

Adaptation to Fluctuating Neuronal Signal Traffic for Brain Connectivity

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Abstract

Brain connectivity is commonly studied in terms of causal interaction or statistical dependency between brain regions. In this analysis paper, we draw attention to the constraining effect the dynamics of fiber tract connections may impose on neuronal signal traffic. We propose a model developed by Copelli and Kinouchi (l.c.) for a different purpose to safeguard signal transmission for brain connectivity by ensuring dynamic adaptation of signal reception to a wide frequency range of traffic flow over connecting fiber tracts. Gap junction connectivity would confer to neuronal groups the capacity of acting as collectives for dynamical adaptability to impinging neural traffic thereby forestalling traffic congestion and overload. It is suggested that applying this model to signal reception in brain connectivity would deliver the required functionality as a collective achievement of the interrelations between neurons and gap junctions, the latter regulated by glia.

Keywords

Brain Connectivity, White Matter, Neuronal Groups, Gap Junctions

1. Introduction and Background

Operating on a high degree of complexity, brain dynamics consist of rapid configuration of network states driven by interactions between network constituents to optimize temporal global evolution [1]. In the framework of theoretical Neuroanatomy [2], relationships between brain connectivity and brain dynamics have become a prominent focus of research for specifying patterns of connectivity between functionally specialized cortical regions. The achievement of this objective involves the application of graph theoretical concepts [3] [4] [5]. Addition of the prominent source of data obtained with brain imaging involving PET

and fMRI, (including also analysis in the wavelet domain [6]) is expected to enable the comprehensive description of species specific connectomes [3] [7]. Despite many variations in details, the common feature of the numerous studies on brain connectivity consists in recording the spatial and temporal relations of the observed brain events at different brain locations. To extract quantitative measures characterizing the inferred connectivity, broadly speaking, two categories of methods are in use: one based on measures of statistical correlations of one kind or another (in which case one generally speaks of functional connectivity); the other, involving neural model construction for statistical validation [8]. In this case, it is customary to speak of efficient connectivity. Numerous publications and meeting reports discuss the various methodological aspects [9] [10], but procedural differences continue to impede comparison between different studies [11].

Brain connectivity data obtained with the methods under discussion do of course reflect that activity on one recording site influences activity appearing on another recording site, but they do not in general allow certainty as to the route (direct or indirect); nor do they permit insight into the dynamics and organization of signal transmission over white matter fiber tracts that sustain the connectivity [5] [12]. For the purposes of the present study, we emphasize that characteristics of the signal transfer *per se* warrant attention in their own right, notably in the context of the graph theoretical considerations mentioned earlier. The application of Diffusion Imaging and related methods has generated substantial insights into the functionality of white matter under normal and pathological conditions: for extensive reviews, see: [13] [14]. Connectivity-based parcellation of grey matter, architectural variability of human white matter connectivity [15] and identifiable “connector hubs” [16] [17] are indicative of white matter organization for sustaining brain connectivity, as are the findings with frequency-specific connections between cortical regions [18] [19].

White matter is made up of myelinated axons (tracts) through which messages quickly pass between different locations of nerve cell bodies or areas of the brain. It exerts modulating functions in the distribution of action potentials and the coordination of communication between different brain regions [20].

In its capacity as data links, white matter sets limits on speed and faithfulness of communication in complex brain networks, measured as communicability function [21]. On this basis, Crofts and Higman [22] studied anatomical networks of human brains and determined a reduction of this measure in brain regions surrounding chronic stroke lesions [23]. An extensive literature on computational models of complex networks is concerned with the opposite situation: breakdown of network function due to overload, congestion and structural bottlenecks for communication [24] [25]. Congestion means in this context the excess of arrival rate of “data packets” exceeding the recipient node’s proc [26]. The dynamics of congestion and network overload control [27], is an issue of great importance for the functioning of the Internet [28]. Failure of congestion

control and instability of traffic routing [29] can induce the dreaded “Internet Storms” [30]. In general, this situation is avoided due to the engineering design of the Transmission Control Protocol (TCP) that automatically detects local network overload for redirecting data flow into alternative pathways.

In the following, we suggest a natural mechanism that is capable of adapting the processing capability of recipient neuronal structures to neuronal traffic input that may fluctuate over a wide range of frequencies. As we will show in the next section, this approach is one that Nature has apparently adopted in a seemingly quite different, though formally equivalent situation.

2. Proposal for Congestion Control in Brain Connectivity

We are noncommittal as to the physical nature of the influence that is being transmitted over the white matter fiber tracts. However, to fix one’s intuition, we suggest the notion of the “wave packet”, introduced by Freeman [31], but the details of the transported content are immaterial for our proposal. Instead of placing the burden of control on a mechanism inherent in the transmission path, we situate it in the recipient neuronal structures which we view as populations of synapses in collectives of mutually interacting neurons. The proposed mechanism is based on the abundant evidence of diffusive (gap junction) coupling between various interneurons and neurogliaform cells in neocortex [32], as is their virtually boundless distribution in neocortex [33]. In addition, we take into account the vast forthcoming evidence of the important role of neuroglia and gap junctions for modulating and coordinating activity in clusters of interconnected neurons. Hormudzi *et al.* [34] consider gap junctions a dynamic signaling system of neuronal networks. Huades *et al.* [35] identified a gap-junction mediated astrocyte networks in mouse barrel cortex. The complexity of these interactions is documented in an exponentially growing literature, based on experimental and computational model studies [36]. Pereira and Furlan [37], Werner and Mitterauer [38] identify the role of gap junctions in the context of the dynamics of Neuromodulation. Lewis and Rinzel [39] demonstrate self-organized synchronous oscillations in networks of excitable cells coupled by simulated gap junctions; and Traub *et al.* [40] examine population oscillations in networks with simulated axo-axonal gap junctions. Models show how gap junctions and astrocytes jointly enable propagation of long distance pulsating calcium waves [41] [42]. The significance of this is related to the well-established versatility and universality of calcium signaling. These citations are but a small sample of the various sources of rapidly accumulating evidence that mandates including the notion of a tripartite neuron-glia-gap-junction [38] [43] in an expanded concept of the original notion of the Neuronal Group [44] [45].

As already intimated before, and will be shown in the following, we re-orient the congestion problem of artificial and man-made networks from message transmission to message reception. This is to be accomplished by adapting the message-receiving neuronal structure to fluctuating demands, varying over an

expanded dynamic range, without compromising sensitivity. For the realization of this objective, we turn to the simple, yet elegant computational model of Copelli *et al.* [46] [47] and Kinouchi and Copelli [48].

The starting point is one of the variants of the Greenberg-Hasting [49] cellular automaton (GBA), originally designed to account for pattern formation in response to external stimuli. When extending the coupling of the GBA's excitable cells over a larger than customary range (thus in effect setting up the equivalent of a field of excitability), Copelli and Kinouchi made the startling observation that the dynamical range of system response to stimuli increased (depending on condition) by several orders of magnitude over and above that of individual cells of GBA [50]. The system response is a then collective achievement of the GBA system as a whole, on account of the electrical coupling among the individual excitable cells. In a separate study, Kinouchi and Copelli [48] replaced the GBA with an Erdos-Renyi random network of variable branching ratio. It could then be shown that enlargement of dynamic response range is maximal at the network's self-organized critical state.

What motivated Copelli and Kinouchi to undertake these studies was their interest to account for the transfer functions in psychophysics, well known as the Stevens and Weber-Fechner laws: how can one explain both the sensitivity and the large dynamic range of sensory systems, given the restricted response range of their components? Based on the observation with the foregoing model, the answer lies in the collective achievement of elementary units, coupled by electrical junctions which, in the model, stand for gap junctions in biological systems.

Capitalizing on these insights, we propose here an analogous situation for neuronal groups receiving input via impinging fiber tracts in brain: gap junction connectivity would confer to neuronal groups the capacity of acting as collectives for dynamical adaptability to impinging neural traffic, thereby forestalling traffic congestion and overload. This, however, we must assume, is but the bare-bone skeleton of a mechanism on which complex gap junction—astrocyte domains, and their multiple biochemical potentials play a modulating tune that, in its totality, still eludes us.

3. Summary

As prerequisite for supporting brain connectivity, signal reception via white matter fiber tracts should be dynamically adaptable to accommodating a wide range of frequencies with equal sensitivity. Thus, the functionality should be analogous to the requirements met in sensory systems, for which Copelli and Kinouchi (l.c.) proposed a plausible model. We suggest that applying this model to signal reception in brain connectivity would deliver the required functionality as the collective achievement of the symbiotic interrelations between neurons and gap junctions, the latter regulated by the abundantly present elements of glia.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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