

# Continuum models in neurobiology and information processing

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## Abstract

Continuum models have been used with considerable success for single neurons but have been neglected in the study of neuronal populations. In more popular discrete neuronal network models, the geometric details of the neuronal centers are usually neglected. We here give a continuum nonlinear dynamical model and an approximate model which admits the possibility of ascertaining the roles of the various connectivity patterns from center to center in the central nervous system. Frequency transfer characteristics are used to incorporate the nonlinear dynamics of single neurons. Simple examples are evaluated both analytically and numerically and the results presented graphically. © 1998 Elsevier Science Ireland Ltd. All rights reserved.

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## 1. Introduction

When the brain processes information, it seems to involve a sequence of centers, as exemplified by visual perception (Lund et al., 1995; Crick, 1996). In this example, since no information can be added from within the nervous system after the light signals have interacted with the retinal receptors, resulting in electrophysiological and chemical changes in the subsequent cell types (horizontal, bipolar, amacrine, ganglion), it follows that the role of multicenter processing is the extraction, amplification and identification of

different features of the visual field. It is very likely that the geometrical features of the connections from center to center play crucial roles in these processes. We wish to explore the use of a continuum approach, in an albeit simple and preliminary way, to examine this geometrical aspect of information processing.

Continuum models have been used for single neurons since the first success of cable theory (Hodgkin and Rushton, 1946), followed a few years later by the appearance of the Hodgkin and Huxley (1952) equations for action potential propagation. An equation which can be used to predict a single neuron's depolarization is

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$$\frac{\partial V}{\partial t} = \frac{\partial^2 V}{\partial x^2} - V + \sum_{i=1}^n g_i(x, t) [V_i - V], \quad (1)$$

where  $g_i$  is the conductance increase at the  $i$ -th synapse whose corresponding reversal potential is  $V_i$ . Such a mathematical representation offers the possibility of a very rich set of possible input patterns, but this is lost when the geometric features of the connections are omitted as in network models of the kind used in many theoretical studies (see for example, Hansel et al., 1995 and Fukai, 1996).

Beurle (1956) introduced a field theoretic approach to modeling the cerebral cortex, but included only excitatory elements—see also Griffiths (1971). A continuum approach was also employed in the mathematical modeling of cortical slow (2 mm/min) potential waves accompanying spreading depression (Tuckwell and Miura, 1978; Tuckwell and Hermansen, 1981). For this phenomenon the mathematical model is of the form of a system of reaction-diffusion equations whose first member is

$$\frac{\partial K_0}{\partial t} = D_K \frac{\partial^2 K_0}{\partial x^2} + F(C), \quad (2)$$

where  $K_0$  is the potassium ion concentration in the extracellular compartment,  $x$  is distance along the structure considered,  $D_K$  is the diffusion coefficient of potassium ions,  $C$  is a vector of various ion concentrations and  $F$  describes the sources and sinks for  $K^+$ . That this system and certain types of cortex support traveling solitary wave solutions illustrates the connectedness of such anatomical structures.

There have been a few recent theoretical nervous system studies in relation to cognitive and perceptual processes which have either involved a partially or complete continuum approach (for example, Cowan, 1985; Kohonen et al., 1985; Parodi et al., 1996; Bresloff and Coombes, 1997). However, most modeling of neural networks adopts a discrete approach.

The origin of the present method began in 1982 when the following rudimentary model for studying epileptic spread was suggested by the author to Aidan Sudbury of Monash University. Consider a slab of cortex, detailing only one space dimension,  $x$ , from  $x=0$  to  $x=L$  and let the

firing rate of cells between  $x$  and  $x+dx$  be  $f(x, t)$  at time  $t$ . Let the densities of excitatory and inhibitory connections from  $x$  to  $x'$  be  $N_E(x', x)$  and  $N_I(x', x)$ , respectively. Assume for simplicity that the EPSP and IPSP magnitudes have fixed amplitudes  $A_E$  and  $A_I$ , respectively. Then roughly we have

$$f(x, t) = g \left[ \int_0^L [A_E N_E(x', x) - A_I N_I(x', x)] f\left(x', t - \frac{|x' - x|}{c}\right) dx' \right], \quad (3)$$

where  $c$  is the speed of conduction in the fibers and  $g$  is a transfer characteristic. This assumes an homogeneous population of neurons with the same  $g$  and  $c$ . This formulation presents a number of problems. At  $t=0$ , the evaluation of the integral requires data for  $t<0$ , but this is not a serious problem as such data may be given. However, consistency may be a problem and factors such as synaptic delays and external sources may need to be included. Eq. (3) may be useful for some long-term steady state calculations but a better approach is outlined below.

## 2. A nonlinear continuum model and an approximation

Consider a region  $M$  of cortex and consider a neuron located at  $\mathbf{x}$ , this point being able to be specified by a unique point such as the center of mass of the soma. We talk about the point  $\mathbf{x}$  and the neuron interchangeably. We first define a first order neuronal receptive field.

Neurons which have direct monosynaptic connections with  $\mathbf{x}$  are called the first order neuronal receptive field of  $\mathbf{x}$  and are denoted by the set  $R_1(\mathbf{x})$ .

Such neurons may be outside of  $M$ . Note that this extends the term receptive field to neuronal connections. Although the term receptive is not perfect it is in accordance with common usage. Similarly we may define a second order receptive field for  $\mathbf{x}$  as those neurons which connect by disynaptic pathways to  $\mathbf{x}$  and denote it by  $R_2(\mathbf{x})$ .

We may put

$$R_2(\mathbf{x}) = R_1(R_1(\mathbf{x})), \quad (4)$$

and generally, with obvious notation,

$$R_n(\mathbf{x}) = R_1^n(\mathbf{x}). \quad (5)$$

Neurons which are monosynaptically driven by  $\mathbf{x}$  are called the first order neuronal target field of  $\mathbf{x}$  and are denoted by the set  $T_1(\mathbf{x})$ . With obvious notation,

$$T_n(\mathbf{x}) = T_1^n(\mathbf{x}) \quad (6)$$

Note that neurons can be in both target and receptive fields and a neuron can be in its own target and receptive fields with recurrent connections.

### 2.1. A nonlinear continuum model

In a discrete network model, let  $\mathbf{X}_i(t) = (V_i(t), X_i(t), Y_i(t), Z_i(t))$  be state variables of neuron  $i \in \{1, 2, \dots, n\}$  at time  $t$ . Here  $V_i$  is a voltage variable and  $X_i, Y_i, Z_i$  are subsidiary variables in a conductance-based model—although there may be more than three. Then we may put in an extended Hodgkin and Huxley (1952) picture,

$$\begin{aligned} \frac{dV_i}{dt} = & f_i(X_i) \\ & + \sum_{j=1}^n J_{ji} G_{Ca}(V_j) (V_j - V_{Ca,j}) (V_i - V_{rev,ij}), \end{aligned} \quad (7)$$

together with the usual equations for  $X_i, Y_i, Z_i$ . Here  $f_i$  describes the intrinsic dynamics of neuron  $i$ ,  $J_{ji}$  is the synaptic strength or amplitude at the synapse from neuron  $j$  to neuron  $i$ ,  $G_{Ca}(V_j)$  is the calcium conductance at the presynaptic terminals of neuron  $j$ ,  $V_{Ca,j}$  is the corresponding equilibrium calcium voltage.  $V_{rev,ij}$  is the reversal potential at the  $j, i$  synapse. Here the postsynaptic conductance change is assumed to be proportional to the concentration of neurotransmitter in the synaptic cleft. Details of the justification of this form for the synaptic input currents is contained in Tuckwell and Miura (1978).

However, if the density of neurons is large enough, we may consider a limiting case where the neurons are distributed along a continuum (one-dimensional for simplicity), so that  $\mathbf{X}_i(t)$  is replaced by  $\mathbf{X}(x, t) = (V(x, t), X(x, t), Y(x, t), Z(x, t))$  and the voltage component satisfies

$$\begin{aligned} \frac{\partial V}{\partial t} = & f(\mathbf{X}) + \int_{y \in R_1(x)} A(y, x) G_{Ca}(V(y, t)) \\ & \times (V(y, t) - V_{Ca}(y, t)) (V_{rev}(x, y, t)) dy, \end{aligned} \quad (8)$$

together with equations for  $\partial X/\partial t$  etc. Here  $A(y, x)$  is a connection density from neurons at  $y$  to neurons at  $x$ . Simplifications occur if the cell population is homogeneous or divides into a few groups of homogeneous cells. However, solutions of such nonlinear continuum models will not be pursued here as we turn our attention to a simpler and more tractable approach.

### 2.2. Basic simplified continuum model

Consider a dense population of neurons in a 3-dimensional region  $M$ . Let  $\mathbf{x} \in M$  and suppose the spike rate density is  $f_M(\mathbf{x}, t)$ , so that  $f_M d\mathbf{x}$  is the number of spikes per s in the small volume element  $(\mathbf{x}, \mathbf{x} + d\mathbf{x})$ . With points (neurons)  $\mathbf{x}'$  in the neuronal receptive field of  $M$  we assume a connectivity function  $A(\mathbf{x}', \mathbf{x})$ . The anatomical configuration is assumed to make both the firing rate density and the connectivity function meaningful. Then we have approximately

$$\begin{aligned} f_M(\mathbf{x}, t) \\ = g \left[ \int_{R_1(\mathbf{x})} A(\mathbf{x}', \mathbf{x}) f_{R_1} \left( \mathbf{x}', t - \frac{d(\mathbf{x}', \mathbf{x})}{c(\mathbf{x}', \mathbf{x})} \right) d\mathbf{x}' \right]. \end{aligned} \quad (9)$$

Here  $d(\mathbf{x}', \mathbf{x})$  is the distance that signals must travel and  $c(\mathbf{x}', \mathbf{x})$  is the corresponding speed of propagation. Thus we have put the nonlinear dynamics in the transfer characteristic  $g$ —the latter may vary from point to point but for now we assume all cells have the same  $g$ . In this approach the firing rate is simply a function of the net synaptic input. For the transfer function we may use an approximate form based on calculations with nonlinear models such as

$$g(y) = bH(y) \tanh(ay), \quad (10)$$

where  $y$  is synaptic input current,  $a$  and  $b$  are constants and  $H$  is a unit step function since the output frequency is zero when the net input is inhibitory. For small positive  $y$  a linear approximation would suffice.

### 2.3. The stochastic case

In the above treatment, the frequencies may be stochastic processes. To find  $f_M$ , a simulation may be performed for a large number of trials for given properties  $f_{R_1}$ . In the linear case and in one space dimension,

$$E[f_M] = \int_{R_1} A(x, x') E \left[ f_{R_1} \left( x', t - \frac{d(x', x)}{c(x', x)} \right) \right] dx'. \quad (11)$$

Note that  $f_{R_1}$  (and hence  $f_M$ ) may be a two (multi) parameter stochastic process. The connectivity function  $A$  may be assumed to be fixed, but if synaptic strengths change  $A$  may be a function of time or other variables.

## 3. Illustrative examples

We do not have space to develop complex examples and will simply illustrate the application of the above approach in a few simple 1-dimensional cases.

### 3.1. Constant $f_{R_1}$ , exponential or Gaussian $A$

Let  $R_1$  extend from  $x' = 0$  to  $x' = L$  and let  $M$  extend from  $x = L + d$  to  $x = 2L + d$  and suppose cells in  $R_1$  are uniformly active with constant firing rate  $f_{R_1}(x, t) = f_E > 0$ . Further we assume that the connectivity is maximal between corresponding points in  $R_1$  and  $M$ . Thus

$$A(x', x) = e^{-|x - (x' + L + d)|}, \quad (12)$$

also that  $C(x', x)$  is constant and set at unity. Then we get

$$f_M(x, t) = g \left[ f_E \int_0^L e^{-|x - (x' + L + d)|} dx' \right], \quad (13)$$

which upon evaluation gives

$$f_M(x, t) = b \tanh[af_E \{2 - e^{-(x-L-d)} - e^{x-2L-d}\}]. \quad (14)$$

A plot of  $f_M$  versus  $x$  for parameter values (all distances in mm)  $b = 50$ ,  $a = 0.05$ ,  $L = 1$ ,  $d = 1$ ,  $f_E = 20$  gives a smooth parabolic curve with a maximum at the midpoint of  $M$ . This illustrates how a given connectivity function can lead to a response with a maximum at a particular location even though the input came from a uniformly active population of neurons. With a Gaussian choice for the connectivity function

$$A(x', x) = \exp \left\{ - \left( \frac{x - (x' + L + d)}{\sigma} \right)^2 \right\}, \quad (15)$$

the result is

$$f_M(x, t) = b \tanh \left[ \frac{af_E \sigma}{2} \sqrt{\frac{\pi}{2}} \left\{ \operatorname{erf} \left( \frac{(d-x)\sqrt{2}}{\sigma} \right) - \operatorname{erf} \left( \frac{(L+d-x)\sqrt{2}}{\sigma} \right) \right\} \right]. \quad (16)$$

### 3.2. Periodic $f_{R_1}$ , exponential $A$

Considering again a 1-dimensional problem, let  $R_1$  have length  $L_1$  and  $M$  have length  $L_2$ . Then if the neurons in the receptive field of those in  $M$  have angular frequency  $\omega$ , mean  $f_E$ , then

$$f_M(x, t) = b \tanh \left[ af_E \left\{ \int_0^{L_1} e^{-|x - (x' + L_2 + d)|} \left( 1 + \sin \left\{ \omega \left( \frac{|x - x'|}{c} \right) \right\} \right) dx' \right\} \right]. \quad (17)$$

The integral can be executed analytically. However, numerical integration was used and  $1 + \sin(\cdot)$  was replaced by  $e^{\sin(\cdot)}$ . On calculating the resulting frequency distribution, with  $a = 0.05$ ,  $b = 50$ ,  $f_E = 1$ ,  $\omega = 20$ ,  $c = 10$ ,  $d = 100$ ,  $L_1 = 2$ ,  $L_2 = 5$ , one obtains the results which are graphed in Fig. 1. It can be seen how, from a uniform, periodic input, an asymmetric, peaked and time-varying response is obtained in the target field.

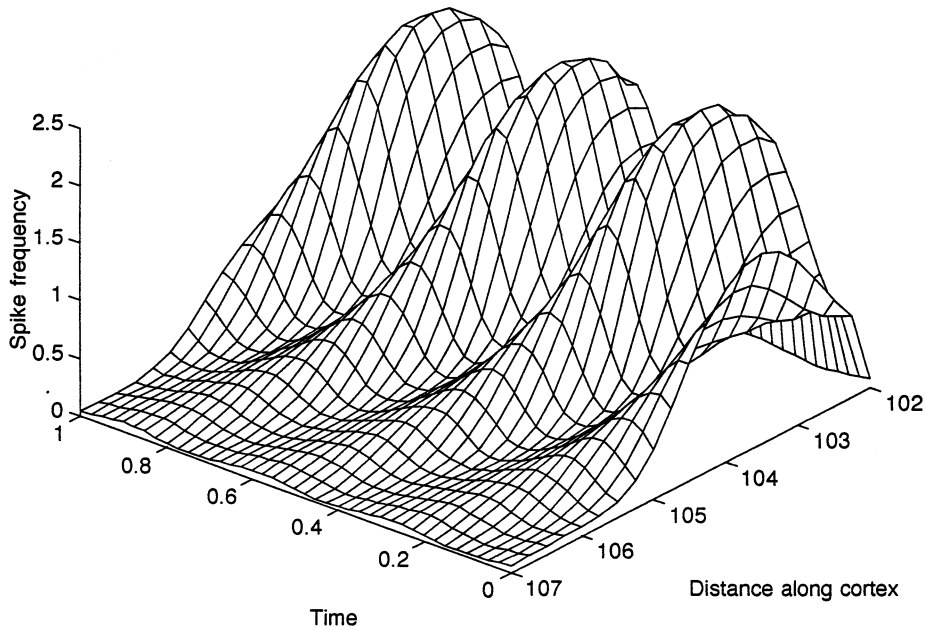


Fig. 1. Spike frequencies as a function of distance along a cortical slab at various times with a uniform source of periodic firing rate feeding in with an exponential connectivity function.

### 3.3. Three populations

There are several examples where signals pass along a sequence of nervous system centers or back and forth, as in the references to vision in the introduction. Other examples occur in proposed memory circuits which are summarized in chapter 9 of Eccles (1984). In Fig. 2 we depict three nervous system centers labeled  $R_1$ ,  $R_2$  and  $M$ . The connectivity function from  $R_1$  to  $M$  is  $A_1$  and that from  $R_2$  to  $R_1$  is  $A_2$ .

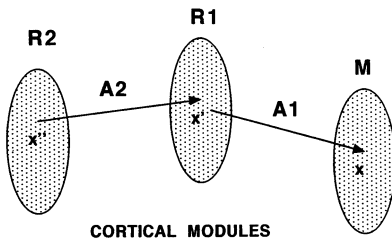


Fig. 2. Illustrating three cortical subpopulations of neurons with connectivity functions  $A_1$  and  $A_2$ .

Again we will make the notation simpler by considering only one space dimension. Letting the transfer function of cells in  $R_1$  be  $g_2$  and that of those in  $M$  be  $g_1$ , we obtain an expression for the frequency distribution in  $M$ :

$$\begin{aligned}
 f_M(x, t) &= g_1 \left[ \int_{x' \in R_1} A_1(x', x) \right. \\
 &\quad \left. g_2 \left\{ \int_{x'' \in R_2} A(x'', x') \right. \right. \\
 &\quad \left. \left. \times f_{R_2} \left( x'', t - \frac{d_1(x', x)}{c_1(x', x)} - \frac{d_2(x'', x')}{c_2(x'', x')} \right) dx'' \right\} dx' \right]. \tag{18}
 \end{aligned}$$

Hence the firing rate distribution in  $M$  is determined by the firing rate distribution in  $R_2$  and the geometry of the anatomical connections as specified by the connectivity functions  $A_1$  and  $A_2$ . In a related article (Tuckwell, 1998) we have shown how a metric space approach is useful in theories of cognitive information processing.

#### 4. Conclusions

In the processing of information by the mammalian central nervous system, signals are propagated from center to center and often back and forth. It is important to be able to understand the role of the anatomy or geometry of the connections between centers in these dynamical processes. We have used an approximate continuum model which enables this feature to be studied and given some simple examples.

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