Ch_e} expresses the error probability of synaptic channel and is defined as follows:

$$p_{Ch_e} = p_{C0} pr\{R = 0\} + p_{C1} pr\{R = 1\}. \tag{6}$$

3.3 Receiver (postsynaptic neuron)

There are hundreds to thousands of synapses between adjacent every pair of successive neurons[6]. While a spike transmission, each synapse has a basic role in the decreasing or increasing the membrane potential of the postsynaptic neuron, respectively. The excitation or inhibition impacts of all synapses, aggregate in the soma of the postsynaptic neuron. Synapses that open cation channels on the postsynaptic neuron and cause to increase of membrane potential are called cooperative synapses. Also, the operation which leads to the aggregation of cooperative synapses impacts is called spatial summation [6]. The process of spatial summation between two neurons i and j can be modeled as a stochastic binary Z-channel with the crossover probability $p_{S_{ij}}$. Considering the physiology

background presented in Section 2, this probability increases by an increase in the number of cooperative synapses between two neurons [11], and it will be decreased by increasing of firing threshold of the postsynaptic neuron. We can model the spatial summation as

$$p_{S_{ij}} = \frac{1}{\mid V_{th_j} - V_{rest_j} \mid} \left(\frac{1}{\mid V_{th_j} - V_{rest_j} \mid} + exp(-N_{ij} p^l_{Ch_{ij}}) \right)^{-1}, \tag{7}$$

where N_{ij} is the number of cooperative synapses between presynaptic neuron i and postsynaptic neuron j. V_{rest_j} and V_{th_j} state the resting potential and firing threshold of the postsynaptic neuron. Also, $p^l_{Ch_{ij}}$ represents the operation probability of the l-th synapse between two neurons i and j, which is obtained by equation (5).

The output signal of the binary spatial summation Z-channel is $S(t)$, which in a short time slot is indicated by the binary variable S. Therefore, $S = 1$ implies a spike firing that means cooperative synapses successfully excite the postsynaptic neuron. Besides, $S = 0$ express that excitation of the postsynaptic neuron is failed and no spike is generated. Also, the binary input variable of this channel is $C = 1$, equivalent to the opening of cation channels and entering positive ions into the postsynaptic neuron or $C = 0$ which means cation channels are not opened. Notice that indices i and j can be removed because a general neuron link has been considered in this model.

On the other side, after a neurotransmitter release, the membrane potential changing of the postsynaptic neuron lasts about 15 ms. Therefore, another neurotransmitter that opens the same channel still could increase the membrane potential, and thereby, the excitation rate increases. Thus, the results of successive releases of neurotransmitters aggregate together. This process that states the postsynaptic neuron response to the successive releases is called temporal summation [6] and can be modeled as $q.h(t)$. In this modeling, $h(t)$ corresponds to the EPSP waveform and deals to the postsynaptic neuron response to a single neurotransmitter release, and q deals to the variable amplitude of the temporal summation. The value of q changes with the number of neurotransmitters releases. Also, $h(t)$ is modeled as an alpha function as follows [1]:

$$h(t) = \frac{h_p}{t_p} exp\left(1 - \frac{t}{t_p}\right) u(t), \tag{8}$$

where h_p and t_p are the peak EPSP magnitude and the corresponding time, respectively, and $u(t)$ indicates the unit step function whose value is one for $t > 0$, and zero otherwise. Also, the probability density function (PDF) of q can be represented as the k-th order Gamma-distribution [12]

$$p(q) = \frac{\beta^k}{(k-1)!} q^{(k-1)} exp(-\beta), \tag{9}$$

both β and k determine the distribution spread. The parameter k modify the variability of q therefore, the case with $k = 1$ refers to an exponential distribution with the highest variability and $k = \infty$ refers to a delta-function is independent to the variability in q.

4 Nervous spike detection

In this section, we evaluate the bit error rate (BER) of nervous spike detection in a neuro-spike communication link. As shown in Fig. 3, the binary variable X implies the existence or absence of a nervous spike in the presynaptic neuron, respectively by X= 1 and 0. Also, Y states the binary decision of spike existence or absence in the postsynaptic neuron, respectively by Y= 1 and 0. The output signal in the receiver measured over the period $0 \leq t \leq T$ is:

$$y(t) = h(t) * \sum_i q_i S_i \delta(t - t_i), \tag{10}$$

where q_i is the variable amplitude of EPSP waveform in response to the i-th nervous spike. S_i is a binary variable stating the spike fire in the soma of the postsynaptic neuron. Also, the symbol $*$ indicates the convolution operation. We consider the period T is divided into several time slots, and each time slot is small enough in which only one spike may occur. We can express the output signal in a single time slot as follows:

$$y(t) = S.q.h(t). \tag{11}$$

Thus, the following rules (Y_0, Y_1) relates the output signal to its binary equivalent:

$$\begin{array}{l} Y_0; Y = 0 \longrightarrow y(t) = 0, \\ Y_1; Y = 1 \longrightarrow y(t) = S.q.h(t). \end{array} \tag{12}$$

Considering initial probabilities as $p_0 = pr\{X = 0\}$ and $p_1 = 1 - p_0 = pr\{X = 1\}$, we can formulate the likelihood ratio for the model as follows [2]:

$$L_x(y) = \frac{f\{Y|X = 1\}}{f\{Y|X = 0\}}, \tag{13}$$

in this equation, $f\{Y|X = 1\}$ implies the probability distribution function of the binary output in the postsynaptic soma conditioned on the spike existence in the presynaptic neuron. Thereby, we can write decision rules according to the model, base on (10) as [1]

$$\begin{cases} if & L_x(y) \geq L_0 & then & Y_1 & is & true \\ if & L_x(y) \leq L_0 & then & Y_0 & is & true \end{cases} \tag{14}$$

where L_0 states the decision threshold which can be defined as follows:

$$L_0 = \frac{p_0 + \frac{1}{SNR_{ax}}}{p_1}. \tag{15}$$

We can also represent the likelihood ratio as a function of other stochastic parameters of the model. Therefore, we rewrite it as

$$L_S(y) = \frac{f\{Y|S=1\}}{f\{Y|S=0\}}, \tag{16}$$

and thereby, the decision rules change to

$$\begin{cases} if & L_S(y) \geq L_1 & then & Y_1 & is & true \\ if & L_S(y) \leq L_1 & then & Y_0 & is & true \end{cases} \tag{17}$$

where L_1 is the new decision threshold and is defined as

$$L_1 = \frac{L_0 A_1 - A_3}{-L_0 A_2 + A_4}, \tag{18}$$

where

$$\begin{aligned} A_1 &= pr\{S=0|X=0\} = 1 - p_{C0}p_S \\ A_2 &= pr\{S=1|X=0\} = p_{C0}p_S \\ A_3 &= pr\{S=0|X=1\} = 1 - p_{C0} + p_R(p_{C0} - p_S + p_S p_{C1}) \\ A_4 &= pr\{S=1|X=1\} = p_R p_S(1-p_{C1}) + (1-p_R)p_S p_{C0}. \end{aligned} \tag{19}$$

Now, according to [13], the $L_S(y)$ can be represented as follows:

$$L_S(y) = \int_0^\infty p(q)\frac{pr\{Y|q:S=1\}}{pr\{Y|S=0\}}dq \tag{20}$$

where $pr\{Y|q:S=1\}$ represents the binary output probability conditioned on the variable amplitude of the EPSP waveform. Then, supposing the AWGN bandwidth is large enough to satisfy $BW_n t_P > 1$, we can simplify $L_S(y)$ as follows:

$$L_S(y) = \int_0^\infty \frac{\beta^k q^{(k-1)}}{(k-1)!} exp(-\beta q + 2q.r(y) - q^2 E_h)dq, \tag{21}$$

where $r(y) = \int_0^T h(t)y(t)dt$, and $E_h = \frac{exp(2)T_p h_P^2}{4}$.

Finally, the average error probability of spike detection in the receiving neuron can be represented as

$$p_{error} = p_0 p_{false} + p_1 p_{miss} \tag{22}$$

where

$$\begin{aligned} p_{false} =& pr\{Y=1 \mid X=0\} = pr\{L_S(y) \geq L_1 \mid S=0\}(1 - p_S p_{C0}) \\ &+ pr\{L_S(y) \geq L_1 \mid S=1\}(p_S p_{C0}), \end{aligned} \tag{23}$$

and

$$\begin{aligned} p_{miss} =& pr\{Y=0 \mid X=1\} = pr\{L_S(y) < L_1 \mid S=0\}(1 + p_S p_R(-1 + p_{C1}) \\ &+ (1-p_R)(-p_S p_{C0})) + pr\{L_S(y) < L_1 \mid S=1\}(p_R(1-p_{C1})p_S \\ &+ (1-p_R)(p_S p_{C0})). \end{aligned} \tag{24}$$

5 Discussion on nervous system diseases and the impact of medicines on neuro-spike communication performance

In this section, the relation between random parameters of the developed model and some nervous system diseases is investigated. Considering the communication background of the nervous system presented in Section 2, a nervous signal may be blocked either while passing the axon, or transmitting in the synaptic channel.

For example in Multiple Sclerosis (MS) which is a mobility disability nervous disease, due to the demyelination of axon, the spike may be disrupted or blocked while passing the axon [9], [14]. In MS disease, while passing a spike in the axon, a large number of positive ions flow out of the neuron and the nervous spike will be blocked. Therefore, the value of (SNR_{ax}) in such diseases is low. Fampridine (Fampyra ®) is known as an efficient medicine for MS and walking disability diseases [15]. Fampridine by blocking the potassium channels prevents excessive efflux of positive electrical charges. As a result, SNR_{ax} increases, and the transmission of the nervous signal through the axon facilitates.

In some other nervous system diseases, the release probability p_R is too small. In such cases, special medicines such as clonidine act on the presynaptic neuron and through a prolonged inhibition of this neuron increase the release probability of neurotransmitters [10].

Also, synaptic channel disruptions cause some nervous diseases such as, Parkinson, Schizophrenia, and Alzheimer [16], [17], [18], and [19]. In these diseases in which the nervous spike passing is failed at the synaptic channel, the value of synaptic parameters p_{C0} and p_{C1} are high. Exercise, enough and good quality sleep as well as the hormone Leptin act on the nervous system to facilitate nervous signal passing through the synaptic channel. Thus, values of p_{C0} and p_{C1} decrease and abilities of learning and memorizing [20] will be improved.

6 Numerical results

In this section, the bit error rate (BER) of a neuro-spike communication link based on the developed model is investigated. Simulations are carried out in the environment of MATLAB [21]. According to [1], we set the predefined parameters as $h_p = 2$ mV and $T_p = 1$ ms for the EPSP waveform. The variable amplitude of EPSP waveform, q, is considered as a Gamma distribution with parameters $\beta = 1$ and $k = 1$. We also considered 10^7 transmitted spikes and computed the average performance. In the following, the results of the error probability analysis versus stochastic parameters are depicted.

Fig. 4 shows the error probability of spike detection in the postsynaptic neuron versus the axon SNR changes. It is observed that by an increase in SNR_{ax}, the spike transmission in the neuron facilitates and as a result, the error probability improves. In cases of axonal diseases such as MS who suffer from weak passing of signal in the axon, SNR_{ax} is low and thus, as we can observe in Fig. 4,

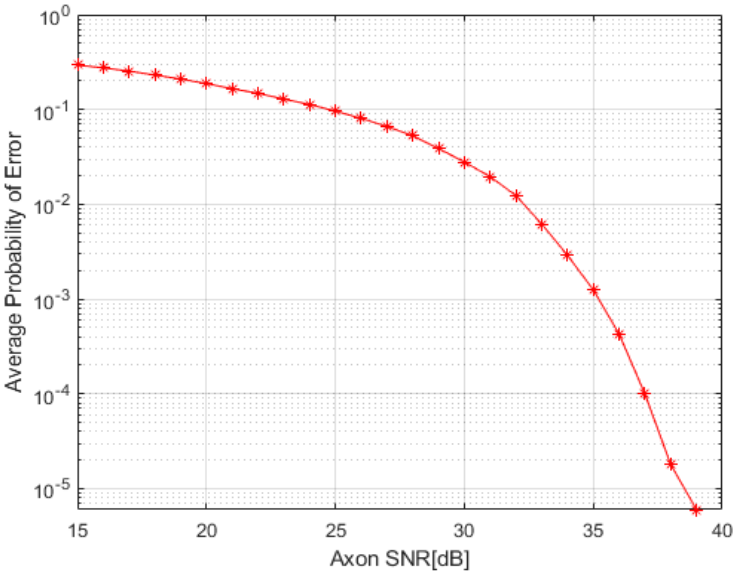

Fig. 4. The average probability of error versus the axon SNR in a neuro-spike communication link with $p_R = 0.8$, $p_{C0} = 0.01$, $p_{C1} = 0.01$, $p_S = 0.4$.

the correct spike detection in the receiver with a high probability will be failed.

In Fig. 5, the average error probability versus the releases probability of neurotransmitters p_R for different cases of $p_{C1} = 0.05$, 0.1, and 0.8 is depicted. It can be seen that with an increase of p_R, the error probability of spike detection decreases. Also, it is observed that for the worst case of $p_{C1} = 0.8$ increasing p_R could not change the error probability. The reason is that in such a case, the synaptic channel is approximately disrupted and thus, the error probability is not sensitive to other parameters.

In Fig. 6, the average error probability versus the spatial summation probability is shown. With an increase of p_S, the average error probability decreases. The reason is that spatial summation probability directly is dependent on the number of cooperative synapses between two neurons. Therefore, more synapses cooperate to excite the postsynaptic neuron the detection of the signal will be more successful.

7 Conclusion

In this paper, the performance of a neuro-spike communication link has been studied. First, we developed a model of neuro-spike communication which consists of two successive neurons that are connected via multiple synapse cleft. Next, we evaluated the error probability of signal detection in this system using

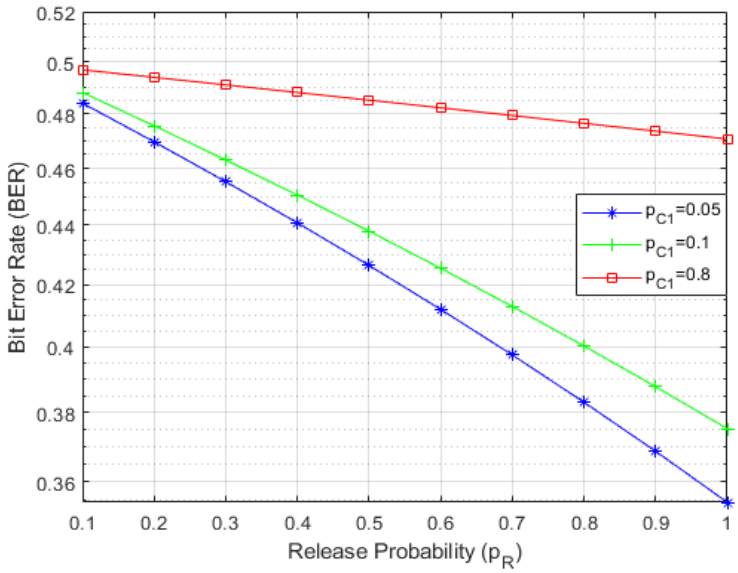

Fig. 5. The bit error probability curves versus the relase probability for different parameters of the synaptic channel in a neuro-spike communication link with $p_{C0} = 0.009$, $p_S = 0.6$, $SNR_{ax} = 15\ dB$.

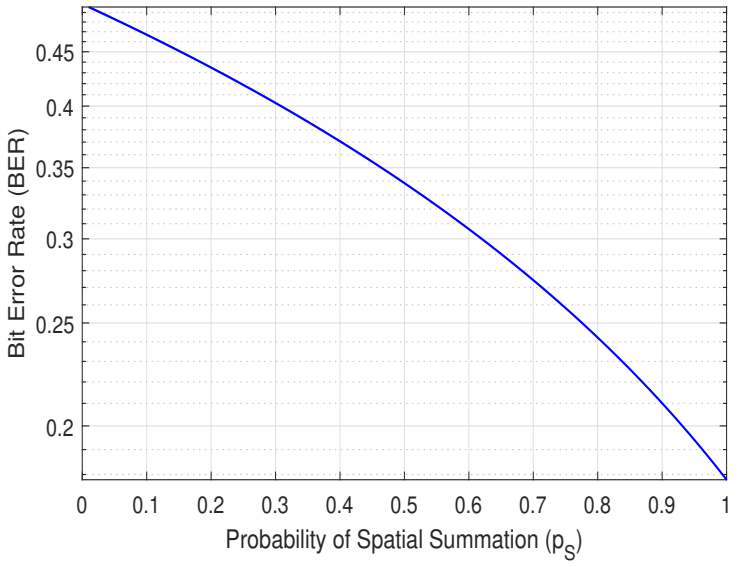

Fig. 6. The bit error rate versus the spatial summation probability in a neuro-spike communication link with $p_R = 0.8$, $p_{C0} = 0.01$, $p_{C1} = 0.09$, $SNR_{ax} = 15\ dB$.

the proposed model. The simulation results reveal the strong dependence of signal detection to the disruption factors such as axonal noise, release probability of neurotransmitters, synaptic channel parameters, and spatial and temporal summation. We also have studied the impact of different nervous system medicines on these stochastic parameters. As part of our future work, we model the cooperation of synapses as a biological concept of synaptic plasticity and develop the neuro-spike communication model by considering the medicine effect.

References

1. A. Manwani and C. Koch, "Detecting and estimating signals over noisy and unreliable synapses: information-theoretic analysis," *Neural Computation*, vol. 13, no. 1, pp. 1–33, 2001.
2. B. Maham, "A communication theoretic analysis of synaptic channels under axonal noise," *IEEE Communications Letters*, vol. 19, no. 11, pp. 1901–1904, 2015.
3. K. Aghababaiyan, V. Shah-Mansouri, and B. Maham, "Joint optimization of input spike rate and receiver decision threshold to maximize achievable bit rate of neuro-spike communication channel," *IEEE Transactions on Nanobioscience*, vol. 18, no. 2, pp. 117–127, 2018.
4. B. Maham, "Spike detection in axonal-synaptic channels with multiple synapses," in *ICASSP 2019-2019 IEEE International Conference on Acoustics, Speech and Signal Processing (ICASSP)*. IEEE, 2019, pp. 1130–1134.
5. L. Galluccio, S. Palazzo, and G. E. Santagati, "Characterization of signal propagation in neuronal systems for nanomachine-to-neurons communications," in *2011 IEEE Conference on Computer Communications Workshops (INFOCOM WKSHPS)*. IEEE, 2011, pp. 437–442.
6. J. E. Hall, *Guyton and Hall textbook of medical physiology e-Book*. Elsevier Health Sciences, 2010.
7. H. Ramezani and O. B. Akan, "Impacts of spike shape variations on synaptic communication," *IEEE Transactions on Nanobioscience*, vol. 17, no. 3, pp. 260–271, 2018.
8. K.-O. Lai and N. Y. Ip, "Central synapse and neuromuscular junction: same players, different roles," *Trends in Genetics*, vol. 19, no. 7, pp. 395–402, 2003.
9. F. Pagnini, C. M. Bosma, D. Phillips, and E. Langer, "Symptom changes in multiple sclerosis following psychological interventions: a systematic review," *BMC Neurology*, vol. 14, no. 1, p. 222, 2014.
10. D. Knight, T. C. Cunnane, and N. A. Lavidis, "Effect of chronic clonidine treatment on transmitter release from sympathetic varicosities of the guinea-pig vas deferens," *British Journal of Pharmacology*, vol. 134, no. 7, pp. 1480–1486, 2001.
11. T. Fares and A. Stepanyants, "Cooperative synapse formation in the neocortex," *Proceedings of the National Academy of Sciences*, vol. 106, no. 38, pp. 16 463–16 468, 2009.
12. J. M. Bekkers and J. D. Clements, "Quantal amplitude and quantal variance of strontium-induced asynchronous epscs in rat dentate granule neurons," *The Journal of Physiology*, vol. 516, no. 1, pp. 227–248, 1999.
13. B. Maham and R. C. Kizilirmak, "Neuro-spike communications with multiple synapses under inter-neuron interference," *IEEE Access*, vol. 6, pp. 39 962–39 968, 2018.

14. J. Shi, X. Wu, and Y. Chen, "Study on dalfampridine in the treatment of multiple sclerosis mobility disability: A meta-analysis," *PloS One*, vol. 14, no. 9, 2019.
15. Y. D. Fragoso, T. Adoni, S. V. Alves-Leon, S. L. Apostolos-Pereira, A. A. Barreira, J. B. B. Brooks, R. Claudino, E. C. Correa, M. L. B. Ferreira, A. Finkelsztejn *et al.*, "Real-life experience with fampridine (fampyra®) for patients with multiple sclerosis and gait disorders," *Neuro Rehabilitation*, vol. 39, no. 2, pp. 301–304, 2016.
16. R. Gao and P. Penzes, "Common mechanisms of excitatory and inhibitory imbalance in schizophrenia and autism spectrum disorders," *Current Molecular Medicine*, vol. 15, no. 2, pp. 146–167, 2015.
17. E. F. Osimo, K. Beck, T. R. Marques, and O. D. Howes, "Synaptic loss in schizophrenia: a meta-analysis and systematic review of synaptic protein and mrna measures," *Molecular Psychiatry*, vol. 24, no. 4, pp. 549–561, 2019.
18. B. Picconi, G. Piccoli, and P. Calabresi, "Synaptic dysfunction in parkinson's disease," in *Synaptic Plasticity*. Springer, 2012, pp. 553–572.
19. J. Laurén, D. A. Gimbel, H. B. Nygaard, J. W. Gilbert, and S. M. Strittmatter, "Cellular prion protein mediates impairment of synaptic plasticity by amyloid-β oligomers," *Nature*, vol. 457, no. 7233, pp. 1128–1132, 2009.
20. J. Harvey, N. Solovyova, and A. Irving, "Leptin and its role in hippocampal synaptic plasticity," *Progress in Lipid Research*, vol. 45, no. 5, pp. 369–378, 2006.
21. M. Release, "The mathworks," *Inc., Natick, Massachusetts, United States*, vol. 488, 2013.