Spiking Activity in Networks of Neurons Impacted by Axonal Swelling

Brian Frost, Stan Mintchev
Department of Mathematics, Cooper Union

Biological Motivation

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's 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 cells electrical dynamics are altered, with significant impact on the manner in which current impulses travel from soma to dendrite within the affected cell. Figure 1 shows how these axonal varicosities manifest in real neural tissue. Due to the localized the nature of this damage, one might consider network-level effects of this damage, and whether or not tissue could adapt through neuroplasticity to mitigate the effects of this sort of damage.

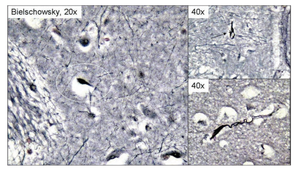

Figure 1: Neural tissue impacted by axonal varicosities[1]

Model Details

We consider a network of spiking neurons in which each neuron processes spikes according to a simplified integrate-and-fire model.[2] A neuron can be either excitatory or inhibitory, and each neuron has three state variables: J_E, J_I and V. Assuming there are no spikes at the input of a given cell, its state variables evolve as

$$\tau_V \frac{dV}{dt} = -V + J_E - J_I$$

$$\tau_J \frac{dJ_E}{dt} = -J_E, \; \tau_J \frac{dJ_I}{dt} = -J_I$$

A spike at the input causes an instantaneous jump in J_E if the spike is produced by an excitatory cell, or an instantaneous jump in J_I if the spike is produced by an inhibitory cell. When V rises above the threshold voltage, V_{TH}, and if a refractory period has passed since the neuron last spiked, V resets to zero and a spike emission is recorded.

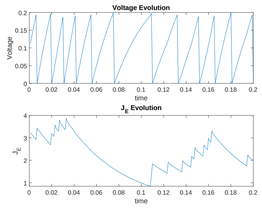

Figure 2: The voltage and J_E evolution for a single cell receiving excitatory stimulus, $V_{TH} = 0.2$.

Neurons are interpreted as nodes on a directed graph in which each arrow represents an axon. A neuron at the head of an arrow processes spikes generated by the neuron at the base of the arrow. Furthermore, all neurons receive a global excitatory stimulus, which is a homogeneous Poisson spike train with frequency parameter λ. The network output is taken to be the spike train output of a single terminal neuron.

Damage is implemented by the replacement of single axons with a filtering scheme which deletes some spikes while transmitting others faithfully. This filtering scheme is based on the work of Maia and Kutz, who introduced a simplified variable-width cable equation model of the swollen axon, showing that axon's subject to certain swelling damages may act as low-pass filters.[3] 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. We have implemented a fast statistical algorithm that accurately replicates the behavior of the cable model.

Problem Description

We look to determine the effects of axonal swelling on the ability of layered feedforward networks of neurons to perform signal processing tasks. In doing so, we look to determine the ways in which modifications due to neuroplasticity can make a network more or less susceptible to damage of this character.

Characterization of Effects of Damage

In assessing the effects of damage on a network's capability for rate-encoding, we propose a measure based on the mean inter-spike interval length (I_{av}) of a network's output. Over a range of input frequency values, many realizations of the input and initial conditions are simulated at each frequency to obtain an I_{av} value. One can then consider a mapping that takes each frequency λ to a mean interspike interval length $I_{av}(\lambda)$ for a given network architecture and damage paradigm. As the frequency of the input spiketrain grows large, the mean inter-spike interval length of the output cell will tend towards its refractory period, T_R, as it is constantly being excited. Thus, at higher frequencies, I_{av} changes very little as frequency changes, staying near T_R.

We define λ_u by

$$\lambda_u = \inf\{l \in [0,1) | I_{av}(\lambda) \leq (1.1)T_R \; \forall \; \lambda > l\}$$

Analogously, let λ_d be such a frequency for the damaged network. We call these values the *cutoff frequencies*. We define the bandwidth measurement, d_{BW}, as

$$d_{BW} = \frac{\lambda_d - \lambda_u}{\lambda_u}$$

The magnitude of this measurement is the amount the bandwidth is affected by damage in proportion to the undamaged bandwidth. The sign determines whether damage makes the bandwidth larger ($d_{BW} > 0$) or smaller ($d_{BW} < 0$).

Approach to Layered Networks

We study a number of simple small prototypical networks consisting of two neurons in a feedforward configuration to determine the effect that damage has on their outputs. We look at the network both undamaged and damaged and compute d_{BW}. We then consider a number of simple modifications to the network including the addition of a single neuron or the addition of a feedback path. We study these networks exhaustively to determine the modifications which most mitigate the effects of axonal damage. We then consider larger layered networks, in which the layers are exactly the prototypical networks. We consider the same modifications layer-wise in order to see how the effects scale with network size. This process is outlined in Figure 3 for a network of two excitatory neurons in a feedforward configuration. Here, circles represent neurons, an "E" label indicate that the neuron is excitatory and an "I" label indicates that the neuron is inhibitory. A solid arrow represent an undamaged axon, and a dashed arrow represents a damaged axon.

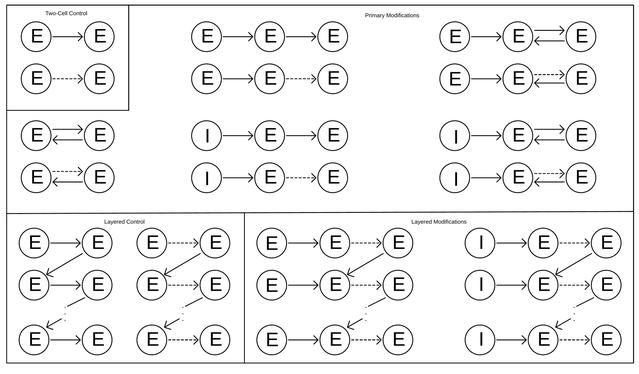

Figure 3: An example of the strategy taken in scaling up our network simulations.

Results

We find that damage can have effects varying in magnitude on the ability of a network of neurons to perform frequency discrimination. Furthermore, modification as a result of neuroplasticity can make networks either more or less susceptible to damage depending on both the architecture and the kind of modification made.

Should networks have the ability to add undamaged connections, we have found that the addition of inhibitory neurons to the front of feedforward chains can, at worst, have no effect on the network's d_{BW} and at best, nullify the effect of damage on the network. Similarly, the addition of an inhibitory cell and a feedback path consistently decreases the absolute value of d_{BW} when both added connections are healthy. Effects of this nature can be seen for the network consisting of two excitatory neurons in a feedforward configuration in the figure below, and similar effects can be seen for all feedforward networks of two cells and their larger layered analogues.

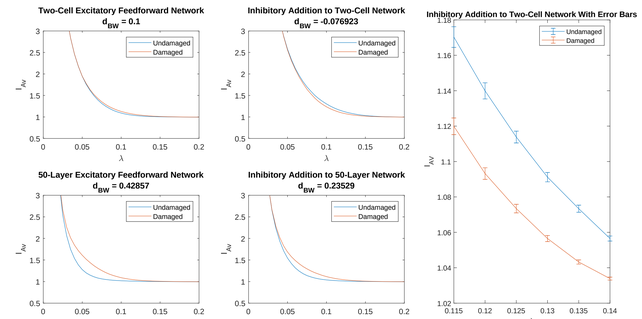

Figure 4: Effects of damage on a two-cell network and a more robust modification, as well as the effects of the analogous modification on a layered network of 200 neurons, showing that the effect is of similar magnitude even at this much larger scale

If the added connections are themselves damaged, however, these results do not necessarily hold – there exist even two-cell networks which cannot be made more robust to damage by the addition of inhibitory neurons with damaged connections.

Conclusions

We have found that for small networks and layered networks of a certain architecture, the addition of inhibitory neurons through undamaged axons often mitigates the effect of damage incurred upon the network's ability to distinguish between global input frequencies and never worsens this effect. However, we find that this is not true when the network modifications are made using damaged connections. This lends itself to physical interpretation in terms of the localized nature of this damage, and the ability of tissue to recover from such damage depending on the distribution of axonal varicosities in surrounding regions.

References

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[3] Maia, Pedro D., and J. Nathan Kutz. Identifying Critical Regions for Spike Propagation in Axon Segments. Journal of Computational Neuroscience, vol. 36, no. 2, 2013, pp. 141-155., doi:10.1007/s10827-013-0459-3.