PARAMETER ESTIMATION FOR RANDOMLY STOPPED DIFFUSION PROCESSES AND NEURONAL MODELING

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SUMMARY

Itô-type stochastic differential equations are developed to describe some aspects of the electrical activity of nerve cells or neurons. It is argued that the subthreshold behavior of the membrane potential of a neuron may be modeled as a diffusion process observed over a random interval. The models contain parameters which reflect important neurophysiological properties. Given independent and identically distributed copies or trajectors of such processes, maximum likelihood estimators of the parameters are explicitly derived and their asymptotic properties such as strong consistency and asymptotic normality are studied.

Although inference for diffusion processes observed over random intervals is of interest in its own right, it is constructive to present his material within the context of applications to neurophysiology to demonstrate its wide applicability. Furthermore, these applications motivate further interesting problems in inference for stochastic processes.

1. Introduction. The objective of this paper is to develop stochastic models of the subthreshold somal transmembrane potential of neurons in the nervous system. These models are Itô-type stochastic differential equations that include parameters which reflect important neurophysiological properties such as effective somal-membrane time constant, potency or amplitude of post-synaptic potentials (PSPs), and variability of synaptic input. Maximum likelihood estimators of these parameters are derived and their asymptotic properties such as consistency and asymptotic normality are studied. Problems concerning the estimation of such parameters from experimentally generated data are considered. Applications of the methods of inference for stochastic processes (developed in the paper) to studies of neuronal plasticity and in particular to synaptic plasticity as a model of neuronal learning are briefly discussed. These methods then offer quantitative means to study plasticity in the nervous system and are expected to shed light on the manner in which the nervous system develops in response to experience. It is clear that detailed knowledge of the mechanics of the manner in which neurons integrate input is an important step toward identifying the mechanisms underlying neuronal learning (Baranyi and Feher, 1981). Furthermore, building, refining and employing models which appropriately describe the electrical behavior of neurons is an important step towards building artificial systems which simulate neuronal information processing. It is clear then that the neuronal models and stochastic methods developed here are essential tools in studies of neuronal learning and artificial intellegence.

More specifically, the subthreshold electrical behavior of the somal-membrane potential of a neuron is modeled as a solution of stochastic differential equations (SDE) driven by Wiener as well as Poisson processes. These models are appropriate for describing the neuron's behavior during spontaneous as well as stimulus driven activity. The method of maximum likelihood (ML) is used to derive estimators of the model's parameters. In this respect the problem of mutual absolute continuity of probability measures induced by solutions of SDEs on the appropriate measurable spaces is briefly considered. Explicite formulae of the ML estimators are derived, where the processes under consideration are assumed to be observed over random intervals. It is also assumed that several independent and identically distributed (iid) copies of the process are observed. Asymptotic properties of the estimators such as consistency and asymptotic normality as the number of observed copies tends to infinity are studied in detail.

In Section 2 a brief introduction of the relevant neurophysiological notions as well as a description of a neuronal model are given. The morphology of nerve cells is briefly described and the relevant aspects of physiological and dynamic processes involved in the subthreshold activity of the somal-membrane potential are addressed. In Section 3, a stochastic neuronal model is developed where the membrane potential is expressed in terms of the amplitudes and rates of occurrence of PSPs. It is also assumed that in the absence of synaptic activity, the membrane potential decays exponentially. For this reason, this neuronal model is known as the leaky integrator, and the membrane potential is modeled

as a stationary Markov process with discontinuous sample paths. These discontinuities occur at the moments of arrival of the PSPs. This model may contain thousands of parameters which make it inapproprite for parameter estimation purposes. Under the appropriate conditions, i.e. if the amplitudes of the PSPs are assumed to be very small and their rates of occurrence are very high, the discontinuous model may be approximated by a diffusion model. That is, the membrane potential is modeled as a solution of a stochastic differential equation with constant coefficients which is driven by a Wiener process. This model is particularly appropriate for describing the subthreshold behavior of the membrane potential of spontaneously active neurons which receive extensive synaptic input with small PSP amplitudes occurring at high rate and with no dominating PSPs with relatively large amplitudes.

In Section 4, the problem of estimation of parameters of the diffusion model is considered. In this respect, briefly discussed is the problem of absolute continuity of probability measures induced by stationary diffusion processes as solutions of SDEs with respect to probability measures induced by Wiener processes on the measurable space of all continuous functions. The likelihood function is then presented and the ML estimators are explicitly derived. In Section 5, strong consistency and asymptotic normality of the MLEs are established. Finally, in Section 6, more general stochastic neuronal models are presented. It is hoped that this will stimulate further interest in considering the problem of parameter estimation for these extended models.

2. A temporal neuronal model. The nerve cell or neuron is a basic anatomical and functional unit for information processing in the nervous system. Morphologically, a neuron consists of three essential regions: The cell body (or soma), the dendrites (or dendretic tree), and the axon. The soma contains the nucleus and many of the other organelles involved in metabolic processes. The dendrites form a series of short highly branched out growths from the cell body. The dendrites and the soma are sites of most specialized junctions (or synapses) where input is received from other neurons. The axon is an extension which exists at the soma at an area called the initial segment (or axon hillock). Near its end, the axon branches into numerous axon terminals, which are responsible for transmitting electrical signals from the neuron to other cells. The junction between two neurons is call the synapse which is a specialized junction between two neurons where the electrical activity of one neuron influences the electrical activity of the other. Most synapses occur between the axonal terminals of one neuron (called the presynaptic neuron) and the dendrites and the cell body of a second one (called the postsynaptic neuron). A neuron in the central nervous system possesses between 5,000 and 100,000 synapses. See Kandel and Schwartz (1981), and Kuffler and Nicholls (1985) for more details concerning the neurophysiology and morphology of neurons.

The entire surface of the neuron is bounded by an electrochemically sensitive membrane, which is selectively permeable to ions. Across the neuronal membrane there exists a difference in potential due to the presence of organic and inorganic electrically charged ions inside as

well as outside the cell with different concentrations. This difference in ionic concentrations is kept by an active metabolism. Among the important inorganic ions are sodium (Na^+), potassium (K^+), and chloride (Cl^-). The transmembrane potential (hereafter called membrane potential) is regulated by active as well as passive membrane transport mechanisms. In the absence of input to the neuron, the membrane potential is kept at a certain level called the resting potential which is about 60 to 70 mV, with the inside negative, due to a higher concentration of K^+ and lower concentration of Na^+ on the inside, relative to the outside.

When a (chemical) synapse is activated due to the arrival of electrical signals along the axon of the presynaptic neuron, a chemical substance called neural transmitter is released into the synaptic cleft (this is a gap separating the pre- and post-synaptic membranes). The transmitter then crosses the synaptic cleft and combines with the receptor sites of the postsynptic membrane and produces a change in potential. This potential change is called post-synaptic potential (PSP). If the PSP results in reducing the potential difference in the post-synaptic membrane (i.e. if the membrane is depolarized) the PSP is called an excitatory post-synaptic potential (EPSP). On the other hand, if the PSP results in increasing the potential difference across the post-synaptic membrane (hyperpolarization), it is called an inhibitory post-synaptic potential. As the EPSPs depolarize the membrane its permeability to both inon Na^+ and K^+ increases, but the increase in permeability to Na^+ is much faster than to K^+. If a certain potential level called the neuron's threshold (-35 to -45 mV) is reached, the

of Na^+ into the cell rapidly depolarizes the membrane, the inside becomes +30 mV relative to the outside within 1 millisecond or less. As the permeability to K^+ exceeds that of Na^+, the membrane potential is reset towards its resting value. This rapid stereotypical process is called an action potential. It is also said, in this case, that the neuron has fired. The action potential is transmitted along the axon down to the axonal terminals causing the release of neural transmitters which generates post-synaptic potential in the post-synaptic neurons. A single EPSP (in a motor neuron) is estimated to be only 0.5 mV, whereas changes of up to 25 mV are necessary to depolarize the membrane from its resting level to threshold. That is, the amplitude of an EPSP is smaller than 2% of the voltage change needed to reach threshold (Calvin, 1975). Since a single synaptic event usually does not bring the post-synaptic membrane potential to its threshold level, an action potential can be generated only by combined effects of many synapses. Of the thousands of synapses on any neuron, probably hundreds are active almost simultaneously so that their effects can summate. Between synaptic events, the membrane potential decays to a resting potential. The membrane potential at any moment, then, is the result of all synaptic activity influencing it at that time. The time interval between the moment when the membrane potential is at a resting level until it reaches threshold is obviously random in nature. In fact it is a stopping time. The task then is to study the problem of estimating the parameters of a stochastic process which is observed over random intervals using several copies or trajectories of the process. A simplified neuronal model is considered in the next section.

3. A temporal stochastic neuronal model. The state of the neuron is assumed to be characterized by the difference in potential across its membrane (membrane potential, for short) near a spatially restricted area of the soma in which the sodium conductance, per unit area, is high relative to that of the remaining somal membrane. This spatially restricted area is called the trigger zone (also initial segment or axon hillock). The membrane potential at any point of time t is subject to instantaneous changes due to the occurrence of post-synaptic potentials (PSPs) which are assumed to arrive at the initial segment according to Poisson processes. This assumption is justified by the well-known fact that if a large number of sparse point-processes are superposed, the result is approximately a Poisson process. The first proof of this result is by Khintchine (1960). It is limited to stationary point-processes and gives only sufficient conditions. Griglionis (1963) extended these results by considering arbitrary point-processes as components and gave necessary and sufficient conditions for convergence to a (possibly non-stationary) Poisson process. Indeed, assume that the number of post-synaptic potentials generated at the synapse at location (n,j) on the neuronal surface is denoted by N_{nj} and that $j=1,2,\ldots,k_n$, and $n=1,2,\ldots$.

Next consider lumped groups of synapses (which belong to the same spatial area together) and the behavior of the resulting process

$$N_n = N_{n1} + N_{n2} + \ldots + N_{nk_n}, \quad n=1,2,\ldots.$$

Griglionis (1963) showed that if

$$\lim_{n\to\infty} \sup_{1\le j\le k_n} P\{N_{nj}(B) \ge 1\} = 0$$

for bounded intervals B of the real line, then the superposition process N_n converges weakly to a Poisson process with mean measure λ if and only if

$$\lim_{n\to\infty} \sum_{j=1}^{k_n} P\{N_{nj}(B) = 1\} = \lambda(B)$$

and

$$\lim_{n\to\infty} \sum_{j=1}^{k_n} P\{N_{nj}(B) \ge 2\} = 0$$

for every finite interval B of the real line. On this basis the PSPs are assumed to arrive at the initial segment according to Poisson processes. See Cinlar (1972) for a review of such results.

Now assume that the membrane potential, V(t), at any point of time t is a random variable which is subject to instantaneous changes due to the occurrence of PSPs of two different types:

(1) Excitatory post-synaptic potentials (EPSPs) which occur according to mutually independent Poisson processes $P(\lambda_k^e, t)$ with rates λ_k^e, $(k=1,2,\ldots,n_1)$, each accompanied by instantaneous displacement of V(t) by a constant amount $\alpha_k^e > 0$ $(k=1,2,\ldots,n_1)$. That is, the dependence on reversal potential is ignored at the moment.

(2) Inhibitory post-synaptic potentials (IPSPs) which occur according to mutually independent Poisson processes $P(\lambda_k^i,t)$, with rates λ_k^i and amplitudes $\alpha_k^i > 0$ $(k=1,2,\ldots,n_2)$.

Between PSPs, V(t) decays exponentially to a resting potential V_0 with a membrane time constant τ.

The PSPs are assumed to be summed linearly at the trigger zone, and when V(t) reaches a certain constant level S, called the neuron's threshold, an action potential is generated or elicited. Following the action potential the neuron is reset to a resting potential.

Based on this physical model, which takes into account only temporal aspects of synaptic inputs, a stochastic model of V(t) is formally built as follows: in the absence of synaptic input, V(t) decays exponentially, i.e., in a small period of time $(t,t + \Delta t]$, V(t) changes by $-\rho V(t)\Delta t$, where $\rho = \tau^{-1}$. On the other hand, the displacement in V(t) due to the arrival of an EPSP during $(t,t + \Delta t]$ is equal to

$$\alpha^e[P(\lambda^e;t + \Delta t) - P(\lambda^e;t)].$$

Similarly, the displacement in V(t) due to the arrival of an IPSP in $(t,t + \Delta t]$ is given by

$$-\alpha^i[P(\lambda^i;t + \Delta t) - P(\lambda^i;t)].$$

The increment $\Delta V(t) = V(t + \Delta t) - V(t)$ may be modeled as

$$\Delta V(t) = -\rho V(t)\Delta t + \sum_{k=1}^{n_1} \alpha_k^e [P(\lambda_k^e; t + \Delta t) - P(\lambda_k^e, t)]$$

$$- \sum_{k=1}^{n_2} \alpha_k^i [P(\lambda_k^i; t + \Delta t) - P(\lambda_k^i, t)].$$

As the time increment becomes small, the above model takes the form

$$(3.1) \qquad dV(t) = -\rho(V(t)dt + \sum_{k=1}^{n_1} \alpha_k^e \, dP(\lambda_k^e; t) - \sum_{k=1}^{n_2} \alpha_k^i \, dP(\lambda_k^i; t),$$

$V(0) = V_0$. The solution of (3.1) is a homogeneous Markov process with discontinuous sample paths.

In this model it is assumed that the tens of thousands of synapses are replaced or approximated by just a few thousand ideal synapses with PSPs occurring according to independent Poisson processes. It may be constructive in certain cases, though, to approximate model (3.1) by a model which contains only a few identifiable, physiologically meaningful parameters for the purpose of parameter estimation using experimentally generated data.

Models in which the discontinuities of the membrane potential, V(t), are smoothed out have been sought where the discontinuous model (3.1) is approximated by a diffusion model (Ricciardi and Sacerdote , 1979; Hanson and Tuckwell, 1983). These approximations are particularly suited for neurons with extensive synaptic input and no dominating

synaptic events with large amplitudes. The approximation to a diffusion model is accomplished by allowing the amplitudes α^e, α^i of the EPSPs and IPSPs to become small and rates λ^e and λ^i to become large in a certain manner.

Kallianpur (1983) rigorously established this diffusion approximation using the functional central limit theorem of Liptser and Shiryayev (1980, 1981). This was simply accomplished by solving the stochastic differential equation (3.1) and then compensating the solution process which is a homogenous Markov process with discontinuous sample paths. The compensated process is easily seen to be a semimartingale. Upon indexing the parameters α^e, α^i, λ^e, and λ^i by n=1,2,... and imposing the appropriate conditions on the asymptotic behavior of these parameters, the Liptser-Shiryayev functional central limit theorem for semimartingales may be applied. To make this protocole precise, the following notations are needed. Let (Ω, F, P) be a probability space and $\{F_t, 0\leq t\leq T\}$, for some fixed T>0, be a filteration, i.e. a nondecreasing family of δ-field contained in $F(F_s<F_t\leq F, s\leq t)$. Also assume that F is P - complete, F_t is augmented by the sets in F having zero P-measure for all t, and $\{F_t\}$ is right continuous, i.e. $F_t=F_{t+}$ for all t, where $F_{t+}=\bigcap_{s>t}F_s$. Let $(D,\mathcal{D})$ be the measurable space of all right-continuous functions defined on the real line, $x=\{x(t),t\geq 0\}$, having left-hand limits endowed with the Skorokhod topology. A stochastic process $X=\{X(t),t\geq 0\}$ is said to be adapted to a filtertion $F=\{F_t,t\geq 0\}$, if X(t) is F_t - measurable for each $t\geq 0$. The notation $(X(t),F_t)$ will be used to indicate that X(t) is F_t - measurable.

A stochastic process $\{M(t),F_t,t\geq 0\}$ is called a martingale if the following two conditions hold:

$$(i)\ E\,|M(t)|<\infty\ ,\ t\geq 0$$

$$(ii)\ E(M(t)|F_s)=M(s),\ s<t.$$

A local martingale $M=(M(t),F_t)$ is an adapted process for which one can find a sequence of stopping times $\{\tau_n,n\geq 1\}$ increasing to infinity such that the stopped processes $M^n=(M(t\wedge\tau_n),F_t)$, $n\geq 1$ are martingales. Let $P(F)$ be the smallest σ-field generated by F-adapted processes with continuous trajectories. An F-adapted process $\{X(t),t\geq 0\}$ is said to be predictable if the mapping $(t,\omega)\to X(t,\omega)$ is measurable with respect to the σ-field $P(F)$. (Processes with left-hand continuous trajectories are predictable processes.)

Let $M(F,P)$, $M_{loc}(F,P)$, $M^c_{loc}(F,P)$, $M^d_{loc}(F,P)$, $M^2_{loc}(F,P)$ denote the classes of uniformly integrable, local, continuously local, purely discontinuously local, and locally square-integrable martingales $X=\{X(t),F_t\ ,t\geq 0\}$, respectively. Next, denote by $B_{loc}\ (F,P)$ the class of stochastic processes $B=(B(t),F_t)$ which have bounded variation on each finite time interval. Let $E_{loc}(F,P)$ be a class of locally integrable processes $E=(E(t),F_t)$. Note that each predictable process of class $B_{loc}\ (F,P)$ belongs to $E_{loc}(F,P)$. If $E\in E_{loc}(F,P)$, there exists a predictable process $\tilde{E}=(\tilde{E}(t),F_t)$ such that $E-\tilde{E}\in M_{loc}(F,P)$. The process $\tilde{E}$ is called the compensator of the process E. A stochastic process $X=(X(t),F_t)$ is said to be a semimartingale if it can be represented in the form

$$X(t)=B(t) + M(t), t\geq 0 \tag{3.2}$$

where $B=(B(t),F_t) \in B_{loc}(F,P)$ and $M=(M(t),F_t) \in M_{loc}(F,P)$. A semimartingale $X=\{X(t),F_t)t>0\}$ also have the canonical representation

$$X(t)=E(t) + M_t^c + \int_0^t \int_{0<|x|<1} x\,\mu(ds,dx) + \int_0^t \int_{0<|x|\leq 1} x\,(\mu-\upsilon)(ds,dx) \tag{3.3}$$

where $E=(E(t),F_t) \in E_{loc}(P,F)$, $M^c=(M^c(t),F_t) \in M^c_{loc}(P,F)$, $\mu(dt,dx)$ is the integral random measure of jumps of the semimartingale X,

$$\mu((0,t],\Gamma)= \sum_{0<s\leq t} I(\Delta X_t s) \in \Gamma), \Gamma \in B(R\setminus\{0\}),$$

$\Delta X(s)=X(s)-X(s-)$, and $\upsilon(dt,dx)$ is the compensator or the dual predictable projection of the measure μ. See Liptser and Shiryayev (1980) for a more detailed discussion of the canonical representation (3.3). Finally, let $\{W(t),F_t\}$ be a standard Wiener process, i.e. a continuous square-integrable martingale with $W(0)=0$, and $E[(W(t)-W(s))|F_s] = (t-s)$ a.s. $[P]$, $t\geq s$.

Now, returning to establishing the diffusion approximation of model (3.1), let

$$P(t) = \sum_{k=1}^{n_1} \alpha_k^e P(\lambda_k^e,t) - \sum_{k=1}^{n_2} \alpha_k^i P(\lambda_k^1,t),$$

and

$$E[P(t)] = (\sum_{k=1}^{n_1} \alpha_k^e \lambda_k^e - \sum_{k=1}^{n_2} \alpha_k^i \lambda_k^i)t = \lambda t.$$

Notice that $M(t) = P(t) - \lambda t$ is a martingale with $M(0) = 0$, and variance

$$\langle M \rangle_t = [\sum_{k=1}^{n_1} (\alpha_k^e)^2 \lambda_k^e + \sum_{k=1}^{n_2} (\alpha_k^i)^2 \lambda_k^i]t = \sigma^2 t.$$

Substituting in (3.1), we have

$$dV(t) = -\rho V(t) + dP(t), \tag{3.4}$$

$V(0) = V_0$. The solution of (3.2) is easily verified to be

$$V(t) = e^{-\rho t} V_0 + e^{-\rho t} \int_0^t e^{\rho s} \, dP(s). \tag{3.5}$$

From the definition of the martingale M given above, (3.5) may be written as

$$V(t) = e^{-\rho t}[V_0 + \frac{\lambda}{\rho} (e^{\rho t} - 1) + \int_0^t e^{\rho s} \, dM(s)]. \tag{3.6}$$

It is clear from (3.6) that V(t) is a semimartingale (see the canonical representation (3.3)). Now let

$$\lambda_n = \sum_{k=1}^{n_1} \alpha_k^e(n)\, \lambda_k^e(n) - \sum_{k=1}^{n_2} \alpha_k^i(n)\, \lambda_k^i(n),$$

$$\sigma_n^2 = \sum_{k=1}^{n_1} [\alpha_k^e(n)]^2 \lambda_k^e(n) + \sum_{k=1}^{n_2} [\alpha_k^i(n)]^2 \lambda_k^i(n),$$

and rewrite (3.4) as

$$(3.7) \qquad dV^{(n)}(t) = -\rho V^{(n)}(t)dt + dP^{(n)}(t),\ V(0) = V_0.$$

The solution of (3.7) may be written in the form

$$V^{(n)}(t) = e^{-\rho t}[V_0 + \rho^{-1}\lambda_n(e^{\rho t} - 1) + \int_0^t e^{\rho s}\, dM^{(n)}(s)],$$

where $V^{(n)}(t)$ is a semimartingale. Using the functional central limit theorem for semimartingales of Liptser and Shiryayev (1980, 1981), Kallianpur (1983) showed that if

$$\lambda_n \to \mu \text{ and } \sigma_n^2 \to \sigma^2 \text{ as } n \to \infty,$$

then

$$P(V^{(n)})^{-1} \Rightarrow PV^{-1} \quad (\text{or } V^{(n)} \xrightarrow{D} V),$$

where V is the solution of the Örnstein-Uhlenbeck equation

$$dV(t) = (-\rho V(t) + \mu)dt + \sigma\, dW(t), \tag{3.8}$$

$V(0) = V_0$, and $W(t)$ is a standard Wiener process, if and only if for every $0<\varepsilon<1$

(A)
$$\sum_{k:\alpha_k^e(n)>\varepsilon} \lambda_k^e(n) + \sum_{\ell:\alpha_\ell^i(n)>\varepsilon} \lambda_\ell^i(n) \to 0$$

(B)
$$\sum_{k:\alpha_k^e(n)>\varepsilon} [\alpha_k^e(n)]^2\, \lambda_k^e(n) + \sum_{\ell:\alpha_\ell^i(n)>\varepsilon} [\alpha_\ell^i(n)]^2 \lambda_\ell^i(n) \to 0$$

as $n \to \infty$.

More general stochastic neuronal models have been considered by Walsh (1981) and Kallianpur and Wolpert (1984 a,b). Then models are discussed in Section 6. For stochastic models of trains of action potentials and related matters, see Habib and Sen (1985 a,b).

4. Parameter estimation for stationary diffusion processes. In this section the problem of absolute continuity and equivalence of probability measures induced, on the appropriate measurable spaces, by the solutions of Itô-type stochastic differential equations is briefly considered. Explicit formulae of the maximum likelihood estimators (MLE) of the model's parameters are given. The processes considered here are assumed to be continuously observed over random intervals. This is particularly appropriate for modeling the subthreshold behavior of the somal membrane potential, V(t), of model neurons, where V(t) is continuously observed starting at a certain point of time (e.g. the moment at which V(t) is equal to the resting potential) up to the moment it reaches the neuron's threshold.

First discussed are conditions for absolute continuity of probability measures induced by randomly stopped diffusion-type processes (which are more general than the ordinary diffusion processes) with respect to probability measures induced by Wiener processes. This problem has been considered by Sørensen (1983). The corresponding Radon-Nikodym derivative is then presented and maximum likelihood estimators of parameters in the special case of stationary diffusion processes are explicitly derived. It should be noted here that the non-stationary diffusion models (i.e. models with time dependent parameters) are more realistic for describing the behavior of neuronal membrane potentials. Studies fo the problems of maximum likelihood estimation of infinite dimensional parameters using Grenander's method of sieves may be found in Grenander (1981) and Habib and McKeague (1985).

Let (Ω,F,P) be a probability space, $\{F_t, 0 \leq t \leq T\}$ be a filtration, and $\{W(t), F_t, t \geq 0\}$ be a standard Wiener process. Let (C_T, A_T) denote the measurable space of continuous functions $x = \{x(t), 0 \leq t \leq T\}$ on $[0,T]$, $x(0) = x_0$ with σ-field $A_T = \sigma\{x: x(s), s \leq T\}$. Also let $A_t = \sigma\{x: x(s), s \leq t\}$. Suppose $X = \{X(t), F_t, 0 \leq t \leq T\}$ is a continuous stochastic process defined on (Ω, F, P). This implies in particular that $X(t)$ is F_t-measurable and that the sample functions of the process X belong to C_T with probability 1. The measure PX^{-1} defined on the σ-field A_T of Borel sets of C_T by

$$PX^{-1}(A) = P\{\omega: X(t,\omega) \in A\}, \quad A \in A_T$$

is called the probability measure induced by the process X on C_T. A measurable function $\tau: \Omega \to [0,\infty]$ is an F_t-stopping time if $[\tau \leq t] \in F_t$ for all $t \geq 0$. The random time τ being an F_t-stopping time, the "past" F_τ at time τ corresponding to the "history" F_t is defined at follows:

$$F_\tau = \sigma\{A \in F_\infty | A \cap [\tau \leq t] \in F_t \text{ for all } t \geq 0\}.$$

The following theorem, which is due to Sørensen (1983), gives sufficient conditions for the absolute continuity of probability measures induced by solution of two stochastic differential equations in the case where these solutions are diffusion-type processes observed over a random interval.

THEOREM 4.1 (Sørensen, 1983). Let X and Y be stochastic processes of the diffuson-type

$$dX(t) = A_t(X)dt + b_t(X)\, dW(t),$$

$$dY(t) = a_t(Y)dt + b_t(Y)\, dW(t),$$

$t \in [0,T]$ and let τ: $C_T \to [0,\infty]$ be an A_t-stopping time, such that:

(i) the non-anticipating functionals $a_t(.)$, $b_t(.)$ satisfy

$$|a_t(x)-a_t(y)|^2+|b_t(x)-b_t(y)|^2 \leq L_1\int_0^t |x(s)-y(s)|^2\, dK(s)+L_2|x(t)-y(t)|^2$$

$$a_t^2(x) + b_t^2(x) \leq L_1\int_0^t (1+x^2(s))\, dK(s) + L_2(1+x^2(t))$$

for each $t \in [0,T]$, $x, y, \in C_T$, where K is a right continuous increasing function such that $0 \leq K \leq 1$;

(ii) for any $t \leq \tau \wedge T$, the equation

$$b_t(X)\, B_t(X) = A_t(X) - a_t(X) \quad [P]$$

has a bounded solution with respect to $B_t(X)$;

$$\text{(iii)} \quad P(\int_0^{\tau\wedge T} B_t^2(X)dt < \infty) = P(\int_0^{\tau\wedge T} B_t^2(Y)dt < \infty) = 1.$$

Then

$$\mu_{\tau,X} \sim \mu_{\tau,Y}$$

and

$$\frac{d\mu_{\tau,Y}}{d\mu_{\tau,X}}(X) = \exp\left(-\int_0^{\tau\wedge T} b_t^+(X)^2(A_t(X) - a_t(X))\, dX_t\right.$$

$$\left. + 1/2 \int_0^{\tau\wedge T} b_t^+(X)^2(A_t(X) - a_t(X))^2 dt\right), \tag{4.1}$$

where

$$b^+(x) = \begin{cases} b_t^{-1}(X) & \text{if } b_t(X) \neq 0 \\ 0 & \text{if } b_t(x) = 0\,. \end{cases}$$

Now proceed to derive the maximum likelihood estimators of the parameters ρ and μ of the stationary diffusion neuronal model

$$dV(t) = (-\rho V(t) + \mu)dt + \sigma\, dW(t),\ 0 \leq t \leq T, \tag{4.2}$$

$V(0) = 0$, from the observation of n independent trajectories $(V_k(t), 0 < t \leq \tau_k)$, $k=1,2,\ldots,n$. Assume that $P(\tau_k < \infty) = 1$, $k=1,2,\ldots,n$. Then every $\tau\wedge T$ in Theorem (4.1) may be replaced by τ. From Theorem (4.1), the log-likelihood function is given by

$$L_n(\rho,\mu) = \sum_{k=1}^{n} \{\int_0^{\tau_k} (-\rho V_k(t) + \mu)\, dV_k(t)$$

$$-1/2 \int_0^{\tau_k} (-\rho V_k(t) + \mu)^2 dt\}. \tag{4.3}$$

The maximum likelihood estimators $\hat{\rho}$ and $\hat{\mu}$ of ρ and μ are the solutions of the equations

$$\frac{\partial L_n(\rho,\mu)}{\partial \rho} = -\sum_{k=1}^{n} \int_0^{\tau_k} V_k(t)\, dV_k(t) + \sum_{k=1}^{n} \int_0^{\tau_k} (-\rho V_k(t) + \mu)\, V_k(t)dt = 0, \tag{4.4}$$

and

$$\frac{\partial L_n(\rho,\mu)}{\partial \mu} = \sum_{k=1}^{n} \int_0^{\tau_k} dV_k(t) - \sum_{k=1}^{n} \int_0^{\tau_k} (-\rho V_k(t) + \mu)dt = 0, \tag{4.5}$$

i.e.

(4.6)

$$\hat{\rho}_n = \frac{[\sum_{k=1}^{n} \tau_k][\sum_{k=1}^{n} \int_0^{\tau_k} V_k(t)dV_k(t)] - [\sum_{k=1}^{n} \int_0^{\tau_k} V_k(t)dt][\sum_{k=1}^{n} \int_0^{\tau_k} dV_k(t)]}{[\sum_{k=1}^{n} \int_0^{\tau_k} V_k(t)dt]^2 - [\sum_{k=1}^{n} \tau_k][\sum_{k=1}^{n} \int_0^{\tau_k} V_k^2(t)dt]},$$

and

(4.7)

$$\hat{\mu}_n = \frac{\left[\sum_{k=1}^{n} \int_0^{\tau_k} V_k(t)dV_k(t)\right]\left[\sum_{k=1}^{n} \int_0^{\tau_k} V_k(t)dt\right] - \left[\sum_{k=1}^{n} \int_0^{\tau_k} V_k^2(t)dt\right]\left[\sum_{k=1}^{n} \int_0^{\tau_k} dV_k(t)\right]}{\left[\sum_{k=1}^{n} \int_0^{\tau_k} V_k(t)dt\right]^2 - \left[\sum_{k=1}^{n} \tau_k\right]\left[\sum_{k=1}^{n} \int_0^{\tau_k} V_k^2(t)dt\right]},$$

Using the fact that the membrane potential $V(t)$ is observed continuously over random intervals, the diffusion coefficient σ^2 may be estimated from an observed trajectory V_k $(k=1,2,\ldots,n)$ by the formula

$$(4.8)\quad \hat{\sigma}^2(k) = \frac{1}{\tau_k} \lim_{m\to\infty} \sum_{j=1}^{2^{m_k}} [V_k(\tau_{k-1}+jd_k2^{-m_k}) - V_k(\tau_{k-1}+(j-1)d_k2^{-m_k})].$$

This result may be proved using the corresponding result of Lévy for Brownian motion by transforming V_k via time substitutions into Brownian motion (or Wiener process). A natural estimate of σ^2 which employs all the observed trajectories is given by

$$(4.9)\qquad \hat{\sigma}_n^2 = \frac{1}{n} \sum_{k=1}^{n} \hat{\sigma}^2(k).$$

By sampling the trajectories $\{V_k(t),\ \tau_{k-1} \le t \le \tau_k\}$ $k=1,2,\ldots,n$, one obtains $\{V_{t_{k,1}}, V_{t_{k,2}},\ldots,V_{t_{k,m_k}}\}$ where $\tau_{k-1} \le t_{k,1} < \ldots < \tau_{k,m_k} \le \tau_k$,

for $k=1,2,\ldots,n$. In this case the integrals in (4.6) and (4.7) may be replaced by sums.

The above methods can be used to estimate the model's parameters for neurons before and after they are subjected to experiments of neuronal conditioning in order to measure the impact of this form of neuronal learning on the membrane time constant, on the drift parameter (which reflects the excess of excitation over inhibition in the synaptic input), and on the variability in synaptic input. It should be noted that this kind of quantitative study of neuronal learning has not been performed before.

5. Asymptotic properties of the ML estimators. In this section, strong consistency and asymptotic normality of the estimators $\hat{\rho}$ and $\hat{\mu}$ (derived in Section 4) are established as the number of observed trajectories or sample paths of the potential process increase to infinity. The sample paths are of course observed over random intervals. A large portion of the literature on inference for stochastic processes deals, though, with the case where only one trajectory or sample path is observed over an extended time interval. Our methods lend themselves to studies of the electrical activity of most types of neurons in the nervous system. It should be noted that there exist few types of neurons in the visual system and in particular in the retina (such as bipolar cells and amacrine cells) which do not spike, i.e. they do not generate action potential. The membrane potentials of these cells change continuously and gradually, and likewise induce gradual and continuous changes in the membrane potential of neighboring cells. This type of behavior of the membrane potential is called graded potential. Lánský (1983) discussed the problem of parameter estimation for Örnstein-Uholenbeck processes as models of neuronal membrane potential. The asymptotic properties of the estimators were discussed as the observation period tended to infinity. This type of inference is only appropriate for studies of the intracellular electrical behavior of non-spiking neurons. The methods discussed in this manuscript though are appropriate for most types of neurons in the nervous system and are therefore more widely applicable. For other discussions of the method of of maximum likelihood estimation for diffusion of processes see

Brown and Hewitt (1975) and Feigin (1976). For an extensive review of statistical inference for stochastic processes in general see Basawa and Prakasa Rao (1980). The following theorem establish strong consistency of the ML estimators.

THEOREM 5.1. The maximum likelihood estimators $\hat{\rho}_n$ and $\hat{\mu}_n$ of ρ and μ which are given by (4.6) and (4.7) are strongly consistent, i.e., $\hat{\rho}_n - \rho \to 0$ and $\hat{\mu}_n - \mu \to 0$ a.s.[P] as $n \to \infty$.

PROOF. Consider the stochastic process I(t) defined by

$$I(t) = \begin{cases} V(t) & \text{if } 0 \leq t \leq \tau \\ 0 & \text{if } \tau < t \leq T. \end{cases}$$

Form (4.4) and (4.5) it follows that

$$A_n + \rho B_n - \mu C_n = 0 \tag{5.1}$$

$$D_n + \rho C_n - \mu E_n = 0, \tag{5.2}$$

where

$$A_n = \frac{1}{n} \sum_{k=1}^{n} \int_0^{\tau_k} V_k(t)\, dV_k(t) \tag{5.3}$$

$$= \frac{1}{n} \sum_{k=1}^{n} \int_0^T I_k(t) [-\rho I_k(t) + \mu]dt + \frac{1}{n} \sum_{k=1}^{n} \int_0^T I_k(t) dW_k(t),$$

$$B_n = \frac{1}{n} \sum_{k=1}^{n} \int_0^T I_k^2(t)\, dt, \tag{5.4}$$

$$C_n - \frac{1}{n} \sum_{k=1}^{n} \int_0^T I_k(t)\, dt \tag{5.5}$$

$$D_n = \frac{-1}{n} \sum_{k=1}^{n} \int_0^T \rho\, I_k(t)dt + \frac{\mu}{n} \sum_{k=1}^{n} \tau_k + \frac{\sigma}{n} \sum_{k=1}^{n} \int_0^{\tau_k} dW_k(t), \tag{5.6}$$

$$E_n = \frac{1}{n} \sum_{k=1}^{n} \tau_k. \tag{5.7}$$

Now, from (5.1) and 5.2) if follows that

$$(C_n^2 E_n^{-1} - B_n)\hat{\rho}_n = A_n - C_n D_n E_n^{-1}$$

and hence from (5.3) it follows that

$$(C_n^2 E_n^{-1} - B_n)\hat{\rho}_n = - B_n \rho + \mu C_n + H_n - C_n D_n E_n^{-1},$$

where

$$H_n = \frac{\sigma}{n} \sum_{k=1}^{n} \int_0^T I_k(t)\, dW_k(t).$$

Therefore,

$$(5.8) \qquad (C_n^2 E_n^{-1} - B_n)\hat{\rho}_n = H_n + E_n^{-1} C_n (\mu E_n - D_n - \rho C_n).$$

Now, by the strong law of large numbers (Shiryayev, 1984), it follows that

$$(5.9) \qquad C_n = \frac{1}{n} \sum_{k=1}^{n} \int_0^T I_k(t)dt$$

$$\to \int_0^T EI(t)\, dt, \text{ as } n \to \infty,$$

$$(5.10) \quad D_n = \frac{-\rho}{n} \sum_{k=1}^{n} \int_0^T I_k(t)\, dt + \frac{\mu}{n} \sum_{k=1}^{n} \int_0^{\tau_k} dt + \frac{1}{n} \sum_{k=1}^{n} \int_0^{\tau_k} dW_k(t)$$

$$\to -\rho \int_0^T EI(t)\, dt + \mu E(\tau), \text{ as } n \to \infty$$

where the fact that $EW(\tau)=0$ was used (see Lemma 4.8 of Liptser and Shiryayev, 1977). Futhermore,

$$(5.11) \qquad E_n = \frac{1}{n} \sum_{k=1}^{n} \tau_k \to E(\tau), \text{ as } n \to \infty,$$

and

$$(5.12) \qquad H_n \to \sigma E[\int_0^T I(t)\, dW(t)] = 0 .$$

It follows from (5.9) - (5.12) that the right hand side of (5.8) tends

to zero as $n \to \infty$, a.s. [p]. It remains to show that $(B_n - C_n^2 E_n^{-1})^{-1}$ converges to a constant a.s. as $n \to \infty$. Indeed, from (5.4) it follows that

$$B_n \to \int_0^T E\, I^2(t)\, dt, \tag{5.13}$$

and from (5.5)

$$C_n^2 = [\frac{1}{n} \sum_{k=1}^{n} \int_0^T I_k(t)\, dt]^2 \to [\int_0^T E\, I(t)\, dt]^2. \tag{5.14}$$

Hence from (5.11), (5.13), and (5.14)

$$(B_n - C_n^2 E_n^{-1}) \to \int_0^T E\, I^2(t)\, dt - [E(\tau)]^{-1} [\int_0^T E\, I(t)\, dt)^2$$

$$= \Delta\ (> 0);\ \text{say, a.s.[P]}.$$

This proves that $\hat{\rho}_n - \rho \to 0$ a.s.[p]. The proof that $\hat{\mu}_n - \mu \to 0$ a.s.[p] follows the same lines and hence is ommitted. □

THEOREM 5.2

With the same notations as above,

$$\sqrt{n}\ (\rho - \hat{\rho}_n) \xrightarrow{\mathcal{D}} N(0, \Sigma_1^2),$$

where

$$\Sigma_1^2 = \frac{(E\int_0^\tau V(t)dt)^2\, E(\tau)^2 + \sigma^2(E\tau)^2\, E\int_0^\tau V^2(t)dt) - 2(E\tau)(E\int_0^\tau v(t)dt)^2}{[(E\int_0^\tau V(t)dt)^2 - (E\tau)(E\int_0^\tau V^2(t(dt)]^2}$$

and

$$\sqrt{n}\,(\mu - \hat{\mu}_n) \xrightarrow{\mathcal{D}} N(0,\ \Sigma_2^2),$$

where

$$\Sigma_2^2 = \frac{(E\int_0^\tau V^2(t)dt)^2 E(\tau)^2 + \sigma^2(E\int_0^\tau V(t)dt)^2 E(\int_0^\tau V^2(t)dt) - 2\sigma(E\int_0^\tau V(t)dt)^2[E(\int_0^\tau V^2(t)dt)]}{[(E\int_0^\tau V(t)dt)^2 - (E\tau)(E\int_0^\tau V^2(t)dt)]^2}$$

PROOF. In order to simplify notation, arguments and limits of integration will be dropped wherever convenient. Now, from (4.6) it follows that

(5.15)
$$\sqrt{n}\,(\rho - \hat{\rho}_n)$$
$$= \sqrt{n}\,\left[\rho - \frac{(\Sigma\tau_k)(\Sigma\int V_k dV_k) - (\Sigma\int V_k dt)\,(\Sigma\, V_k(T_k))}{(\Sigma\int V_k dt)^2 - (\Sigma\tau_k)(\Sigma\int V_t^2 dt)}\right]$$

$$= \sqrt{n}\,[\rho - \frac{(-\rho(\Sigma\tau_k)(\Sigma\int V_k^2 dt) + \mu(\Sigma\tau_k)(\Sigma\int V_k dt) + \sigma(\Sigma\tau_k)(\Sigma\int V_k dW_k) - (\Sigma\int V_k dt)(\Sigma V_k(\tau_k))}{(\Sigma\int V_k dt)^2 - (\Sigma\tau_k)(\Sigma\int V_k^2 dt)}]$$

$$= \sqrt{n}\,[-\frac{\rho(\Sigma\int V_k dt)^2 - \mu(\Sigma\tau_k)(\Sigma\int V_k dt) - \sigma(\Sigma\tau_k)(\Sigma\int V_k d W_k) + (\Sigma\int V_k dt)(\Sigma V_k(\tau_k)}{(\Sigma\int V_k dt)^2 - (\Sigma\tau_k)(\Sigma\int V_k^2 dt)}]$$

$$= \frac{\sqrt{n}\,[(\Sigma\int V_k dt)(\Sigma(\rho\int V_k dt - \mu\tau_k + V_k(\tau_k)) - \sigma(\Sigma\tau_k)(\Sigma\int V_k dW_k)]}{(\Sigma\int V_k dt)^2 - (\Sigma\tau_k)(\Sigma\int V_k^2 dt)}$$

$$= \frac{(n^{-1}\Sigma\int V_k dt)[n^{-1/2}\Sigma W_k(\tau_k)] + \sigma(n^{-1}\Sigma\tau_k)(n^{1/2}\Sigma\int V_k dW_k)}{(n^{-1}\Sigma\int V_k dt)^2 - (n^{-1}\Sigma\tau_k)(n^{-1}\Sigma\int V_k^2 dt)}$$

$$= (\xi_n \ \eta_n)\begin{pmatrix}\alpha_n \\ -\beta_n\end{pmatrix}$$

where

$$\xi_n = \frac{1}{\sqrt{n}} \sum_{k=1}^{n} W_k(\tau_k),$$

$$\eta_n = \frac{1}{\sqrt{n}} \sum_{k=1}^{n} \int_0^{\tau_k} V_k(t)dW_k(t),$$

$$\alpha_n = (\frac{1}{n} \sum_{k=1}^{n} \int_0^{\tau_k} V_k(t)dt) \; / \; [(\frac{1}{n} \sum_{k=1}^{n} \int_0^{\tau_k} V_k(t)dt)^2 - (\frac{1}{n} \sum_{k=1}^{n} \tau_k)(\frac{1}{n} \sum_{k=1}^{n} \int_0^{\tau_k} V_k^2(t)dt)]$$

and

$$\beta_n = \sigma(\frac{1}{n} \sum_{k=1}^{n} \tau_k) \; / \; [(\frac{1}{n} \sum_{k=1}^{n} \int_0^{\tau} V_k(t)dt)^2 - (\frac{1}{n} \Sigma\tau_k)(\frac{1}{n} \sum_{k=1}^{n} \int_0^{\tau_k} V_k^2(t)dt)].$$

Now, $E\,\xi_n = 0$, $E\,\eta_n = 0$, forall n, $Var\,(\xi_n) = \frac{1}{n} \sum_{k=1}^{n} E[W_k(\tau_k)]^2 = E\tau^2$, since $EW^2(\tau) = E\,\tau^2$ (See Lemma 4.8 of Liptser and Shiryayev, 1977),

$$Var(\eta_n) = \frac{1}{n} \sum_{k=1}^{n} [\int_0^{\tau_k} V_k(t)dW_k(t)]^2$$

$$= E\,[\int_0^{\tau} V^2(t)dt],$$

and

$$E\,[\xi_n\,\eta_n] = \frac{1}{n} E\,[(\sum_{k=1}^{n} W(\tau_k))(\sum_{k=1}^{n} \int_0^{\tau_k} V_k(t)dW_k(t)]$$

$$= \frac{1}{n} \sum_{k=1}^{n} E\,[\int_0^{\tau_k} dW_k(t) . \int_0^{\tau_k} V_k(t)dW_k(t)]$$

$$= E\,[\int_0^{\tau} V(t)dt].$$

Furthermore,

$$\alpha_n \to \alpha = \frac{E\left(\int_0^\tau V(t)dt\right)}{\left(E\int_0^\tau V(t)dt\right)^2 - (E\tau)\left(E\int_0^\tau V^2(t)dt\right)},$$

and

$$\beta_n \to \beta = \frac{\sigma E(\tau)}{\left(E\int_0^\tau V(t)dt\right)^2 - (E\tau)\left(E\int_0^\tau V^2(t)dt\right)}.$$

Now applying the central limit theorem in two dimensions it follows that $\sqrt{n}\,(\rho - \hat{\rho}) \xrightarrow{\mathcal{D}} N(0,\Sigma_1^2)$, where Σ_1 is defined in the statement of the theorem. The proof of the second assertion is similar to that of the first one and hence is omitted. □

See Gihman and Skorokhod (1972) for properties of Itô-type stochastic integrals which have been used in the proofs of Theorems 5.1 and 5.2.

6. Extended stochastic neuronal models. Before concluding it should be noted that model (3.8) describes the subthreshold behavior of the membrane potential of neurons with extensive (or rapid) synaptic input with relatively small amplitudes. It is also assumed that there are no post-synaptic potentials with large amplitudes. This last assumption might be too stringent since in many situations and specially for in case of stimulus driven neurons. Therefore, consider a stochastic neuronal model which takes into account the influence of extensive low amplitude synaptic input as well as PSPs with large amplitudes, which may be reflecting an influence of a number of dominating syanpses. These synapses may be electrotonically close to the initial segment. The activity of these synapses will be modeled by a linear combination of independent point-processes. This mixed model is a special case of a well-known class of stochastic processes called Itô-Markov processes (See Ikeda and Watanabe, 1981).

Now assume that in addition to the extensive synaptic input leading to the diffusion model (3.8), there are n_1 EPSPs arriving according to independent point-processes $N(\lambda_k^e(t),t)$ with random intensities $\lambda_k^e(t)$, and EPSP amplitudes α_k^e, k=1,2,...,n. In addition, IPSPs are arriving according to the independent processes $N(\lambda_k^i(t),t)$, with the corresponding parameters $\lambda_k^i(t)$ and α_k^i, k=1,2,...,n_2. An extended mixed model to describe the membrane potential of a stimulus driven neuron may be given by

$$dV(t) = (-\rho V(t) + \mu)\,dt + \sigma\,dW(t) + \sum_{k=1}^{n_1} \alpha_k^e\, dN(\lambda_k^e(t),t) - \sum_{k=1}^{n_2} \alpha_k^i\, dN(\lambda_k^i(t),t). \tag{6.1}$$

Reversal potentials. A feature which undoubtedly plays an important role in information processing in the nervous system is the dependence of the amplitudes of post-synaptic potentials on the pre-existing value of the membrane potential. It is well established that arrival of an action potential at a pre-synaptic terminal causes a release of a transmitter substance (for the cerebral cortex this could be a variety of substances including acetylcholine, glutamate, or glycine). In any case, a transmitter's action on the neuronal membrane at a given synaptic junction can be characterized by means of the experimentally observable reversal potential. This is the membrane potential at which the observed change in membrane potential caused by transmitter induced conductance change is zero. Reversal potentials have been utilized in deterministic modeling of neuronal membranes (Rall, 1964).

The neuronal model (3.8) is then extended to take the form

$$dV(t) = (-\rho V(t) + \mu)\, dt + \sigma\, dW(t) + \sum_{n=1}^{n_1} \alpha_n^e [V_n^e - V(t)]\, dN(\lambda_n^e(t), t) - \sum_{k=1}^{n_2} \alpha_k^i [V_k^i - V(t)]\, dN(\lambda_k^i(t), t), \tag{6.2}$$

where it is assumed that the neuron has excitatory synapses which, when activated, result in displacing $V(t)$ toward the reversal potential V_m^e

$(m=1,2,\ldots,n_1)$, and inhibitory synapses, which when activated, result in displacing V(t) away from the reversal potential $V_k^i(k=1,2,\ldots,n_2)$.

Spatial aspects of synptic input. Another important characteristic of central nervous system (CNS) information processing is the dependence of both the magnitude and time course of the post-synaptic potential, evoked by a given synapse, on the spatial location of the active synaptic junction. This important feature is not considered in most existing stochastic models of single neurons, which have concerned themselves only with the influences of temporal summation of synaptic inputs. Model (3.10) may be extended to incorporate the important feature of **spatial distribution.** This extension is based on Rall's model neuron (Rall, 1978). In Rall's model neuron the cable properties of a system of branched dendrites are reduced to a one-dimensional equivalent dendrite, with synapses made at specific distances along the equivalent dendrite. Considering the nerve cell as a line segment of finite length L, we propose that the subthreshold behavior of the membrane's potential, V(t,x) be modeled as

$$(6.3)\quad dV(t,x) = (-\rho V(t,x) + (\partial^2/\partial x^2)V(t,x) + \mu)\,dt + \sigma\,dW(t,w)$$

$$+ \sum_{j=1}^{n_1} \alpha_j^e\, \partial(x-x_j^e)[V_j^e(x)-V(t,x)]\, dN(\lambda_j^e(t),x,t)$$

$$- \sum_{k=1}^{n_2} \alpha_k^i\, \partial(x-x_k^i)[V_k^i(x)-V(t,x)]\, dN(\lambda_k^i(t),x,t)$$

where δ is the delta distribution (or generalized function), and $x_j^e(x_k^i)$ is the location of the excitatory (inhibitory) synaptic inputs which occur according to independent point-processes with rates $\lambda_j^e(\lambda_k^i)$ and amplitudes of $\alpha_j^e(\alpha_k^i)$, $j=1,2,\ldots,n_1$; $k=1,2,\ldots,n_2$. The solution of (2.6) is a stochastic process $\{V(t,x),\ 0 < x < L,\ t \geq 0\}$.

Walsh (1981) considered a partial stochastic differential equation model that describes the subthreshold behavior of the membrane potential and studied the properties of the sample paths of the solution of the partial stochastic differential equation. The model is a special case of the neuronal model (6.3). Killianpur and Wolpert (1984a) modeled the membrane potential as a random field driven by a generalized Poisson process. The authors studied the approximations of this model by an Örnstein-Uhlenbeck type process in the sense of weak convergence of the probability measures induced by solutions of stochastic differential equations in Skorokhod space. The problem of reversal potential was taken into consideratin in modeling the membrane potential of a neuron by Kallianpur and Wolpert (1984b).

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Ito-type stochastic differential equations are developed to describe some aspects of the electrical activity of nerve cells or neurons. It is argued that the subthreshold behavior of the membrane potential of a neuron may be modeled as a diffusion process observed over a random interval. The models contain parameters which reflect important neurophysiological properties. Given independent and identically distributed copies or trajectors of such processes, maximum likelihood estimators of the parameters are explicitly derived and their asymptotic properties such as strong consistency and asymptotic normality are studied.

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