

### Brain Implantable Devices: A Step Forward or a Step Away?

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#### COLUMN ARTICLE

“Presuming that brain implant devices interface with a neural network that operates in a fashion similar to peripheral nerves is likely to be mistaken”.

Implantable medical devices for peripheral nerves such as cochlear or retinal implants are regularly employed to assist or replace impaired neural functions [1]. Increasingly, implantable devices are also viewed as prospective therapy for impaired brain tissue [2]. To date, proposed designs for brain implants have adopted approaches used in peripheral nerves on the premise that brain physiology mimicks their operation. This presupposition, however, is likely to be misplaced.

Strategies for neural interfacing outside the brain rely on a conception of nerve operation described by the Hodgkin-Huxley, biophysical model of action potential propagation. In this model nerve signals depend on the creation of a non-equilibrium, electropotential gradient that is transiently collapsed by the activation of membrane permeability changes to Na and K ions. Ensuing permeability changes eventually traverse the length of the axon allowing signal propagation to reach other, often spatially distant, neurons. Based on this model, mechanisms of nerve operation are characterized by operational inactivity and transience; hence, signal propagation is generally maintained in an off mode until needed. Implantable devices that are intended

to replace lost function in peripheral nerve tissue, accordingly, attempt to reestablish signal propagation by the generation of spikes temporally coinciding with input to impaired nerves [1]. In such cases, implantable devices must both sense input that ordinarily would generate spikes in impaired nerve tissue and also provide stimulation to correct for lost signal transmission. Design strategies for neural interfacing in these devices are relatively well established and have greatly assisted patients who have lost neural function.

Designs for neural interfacing in brain implants currently pursue a similar approach on the assumption that brain tissue operation is directly analogous to that of peripheral nerves. Attempts to decode local field potential (LFP) in focal brain regions, for example, do so with the intention of identifying underlying contributions from individual neurons or groups of neurons, often resorting to mathematical decoding algorithms that filter the complex contribution of neuronal spikes to the LFP [3]. While there is a general acknowledgement of significant quantitative differences between cortical and peripheral nerves, especially in the relative complexities of their networks, performance features are otherwise assumed to be the same.

This presupposition, however, is likely to be only partially valid. While both domains employ gated membrane permeability changes to generate electrical potential changes, anatomically and dynamically there are substantial differences between the two. Morphologically, cortical neurons

exhibit a much higher percentage of recursive feedback; existing data indicate that nearly 95% of all brain neurons display significant synaptic feedback contacts from post-synaptic neurons [4]. The physiological effect of this morphology is the construction of topologies permitting cyclical information flow that dynamically and temporally are potentially indefinite. By maintaining such information flows, network topologies create stabilized zones termed attractors that are robust to spurious input [5,6]. This is essential for brain function since the brain is continually adjusting to the input of neural activity, making fluctuations the norm rather than the exception. Mathematically an attractor is an invariant solution of dynamic brain states toward which brain activity converges; thus, perturbations that push these states away from their attractors are resisted, returning them to their original configuration.

Stability, moreover, is not the only dynamic feature distinguishing brain operation. Brain activity must also be capable of alternating between stabilized zones. Excess stability would prevent the possibility of responding to actual, as opposed to stochastic, signals. Flexible operation is achieved by maintaining energy profiles of stable zones close to levels that introduce instability, where sufficient input can influence movement away from one attractor to another. Such transitions can process through one bifurcation or, alternatively, establish trajectories involving movement through multiple zones [7]. Significantly, numerous studies indicate that global brain activity is naturally maintained at or near energy levels that are potentially unstable enabling access to multiple trajectories. Mean field analyses of attractor landscape, for example, show that fixed point attractors attain a maximum as a function of the variability of cortical activity [8].

For brain implantable devices, of the sort that may be used for closed loop devices or brain computer interfacing, these features have implications not only for interfacing design strategies, but, potentially, also for patient safety. These implications become evident when considering traditional interfacing designs for recording and/or stimulation. Implants used for brain computer interfacing (BCI), for example, must identify and record brain signals that ultimately effect behavioral expression. This requirement necessitates

the determination of a direct relationship between the brain signal and its generation of a unique motor output. However, determining such a relationship is considerably complicated by the nonlinearity of dynamical brain activity. Cases that combine both recording and stimulation are further complicated by the need to gauge a stimulus for a system maintained close to criticality and easily shifted. Such complications make a design based on direct signal conversion not only imprecise but potentially deleterious.

Adjusting information flow by means of brain implant devices is not simply a matter of replacing aberrant spiking activity in brain circuits. These must, instead, modulate activity patterns that recreate the dynamic circumstances overlaying neuronal activity and that are the basis of brain operation.

#### CONFLICT OF INTEREST

None.

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