Dynamical models of interacting neuron populations in visual cortex

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Abstract

Over the past several years, with increasing frequency, supercomputers have been used for the direct dynamical simulation of large populations (totalling thousands to tens of thousands) of interacting visual cortical neurons. The full simulations, which a researcher would choose to carry out, are far beyond the capabilities of current or presently anticipated supercomputers, and consequently those simulations which have been implemented have necessitated major compromises. One sort of compromise is to set an unrealistically low limit on the number of neurons of a given population type. A second compromise is to use an abbreviated neuron dynamics ("integrate-and-fire" neuron model) rather than to use the full realistic Hodgkin-Huxley type neuronal model which is available. The difficulty and challenge here is the wide range of different time-scales which appear in the dynamics of each of a large number of neurons.

With more ambitious future simulations in mind, we have undertaken the computationally efficient reformulation of the problem in terms of the dynamics of whole neuronal sub-populations. We note that a set of neurons of a given type may be represented in terms of an evolving "density" that is spread within the Hodgkin-Huxley state-space which defines the dynamics of that neuron type. That density's evolution is described in detail by a partial differential equation which in turn may be efficiently approximated by a small set of simple ordinary differential equations. These equations also have a simple interpretation in terms of the underlying neuronal dynamics.

Our method is a means to remove the high redundancy which exists in a direct simulation of many similar neurons, and to furnish instead a compressed type of representation which is capable of undertaking more extensive and more realistic simulations of visual cortex.

A. Introduction

There is good hope that neuroscience is approaching an ability to study realistic models of parts of the cerebral cortex. This expectation arises from the convergence of three active scientific endeavors. The first is our expanding quantitative knowledge of neuronal interconnections. The second is our maturing understanding, even down to the level of macromolecules, of the biophysics which underlies the dynamics of electrically interacting nerve cells. Third is the current rapid growth of available computing power. Regarding the third endeavor, a pessimist may point to the fact that realism in neural simulation may demand the following of parallel activity of tens of thousands of interacting neurons in a patch of cortex; while each of these neurons talks to hundreds or thousands of neighbors and exhibits essential time scales which range from the sub-millisecond regime for the progression of a nerve impulse, to several seconds in the case of important low-frequency components in a visual stimulus. Such numbers seem to emphatically rule out realistic direct simulation by any computer system now projected. The comments here address this issue.

A nerve cell body is contained by a surrounding membrane which is a good insulator and is so thin that it endows the cell with a substantial electrical capacitance. The rate at which voltage across this membrane changes is proportional to the flow of transmembrane current and is inversely proportional to the membrane capacitance:

$$dV/dt = (1/c)\, I\,(V; m, h, n; s)\,. \tag{1}$$

Present knowledge enables us to write out the right-hand side explicitly.[1] Here the dependence of I upon V is by Ohm's law as currents flow through molecular ion-selective channels whose conductances to sodium and potassium currents are set by the parameters m, h, n. Conduction by other ions (calcium, chloride) may be governed by similar parameters. The voltage difference is maintained by the down-gradient flows of ions whose concentrations are different on the two sides of the membrane (high potassium inside, high sodium outside). The

variable s in (1) indicates the response of the transmembrane current flow to signals from other neurons.

The variables m, h, n satisfy dynamical equations of their own[1] which include a dependence on V. The time-constants in these equations tend to be fast compared to the capacitative relaxation time of the cell membrane. If s is held fixed, the remaining variables tend to pursue a limit-cycle in the 4-space of V, m, h, n. That limit-cycle shows a slow rise in V followed by a much faster rise followed by an abrupt drop, which high-speed feature is the nerve impulse. Changing the input s changes the location of the limit-cycle in 4-space and changes the rate of nerve-impulse production.

B. Population Model

We may measure the system's position on the limit cycle by a variable x which ranges from 0 to 1 and repeats. Except during the brief return of the nerve-impulse (which we may put at $x = 1$), x may be interpreted as voltage rescaled. We now ask what is the neuron's dynamical response to changes in the input s. Because m, h, n adjust with rapid time-constants, they will not be removed much from their limit-cycle values, and (1) takes the simplified form

$$dx/dt = f(x, s), \tag{2}$$

with the understanding that x returns to 0 upon achieving the value 1.

In the cortex we find whole sub-populations of similar neurons which respond to similar input but are distributed rather than synchronized on the firing cycle. We may characterize the state of such a population by a distribution density function $P(x, t)$, around the firing cycle. The way this density evolves in time is mandated by equation (2); an easy exercise derives the dynamical equation

$$\frac{\partial P}{\partial t} = -\frac{\partial}{\partial x}\left(f(x, s)\, P\right). \tag{3}$$

which is a particular case of the general relation

$$\frac{\partial P}{\partial t} = -\frac{\partial J}{\partial x}. \tag{4}$$

Here $J(x, t)$ is the "density current" and states the rate at which members of the population are crossing the point x toward larger values. A natural boundary condition is

$$J(x = 0) = J(x = 1), \tag{5}$$

so that each neuron which fires also returns. If we integrate (4) over x, we see that (4) states that the population size does not change with time.

The neuronal behavior remains largely intact if equation (2) above is specialized to the very simple form

$$dx/dt = -\gamma x + s. \tag{6}$$

If we regard x as voltage normalized by capacitance, then here s is clearly electric current imposed from without, while $-\gamma x$ is the voltage-driven leakage current back through the membrane, and $1/\gamma$ is the "electrical time constant" or "RC time" of the system, while $x = 1$ is the "nerve-impulse firing threshold". Equation (6) is sometimes called the "leaky" or "forgetful integrate-and-fire" model[2]; it is a reasonable guide to the behavior of more elaborate neuron models and it is currently used in direct simulations of cortex, to relieve the massive requirement of computation time.

At this point we can see that equation (3) suggests alternative simulation techniques capable of sidestepping the need for direct simulation of multitudinous duplicate neurons. However first we must include one additional important biophysical effect, that of random independent fluctuations in the inputs of the population's member neurons. The effect of such fluctuations is to superimpose on each neuron's voltage time-course an additional "random walk" in voltage. The quantitative effect of such a random walk upon the density function has been addressed in statistical physics: it is manifested as a "diffusion current" down the gradient of the population density, so that the density current of equations (3), (4) is modified by an additional term

$$J(x, t) = -D(x, s)\left(\partial P/\partial x\right) + f(x, s)\, P \tag{7}$$

which gives for (4) the dynamical equation

$$\frac{\partial P}{\partial t} = \frac{\partial}{\partial x}\left(D(x, s)\frac{\partial}{\partial x} - f(x, s)\right) P. \tag{8}$$

Here s is that part of the input signal - the "average input" - which is common to all the neurons. In the particular case of a population of forgetful integrate-and-fire neurons (6) we have the explicit equation[3],[4],[5]

$$\frac{\partial P}{\partial t} = \frac{\partial}{\partial x}\left(D\frac{\partial}{\partial x} + \gamma x - s\right) P. \tag{9}$$

This equation requires two boundary conditions, one of which is (5). For the second observe that in this model we have squeezed the nerve impulse to a point at $x = 1$ where a neuron proceeds with certainty to $x = 0$; this is an absorbing boundary at which, by diffusion theory, we must have

$$P(x = 1) = 0. \tag{10}$$

C. Diffusion Coefficient

To see how the diffusion coefficient D may be evaluated explicitly from the input fluctuations, we may compare evaluations of (6) and (9) in the simple case where $\gamma = 0$. In (6) we assume a time-stationary fluctuating input $\hat{S}(t)$ which has zero mean (that will set the average s in (9) to zero as well) and whose autocorrelation is

$$c(\tau) = \left\langle \hat{S}(t)\,\hat{S}(t+\tau) \right\rangle, \tag{11}$$

the average taken over the population. From (6) the random variable $x(t)$, starting from 0 at $t = 0$, is

$$x(t) = \int_0^t dt' \hat{S}\left(t'\right). \tag{12}$$

We observe that if t is large compared to a value of τ which will make $c(\tau)$ in (11) drop close to zero then by (12) $x(t)$ is a sum of numerous similarly distributed independent random variables, hence $x(t)$ will have a gaussian probability distribution. A centrally located gaussian is fully characterized by the mean-square of its variable, so from (12) we evaluate

$$\begin{aligned} \left\langle x^2(t) \right\rangle &= \int_0^t dt'' \int_0^t dt' \left\langle \hat{S}(t'')\hat{S}(t') \right\rangle \\ &= \int_0^t dt'' \int_0^t dt'\, c(t' - t'') \\ &\cong \int_0^t dt'' \left(\int_{-\infty}^{\infty} d\tau c(\tau) \right) = \left(\int_{-\infty}^{\infty} d\tau c(\tau) \right) t. \end{aligned} \tag{13}$$

Thus $\left\langle x^2 \right\rangle$ grows linearly with t, with a coefficient dependent on the autocorrelation as shown. The approximating step in (13) assumes as before that $c(t' - t'')$ drops to zero when its argument exceeds a small fraction of t. Now equation (9) with $\gamma = 0$ and $s = 0$, and with $P(x,0)$ concentrated at $x = 0$, is a familiar exercise, whose solution is a gaussian which spreads with time, whose mean-square is given by

$$\left\langle x^2(t) \right\rangle = 2Dt. \tag{14}$$

By comparing (13) and (14) we see that

$$D = \frac{1}{2} \int_{-\infty}^{\infty} d\tau c(\tau). \tag{15}$$

Work which appears above is discussed in various perspectives in refs.[3 4 5].

The stochastic input to each neuron, which gives rise to the autocorrelation $c(\tau)$, may arise from different sources, among which there is not yet a clear enough base of laboratory data to always choose one dominating source. One sort of source is the variety of voltage inputs which act independently on each cell, such as the "Johnson noise" which thermal fluctuations produce across the electrically resistive membrane. Fluctuations also arise because synaptic input to a neuron arrives as a fusillade of discrete "shots", $b(t)$, released from the arrivals of individual nerve impulses:

$$s(t) = \sum_m b(t - t_m), \tag{16}$$

where if there are enough independent inputs then the arrival times t_m will be Poisson distributed. If the mean arrival rate in (16) is λ, then the autocorrelation which results[6] is (reasonably)

$$c(\tau) = \lambda \int_{-\infty}^{\infty} dt\; b(t)\, b(t+\tau) \tag{17}$$

and the diffusion coefficient (15) becomes

$$D = \frac{1}{2}\lambda \left(\int_{-\infty}^{\infty} dt\; b(t) \right)^2. \tag{18}$$

Our input signal (16) above was a bit idealized by making the "shots" all the same size. If their sizes have a distribution[6] then the expressions above have a simple natural generalization. Clearly the presentation here assumes that the input signal changes on a scale slow compared to the shot-arrival rate. We might informally average (16) over a moving time interval whose reciprocal is intermediate between the signal rate and the shot arrival rate, to obtain

$$s(t) \cong \lambda(t) \int_{-\infty}^{\infty} dt'\, b\left(t'\right). \tag{19}$$

From this we note that D in (18) is proportional (through λ) to the size of the input signal.

D. Eigenfunction Analysis

These considerations lead to an alternative kind of simulation algorithm expressed directly in terms of subpopulations of like neurons. The first steps are standard steps in applied analysis. Equation (8) may be written

$$\frac{\partial P}{\partial t} = Q(s)\, P \tag{20}$$

and the operator Q of (8) has a set of eigenfunctions and eigenvalues:

$$Q\phi_n = \lambda_n \phi_n. \tag{21}$$

The euclidean space of smooth functions of x between 0 and 1 has a natural inner product

$$(\psi, \phi) = \int_0^1 dx\ \psi\phi. \tag{22}$$

An operator such as Q above has an adjoint operator $\hat{Q}$ which satisfies

$$(\psi, Q\phi) = \left(\hat{Q}\psi, \phi\right). \tag{23}$$

Equations (8) and (22) - with integrations by parts - show us that

$$\hat{Q} = \frac{\partial}{\partial x} D \frac{\partial}{\partial x} + f(x,s)\frac{\partial}{\partial x} \tag{24}$$

with adjoint boundary conditions

$$\hat{\phi}(0) = \hat{\phi}(1), d\hat{\phi}(0)/dx = 0. \tag{25}$$

As an adjoint operator, $\hat{Q}$ has a set of adjoint eigenfunctions which satisfy

$$\hat{Q}\hat{\phi}_n = \lambda_n \hat{\phi}_n \tag{26}$$

with the same eigenvalues as Q. With appropriate choice of normalization, the two sets of eigenfunctions are biorthonormal:

$$\left(\hat{\phi}_n, \phi_m\right) = \delta_{nm}. \tag{27}$$

Above, the two operators $Q, \hat{Q}$, the eigenvalues λ_n, and the two sets of eigenfunctions $\phi_n, \hat{\phi}_n$ are functions of the parameter s, with the exception that from (24), clearly

$$\hat{\phi}_0(x) = 1, \lambda_0 = 0 \tag{28}$$

solves (26).

E. Modal Reduction

The population density function may be expanded, at any value of s, in the eigenfunctions of Q:

$$P(x,t) = \sum_m a_m(t)\, \phi_m(x,s) \tag{29}$$

where the coefficients a_m are given by

$$a_m = \left(\hat{\phi}_m, P\right). \tag{30}$$

If the $a_m(t)$ are on hand, we may use (29) to recover $P(x,t)$, and by (7) $J(x,t)$ which at $x = 0$ is the population's firing rate of nerve-impulses.

From (30) we have (letting $\partial\hat{\phi}_n/\partial s = \hat{\phi}_{n,s}$)

$$\begin{aligned} \frac{da_n}{dt} &= \left(\hat{\phi}_n, \frac{\partial P}{\partial t}\right) + \left(\hat{\phi}_{n,s}\frac{ds}{dt}, P\right) \\ &= \left(\hat{Q}\hat{\phi}_n, P\right) + \left(\frac{ds}{dt}\right)\left(\hat{\phi}_{n,s}, P\right) \\ &= \sum_m a_m \left\{\left(\lambda_n \hat{\phi}_n, \phi_m\right) + \left(\frac{ds}{dt}\right)\left(\hat{\phi}_{n,s}, \phi_m\right)\right\} \\ &= \lambda_n(s)\, a_n + \left(\frac{ds}{dt}\right)\sum_m M_{nm}(s)\, a_m \end{aligned} \tag{31}$$

where in the final step we have substituted

$$\left(\frac{\partial\hat{\phi}_n}{\partial s}, \phi_m\right) = M_{nm}(s). \tag{32}$$

Now the $\lambda_n(s)$ and the $M_{nm}(s)$ may be evaluated for interpolation, once and for all, so that for specified $s(t)$ (31) is a set of explicit ordinary differential equations for the $a_n(t)$. These, in turn, explicitly evaluate P, J, and the firing rate in the population.

Our hope and expectation of course is that a few terms of (29) will serve, so only a few of the equations (31) will have to be integrated. More detailed investigation confirms that this is commonly true. In particular it follows from (28) that not only

$$\lambda_0 = 0 \text{ but also } \partial\hat{\phi}_0/\partial s = 0 \text{ whence } da_0/dt = 0. \tag{33}$$

If we normalize $P(x,0)$ to an integral of unity (as a probability density) then (33) gives

$$a_0(t) \equiv 1. \tag{34}$$

Since $\lambda_0 = 0, \phi_0(x,s)$ corresponds to the equilibrium distribution of the population. If $s(t)$ changes slowly (ds/dt small in (31)), then as it changes the population simply passes through a succession of equilibrium states and simulation involving large subpopulations becomes very tractable. The remaining equations of (31) serve as corrections if faster time-scales are important in $s(t)$.

If we specialize to $Q(s)$ in equation (9), then for small constant D we can obtain detailed analytic results for λ_n and M_{nm} in equation (31). Equation (6) gives us a transit time whose reciprocal (the firing rate) we may call

$$f_0 = -\gamma/s\left(\ell n\left(1-\frac{\gamma}{s}\right)\right). \tag{35}$$

In terms of this frequency the eigenvalues are of the form

$$\lambda_n = i\cdot 2\pi\left(f_0 + Da(s)\right)\cdot n - Db(s)\cdot n^2 \tag{36}$$

where a and b arise from solving the problem through first order in D, and n runs through both positive and negative integers. Also to lowest order

$$M_{nm}(s) = \frac{1}{(\gamma/f_0) + 2\pi i(n-m)}\frac{n}{n-m}c(s) \tag{37}$$

(for $n \neq m$).

$$M_{nn}(s) = 2\pi i\ n\ f_0\cdot d(s). \tag{38}$$

Referring back to equation (31) we see that the factor $-Dn^2$ in (36) will cause strong damping as n becomes large. (This is the familiar damping of diffusion at short wavelengths.) Equation (37) decouples member equations of (31) which differ much in index. The eigenvalues (36) show that the system has some tendency to "ring" with damped oscillations at low harmonics of the passage-time frequency. This leads to the appearance of complex numbers, with the result that computationally it is natural to reorganize the equations (31) for

$$a_n = a_{rn} + ia_{in}\ and\ a_{-n} = a_{rn} - ia_{in} \tag{39}$$

in coupled pairs of real equations for the real variables a_{rn} and a_{in}.

F. Concluding Remarks

The analytic methodology just described may be applied to the simulation of visual cortex, and clearly to other sorts of cortex as well. In the most direct sort of simulation, which features the dynamics of every neuron, the neurons may be identified by type and by location, with many neurons of each type falling within narrow boundaries surrounding any given location; such a collection of nearby neurons constitute the sort of sub-population discussed above, and their numerous sets of individual dynamical equations may be replaced by a small set of ordinary differential equations of the form (31) above. Currently we are developing this methodology with a computer program in which the equations (31) for one sub-population may be exchanged for the much more laborious full simulation of that sub-population, in order to verify the concurrence of the two sorts of computational results.

G. Acknowledgements

The authors gratefully acknowledge support from the Office of Naval Research under N00014-95-1-0281 and N00014-93-1-0279.

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