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# A Study of Compound Action Potentials in Current-Coupled Tracts: The General Case

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## Abstract

In this paper, the authors investigate compound action potentials formed when the underlying tract's axons have current-mediated coupling amongst themselves, and no field-mediated coupling. The key finding of the paper is that, for the case of biophysically inhomogeneous axon tracts, the compound action potential is governed by a Hodgkin-Huxley like equation itself in certain cases. The paper extends an earlier result for the identical axon case.

## Keywords

Compound Action Potentials, Current-Mediated Coupling, Biophysically Inhomogeneous Axon Tracts, Hodgkin-Huxley Equation, Identical Axon Case

## 1. Introduction

The human brain is a marvelous communication and computation [1] device, perhaps one of the most complex found in the universe. The signals that flow in the brain, if interpreted, are key to understanding how it functions. Furthermore, the structure of the brain is related to the signals that flow in the brain [2] and there is a tight integration between the brain and the environment. For example, recent work has suggested the impact of metric perturbations on the brain's signaling system [3].

What is the unitary signal in the brain? Is it at the ion channel level [4], the single axon level (for example, consider cellular connectionism [5]) or at a higher level? This question, though seemingly obvious in its solution, is not so straightforward. For example, if one considers the consciousness [6] [7] of the organism as a whole, then the entire brain's state becomes relevant in some sense. Nevertheless, it is generally accepted that axon signals are quite funda-

mental. In this paper we will go one step higher, to the compounded nerve signal.

The compound action potential (CAP) [8] is a more relevant quantity than the single-fiber action potential for the neurophysiologist who does not often have access to individual fiber voltages, though its relevance is less for single neuron investigations. Thus its detailed study is of some importance. Historically as well, these were probably the first potentials recorded from the frog sciatic nerve. In this paper, we take an analytical approach and develop the resulting compounded signal equation for the ephaptic case.

Some of the questions we are interested in answering include: Can an ephaptically current-coupled nerve be treated like an axon [9] mathematically when compounded? If so, can there be inter-nerve current- or field-mediated coupling [10], say, when there is minimal insulation [11] on the considered nerves? Further, if a nerve is like an axon, then all synapses [12] emerging from a given nerve may not only be synchronized, but they may act as one unified, though distributed synapse. So, can nerve formation be seen as a case of the organism trying to accomplish a task requiring amplification of the control signal? In this paper, we don't directly address all these questions, but our work illumines some of them.

This paper is organized as follows. In Section 2 we review the axon tract model used throughout this paper. Then we present a table of notation. In Section 3 we review an important paper from the literature. In Section 4 we describe the model being studied for two identical axons and in Section 5 we extend it to the general case. Finally, we conclude with a discussion in Section 6.

## 2. Overview of the Axon Tract Model

In this section we take a quick look at the axon tract model that we are using throughout this paper. Axons are modeled as oriented straight segments arranged in a tract. These oriented segments consist of nodal sub-segments placed alternately with internodal sub-segments, and such axons interact with one another via an extracellular return path current [11]. The equation for such an oriented, interacting, axon is:

$$C_i \frac{\partial V_i}{\partial t} = G_i^{ax} \cos^2 \theta_i \left[ \frac{\partial^2 V_i}{\partial z^2} - \sum_{axons,p} W_{ip} K_p \frac{\partial^2 V_p}{\partial z^2} \right] - G_i^{my} V_i + I_i^{inj} \tag{1}$$

where $i$ runs from $1, \cdots, N$. The reader is referred to **Table 1** for details on the notation. In what follows, we will club together some of the quantities and represent them succinctly by the symbols $\alpha$ and $\beta$. These are defined below as,

$$\alpha = G_i^{ax} \cos^2 \theta_i \tag{2}$$

and

$$\beta = -\alpha \cdot W_{ip} K_p. \tag{3}$$

Lastly, we use

$$g = G_i^{my}. \tag{4}$$

The injected current term is set to zero for notational convenience. This doesn't substantially affect the validity of the derivations presented in the rest of the paper. This is clear by noting that, given freedom in $g$, the amount of current injection can be included as a fractional part of the term containing $g$ by setting,

$$gV + I_i^{inj} = g'V. \tag{5}$$

The interested reader is referred to [13] for a derivation of Equation (1), as well as its simulations. Augmented versions of that equation are presented in [2] and [3], and simulated in MATLAB, but will not be necessarily directly useful to the reader here. In the next section, Section 3, we present a quick literature review of past work by other authors.

### Notation

The notation used in this paper and specifically in this section, is succinctly summarized in **Table 1**.

## 3. Wijesinghe's CAP Model: A Review

Prior theoretical work on compound action potentials includes [14] [15] [16] as well as [17], and experimental papers include [18]-[25], while clinical work includes [26]. In this literature review we will focus on [14] wherein the authors study the compound action potential and develop a model for its description on

**Table 1.** Table of notation.

| S. No. | Symbol | Meaning |
|---|---|---|
| 1 | $C, C_1, C_2$ | fiber capacitance per unit length |
| 2 | $G_{ext}, G_i^{ax}, G_i^{my}$ | {extracellular, axoplasmic, myelin} conductance (of the i-th axon) |
| 3 | $\alpha, \beta, \alpha_{\{1,2\}}, \beta_{\{1,2\}}$ | constants related to geometry, intra- and extra-cellular resistivity, specified in Equations (2) and (3) |
| 4 | $g, g_{\{1,2\}}$ | constants related to conductance of myelin |
| 5 | $V_{\{1,2\}}$ | transmembrane potential |
| 6 | $W_{ip}$ | inter-axonal distance matrix |
| 7 | $K_p$ | axon number-parametrized geometric constant defined in [13] as $\frac{G_p^{ax}\cos\theta_p}{G_{ext} + \sum_p G_p^{ax}\cos\theta_p}$ |
| 8 | $I_i^{inj}$ | current injected into the i-th axon |
| 9 | $\tau_{\{1,2\}}$ | time delay between stimulus onset and the action potential initiation time |

the basis of single fiber action potentials. They study the effect of the myelin sheath and also the effects of temperature and fiber diameter on the compound action potential. Their forward model consists of summations of the single fiber action signals where each signal is time-shifted by the corresponding delay $\tau_j$ between the stimulus time and the arrival time at the recording electrode of that fiber. They present a block diagram for the compound action current (CAC) and present an algorithm for computing the compound action signal. They present time-domain simulation results. They also study variation of the peak-to-peak amplitude of anisotropy of the nerve bundle. Their principal result is the relation between the conduction velocity distribution and the specific compound action potential studied. In contrast, the key contribution of the present paper is to show that when there is ephaptic coupling between the axons in a nerve bundle, they may jointly behave as single axons. As a note, the coupling condition is not looked at by Wijesinghe *et al.* in their paper.

## 4. Identical Axons: The Model and Its Study

In this section, we recall the work done in [27]. As per [14], under the assumption of superposition, the compounded action potential is given in terms of time-shifted versions of the single fiber action potentials:

$$CAP(x,t)=\sum_{j=1}^{N}V_j\left(v_j,t-\tau_j\right) \tag{6}$$

where $\tau_j$ is the time-delay between the stimulus onset and the arrival time at the *j*-th fiber, $x$ is the propagation distance, and the variables $v_j$ represent the conduction velocities of the various fibers. In [14], the $v_j$ are distinct; in our case, they are identical. Nevertheless a variable propagation delay arises due to the geometry of the situation [13]. More specifically, as in [2], these delays are related to the action potential initiation times at the current-coupled axons.

Consider the [11] equations for two coupled axons (that is, $N=2$), both being identical biophysically[1]:

$$C\frac{\partial V_1}{\partial t}=\alpha\frac{\partial^2 V_1(t)}{\partial x^2}+\beta\frac{\partial^2 V_2(t)}{\partial x^2}-gV_1 \tag{7}$$

and

$$C\frac{\partial V_2}{\partial t}=\alpha\frac{\partial^2 V_2(t)}{\partial x^2}+\beta\frac{\partial^2 V_1(t)}{\partial x^2}-gV_2 \tag{8}$$

As indicated in **Table 1** and specified in Equations (2) and (3), $\alpha$ and $\beta$ are related to the interaxonal distances, angular axonal inclinations and the various conductances of the axons and extracellular space.

Next, let $V=V_1(t-\tau_1)+V_2(t-\tau_2)$ be the compounded signal. Then,

$$C\frac{\partial V(t)}{\partial t}=(\alpha+\beta)\frac{\partial^2 V(t)}{\partial x^2}-gV(t) \tag{9}$$

[1]The velocity variables are omitted, being identical.

is the equation for the compounded signal. This resembles the Hodgkin-Huxley equation for a single fiber [9]. Thus, the compounded signal's propagation is similar to that of the single fiber signal, in the case considered (identical current-coupled fibers).

Most nerves do not have identical axons. The shapes and sizes of axons differ in a typical nerve cross-section, such as the one shown in Figure 7A of [28], in healthy as well as diseased cases. Thus it becomes important to generalize Equation (9) to the case of non-identical axons. This line of investigation is the key contribution of the present work and is presented next in Section 5.

## 5. General Axons: The Model and its Study

In this section, we relax the values $\alpha$ and $\beta$, allowing them to be different for the component axons. For the following two axons,

$$C_1 \frac{\partial V_1}{\partial t} = \alpha_1 \frac{\partial^2 V_1(t)}{\partial x^2} + \beta_1 \frac{\partial^2 V_2(t)}{\partial x^2} - g_1 V_1 \tag{10}$$

and

$$C_2 \frac{\partial V_2}{\partial t} = \alpha_2 \frac{\partial^2 V_2(t)}{\partial x^2} + \beta_2 \frac{\partial^2 V_1(t)}{\partial x^2} - g_2 V_2 \tag{11}$$

we obtain the following linear matrix equation,

$$C' \frac{\partial}{\partial t}\begin{bmatrix} V_1 \\ V_2 \end{bmatrix} = \begin{bmatrix} \alpha_1 & \beta_1 \\ \alpha_2 & \beta_2 \end{bmatrix} \frac{\partial^2}{\partial x^2}\begin{bmatrix} V_1 \\ V_2 \end{bmatrix} - G\begin{bmatrix} V_1 \\ V_2 \end{bmatrix} \tag{12}$$

where

$$C' = \begin{bmatrix} C_1 & 0 \\ 0 & C_2 \end{bmatrix} \tag{13}$$

and

$$G = \begin{bmatrix} g_1 & 0 \\ 0 & g_2 \end{bmatrix}. \tag{14}$$

If we express it compactly, using

$$V' = \begin{bmatrix} V_1 \\ V_2 \end{bmatrix} \tag{15}$$

and

$$A = \begin{bmatrix} \alpha_1 & \beta_1 \\ \alpha_2 & \beta_2 \end{bmatrix} \tag{16}$$

we see that we have an equation in the form of the equation of a single axon:

$$C' \frac{\partial}{\partial t} V' = A \frac{\partial^2}{\partial x^2} V' - GV' \tag{17}$$

Take two such "single" axons (for a total of four axons), each with the same properties ($C', A, G$), and using the result from Section 4, we find that if we couple them as per Equations (7) and (8), and compound them as per Equation

(9), this compounded signal again follows the single axon law. This is explicated as follows.

The "single axons" are,

$$C'\frac{\partial}{\partial t}V_1' = A\frac{\partial^2}{\partial x^2}V_1' - GV_1' \tag{18}$$

and

$$C'\frac{\partial}{\partial t}V_2' = A\frac{\partial^2}{\partial x^2}V_2' - GV_2' \tag{19}$$

where

$$V_1' = \begin{bmatrix} V_1 \\ V_2 \end{bmatrix} \tag{20}$$

and

$$V_2' = \begin{bmatrix} V_3 \\ V_4 \end{bmatrix}. \tag{21}$$

Upon cross-coupling them, we have

$$C'\frac{\partial}{\partial t}V_1' = A\frac{\partial^2}{\partial x^2}V_1' + B\frac{\partial^2}{\partial x^2}V_2' - GV_1' \tag{22}$$

and

$$C'\frac{\partial}{\partial t}V_2' = A\frac{\partial^2}{\partial x^2}V_2' + B\frac{\partial^2}{\partial x^2}V_1' - GV_2'. \tag{23}$$

Next we define,

$$V_3' = V_1' + V_2' \tag{24}$$

to be the (partially) compounded signal. This will obey the law,

$$C'\frac{\partial V_3'}{\partial t} = (A+B)\frac{\partial^2 V_3'}{\partial x^2} - GV_3'. \tag{25}$$

In this way, we find that certain combinations of (not necessarily all identical) coupled axons yield very simple compound action potentials that follow the usual Hodgkin-Huxley (vector) law. By mathematical induction, Equation (25) can likely be extended into a more general statement, for arbitrary numbers of axons. Following the guidelines of the previous and present sections, the compounded signals might generally contain $2^n$ voltage components where $n = 1, 2, 3, \cdots$.

## 6. Discussion and Conclusion

To summarize, in this paper we found that when the underlying current-coupled axons are biophysically identical in pairs, then the compounded signal may be like a Hodgkin-Huxley signal and we can respond affirmatively to the first question raised in Section 1. An appropriate name for such a compounded signal is an *ephaptic compound action potential* or eCAP. The paper extended results previously shown for tracts containing identical axons. This result has bearing

on our understanding of synchronization and binding in the brain. If multiple axons, when coupled together, act as one, as shown herein, it may be how the brain "binds" features related to various different percepts, particularly property and location binding [29].

A limitation of our work is that we didn't explore the case of sensorimotor nerves wherein individual fibers carry signals in two opposing directions [30], nor did we study nonlinearities in axon-axon interaction [31] in this context. In future work, we can consider simulations of the propagation of eCAPs under focal demyelination conditions [32] as well as healthy conditions. Another investigation that may yield novel insight is the impact of single fiber internodal lengths on the conduction velocity of eCAPs. Indeed, many of the theoretical and simulation studies designed for single axons and CAPs might be adapted to the case of eCAPs. In this way, this paper opens up a new field of study.

Further, the most important aspect of the present work, even beyond [27], is that it illumines future studies of quantum effects for entire nerves, in the context of [33] and [34]. In these papers, it was shown how metric perturbations perform quantum computation in single axons and how multiple such computed axons can possibly be entangled, leading to brain-wide quantum computations. If eCAPs behave as shown in this paper, then we can go one step up hierarchically and again (more easily perhaps) postulate brain-wide quantum computations since multiple axons will carry signals that are identically governed. The findings of this paper therefore have relevance for neuroscience, beyond just the traditional binding problem; they also bear on deeper questions related to consciousness [35].

## Conflicts of Interest

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

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