# Studies With Spike Initiators: Linearization by Noise Allows Continuous Signal Modulation in Neural Networks

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*Abstract*—**Engineers and neuroscientists generally believe that noise is something to be avoided in information systems. In this paper we show that noise, in fact, can be an important element in the translation of neuronal generator potentials (summed inputs) to neuronal spike trains (outputs), creating or expanding a range of amplitudes over which the spike rate is proportional to the generator potential amplitude. Noise converts the basically nonlinear operation of a spike initiator into a nearly linear modulation process. This linearization effect of noise is examined in a simple intuitive model of a static threshold and in a more realistic computer simulation of a spike initiator based on the Hodgkin–Huxley (HH) model. The results are qualitatively similar; in each case larger noise amplitude results in a larger range of nearly-linear modulation.**

**The computer simulation of the HH model with noise shows linear and nonlinear features that we earlier had observed in spike data obtained from the VIIIth nerve of the bullfrog. This suggests that these features can be explained in terms of spike initiator properties, and it also suggests that the HH model may be useful for representing basic spike initiator properties in vertebrates.**

## INTRODUCTION

INVESTIGATIONS of multidimensional signal processing (e.g., pattern classification) possibilities of artificial neural networks seem to be divided into two categories: 1) those in which neurons are treated as essentially binary threshold devices, and 2) those in which neurons are treated as analog processors of continuous-valued signals (e.g., see [1], [2]). Real nervous systems evidently exhibit both categories of operation. In this paper, we develop a model of spike generation that can explain both categories of operation in terms of known biophysical processes. Furthermore, we show that a single parameter (the amplitude of the noise current at the spike initiator) can determine whether the operation of a spiking neuron falls in category 1) or category 2).

Regarding category 2), it is generally accepted among neuroscientists that there is a large class of spiking neurons in which the interval between successive spikes is a random variable, and in which continuous analog input signals are translated into continuous modulation of the instantaneous mean spike rate. One easily can find many members of this class (in our laboratory we see them repeatedly in the vertebrate auditory and vestibular systems). Members of this class could provide the basis for neural networks involved in massively parallel analog signal processing. Unfortunately, although we know that such neurons occur widely, the physiology and biophysics communities presently do not have a satisfactory explanation of the operation of continuous spike-rate modulation in neurons.

Although detailed knowledge now is available regarding the production of a single spike (e.g., [15]), modelers so far have been unable to use that knowledge to explain one of the most important features of repetitive spike production—namely the wide dynamic range (often more than 60 dB) of spike-rate modulation in real neurons. Mean spike rates typically can be modulated over a range from nearly 0 spikes/s to a saturation rate (from less than 50 spikes/s to more than 1000 spikes/s) determined by refractoriness and the consequent inability of axons to conduct spikes at very high rates.

The models developed up to now to describe or explain continuous spike-rate modulation can be divided into three general categories. One category comprises models which mainly are abstract stochastic point processes (e.g., Poisson processes, random walks, birth–death processes, etc.) that produce statistics similar to those observed in spike trains from specific nerve cells. Although the simpler of these models have been useful as representatives of neurons in theoretical studies of neural coding or neural networks, they have given little physical insight about the mechanism of spike train production. Furthermore, the lack of understanding of spike train firing mechanism has resulted in some stochastic models that seem to be unnecessarily complicated.

The second category comprises models that include subsets of the physiological phenomena associated with spike initiation, but in which, for the sake of mathematical tractability, the biophysical underpinnings of those phenomena are not represented explicitly. Such models include variations on the classical "one and two time constant models" [7], [6].

The third category comprises models that explicitly include biophysical phenomena related to spike generation. The principal example is the Hodgkin–Huxley (HH) model. That model generally is accepted as a good model of single spike initiation in excitable cells and has led to

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much physical insight about the generation of a single spike. Therefore, much work has been done to extend the HH model to account for repetitive firing activity. The results of these studies (e.g., [3], [4], and [8]) revealed a major problem; when the input is noise-free, constant current, the lowest nonzero repetitive spike rate is within 10 dB of the maximum or saturation rate (the rate at which the local spike amplitudes begin to decline to the extent that the spikes will not propagate along an axon). For the HH model with parameters based on the squid axon at 6.3°C, this lowest achievable nonzero rate is approximately 50 spikes/s. This contradicts considerable experimental data (e.g., those from many primary sensory neurons and those from many motor neurons) which show modulation ranges extending nearly to 0 spikes/s and covering a dynamic range of 60 dB or more. Because of this problem, the HH model is considered unsuitable as a model of repetitive spike firing in which the spike rate is continuously modulated [i.e., unsuitable as a basis for operation of neural networks in category 2)] [4]. On the other hand, the fact that it predicts repetitive firing in which the spike rate is either zero or nearly saturated makes it an excellent model for the binary operation of neural networks in category 1).

To explain the inadequacy of the Hodgkin–Huxley model with respect to category 2) operation of neural networks, some researchers suggested that repetitive spike firing depends on nonlinear dynamical phenomena not included in the Hodgkin–Huxley model, perhaps overlooked in the squid-axon data [9], [10]. Investigators modified the HH model in various ways, attempting to achieve a much lower bottom frequency limit and thus achieve a larger modulation range ([4], see references in [11], [12]). For example, by making considerable changes in the commonly accepted HH parameters and by adding a new transient potassium channel species to the model, Connor [11] was able to extend the spike-rate modulation down to about 2 spikes/s. However, up to now there is no modified version of the HH model that can solve the problem completely, i.e., take the modulation range arbitrarily close to zero (as one typically sees in real neurons); and there is no evidence that the changes made to the widely accepted HH model parameters and the transient potassium channel species added to the HH model are generally present in spike initiators.

In these modeling studies, researchers generally considered noise in the spike initiator to be something that causes errors in neural coding. Hence, noise has been considered to be a nuisance rather than an essential ingredient in repetitive spike firing mechanisms. However, French and Stein [5]–[7] showed that in a variation on the two-time constant model, the addition of noise to a sinusoidal input broke up strict phase-locking between the spikes and the input sinusoid and allowed the average spike rate to follow the amplitude of the sinusoid smoothly. Unfortunately, the significance of this phenomena with respect to spike coding by real neurons evidently has not been recognized.

In this paper, we show that noise can in fact be a useful element in spike initiation, allowing the spike-rate modulation range to be broad and to extend to 0 spikes/s. Within the broad modulation range created by the presence of noise, there will be subranges over which the transformation from input current to spike rate is nearly linear. Consequently, noise can effectively convert the inherently nonlinear operation of a spike initiator into a modulation process that is approximately linear. In the following report, this linearizing effect of noise is explained first by a general intuitive model. Then the results of computer simulation of a spike-initiator model comprising the HH model with noise added (an HHN model) are presented and compared with spike data obtained from axons in the VIIIth nerve of the bullfrog. The results of this comparison suggest that the general properties of repetitive spike initiator can be well explained and modeled by the HHN model.

The idea that noise linearizes nonlinearities in a stochastic way gives us insights for deriving simplified stochastic models of spike train generation. It also could provide a simple realization of category 2) neural networks for massively parallel analog signal processing in real and synthetic nervous systems.

## Physiological Methods

The bullfrog preparation was the same as previously reported [13]. After the animal was anesthetized, a small hole was made in the roof of the mouth to expose the VIIIth cranial nerve on its way from the intact otic capsule (with intact circulation) to the brain. Each animal was mounted on a thick platform, the underside of which was connected to an electromagnetic vibrator. A vibration isolation system attenuated ambient seismic signals to an insignificant level compared to the applied seismic stimulation. Individual axons were penetrated with glass microelectrodes filled with KCl solution. Electrical signals from the microelectrode were recorded on tape during the experiments.

## The Linearization by Noise

To understand the potential for linearization by noise, consider the system modeled in Fig. 1.

$U(t)$ is the input to the system; $Y(t)$ is its output. $N(t)$ is noise, uncorrelated with $U(t)$. $X(t)$ is the sum of $U(t)$ and $N(t)$, and $x$ is the instantaneous value of $X(t)$. $F(x)$ is a static threshold function. The instantaneous value $z$ of $Z(t)$ is a random variable; and $E[z]$ is its expectation.

$$F(x) = \begin{cases} k, & x \geq C,\ k = \text{constant} \\ 0, & x < C \end{cases}$$

$$Z(t) = F(X(t)).$$

Suppose $N(t) = 0$. Then

$$Y(t) = E\big[F(U(t))\big] = \begin{cases} k, & U(t) \geq C \\ 0, & U(t) < C. \end{cases}$$

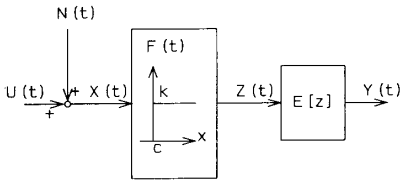


Fig. 1. Diagram of the simple threshold model.

In this case, output $Y(t)$ is a step function of the amplitude of $U(t)$.

Suppose $N(t)$ is a stationary random process such that $E[N(t)] = 0$ for any $t$, and $N(t)$ is uniformly distributed in the interval $[-a, a]$. Then

$$Y(t) = \begin{cases} 0, & U(t) < C - a \\ k/2 + (k/2a)(U(t) - C), & \\ & C - a < U(t) \leq C + a \\ k, & U(t) \geq C + a. \end{cases}$$

Now $Y(t)$ is a linear (actually, affine) function of $U(t)$ when $U(t) \in [C - a, C + a]$. The variance of $N(t)$ is

$$\sigma_N^2 = a^2/3.$$

For a given variance,

$$a = \sqrt{3}\sigma_N$$

$$[C - a, C + a] = [C - \sqrt{3}\sigma_N, C + \sqrt{3}\sigma_N].$$

Note that $\sigma_N$ is the rms deviation of the instantaneous amplitude of $N(t)$ from its mean, zero. Thus, $\sigma_N$ is the rms amplitude of the noise.

It is apparent that the noise $N(t)$ statistically linearizes the previously nonlinear system. The range of this linearization increases with increasing noise amplitude ($\sigma_N$) [Fig. 2(a)].

Suppose $N(t)$ is a stationary Gaussian random process with zero mean and standard deviation $\sigma$. Then

$$Y(t) = (k/2) + k \int_0^{U(t)-C} \cdot [1/2\pi\sigma^2]^{1/2}[1 - x^2/2\sigma^2 + \cdots]\, dx.$$

When $U(t) - C \ll \sigma$,

$$Y(t) = (k/2) + [1/2\pi\sigma^2]^{1/2}(U(t) - C).$$

Thus, we have the same results as above: $N(t)$ locally linearizes the step-wise (threshold) nonlinearity, and the range of linearization increases with increasing noise amplitude [Fig. 2(b)].

Suppose this simple model represents spike-train generation, with $U(t)$ representing the neural input signal, $Y(t)$ representing the mean rate of repetitive firing, and $N(t)$ representing noise added to the input signal. When

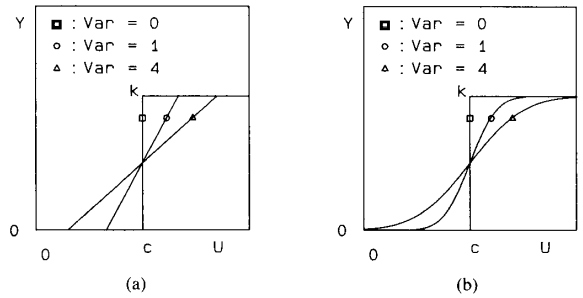


Fig. 2. Relationships between the input $U$ and the output $Y$ of the simple threshold model. (a) The noise $N(t)$ has a uniform amplitude distribution for all $t$. (b) $N(t)$ has a Gaussian distribution for all $t$. Var = variance of $N(t)$.

$N(t) = 0$, $Z(t)$ is a deterministic constant. This means that the modeled output spike rate is either zero or is saturated at some nonzero level, depending on whether $U(t)$ is bigger or smaller than the threshold value $C$. Furthermore, when its rate is saturated, the modeled spike train is periodic, with no randomness. These results are qualitatively consistent with simulation studies of HH model (e.g., [4]; and our own in the next section of this paper). They also are consistent with recent observations by Chapman [14] on space-clamped squid axons (which demonstrated that the HH equations are a good model of the space-clamped squid axon for repetitive firing).

When the noise $N(t)$ is not equal to zero and the input $U(t)$ lies within a particular interval of values, then $Z(t)$ is a random variable with a mean value approximately proportional to $U(t)$. Thus, the spike train would be aperiodic (random) with a mean rate proportional to the input. This is consistent with observations from a wide variety of nerve cells operating normally (i.e., not under space clamp). From these analyses we can see that this simple model predicts concomitancy between nearly periodic spike-train generation and all-or-nothing spike-rate modulation by applied dc stimuli (both of which are observed in the space-clamped squid giant axon). It also predicts concomitancy between aperiodic spike-train generation and broadly graded spike-rate modulation by applied dc stimuli (both of which are observed in a wide variety of neurons). In the graded modulation process, noise is an essential element, responsible for creating the graded modulation range. Both the overall extent of that range and the portion over which modulation is nearly linear are proportional to the amplitude of the noise.

## Computer Simulation of Repetitive Firing Based on the HHN Model

To study the effect of noise on repetitive spike production in a more realistic model, we simulated a spike initiator based on an HHN (HH model plus noise) model with various noise amplitudes and various kinds of inputs. The time of occurrence of each spike was recorded in a data file during the simulation. Then the data file was analyzed in the same ways that real spike data from the frog

VIIIth nerve were analyzed in our laboratory. The HHN model can be written in the following form:

$$dV_m/dt = (1/C_m)\left[I(t) + N(t) - g_K n^4(V_m - V_K) - g_{Na} m^3 h(V_m - V_{Na}) - g_l(V_m - V_l)\right]$$

where $I(t)$ is the input current to the spike initiator (including inputs from all the various neuronal loci surrounding it plus any nonHodgkin–Huxley currents in the spike initiator itself); $N(t)$ is white-noise current (from sources inside or outside of the spike initiator). The parameters (for the squid axon at 6.3°C) and the state equations for $n$, $m$, and $h$ are given by Hodgkin–Huxley [15]. The solutions of the HHN model for various inputs and various noise levels were generated on an IBM PC AT computer by the following simple numerical integration algorithm:

$$V(i+1) = V(i) + (\Delta t/C_m)\left[I(i) + N_d(i) - g_K n^4(i) \cdot (V(i) - V_K) - g_{Na} m^3(i) h(i) \cdot (V(i) - V_{Na}) - g_l(V(i) - V_l)\right].$$

$n(i)$, $m(i)$, and $h(i)$ are calculated in the same way. $\Delta t$ is usually in the range of 5–50 $\mu$s. When $\Delta t$ is suitably chosen, the algorithm gives a stable consistent solution.

$N_d(i)$ is a random number generated by a conventional computer algorithm. To see how the continuous random variable $N(t)$ can be translated into a discrete random variable such as $N_d(i)$, consider the following model: let $N(t)$ be the (formal) time derivative of a Brownian motion $W(t)$ (e.g., [16]) where

$$E[W(t)\,W(s)] = \sigma^2 \min[t, s]$$

$$N(t) = dW(t)/dt \cong [W(t + \Delta t) - W(t)]/\Delta t$$

Let $N_d(i) = [W(t + \Delta t) - W(t)]/\Delta t$

then

$$E[N_d(i)] = 0$$

$$E[N_d(i)\,N_d(j)] = 0 \qquad \text{for } i \neq j$$

$$E[N_d(i)\,N_d(j)] = \sigma^2/\Delta t \qquad \text{for } i = j \qquad (1)$$

where $\sigma^2$ is the power spectral density of $N(t)$. Additionally, since it was derived from a Brownian motion, the amplitude of $N_d(i)$ should have a Gaussian distribution.

In the actual simulation, we use a discrete random variable that is uniformly distributed (over the interval $[-\alpha, \alpha]$), with the same mean (zero) and the same power spectrum as the ideal $N_d(i)$ of the previous paragraph. To relate $\sigma$ to $\alpha$, we can use

$$E[N_d(i)\,N_d(j)] = \alpha^2/3 \qquad \text{for } i = j$$

combining this with (1), we have

$$\sigma^2 = \Delta t \alpha^2/3. \qquad (2)$$

To estimate the relationship between the variance of the noise signal $N(t)$ and the membrane-potential variance ($\sigma_v^2$) produced by the noise, we use a simplified HH model

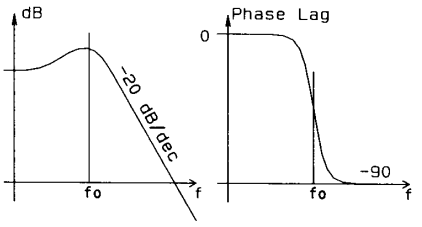


Fig. 3. Small signal, sinusoidal steady-state relationship between input current and membrane potential from the HH model.

operating in the subthreshold range (note: to estimate the effects of the noise on spike-initiation, we use the complete HH model). Fig. 3 shows the approximate steady-state input-output relations of the simulated HH model when the input current $I(t)$ is a sinusoid whose amplitude is small enough not to cause spike generation. From that figure we can see that for the small signals, the HH model (with parameters set at their values for the 6.3°C axon) can be approximated by a simple parallel $RC$ model:

$$V(s)/I(s) = kw_0/(s + w_0)$$

where

$$w_0 = 502 \text{ rad/s } (f_0 = 80 \text{ Hz})$$

$$k = 0.8.$$

This is not surprising because, as many other investigators have already shown, when input is small the HH model reduces to a parallel combination of constant resting membrane capacitance and constant resting membrane conductance. However, even in the subthreshold range, the HH model responds in a slightly nonlinear manner, so that the voltage response sinusoid is distorted. The approximate relationship of Fig. 3 was obtained by hand fitting a true sinusoid to the voltage response. Interestingly, when this was done, the estimates of $w_0$ and $k$ were robust (within a factor of 2) over the full range of amplitudes of $I$, from zero to just below threshold. If the transfer function $V(s)/I(s)$ truely conformed to that of a parallel $RC$ circuit, then if $I(t)$ [or, alternatively, $N(t)$] were Gaussian white noise, $V(t)$ would be an Ornstein–Uhlenbeck process. The variance of $V(t)$ in that case would be given by

$$\sigma_v^2 = \sigma^2 k^2 w_0.$$

Combining (2) into this expression, we derive

$$\sigma_v^2 = \Delta t k^2 w_0 \alpha^2/3.$$

This equation was used to estimate the amplitude of $N_d$ required to achieve a given noise level $V_m(t)$ in the HH simulation.

Fig. 4 shows simulation results from the HHN model when $I(t)$ is a dc current of various amplitudes and $N_d(i)$ is uniformly distributed discrete white noise of various amplitudes. The results in this figure clearly show that noise effectively linearizes the nonlinear behavior of the HH model and extends the bottom limit of the spike fre-

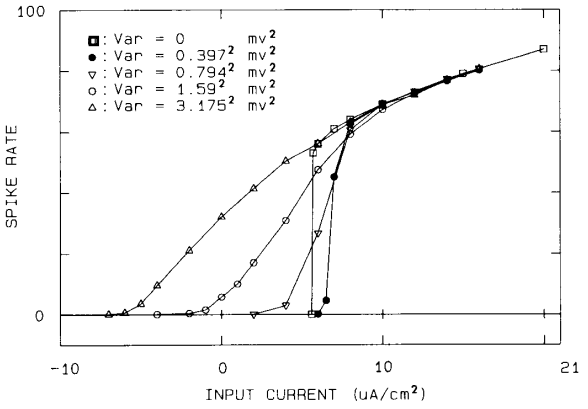


Fig. 4. The input-output relationships from the HHN model. Var = variance of membrane potential noise. Each data point in the figure represents ten seconds of neuron sampling time in the simulation.

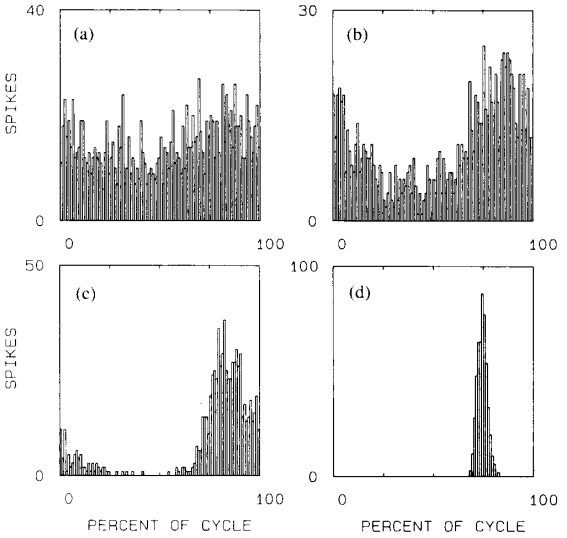


Fig. 5. Cycle histograms for steady-state, spike-train responses of a frog saccular axon to sinusoidal acceleration stimuli. Stimulation frequency ($f$) = 50 Hz. (a) Sample time (st) = 40 s; peak stimulation acceleration (pa) = $1.2 \times 10^{-5}$g. (b) st = 30 s; pa = $2 \times 10^{-5}$g. (c) st = 20 s; pa = $1.2 \times 10^{-4}$g. (d) st = 10 s; pa = $5 \times 10^{-4}$g.

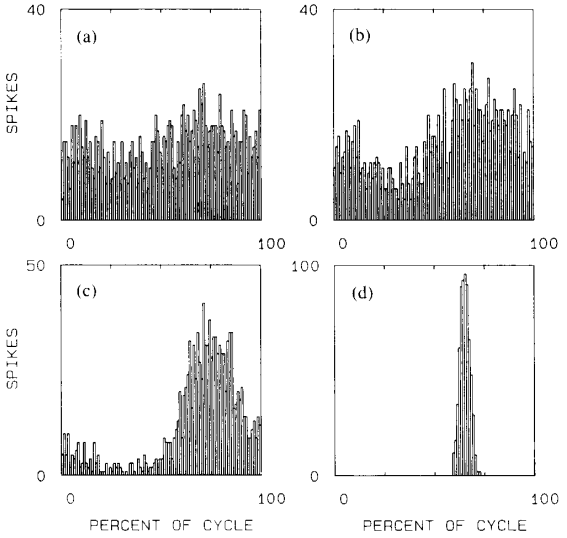


Fig. 6. Cycle histograms for steady-state spike-train responses of the HHN model to sinusoidal currents. Variance of membrane potential noise = $3.175^2$ mV$^2$; stimulation frequency $f$ = 50 Hz. (a) Sample time (st) = 45 s; peak stimulation strength (ps) = 0.15 uA/cm$^2$. (b) st = 45 s; ps = 0.31 uA/cm$^2$. (c) st = 30 s; ps = 1.25 uA/cm$^2$. (d) st = 13 s; ps = 10 uA/cm$^2$.

quency modulation range to zero. The relationships in Fig. 4 are consistent with spike data reported in the literature from many different axons (e.g., frog vestibular afferents [17], rat hippocampal pyramidal cells [18]).

When investigators apply sinusoidal stimuli to neural structures, the steady-state response spike trains often are analyzed by means of cycle histograms (which show spike occurrence as a function of phase of the stimulus sinusoid). Fig. 5 shows cycle histograms obtained from a frog representative saccular afferent axon responding to sinusoidal motion of various amplitudes. In the absence of applied stimulus, this axon exhibited spontaneous spike generation—about which both positive and negative modulation could occur. For comparison, Fig. 6 shows cycle histograms obtained from the HHN model with $I(t)$ a sinusoidal current of various amplitudes. A background spike rate, about which modulation could occur, was generated in the simulation by $N_d(i)$ added to $I(t)$.

For sinusoidal stimuli at low amplitudes and frequencies, the response modulation in the cycle histogram is very close to being sinusoidal. Fig. 5 shows the distortion that arises as the stimulus amplitude is increased. This same pattern is seen consistently in inner-ear afferent axons at low stimulus frequencies. The nonlinear distortion consistently is related directly to the percentage of modulation of the spike rate (relative to the spontaneous rate), and is essentially independent of the absolute amplitude of the stimulus and the actual value of spontaneous spike rate. Over the same relative response (percent modulation) range, at low frequencies, the same distortion pattern is robustly reproduced in the HHN model. Furthermore, the distortion pattern is robust with respect to the combination of noise and dc current used to establish the spontaneous spike rate—as long as the noise amplitude is not too small and the dc current is not too big.

Two distortion features [apparent in Fig. 5(c)] that are seen consistently at these stimulus frequencies and response amplitudes (in terms of percent modulation) are the following: 1) the positive slopes of the modulation waveform are steeper than the negative slopes (making the front edge of the positive half-cycle steeper than the back edge); 2) the width of the negative half-cycle is larger than that of the positive half-cycle. These two characteristics occur robustly in the HHN model, over the same range of response amplitudes, as shown in Fig. 6(c).

Whereas the distortion pattern in the cycle histogram

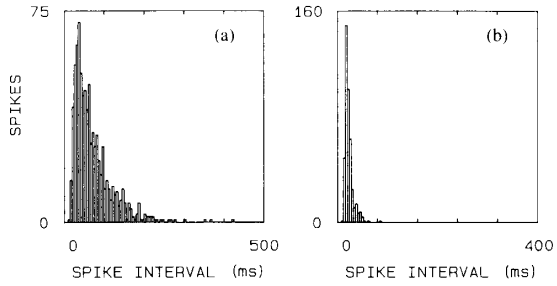


Fig. 7. Spike interval histograms from the HHN model. (a) Variance of membrane potential noise (var) = $4.1^2$ $mV^2$; sample time (st) = 60 s; hyperpolarizing current = $-4.5$ $uA/cm^2$. (b) Var = $4.76^2$ $mV^2$; st = 10 s (no hyperpolarizing current).

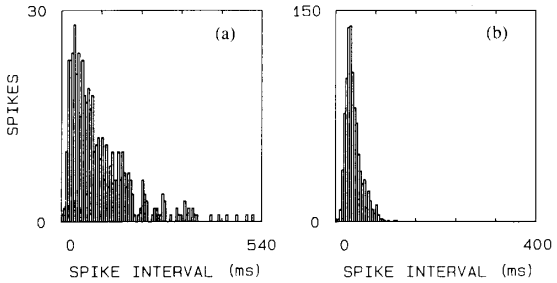


Fig. 8. Spike interval histograms for spontaneous firing in two frog VIIIth-nerve axons. (a) From a frog utricular axon: sample time = 50 s. (b) From a frog saccular axon: sample time = 36 s.

from the HHN model was robustly independent of the combination of dc current and noise used to generate the spontaneous spike rate, that combination does affect the interval histogram of the spontaneous spikes. Fig. 7 shows spike-interval histograms obtained from the HHN model with different combinations of dc current and noise amplitudes. For comparison, similar spontaneous spike-interval histograms from frog saccular and utricular axons are shown in Fig. 8.

Fig. 7 shows that the mean spike rate increases and the spike interval variance decreases in the HHN model as the dc input signal strength increases. This relationship between spike rate and spike interval variance is a basic property of Poisson and Poisson-like processes, and is commonly reported as a feature of repetitive firing in nerve cells. Thus, modulation by dc input signal seems to be closely related to lambda-modulation in Poisson processes (see [24]).

Occasionally, spike interval histograms show multiple modes, reflecting periodicities either in internal signals (as in neuronal pacemaker signals) or in externally-applied stimulus signals. Fig. 9(a) shows an interval histogram from the HHN model when $I(t)$ comprised a dc component plus a sinusoidal component. This histogram is similar to those observed from a number of axons (e.g., frog saccular axons [20], turtle basilar papilla afferents [19], and cat lateral geniculate neurons [21]). An example from a seismic-sensitive axon of the bullfrog sacculus is shown in Fig. 9(b). The shape of the histogram from the

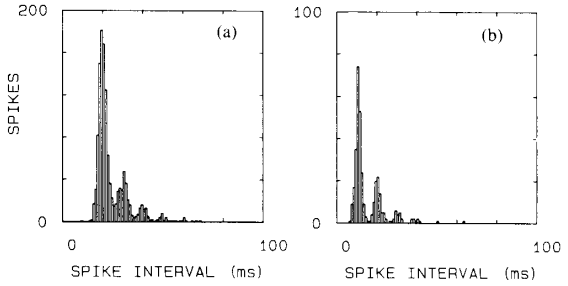


Fig. 9. Multimodal spike interval histograms from the frog VIIIth nerve and the HHN model, each stimulated with 100 Hz inputs. (a) Data from the HHN model: variance of membrane potential noise = $3.175^2$ $mV^2$; sample time (st) = 30 s; peak amplitude of sinusoidal input current 2 $uA/cm^2$. (b) Data from a frog saccular axon: st = 5.3 s.

HHN model depended on the combination of noise, dc current, and sinusoidal current amplitudes.

From all of these simulation results, one can see that many common characteristics of repetitive spike firing can be reproduced well by the HHN model with suitable combinations of noise, dc current input, and, where applicable, sinusoidal current input.

## Discussion

Chapman [14] shows that the characteristics of the repetitive response induced in squid giant axons by the application of sustained (dc) depolarizing currents under space clamp conditions are consistent with the characteristics of repetitive firing simulations based on the HH model. Both squid experimental data and the HH model computer simulation data (e.g., Fig. 4 in the previous section; [4], [8]) show that the relationships between depolarizing membrane current and the rate of repetitive firing can be divided into three regions. Region I is wholly below threshold. Here there is no repetitive spike firing at all. Region II comprises two subregions: one is an abrupt transition between zero spike rate and a near-saturation spike rate, the other is a subregion over which the nearly-saturated spike rate can increase slightly (in direct proportion to further increases in dc current) without affecting the spike amplitude much. Region III is beyond region II. There the amplitude of the spike decreases markedly (to less than 25 percent of its normal height) with further increases of the dc current; and the spike firing rate first increases and then decreases to zero as the dc depolarizing current is increased. This third region of the frequency-current relationship in fact represents an overdriven condition of the spike initiator where the generated spikes will not conduct along a nonspace-clamped axon [4]. In our HH simulation, for example, when the spike rate is higher than 120 spikes per s, the spike amplitude is less than two thirds of the amplitude of spikes at lower rates. In frog and gerbil VIIIth-nerve axons, even when they are driven at extremely high rates by strong stimuli, we do not see this sort of spike amplitude shift. Region III therefore evidently is out of the normal biophysical operating range of real axons. Thus, for the space-clamped squid

axon where normal neuronal noise is absent, operating regions I and II could be considered to represent two binary states, suitable for category 1) operation of neural networks.

In Fig. 4, the spike rate versus current relationship tends to a shallow-sloped straight line as the mean spike rate ranges approximately between 50–100 spike per s (a dynamic range of 6 dB). This corresponds to region II of the previous paragraph. This region has been cited repeatedly in the literature as accounting for continuous spike-rate modulation in nerve cells. However, spike trains in real axons (e.g., those in the frog VIIIth nerve) commonly show dynamic ranges much wider than the 6 dB available here, with spike rates ranging down to or very close to zero. A 6 dB operating range hardly seems an adequate basis for category 2) operation of neural networks.

The noise current generator in the HHN model is a lumped element. We intend it to represent many different noise sources lumped together [22]. Since most of these noise sources result in membrane potential fluctuations, one would expect the statistical characteristics of the spike train to be strongly related to the membrane potential noise. This conclusion was reached long ago by Calvin [23] on the basis of observations of repetitive firing in cat motorneurons. Furthermore, the noise amplitudes (approximately 2–8 mV peak-to-peak) he observed are within the range of noise amplitudes that were effective in our HHN simulations (e.g., the 0.8–4 mV range shown in Fig. 4). With the addition of noise in this amplitude range, the Hodgkin–Huxley spike initiator is transformed from a binary element, suitable for category 1) neural network operation, to a continuous analog element, suitable for category 2) neural network operations.

For noise amplitudes below this range, the operation of the HHN spike initiator is intermediate, switching randomly in a binary manner between "on" periods and "off" periods. During "off" periods there are no spikes; during each "on" period there is a random number of spikes, with nearly constant intervals. Thus, the HHN model with low noise amplitudes provides a good explanation of random bursting activity often seen in neurons [9].

## Conclusions

We have shown that the Hodgkin–Huxley model, with noise added to it, provides an excellent general model for spike-train generation in the nervous system. With just two parameters, the noise amplitude and the amplitude of a dc bias current (depolarizing or hyperpolarizing), this model can reproduce most of the qualitative features of the spike trains with which we are familiar. In addition, it can reproduce very well spike-rate modulation by sinusoidal stimuli, including the frequency and amplitude dependent distortion patterns observed in cycle histograms.

We know that noise-generating mechanisms are present in real neurons. We conclude that the noise associated with spike-initiator loci is an essential ingredient in spike-train production, allowing the nervous system to operate large neural networks in analog fashion.

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