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Spiking Activity in Networks of Neurons Impacted by Axonal Swelling

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Abstract: Experiments on traumatic brain injury such as concussion have identified the emergence of axonal abnormalities for neurons within affected brain tissues. When microtubules involved in various transport mechanisms along the nerve cell membrane are severed, material pile-ups can lead to focal axonal swelling, wherein an area of nerve cell body is widened as a result of nonuniform pressure from fluid buildup or redistribution. As a consequence, the nerve cell's electrical dynamics are altered, with significant impact on the manner in which current impulses travel from soma to dendrite within the affected cell.

A mathematical investigation to understand the effects of focal axonal swellings on propagating pulses of electrical current was previously undertaken by Maia and Kutz, who introduced a simplified variable-width cable equation model in order to identify potential phenomena of interest at the single-cell level. Among the results obtained in that study, the authors identified a mechanism by which an axon augmented by swelling acts as a low-pass filter, allowing propagation of impulses at low frequencies while blocking those at higher frequencies. The specifics of this filtering depend entirely on the character of the damage, and require the numerical solution of a system of partial differential equations. For the purposes of numerical simulations, this imposes a computational challenge that is in part responsible for a lack of literature on network-level effects of such damage.

In the present study, we have implemented a fast statistical algorithm that accurately replicates the behavior of the damaged axon when simulated via solution of the cable equation. This advance allows an efficient investigation into how this type of traumatic stress affects the spiking activity and frequency encoding properties of networks of neurons. The cell (network node) model employed is a simplified version of the integrate-and-fire paradigm, and axonal damage is interpreted as a physical flaw in the connection (arrow) between two such cells. Cells in the network come in two types - excitatory and inhibitory - depending on whether an outgoing action potential from such a cell results in a positive or negative contribution to the voltage evolution of cells receiving input from it.

We study a number of simple small prototypical networks to determine the effect that damage has on their outputs. We characterize this both in terms of specific spiking times and the mean inter-spike interval at the network output over varying input frequencies. As such, we can quantify the effect of axonal swelling on a network's ability to encode a stimulus within the paradigm of either spike-time or frequency encoding. We find that these effects are highly dependent on network architecture, including cell type and the presence of recurrent connections. We further identify various mechanisms by which augmentation of network structures through

plasticity (in this context, the introduction of additional cells and alternate connections) can serve to make a network more robust to this form of damage. We have found in the case of small feedforward networks that the addition of inhibitory cells at the beginning of the feedforward chain invariably creates a network which is less susceptible to damage of this type, both in terms of spike arrival time and frequency encoding (where the network output is considered as the output of the final cell in the feedforward chain). Conversely, the addition of an excitatory cell in this position makes the same network more susceptible to damage. This result informs an exploration of larger networks of similar architecture to determine if the addition of cells has an analogous effect at all scales.