COMPUTER SIMULATION OF NOISE RESULTING FROM RANDOM SYNAPTIC ACTIVITIES

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Abstract—Neuronal behavior is dependent on random inputs from a multitude of synaptic contacts on the soma and dendritic tree. Therefore, simulations of different types of noise are often required in the experimental and theoretical investigation of the properties of neurons and neuronal assemblies. The direct simulation of these noise sources by simple difference equations may therefore be quite useful and a general approach is presented in this paper. Initially, a first order model and its time-discretization are analyzed in detail, followed by a generalization to more complex models.

The firing patterns of neurons are dependent on the random behaviors of their membrane potentials at the trigger zone. These depend on the propagation of the randomly occurring postsynaptic potentials from specific places on the dendritic tree or soma to the trigger zone. Different models may represent a variety of circumstances in which random membrane potentials arise at the trigger zone. Simulations of different types of noise are often required in the experimental and theoretical investigation of the properties of neurons and neuronal assemblies. The direct simulation of these noise sources by simple difference equations may therefore be quite useful and a general approach is presented in this paper. This paper presents a detailed analysis of the very useful first order model and its time discretization. The criterion used is that the autocovariance sequence of the discrete time model be a sample of the original autocovariance function. Several cases are presented which are of practical interest, including the case of constant output variance independent of the model's time constant. General models are time-discretized by the impulse response invariance method. Two applications are presented, one is related to the modeling of the synaptic currents by the alpha function instead of the delta function and the second deals with analog synaptic noise generation by D/A conversion of computer generated noise sequences. © 1997 Elsevier Science Ltd.

Computer simulation of neuronal noise   Computer simulation of synaptic noise
Algorithms for the simulation of synaptic noise   Simulation of neuronal noise
Simulation of synaptic noise

1. INTRODUCTION

In most neurons in vertebrate central nervous systems (CNS) the random fluctuations in the membrane voltage at the trigger zone are mainly due to the multitude of randomly occurring propagated postsynaptic potentials arising from the dendritic tree and the soma. Some refer to this randomness in somatic membrane potential as synaptic noise [1,2] and usually a white noise model will be inadequate to represent all the dynamics involved from the postsynaptic patches to the trigger zone. The existence of random behaviors in neurons has been acknowledged for a long time and much research, experimental and theoretical, has been done trying to answer questions related to the effects of different noise sources on neuronal dynamics [3]. More recently, there has been a great effort in the study of the dynamics of neuronal networks both deterministic and random. Unfortunately, their analytical study is usually forbidding, except under very unrealistic assumptions from a biological viewpoint, and hence much work has to rely on large scale neuronal network simulators [4,5]. When the elements of the network are noisy, the simulation has to generate a much larger number of action potentials from each neuron so that statistics such as cross-correlations can be estimated with adequate statistical significance. This requires an extremely large number of simulated membrane potential samples. The computer overhead will be extremely large if for each neuron a model for dendritic propagation of synaptic

potentials (e.g. based on partial differential equations) has to be integrated numerically with noise inputs. The more efficient approach generates the noises at the trigger zone by simple difference equations and without numerical integration of very complicated differential equations. Sometimes a given model neuron is to be studied with different noise characteristics at the trigger zone and it usually is an advantage to have the noise and the trigger zone models simulated independently [6]. Another quite interesting use of noise sequences is to apply them as input currents into real neurons [2] to mimic the effects of dendritic or somatic propagation dynamics on synaptic activities. A microelectrode inside the cell soma injects the D/A-converted random waveforms generated by a computer and the resulting trains of action potentials are analyzed.

In many parts of the CNS, specific inputs to neurons are usually segregated to specific regions of the dendritic tree when they are not on the soma [7]. Hence, the synaptic influences from each type of input (e.g. Ia synaptic inputs on motoneurons) can be approximated by a lumped parameter model instead of a stochastic partial differential equation model. This representation of activities at the neuron trigger zone due to one or more populations of synaptic sources at specific regions of the dendritic tree or soma gives a tremendous simplification to the computer simulation of the problem and is one of the guiding lines of the present work.

This paper presents a careful analysis of algorithms for the computer generation of noise sequences originating from a first order neuronal or dendritic model with noise input. This is followed by the presentation of a general approach to the computer simulation of higher order models with noise input.

2. CONTINUOUS TIME MODEL

2.1. *White noise approximation of the equivalent input synaptic current*

Most central nervous system neurons are continually being bombarded by a large number of rather weak synaptic inputs which cause a noisy looking membrane potential when recorded at the soma. The random process at the trigger zone may be viewed as the result of a filtering process by the dendrites and soma of all the random synaptic activations. Let us fix our attention on a population of synapses occurring at a certain region of the soma-dendritic tree complex. Very brief excitatory and inhibitory postsynaptic currents $\rho_e(t)$ and $\rho_i(t)$, respectively, are generated at that region and their equivalent model can be approximated by a white noise process. One justification for this is by assuming linearity and invoking the result that the superposition of a large number of point processes (each associated with a different synapse) is approximated by a Poisson process [8]. This means that, in approximation, the synaptic currents will be described by

$$i(t) = \sum_k \rho_e(t - t_k) + \sum_n \rho_i(t - t_n), \tag{1}$$

where the t_k and t_n are time instants in two independent Poisson processes with mean rates λ_e and λ_i, respectively. Each term in expression (1) is basically a shot noise and the power spectral density (the Fourier transform of the autocovariance function) is:

$$S_{ii}(\omega) = \lambda_e |V_e(\omega)|^2 + \lambda_i |V_i(\omega)|^2, \tag{2}$$

where $V_e(\omega)$ and $V_i(\omega)$ are the Fourier transforms of $\rho_e(t)$ and $\rho_i(t)$, respectively.

As the pulses $\rho_e(t)$ and $\rho_i(t)$ are much briefer than the time constants of interest in somatic and dendritic propagations, the terms $|V_e(\omega)|^2$ and $|V_i(\omega)|^2$ in equation (2) may be approximated by a flat spectrum in the relevant range of ω.

Another approach to justify the white noise approximation may be found in the derivation of the diffusion approximation of a neuron model receiving a large number of excitatory and inhibitory synapses exerting very small influences at the trigger zone [9].

2.2. *First order linear model for the current-to-voltage transformation from the region of synaptic bombardment to the trigger zone*

In some cases, such as when the dendritic tree is electronically compact and behaves linearly, a simple first order linear model can describe approximately the membrane

potential $v(t)$ at the trigger zone when the synapses occur at the soma or dendrites [10]. The model is a parallel association of a resistance R with a capacitance C, the input $i(t)$ being the equivalent current source corresponding to all the synaptic actions and the output $v(t)$ being the membrane potential measured across the resistance–capacitance association. Sometimes such a model is called the RC or "leaky integrator" model [10] and has been widely used in the neural modeling literature. The resulting differential equation is

$$\frac{dv(t)}{dt} = -\omega_0 v(t) + \frac{1}{C} i(t) \tag{3}$$

with $\omega_0 \triangleq 1/R = 1/\tau$, where $\tau = RC$ is the time constant measured at the soma.

The differential equation in (3) has the general solution

$$v(t) = v_0 \exp(-t\omega_0) + \frac{1}{C} \int_0^t \exp[-(t-\lambda)\omega_0]i(\lambda)d\lambda \tag{4}$$

where v_0 is the membrane potential at time zero: $v(0) = v_0$.

If $v_0 = 0$ and $i(t)$ is a very brief pulse applied at time zero, approximated by $\delta(t)$, the solution to (3) is

$$h(t) = \gamma \exp(-t/\tau) = \gamma \exp(-t\omega_0), \tag{5}$$

where $\gamma = 1/C$ and $h(t)$ is the impulse response of the system described by equation (3).

When $i(t)$ is a random process so is $v(t)$ and from our previous considerations $i(t)$ will be a white noise. If its mean $E[i(t)] = i_{DC}$ then the mean of the output random process can be obtained from (4):

$$\mu_v(t) = E[v(t)] = v_0 \exp(-t\omega_0) + \frac{i_{DC}(1 - \exp(-\omega_0 t))}{C\omega_0} \tag{6}$$

which is time-varying even if the initial state v_0 is zero, the transient decaying with a time constant equal to $\tau = 1/\omega_0$ towards the steady state value $i_{DC}/C\omega_0 = R \cdot i_{DC}$. No transient occurs if both v_0 and i_{DC} are equal to zero.

The analysis that follows assumes *zero mean white noise* in the computation of the auto-covariance ACV of the random process $v(t)$: $ACV_{vv}(t,s) \triangleq E[(v(t) - \mu_v(t))(v(s) - \mu_v(s))]$. By defining $y(t) \triangleq v(t) - \mu_v(t)$ we have that $E[y(t)] = 0$, $\forall t$, $y(0) = 0$ and $ACV_{yy}(t,s) = ACV_{vv}(t,s)$. From this:

$$E[y(t)y(s)] = \int_0^t \int_0^s \frac{1}{C} \exp[-(t-\lambda)]\omega_0] \frac{1}{C} \exp[-(s-\tau)\omega_0]E[i(\lambda)i(\tau)]d\lambda d\tau.$$

As $Y(t)$ is generated using an input current process $i(t)$ which is a zero mean white noise we have that $E[i(t)i(s)] = \beta^2 \delta(t-s)$, where β^2 is the finite value of the constant power spectral density of the input white noise, i.e. $S_{ii}(\omega) = \beta^2$ (notice that β^2 is *not* the variance of the input noise because the variance or power of continuous time white noise is infinite since variance $= \int_{-\infty}^{\infty} \beta^2 df = \infty$. For $s > t$ the result above becomes

$$E[y(t)y(s)] = \frac{1}{C^2} \exp[-(t+s)\omega_0] \int_0^t \exp(\omega_0\lambda)\exp(\omega_0\lambda)\beta^2 d\lambda$$

which results in

$$E[y(t)y(s)] = \frac{\beta^2}{C^2} \exp[-(t+s)\omega_0] \frac{1}{2\omega_0} [\exp(2\omega_0 t) - 1]$$

and making $s = t + \tau$ ($\tau \geq 0$)

$$E[y(t)y(t+\tau)] = \frac{\beta^2}{2\omega_0 C^2} \exp(-\tau\omega_0) - \frac{\beta^2}{2C^2\omega_0} \exp[-\omega_0(2t+\tau)]$$

which gives the autocovariance function of the nonstationary process $v(t)$:

$$ACV_{vv}(t,t+\tau) = \frac{\beta^2}{2\omega_0 C^2} \exp(-\tau\omega_0) - \frac{\beta^2}{2\omega_0 C^2} \exp(-\omega_0(2t+\tau)); \quad \tau > 0. \tag{7}$$

As a test of expression (7) we have that for $t=0$ and $\tau=0$ the autocovariance is zero, which is correct because the system always starts from the same initial state. According to equation (7), the autocovariance depends on the ongoing time t but it decays with a time constant equal to $\tau/2$ to the first expression on the right side of the equation for increasing values of t. In practical terms, this means that if we want to obtain an approximately stationary (wide-sense) random process, then we have to start measuring $v(t)$ only after an adequate interval of time from the initial time (a few time constants will do). In this case, when the nonstationarities (the transients) will have died out, the autocovariance will be

$$ACV_{vv}(\tau) = \frac{\beta^2}{2\omega_0 C^2} \exp(-\omega_0 \tau); \quad \tau > 0$$

or

$$ACV_{vv}(\tau) = \frac{\beta^2}{2\omega_0 C^2} \exp(-\omega_0 |\tau|); \quad \tau \in \mathbb{R}. \tag{8}$$

An exponential autocovariance function of the membrane potential has been found, for example, in cat motoneurons [1] and in invertebrate sensory receptors [11,12].

The variance or power is obtained from (7) by making $\tau=0$:

$$\sigma_v^2(t) = \frac{\beta^2}{2\omega_0 C^2} - \frac{\beta^2}{2\omega_0 C^2} \exp(-\omega_0 2t); \quad \tau > 0$$

and if we wait long enough the variance tends to the steady state value

$$\sigma_v^2 = \frac{\beta^2}{2\omega_0 C^2} = \frac{\beta^2 \tau}{2C^2}. \tag{9}$$

Here one should notice that altering the time constant τ while keeping C fixed will alter the output noise variance.

The power spectral density $S_{vv}(\omega)$ is the Fourier transform of (8):

$$S_{vv}(\omega) = \frac{\beta^2}{C^2} \frac{1}{(\omega^2 + \omega_0^2)}; \quad \omega \in \mathbb{R}. \tag{10}$$

This power spectrum is sometimes called Lorentzian and is typical of the output of a first order lowpass system that has white noise at its input. It can also be derived from the relation

$$S_{vv}(\omega) = |H(j\omega)|^2 S_{ii}(\omega), \tag{11}$$

where $S_{ii}(\omega) = \beta^2$ and $H(j\omega)$ is the frequency response of the system and can be found from the transfer function $H(s)$ by substituting $s = j\omega$. In the case of the system described by (3) the transfer function is

$$H(s) = \frac{V(s)}{I(s)} = \frac{R}{1 + s\tau} = \frac{R\omega_0}{\omega_0 + s} = \frac{1}{C(s + \omega_0)}. \tag{12}$$

2.3. Models with impulse responses composed of a sum of a finite number of exponentials

For a general dendritic tree and with the linearity property satisfied, the impulse response for synaptic input at the soma and the output at the soma or trigger zone is an infinite sum of exponentials [13]:

$$h(t) = \sum_{k=1}^{\infty} \gamma_k \exp(-t/\tau_k) = \sum_{k=1}^{\infty} \gamma_k \exp(-t\omega_k) \tag{13}$$

where $\omega_k = 1/\tau_k$.

In practice, a finite number of terms in the sum will usually yield an acceptable approximation. Recently, a new method was proposed for fitting neuronal or other experimental data to such sums of exponentials [14]. Assuming a sum of K exponentials in

(13), the resulting transfer function is:

$$H(s) = \sum_{k=1}^{K} \frac{\gamma_k}{s - s_k} \tag{14}$$

where $s_k = -\omega_k = -1/\tau_k$.

When input synaptic currents occur at a certain region of a dendritic tree, the impulse response at the soma or trigger zone will depend on characteristics such as the geometries involved, membrane resistivities and capacitances, intracellular specific resistance and the types of boundaries [10,15]. Analytic expressions from cable theory may vary in difficulty, many times an infinite series will have to be truncated so that a sum of a finite number of functions results. Other times the impulse response will be an expression that is not a function of pure exponentials [10,15].

Finally, an approach which has been used in neuronal computer simulations is the compartmental modeling of the dendritic tree. If the structures are passive (dynamically linear) then the impulse response is of the form $h(t) = \sum_{k=1}^{K} \gamma_k \exp(-t/\tau_k)$ [16] and hence the transfer function is given by (14). As a generalization of all we have seen, if the synaptic bombardment comes from more than one source acting on more than one region of the neuron, and if linearity in the propagation dynamics may be assumed for all the different paths, then the contributions from each source may be summed at the trigger zone. Therefore, the overall impulse response or transfer function will be a sum of different impulse responses or partial transfer functions, each given by equation (14) with a specific K value. Difference equations simulating this overall transfer function (by simulating the partial equations) will permit the generation of the desired synaptic noise at the trigger zone.

3. TIME-DISCRETIZATION OF CONTINUOUS TIME MODELS

One fundamental issue in the discretization of the continuous time models presented in the previous section is what criterion should be used to obtain the corresponding difference equations. In digital filter theory there are a few methods to obtain discrete-time versions of continuous time systems. These include: impulse response invariance, bilinear transformation, numerical solution of a differential equation, minimization of a frequency domain approximation criterion [17]. Those based on the frequency domain are usually inappropriate for the simulation of synaptic noise. This stems from the fact that the most usual applications of digital filters are related to spectral shaping while in neuronal dynamics the time domain characteristics are the relevant ones [18,19]. In other words, a reproduction of the autocovariance is much more important in synaptic noise generation than that of the power spectral density and any discrete time simulation should have an output autocovariance sequence which is a good approximation to the sampled version of the original continuous time system autocovariance function.

In what follows, some issues will be presented in more detail for the simple model of equation (3). The objective will be to discretize the time, so that we only generate noise samples at every T units of time. The difference equations will be a function of the counting variable n ($n=0$, 1, 2,...) which actually means that input and output variables are obtained at multiples nT of the sampling period T. The sampling rate in samples/s or Hz is the inverse of T.

3.1. Time-discretization of equation (3)

From the general solution (4) to the system (3) we have for a time step T between two consecutive sampling times:

$$v(t+T) = \exp(-T\omega_0) \cdot v(t) + \frac{1}{C} \int_t^{t+T} \exp[-(t+T-\lambda)\omega_0] \cdot i(\lambda) d\lambda$$

with $v(0) = v_0$.

Different approaches to approximate the expression above (e.g. for small τ the exponential term under the integral can be assumed constant in the interval and taken out of the integral) give the general result:

$$w(t+T)=a \cdot w(t)+b \cdot i(t),$$

where $w(t)$ is the approximation to $v(t)$ and a and b are constants that depend on T, ω_0 (or τ) and C. For convenience, the input white noise mean i_{DC} will be represented separately in the equation above, resulting

$$w(t+T)=a \cdot w(t)+b \cdot i(t)+c \cdot i_{DC}$$

where $i(t)$ is a *zero mean* white noise.

As the time axis is being sampled so that only values such as $t=nT$ are relevant, we can leave out the factor T in denoting $w((n+1)T)$ and $w(nT)$ by $w(n+1)$ and $w(n)$, respectively:

$$w(n+1)=a \cdot w(n)+b \cdot i(n)+c \cdot i_{DC} \tag{15}$$

with $w(0)=v_0$.

The general solution of (15) is:

$$w(n)=a^n v_0+ \sum_{j=1}^{n} a^{n-j}bi(j-1)+ \frac{c \cdot i_{DC} \cdot (1-a^n)}{1-a}, \; n=1,2,\ldots. \tag{16}$$

By applying expected values to both sides of (16) we have:

$$E[w(n)]=a^n v_0+ \frac{c \cdot i_{DC} \cdot (1-a^n)}{1-a}$$

which when compared with (6) sampled at $t=nT$ gives:

$$a=\exp(-\omega_0 T) \tag{17}$$

$$c= \frac{1-\exp(-\omega_0 T)}{C\omega_0} . \tag{18}$$

The values of a and c given by (17) and (18), respectively, assure that the difference equation will have steady state and transients due to the initial state and to the nonzero mean i_{DC} of the input noise which are exact sampled versions of the continuous time result given in (6). After the transients die away the mean of $w(n)$ is $i_{DC}/C\omega_0=R \cdot i_{DC}$. Only in the case $v_0=0$ and $i_{DC}=0$ there will be no transient in the output mean value.

The resulting difference equation (15) will convert a white noise sequence $i(n)$ into a colored noise sequence $w(n)$. A white noise *sequence* has a constant power spectral density $S(f)=\beta^2$ for $f\in[-1/2T,1/2T]$ and a *finite* variance (power) equal to $\int_{-1/2T}^{1/2T} \beta^2 dt=\beta^2/T$, where $1/T$ is the sampling frequency. From a different perspective, it is important to note that if a white noise sequence is generated with a pre-established variance σ^2 then the power spectral density will be $\beta^2=\sigma^2 \cdot T$. In this situation, when the sampling frequency increases the power spectral density decreases so that the area remains constant. Sometimes confusions arise in the literature when these issues of constant power spectral density versus constant variance are not clearly established.

It is important to check if the second order time statistics of the discrete-time version of (3) can be made compatible with the original continuous time statistics. For this we shall find the autocovariance sequence of the output sequence $w(n)$ of equation (15), assuming a zero mean white noise input. The autocovariance should ideally be a perfect reproduction of that for the original continuous time model, or at least it should tend to the continuous time autocovariance when the step size tends to zero.

To find $ACV_{ww}(n)$ one should take $i(n)$ with zero mean and $v_0=0$ and then compute $E[w(k)w(k+n)]$. The input power spectral density is assumed to be β^2 and therefore the corresponding autocovariance is $E[i(k)i(j)]=(\beta^2/T)\delta(k-j)$. Therefore:

$$E[w(k)w(p)]= \sum_{j=1}^{k} \sum_{\ell=1}^{p} a^{k+p-j-\ell}b^2 E[i(j-1)i(\ell-1)]$$

where $p=k+n$ ($p>k$ or in other words $n>0$). The equation results

$$E[w(k)w(p)] = \frac{a^{k+p}b^2}{T} \sum_{j=1}^{k} a^{-2j}\beta^2 = a^{k+p}b^2\beta^2 \frac{(a^{-2k}-1)}{T(1-a^2)}$$

or with $p=k+n$:

$$E[w(k)w(p)] = a^p b^2 \beta^2 \frac{(a^{-k}-a^k)}{T(1-a^2)} = \frac{b^2\beta^2}{T(1-a^2)} a^n(1-a^{2k}).$$

Using the expressions for a given in (17) we have:

$$ACV_{ww}(k,k+n) = \frac{b^2\beta^2}{T(1-\exp(-2T\omega_0))} \exp(-nT\omega_0)\cdot(1-\exp(-2kT\omega_0)), \qquad (19)$$

or still

$$ACV_{ww}(k,k+n) = \frac{b^2\beta^2}{T} \frac{\exp(-nT\omega_0)}{(1-\exp(-2T\omega_0))} - \frac{b^2\beta^2}{T} \frac{\exp(-\omega_0 T(2k+n))}{(1-\exp(-2T\omega_0))}. \qquad (20)$$

Remembering that $nT=\tau$ and that $kT=t$, the comparison of equations (7) and (20) gives

$$b = \frac{\sqrt{T}\sqrt{1-\exp(-2T\omega_0)}}{\sqrt{2\omega_0}C}. \qquad (21)$$

The resulting difference equation is then obtained by substituting (17) and (21) in (15):

$$w(n+1) = \exp(-T\omega_0)\cdot w(n) + \frac{\sqrt{T}\sqrt{1-\exp(-2T\omega_0)}}{\sqrt{2\omega_0}C} \cdot i(n). \qquad (22)$$

For completeness we give the corresponding discrete time transfer function:

$$\frac{W(z)}{I(z)} = \frac{z^{-1}\sqrt{T}\sqrt{1-\exp(-2T\omega_0)}}{\sqrt{2\omega_0}C[1-z^{-1}\exp(-T\omega_0)]}. \qquad (23)$$

If the input noise has $i_{DC}\neq0$ then (22) will be

$$w(n+1) = \exp(-T\omega_0)\cdot w(n) + \frac{\sqrt{T}\sqrt{1-\exp(-2T\omega_0)}}{\sqrt{2\omega_0}C} \cdot i(n) + \frac{1-\exp(-\omega_0 T)}{C\omega_0} \cdot i_{DC}. \qquad (24)$$

The result we have just derived shows that for the simple first order system given in (3) it is feasible to obtain a difference equation whose output has an autocovariance sequence (transient and stationary parts) that is a perfect sampled version of the continuous time autocovariance function. For more complicated systems the above derivations may be unwieldy and approximate methods have to be used. In these cases it could be desirable to check if the discrete time autocovariance tends to the continuous time when the step size tends to zero.

Note that the discrete time autocovariance of the output noise from (22) is

$$ACV_{ww}(k,k+n) = \frac{\beta^2}{2\omega_0 C^2} \exp(-nT\omega_0) - \frac{\beta^2}{2\omega_0 C^2} \exp(-T\omega_0(2k+n)) \qquad (25)$$

and that for $T\to0$ k and n will have to tend to ∞ to make $kT=t$ and $nT=\tau$ both finite.

From this last expression we obtain the evolution of the variance of $w(n)$

$$\sigma_w^2(k) = \frac{\beta^2}{2\omega_0 C^2} - \frac{\beta^2}{2\omega_0 C^2} \exp(-T\omega_0 2k)$$

which shows that after a transient the variance tends to

$$\sigma_w^2 = \frac{\beta^2}{2\omega_0 C^2} = \frac{\beta^2\tau}{2C^2} = \frac{\beta^2 R}{2C}$$

for any finite fixed step size T. As in the continuous time case, we point out that changing τ while keeping C constant will also change the output noise power. If different time constants $\tau = RC$ are desired but without changing the output noise variance then one should change the RC product but keep the R/C ratio constant. For example, if $R = C = \sqrt{\tau}$ then $\sigma^2 = \beta^2/2$ for any time constant τ.

In the derivations above a discrete time white noise input was used with a power spectral density equal to β^2 (i.e. autocovariance $= (\beta^2/T)\delta(k-j)$). The discrete approximation (15) to equation (3) will give results that converge to the correct solution (of the continuous time system) when the step size T tends to 0, but with no error in terms of the autocovariance sequence. It is important to emphasize that while β^2/T is the variance of the discrete time white noise at the input of (15) the white noise at the input of the continuous time system (3) has infinite variance (or power) but has a constant power spectral density equal to β^2. In this way when $T \rightarrow 0$ the discrete time system tends to the continuous time system and the discrete time white noise variance tends to ∞, which agrees with the variance of the continuous time white noise.

Finally, a simpler difference equation can be obtained from (24) using an approximation for small T (say $T \leq \tau/10$):

$$w(n+1) = (1 - T/\tau) \cdot w(n) + (T/C) \cdot i(n) + (T/C) \cdot i_{DC}, \tag{26}$$

where $i(n)$ is zero mean white noise with variance β^2/T.

3.2. Time-discretization of the first order model of equation (3) by the method of impulse response invariance

The method of time-discretization by impulse response invariance [17] consists in imposing

$$h_d(n) = T \cdot h(nT) \tag{27}$$

where $h(nT)$ is the continuous time impulse response and $h_d(n)$ is the discrete time version. This is equivalent to a mapping of the following transfer function in the complex variable s (associated with the continuous time system)

$$H(s) = \sum_{k=1}^{K} \frac{\gamma_k}{(s - s_k)}$$

on the transfer function in the complex variable z (associated with discrete time system) given below

$$H_d(z) = \sum_{k=1}^{K} \frac{T\gamma_k}{[1 - z^{-1}\exp(Ts_k)]}, \tag{28}$$

where z^{-1} corresponds to a unit delay in time.

We shall apply this method to the case of the system described by equation (3). The impulse response and the transfer function give the same information, having one you can get the other by Laplace transformations. As model (3) has the transfer function given in (12), it is straightforward to obtain $H(z)$ from (28), with $\gamma_k = R\omega_0$ and $s_k = -\omega_0$:

$$H(z) = \frac{TR\omega_0}{1 - z^{-1}\exp(-T\omega_0)} = \frac{W(z)}{I(z)}, \tag{29}$$

where $W(z)$ and $I(z)$ are the z-transforms of the output and input sequences, respectively. From this transfer function the corresponding difference equation is obtained by cross-multiplying and anti-transforming:

$$w(n) = \exp(-T\omega_0) \cdot w(n-1) + TR\omega_0 i(n)$$

but since $\omega_0 \triangleq 1/RC = 1/\tau$

$$w(n) = \exp(-T\omega_0) \cdot w(n-1) + \frac{T}{C} i(n) \tag{30}$$

for $n = 1, 2, \ldots$ and $w(0) = x_0$.

The difference equation (30) should now be compared with the one obtained before in (22). Besides a delay of one sample in the input, which is innocuous for the purpose of generating noise samples $w(n)$, the other difference is in the constant that multiplies $i(n)$. In (30) it is T/C, while in (22) it is $\sqrt{T}\sqrt{1 - \exp(-2T\omega_0)}/\sqrt{2\omega_0} \cdot C$, which, nevertheless, can be approximated by T/C if we take a small enough T. Therefore, the two approaches yield similar results if T is made small enough (e.g. $T \le 0.1\tau$), although (22) is more precise.

3.3. Special cases of practical interest

3.3.1. If the *input* has a *constant power spectral density* β^2, i.e. a variance that increases linearly with the inverse of the time step T, equation (22) should be used, or its approximate expression (30). The theoretical steady state variance is $\sigma_w^2 = \beta^2/2\omega_0 C^2$.

3.3.2. If the *input* white sequence $i(n)$ is to have a *fixed variance* σ^2 independent of the step size T, then (22) should have the input coefficient divided by $\sqrt{T}$:

$$w(n+1) = \exp(-T\omega_0) \cdot w(n) + \frac{\sqrt{1 - \exp(-2T\omega_0)}}{\sqrt{2\omega_0 C}} \cdot i(n) \tag{31}$$

and similarly for (30):

$$w(n) = \exp(-T\omega_0) \cdot w(n-1) + \frac{\sqrt{T}}{C} i(n). \tag{32}$$

The theoretical steady state output variance is $\sigma_w^2 = \sigma^2/2\omega_0 C^2$.

To have a feeling of how the two approaches behave, we made simulations of the two difference equations (given by (31) and (32)) with different values of the step size T. Each equation, with $\omega_0 = 5$ and $C = 1$, always received as input the same 30,000 Gaussian samples from a unit variance white noise sequence and, therefore, the theoretical output noise variance σ_w^2 is 0.1. The first 1000 samples of the output noise were not used to compute the variance estimate. In Table 1 it can be seen that the estimated variances $\hat\sigma_{w1}^2$ and $\hat\sigma_{w2}^2$ of the output noises generated by the two systems (equations (31) and (32), respectively) are roughly similar even though the variance of the noise generated by (31) is closer to the theoretical value. Had we used the original equations (22) and (30) the variances would have depended very strongly on the step size T.

3.3.3. If the available *input* white sequence $\theta(n)$ always has *unit variance*, which may be convenient in terms of computer routines or if the same input sequence (meaning waveshape) is to be used but with different "amplitudes", i.e. different standard deviations, then equations (31) and (32) become respectively:

$$w(n+1) = \exp(-T\omega_0) \cdot w(n) + \frac{\sigma\sqrt{1 - \exp(-2T\omega_0)}}{\sqrt{2\omega_0 C}} \cdot \theta(n) \tag{33}$$

Table 1. Variances of the output noises for two difference equations as a function of T

	$T=0.02$	$T=0.01$	$T=0.002$
$\hat\sigma_{w1}^2$	0.1001	0.0983	0.0991
$\hat\sigma_{w2}^2$	0.1104	0.1034	0.1001

and

$$w(n)=\exp(-T\omega_0)\cdot w(n-1)+\frac{\sigma\sqrt{T}}{C}\,\theta(n), \tag{34}$$

where $\theta(n)$ is a zero mean white noise with unit variance and σ^2 is the actual desired variance for the input. The theoretical steady state output variance is $\sigma_w^2=\sigma^2/2\omega_0 C^2$.

3.3.4. If in the previous case we impose in addition that the steady state *output noise variance be independent of* τ (or of ω_0) we can make $R=C=\sqrt{\tau}$ to obtain $\sigma_w^2=\sigma^2/2$. The equations become:

$$w(n+1)=\exp(-T/\tau)\cdot w(n)+\frac{\sigma\sqrt{1-\exp(-2T/\tau)}}{\sqrt{2}}\cdot\theta(n) \tag{35}$$

and

$$w(n)=\exp(-T/\tau)\cdot w(n-1)+\sigma\sqrt{T/\tau}\,\theta(n). \tag{36}$$

This case is relevant, for example, in the study of the effects of different colored noises on neuronal behavior. If we use any of the previous algorithms, a decrease in the frequency cutoff, i.e. an increase in the time constant, will decrease the variance or power of the resulting output noise with the probable consequence that less neuronal discharges will occur, *independently of the differences in frequency content in the noise*. The use of any of the equations (35) or (36) avoids this pitfall and the difference in neuronal behavior will only reflect the differences in the time structure of the noise signals.

3.3.5. If the *output noise* is desired with a *fixed plateau value in the power spectral density* (at small ω) which does not depend on the system time constant τ then, from (10) we must have $R=$constant. If, for example, $R=1$, then $\tau=C$ and the equations (33) and (34) become:

$$w(n+1)=\exp(-T/\tau)\cdot w(n)+\frac{\sigma\sqrt{1-\exp(-2T/\tau)}}{\sqrt{2\tau}}\cdot\theta(n)$$

and

$$w(n)=\exp(-T/\tau)\cdot w(n-1)+\frac{\sigma\sqrt{T}}{\tau}\,\theta(n)$$

3.3.6. In any of the cases above, if the *input noise* is to have a *non zero mean* i_{DC} then a term $i_{DC}\cdot(1-\exp(-\omega_0 T))/C\omega_0$ should be added to the respective difference equation, as done, for example, in equation (24). If the step size is small enough the term would simplify to $i_{DC}\cdot T/C$.

3.3.7. Any of the difference equations presented in this paper may be used for the generation of *analog* noise signals from computer-generated noise sequences. In this setting, let T_s be the interval between the samples or the inverse of the sampling frequency f_s of the D/A converter. If a noise sequence with an autocovariance having a time constant τ is D/A converted with $T_s=\alpha T$ (α being a positive constant), then the resulting *analog* noise will have an autocovariance function with time constant $\alpha\tau$. An illustration of this result will be given later in Application Example II.

3.4. *Time-discretization of an impulse response that is a sum of a finite number of exponentials*

When the impulse response is a sum of exponentials $\sum_{k=1}^{K}\gamma_k\exp(-t\omega_k)$ the suggested method of discretization will be based on the impulse response invariance and the main result to be taken from the previous derivations is that for an input white noise sequence with a fixed *unit variance* the calculated coefficient multiplying the input sequence should be multiplied by $\sigma/\sqrt{T}$. This will be done below to find equation (38) from (37). Each

exponential in the sum $\sum\limits_{k=1}^{K} \gamma_k \exp(-t\omega_k)$ will result in a first order transfer function and the total transfer function will be given by (14). The method of impulse response invariance generates the transfer function in the z domain given by (28), from which we obtain:

$$W(z) = H(z) \cdot I(z) = \sum_{k=1}^{K} \frac{T\gamma_k I(z)}{[1 - z^{-1}\exp(Ts_k)]} = \sum_{k=1}^{K} Q_k(z),$$

where $s_k = -\omega_k$ and each $q_k(n)$ is given by

$$q_k(n) = \exp(-T\omega_k) \cdot q_k(n-1) + T\gamma_k i(n) \tag{37}$$

for $n = 1, 2, 3,...$; $k = 1, 2, 3,..., K$ and $q(0) = 0$. However, as mentioned above, the use of a standard input white sequence $\theta(n)$ with variance equal to 1 requires a correction to (37):

$$q_k(n) = \exp(-T\omega_k) \cdot q_k(n-1) + \gamma_k \sqrt{T}\sigma \cdot \theta(n). \tag{38}$$

The overall output is $w(n)$ given by

$$w(n) = q_1(n) + q_2(n) + ... + q_K(n). \tag{39}$$

Therefore, K simultaneous difference equations like (38) are used with the same white noise input sequence $\theta(n)$, and at each time step the values of all the $q_k(n)$ are summed to yield the value of the output $w(n)$ at the same time step. Some of the observations given in the previous item for the first order system also apply here.

4. FINAL REMARKS

To *generate the input white sequence*, either a uniform $(0,1)$ generator or a $N(0,1)$ Gaussian sample generator is used. In the uniform $(0,1)$ case, each sample should have 0.5 subtracted and the result multiplied by $\sqrt{12}$ (to get a zero mean unit variance white noise). It should be noted that, due to the central limit theorem, the output (after a short transient) of the difference equations given in this paper will be Gaussian even when the input is non-Gaussian.

In case a desired dendritic equivalent impulse response is not expressed as a combination of exponentials [15], an optimization method may be employed to obtain a difference equation approximation, as described in section 5.3.3 of [17].

The step size should be chosen smaller than the *smallest* time constant involved in the impulse response (e.g. between $T = \tau_{min}/5$ and $\tau_{min}/10$).

If steady state statistics are desired, the output noise sequences must be taken after the transients have decreased enough, e.g. after five or ten times the *largest* time constant involved in the impulse response. The starting sample number to be used in the output noise sequence n_{min} will depend on the step size T, e.g. $n_{min} = 10\tau_{max}/T$. For example, if $\tau_{min} = 1$ ms, $\tau_{max} = 15$ ms and $T = 0.1$ ms, then $n_{min} = 1500$.

5. APPLICATION EXAMPLES

(I) In some applications a more refined model for the postsynaptic currents, such as the popular alpha function [10], may be desired. The objective here will be to simulate synaptic noise using the alpha function impulse response for the postsynaptic currents and the simple first order model of equation (3) for the generation of the postsynaptic potentials as propagated to the trigger zone. For the latter we can use (22) or (30) except that instead of having a white noise input $i(n)$, it will have the colored noise $x(n)$ as its input. For the former we shall derive in what follows the corresponding difference equation relating the output $x(n)$ to the input white noise sequence $\theta(n)$ with zero mean and unit variance.

The alpha function is $\alpha^2 t \exp(-\alpha t)$ and hence an impulse response of the postsynaptic current is

$$h_{sc}(t) = \alpha^2 t \exp(-\alpha t)$$

the input impulse being associated with a presynaptic action potential (ignoring the synaptic delay) and α setting the postsynaptic current rise time. In this example we shall use alpha values 20, 40 and 100.

As the time will be discretized with step size T, from (27) the discrete time impulse response will be

$$h_{sc}(n) = T\alpha^2 nT \exp(-\alpha nT).$$

This expression is valid when the input power spectral density is a constant β^2. The corresponding transfer function may be found from a table of z transforms [17] as:

$$H_{sc}(z) = \frac{T^2\alpha^2 \exp(-\alpha T)z^{-1}}{(1 - \exp(-\alpha T)z^{-1})^2} = \frac{X(z)}{I(z)}. \tag{40}$$

As an analogy to what was done when we wanted a white noise input $\theta(n)$ with unit variance the final transfer function has to have an additional factor $\sigma/\sqrt{T}$ multiplying the numerator. From this modified transfer function we obtain the corresponding difference equation:

$$x(n) = 2\exp(-\alpha T)x(n-1) - \exp(-2\alpha T)x(n-2) + \sigma T^{3/2}\alpha^2 \exp(-\alpha T)\theta(n-1) \tag{41}$$

with $x(0) = 0$, $x(1) = 0$ and $n = 2, 3, 4, \ldots$. This difference equation should be used together with either equation (22) or (30), e.g.
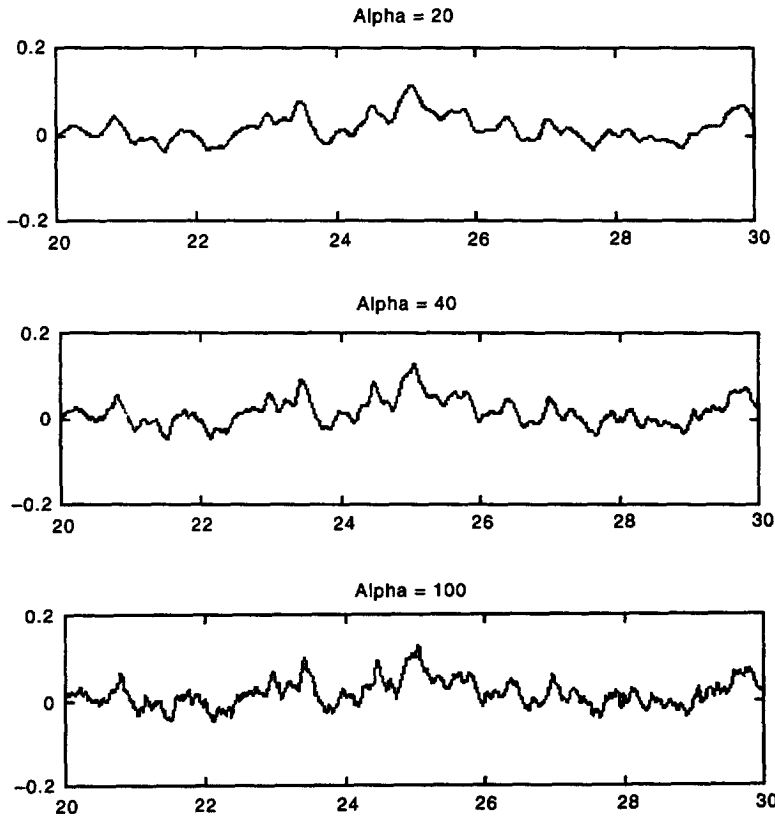

Fig. 1. Time course of noise signals generated by simulations of alpha impulse response for synaptic currents followed by a first order system. Larger alpha values yield waveforms with sharper peaks and faster transitions.
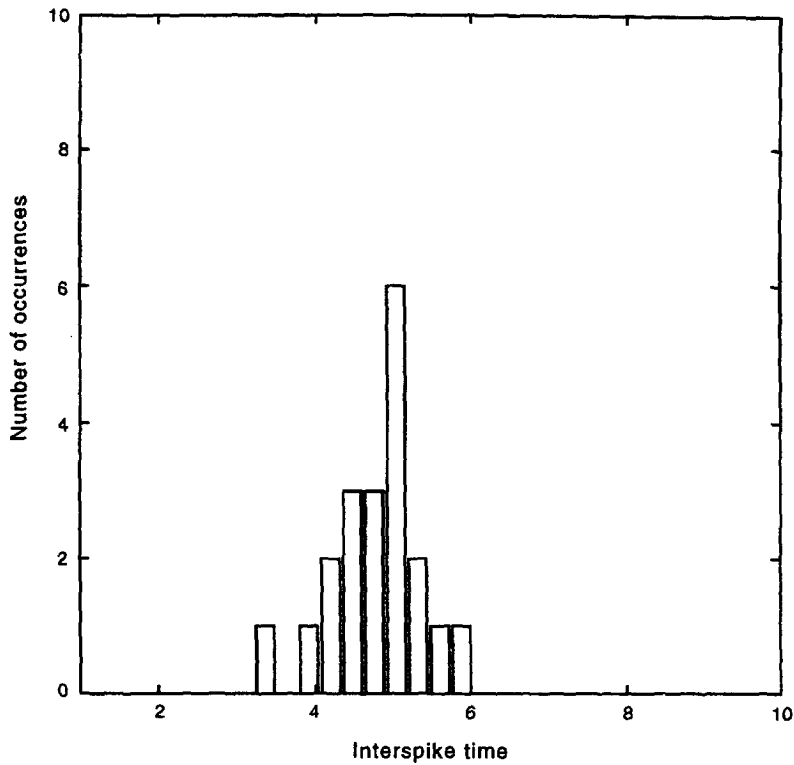
Fig. 2. Inter-spike interval histogram for leaky integrator with threshold model with noise input
corresponding to $\alpha=40$.

$$w(n)=\exp(-T\omega_0)\cdot w(n-1)+ \frac{T}{C}\cdot x(n) \tag{42}$$

with $w(0)=w(1)=0$ and $n=2, 3, 4,....$ As explained before, the initial zero samples should
be discarded from the output noise sequence $w(n)$ before using it in a simulation. An
alternative approach would be to obtain the overall transfer function by multiplying the two
transfer functions given by (40) and either (23) or (29). The result would have to be
corrected (as seen before) by multiplying the numerator by $\sigma/\sqrt{T}$ so that the overall input
is white noise with unit variance. From this overall transfer function the corresponding
difference equation may be derived. This alternative approach, besides giving a single
difference equation algorithm, also justifies why in (42) we used (30) and not (32). Figure
1 shows noise signals generated by (41) and (42) for alpha values of 20, 40 and 100, from
which we can see that the high frequency content for $\alpha=100$ is more pronounced than for
$\alpha=20$. This difference in the time structure may or may not cause statistical differences in
the neuronal spike trains. For the sake of illustration, a simple leaky-integrator-with-
threshold neuronal model was simulated having as input the noise signals we have just
described. To generate 21 action potentials 10,000 input noise samples had to be generated.
It should be emphasized that in order to get stable and significant spike train statistics a
much larger number of action potentials is needed (say, at least 1000). Figure 2 shows the
inter-spike interval histogram for the simulation with $\alpha=40$, the histograms for the other
alpha values being very similar to this one (using a visual comparison). Indeed, the
histogram from a simulation without using the alpha system, i.e. assuming the synaptic
currents to be modeled by impulses, was also similar to Fig. 2. It may be that other statistics
would show a dependence on alpha values and, also, it may be that a different trigger zone
model would be more dependent on the different alpha values used. As a final illustration
in this example, the neuronal membrane potentials are shown in Fig. 3 for $\alpha=40$ and the
same input current noise sequence, one with standard deviation 0.1131 and the other

0.2262. The noisier membrane potential results in more variability in the interspike intervals.

(II) In this application the objective is to generate *analog* colored noise signals by D/A conversion of computer generated noise sequences. One use would be to inject as current in a neuron's soma. In this example, the D/A converter is used with two different rates yielding two noise signals, the autocovariance function of one being a time-scaled version of the other. The simple first order model (35), with $\tau=1$ ms and $T=0.1$ ms, is used to filter a Gaussian white noise sequence (zero mean and unit variance) with 10,000 samples generated by Matlab. When the D/A converter outputs samples at every $T_s = 100$ μs ($=T$), the autocovariance function of the analog noise at the output of the D/A should have a time constant of 1 ms, but when the noise samples are sent by the D/A at every $T_s = 20$ μs (i.e. 5 times faster) then the analog noise will have a 5 times ($100 \mu s/20 \mu s$) shorter autocovariance time constant, i.e. equal to 0.2 ms. An alternative view is in the frequency domain: when we pass from $T_s = 100$ μs to $T_s = 20$ μs the analog noise bandwidth will increase 5 times.

A program in C implements the algorithm given by (35) and sends the resulting sequence to a D/A converter at a rate equal to $f_s = 1/T_s$. Figure 4 shows the resulting analog noise autocovariances when the D/A clock is 10 kHz and 50 kHz, i.e. $T_s = 100$ μs and $T_s = 20$ μs, respectively. The slower curve corresponds to $T_s = 100$ μs. The time constants for the two autocovariances were estimated graphically to be equal to 1.03 ms and 0.18 ms, which are close to the theoretical values 1.0 ms and 0.2 ms. Note that the variance in both cases is approximately 0.42, which is somewhat lower than the theoretical value 0.5, probably due to sampling variations. It should be emphasized that in these procedures the value of T in the difference equations should stay constant, only the D/A output rate $1/T_s$ is changed.
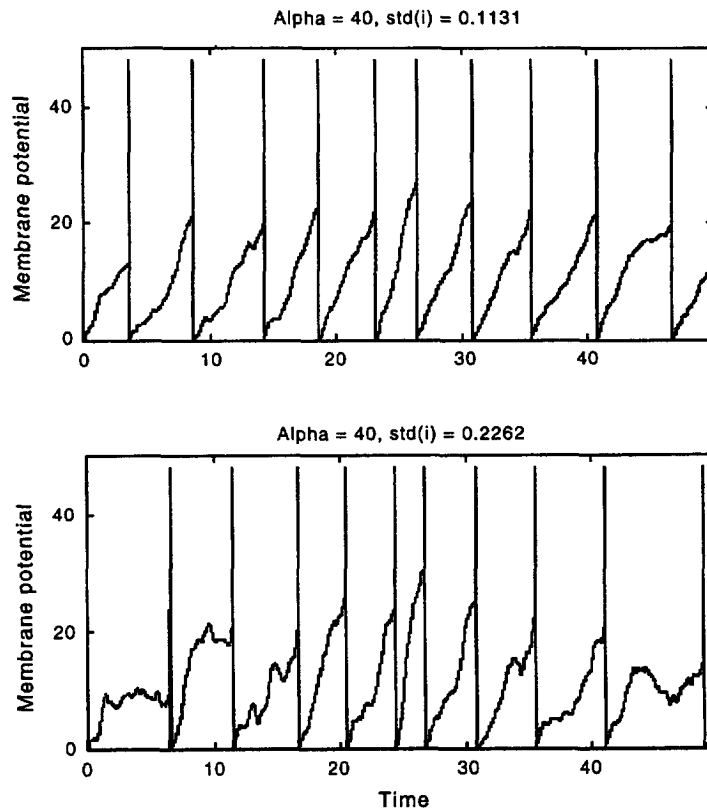

Fig. 3. Membrane potential time courses for two simulations with the same alpha value but with different variance of the synaptic input noise. The lower figure is for higher input variance and shows larger inter-spike interval variability.

ACV of D/A output with 100 μs and 20 μs output interval
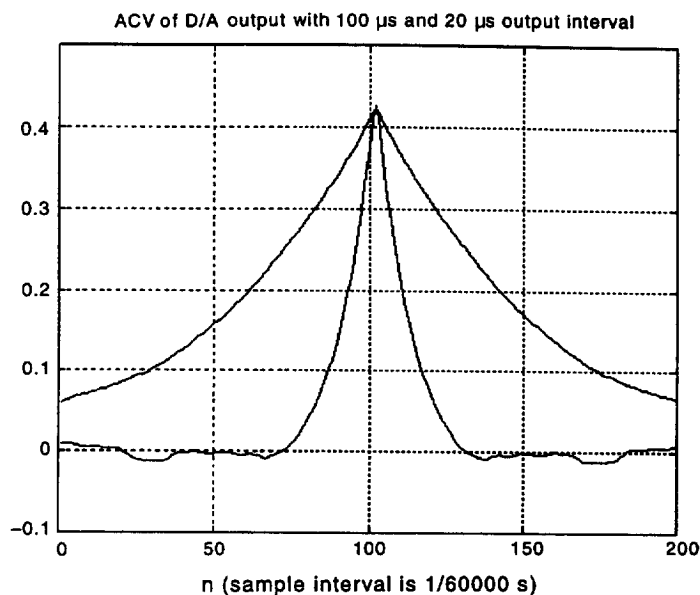

n (sample interval is 1/60000 s)

Fig. 4. Autocovariances for two analog noise signals generated from the same sequence stored in a computer but with different D/A sampling intervals. The abscissa is the sample number, where the interval between two adjacent samples corresponds to 16.67 μs. The ordinate is in V^2, the peak of the autocovariances indicating the respective noise variances. These autocovariances were computed with Matlab after A/D conversion of the analog noise signals at a rate of 60,000/s.

From this example we can see that a noise sequence may be used repeatedly to generate different analog noises if a D/A converter is used at different rates. The resulting analog noise autocorrelation function will change in time scale according to the D/A sampling interval but its form will stay the same.

REFERENCES

1. W.H. Calvin and C.F. Stevens, Synaptic noise and other sources of randomness in motoneuron interspike intervals, *J. Neurophysiol.*, **31**, 574–587 (1968).
2. A.V. Poliakov, R.K. Powers, A. Sawczuk and M.D. Binder, Effects of background noise on the response of rat and cat motoneurons to excitatory current transients, *J. Physiol.*, **495.1**, 143–157 (1996).
3. J.P. Segundo, J.F. Vibert, K. Pakdaman, M. Stiber and O. Diez-Martinez, Noise and the neurosciences: a long history, a recent revival and some theory. In K. Pribaum (Ed.) *Origins: Brain and Self Organization*, pp. 300–301. Lawrence Erlbaum, New Jersey (1994).
4. R.J. MacGregor, *Neural and Brain Modeling*. Academic Press, San Diego (1987).
5. J.F. Vibert, K. Pakdaman, F. Cloppet and N. Azmy, NBC: A workstation for biological neural network simulation. In J. Skrzypek (Ed.) *Neural Network Simulation Environments*, pp. 113–133. Kluwer, Boston (1994).
6. A.F. Kohn, Dendritic transformations on random synaptic inputs as measured from a neuron's spike train, *IEEE Trans. Biomed. Eng.*, **36**, 44–54 (1989).
7. G.M. Shepherd, *The Synaptic Organization of the Brain*. Oxford University Press, Oxford (1990).
8. D.R. Cox and P.A.W. Lewis, *The Statistical Analysis of Series of Events*. Methuen, London (1966).
9. M. Musila and P. Lánský, Generalized Stein's model for anatomically complex neurons, *BioSystems*, **25**, 179–191 (1991).
10. J.J.B. Jack, D. Noble and R.W. Tsien, *Electric Current Flow in Excitable Cells*. Clarendon Press, Oxford (1975).
11. R.S. Stephenson, On the interpretation of voltage noise in small cells, *J. Neurosci. Meth.*, **26**, 141–149 (1988).
12. L.J. DeFelice and D.L. Alkon, Voltage noise from hair cells during mechanical stimulation, *Nature*, **269**, 613–615 (1977).
13. W. Rall, R.E. Burke, W.R. Holmes, J.J.B. Jack, S.J. Redman and I. Segev, Matching dendritic neuron models to experimental data, *Physiol. Rev.*, **72**, S159–186 (1992).
14. J.R. Knisley and L.L. Glenn, A linear method for the curve fitting of multiexponentials, *J. Neurosci. Meth.*, **67**, 177–183 (1996).
15. H.C. Tuckwell, *Introduction to Theoretical Neurobiology*, Vol. 1. Cambridge University Press, Cambridge (1988).
16. D.H. Perkel, B. Mulloney and R.W. Budelli, Quantitative methods for predicting neuronal behavior, *Neurosci.*, **6**, 823–838 (1981).
17. A.V. Oppenheim and R.W. Schafer, *Digital Signal Processing*. Prentice-Hall, New Jersey (1975).

18. H.L. Bryant and J.P. Segundo, Spike initiation by transmembrane current: a white noise approach, *J. Physiol.*, **260**, 279–314 (1976).
19. D.R. Brillinger, H.L. Bryant and J.P. Segundo, Identification of synaptic interactions, *Biol. Cybern.*, **22**, 213–228 (1976).

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