Electric Conduction Effects in the Neuronal Cytoskeleton Hold the Key to Our Understanding of the Biophysics of Consciousness

Jack A. Tuszyński[*1,2]

Department of Oncology, Dept. of Physics, University of Alberta, Edmonton, T6G 2J1, Canada[1]
Department of Mechanical and Aerospace Engineering, Politecnico di Torino, Torino, Italy[2]
jack.tuszynski@gmail.com

Abstract

Electrical activity of the brain is the basis of our understanding of neurophysiology. Electrical signals in the form of action potentials propagate along axons and are relayed via synaptic connections between neurons. Neuronal cytoskeleton is constructed from parallel bundles of microtubules interconnected by microtubule associated proteins (MAPs). In this paper we provide an overview of the electrical properties of microtubules and actin filaments which act as bioelectric circuits. It is well known that impairment of neuronal cytoskeleton results in various neurodegenerative diseases. Therefore, it stands to reason that these electrical properties of neuronal cytoskeleton are of critical importance to our understanding of consciousness as an emergent property. This short paper provides an overview of this issue.

In this brief document, we give a high level overview and relevant references that form the basis for the arguments implicating neuronal cytoskeleton's electric conduction and signaling in the cognitive functions of the human brain. A recently published book, which is a collection of

Journal of Cognitive Science 19-2:109-114, 2018

contributed chapters on the topic of the biophysics of consciousness is an excellent source of detailed information on this topic[1]. In earlier work, computational and theoretical modeling was performed at both atomistic and coarse-grained levels in order to gain insight into electrostatic and electro-conductive properties of the cytoskeleton[2]. Specifically, computer simulations corroborated some very intriguing experimental measurements carried out for actin filaments[3] and microtubules[4]. In the case of actin filaments, it was shown that they propagate ionic pulses in a lossless fashion consistent with a solitonic model of wave propagation in nonlinear systems[3]. In the case of microtubules (MTs), the unusual behavior of ionic conductions along their lengths exhibited amplification effects that are comparable to the behavior of a transistor[4]. Continuum approximations for cable equations describing actin filaments and microtubules were derived and their analytical solutions compare favorably to measurements in buffer solutions showing these nonlinear waves of ionic signals[3-5]. More recent measurements of the changes in conductivity and capacitance of buffer solutions containing ensembles of microtubules supported these intriguing results and also provided estimates of the conductivity of individual microtubules[6]. They showed that a dramatic change in conductivity occurs when tubulin forms microtubules with unpolymerized tubulin lowering the conductivity of the systems while microtubules significantly increasing it[6]. In living cells, this intra-cellular reorganization taking place in the cytoskeleton signals a conductive phase transition coinciding with mitosis in dividing cells. In non-dividing cells, such as neurons, microtubules and actin filaments not only provide a network of "roadways" for material transport via motor proteins but also cable-like ionic signal propagation circuitry[7]. Information processing is a key process involved in cognitive brain functions, hence it is important to link the structure of neuronal cytoskeleton to the biophysical functions of MTs, specifically those functions related to signaling, conduction and cellular transport, and to find possible mechanisms for MTs to influence brain cell firing. The question is how this can be integrated into the entire neuron's electrical excitatory dynamics. Below we list components of such a scheme:

1. Synaptic transmission signals arrive at the postsynaptic density, which may be causing ionic waves to move along associated actin filaments. The

latter, as demonstrated earlier, participate in lossless signal transmission.

2. These waves can then propagate along MAP2 via the movement of counter-ions from the actin filaments to MTs in their proximity. As stated above, MTs can amplify these signals and send them toward or away the soma depending on the propagation direction.

3. These waves in turn affect the conformational states of the C-termini on the MT as was shown in computational simulations[8, 9].

4. The change in C-termini states affects the processivity of kinesin movement along MTs as well as the MAP2 connections along the MT affecting memory and learning.

5. The resultant change in MAP2 connections can then lead to an alteration of the architecture of the network and consequently the overall signaling patterns and their distribution.

6. The ionic waves may then propagate along the new connections to other actin filaments that in turn could affect ion channels and neuron signaling changing their threshold for activation and deactivation.

The above scheme may elucidate the way by which external stimuli affect our learning and memory as well as our conscious perception. While we have not invoked quantum aspects of consciousness yet, quantum events may also take place as we discuss briefly next. While classical ionic conduction may be a major part of it but necessarily the only aspect worth considering. Several recent papers[10-12] made predictions about the binding of anesthetic molecules to tubulin and microtubules. It was shown that there exist numerous binding sites on tubulin, which is one of very few proteins in the cytoskeleton that has this property and is involved in cognitive functions. Moreover, it was demonstrated that some of these binding sites are close enough to the tryptophan locations to affect exciton dynamics in the electronic degrees of freedom of the lattice of tryptophans within the structure of a microtubule. This change in tryptophan excitation dynamics, very importantly, correlates to a high degree with the potency of the anesthetic molecules studied[13]. This is an indirect proof that quantum degrees of freedom in microtubules could be strongly involved in consciousness.

While theoretical predictions indicate that this may not be so, direct experimental evidence of quantum effects within MTs is required[14].

Experimental tests to investigate quantum effects in MTs have been outlined in the past, however concrete results are still needed and we hope to participate in such empirical studies in the near future.

Finally, there has been a strong link made between microtubules in neurons and their participation in memory formation at a molecular level through phosphorylation events involving calmodulin kinase II enzyme[15]. Conversely, almost all neurodegenerative diseases can be linked to aberrations in the structure and function of microtubules and cytoskeletal motor traffic[16]. A case in point is the molecular basis of Alzheimer's disease that is well documented to involve MAP tau, an important protein cross-linking microtubules and a computational model elucidating this pathology clearly shows how zinc binding to tubulin plays a central role in this pathology[17].

References

1. R. R. Poznanski, J.A. Tuszynski and T.E. Feinberg (eds.), *Biophysics of Consciousness: A Foundational Approach*, ISBN 9789814644259, World Scientific, Singapore, 2016

2. A.Priel, J. A. Tuszynski and H. F. Cantiello, Electrodynamic Signaling by the Dendritic Cytoskeleton: Towards and Intracellular Information Processing Model, *Electromagnetic Biology and Medicine, 24*, no.3, 221-231

3. J.A. Tuszynski, S. Portet, J.M. Dixon, C. Luxford and H.F. Cantiello, Ionic Wave Propagation Along Actin Filaments, *Biophysical Journal 86*, 1890-1903 (2004)

4. A.Priel, A.J. Ramos, J.A. Tuszynski and H.F. Cantiello, Effect of calcium on electrical energy transfer by microtubules, *Journal of Biological Physics 34*. No. 5 (2008) 475-485,

5. A.Priel, A.J. Ramos, J.A. Tuszynski and H.F. Cantiello, A Bio-Polymer Transistor: Electrical Amplification by Microtubules, *Biophysical Journal* vol. 90 issue12: 4639-4643 (2006)

6. I. B. Santelices, D.E. Friesen, C. Bell, J. Lewis, J. Xiao, C.M. Hough, H. Freedman, V. Rezania, K. Shankar and J.A. Tuszynski, Response to Alternating Electric Fields of Tubulin Dimers and Microtubule Ensembles in Electrolytic Solutions, *Scientific Reports 7: 1*, 9594 (2017)

7. D.E. Friesen, T.J.A. Craddock, A.P. Kalra, and J.A. Tuszynski. Biological wires, communication systems, and implications for disease. *Biosystems* 127: 14-27 (2015).

8. H. Freedman, V. Rezania, A. Priel, E. Carpenter, S. Y. Noskov, and J. A. Tuszynski. Model of ionic currents through microtubule nanopores and the lumen. *Physical Review E 81*, no. 5 (2010): 051912.

9. T.J.A. Craddock, J. A. Tuszynski, A. Priel, and H. Freedman. Microtubule ionic conduction and its implications for higher cognitive functions. *Journal of integrative neuroscience 9*, no. 02 (2010): 103-122.

10. S.R. Hameroff, T.J. A. Craddock and J.A. Tuszynski, Quantum Effects in the Understanding of Consciousness, *Journal of Integrative Neuroscience* 13(2):229-52 (2014)

11. T. J. A. Craddock, M. St. George, H. Freedman, K. H. Barakat, S. Damaraju and J. A. Tuszynski, Computational Predictions of Volatile Anesthetic Interactions

with the Microtubule Cytoskeleton: Implications for Side Effects of General Anesthesia, *PLoS One* (2012) 7(6):e37251

12. T.J.A. Craddock, A. Priel and J.A. Tuszynski, Keeping Time: Could Quantum Beating in Microtubules Be the Basis for the Neural Synchrony Related to Consciousness? *Journal of Integrative Neuroscience* 13 (02), 293-311 (2014)
13. T. J. A. Craddock, P. Kurian, J. Preto, K. Sahu, S. R. Hameroff, M. Klobukowski, and J. A. Tuszynski, Anesthetic Alterations of Collective Terahertz Oscillations in Tubulin Correlates with Clinical Potency: Implications for Anesthetic Action and Post-Operative Cognitive Dysfunction, *Scientific Reports 7:1*, 9877 (2017)
14. J.A. Tuszynski, The Need for a Physical Basis of Cognitive Process. Comment on Consciousness in the Universe. A Review of the "Orch OR" Theory by Hameroff and Penrose, *Physics of Life Reviews* (2014) Mar;11(1):79-80;
15. T.J.A. Craddock, S.R. Hameroff and J.A. Tuszynski, Cytoskeletal signaling: Is molecular memory encoded in microtubule lattices by CaMKII phosphorylation, *PloS Computational Biology* (2012) 8(3): e1002421. doi:10.1371/journal.pcbi.1002421.
16. N.J. Woolf, A. Priel and J.A. Tuszynski. Nanoneuroscience: structural and functional roles of the neuronal cytoskeleton in health and disease. Springer Science & Business Media, 2009.
17. T.J.A Craddock, J. A. Tuszynski, D. Chopra, N. Casey, L. E. Goldstein, S. R. Hameroff, and R. E. Tanzi. "The zinc dyshomeostasis hypothesis of Alzheimer's disease." *PLoS One* 7, no. 3 (2012): e33552.