

**IDENTIFICATION OF SEMIMARTINGALE NEURONAL SYSTEMS**

by

M.K. Habib and A. Thavaneswaran

The University of North Carolina at Chapel Hill  
Department of Biostatistics

Institute of Statistics Mimeo Series No. 1848

March 1988

Identification of Semimartingale

Neuronal Systems

by

M.K. Habib and A. Thavaneswaran

The University of North Carolina at Chapel Hill

Department of Biostatistics

Chapel Hill, North Carolina 27514 USA

AMS 1980 Subject Classification: 60G55, 60K99, 62F99

KEYWORDS AND PHRASES: Cross covariance, neuron, nervous system, point processes, semimartingales, spike trains, system identification, variance process

Research supported by the Office of Naval Research under contract number N00014-83-K-0387

## ABSTRACT

In this paper a nerve cell (or neuron) is modeled as a system that transforms a semimartingale input into a point process output. This extends a result of van der Boogaard et al. (1986) in which neurons transform point process inputs into point process outputs. The semimartingale input model proposed here encompasses Poisson, Gauss-Poisson, diffusion and Itô-Markov processes which have been considered in the literature. Using Itô's formula, the intensity (or pulse generation function) of the output point process is expressed explicitly in terms of the input process under mild differentiability conditions on the intensity. The conditional mean and quadratic variation of the output process are derived in terms of the corresponding mean and quadratic variation of the input process. Some related problems of parameter estimation are also considered.

## 1. INTRODUCTION

A basic unit of the nervous system which receives, processes and transmits information is the nerve cell or neuron. For many types of neurons, this information is transmitted in the form of brief impulse-like electrical events which are called action potentials (or spikes). The action potentials of a particular neuron are nearly identical in the shape of wave forms. Furthermore, because action potentials have short temporal durations (2-3 m.s.) with respect to the time intervals between their occurrences, a train of action potentials may be modeled as a realization of a stochastic point process. This point of view is quite prevalent in the literature (see e.g. Perkel et al., 1967; Moore et al., 1970; Yang and Chen, 1978; DeKwaadsteniet, 1982). It is widely believed that the temporal patterns of spike trains are the information carriers in many areas in the nervous system. For this reason, theoretical and experimental neuroscientists have paid a great deal of attention to the statistical analysis of both single and simultaneously recorded spike trains, which are recorded extracellularly from one or more neurons respectively. (See e.g. Perkel et al., 1968; Bryant et al., 1973; Toyama et al., 1981; Tanaka, 1983; Borisyuk et al., 1985; Habib and Sen, 1985.)

Consider a neuronal system with an input process,  $X_t$ , and output point process,  $N_t$ , with intensity process,  $\lambda_t$ , where  $\lambda_t = F(X_t)$ .  $\lambda_t$  is also known as the pulse generating function. The following cases are encountered in studies of stochastic transformation systems:

- (a) Both  $X_t$  and  $N_t$  are observable, but the pulse generator  $\lambda_t$  is not known. This set up corresponds to an identification problem in which one is interested in knowing the mechanism involved, i.e. how a neuron transforms the input process into an observable output process.
- (b)  $X_t$  is not observable,  $N_t$  is observable, and the pulse generator is a known function. This corresponds to the problem of estimation of random intensities (see e.g. Karr, 1986). In general, this set up can also be interpreted as a Bayesian problem in which the input process corresponds to the prior, and the unknown parameter in the prior corresponds to the hyperparameter. Preliminary investigation of this problem may be found in Konecny (1984).

(c) Both  $X_t$  and  $N_t$  are observable and the pulse generator  $\lambda_t$  is known up to an unknown parameter  $\theta$ . In this case,  $\theta$  may be estimated as in Habib and Thavaneswaran (1988).

Before discussing the neuronal systems which will be considered in this paper, we briefly review some relevant literature. Knox (1974) proposed a simplified model for a neuron in which the somal-membrane of a post-synaptic (driven) cell was modeled as a linear time-invariant filter. The neuron was assumed to have a constant threshold,  $\theta$ . After crossing the threshold, the membrane potential was reset to a resting potential (i.e. the refractory period was not taken into consideration), and only excitatory post-synaptic potentials were considered. The pre-synaptic spikes were assumed to arrive at random over a single excitatory channel and are idealized as Dirac delta functions, i.e. the input was modeled by  $X_t = \sum_k \delta(t-r_k)$ , where  $\{r_k\}$  are the instances of arrivals of presynaptic action potentials. The membrane potential,  $Y$ , was modeled by

$$Y_t = \int_{t_0}^t X_u h(t-u) du = \sum_{t_0 < r_k \leq t} h(t-r_k),$$

as long as  $Y_t$  remains less than the constant threshold  $\theta$ , where  $h(t)$  is the impulse response function of the filter. The author considered both the case of the perfect integrator (where the membrane sums the synaptic input linearly and without decay in the absence of synaptic events), as well as the case of the leaky integrator (where the membrane potential decays exponentially between synaptic inputs). In the stationary case, the cross-correlation function of pre- and post-synaptic spike trains was derived from a linear system as a convolution of the input auto-correlation function with the impulse response function of the system. The cross-correlation function was also derived when the input  $X_t$  was a Poisson process. See also Knox and Poppele (1977a; 1977b).

Brillinger, Bryant, and Segundo (1976) applied an identification method of point processes, developed by Brillinger (1974; 1975), to a large data set of spike trains recorded from a neural network in Aplysia. The neurons were connected by monosynaptic inhibitory or excitatory post-synaptic potentials and either discharged spontaneously or were driven by intracellular current pulses. The cross-intensity function of two jointly weakly-stationary spike trains recorded simultaneously from two cells A and B is defined by

$$I_{AB}(u) = \lim_{h \rightarrow \infty} P \{B \text{ spike in } (t, t+h) \mid A \text{ spike at } t-u\}/h.$$

Brillinger et al. (1976) expressed the cross-intensity function of two cells, A and B, as a functional series, using "kernels," which is a point process analog of the Volterra-Wiener expansion of ordinary time series (Marmarelis and Naka, 1973a; 1973b). The kernels were expressed as functions of time arguments, and were meant to be invariant of the system, i.e., they retained the same essential characteristics even when the pre-synaptic discharges vary and the kernels were estimated from the corresponding pre- and post-synaptic spike trains.

The above studies were based on the assumptions that the point processes representing the spike trains were weakly-stationary and were also assumed to be jointly weakly-stationary. In reality, it is well documented that many spike trains are neither weakly-stationary nor jointly so. For example, Correia and Landolt (1977) studied the spontaneous activity of anterior semicircular canal afferents and found that spike activity of 57.5% of the studied units was non-stationary as determined by the Wald-Wolfowitz runs test for trends. It is reasonable, then, to expect that lack of stationarity will be even more pronounced in stimulus driven activity. Recently, van den Boogaard et al. (1986) have proposed a neuronal model neuron in which a neuron transforms Gauss-Poisson point processes into an output which is a doubly-stochastic Poisson process. The intensity of the output process,  $g$ , was assumed to be of the form  $g(u) = ae^u$ .

In the present paper, we extend the neuronal models described above to a system that transforms a semimartingale input,  $X_t$ , into an output point process,  $N_t$  with random intensity,  $\lambda$ . Assuming that the intensity  $\lambda$  is a non-negative twice continuously differentiable function of the input, i.e.  $\lambda_t = F(X_t)$ , formulae are derived that explicitly express the conditional mean and variance of the output counting process in terms of the input semimartingale.

In symbolic notation the proposed transformation is formulated by

$$N_t = S \left[ X_t \right]. \quad (1.1)$$

The input process  $X_t$  can be modeled in several ways depending on the experimental situation at hand. For instance, in the case of simultaneous extracellular recording of spike trains from two or more neurons, the spike trains of a driven cell may be modeled as a point process,  $N_t$ . The input,  $X_t$ , to the neuronal system may be given by

$$dX_t = \sum_{\tau_j \leq t} w(\tau_j) - w(t) dN(t),$$

where  $w(t)$  is the synaptic weight, and  $(\tau_1, \tau_2, \dots)$  are the firing times of the presynaptic neuron projecting to the synapse of concern. This may be extended to the case where  $X_t$  is modeled as a linear combination of counting processes  $N_1, N_2, \dots, N_k$  which represent the temporal firing patterns of the presynaptic neurons projecting to the neuron under consideration.  $X_t$  can be viewed as the solution of a stochastic differential equation of the form

$$dX_t = \sum_{k=1}^K \sum_{\tau_j^{(k)} \leq t} w_k(\tau_j^{(k)}) \quad (1.2)$$

$$= \sum_{k=1}^K w_k(t) dN(\lambda_k(t), t),$$

where  $w_k(t)$  are synaptic weights (or amplitudes of post-synaptic potentials),  $\lambda_k(t)$  are the presynaptic firing rates or intensities which may be stochastic processes,  $k=1, 2, \dots, K$ , and  $(\tau_1^{(k)}, \tau_2^{(k)}, \dots)$  are the firing times of the neuron projecting to the  $k$ th synapse. Equation (1.2) may also be written in an integral form

$$X_t = X_0 + \sum_{k=1}^K \int_0^t w_k(s) dN_k(\lambda_k(s), s). \quad (1.3)$$

This model is schematically represented in Figure 1.1. Variations of model (1.3) have been considered by many authors among them Knox (1974), Brillinger et al. (1976) and van den Boogaard et al. (1986). In the special case when the  $w$ 's and  $\lambda$ 's are constants and  $N_1, N_2, \dots, N_k$  are independent Poisson processes, it is well known that the solution of (1.2) or (1.3) is a Markov process with discontinuous sample paths. Model (1.3) in this case is called

Stein's model (Stein, 1965). See Snyder, (1975) for a discussion of Poisson driven Markov processes.

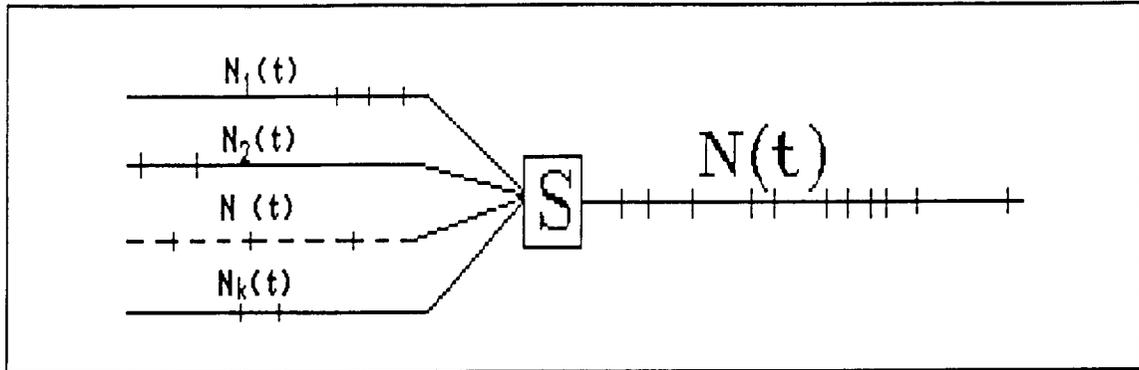


Figure 1.1. A neuronal system that transforms a linear combination of point-process inputs into point-process output.

Another neuronal system considered in this paper is one which transforms a diffusion process input into a point process output. The model is suited to experiments in which both the intracellularly recorded membrane potential of a neuron and the action potential generated by the same neuron are available. The choice of a diffusion process as a model for the effective potential input of the system may be based on the observation that in many types of neurons, in particular those in the brain, the number of synapses ranges from a few thousands to tens of thousands. A single motor neuron in the spinal cord probably receives some 15,000 synaptic junctions while certain types of neurons in the brain may have more than 100,000 synapses. If the synaptic weights (or the amplitudes of the postsynaptic potentials) are relatively small and the firing rates are relatively high, it can be argued that models (1.2) or (1.3) may be approximated by diffusion models in the form

$$X_t = X_0 + \int_0^t a(s, X_s) ds + \int_0^t b(s, X_s) dW_s \quad (1.4)$$

where  $W_t$  is a standard Wiener process and the processes  $a$  and  $b$  satisfy the appropriate Lipschitz and growth conditions which guarantee the existence of a strong solution of equation (1.4). (See e.g. Liptser and Shiriyayev, 1977; Sørensen, 1983.) The diffusion approximation in the neurophysiology set up has been considered by Johannesma (1968), Ricciardi (1976) and recently by

Kallianpur (1983) where a proof of the diffusion approximation was given using the functional central limit theorem for semimartingales (Liptser and Shiriyayev, 1980, 1981). Model (1.4) is appropriate for modeling neurons which receive extensive synaptic input with low amplitudes (Lansky, 1983; Habib, 1985). This model is represented in Figure 1.2.

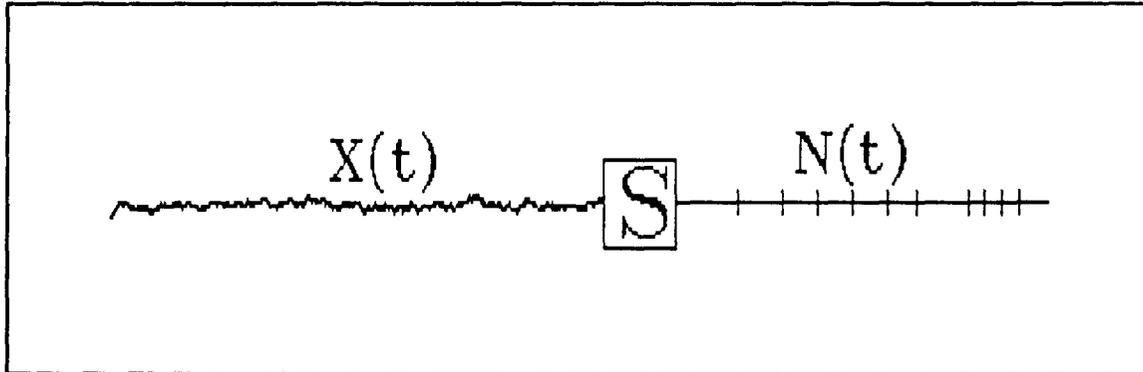


Figure 1.2. A neuronal system that transforms a diffusion process input into a point process output.

A third example of the neuronal system considered here is one which transforms a mixed input process, that is, an input process which is a combination of point and diffusion processes. This model is suitable for experiments in which both the extracellular and intracellular records of a neuron are available. The model is based on the observation that in the sensory areas such as the auditory, somatosensory, and visual cortices, a limited number of pre-synaptic neurons will be firing above the background level in response to an effective stimulus while the rest of the presynaptic neurons may be firing spontaneously (see Tanaka, 1983). In this case, in addition to diffusion input, the neuron receives input in the form of a linear combination of counting processes. The effective potential input may then be modeled as a mixed stochastic model of the form

$$X_t = X_0 + \int_0^t a(s, X_s) ds + \int_0^t b(s, X_s) dW_s + \sum_{k=1}^K \int_0^t w_k(s) dN_k(\lambda_k(s), s). \quad (1.5)$$

This model is schematically represented in Figure 1.3.

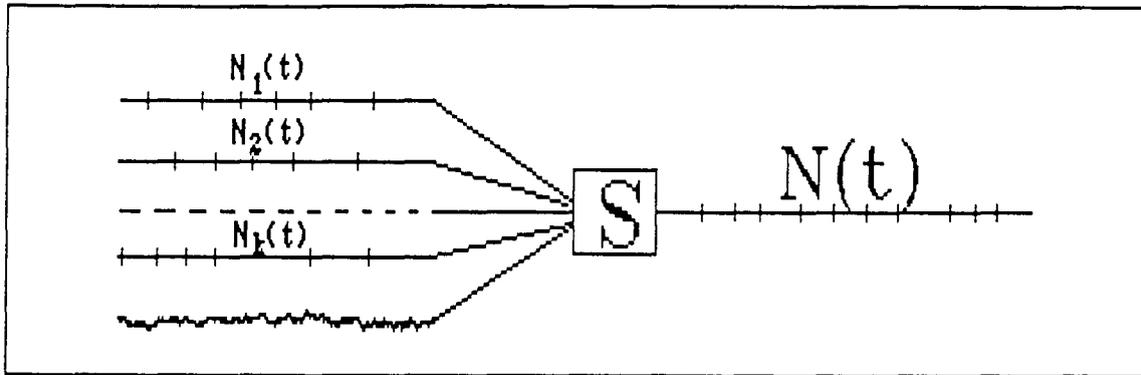


Figure 1.3. A neuronal system that transforms a mixed diffusion and point-process (Ito-Markov) inputs into a point-process output.

A semimartingale model for the input process will include all the models discussed above as special cases. Therefore, it is more convenient to assume that a neuron transforms a semimartingale input into a counting process output with random intensity.

In Section 2, we take a more general approach than that of van den Boogaard et al. (1986) by considering a class of twice differentiable functions as pulse generators. In van den Boogaard et al. (1986), the pulse generating function had an exponential form and the input process was assumed to be a Gauss-Poisson process. Thus, the entire distribution can be characterized by its first two moments and the output process to be a doubly stochastic Poisson process. This does not incorporate feedback, while the output models considered in our work include self-exciting processes, and hence incorporate feedback. The approach adapted in this paper generalizes the work of van den Boogaard et al. (1986) in three directions allowing.

(a) consideration of a general class of inputs, namely semimartingales, (b) consideration of a general class of impulse generators, and (c) inference about the functional relationship between input and output processes from real data.

## 2. A SEMIMARTINGALE MODEL

In this section, we model a neuron as a system that transforms a semimartingale input into a point process output with random intensity (or pulse generating function) which is assumed to be an arbitrary continuously twice differentiable function. This extends the exponential impulse generating function considered by van den Boogaard et al. (1986). The following notation will be used in the sequel. Let  $(\Omega, \mathcal{F}, P)$  be a complete probability space, and  $(\mathcal{F}_t, t \geq 0)$  be a filtration, i.e. a non-decreasing family of sub- $\sigma$ -fields of  $\mathcal{F}$ . Assume that  $(\mathcal{F}_t)$  is augmented by the sets of  $\mathcal{F}$  having zero  $P$ -measure, and that  $(\mathcal{F}_t)$  is right continuous, i.e.  $\mathcal{F}_t = \mathcal{F}_{t+} (= \bigcap_{s \geq t} \mathcal{F}_s)$ . A stochastic process  $X = (X_t, t \geq 0)$  is said to be adapted to a filtration  $\mathcal{F} = (\mathcal{F}_t, t \geq 0)$ , if  $X_t$  is  $\mathcal{F}_t$ -measurable for each  $t \geq 0$ . The notation  $(X_t, \mathcal{F}_t)$  will be used to indicate that  $X_t$  is  $\mathcal{F}_t$ -measurable for each  $t \geq 0$ . Let  $\mathcal{P}$  be the smallest  $\sigma$ -field which contains the class of all left continuous stochastic processes.  $\mathcal{P}$  is called the predictable  $\sigma$ -field. A stochastic process which is measurable with respect to  $\mathcal{P}$  is called predictable.

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

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

$$(ii) \quad E(M_t | \mathcal{F}_s) = M_s, \quad s \leq t.$$

If the equality in (ii) is replaced by  $\geq$  ( $\leq$ ), the process is called supermartingale (submartingale). A stopping time,  $\tau$ , is a random variable such that the event  $[\tau \leq t]$  is  $\mathcal{F}_t$ -measurable. A local martingale  $M = (M_t, \mathcal{F}_t)$  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  $M^n = (M_{t \wedge \tau_n}, \mathcal{F}_t)$ ,  $n \geq 1$  are martingales. Each local martingale  $M$  admits the decomposition  $M = M^c + M^d$ , where  $M^c$  is a continuous local martingale and  $M^d$  is a purely discontinuous local martingale. If  $M$  is a square-integrable martingale, then  $M^2$  is a submartingale, and according to the Doob-Myer decomposition there exists a predictable increasing process, denoted by  $\langle M \rangle$

(or  $\langle M, M \rangle$ ), which is called the quadratic characteristic or the variance process of the martingale  $M$ .  $\langle M \rangle$  may be calculated from the formula

$$\langle M \rangle_t = \lim_{n \rightarrow \infty} \sum_{k=0}^{n-1} E \left[ (M_{t(k+1)/n} - M_{tk/n})^2 \mid \mathcal{F}_{tk/n} \right].$$

The covariance process of two square-integrable martingales  $M$  and  $N$  may be defined by

$$\langle M, N \rangle_t = \frac{1}{4} \left[ \langle N + M \rangle - \langle N - M \rangle \right].$$

Statistical analysis of the trajectories of random processes  $(X_t, t \geq 0)$  shows that rather often their structure is such that  $X_t, t \geq 0$  consists of the sum of two components, namely a slowly changing (trend)  $A_t, t \geq 0$ , and a rapidly changing component (noise)  $M_t, t \geq 0$ . The slowly changing component is modeled as a process with bounded variation. A stochastic process  $(A_t, t \geq 0)$  is of locally bounded variation if for arbitrary  $t \geq 0$  and  $\omega \in \Omega$  the variation

$\int_0^t |dA_s(\omega)| < \infty$ . The rapidly changing process  $M$  is modeled as a local martingale.

Definition: A stochastic process  $X=(X_t, \mathcal{F}_t, t \geq 0)$  is called a semimartingale, if it can be written in the form

$$X_t = A_t + M_t, \quad t \geq 0 \quad (2.1)$$

where  $A$  is a process of locally bounded variation and  $M$  is a local martingale.

Model (2.1) encompasses models (1.3) - (1.5) as special cases. For model (1.3),

$$A_t = X_0 + \sum_{k=1}^K \int_0^t w_k(s) \lambda_k(s) ds,$$

and

$$M_t = \sum_{k=1}^K \int_0^t w_k(s) dM_k(\lambda_k(s), s)$$

where  $dM_k(\lambda_k(t), t) = dN_k(\lambda_k(t), t) - \lambda_k(t)dt$ . For model (1.4)

$$A_t = X_0 + \int_0^t a(s, X_s) ds,$$

and

$$M_t = \int_0^t b(s, X_s) dW_s.$$

For model (1.5)

$$A_t = X_0 + \int_0^t a(s, X_s) ds + \sum_{k=1}^K \int_0^t \lambda_k(s) ds,$$

and

$$M_t = \int_0^t b(s, X_s) dW_s + \sum_{k=1}^K \int_0^t w_k(s) dM_k(\lambda_k(s), s),$$

where  $dM_k(\lambda(t), t) = dN_k(\lambda(t), t) - \lambda(t)dt$ .

Now, we present the celebrated Itô-formula which is the basic stochastic calculus rule for computing differentials of functions of general stochastic processes such as semimartingales.

Let  $X_t$  be an  $R^n$ -valued input semimartingale (i.e.  $X \in R^n$ ), where each component  $X^i$  is itself a semimartingale. Suppose that the pulse generating function  $F$  of the output process  $N_t$  is a real valued, positive, continuously twice differentiable function on  $R^n$ . That is, the intensity process  $\lambda_t$  of the output counting process  $N(t)$  is given by  $\lambda_t = F(X_t)$ . The application of Itô's formula to  $F$  leads to

$$\begin{aligned}
 F(X_t) = & F(X_0) + \sum_{i=1}^n \int_0^t \frac{\partial}{\partial x_i} F(X_{s-}) dX_s^i \\
 & + \frac{1}{2} \sum_{i,j=1}^n \int_0^t \frac{\partial^2}{\partial x_i \partial x_j} F(X_{s-}) d\langle X^{ic}, X^{jc} \rangle_s \\
 & + \sum_{0 < s \leq t} \left[ (F(X_s) - F(X_{s-})) - \sum_{i=1}^n \frac{\partial}{\partial x_i} F(X_s^i) \Delta X_s^i \right] \quad (2.3)
 \end{aligned}$$

where  $\Delta X_s = X_s - X_{s-}$ ,  $X^{ic}$ , is the continuous part of  $X^i$ , and  $\langle X^{ic}, X^{ic} \rangle_s$  is the variance-covariance process of  $X^{ic}$  and  $X^{jc}$ .

Note: The above formula shows that the intensity process  $\lambda_t = F(X_t)$  is a semimartingale.

### 3. APPLICATIONS

In this section we consider special cases of the input process such as point, diffusion, and Itô-Markov processes. The output process is assumed to be a point process with random intensity with pulse generating function which is assumed to be continuously twice differentiable.

#### Example 3.1:

Consider an experimental setup where one is able to record simultaneously two spike trains from two neurons. For definiteness, assume that we have extracellular records of two neurons with one driving the other. For this set up, the input process  $X_t$  is modeled by a point process of the form

$$X_t = \int_0^t \mu_s ds + m_t^d$$

where  $m_t^d$  is a zero-mean purely discontinuous martingale. The output process is assumed to have a pulse generator or intensity,  $\lambda_t$  of the form

$$\lambda_t = e^{aX_t} (-F(X_t)), \quad a \in \mathbb{R}^+.$$

See Aalen (1978) for a discussion of the problem of non-parametric inference for waiting processes with multiplicative random intensities. Applying Itô's formula (2.3) gives

$$\lambda_t = \lambda_0 + \int_0^t \mu_s \lambda_s ds + \int_0^t [\lambda_s - \lambda_{s-} - \lambda_{s-} \Delta m_s^d] ds.$$

Hence  $\lambda_t$  is a semimartingale with a conditional mean

$$E[\lambda_t | F_t^\lambda] = \lambda_0 + \int_0^t \mu_s \lambda_s ds,$$

and conditional second variance

$$\begin{aligned}
\text{Var} \left[ \lambda_t | F_t^\lambda \right] &= E \left[ (\lambda_t - E [\lambda_t | F_t^\lambda])^2 | F_t^\lambda \right] \\
&= E \left[ \left( \sum_{s \leq t} [\lambda_{s-} \Delta m_s^d] \right)^2 | F_t^\lambda \right] \\
&= \int_0^t \lambda_{s-}^2 \langle dm^d \rangle_s \\
&= \int_0^t \lambda_{s-}^2 \mu_s ds.
\end{aligned}$$

Example 3.2:

Assume that both the intracellular record of the somal membrane potential and extracellular record of spike trains of a certain neuron are available. In this situation the somal membrane potential  $X_t$  may be modeled as a diffusion process of the form

$$X_t = X_0 + \int_0^t \theta_s ds + W_t,$$

where  $\theta_s$  is assumed to be a deterministic function and  $W_t$  is a standard Wiener process. This model is appropriate for neurons which receive extensive synaptic input with small post-synaptic potential amplitudes.

Then, for a pulse generator  $\lambda_t = e^{aX_t}$  ( $=F(X_t)$ ), where  $a \in \mathbb{R}^+$  it follows that for all  $a \in \mathbb{R}^+$

$$\lambda_t = \lambda_0 + \int_0^t \lambda_s \left( a\theta_s + \frac{a^2}{2} \right) ds + a \int_0^t \lambda_s dW_s.$$

Hence  $\lambda_t$  is a semimartingale with a conditional mean

$$E[\lambda_t | F_t^\lambda] = \lambda_0 + \int_0^t \lambda_s \left[ a\theta_s + \frac{a^2}{2} \right] ds ,$$

and conditional second moment

$$E[\lambda_t^2 | F_t^\lambda] = a^2 \int_0^t \lambda_s^2 ds .$$

In this case the output process is given by

$$N_t = \int_0^t \lambda_s ds + m_t$$

with variance process  $\langle N, N \rangle_t = \int_0^t \lambda_s ds$ . Both the conditional and

unconditional means are given by  $E[N_t] = \int_0^t \lambda_s ds$ . If the pulse generator

is exponential, i.e.  $F(\cdot)$  is of the form  $F(u) = \nu e^{-u}$  as in van de Boogaard et al. (1986), then for the input process in (3.4),

$$\lambda_t = F(X_t) = \nu e^{-X_t} ,$$

$$\lambda_t = \lambda_0 + \int_0^t \lambda_s \left( \phi_s + \frac{1}{2} \right) ds + \int_0^t \lambda_s dW_s ,$$

$$dN_t = \lambda_t dt + dm_t ,$$

$$\langle N, N \rangle_t = \int_0^t \lambda_s ds ,$$

$$E \left[ \lambda_t | F_t^X \right] = \lambda_0 + \int_0^t \lambda_s \left[ \phi_s + \frac{1}{2} \right] ds ,$$

and

$$\text{Var} \left[ \lambda_t \mid \mathcal{F}_t^\lambda \right] = \int_0^t \lambda_s \, ds.$$

Example 3.3:

Consider the same experimental set up as in Example 3.2 with the diffusion input  $X_t$  replaced by an Itô-Markov process of the form

$$X_t = X_0 + \int_0^t f(s, x_s) da + \int_0^t g(s, x_s) dW_s + \int_0^t h(s, x_s) dM_s^d,$$

where  $W_t$  is a standard Wiener process and  $M_s^d$  is a purely discontinuous martingale. Then

$$\lambda_t = e^{ax_t} (-F(x_t)), \quad a \in \mathbb{R}^+.$$

It follows that

$$\begin{aligned} \lambda_t &= \lambda_0 + \int_0^t a \lambda_s [f(s, X_s) + a^2/2] \, ds \\ &\quad + \int_0^t u \lambda_s g(s, X_s) dW_s + \int_0^t h(s, X_s) (a\lambda_s + 1) dM_s^d \\ &\quad + \sum_{0 \leq s \leq t} \left[ \lambda_s - \lambda_{s-} - \lambda_{s-} h(s, \lambda_{s-}) \Delta M_s^d \right]. \end{aligned}$$

The cross-covariances of the input process,  $X_t$ , and output process,  $N_t$ , may be derived using Itô's formula for the product of two semimartingales. (See e.g. Elliot, 1982.) In the set up described above, the input,  $X_t$ , is given by

$$X_t = V_t + m_t,$$

and the output process,  $N_t$ , is given by

$$N_t = \int_0^t \lambda_s ds + M_t = \Lambda_t + M_t ,$$

where  $m$  and  $M$  are zero mean purely discontinuous martingales. Itô's formula gives

$$d(XN)_t = V_t d\Lambda_t + \Lambda_t dV_t + d\langle M, m \rangle_t ,$$

provided that  $M_t$  and  $m_t$  have no common jumps. Hence

$$E[X_t N_t] = E \int_0^t V_s d\Lambda_s + E \int_0^t \Lambda_s dV_s + E\langle M, m \rangle_t .$$

In conclusion, we briefly describe how to use the first two conditional moments to study the relationship between the input and output processes when both the input process,  $X_t$ , and the output process,  $N_t$ , are observable and the pulse generator is known up to an unknown parameter  $\theta$ . In this case the output process  $N_t$  can be written as

$$N_t = \int_0^t \lambda_s(X_s, \theta) ds + M_t$$

where the predictable process  $\lambda_s$  is observable (known) except for the parameter  $\theta$ . Then an optimal estimate for  $\theta$  may be obtained as in Habib and Thavaneswaran (1987). Indeed, using the method of optimal estimating functions (Thavaneswaran and Thompson, 1986), the parameter  $\theta$  may be estimated by solving the optimal estimating equation

$$\int_0^t [\lambda_s(X_s, \theta)]^{-1} [\partial \lambda_s(X_s, \theta) / \partial \theta] [dN_s - \lambda_s(X_s, \theta) ds] = 0 .$$

In particular if  $\lambda_s(X_s, \theta) = \theta f(X_s)$ ,  $\theta > 0$ , where  $f$  is a known function (not necessarily linear), then the optimal estimate of  $\theta$  turns out to be

$$\theta^0 = \frac{\int_0^t f(X_s) dN_s}{\langle M \rangle_t} = \frac{\int_0^t f(X_s) dN_s}{\int_0^t f(X_s) ds}$$

That is, in this case it is easy to fit a model with a known functional form from  $\lambda_t(X_t, \theta)$ . For example, if  $\int_0^t \theta f(X_t) dt$  gives a good fit to the observed data for a given  $f$ , we may argue that the rate of firing of the post synaptic neuron is proportional to  $f(X_t)$ , where  $f$  is known. More interestingly,  $\lambda_t = f(\theta, X_t) = \sum_{i=1}^n \theta_i X(t-t_i)$  may be considered to study the effect in the rate of firing due to the changes in  $X$  at  $t_1, \dots, t_n$ .

## REFERENCES

- O.O. Aalen, Non-parametric inference for a family of counting processes, Ann. Statistic 6:701-726 (1978).
- G.N. Borisyuk, R.M. Borisyuk, A.B. Kirillov, E.I. Kovalenko, and V.I. Kryukov, A new statistical method for identifying interconnections between neuronal network elements, Biol. Cybern. 52:301-306 (1985).
- D.R. Brillinger, Cross-spectral analysis of processes with stationary increments including the stationary G/G/queue, Ann. Probab. 2:815-827 (1974).
- D.R. Brillinger, The identification of point process systems, Ann. Probab. 3:909-924 (1975).
- D.R. Brillinger, H.L. Bryant Jr., and J.P. Segundo, Identification of synaptic interactions, Biol. Cybernetics 22:213-228 (1976).
- H.L. Bryant, A. Ruiz Marcos, and J.P. Segundo, Correlations of neuronal spike discharges produced by monosynaptic connections and of common inputs, J. Neurophysiol. 36:205-225 (1973).
- R.M. Capocelli and L.M. Ricciardi, Diffusion approximation and first passage time problem for a model neuron, Kybernetik 8:214-223 (1971).
- M.J. Corriea and J.P. Landolt, A point process analysis of spontaneous activity of anterior semicircular canal units in the anesthetized pigeon, Biol. Cybernetics 27:199-213 (1977).
- J.W. DeKwaadsteniet, Statistical analysis and stochastic modeling of neuronal spike-train activity, Math. Biosciences 60:17-71 (1982).
- R.J. Elliot, Stochastic Calculus and Applications, Springer-Verlag, New York, 1982.
- M.K. Habib, Parameter estimation for randomly stopped processes and neuronal modeling, UNC Institute of Statistics, Mimeo Series No. 1492 (1985).
- M.K. Habib and P.K. Sen, Non-stationary stochastic point-process models in neurophysiology with applications to learning. Biostatistics - Statistics in Biomedical, Public Health and Environmental Sciences, The Brenard G. Greenberg Volume, P.K. Sen, ed., North Holland, Amsterdam, 1985, pp. 481-509.
- M.K. Habib and A. Thavaneswaran, Optimal estimation for semimartingale neuronal models, Proceedings of the conference on Stochastic Methods for Biological Intelligence, Plenum Press, New York, 1988 (to appear).
- P.I.M. Johannesma, Diffusion models for the stochastic activity of neurons, In Caianello, E.R., (ed.) Neuronal Networks, Springer-Verlag, New York, 1968.

G. Kallianpur, On the diffusion approximation to a discontinuous model of a single neuron, Contributions to Statistics: Essays in Honor of Normal L. Johnson. (ed. by P.K. Sen), North Holland, Amsterdam, 1983.

A.F. Karr, Point Processes and Their Statistical Inference, Dekker, New York, 1986.

C.K. Knox, Cross correlation functions for a neuronal model, Biophys. J. 14:567-582 (1974).

C.K. Knox and R.E. Poppele, Correlation analysis of stimulus-evoked changes in excitability of spontaneously firing neurons, J. Neurophysiol. 31:616-625 (1977a).

C.K. Knox and R.E. Poppele, A determination of excitability changes in dorsal spinocerebellar tract neurons from spike-train analysis, J. Neurophysiol. 31:626-646 (1977b).

F. Konecny, Parameter estimation for point process with partial observations, a filtering approach, Systems and Control Letters 4:281-286 (1984).

P. Lansky, Inference for the diffusion models of neuronal activity, Math. Biosci. 67:247-260 (1983).

R.S. Liptser, and A.N. Shirayayev, Statistics of Random Processes I., Springer-Verlag, New York, 1977.

R.S. Liptser, and A.N. Shirayayev, A functional central limit theorem for semi-martingales, Theor. Probab. Appl. XXV. 4:683-703 (1980).

R.S. Liptser, and A.N. Shirayayev, On necessary and sufficient conditions on a central limit theorem for semi-martingales, Theor. Prob. Appl. XXVI. 1:123-137 (1981).

P. Marmarelis, and K.I. Naka, Non-linear analysis and synthesis of receptive field responses in the catfish retina. I. Horizontal cell ganglion cell chains, J. Neurophysiol. 36:605-618 (1973a).

P. Marmarelis, and K.I. Naka, Non-linear analysis and synthesis of receptive field responses in the catfish retina. II. One-input white-noise analysis, J. Neurophysiol. 36:619-633 (1973b).

G.P. Moore, J.P. Segundo, D.H. Perkel, and H. Levitan, Statistical signs of synaptic interaction in neurons, Biophys. J. 10:876-900 (1970).

D.H. Perkel, G.L. Gerstein, and G.P. Moore, Neural spike trains and stochastic point-processes. II. Simultaneous spike trains, Biophys. J. 1:419-440 (1967).

L.M. Ricciardi, Diffusion approximation for a multi-input model neuron, Biol. Cybern. 24:237-240 (1976).

L.M. Ricciardi and L. Sacerdote, The Ornstein-Uhlenbeck process as a model for neuronal activity. Biological Cybernetics, 35:1-9 (1979).

D.L. Snyder, Random Point Processes, Wiley, New York, 1975.

L.M. Sørensen, On maximum likelihood estimation in randomly stopped diffusion-type processes, Intern. Statist. Rev. 53:93-110 (1983).

K. Tanaka, Cross-correlation analysis of geniculostriate neuronal relationships in cats, J. Neurophysiol. 49:1303-1318 (1983).

A. Thavaneswaran and M. Thompson, Optimal estimation for semimartingales, J. Appl. Prob. 23:409-417 (1986).

K. Toyama, Kimura, and K. Tanaka, Cross-correlation analysis of interneuronal connectivity in cat visual cortex, J. Neurophysiol. 40:191-201 (1981).

H.C. Tuckwell and D.K. Cope, Accuracy of neuronal interspike times calculated from a diffusion approximation, J. Theor. Biol. 83:377-387 (1980).

H. van den Boogaard, G. Hesselmann, and P. Johannesma, System identification based on point processes and correlation densities. 1. The nonrefractory neuron model, Mathematical Biosciences 80:143-171 (1986).

G.L. Yang and T.C. Chen On statistical methods in neuronal spike-train analysis, Math. Biosciences 39:1-34 (1978).