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Contribution to Chapter One of Book

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1.3 STOCHASTIC DYNAMICAL SYSTEMS

1.3.1 Jump processes

The observed electrical potentials of neurons as determined either by extracellular or intracellular recording are never constant. The same is true for grossly recorded field potentials and brain recordings such as the electroencephalogram. Often such recordings of potential exhibit quite sudden changes or jumps. If the sample paths of a continuous time random process have **discontinuities** then it is called a **jump process**. A process may be a pure jump process, like a **Poisson process** or a random walk, or there may be drift and or diffusion between the jumps.

Motivation for using jump processes in neurobiological modeling sprang primarily from observations on excitatory and inhibitory synaptic potentials (EPSP's and IPSP's). Examination of, for example, motoneuron or pyramidal cell somatically recorded EPSP's may show a rapid depolarization of several millivolts relative to resting potential, followed by an exponential decay with a characteristic time constant (Coombs *et al.*1959; Thompson, 1997). A complete understanding of these events requires the use of complex **spatial models**, (see below) but in the majority of studies attempting to model neuronal electrophysiological properties in the last several decades, spatial extent has, regrettably, been ignored, probably because of the unwillingness of but a few theorists to confront partial differential equations rather than ordinary ones.

Putting aside the matter of spatial versus "**point models**", if $N = \{N(t), t \geq 0\}$ is a simple standard (unit jumps) Poisson process, with rate parameter λ , then a simple one-dimensional model for the subthreshold (less than $V_\theta \approx 10\text{-}20\text{mV}$) depolarization of a single neuron can be written as the stochastic differential equation (SDE)

$$dV = -\frac{V}{\tau}dt + a_E dN, \quad V < V_\theta, \quad V(0) = V_0, \quad (1.3.1)$$

where τ is the time constant of decay and $a_E > 0$ is the magnitude of an EPSP. In the very small time interval $(t, t + \Delta t]$, either N and hence V jumps, with probability $\lambda\Delta t$ or doesn't; if it doesn't then V decreases according to $dV/dt = -V/\tau$.

A characteristic of a Poisson process is that the (random) time T between jumps or events has an **exponential distribution** with mean $1/\lambda$:

$$Pr\{T \leq t\} = 1 - \exp(-\lambda t), t \geq 0.$$

We may suppose that jumps still occur at rate λ , but that the jump size is random with probability density $\phi(u)$ or a distribution function $\Phi(u)$. This gives a **compound Poisson process** X . This means that jumps with amplitudes in $(u, u + du]$ occur with a relative rate of $\phi(u)du$ or an absolute rate of $\lambda\phi(u)du$. We let $N(du, t)$ count the number of such events in $(0, t]$ and the total contribution of these events will be $uN(du, t)$, being jump amplitude multiplied by the number of jumps with this amplitude. The whole compound Poisson process will be obtained by integrating over all possible amplitudes

$$X(t) = \int_{-\infty}^{\infty} uN(du, t),$$

where the total jump or event rate is of course $\int \lambda\phi(u)du = \lambda$.

The above **“leaky integrate and fire”** model (1.3.1) may thus be extended to include an arbitrary distribution of postsynaptic potential amplitudes:

$$dV = -\frac{V}{\tau}dt + \int_{-\infty}^{\infty} uN(du, dt), \quad V < V_\theta, \quad V(0) = V_0. \quad (1.3.2)$$

Since the positions of inputs are not distinguished in such point models, the input here could arise from many separate excitatory and inhibitory synapses. The representation

$$V(t) = V(0)e^{-\frac{t}{\tau}} + \int_0^t e^{-\frac{(t-s)}{\tau}} \int uN(du, ds),$$

(Tuckwell, 1989) enables us to find the mean of the unrestricted potential at time t

$$E[V(t)] = E[V(0)]e^{-\frac{t}{\tau}} + \mu_1(1 - e^{-\frac{t}{\tau}})$$

where $\mu_1 = \int u\phi(u)$ is the mean postsynaptic potential amplitude. Similarly, the variance is found to be

$$Var[V(t)] = \frac{\mu_2}{2}(1 - e^{-\frac{2t}{\tau}}),$$

where μ_2 is the second moment of ϕ .

For the model (1.3.1) analytical solutions for the firing time (ISI) are difficult to obtain because they involve differential-difference equations. These were first solved in Tuckwell (1975) and later using analytical and numerical methods for excitation and inhibition in Cope and Tuckwell (1979). Such discontinuous processes had been neglected because it was easier to deal with differential equations, which arise in the theory and properties of diffusion processes (see below). However, with the

great power of the desktop computers now available, it is a simple task to quickly estimate the interspike time distribution generated by a model such as (1.3.1) or (1.3.2) using simulation.

We may add physiological realism to (1.3.2) by including synaptic **reversal potentials**. These make postsynaptic potential amplitudes smaller when the equilibrium potentials for transmitter-induced conductance changes are approached (Tuckwell, 1979). This gives,

$$dV = -\frac{V}{\tau}dt + (V - V_E) \int_{-\infty}^{-\infty} uN_E(du, dt) + \\ + (V - V_I) \int_{-\infty}^{-\infty} uN_I(du, dt), \quad V < V_\theta, \quad V(0) = V_0, \quad (1.3.3)$$

where V_E and V_I are the reversal potentials for excitation and inhibition and N_E and N_I give the input frequency and amplitude distributions.

A **spatial model** may similarly be constructed with jump processes (Tuckwell, 1988a) using the linear cable equation

$$\frac{\partial V}{\partial t} = -V + \frac{\partial^2 V}{\partial x^2} + (V - V_E) \sum_{i=1}^{n_E} \delta(x - x_{E,i}) a_{E,i} \frac{dN_{E,i}}{dt} \\ + (V - V_I) \sum_{j=1}^{n_I} \delta(x - x_{I,j}) a_{I,j} \frac{dN_{I,j}}{dt}. \quad (1.3.4)$$

This gives a better representation of a neuron than either (1.3.2) or (1.3.3) because now the postsynaptic potentials have finite rise times according to experimental data and separate spatial locations for inputs are distinguished. Here there are n_E excitatory synaptic inputs at positions $x_{E,i}$, $i = 1, \dots, n_E$ with amplitudes $a_{E,i}$ and n_I inhibitory synaptic inputs at positions $x_{I,j}$, $j = 1, \dots, n_I$ with amplitudes $a_{I,j}$ and it is assumed that all excitatory (inhibitory) inputs have the same reversal potential, which is often the case. A region of low threshold is chosen as a trigger zone, at say $x = 0$, and boundary conditions must be imposed at $x = a$ and $x = b$. A realistic boundary condition at the soma could be a lumped-soma, being a capacitance and resistance in parallel to represent somatic membrane.

General jump process point model with drift

Multidimensional continuous time Markov processes are well suited for describing much of the electrophysiological and biochemical behavior of neurons and networks of neurons, especially when neuronal spatial extent is ignored. Thanks mainly to Itô (1951), Feller and Kolmogorov, the analytical theory of such processes and their representations by **stochastic integrals** (or equivalently stochastic differential equations) was rigorously developed in the middle of the 20th century. Consider

a deterministic differential equation for the n -vector $\mathbf{X}(t)$ of the form

$$\frac{d\mathbf{X}(t)}{dt} = \mathbf{f}(\mathbf{X}(t), t),$$

with initial value $\mathbf{X}(0)$. Interrupting the deterministic trajectories there may be superimposed jumps of various amplitudes and frequencies, both possibly time-dependent or depending on the values of the components of $\mathbf{X}(t)$, representing synaptic inputs. The function \mathbf{f} is called the **drift** and with the discontinuous components representing synaptic inputs of various amplitudes and frequencies we have

$$d\mathbf{X}(t) = \mathbf{f}(\mathbf{X}(t), t)dt + \int \mathbf{h}(\mathbf{X}(t), t, \mathbf{u})N(d\mathbf{u}, dt),$$

N being a Poisson random measure defined on subsets of $R^n \times [0, \infty)$. Such a general system covers all non-spatial conductance-based models such as Hodgkin-Huxley or approximations like Fitzhugh-Nagumo with almost every possible pattern of synaptic input. For more details in relation to neuronal modeling and extensions to the spatially distributed case see Tuckwell (1988a and 1989).

1.3.2 Diffusion processes

Diffusion processes are an abstract approximation to empirical processes which have the advantage of being less cumbersome to analyze than processes with jumps. Providing the postsynaptic potentials as seen at the soma are not very large and are fairly frequent, a diffusion model should perform reasonably well.

The simplest diffusion model

The simplest diffusion process employed for modeling a neuron is based on the unrealistic “**perfect integrator**” model and hence is only of historical interest. Unfortunately it is the only diffusion model which can be solved exactly for all parameter values. It consists of a **Wiener process** (Brownian motion) with drift and was introduced by Gerstein and Mandelbrot (1964). Consider a random walk consisting of the difference of two Poisson processes N_E and N_I , corresponding to excitatory and inhibitory input respectively,

$$dX = a_E dN_E - a_I dN_I,$$

where $a_E \geq 0$ and $a_I \geq 0$ are the magnitudes of steps up or down. Since, using the properties of Poisson random variables, the mean of $X(t)$ is $E[X(t)] = (\lambda_E a_E - \lambda_I a_I)t$ and its variance is $Var[X(t)] = (\lambda_E a_E^2 + \lambda_I a_I^2)t$, a diffusion approximation V to X is given by

$$dV = (\lambda_E a_E - \lambda_I a_I)dt + \sqrt{(\lambda_E a_E^2 + \lambda_I a_I^2)}dW, \quad V < V_\theta, \quad V(0) = V_0.$$

(Note that W , a standard Wiener process, is equivalent to a standard Brownian motion B).

Putting $\mu = \lambda_E a_E - \lambda_I a_I$ and $\sigma^2 = \lambda_E a_E^2 + \lambda_I a_I^2$, it can be shown that V will reach $V_\theta > V(0)$ with probability one if and only if $\mu \geq 0$; that is, the net excitatory drive is greater or equal to the net inhibitory drive. This is not true for more realistic models. When $\mu \geq 0$ the probability density of the time for V to get from a value $V(0) < V_\theta$ to threshold is the *inverse Gaussian*

$$f(t) = \frac{(V_\theta - V(0))}{\sqrt{2\pi\sigma^2 t^3}} \exp\left[-\frac{(V_\theta - V(0) - \mu t)^2}{2\sigma^2 t}\right], t > 0.$$

Gluss Model - Ornstein-Uhlenbeck process (OUP)

The jump process model with exponential decay given by (1.3.2) can be similarly approximated by a diffusion model which is, for subthreshold V

$$dV = \left(-\frac{V}{\tau} + \mu_1\right)dt + \sqrt{\mu_2}dW. \quad (1.3.5)$$

This defines an **Ornstein-Uhlenbeck process**, which as a neuronal model was first derived and analyzed by Gluss (1967). Here V has continuous paths and, if unrestricted, the same first and second moments as X . The jump process X and the diffusion process V may get to the same values, such as a threshold for an action potential, at about the same time, but in many cases this will be far from the truth, depending on the values of the four parameters $\lambda_E, a_E, \lambda_I$ and a_I - see Tuckwell and Cope (1980) for a complete discussion. Thus **extreme caution** must be exercised if using a diffusion model such as (1.3.5) to obtain input-output relations for neurons. Roy and Smith (1969) solved the difficult problem of obtaining an exact expression for the mean firing time in the case of a constant threshold. Even recently this model has attracted much attention (Plesser and Tanaka, 1997; Plesser and Gerstner, 2000; Lansky and Sacerdote, 2001; Feng *et al.*, 2001). The OUP has also been shown to be a suitable approximation for **channel noise** (Tuckwell, 1987a).

The general theory of diffusion processes is broad and often quite abstract. Such fundamental matters as (appropriate) definition of stochastic integral and boundary classifications are important but generally outside the domain of most computational neuroscientists. Fortunately such matters can be sidestepped as most modeling is pragmatic and will involve trial and error **simulation methods** using software packages. However, it is useful to realize that diffusion processes, whether of one or several dimensions, have an associated linear partial differential equation satisfied by the transition probability function or its density. This is also true for Markov jump processes, but the corresponding equations are more complicated and far less studied.

Letting $\mathbf{X}(t)$ be a vector with n components, all neuronal ordinary differential equation models in which the input current is approximated by white noise have the general form

$$d\mathbf{X}(t) = \mathbf{f}(\mathbf{X}(t), t)dt + \mathbf{g}(\mathbf{X}(t), t)d\mathbf{W}(t),$$

where \mathbf{f} also has n components, \mathbf{g} is an $n \times m$ matrix and \mathbf{W} is an m -vector of (possibly) independent standard Wiener processes. This form covers nonlinear models such as Hodgkin-Huxley, Fitzhugh-Nagumo etc. and certain network approximations. Let $p(\mathbf{y}, t|\mathbf{x}, s)$ be the transition probability density function of the process \mathbf{X} , defined with $s < t$ through, $p(\mathbf{y}, t|\mathbf{x}, s)d\mathbf{y} = \Pr\{\mathbf{X}(t) \in (\mathbf{y}, \mathbf{y}+d\mathbf{y})|\mathbf{X}(s) = \mathbf{x}\}$. Then p satisfies two partial differential equations. Firstly, the **forward Kolmogorov equation** (sometimes called a Fokker-Planck equation)

$$\frac{\partial p}{\partial t} = - \sum_{k=1}^n \frac{\partial}{\partial y_k} [f_k(\mathbf{y}, t)p] + \frac{1}{2} \sum_{l=1}^n \sum_{k=1}^n \frac{\partial^2}{\partial y_k \partial y_l} [(\mathbf{g}(\mathbf{y}, t)\mathbf{g}^T(\mathbf{y}, t))_{kl}p],$$

where superscript T denotes transpose. Secondly, holding forward variables fixed gives the **backward Kolmogorov equation**

$$\frac{\partial p}{\partial s} = - \sum_{k=1}^n [f_k(\mathbf{x}, s)] \frac{\partial p}{\partial x_k} - \frac{1}{2} \sum_{l=1}^n \sum_{k=1}^n (\mathbf{g}(\mathbf{x}, s)\mathbf{g}^T(\mathbf{x}, s))_{kl} \frac{\partial^2 p}{\partial x_k \partial x_l}.$$

We may write this as

$$\frac{\partial p}{\partial s} + L_{\mathbf{x}}p = 0,$$

to define the operator $L_{\mathbf{x}}$ which is useful in finding first passage times such as the time to reach a specified electrophysiological state - see Tuckwell (1989) for details.

An example - analytical results for the OUP

For the model (1.3.5), the analytical theory is simple and the resulting differential equations are easily solved. Putting the time unit as the membrane time constant, the forward equation is

$$\frac{\partial p}{\partial t} = - \frac{\partial}{\partial y} [(-y + \mu_1)p] + \frac{\mu_2}{2} \frac{\partial^2 p}{\partial y^2}.$$

In Feller's terminology, the points at $y = \pm\infty$ are *natural* boundaries and p must vanish there. All other points are *regular* so they are visited with probability one in a finite time. The **unrestricted process** is Gaussian and its distribution is easily found using the mean and variance for (1.3.2). If a **threshold** is put at $y = a$, an absorbing condition $p(a, t|x, s) = 0$ gives a solution from which the neuronal firing time distribution can be found. Alternatively one may solve on $(-b, a)$ with $a, b > 0$ the equation for the mean exit time from $M(x)$ starting at x from $(-b, a)$

$$L_x M(x) = \frac{\mu_2}{2} \frac{d^2 M}{dx^2} + (\mu_1 - x) \frac{dM}{dx} = -1$$

with boundary conditions $M(-b) = M(a) = 0$. Letting $b \rightarrow \infty$ gives the mean time for the neuronal depolarization from rest to get to the threshold for an action potential. The solution is in a series of parabolic cylinder functions (Roy and Smith, 1969).

Spatial diffusion models - SPDE's

If the postsynaptic potentials are not too large and fairly frequent, a diffusion approximation for a spatial model such as (1.3.4) may be employed. Linear models of this kind may involve distributed one-parameter white noises representing each synaptic input or group of synaptic inputs

$$\begin{aligned} \frac{\partial V}{\partial t} = & -V + \frac{\partial^2 V}{\partial x^2} + (V - V_E) \sum_{i=1}^{n_E} \delta(x - x_{E,i}) (a_{E,i} \lambda_{E,i} + |a_{E,i}| \sqrt{\lambda_{E,i}} \frac{dW_{E,i}}{dt}) \\ & + (V - V_I) \sum_{j=1}^{n_I} \delta(x - x_{I,j}) (a_{I,j} \lambda_{I,j} + |a_{I,j}| \sqrt{\lambda_{I,j}} \frac{dW_{I,j}}{dt}). \end{aligned}$$

Simplified versions of this and similar models were analyzed in Tuckwell *et al.* (1984, 2002). Alternatively, if the synapses are very densely distributed, a two-parameter white noise may be employed as an approximation:

$$\frac{\partial V}{\partial t} = -V + \frac{\partial^2 V}{\partial x^2} + f(x, t) + g(x, t) \frac{\partial^2 W}{\partial t \partial x},$$

where $W(t, x)$ is a standard two-parameter Wiener process. For details see Tuckwell and Walsh (1983). Nonlinear spatial models are discussed in Section 1.3.4.

1.3.3 Jump-diffusion models

It is possible that some inputs to a neuron, including channel noise are frequent and of small amplitudes whereas others are less frequent and large amplitude, such as occur at certain large and critically placed synapses or groups of synapses of the same type. Such a model was introduced by Tuckwell (1981) and in its simplest form has the stochastic equation

$$dV = -V dt + a_E dN_E + a_I dN_I + \sigma dW,$$

where the unit of time is the time constant. The corresponding equations for the n -th moments of the firing time for an initial potential x can be obtained by solving:

$$\frac{\sigma^2}{2} \frac{d^2 M_n}{dx^2} - x \frac{dM_n}{dx} + \lambda_E M_n(x + a_E) + \lambda_I M_n(x - a_I) - (\lambda_E + \lambda_I) M_n(x) = -n M_{n-1}(x),$$

$n = 1, \dots$, with $M_0 = 1$. Here λ_E, λ_I are the mean frequencies of excitation and inhibition, respectively. However, for particular parameter values, solutions can be readily obtained by simulating the Poisson and white noise inputs.

1.3.4 Perturbation of deterministic dynamical systems

One of the key topics addressed in the theory of differential equations or dynamical systems is the asymptotic (large time) effect of a small disturbance or perturbation on a reference solution or orbit, such as an equilibrium point or limit cycle. The fundamental methods employed for deterministic systems are called Lyapunov's first and second methods. For stochastic dynamical systems, which have an extra dimension, results on stability are naturally more difficult to obtain (Arnold, 1998). Here we consider the effects (or methods of determining them) on neuronal systems of perturbations with small Gaussian white noise.

Firing time of a model neuron with small white noise

Consider a OUP model with threshold θ and stochastic equation

$$dV = (-V + a)dt + b dW.$$

It should be noted that in the absence of noise and in the absence of a threshold, the steady state potential is a . If $a \leq \theta$ the deterministic neuron never fires whereas if $a > \theta$ the firing time is

$$T = T_R + \ln\left(\frac{\alpha}{\alpha - 1}\right),$$

where $\alpha = \frac{a}{\theta}$ and T_R is the refractory period. If we define the small noise parameter $\epsilon^2 = \frac{b}{\theta}$ then using perturbation techniques (Wan and Tuckwell, 1982) the mean and variance of the firing time can be found to order ϵ^2 as follows.

Steady state well above threshold. When $\alpha \gg \epsilon + 1$,

$$E[T] = T_R + \ln\left(\frac{\alpha}{\alpha - 1}\right) - \frac{\epsilon^2}{4} \left[\frac{1}{(\alpha - 1)^2} - \frac{1}{\alpha^2} \right],$$

$$Var[T] \approx \frac{\epsilon^2}{2} \left[\frac{1}{(\alpha - 1)^2} - \frac{1}{\alpha^2} \right].$$

These results show clearly how small noise reduces the mean interspike interval.

Steady state well below threshold. When $\alpha \ll 1 - \epsilon$, the expectation of the interspike interval is

$$E[T] \approx T_R + \frac{\epsilon\sqrt{\pi}}{1 - \alpha} \exp\left[\frac{(1 - \alpha)^2}{\epsilon^2}\right],$$

and the variance is

$$Var[T] \approx \frac{\epsilon^2\pi}{(1 - \alpha)^2} \exp\left[\frac{2(1 - \alpha)^2}{\epsilon^2}\right],$$

Many other results are given in the aforementioned reference, which includes an exhaustive study of the dependence of the **coefficient of variation** of T on the input parameters.

Differential equations for moments under Gaussian white noise perturbations

Ordinary differential equations have been derived for the asymptotic moments of the dynamical variables in a general system of coupled (nonlinear) stochastic differential equations with white noise perturbations of the form

$$dX_j = f_j(\mathbf{X}, t)dt + \sum_{k=1}^m g_{jk}(\mathbf{X}, t)dW_k$$

where the W_k are standard Wiener processes - see Rodriguez and Tuckwell (1996). For example, consider the Fitzhugh-Nagumo system

$$dX = [f(X) - Y + I]dt + \beta dW$$

$$dY = b[X - \gamma Y]dt,$$

where $f(X) = kX(X - a)(1 - X)$. The means of X and Y , denoted by m_1 and m_2 respectively, satisfy the equations

$$dm_1/dt = f(m_1) - m_2 + f''(m_1)S_1/2 + I(t)$$

$$dm_2/dt = b(m_1 - \gamma m_2)$$

where S_1 is the variance of X . Denoting the variance of Y by S_2 and the covariance of X and Y by C_{12} we also have

$$dS_1/dt = 2f'(m_1)S_1 - 2C_{12} + \beta^2$$

$$dS_2/dt = 2b(C_{12} - \gamma S_2)$$

and

$$dC_{12}/dt = bS_1 - S_2 + C_{12}[f'(m_1) - \gamma b].$$

This system of five ordinary differential equations may be easily solved and gives good agreement with moments from simulations (see Tuckwell and Rodriguez, 1998). The method can also be used for small biological neuronal networks.

White noise perturbation of spatial nonlinear neuronal models

The analysis of spatial neuronal nonlinear model equations under the effects of white noise perturbations has been performed for both scalar and vector forms of the Fitzhugh-Nagumo model. In all cases a perturbation expansion was used to obtain the moments of the dynamical variables. As a simple example consider the Fitzhugh-Nagumo system without recovery driven by white noise of small amplitude:

$$u_t = u_{xx} + f(u) + \epsilon(\alpha + \beta W_{xt})$$

where W is a two-parameter Wiener process. An expansion in powers of ϵ

$$u = u_0 + \sum_{k=1}^{\infty} \epsilon^k u_k$$

yields a recursive system of linear stochastic partial differential equations for the u_k . Solving the system recursively yields series expressions for the moments and spectrum of the potential. These results, results on the full Fitzhugh-Nagumo system of SPDE's and a general result on perturbation of a nonlinear PDE with white noise are derived in Tuckwell (1987, 1988b and 1992).

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