BLOCKING OF WEAK SIGNAL PROPAGATION VIA AUTAPTIC TRANSMISSION IN SCALE-FREE NETWORKS

Veli BAYSAL [1], Ergin YILMAZ [1], Mahmut ÖZER [2]

[1]Department of Biomedical Engineering, Ergineering Faculty, Bülent Ecevit University, 67100 Zonguldak, Turkey
[2]Department of Electrical and Electronics Engineering, Ergineering Faculty, Bülent Ecevit University, 67100 Zonguldak, Turkey
veli.baysal@beun.edu.tr, erginyilmaz@yahoo.com, mahmutozer2002@yahoo.com

Abstract: *In this paper, the effects of autapse, a kind of synapse formed between the axon or soma of a neuron and its own dendrite, on the transmission of weak signal are investigated in scale-free neuronal networks. In the study, we consider that each neuron has an autapse modelled as chemical synapse. Then, a weak signal that is thought to carry information or an unwanted activity such as virus is applied to all neurons in the network. It is seen that the autapse with its small conductance values can slightly increases the transmission of weak signal across the network when the autaptic time delay is equal to the intrinsic oscillation period of the Hodgkin-Huxley neuron. Interestingly, when the autaptic time delay becomes equal to half of this intrinsic period or its integer multiples the autapse can prominently blocks the weak signal transmission. Also, as the autaptic conductance is increased the weak signal transmission is completely impeded by the autapse with its proper auatptic time delays. One consider that the weak signal is an unwanted or virius threatening the whole network, this autaptic mechanism is an efficient way to protect the network from attacks.*
Keywords: *Autapse, Scale-free, Blocking of weak signal.*

1. Introduction

Information exchange among neurons is fulfilled via special structures called synapse. There are two different types of synapses: electrical synapses and chemical synapses [1]. Synaptic connections are commonly occurred between two different neurons. On the other hand, a different type of synaptic connection called autapse, which is established between the axon and the dendrites of the same neuron, was firstly introduced by Vander Loos and Glaser [2]. Autapse could be electrical synapse or chemical synapse [3, 4]. Presence of this synaptic connection in different brain regions was uncovered various experimental studies by using different experimental techniques [5-11]. Tamas et al. showed that neurons in visual cortex could have roughly between 10 to 30 inhibitory autapses [11]. Lübke at al demonstrated that the 80 percent of cortical pyramidal neurons have autaptic connections in neocortex of human brain [5]. Bacci et al reported that GABAergic autaptic activity is present in fast-spiking interneurons of layer V in neocortical slices. Also they demonstrated that autaptic activity has significant inhibitory effect on the repetitive firing, and can increase current threshold for evoking action potential [12].

In addition to above studies where the presence of autapse have been shown with experimental studies, there are some studies investigating the effects of autapse on neuronal dynamics[13-24]. Saada et al. showed that autapse can cause persistent activity in B31/B32 neurons of Aplysia [13]. Bacci and Huguenard indicated that autapse can have determinative effect on the spike time of interneurons in neocortical slices [14]. Li et al. showed via histogram analysis that the number of spikes in stochastic Hodgkin-Huxley neuron is decreased in the presence of autapse [15]. Autapse can trigger the formation of spiral wave in regular network comprised of Hindmarsh-Rose (HR)[16]. Masoller et al. [17] studied how the subthreshold dynamics of Hodgkin-Huxley (HH) neuron interacts with time-delayed feedback and noise. They reported that for negative feedback, the firing rate can be lower than in the noise-free situation, for positive feedback, there are regions of delay values where the noise-induced spikes are inhibited by the feedback (i.e., autapse). Connelly found that autapse enhances the synchrony of basket cell membrane potentials across the network during neocortical gamma oscillations [18]. Wang et al studied that autapse-induced transition of firing pattern using the HR neuron model theoretically. They indicated that delayed autaptic feedback connection switches the electrical activitie of the HR neuron among quiescent, periodic and chaotic firing patterns [19]. In Ref [20], it was shown that the autapse can enhance or abolish the status of mode-locking and can effectively regulate the neuronal response. Sainz-Trapaga et al. investigated the dynamics of thermally sensitive neurons that display intrinsic oscillatory activity. They reported that a self-feedback causes spikes by

Received on: 31.01.2017
Accepted on: 14.03.2017

increasing the amplitude of the subthreshold oscillations above the threshold [21]. In Ref [22], it was shown that single spikes and burst type spikes is a sensitive function of autaptic time delay. Besides, Yılmaz et al. revealed that the presence of autapse can significantly enhances the propagation of pacemaker activity across both scale-free (SF) and small world (SW) neuronal networks [23-24].

In the above studies conducted in network level, it is considered that only pacemaker neuron has autaptic connection. But in realistic conditions, many neurons in the network can have this type of connection. In this study, we take into account that all neurons in the network have autapse modeled as chemical synapse. A weak signal which can be thought an unwanted signals (may be virus or an anomaly) is injected to all neurons. Then, the effects of autapse on the transmission or propagation of this weak signal is investigated in scale-free neuronal networks. When the obtained results evaluated, we briefly say that, autapse can become an efficient control mechanism to prevent the spreading of unwanted signals in scale-free neuronal networks.

2. Model and Methods

In order to simulate the stochastic neuronal dynamics in the scale-free network effectively, we employ the Hodgkin-Huxley equations [25].

$$C_m \frac{dV_i}{dt} + g_K^{max} n_i^4 (V_i - E_K) + g_{Na}^{max} m_i^3 h (V_i - E_{Na}) + g_l (V_i - E_l) = I_{inj} - I_i^{aut} + \sum_{j=1}^{N} \varepsilon_{ij} (V_j - V_i), i = 1, 2, \dots N \quad (1)$$

where $C_m = 1\mu F/cm^2$ is the capacity of the cell membrane, V_i denotes the membrane potential of neuron i. $g_{Na}^{max} = 120 mS cm^{-2}$ and $g_K^{max} = 36 mS cm^{-2}$ respectively denote the maximal potassium and sodium conductance, when all ion channels are open. The leakage conductance is assumed to be constant, equaling $g_l = 0.3$. $E_K = -77$ mV, $E_{Na} = 50$ mV and $E_l = -54.4$ mV are the reversal potentials for the potassium, sodium and leakage current, respectively. N is total number of neuron in the netwoks. In this paper it is assumed that $\varepsilon_{ij} = \varepsilon$, if the neurons *i* and *j* are connected; otherwise $\varepsilon_{ij} = 0$. Here, I_{inj} is given with the following equation [15]:

$$I_{inj} = \sin(0.3t) \quad (2)$$

I_i^{aut} is the autaptic current stemming from the autaptic connection of neuron i. Autapse is assumed as chemical synapse in this paper and modeled using the so-called fast threshold modulation given by the following function.

$$I_i^{aut} = -\kappa (V_i(t) - V_{syn}) S(t - \tau) \quad (3)$$

$$S(t - \tau) = 1/\{1 + \exp(-k(V_i(t - \tau) - \theta))\} \quad (4)$$

where κ denotes the conductance of line that is flowed autaptic current on, and τ represents the autaptic time delay, which occurs because of the finite propagation speed during axonal transmission. $V_{syn} = 2$ mV for excitatory chemical autapse, $k = 8$ and $\theta = -0.25$.

m_i and h_i represent the activation and inactivation variables for sodium channels of neuron i, respectively. The activation variables for potassium channels of neuron of i is expressed with n_i. The gating dynamics is described by the Langevin generalization that based on Fox's algorithm as follows [26]:

$$\frac{dx}{dt} = \alpha_x(V)(1 - x) - \beta_x(V)x + \zeta_x(t), x = m, n, h \quad (5)$$

where $\alpha_x(V)$ and $\beta_x(V)$ are the voltage-dependent rate functions for the gating parameter x [25].

$$\alpha_m(V) = \frac{0.1(V+40)}{1-\exp(-(V+40)/10)} \quad (6)$$

$$\beta_m(V) = 4\exp[-(V + 65)/18] \quad (7)$$

$$\alpha_h(V) = 0.07\exp[-(V + 65)/20] \quad (8)$$

$$\beta_h(V) = \frac{1}{1+\exp[-(V+35)/10]} \quad (9)$$

$$\alpha_n(V) = \frac{0.01(V+55)}{1-\exp[-(V+55)/10]} \quad (10)$$

$$\beta_h(V) = 0.125\exp[-(V + 65)/80] \quad (11)$$

ζ_x denotes the independent zero mean Gaussian white noise whose autocorrelation functions are given as follows [25]:

$$\langle \zeta_m(t)\zeta_m(t') \rangle = \frac{2\alpha_m\beta_m}{N_{Na}(\alpha_m+\beta_m)} \delta(t - t') \quad (12)$$

$$\langle \zeta_h(t)\zeta_h(t') \rangle = \frac{2\alpha_h\beta_h}{N_{Na}(\alpha_h+\beta_h)} \delta(t - t') \quad (13)$$

$$\langle \zeta_n(t)\zeta_n(t') \rangle = \frac{2\alpha_n\beta_n}{N_K(\alpha_n+\beta_n)} \delta(t - t') \quad (14)$$

where N_{Na} and N_K represent the total numbers of sodium and potassium channel, and calculated as $N_{Na} = \rho_{Na} S$ and $N_K = \rho_K S$, respectively. S is the cell size or the membrane area used for the scaling of channel noise intensity. The number of channels per square micrometer of cell size is $\rho_{Na} = 60\ \mu m^{-2}$ for sodium and $\rho_K = 18\ \mu m^{-2}$ for potassium. It is given in Eq. (12, 13, 14) that when the cell size is large enough the stochastic effect added by the ion channels to the membrane potential is trivial, but when the cell size is small the stochastic effect due to the ion channels is very crucial [31].

Following the procedure in [28], we construct the scale-free neuronal network, using N=200 neurons with different average degree of connectivity, k_{avg}. To quantitatively demonstrate the weak signal propagation degree, we calculate Fourier series coefficients. To do so, we first calculate the average membrane potential $V_{avg}(t) =$

$\frac{1}{N}\sum_i^N V_i(t)$ during N = 1000 periods. Then, we calculate the Fourier coefficients as follows:

$$Q_{sin} = \frac{\omega}{2N\pi}\int_0^{2N\pi/\omega} 2V_{avg}(t)(t)\sin(\omega t)\,dt \quad (15)$$

$$Q_{cos} = \frac{\omega}{2N\pi}\int_0^{2N\pi/\omega} 2V_{avg}(t)\cos(\omega t)\,dt \quad (16)$$

$$Q = \sqrt{Q_{sin}^2 + Q_{cos}^2} \quad (17)$$

where, $\omega = 2\pi/t_s$ is the frequency of the weak signal. Notably, the larger the Q the better the weak signal propagation.

3. Results and Discussion

In all previous studies where the propagation of the weak localized pacemaker activity is considered, only one neuron acting as pacemaker has an autapse. But, here we consider that each neuron in the network has one autapse modeled as chemical synapse. Then, we investigate the effects of autapse on the transmission or propagation of weak signal applied to the all neurons. To do so, we initially fix the cell size $S = 16\mu m^2$ and the average degree of connectivity $k_{avg} = 10$ and the coupling constant $\varepsilon = 0.05$. In Fig.1, we give the dependence of Q on the autaptic time delay for low levels of autaptic conductances. Also to make a comparison, we demonstrate Q values of the network in the absence of autapse (black straight line in Fig.1).

It is seen in Fig.1 that the weak signal propagation capacity of the network slightly increases for finely tuned τ. But, interestingly, when τ is equal to half of the intrinsic oscillation period of HH neuron ($T_{osc} \approx 21ms$ [23]) or its odd multiples, the weak signal propagation throughout network decreases prominently compared with the without autapse.

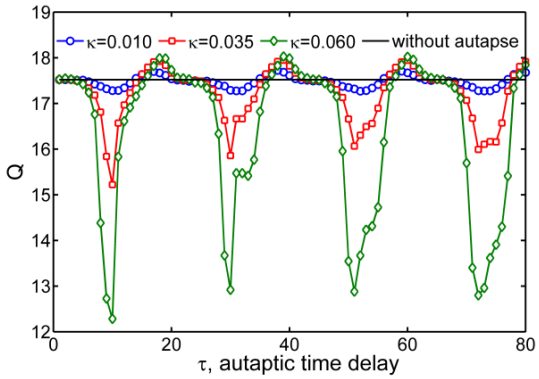

Figure 1. Effect of low autaptic conductance levels on the transmission of weak signal (ε=0.05, S=16 μm², N=200, k_{avg}=10)

To provide clear evidence for the results in Fig.1, we give the average membrane potential and the weak signal in the same panel for three different autaptic time delay values when autaptic conductance $\kappa = 0.06$ in Fig 2.

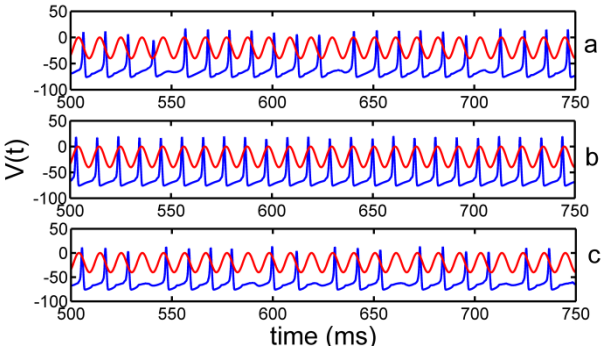

Figure 2. Average membrane potential at different autaptic time delay value with weak signal (weak signal is magnified 20 times and is shifted towards below20 units at vertical axis) a) τ = 30 ms b) τ = 17 ms c) τ = 10 ms (ε=0.05, S=16 μm², N=200, k_{avg}=10, $\kappa = 0.06$)

It is seen that the overlap between the weak signal and average membrane potential is maximum, and the average membrane potential fires when the weak signal is maximum. But in Fig 2a and Fig. 2c, matching between weak signal and average membrane potential is disrupted. Particularly in Fig 2c, the average membrane potential spikes do not occur at the time when the weak signal takes the peak value, and cycle skipping occurs. As a consequences, when the match between the weak signal and average membrane potential is well, the obtained Q values are high, which indicates better propagation of weak signal across the network. If the match between average membrane potential and the weak signal is bad and cycle skipping occurs, low Q values are obtained.

In Fig. 3, we show the dependence of Q on τ values for intermediate and high level of autaptic conductance levels. As seen in Fig.3, as the autaptic conductance level increases the propagation of weak signal across the network reduces, and even, at a strong autaptic conductance level ($\kappa = 0.76$) the propagation of weak signal is ceased by autapse for some autaptic time delay intervals when compared to the without autapse. Interestingly, when the auatptic time delay equals to the intrinsic oscillation period (T_{osc}) of HH neuron or its integer multiples the level of weak signal propagation takes the values roughly equal to the ones obtained in the absence of autapse.

To provide more evidence about the blockage of weak signal transmission, we plot the average membrane potential and the weak signal in the same panel for different autaptic time delay values in Fig 4.

As seen in Fig.4a, average membrane potential of the network has spikes occurring at approximately time instances when the weak signal has peak value. This coherence between average membrane potential and weak signal causes high Q values. But, in Fig.4b, the spike times of average membrane potential match the negative peak of the weak signal, that is, the synchronization between weak signal and spiking activity is destroyed, which leads to obtain small Q values.

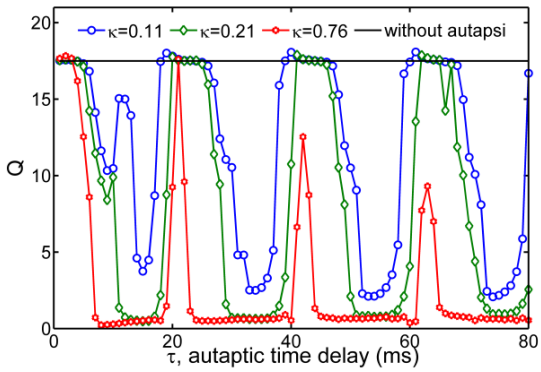

Figure 3. Effect of autaptic conductance on transmisson of weak signal depend on autaptic time delay (ε=0.05, S=16 μm^2, N=200, k_{avg}=10)

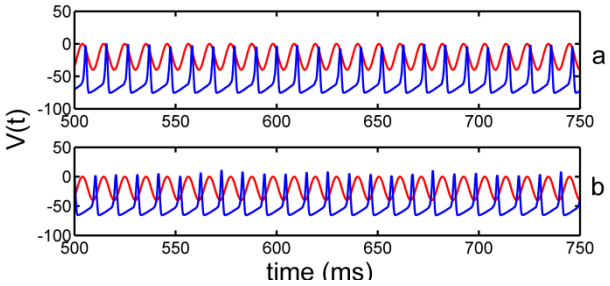

Figure 4. Average membrane potential and weak signal (weak signal is magnified 20 times and is shifted 20 units at vertical axis) for different auatptic time delays. a) $\tau = 21$ ms b) $\tau = 35$ ms (ε=0.05, S=16 μm^2, N=200, k_{avg}=10, $\kappa = 0.21$)

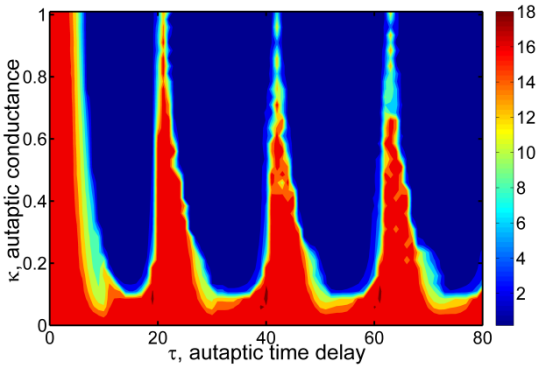

Figure 5. The dependence of Q on autaptic conductance and autaptic time delay (ε=0.05, S=16 μm^2, N=200, k_{avg}=10)

To get a global view, we show the contour plot of Q on $\kappa - \tau$ parameters space in Fig. 5. Results reveal that for low values of autaptic time delay (roughly $\tau < 10\ ms$), the weak signal propagation across the network is not affected by the variations in autaptic conductance, and the Q values take approximately the same value obtained in the absence of autapse. Similarly, when the autaptic conductance is lower than $\kappa = 0.1$, there is not any effect of autaptic time delay on the propagation of weak signal in the network. When $\tau > 10\ ms$ and $\kappa > 0.1$, we obtain different resonance islands where the degree of propagation of weak signal is almost the same with that obtained in the absence of auatpse (red shaded region). Outside of these resonance islands, we obtain that the presence of autapse significantly blocks the propagation of weak signal.

4. Conclusions

In sum, the effects of autapse on the propagation of weak signal are investigated in scale-free neuronal networks where each neuron has a chemical autapse. We obtain that when each neuron has autaptic connection in the network, the presence of autapse does not augment the propagation of weak signal in contrast it prevents the propagation of weak signal in the network. If someone assumes that this weak signal carries an unwanted signal such as infectious disease, virus, schizophrenic signal etc., the presence of autapse will be an efficient way to cope with this unwanted disturbances.

5. References

[1] EJ. Furshpan, DD. Potter, "Transmission at the giant motor synapses of the crayfish.", *J. Physiol*., vol. *145*, no. *2*, pp. *289-325*, March 1959.

[2] H. Van der Loos, E.M. Glaser, "Autapses in neocortex cerebri: synapses between a pyramidal cell's axon and its own dendrites.", *Brain Res*., vol. *48*, no. *24*, pp. *355-360*, December 1972.

[3] JM. Bekkers, "Neurophysiology: are autapses prodigal synapses?", *Curr Biol.*, vol. *8*, no. *2*, pp. *52-55*, January 1998.

[4] K. Yamaguchi, "Autapse Encyclopedia of Neuroscience" (M. D. Binder ed.), N Hirokawa and U Windhorst (Springer Berlin Heidelberg) 2008.

[5] J. Lübke, H. Markram, M Frotscher, B. Sakmann, "Frequency and dendritic distribution of autapses established by layer 5 pyramidal neurons in the developing rat neocortex: Comparison with synaptic innervation of adjacent neurons of the same class.", *J. Neurosci.*, vol. *16*, no.*10*, pp *3209-3218*, May 1996.

[6] M. H. Flight, "Neuromodulation: Exerting self-control for persistence.", *Nat. Rev. Neurosci*., vol. *10*, no. *316*, May 2009

[7] T. Branco, K. Staras "The probability of neurotransmitter release: variability and feedback control at single synapses.", *Nat. Rev. Neurosci*., vol. *10*, pp. *373-383*, May 2009.

[8] A.B. Karabelas, D.P. Purpura, "Evidence for autapses in the substantia nigra" *Brain Res.*, vol. *200*, no. *2*, pp. *467-473*, November 1980.

[9] M.R. Park, J.W. Lighthall, S.T. Kitai, "Recurrent inhibition in the rat neostriatum.", *Brain Res*., vol. *194*, no *2*, pp. *359-369*, August 1980.

[10] F. Kimura, Y. Otsu, T. Tsumoto, "Presynaptically silent synapses: spontaneously active terminals without stimulus-evoked release demonstrated in cortical autapses.", *J. Neurophysiol.*, vol. *77*, no. *5*, pp. *2805-2815*, May 1997.

[11] G. Tamás, E.H. Buhl, P. Somogyi, "Massive autaptic self-innervation of GABAergic neurons in cat visual cortex", *J. Neurosci*., vol. *17*, no. *16*, pp *6352-6364*, August 1997.

[12] A. Bacci, J.R. Huguenard, D.A. "Prince Functional autaptic neurotransmission in fast-spiking interneurons: a novel form of feedback inhibition in the neocortex", *J. Neurosci.*, vol. *23*, no *3*, pp. *859–866*, February 2003.

[13] R. Saada, N. Miller, I. Hurwitz, A. J. Susswein, "Autaptic excitation elicits persistent activity and a plateau potential in a neuron of known behavioral function.", *Curr. Biol*., vol. *19*, no. *6*, pp. *479-484*, March 2009.

[14] A. Bacci, J.R. Huguenard, "Enhancement of Spike-Timing Precision by Autaptic Transmission in Neocortical Inhibitory

Interneurons", *Neuron*, vol. *49*, no. *1*, pp. *119-130*, January 2006.
[15] Y. Li, G. Schmid, P. Hänggi, L. Schimansky-Geier, "Spontaneous spiking in an autaptic Hodgkin-Huxley setup", *Phys. Rev. E.,* vol. *82*, no. *6*, pp. *061907*, December 2010.
[16] H.X Qin, J. Ma, C. Wang, R. Chu, "Autapse-induced target wave, spiral wave in regular networkof neurons", *Physics, Mechanics and Astronomy*, vol. *57*, no. *10*, pp. *1918-1926*, October 2014.
[17] C. Masoller, M.C. Torrent, J. García-Ojalvo, "Interplay of subthreshold activity, time-delayed feedback, and noise on neuronal firing patterns" *Phys. Rev. E*, vol. *78*, no. *4*, pp. *041907*, October 2008.
[18] W.M. Connelly, "Autaptic connections and synaptic depression constrain and promote gamma oscillations" *PLoS ONE*, vol. *9*, no. *2*, pp. *e89995*, February 2014.
[19] H. Wang, J. Ma, Y. Chen, Y. Chen, "Effect of an autapse on the firing pattern transition in a bursting neuron." *Commun. Nonlinear Sci. Numer. Simul*., vol. *19*, no. *9*, pp. *3242–3254*, September 2014.
[20] H. Wang, Y. Sun, Y. Li, Y. Chen, "Influence of autaptic self-feedback on mode-locking structure of a Hodgkin–Huxley neuron under sinusoidal stimulus.", *J. Theoret. Biol*., vol. *358*, pp. *25–30*, May 2014.
[21] M. Sainz-Trapaga, C. Maseller, H.A. Braun, M.T. Huber "Influence of time-delayed feedback in the firing pattern of thermally sensitive neurons.", *Phys. Rev. E*, vol. *70*, no. *3*, pp. *031904*, September 2004.
[22] GC Sethia, J Kurths, A Sen, "Coherence resonance in an excitable system with time delay.", *Physics Letters A*, vol. *364*, no. *3*, pp. *227-230*, April 2007.
[23] E. Yılmaz, V. Baysal, M. Ozer, M. Perc, "Autaptic pacemaker mediated propagation of weak rhythmic activity across small-world neuronal networks.", *Physica A*, vol. *444*, pp. *538-546*, February 2016.
[24] E. Yılmaz, V. Baysal, M. Perc, M. Ozer, "Enhancement of pacemaker induced stochastic resonance by an autapse in a scale-free neuronal network.", *Science China Technological Sciences*, vol. *59*, no.*1*, pp. *1–7*, March 2016.
[25] E. Yılmaz, M. Ozer, V. Baysal, M. Perc, "Autapse-induced multiple coherence resonance in single neurons and neuronal networks.", *Scientific Reports*, vol. *6*, pp. *30914*, August 2016.
[26] A L. Hodgkin, A F. Huxley, "A quantitative description of membrane current and its application to conduction and excitation in nerve.", *J Physiol*, vol. *117*, no. *4*, pp. *500–544*, August 1952.
[27] R.F. Fox, "Stochastic versions of the Hodgkin–Huxley equations.", *Biophys. J*., vol. *72*, pp. *2068–2074*, no. *5*, May 1997.
[28] A L. Barabasi, R. Albert "Emergence of Scaling in Random Net-works." *Science*, 1999, 286: 509-512.