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Computing by physical interaction in neurons

Dorian Aur[*,§], Mandar Jog[†] and Roman R. Poznanski[‡]

[*]*Department of Comparative Medicine, Stanford University*
Palo Alto, CA 94305, USA

[†]*Faculty of Medicine and Dentistry*
Department of Clinical Neurological Sciences
University of Western Ontario
London Ontario, N6A 5A5, Canada

[‡]*Department of Physical and Mathematical Science*
Universiti Tunku Abdul Rahman, Perak, 31900, Malaysia

[§]*Department of Mathematics and Statistics*
University of Victoria, BC V8W 3R4, Canada
[§]*DorianAur@gmail.com*

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The electrodynamics of action potentials represents the fundamental level where information is integrated and processed in neurons. The Hodgkin–Huxley model cannot explain the non-stereotyped spatial charge density dynamics that occur during action potential propagation. Revealed in experiments as spike directivity, the non-uniform charge density dynamics within neurons carry meaningful information and suggest that fragments of information regarding our memories are endogenously stored in structural patterns at a molecular level and are revealed only during spiking activity. The main conceptual idea is that under the influence of electric fields, efficient computation by interaction occurs between charge densities embedded within molecular structures and the transient developed flow of electrical charges. This process of computation underlying electrical interactions and molecular mechanisms at the subcellular level is dissimilar from spiking neuron models that are completely devoid of physical interactions. Computation by interaction describes a more powerful continuous model of computation than the one that consists of discrete steps as represented in Turing machines.

Keywords: Physical theory; electric field; intraneuronal computation; spike stereotypy; subcellular signaling; neural code; Turing-machines.

1. Introduction

Modern experimental science has reshaped the theoretical framework and our thinking regarding physical world that we live in. Accidentally discovered, chemical reactions that occur far-from-thermodynamic equilibrium (Murray, 1974) or experimental data regarding quasiperiodic crystals (Shechtman *et al.*, 1951) have shown the limits of theoretical models and previous experiments. However, far from an initial

[§]Corresponding author.

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goal, the impact of the Hodgkin−Huxley (HH) model (Hodgkin & Huxley, 1952) expanded fast in many different areas of science from biology to artificial intelligence. Even though Rashevsky (1960) had described the potential limits of the HH model:

"*HH proposed a kind of semiinformal theory which represents very well a large number of experimental data. It is, however, to be hoped that further developments of definite physico-chemical models will lead to a derivation of the HH equations or of some equations which are equivalent to them...*"

The HH model does not seem to reveal relevant important aspects regarding information-processing in neurons since many computational processes are not included. In particular, recent analyses show that the electrodynamics of action potential propagation displays significant meaningful changes (Aur *et al.*, 2005; Aur & Jog, 2007; Aur *et al.*, 2006; Aur & Jog, 2010). Additionally, it is well known that the arrangements in macromolecular structures inside the cell are not random. Theoretical models and previous experimental data that analyzed structural elements within proteins confirmed this important phenomenon (Levitt & Chothia, 1976). More importantly, since the roots of intelligent action lie deep in computing by physical interaction in single neurons (Ford, 2009; Aur, 2011) in many simple organisms, the decision-making abilities are taken without delivering spikes within a millisecond range (Ford, 2010). The process of physical interaction when information is "read", "written" or processed within a neuron are related to semantics of cognitive phenomena. Therefore, the HH model is an incomplete model underlying the biophysics of spike computation across organizational levels.

This study bridges different levels of computation and hypothesizes that the fundamental process of computation in neurons can be revealed at the subcellular level. Therefore, we identify the spiking activity dynamics and interaction of electric charges as the fundamental level where information is integrated and processed in neurons. During action potential (AP) generation, electric charges that locally interact perform computations at a molecular level within active neurons (Krishtalik & Topolev, 2000). The model of computation using physical interaction develops during spikes (both axonal and dendritic), involves internal molecular processes, the effects of neurotransmitters and generated electric fields which provide a continuous form of communication. Therefore, one can consider that computation developed by electric interactions is subject to endogenous and exogenous inputs reflected in electric field changes (Pidaparti *et al.*, 2007; Woolf *et al.*, 2009; Poznanski, 2010). Our framework supports the idea of "memories" stored within densities of electric charges in molecular structures and that the process of interaction is required to access information stored, to write additional information and intrinsically to build semantics (Woolf *et al.*, 2009; Aur & Jog, 2010).

2. Spike directivity: The charge density dynamics revealed

Spike directivity is a vector representation of transient charge density during AP occurrence. Spike directivity depends on spatial occurrence of electrical patterns and

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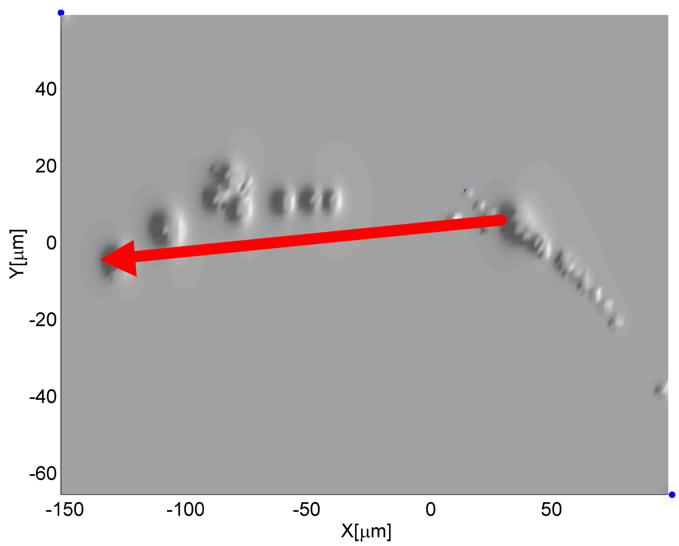
reflects changes in the charge density dynamics during AP propagation (Aur *et al.*, 2005; Aur & Jog, 2006). The dynamics and interaction of electric charges under the influence of electric fields and concentration gradients during AP occurrence was modeled using the charge movement model (Aur *et al.*, 2005). The existence of electrical patterns within neurons highlights the existence of a fast complex behavior that occurs within a millisecond during AP propagation. Our hypothesis relates significant meaningful changes in spike directivity to changes at a molecular level developed inside the neuron. Within this formulation, computation can be seen to occur in the neuron as a process of electrical interaction. Therefore, in this case, information processing occurs physically within the neuron and can be evidenced by electrical patterns during AP propagation (see Fig. 1). The measurement of temporal variables only provides the moments in time when information is communicated between neurons which tells little regarding the content or information that has been processed inside the neuron. However, few theoretical models have revealed these complex subcellular electrical phenomena and related them to physical models of information processing (Poznanski, 2010; Freedman *et al.*, 2010; Hameroff *et al.*, 2002; Pidaparti *et al.*, 2007). Remarkably, these models are



(a)

Fig. 1. Schematic representation of changes in spatial distribution of electrical patterns from a single extracellularly recorded spike in a freely behaving rodent is shown in the middle image (b). The protuberances represent agglomeration of electric charges and the red arrow represents the spike directivity. The two other images show changes in spike directivity when electrical patterns are removed from the lower axonal branch as shown in the bottom image (c) and removed from the upper axonal branch as shown in the top image (a). In this sense, the removel of charges mimics the propagation of action potentials solely in a single axonal branch which determines a slight change in spike directivity orientation. A tetrode tip represents the spatial frame of reference of the reconstructed image where X and Y represent the coordinates in microns of 2D-view with the origin representing one selected tip of the tetrode. Each division on the Y axes is approximately 20 microns and each division on the X axes is approximately 50 microns.

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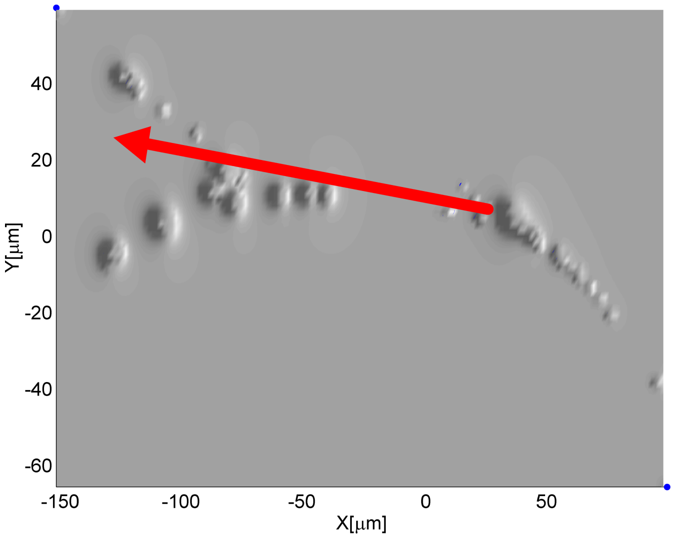
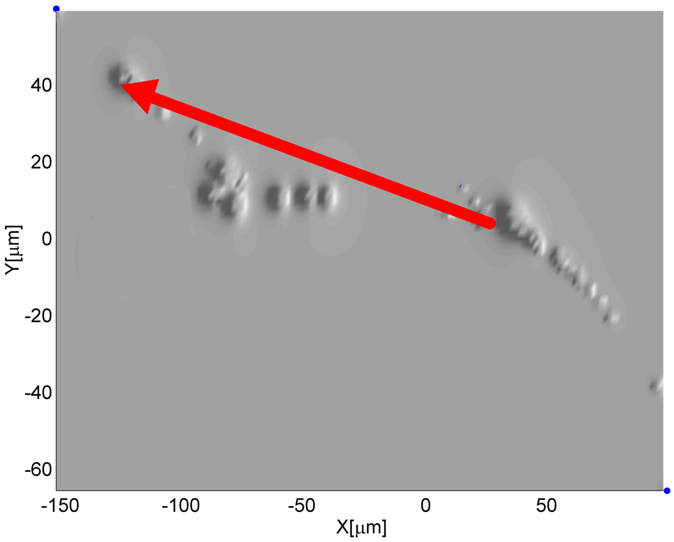


(b)



(c)

Fig. 1. (*Continued*)

reinforced by experimental results (Aur *et al.*, 2005; Aur & Jog, 2006, 2010; see also Fig. 1) that show changes in spatial distribution of electrical patterns in recorded spikes.

3. Computation by interaction

Natural phenomena involve the presence of interactions that develop during computation. The Turing formalism describes a form of computation which is not universal and does not seem to describe the most powerful mechanism of computation (Goldin *et al.*, 2006; Goldin & Wegner, 2008). Indeed, any process of computation requires information communication; however, a simple communication of information does not always reflect the entire process of computation. Specifically, in order to add two values (e.g., α and β) information about these two numbers is read from memory and then this information is communicated to the arithmetic logic unit. In this case, "computation" is complete only when information is processed; the two values are added, communicated and stored in memory. Therefore, in a Turing Machine framework, the simple process of communication of α and β values cannot replace the entire process of computation.

The existence of electric fields (and to a lesser extent, magnetic field) provides means by which information can be carried at distance. In this natural model of computation, communication is continuous and not restricted to a certain time sequence of information communication as in the Turing model. Therefore, communication can develop in the neurons while computations are performed (see Fig. 2).

A major prediction from neuroelectrodynamics is that fragments of information regarding our memories are stored within molecular structures in proteins (Aur & Jog, 2010). This prediction is consistent with several observations and theoretical models (Hameroff *et al.*, 2002; Woolf *et al.*, 2009). Since fragments of information are stored within biological substrates, many related processes that involve protein structures become part of information processing. In a neuroelectrodynamical description, the models of physical interaction include internal molecular processes, the generated electric field which provides a continuous form of communication. Hence, one can consider that computation developed by interaction is subject to endogenous or exogenous inputs that reflect changes in electric field. In addition, the arrangements in macromolecular structures inside the cell are not random. Early theoretical models and experimental data that analyzed structural elements within proteins (Levitt & Chothia, 1976; Krishtalik & Topolev, 2000) confirmed this important aspect and have predicted the presence of intraprotein electric fields (Krishtalik & Topolev, 2000).

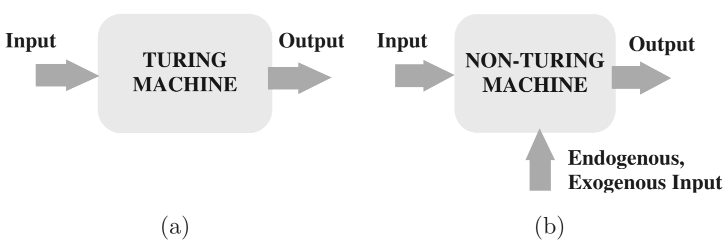


Fig. 2. Schematic difference between two different forms of computation. Early models of interactive computation developed in computer science show that during the computing process the transformation between input and output can be changed. In (a), the input−output representation of a Turing machine. In (b), a non-Turing machine, interaction during computation changes the nature and the outcome of computation and is, in general, assimilated with an endogenous or exogenous input.

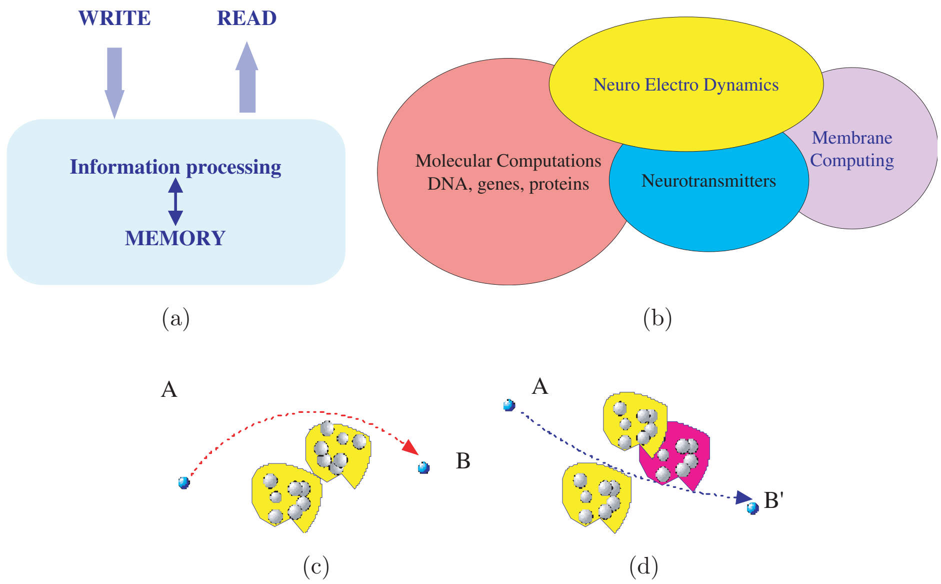


Fig. 3. The neuron is a complex physico-chemical system where intra-neuronal information processing registers different forms of computations. (a) A schematic Turing model of computation where the system has to access the memory and is required to write (code), read (decode) and process information. (b) The dynamics and interaction of electric charges captures and integrates important characteristics and is directly influenced by the release of neurotransmitters. (c) Schematic representation of computation by interaction (non-Turing model) as a dynamic process where the moving charge starts in **A** (in blue color) interacts with other groups of charges embedded in molecular structures (in grey colors) and arrives in **B**. (d) The change of final position of electric charge from **B** in **B**′ depends on the distribution of electric charges in the structure, protein polarization, new synthesized proteins (in magenta color).

In a Turing framework, the process of accessing data stored in memory to read (decode) or to write (encode) information is represented with a conventional scheme (Fig. 3(a)). Within the neuron, the similar process of encoding and decoding information can be explained based on dynamics and interaction of electric charges and generated electric field. Schematically, this process is revealed in (Figs. 3(c)–3(d)). Information is communicated in space due to the movement of electric charge and electric field propagation. Therefore, the movement of a charge from point A to point B deletes information in point A and transfers information to point B. The final position of electric charge in B (Fig. 3(c)) or in B′ (Fig. 3(d)) depends on the distribution of electric charges in the structure and in this sense may be said to decode (read) the stored information. Since, regulated by gene expression, new proteins can be synthesized (Wächter *et al.*, 2010) then long-term storage may be seen as a continuous process of creating large molecular assemblies and refining spatial distribution of charges within macromolecular structures (protein formations). In this sense, the process may be said to encode (write) information in the molecular structure. While decoding information can be performed fast during transient events, the process of remodeling molecular structure to store information is a longer process. Since the arrangements in macromolecular structures inside the cell are not random, they

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constrain the intraprotein electric field (Krishtalik & Topolev, 2000; Krishtalik, 2005; Rubinstein & Sherman, 2004) changes in the induced dipoles, polarization characteristics and charge-transfer effects (Murray & Sen, 1996; May & Kühn, 2000). In this sense, the information is "stored" endogenously within the structure at molecular level and revealed only during spiking activity. The entire process of computation where electric charges have to be moved requires a metabolic cost and is modulated by the presence of neurotransmitters and neuromodulators (Laughlin *et al.*, 1998).

The phenomenon of computation develops as an open process and includes a continuous, intrinsic communication with the external world through electric field. Complex molecular regulatory mechanisms from gene selection (expression), DNA computations to membrane properties become intrinsic forms of information processing directly involved in computation (Fig. 3). In fact, these forms of computation can bring massive parallelism and transcend the limits of Turing computability and are part of information processing that develops at the subcellular level. Research in DNA computing (Adelman, 1994; Kari & Rozenberg, 2008) and membrane computing has shown that these models can express hypercomputational power (Calude & Păun, 2008).

Including all these forms of subcellular computation suggests that transient electric interactions can have an integrative role in reading, writing and retrieval of information within the neuron at molecular scale. Indeed, these open non-terminating processes are not easily modeled within a Turing machine framework. The input−output framework then always becomes a reductionist model of developed interactions. The model of computation by interaction shows also that information can be embedded in a distribution of electric charges (spatial density of charges) rather than in temporal patterns. During synaptic activity, a similar process of computation by interaction occurs between biological substrate (synaptic proteins) and electric flux. The neurotransmitter interaction causes specific ion channels to open and since the molecular structures embed information during the electric transport, *synaptic protein structures take part in computation* and information is bidirectionally exchanged between proteins and the motion of charged particles in an electric field. This model of computation by physical interaction can be effectively extended to other parts within the neurons. Since alterations in electrical patterns occur within the entirety of the neuron, in soma, dendrites and axon, by definition, "plasticity" cannot be considered only an attribute of synapses.

4. Discussion

We have shown that particularities of spiking activity including electrical patterns that occur during every AP can be relevant to information coding and information transfer. These results have broader implications regarding *the nature* of the *neural code* and confirm the existence of a "*lower level*" where information is processed within every neuron (Hameroff, 1999; Hameroff *et al.*, 2002; Poznanski, 2002; Freedman *et al.*, 2010; Pidaparti *et al.*, 2007; Craddock *et al.*, 2010; Woolf *et al.*, 2009; Aur, 2011).

Therefore, temporal coding that has been presented as a form of "neural computation" is in fact *information communication*. The real process of "neural computation" occurs within neurons where information is processed. The entire phenomenon of computation relates rhythmic transient events when information is communicated with slow changes in biological substrate (proteins) where new information has to be stored. The existence of complex signaling pathway where electrostatic interactions regulate protein phosphorylation and transcription plays a significant role to memory encoding at the level of individual proteins (Hameroff *et al.*, 2010).

Recent physiological investigations within *in vivo* experimental data and changes in spike directivity reveal that computations are built at different scales inside the neuron shaped by molecular interactions, regulating genes, and protein expression. All these phenomena remodel how electric interactions are performed and implicitly how information is processed and stored inside the neuron. Unfortunately, these levels of computation are missing in the HH model description; however they are critically important. They are required to achieve real-time information processing and bridge between the electrical nature of the brain (including AP generation) and intrinsic information processing at a molecular level. Therefore, from a computational perspective, the HH model is incomplete since subtle spatial changes in charge density within the neuron during spike generation are missing and therefore provides a limited ability to account for important experimental observations.

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