World Academy of Science, Engineering and Technology
International Journal of Biotechnology and Bioengineering
Vol:11, No:1, 2017

Thermodynamic Analyses of Information Dissipation along the Passive Dendritic Trees and Active Action Potential

Bahar Hazal Yalçınkaya, Bayram Yılmaz, Mustafa Özilgen

***Abstract*—**Brain information transmission in the neuronal network occurs in the form of electrical signals. Neural work transmits information between the neurons or neurons and target cells by moving charged particles in a voltage field; a fraction of the energy utilized in this process is dissipated via entropy generation. Exergy loss and entropy generation models demonstrate the inefficiencies of the communication along the dendritic trees. In this study, neurons of 4 different animals were analyzed with one dimensional cable model with N=6 identical dendritic trees and M=3 order of symmetrical branching. Each branch symmetrically bifurcates in accordance with the 3/2 power law in an infinitely long cylinder with the usual core conductor assumptions, where membrane potential is conserved in the core conductor at all branching points. In the model, exergy loss and entropy generation rates are calculated for each branch of equivalent cylinders of electrotonic length (L) ranging from 0.1 to 1.5 for four different dendritic branches, input branch (BI), and sister branch (BS) and two cousin branches (BC-1 & BC-2). Thermodynamic analysis with the data coming from two different cat motoneuron studies show that in both experiments nearly the same amount of exergy is lost while generating nearly the same amount of entropy. Guinea pig vagal motoneuron loses twofold more exergy compared to the cat models and the squid exergy loss and entropy generation were nearly tenfold compared to the guinea pig vagal motoneuron model. Thermodynamic analysis show that the dissipated energy in the dendritic tress is directly proportional with the electrotonic length, exergy loss and entropy generation. Entropy generation and exergy loss show variability not only between the vertebrate and invertebrates but also within the same class. Concurrently, single action potential Na^+ ion load, metabolic energy utilization and its thermodynamic aspect contributed for squid giant axon and mammalian motoneuron model. Energy demand is supplied to the neurons in the form of Adenosine triphosphate (ATP). Exergy destruction and entropy generation upon ATP hydrolysis are calculated. ATP utilization, exergy destruction and entropy generation showed differences in each model depending on the variations in the ion transport along the channels.

***Keywords*—**ATP utilization, entropy generation, exergy loss, neuronal information transmittance.

I. Introduction

THE involuntary and voluntary communication along the body are established via the nervous system. The core component of nervous system and brain is neuron, an electrically excitable cell that can process and transmit electro-chemical signals to other neurons and/or target cell (e.g. muscle cells). Each neuron possesses three distinct morphological subcellular domains; soma (cell body), axon (nerve fiber) and dendrite.

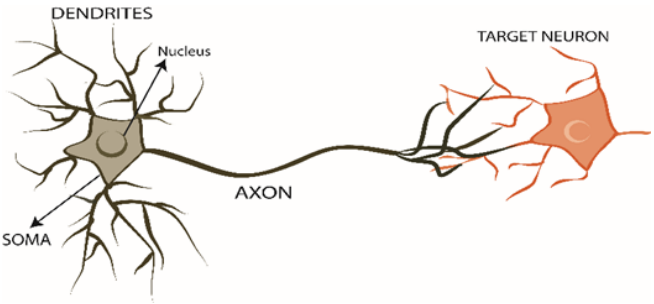

Fig. 1 Schematic description of typical neuron

Cytosol, nucleus and cytoplasmic organelles e.g. mitochondria located in soma. Synthesis of the necessary proteins and metabolic activities to sustain neuronal viability and functions all occur in soma. The axon transmits the upcoming signal from the soma to the axonal terminus in series of action potential (AP) initiations. AP uses sodium and potassium concentration gradient to encode and transmit upcoming information via ion exchange through the cell membrane Na+/K+ ATPase pumps with the use of metabolic energy in the form of ATP, where each 3 Na+/2 K+ exchange consumes 1 ATP.

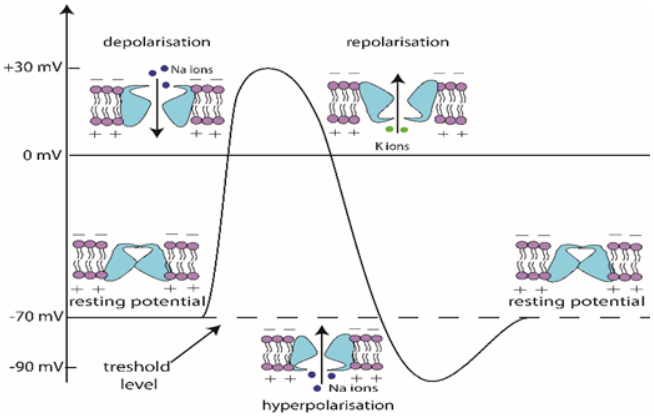

Fig. 2 Schematic description of AP in voltage- time graph and Na+/K+ ATPase pumps behavior under voltage

B. H. Yalçınkaya is with the Department of Biotechnology, Yeditepe University, 34755 Istanbul, Turkey (phone: +90 536 420 14 83; e-mail: baharhazalyalcinkaya@gmail.com).

B. Yılmaz is with the Department of Physiology, Faculty of Medicine, Yeditepe University, 34755 Istanbul, (e-mail byilmaz@yeditepe.edu.tr).

M. Özilgen, is with Department of Food Engineering, Yeditepe University, 34755 Istanbul, Turkey (e-mail: mozilgen@yeditepe.edu.tr).

At a site, where electrochemical signals arrive and propagate into cell body, neurons show extensive branching. The communication between the neuron to neuron or/and target cell is in a form of synaptic transmission (Fig. 3).

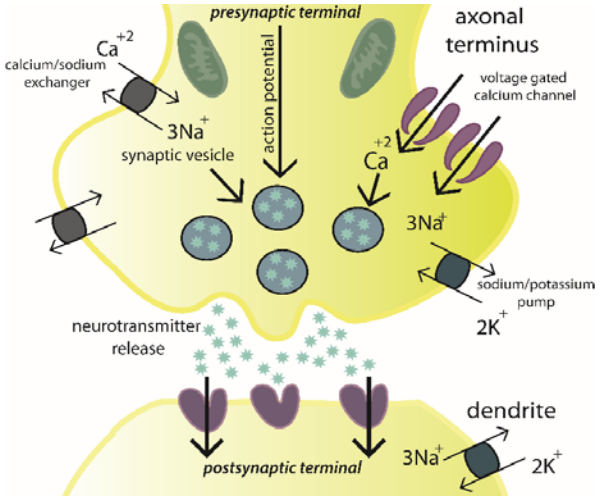

Fig. 3 Schematic description of synapses between axonal terminus of presynaptic cell and dendrite of postsynaptic cell

Each information transmission step creates an energy demand, in the form of ATP, in the brain. At the resting state, brain consumes about 20% of the total oxygen demand of the body [1]. Energy allocation calculations in the rat cerebral cortical gray matter in subcellular processes showed brain signaling activity uses nearly 75% of total ATP while the remaining is used for production of proteins, lipids and transportation etc. [2]. In brain signaling activity, most of the energy is consumed by synaptic transmission. Action potential has the second highest energy consumption ratio. The remaining energy allocated for maintain resting potential, recycle neurotransmitter and establish calcium ion entry.

Mathematical analysis of the neuronal signal transmission is very important to understand functioning and related diseases of the brain. The electric current propagation over the electrotonic length of the neuron is referred to as the cable properties of the neurons. The cable theory was first applied to the squid giant axon by Hodgkin and Huxley [3]-[6]. Later, massive dendritic trees modelled by Rall [7]-[14]. Rall's model 'trees equivalent cylinder' approximates electric current propagation along passive dendritic trees. In the model, the cylindrical trunk and other dendritic components were assumed to have M order of symmetrical branching in N order of identical trees, satisfying 3/2 power law in an infinitely long cylinder with the usual core conductor assumption, and the membrane potential was conserved in core conductor at all branching points.

In the present study, thermodynamic analyses of energy dissipation were carried out at a dendrite comprised of input (BI), sister (BS) and two cousin (BC-1 & BC-2) branches with varying electrotonic lengths in squid giant axon (SA) [4], cat motoneuron 1 (CA_1) [15], cat motoneuron 2 (CA_2) [14] and guinea pig motoneuron (GP) [16]. Use of the metabolic ATP in AP was assessed for squid giant axon SA [4] and mammalian motoneuron (MM) [17].

II. Methodology

A. Thermodynamic Analyses of Dissipated Energy

The model was established with the same assumptions as Rinzel and Rall where each branch was bifurcating symmetrically, satisfying 3/2 power law [13]. Order of symmetric branching was M=3, and the order of identical trees was N=6, the electrotonic length L was 0.1, 0.4, 0.8, 1.0, 1.2 and 1.5. Thermodynamic analyses were carried out for SA, CA_1, CA_2 and GP animal models. Each of these motoneurons has different membrane resistivity, input resistance, intracellular resistivity, membrane capacitance, diameter of membrane cylinder, and dimensionless conductance ratio. The convolution of the signals and the responses are calculated as defined by Rinzel and Rall [13] for the entire branch over time with an in-house developed computer code. Exergy loss in each motoneuron was calculated with varying electrotonic lengths with the consideration of the work done in electric field:

$$W = Vq \tag{1}$$

where V is voltage difference (taken as constant for mammalian 120 mV while for invertebrate 110 mV) and q is the involuntary dissipated charge. The work potential treated as loss work potential and entropy generation of each model for each L calculated.

B. Thermodynamic Analyses of Action Potential

The model was based on kinetic approach of Hodgkin and Huxley for the quantitative analyses of membrane current in [4] and calculations were done with an in-house developed computer code. The membrane current dynamism is governed with (1):

$$C_m \frac{dV}{dt} = \overline{g_K} n^4 (V_m - V_K) + \overline{g_{nA}} m^3 h (V_m - V_{Na}) + \overline{g_I} (V_m - V_I) - I_{stim} \tag{2}$$

where, C_m is the membrane capacitance, g_{Na}, g_K and g_l are the conductance's per unit area for the Na channel K channel and leak channel and m, h and n are set of activation and inactivation variables. The model steady state activation, inactivation and time constants satisfy boundary conditions $m=m_0$ and $h=h_0$ at t=0 with (3)-(5):

$$m = m_\infty - (m_\infty - m_0)\exp\left(-\frac{t}{\tau_m}\right) \tag{3}$$

$$h = h_\infty - (h_\infty - h_0)\exp\left(-\frac{t}{\tau_h}\right) \tag{4}$$

$$n = n_\infty - (n_\infty - n_0)\exp\left(-\frac{t}{\tau_n}\right) \quad (5)$$

where

$$m_\infty = \frac{\alpha_m}{\alpha_m + \beta_m}, \tau_m = \frac{1}{\alpha_m + \beta_m} \quad (6)$$

and

$$h_\infty = \frac{\alpha_h}{\alpha_h + \beta_h}, \tau_h = \frac{1}{\alpha_h + \beta_h} \quad (7)$$

The sodium conductance model agreed with the experimental data when three 'm' and one 'h' gating parameters are employed in the model. Kinetic parameter used for the simulations taken from literature [4], [17].

Calculation of the ATP utilization was based on Na^+ kinetics [18]. Over the entire process, Na^+ load was calculated for SA and MM. The number of the ATP molecules utilized in a single AP is calculated by multiplying the Na^+ load with the Avogadro's number and dividing into Faraday's constant. Standard Gibbs energy and the enthalpy of formation of the ATP and ADP molecules in the undergoing biochemical reaction is calculated based on the method described by [19] and by following the same procedure as [20], [21]. At a given pH, biophysical conditions set for mammalian motoneuron model are as pH=7, T=310.15 and I=0.18, and for squid giant axon model pH=7, T=298.15 and I=0.25 computed with in-house computer code where temperature (T) in Kelvin and ionic strength (I) is in molar. The exergy loss and entropy generation of ATP utilization in a single AP in SA and MM were calculated.

III. Results

A. Thermodynamic Analyses of Dissipated Energy

Calculations showed that entropy generation and exergy loss was directly proportion with the electrotonic length (Fig. 1).

Table I shows that the cat motoneurons lose nearly the same amounts of exergy while generating nearly the same amount of entropy. Exergy loss in the Guinea pig vagal motoneuron caused generation of almost twofold exergy, when compared to the CA_2 model. Exergy loss and entropy generation with the squid motoneuron was nearly 10% of those of the guinea pig vagal motoneuron.

B. Thermodynamic Analyses of Action Potential

Upcoming signal cause AP initiation in the plasma membrane with rapid, transient and increased membrane permeability to the Na^+ ions and then the action slows down and extends to the K^+ ions. To maintain signaling, 1 mole of ATP is utilized by a Na^+/K^+ ATPase pump for the transport of every 3 Na^+ and 2 K^+ ions. The Na^+ load and ATP utilization of single AP was calculated for SA and MM. Calculations (Table II) show that SA became permeable to 1525.3 nC/cm^2 with utilization of 3.17x10^{12} ATP molecules per unit area while MM became permeable to 11223 nC/cm^2 with utilization of 23.3x10^{12} ATP molecules per unit area.

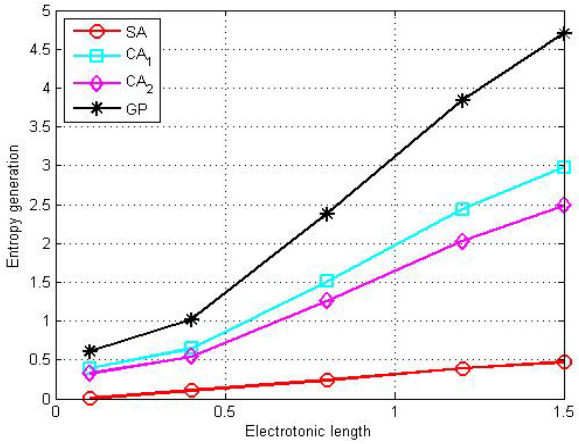

Fig. 4 Entropy generation in a varying length for SA, CA_1, CA_2 and GP models

TABLE I
EXERGY LOSS AND ENTROPY GENERATION WHEN L=1.0 FOR ALL MODELS

Models	Exergy loss (pJ)	Entropy generation (pJ)
SA	0.95	0.003
CA_1	6.19	0.020
CA_2	5.16	0.017
GP	9.75	0.031

TABLE II
THERMODYNAMIC PROPERTIES OF ACTION POTENTIAL

Models	Na load (nC/cm^2)	ATP molecules (10^{12})	Entropy Generation (nJ/mol)	Exergy Loss (nJ(/molK)
SA	1525.3	3.17	182.4	0.61
MM	11223	23.3	862.8	2.78

ATP hydrolysis exergy loss and entropy generation are calculated for different physiological conditions. SA motoneuron generated nearly 5 fold entropy compared to the MM motoneuron.

IV. Discussion

A. Thermodynamic Analyses of Dissipated Energy

Table I summarizes the main results of the thermodynamic analysis of the propagation entropy generation and exergy loss for unit electrotonic length. Vertebrate motoneurons (cat and Guinea pig motoneurons) have higher exergy loss and entropy generation than invertebrate motoneuron (squid giant axon) implying that the electrical transmission from to input branch to other branches was more efficient in the invertebrate motoneuron than mammalian motoneurons. Fig. 4 shows that the entropy generation was directly proportional with the electrotonic length. The electrotonic length was estimated as 1.5 for the spinal motoneurons [22] and 0.9 for the hippocampal pyramidal [23] and 1.2 for the granule cells [24]. Fig. 4 shows that effective reduction in the electrotonic length in simple cylinder motoneurons reduces the propagation loss

significantly.

B. Thermodynamic Analyses of Action Potential

The results of this study summarize thermodynamic analysis of the AP for invertebrate and mammalian motoneuron. According to the results, AP is more efficient in the squid giant axon, than that of mammalian motoneuron in terms of sodium ion load and ATP utilization. Accordingly, entropy generation and exergy loss of ATP consumption was nearly 5 fold more in the MM. ATP expenditure in the AP is highly dependent to sodium ion transfer kinetics [25] pointing that 13.5% more sodium ions enter in to the MM in action potential, which utilizes more ATP. Reference [26] showed that in the rising phase at 37 ^{o}C in mossy fiber boutons of hippocampal granule neurons, sodium entry was confined much more than that of squid giant axon as observed with 30% more sodium entry. The difference in action potential efficiency could be attributable to differences in sodium channel kinetics in different cell types [27]. It may also be possible that the sodium channel kinetics and the physiological conditions of the motoneurons may differ from each other.

V. Conclusion

In the present paper, propagation loss and its thermodynamic cost in passive propagation along the dendritic cylinders was assessed.

The results have shown that, electrotonic length has a great importance in the propagation loss and its thermodynamic costs and much more information lost during propagation in vertebrate motoneurons than those of the invertebrate. Furthermore, in active propagation along axon of the mammalian motoneuron, metabolic energy demand was higher than that of the squid giant axon. Thermodynamic evaluation of metabolic cost also gave higher amount of entropy generation and exergy loss in the mammalian motoneurons.

References

[1] P. J. Magistretti, "Brain energy metabolism," in Fundamental Neuroscience, F. E. B. M. Zigmond, S. Landis, J. Roberts and L. Squire Ed., ed San Diego: Academic Press, 1999, pp. 389-413.W.-K. Chen, *Linear Networks and Systems* (Book style). Belmont, CA: Wadsworth, 1993, pp. 123–135.

[2] C. Howarth, P. Gleeson, and D. Attwell, "Updated energy budgets for neural computation in the neocortex and cerebellum," Journal of Cerebral Blood Flow & Metabolism, Vol. 32, pp. 1222-1232, 2012.

[3] A. L. Hodgkin, A. Huxley, and B. Katz, "Measurement of current-voltage relations in the membrane of the giant axon of Loligo," The Journal of physiology, Vol. 116, pp. 424-448, 1952.

[4] A. L. Hodgkin and A. F. Huxley, "A quantitative description of membrane current and its application to conduction and excitation in nerve," The Journal of physiology, Vol. 117, pp. 500-544, 1952.

[5] A. L. Hodgkin and A. F. Huxley, "Currents carried by sodium and potassium ions through the membrane of the giant axon of Loligo," The Journal of physiology, Vol. 116, pp. 449-472, 1952.

[6] A. L. Hodgkin and A. F. Huxley, "The dual effect of membrane potential on sodium conductance in the giant axon of Loligo," The Journal of physiology, Vol. 116, pp. 497-506, 1952.

[7] W. Rall, "Membrane potential transients and membrane time constant of motoneurons," Experimental neurology, Vol. 2, pp. 503-532, 1960.

[8] W. Rall, "Theory of physiological properties of dendrites," Annals of the New York Academy of Sciences, Vol. 96, pp. 1071-1092, 1962.

[9] W. Rall, "Theoretical significance of dendritic trees for neuronal input-output relations," Neural theory and modeling, pp. 73-97, 1964.

[10] W. Rall, "Distinguishing theoretical synaptic potentials computed for different soma-dendritic distributions of synaptic input," 1967.

[11] W. Rall, "Time constants and electrotonic length of membrane cylinders and neurons," Biophysical Journal, Vol. 9, p. 1483, 1969.

[12] W. Rall, "Cable properties of dendrites and effects of synaptic location," Excitatory synaptic mechanisms, Vol. 1, pp. 175-187, 1970.

[13] J. Rinzel and W. Rall, "Transient response in a dendritic neuron model for current injected at one branch," Biophysical Journal, Vol. 14, p. 759, 1974.

[14] W. Rall, "Core conductor theory and cable properties of neurons," Comprehensive physiology, 2011.M. Young, *The Techincal Writers Handbook*. Mill Valley, CA: University Science, 1989.

[15] F. Dodge and J. Cooley, "Action potential of the motorneuron," IBM Journal of Research and Development, Vol. 17, pp. 219-229, 1973.

[16] R. Nitzan, I. Segev, and Y. Yarom, "Voltage behavior along the irregular dendritic structure of morphologically and physiologically characterized vagal motoneurons in the guinea pig," Journal of neurophysiology, Vol. 63, pp. 333-346, 1990.

[17] A. Singh, R. Jolivet, P. Magistretti, and B. Weber, "Sodium entry efficiency during action potentials: A novel single-parameter family of Hodgkin-Huxley models," in Advances in Neural Information Processing Systems, 2010, pp. 2173-2180.

[18] B. Sengupta, M. Stemmler, S. B. Laughlin, and J. E. Niven, "Action potential energy efficiency varies among neuron types in vertebrates and invertebrates," PLoS Comput Biol, Vol. 6, p. e1000840, 2010.

[19] R. A. Alberty, Thermodynamics of biochemical reactions: John Wiley & Sons, 2005.

[20] S. Genc, E. Sorguven, I. A. Kurnaz, and M. Ozilgen, "Exergetic efficiency of ATP production in neuronal glucose metabolism," International Journal of Exergy, Vol. 13, pp. 60-84, 2013.

[21] B. H. Yalçınkaya, Ş. Erikli, B. A. Özilgen, A. B. Olcay, E. Sorgüven, and M. Özilgen, "Thermodynamic analysis of the squid mantle muscles and giant axon during slow swimming and jet escape propulsion," Energy, Vol. 102, pp. 537-549, 2016.

[22] L. L. Glenn, B. G. Samojla, and J. F. Whitney, "Electrotonic parameters of cat spinal α-motoneurons evaluated with an equivalent cylinder model that incorporates non-uniform membrane resistivity," Brain research, Vol. 435, pp. 398-402, 1987.

[23] T. H. Brown, R. A. Fricke, and D. H. Perkel, "Passive electrical constants in three classes of hippocampal neurons," Journal of Neurophysiology, Vol. 46, pp. 812-827, 1981.

[24] L. L. Glenn, "Overestimation of the electrical length of neuron dendrites and synaptic electrotonic attenuation," Neuroscience letters, Vol. 91, pp. 112-119, 1988.

[25] B. C. Carter and B. P. Bean, "Sodium entry during action potentials of mammalian neurons: incomplete inactivation and reduced metabolic efficiency in fast-spiking neurons," Neuron, Vol. 64, pp. 898-909, 2009.

[26] H. Alle, A. Roth, and J. R. Geiger, "Energy-efficient action potentials in hippocampal mossy fibers," Science, Vol. 325, pp. 1405-1408, 2009.

[27] I. M. Raman and B. P. Bean, "Resurgent sodium current and action potential formation in dissociated cerebellar Purkinje neurons," The Journal of neuroscience, Vol. 17, pp. 4517-4526, 1997.