

Waves and oscillations in networks of coupled neurons

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1 Introduction

Neural systems are characterized by the interactions of thousands of individual cells called neurons. Individual neurons vary in their properties with some of them spontaneously active and others active only when given a sufficient perturbation. In this note, I will describe work that has been done on the mathematical analysis of waves and synchronous oscillations in spatially distributed networks of neurons. These classes of behavior are observed both *in vivo* (that is, in the living brain) and *in vitro* (isolated networks, such as slices of brain tissue.) We focus on these simple behaviors rather than on the possible computations that networks of neurons can do (such as filtering sensory inputs and producing precise motor output) mainly because they are mathematically tractable. The chapter is organized as follows. First, I will introduce the kinds of equations that are of interest and from these abstract some simplified models. I will consider several different types of connectivity – from “all-to-all” to spatially organized. Typically (although not in every case), each individual neuron is represented by a scalar equations for its dynamics. These individuals can be coupled together directly or indirectly and in spatially discrete or continuous arrays.

Neural models are roughly divided into two main classes: spiking models and firing rate models. We will concentrate on spiking models in this chapter. A comprehensive review of neural network models is given in Ermentrout (1998b). In spiking models, we track the firing (or spikes) of individual units, while in firing rate models, we are interested mainly in the average frequency that each unit fires. Individual neurons are highly complex spatially extended nonlinear systems. However, in most models that involve networks of neurons, they are reduced to points in space. The description of these point neurons is itself often

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very complicated involving dozens of nonlinear differential equations. Again, most modelers simplify the neurons considerably often reducing them to one- or two-dimensional dynamical systems.

The canonical representation of point neurons is due the Hodgkin and Huxley wherein each cell is considered to be an equivalent electrical circuit with a single capacitor and several resistors in parallel. Thus, the neuron satisfies the differential equation:

$$C \frac{dV}{dt} = I - \sum_k g_k(t)(V - E_k) \quad (1)$$

where I is the experimentally applied current, C is the capacitance of the neuron, E_k are constant reversal potentials, one for each ionic species that travels across the membrane, and $g_k(t)$ are the time-dependent conductances (reciprocal of resistances). The key theoretical point that Hodgkin-Huxley advanced is that $g_k(t)$ are themselves dependent on voltage. That is,

$$g_k(t) = \bar{g}_k m^p h^q$$

where p, q are nonnegative integers (sometimes 0), \bar{g}_k is a nonnegative constant, and $x = \{m, h\}$ satisfy equations of the form:

$$\tau_x(V) \frac{dx}{dt} = x_\infty(V) - x.$$

Without these extra variables, the voltage dynamics is just linear. The original Hodgkin-Huxley model for the squid axon membrane has three of these extra variables, one for the potassium current and two for the sodium current. The simplest model (and one which is commonly used in simulations) is called the leaky integrate-and-fire (LIF) model. There is only one current and it is passive:

$$C \frac{dV}{dt} = I - g_L(V - E_L). \quad (2)$$

However, there is an additional rule that states that if $V(t)$ crosses a proscribed value, V_S , then it is reset to $V_R < V_S$ and the neuron is said to have fired. If I is sufficiently large, the neuron will fire repetitively with a frequency, ω given by:

$$\omega^{-1} = \frac{C}{g_L} \log \frac{I - g_L(V_R - E_L)}{I - g_L(V_S - E_L)}.$$

This makes sense only if $I > g_L(V_S - E_L)$. For I large, the frequency is linear with I . Another related model is called the quadratic integrate-and-fire (QIF) model:

$$C \frac{dV}{dt} = I + g_L(V - V_L)(V - V_T)/(V_T - V_L). \quad (3)$$

As with the LIF, when $V(t)$ reaches V_S it is reset to V_R . By choosing $V_S = +\infty$ and $V_R = -\infty$, we recover the dynamics for the normal form of a dynamical

system near a saddle-node on a limit cycle (Ermentrout & Kopell, 1986, Hoppensteadt & Izhikevich, 1997, Izhikevich, 2000). If $I > g_L(V_T - V_L)/4 \equiv I^*$, then the QIF fires repetitively with frequency:

$$\omega = K(I)\sqrt{I - I^*}$$

where $K(I)$ is a complicated expression tending to a constant as $V_S \rightarrow +\infty$ and $V_R \rightarrow -\infty$. Thus, unlike the LIF model, the QIF model has a square-root dependence of frequency on current for large currents.

Almost all of the neural models that we are concerned with in this chapter fire repetitively when sufficient current is injected into them. There are essentially two mechanisms for going from rest to periodic activity. One of these is the saddle-node on a limit cycle which we have already described. The other mechanism is through a Hopf bifurcation. Near this bifurcation, the behavior of the neuron is similar to its normal form (Brown et al 2004):

$$\frac{dz}{dt} = z(a - b|z|^2)$$

where a, b, z are complex. If we take $a = 1 + i$ and $b = 1$ we recover the “radial isochron clock” (RIC; Winfree, 1980).

Finally, there are many interesting cases in which the dynamics of the neuron are essentially two-dimensional with V as one dimension and x as the other, where x is one of the auxiliary variables in the Hodgkin-Huxley formalism. For example, suppose that there are only two ionic species: a linear leak and a calcium current. Then the model has the form:

$$C \frac{dV}{dt} = I - g_L(V - E_L) - g_{Ca} m_\infty(V) h(V - E_{Ca}) \quad (4)$$

$$\tau_h(V) \frac{dh}{dt} = h_\infty(V) - h. \quad (5)$$

m_∞ is monotonically increasing while h_∞ is a decreasing function of V . For this model, τ_h is sometimes very large, so that it is justifiable to use singular perturbation methods to analyze it. We will do this later in this chapter.

Now that we have briefly described the dynamics of neurons we can ask how to couple them. Neurons communicate in many ways, but the most common mechanism is through chemical synapses. When the presynaptic neuron fires, it produces currents in the post-synaptic neuron. Synapses are modeled similarly to the ionic channels but the auxiliary variables depend on the presynaptic voltage rather than the postsynaptic potential. Thus, a network of neurons is described by equations of the form:

$$C \frac{dV_j}{dt} = I_j - I_{ionic,j} - \sum_k c_{jk} s_k (V_j - E_{R,k}) \quad (6)$$

$$\frac{ds_j}{dt} = \alpha(V_j)(1 - s_j) - s_j/\tau_j \quad (7)$$

where $c_{j,k}$ are nonnegative constants, $E_{R,k}$ is the reversal potential of the k^{th} synapse and $I_{ionic,j}$ are the intrinsic currents for neuron j . When convenient, we will go to the continuum limit to study spatially organized systems. Thus, our goal in the rest of this chapter is to describe the behavior of coupled systems of neurons.

2 PRC theory and coupled oscillators.

We suppose that each neuron is, by itself, an oscillator and that the interactions between neurons are brief and pulsatile. Then, instead of treating the full equations for each oscillator, we suppose that without any external signal, each cell traverses its limit cycle in a regular periodic manner. Thus, we consider each neuron to lie on a one-dimensional circle and satisfy the equation $\theta' = 1$ where θ is the phase of the cycle. Each time θ crosses an integer, we say that the neuron has spiked. Experimental biologists often treat rhythms of unknown mechanism as such black boxes. In order to do some interesting mathematics on this black box, we ask what the effects of brief external perturbations are on the timing of the spikes of our model. Again, this technique has been used for decades to quantify the behavior of biological oscillators (Best, 1979; Ypey et al, 1982; Ayers & Selverston, 1984, Canavier et al.,1997; Oprisan et al 2004). Suppose that the oscillator fires at $t = 0, 1, 2, \dots$ in absence of any external perturbations. Now suppose at $t = \phi \in [0, 1)$, we apply a brief stimulus. This will cause the oscillator to fire at some time $t = T(\phi)$. In absence of the stimulus, the oscillator fires at $t = 1$ so that the effect of the stimulus has been to advance the timing by an amount $1 - T(\phi)$. If $T > 1$, then a “negative” advance is actually a delay. We call the function, $\Delta(\phi) = 1 - T(\phi)$, the phase-resetting curve or PRC. The PRCs of cortical neurons have been measured by several groups, (Reyes & fetz, 1993; Stoop, et al, 2000).

Figure 1 shows the PRCs from the three simplified models described in the above text. In each of these models, at a time $t = \phi$ the voltage was incremented by an amount a , either positive or negative. For the experimental neuron, the current is held constant to induce repetitive firing and then a brief square pulse of current is superimposed on this background. We note that for small stimuli, the PRC of the RIC is roughly, $\Delta_{RIC}(\phi) = -a \sin 2\pi\phi$ and for the QIF, it is roughly, $\Delta_{QIF}(\phi) = a(1 - \cos 2\pi\phi)$. The PRC for the RIC is very similar to that measured for the flashing rhythm of *Pteroptyx malacca*, a Malaysian firefly species known for its dramatic synchronous displays.

Given that we have computed a PRC for a neuron, how can we use this in a mathematical model? In general, the PRC depends in a complicated fashion on the amplitude but for small stimuli, this is almost linear. Consider, first a pair of identical neural oscillators such that each time one fires, the other is adjusted using its PRC. Formally, we can write (Izhikevich, 1999):

$$\begin{aligned}\theta'_1 &= 1 + \Delta(\theta_1)\delta(\theta_2) \\ \theta'_2 &= 1 + \Delta(\theta_2)\delta(\theta_1).\end{aligned}$$

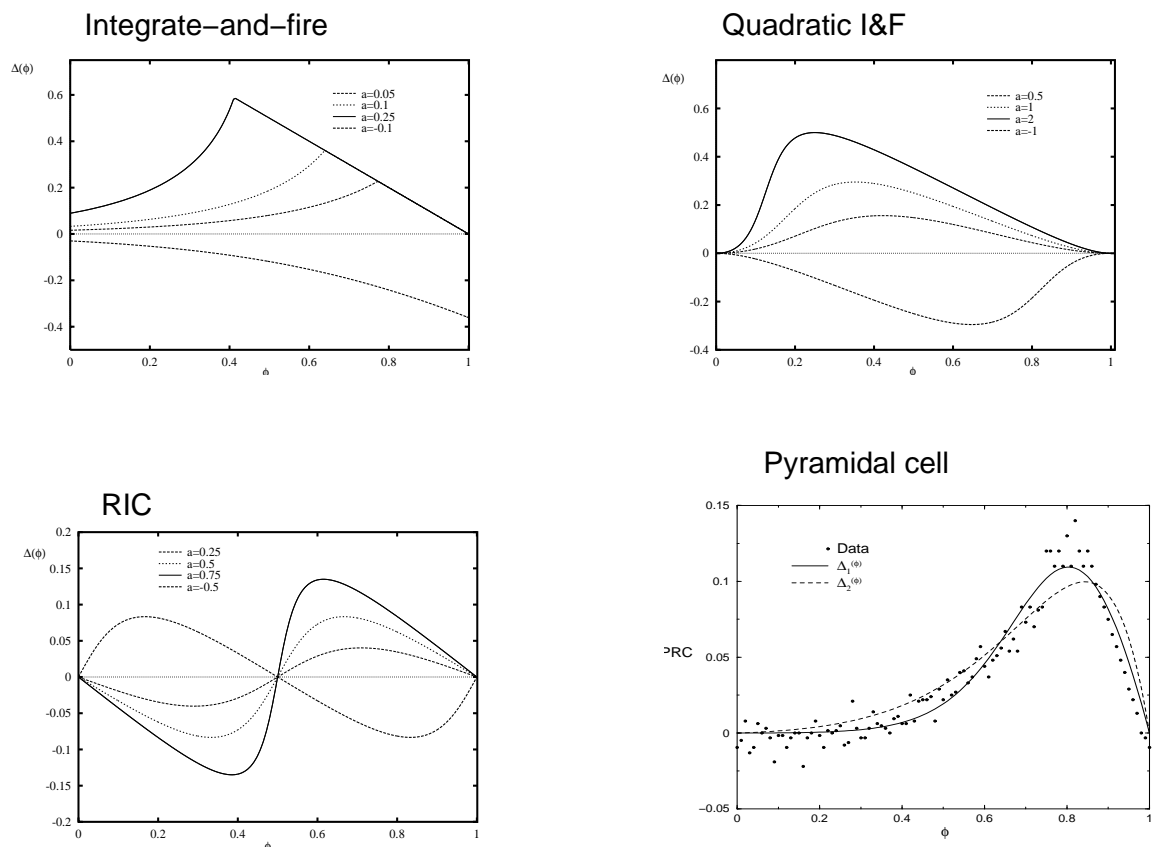


Figure 1: PRCs from three common models of single neurons and the PRC from a pyramidal cell with some fits to a conductance-based model.

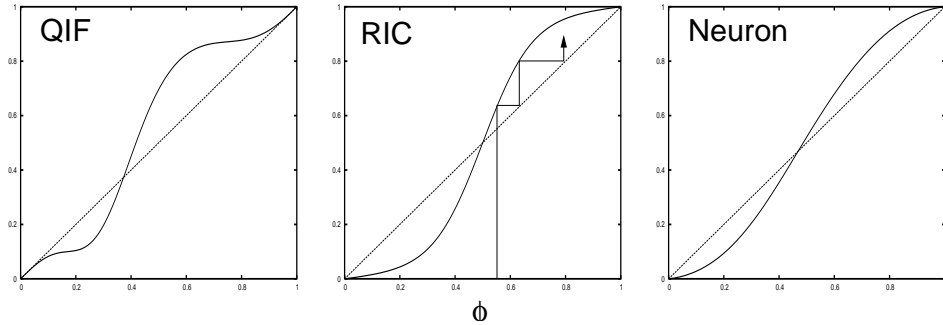


Figure 2: Maps derived from the PRCs in the previous figure.

Here δ is the Dirac impulse function. This formulation is readily generalized to arbitrary networks of oscillators and by changing the “1” to, say, ω_j we can endow each oscillator with its own intrinsic frequency. Let’s first study the two-oscillator system by reducing it to a map. Let $F(\phi) = \phi + \Delta(\phi)$. We make two important assumptions about F : (i) $F'(\phi) > 0$ and (ii) $F(0) = 0$. Note that (ii) implies that $F(1) = 1$ since $\Delta(\phi)$ is periodic. Clearly, the PRC for the LIF violates (ii), but the neural PRC and those of the RIC and QIF both satisfy (ii). For weak enough coupling, a small, they also satisfy (i). Physically, these assumptions say that no stimulus can instantly make the neuron fire and that at the moment of spiking, the neuron ignores all stimuli.

We now construct a map for a pair of oscillators. Suppose that when 1 fires, 2 is at ϕ so that the new phase for 2 is $F(\phi)$ and 1 is reset to 0. At $t = t_2 \equiv 1 - F(\phi)$ oscillator 2 fires and oscillator 1 has traveled exactly t_2 since its frequency is 1. Thus, the phase of oscillator 1 is set to $F(t_2)$ and oscillator 2 is set to zero. Finally, oscillator 1 will fire once again at $t_1 = 1 - F(t_2)$ and the phase of oscillator 2 will be t_1 . This yields the map

$$\phi \longrightarrow 1 - F(1 - F(\phi)) \equiv G(\phi). \quad (8)$$

We see immediately that $G(0) = 0$ so that there is a synchronous solution. By looking at the iteration, $\phi_{n+1} = G(\phi_n)$, we can analyze the approach to and stability of fixed points. Figure 2 shows $G(\phi)$ for the three oscillators, QIF, RIC, and the real neuron. (For the neuron, we use the approximation, $\Delta(\phi) = \phi(1 - \phi)/(1 + \exp(-6(\phi - 0.6)))$) which is a reasonable fit.) For each of these maps, there is also a non-zero fixed point corresponding roughly to the “anti-phase” solution in which the oscillators fire alternately. The fixed point $\phi = 0$ is stable if and only if $|G'(0)| < 1$ or

$$|F'(1^-)F'(0^+)| = |1 + \Delta'(1^-)||1 + \Delta'(0^+)| < 1.$$

We have used limits, 1^- and 0^+ since the PRCs are continuous, but may not be continuously differentiable at endpoints. (This is certainly true of the neural

PRC which is nearly flat at 0 and has a negative slope at 1.) For $a > 0$ in the RIC, synchrony is asymptotically stable as it also is for the neural PRC. The linear stability gives no information for the QIF since $\Delta'(0) = 0$ for this model, but the graphical picture shows that synchrony is stable.

We next turn to some questions about synchrony in more complex networks. Suppose that we have N identical oscillators and each is connected to all the others in exactly the same fashion. Then clearly, synchrony is a solution. In Goel and Ermentrout (2003), we analyzed this and proved the following condition for stability. Let $\alpha_0 = F'(0^+)$ and $\alpha_1 = F'(1^-)$. Then synchrony is linearly stable if and only if each of the quantities $\beta_l \equiv \alpha_0^l \alpha_1^{N-l}$, $1 \leq l < N$ is less than 1. This leads to a rather interesting situation. Suppose that $\alpha_0 > 1$ and $\alpha_1 < 1$ as is the case for the neural PRC. Then for l sufficiently large, we can guarantee that β_l is positive. Thus, for a small network, it is possible that synchrony is stable but for a larger network, it becomes unstable!

Surprisingly, the analysis of synchrony for locally coupled networks is much more difficult than the all-to-all case. The reason for this is that with all-to-all coupling, the ordering of the firing is preserved because of the monotonicity of $F(\phi)$ and the fact that each time an oscillator fires, *all* other oscillators are affected identically. We conjecture that if synchrony is pairwise stable, then it is also stable in a one-dimensional network of nearest-neighbor coupled oscillators. Here, by pairwise stability of synchrony, we mean that for two identical symmetrically coupled oscillators, synchrony will be stable. In one-dimensional rings of sufficient size, there is also the possibility of waves. That is, there is a constant phase-difference between successive oscillators so that the net phase change around the ring is an integer. Consider the network of N nearest neighbor oscillators:

$$\theta'_j = 1 + \Delta(\theta_j)[\delta(\theta_{j-1}) + \delta(\theta_{j+1})]$$

where we identify 0 with N and $N + 1$ with 1. Suppose that when oscillator j fires, oscillator $j - 1$ has phase τ so that its new phase is $F(\tau)$. After N iterations of this, we want to have traversed a single cycle. This leads to the following algebraic condition for the existence of a wave:

$$G(\tau, N) \equiv F(F(\tau) + (N - 2)\tau) + \tau = 1.$$

Basically, this just says that each oscillator receives two inputs from its two neighbors and that after these it must traverse one cycle. Waves with multiple cycles replace the 1 with m . The wave is linearly stable if and only if (i) $\alpha_N < 1$; (ii) $\alpha_1 \alpha_N < 1$; and (iii) $1 + \alpha_1 \alpha_N > \alpha_N$, where $\alpha_1 = F'(\tau)$ and $\alpha_N = F'((N - 2)\tau + F(\tau))$. The last condition is trivially satisfied if the first two hold. These simple conditions are analogous to the conditions for synchrony for a pair of neurons. We point out that this formula is not valid for $\tau = 0$ which is the synchronous solution since it assumes that the firing order is fixed (which is valid near a traveling wave).

In two-dimensions, it is possible to find rotating waves. For example, consider a 4×4 network with nearest neighbor coupling using the RIC PRC. Cells at

the corners receive only two inputs, those at the edges, three, and interior cells, four from their neighbors to the north, east, south, and west. The following table summarizes the various firing times in terms of four $((N/2)^2)$ unknowns:

0	α	$\tau/4 - \beta$	τ
$\tau - \beta$	γ	$\tau/4 + \gamma$	$\tau/4 + \alpha$
$3\tau/4 + \alpha$	$3\tau/4 + \gamma$	$\tau/2 + \gamma$	$\tau/2 - \beta$
$3\tau/4$	$3\tau/4 - \beta$	$\tau/2 + \alpha$	$\tau/2$

The structure of this table depends crucially on the fact that the PRC we use is odd-symmetric. Like the work of Paultet and Ermentrout (1994), we can exploit this symmetry to reduce the number of equations. In Paultet and Ermentrout further symmetries allowed us to reduce the system even more. If $\Delta(-\phi) \neq -\Delta(\phi)$ then there can generally be no reduction. We can use this to derive a series of algebraic conditions for the existence of a rotating wave. Goel and Ermentrout (2003) find these explicitly for $N = 4, 6, 8$ and also continue the solutions in the amplitude parameter a for the RIC.

Before moving on to propagation of waves in active media, I want to state a general result about coupled PRCs which is possible when we replace the impulse coupling with a smooth version. Consider the following model:

$$\frac{d\theta_j}{dt} = 1 + \sum_k c_{jk} P(\theta_k) \Delta(\theta_j). \quad (9)$$

The function $P(\theta)$, called the *coupling function*, should be regarded as a pulse-like function; for example $P(\theta) = A \exp(-B(1 - \cos 2\pi\theta))$ where B is a large positive number and A is chosen so that the area under P over one period is 1. As $B \rightarrow \infty$ this function tends to an impulse function. Suppose that $c_{jk} \geq 0, c_{jk} = c_{kj}$ and that

$$\sum_k c_{jk} = c$$

is a constant. The last assumption implies that $\theta_j(t) = \phi(t)$ where

$$\frac{d\phi}{dt} = 1 + c\Delta(\phi)P(\phi) \equiv f(\phi).$$

We assume that $f(\phi) > 0$ so that $\phi(t)$ is a periodic solution with period:

$$T = \int_0^1 \frac{ds}{f(s)}.$$

The first two assumptions allow us to find a simple condition for the stability of the synchronous state. Suppose the matrix c_{jk} is irreducible and

$$Q \equiv \int_0^T P(\phi(t)) \Delta'(\phi(t)) dt < 0.$$

Then the synchronous state is asymptotically stable. The condition on Q is intuitively appealing and has a simple interpretation. Suppose that P is positive

near the firing time and nearly zero the rest of the time. Then we require the slope of the PRC to be negative at the firing phase. This is not true for the QIF or the real neuron, but it is true for the RIC. However, for the real neuron, the PRC has a big negative slope on one side of 0 and a very shallow positive slope on the other, so for a symmetric pulse, $P, Q < 0$ as required. The assumptions on c_{jk} are not unreasonable, for example, any ring of oscillators with symmetric positive coupling will work.

3 Waves in spiking models.

In the first half of these notes, we examined coupled networks of oscillatory neurons. I want to turn now to networks of synaptically coupled units which are not intrinsically oscillatory. Rather, we will assume that the network is “excitable”; that is small perturbations decay to rest, but large enough ones lead to an action potential. Each cell could be a full conductance-based model such as equation (1), or a simpler scalar model such as the LIF or QIF model. Consider the following general class of scalar models:

$$\frac{dV(x, t)}{dt} = f(V(x, t)) + g[V(x, t), \int_{\Omega} k(x, y)s(y, t) dy] \quad (10)$$

The functional $s(x, t)$ is effect of the cell at x firing. This could satisfy its own differential equation or be a proscribed function of t or just a nonlinear function of V .

3.1 Theta model.

Let me start with a simple model in which the function s has no independent dynamics. Recall the QIF model, equation (3). This is a scalar model, but it is not convenient for mathematical analysis, so that we transform it to the so-called theta model by setting $V = V_0 + V_1 \tan(\theta/2)$:

$$\frac{d\theta}{dt} = 1 - \cos \theta + (1 + \cos \theta)I \quad (11)$$

where I represents all the inputs. The spiking threshold is $\theta = \pi$ or $V = +\infty$ and the reset is $\theta = -\pi$ or $V = -\infty$. Since $-\pi = \pi$, the theta model is smooth around the spiking so that it represents a smooth dynamical system on the circle. If $I < 0$ then θ tends to a stable fixed point and if $I > 0$, then θ traverses the circle with frequency \sqrt{I}/π . (See figure 3A.) Suppose that the coupling function is as in the previous section; just a pulse like function of θ (see figure 3B) and that the domain is the whole line with homogeneous coupling. Then, we arrive at:

$$\frac{d\theta(x, t)}{dt} = 1 - \cos \theta + (1 + \cos \theta)(I + g \int_{-\infty}^{\infty} K(x - y)P(\theta(y, t)) dy).$$

$K(x)$ is nonnegative, symmetric, and monotone non-increasing for $x > 0$. $I < 0$ so that the medium is not spontaneously active. Intuitively, we might suspect that if we excite a region above threshold, then the coupling might induce propagation of activity and lead to a traveling wave. This is in fact true under a rather broad range of conditions. Figure 3C shows a simulation of the model and the profiles of two values of $\theta(x, t)$. A traveling pulse satisfies, $\theta(x, t) = U(\xi)$ where $\xi = x - ct$. At $\xi = +\infty$ we want $U(\xi) = \theta_{rest}$ and at $x = -\infty$, $U(\xi) = 2\pi + \theta_{rest}$. This says that the wave traverses exactly one cycle. While there is no published proof of the existence of such a wave front for this model, existence and stability follow with minor changes from a theorem of Xinfu Chen as long as

$$Q(u) = 1 - \cos u + (1 + \cos u)(I + gP(u))$$

has two roots in $[0, 2\pi)$. If $I < 0$, $P(u)$ is narrow enough, and the peak, θ_T of $P(u)$ is close enough to π , then $Q(u)$ will have the required roots. In two spatial dimensions, we can expect spiral waves as shown in part D of the figure.

Osan, et al, have considered the same theta model but the coupling function is no longer a simple function of the state θ . Instead, $s(x, t) = \exp[-(t - t^*(x))/\tau]$ where $t^*(x)$ is the time at which $\theta(x, t)$ crosses π . Osan et al proved the existence of a traveling wave solution to this problem and in a subsequent paper, Rubin formulated the stability questions.

3.2 Thalamic models.

We conclude with a rather complicated conductance-based model of the a region of the brain called the thalamus. At its simplest, the network consists of two layers of neurons, the thalamocortical cells (TC) and the reticular nucleus cells (RE). Each neuron satisfies an equation of the form (4) with an additional equation for the synapses. The phaseplane for an individual cell is shown in figure 4A. Each cell is endowed with a calcium current which produces rebound excitation. That is, suppose the cell is inhibited for a period of time. This raises the V -nullcline as seen in the figure ($s = \phi$). The equilibrium moves toward the new fixed point. If the inhibition is rapidly removed, the V -nullcline falls back to the original position ($s = 0$) which leaves (V, h) above h_{max} . This causes the voltage to jump to the right branch of the nullcline (a rebound spike), before returning to rest. (More details on this cycle are provided in the next paragraph.) If the a two layer network of these cells is wired up as in figure 4B, then under some circumstance, the result is a wave of activity across the network. Such a wave is shown in figure 4C. This is not a smooth wave; rather we call this a lurching wave. Here is what happens. A group of TC cells fires. This excites RE cells nearby causing them to fire. They inhibit the TC cells including those surrounding the original population of firing cells. The fresh population is inhibited and when the inhibition wears off, they fire as a group.

We now attempt to explain this and find a formula for the size of the groups that fire as well as the time it takes for them to fire. In order to do this, we will simplify a bit and consider a single layer of cells with inhibitory coupling.

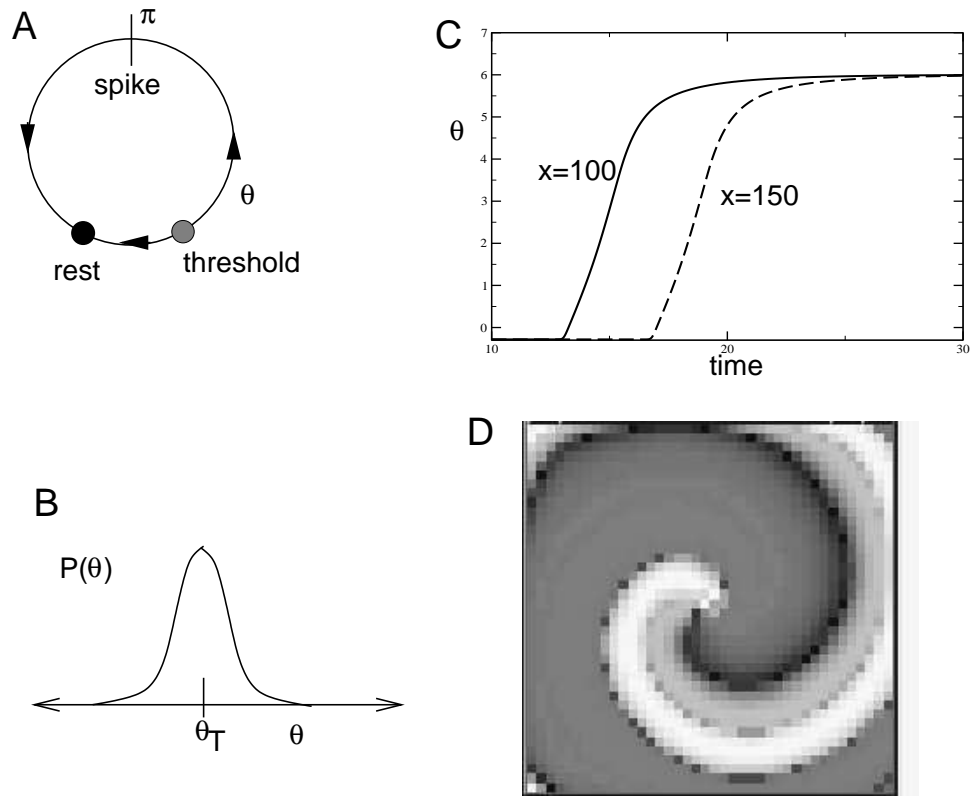


Figure 3: Waves in a theta model. (A) Phase space of the theta model; (B) Coupling function of θ ; (C) Traveling wave for a line of cells; (D) Spiral wave for a two-dimensional array.

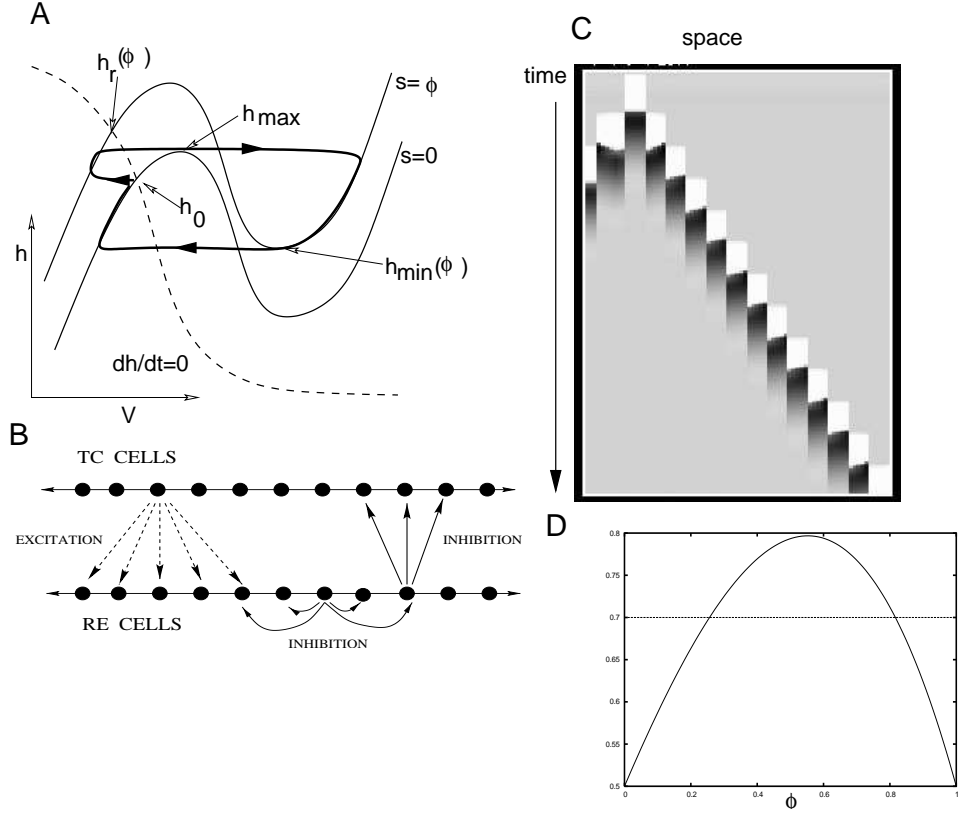


Figure 4: Thalamic network model. (A) Phaseplane showing the h -nullcline (dashed) and the V -nullcline at rest ($s = 0$) and when a region of length ϕ is inhibiting ($s = \phi$). Several important values of h are shown. The approximate singular trajectory of a lurching wave is drawn in thick lines. (B) The architecture of the full model. (C) A simulation of a lurching wave. Grey scale depicts voltage; white=40 mv and black=-90 mV. (D) The function $F(\phi)$ from equation (15) with $h_{max} = .7$, $h_{min}(\phi) = .2 + .5\phi$, $h_r(\phi) = .5 + \phi$, $\tau_R/\tau_L = 2$.

Thus, when a group of cells fires, it inhibits a neighboring group. After the inhibition wears off, the next group fires and so on. (In the next section, we will look at the transition from smooth waves to lurchers through a different set of simplified models.) To analyze this model, we use singular perturbation. The present exposition will be a drastic approximation to a fuller analysis of the model which can be found in Terman et al. The equations of interest are

$$\epsilon \frac{\partial V}{\partial t} = f(V, h) - g \int_{-\infty}^{\infty} W(x-y)s(y, t) dy (V - V_{in}) \quad (12)$$

$$\frac{\partial h}{\partial t} = (h_{\infty}(V) - h)/\tau(V) \quad (13)$$

$$\epsilon \frac{\partial s}{\partial t} = \alpha H(V - V_T)(1 - s) - \beta s. \quad (14)$$

$f(V, h)$ is all the intrinsic currents of the cell. We suppose that the interaction kernel, $W(x)$ is a square and without generality, assume it is zero outside of $x = (-1/2, 1/2)$. We assume that $\tau(V)$ takes on two values, τ_R when V is on the right branch of the V -nullcline and τ_L when V on the left branch. The parameter ϵ is small indicating that the dynamics is governed by the calcium recovery variable, h . (We should really start with ϵ multiplying the right-hand side of the h equation and then rescale time. In the interest of brevity, I have already done this.) By letting $\epsilon \rightarrow 0$, we analyze the singular trajectory and compute the properties of the wave. Figure 4A shows the singular trajectory of a group of cells. Suppose that ϕ is the size of the group of cells that is turned on. This inhibits a neighboring group, which are all at rest, h_0 . As long as the first group remains on the right-branch of the V -nullcline, the second group crawls up the left branch of V -nullcline toward $h_r(\phi)$ the resting state. When the first group reaches the bottom of the inhibited ($s = \phi$) V -nullcline, the inhibition disappears. All cells that are above h_{max} will jump to the right branch, starting the cycle again. With this simple description of the wave, we can derive formulas for the time between jumps and the size of group that jumps. Suppose the group that jumps is on $x \in (-\phi, 0)$. This means that all the synaptic variables, $s(x, t)$, in the group are at their equilibrium values, $a \equiv \alpha/(\alpha + \beta)$. Thus

$$S_{tot}(x) \equiv \int_{-\infty}^{\infty} W(x-y)s(y, t) dy = a \int_{-\phi}^0 W(x-y) dy.$$

We assume that ϕ is smaller than the synaptic footprint, so that $S_{tot}(x) = a\phi$ for $x \in (0, \phi)$. For the time in which this group of cells is on the right branch of the V -nullcline, All cells in $(-\phi, \phi)$ feel the same common inhibition parameterized by ϕ and they see the V -nullcline labeled $s = \phi$ in the figure. At the up-jump, all the cells roughly jump horizontally with $h = h_{max}$, the maximum of the $s = 0$ V -nullcline. They remain on the right branch until they reach $h_{min}(\phi)$ where they jump back. For V on the right branch, $h_{\infty}(V) = 0$, so the time it takes is

$$T = \tau_R \ln \frac{h_{max}}{h_{min}(\phi)}.$$

In the meantime, the group of cells at $x \in (0, \phi)$ is feeling the inhibition, so, starting from rest, they are heading toward the upper equilibrium point at $h_r(\phi)$. During this period h satisfies

$$\tau_L \frac{dh}{dt} = h_\infty(V_L(h)) - h, \quad h(0) = h_0,$$

where $V_L(h)$ is the value of the voltage on the $s = \phi$ V -nullcline. We approximate $h_\infty(V_L(h))$ as $h_r(\phi)$ so that we can solve for h in this time period:

$$h(x, t) = h_r(\phi) + (h_0 - h_r(\phi))e^{-t/\tau_L}.$$

When the inhibition wears off at $t = T$ only the cells above h_{max} will make the jump. Thus, for self-consistency, we must have

$$h(\phi, T) = h_{max}$$

or:

$$h_{max} = h_r(\phi) + (h_0 - h_r(\phi)) \left(\frac{h_{min}(\phi)}{h_{max}} \right)^{\tau_R/\tau_L} \equiv F(\phi). \quad (15)$$

Thus, we reduce the problem to a single equation for ϕ . $F(0) = h_0 < h_{max}$ so that for small ϕ , $F(\phi) < h_{max}$. If the synaptic coupling g is large enough and τ_R/τ_L is also large, then $F(\phi)$ will be larger than h_{max} for ϕ in some range. Indeed, the function $F(\phi)$ is parabolic in shape (see figure 4, so there will either be two roots or no roots to this equation. Having found ϕ we can then plug it back to get T and thus get the speed of the lurching wave. In Terman, et al, a more correct and precise analysis is presented and compares very closely to the solutions obtained by numerically simulating the full model.

3.3 Integrate-and-fire.

We close this chapter with an example system which shows the transition from smooth waves to lurching waves as a parameter varies. We will examine the simplest neuronal dynamics, the LIF, in which there is a fixed delay between the time that a cell fires and the time that it excites the neighboring cells. For small delays, the system is like the coupled theta-cell model and a solitary smoothly propagating wave exists and is stable. For large delays, we can think of this as analogous to the thalamic model based on inhibition and rebound. The delay is analogous to the time for the inhibition to wear off allowing the stimulated cell to fire; if this is large enough lurching occurs. Suppose that each time a cell fires, the result on a neighboring cell is a proscribed function of time, $\alpha(t)$. The domain is the real line. Then the equation of each cell is:

$$\tau_0 \frac{\partial V(x, t)}{\partial t} = -V(x, t) + g_{syn} \int_{-\infty}^{\infty} w(x - y) \alpha(t - T(y) - \tau_d) dy + I,$$

where I is a constant applied current and $T(x)$ is the time at which the cell at x fires. We say that a cell fires when $V(x, t)$ crosses V_T , the threshold. Typically,

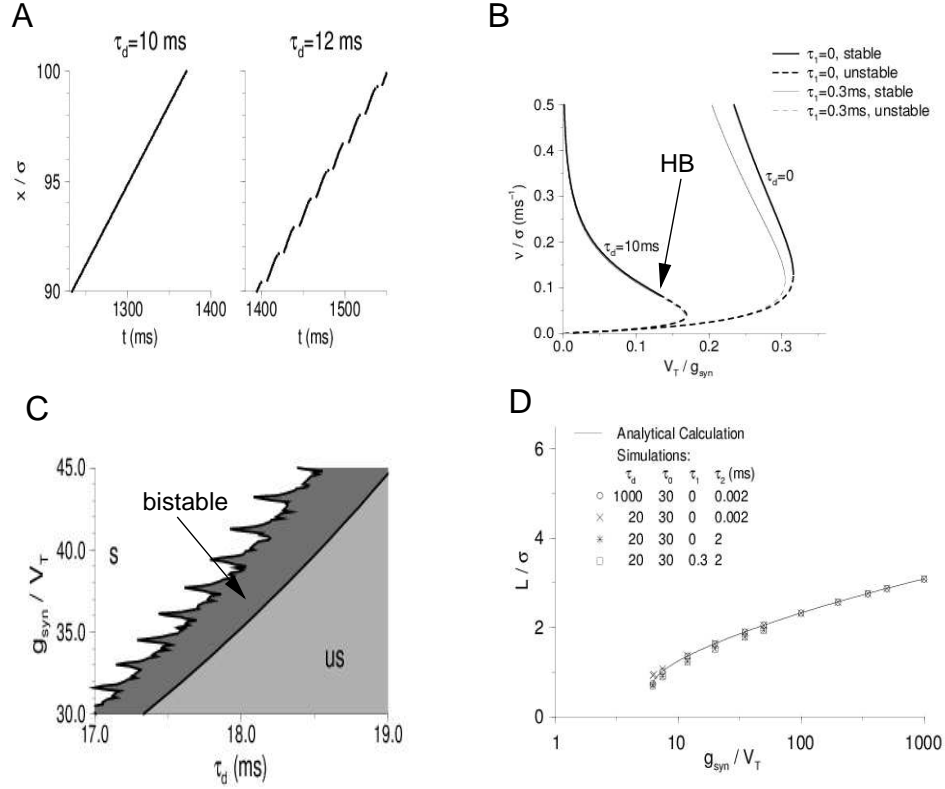


Figure 5: The integrate-and-fire model with delays. (A) a raster plot showing the time of firing of cells in a numerically computed wave for two delays. (B) velocity as a function of the threshold for different α functions. Note the Hopf bifurcation leading to instability of the smooth wave. (C) Complex behavior of the network; white region – only smooth waves are stable; light grey – only lurching waves are stable; dark grey – both waves are stable. (D) Lurching period as a function of synaptic strength.

$\alpha(t) = (\exp(-t/\tau_1) - \exp(-t/\tau_2))/(\tau_1 - \tau_2)$ for $t > 0$ and 0 otherwise. $w(x)$ will be either a square, Gaussian, or exponential interaction.

Since V satisfies a linear differential equation, we can integrate this equation once to obtain a Volterra integral equation for $V(x, t)$. We then note that $V(x, T(x)) = V_T$ by definition which leads to a very interesting functional equation for $T(x)$:

$$\frac{V_T}{g_{syn}} = \int_{-\infty}^{\infty} dy w(y) G[T(x) - T(y) - \tau_d], \quad (16)$$

where

$$G(t) = \int_0^{\infty} e^{-(t-s)/\tau_0} \alpha(s) ds.$$

Equation (16) is equivalent to the original model under the assumption that each cell fires at most one time. We could justify the ‘‘one-spike’’ assumption by assuming a very strong hyperpolarizing afterpotential or strong synaptic depression, both preventing further spikes.

Figure 5A shows the firing pattern of a network of LIF neurons with two different delays. In the left, a smooth wave appears so that $T(x) = x/\nu$ where ν is the wave velocity. On the right, this simple description no longer holds. However, we do have that $T(x + L) = T(x) + T_{per}$ and the average velocity is $\nu = L/T_{per}$. That is, $T(x) - x/\nu$ is a periodic function of x . The smooth wave is simple to analyze since we know the exact form of $T(x) = x/\nu$. Plugging this into (16), we obtain:

$$\frac{V_T}{g_{syn}} = \int_0^{\infty} dy w(y + \tau_d \nu) G(y/\nu) \equiv F(\nu).$$

The function $F(\nu)$ can be analytically determined in several interesting cases, for example if $w(x) = \exp(-|x/\sigma|)/(2\sigma)$ and $\tau_1 = 0$, we find

$$F(\nu) = \frac{2(\tau_0 \nu + \sigma)(\tau_2 \nu + \sigma)}{\tau_0 \nu \sigma} \exp(\tau_d \nu / \sigma).$$

In general, this is a parabolic function of ν so that there are either no roots, one root, or two roots. Figure 5B shows the velocity as a function of the threshold for several different parameters and delays. Ermentrout (1998a) showed that this was generally the case for conductance-based neurons using a combination of numerical shooting and asymptotics.

Following Golomb and Ermentrout (2000) or Bressloff (2000), we can look at the stability of these traveling waves. Substituting, $T(x) = x/\nu + \epsilon e^{\lambda x}$ into (16) and taking the $O(\epsilon)$ terms, we obtain an equation for λ :

$$E(\lambda) \equiv \int_0^{\infty} dy w(y + \tau_d \nu) G'(y/\nu) \left[1 - e^{-\lambda(y + \tau_d \nu)} \right] = 0. \quad (17)$$

The function $E(\lambda)$ is called the Evans function; $E(0) = 0$ since there is translation invariance. If the real part of λ is positive, the perturbation of the wave will grow exponentially as it advances through space and it is thus unstable. Bressloff

(2000) and Golomb and Ermentrout (2000) showed that the lower branch of solutions (the slow waves) are unstable for all parameters. The fast waves are stable if there is no delay. What is relevant to lurching waves is that Golomb and Ermentrout showed that for a large enough delay, the fast waves lose stability at a Hopf bifurcation and give rise to waves that have periodic modulation. That is, $T(x) - x/\nu$ is a periodic function. We have not yet computed the direction of bifurcation for this problem; however, we have done careful numerical analysis the results of which are shown in figure 5C. There is a complex regime of bistability between lurching waves and smooth waves. We conjecture that the borders of this region are precisely those places where the Hopf bifurcation switches from sub- to super-critical. (Oscillations branching from subcritical Hopf bifurcations undergo turning points to become stable leading to a regime of bistability between the fixed point and the oscillation.) These results suggest that the transition between smooth waves and lurching waves in the thalamic model is a consequence of changing the effective delay to excitation. Golomb and Ermentrout (1999) showed simulations of a conductance-based model of TC and RE cells that undergoes a transition from smooth to lurching waves as the strength of inhibition (and thus the effective delay to firing) increases.

As in the previous section of this chapter, we can estimate the size of a lurching group of neurons in certain asymptotic regimes. Recall that for the singular perturbation arguments, we let ϵ , the recovery rate for the T-current tend to zero. In unscaled time, this means that the period between lurching groups tends to infinity. The analogue in the present model is to let the delay become arbitrarily large. We obtained the following estimate for the size, L of a group of neurons which fire together during a lurching cycle:

$$\frac{V_T}{g_{syn}} = \int_L^{2L} dy w(y) \equiv W(L).$$

This implicitly defined function gives an excellent approximation for the size of the lurching group as shown in figure 5D. For an exponential footprint,

$$L \sim \sigma \ln \left(\frac{g_{syn}}{2V_T} \right)$$

for large g_{syn} while for a Gaussian footprint,

$$L \sim \sqrt{2}\sigma \sqrt{\ln(g_{syn}/V_T)}.$$

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