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ABSTRACT

A "pacemaker" neuron with the following properties is considered: After a firing, the membrane potential is reset to a constant value from which it increases to the firing threshold during a time t_0. The neuron receives strong synaptic input producing postsynaptic potentials which change the membrane potential to the reversal potential of the synapse, from which level the potential increases to the firing threshold during a time t_1. Provided that interarrival times for the PSPs are independent and identically distributed, successive interspike intervals in this class of model neurons can be described by a regenerative stochastic process simple enough to allow the derivation of tractable expressions for the limiting distribution of the interspike intervals, including a simple expression for the mean firing rate. A central limit theorem for the partial sums of interspike intervals can also be proved. This class of models is a generalization of a model of the crayfish's stretch receptors [1], a commonly used neuro-physiological system. In two examples the model is studied under varying temporal patterns for the PSPs to illustrate respectively phaselocking and certain principles of summation of excitation and inhibition.

1. Introduction

We consider a "pacemaker" neuron, for instance a slowly adapting sensory neuron under steady state conditions, recieving strong synaptic input with different temporal patterns.

The neuron is assumed to have the following properties: After a firing, the membrane potential is reset to a constant value. If no synaptic activity interfer, the membrane potential increases to the firing threshold during a certain time t_0. The synaptic input to the neuron produces postsynaptic potentials (PSPs) which change the membrane potential to the reversal potential of the synapse, from which the potential increases to the firing threshold during a time t_1 (figure 1).

The motives for studying this model may be summarized as follows:
a) The model is a generalization of a model of the crayfish's stretch receptors suggested by Fenstad, Njå and Walløe [1] on the basis of intracellular recordings reported in [2]. This is probably the mechanoreceptor system studied in the greatest detail. It has been used in studies of the morphology and physiology of sensory receptors, e.g. [3,4], summation of inhibition and sensory excitation [1,2,5], lateral inhibition [6], and "phaselocking" [7,8,9].
b) To our opinion, phenomena related to phaselocking provide useful illustrations of likely constraints on the way the nervous system can transmit and transform information. In the present model the phaselocking-effects are particularly evident: when the input is sufficiently regular, the output spikes from the pacemaker may be "locked" to the input in such a way that for certain frequency intervals, an increase in the arrival rate of spikes causing inhibitory postsynaptic potentials may increase the firing rate of the

pacemaker [7]. c) The behaviour of similar systems have been studied earlier by simulation, [7], and, for nonrandom input, by analytical methods [8]. However, provided the interarrival times for the PSPs are independent and identically distributed, successive interspike intervals in the pacemaker form a regenerative stochastic process, simple enough to allow the derivation of tractable expressions for the limiting distribution of the interspike intervals in the pacemaker, including a simple expression for the mean firing rate. A central limit theorem for the partial sums of interspike intervals can also be proved and the relevant limiting quantities computed. The latter quantities describe what could be termed time averages of the system, and do apply if we assume that the information from the pacemaker is "averaged" over long time intervals. The model thus appears to provide an adequate description of an actual biological system where the steady state properties can be studied by means of stochastic process theory. In example 1 the model is used to illustrate phaselocking phenomena. Another application is given in example 2 where we extend some results from [1] concerning the effect of inhibition on the sensitivity to changes in excitatory drive.

The present model is in certain respects related to the selective interaction class of models (reviewed in [1o] and [11]).

2. The model.

Let $T_1, T_2, \ldots$ denote the arrival times for the PSPs, and let

$$X_n = T_n - T_{n-1}, \quad n = 2,3,\ldots$$

be the interarrival intervals for the PSPs. We assume $X_2, X_3, \ldots$ to be a sequence of independent, identically distributed (i.i.d.) real valued random variables with distribution F. The initial conditions determining X_1 will be chosen later.

Let $S_0(=0)$, $S_1, S_2, \ldots$ denote the epochs of the firings in the pacemaker neuron, and define

$$V_n = S_n - S_{n-1}, \quad n = 1,2,\ldots .$$

Hence, $V_1, V_2, \ldots$ are the length of the successive interspike intervals in the pacemaker.

To avoid ambiguities we will assume that F has a density f. In this case with probability one no PSP will arrive at the epoch of a firing in the pacemaker neuron and the system is welldefined.

If no PSPs interfere, $V_n = t_0$. After the arrival of a PSP at T_i, the neuron will fire at $T_i + t_1$, if $X_{i+1} > t_1$ (figure 1). Note that if $t_1 \geqq t_0$ the PSPs are inhibitory, while if $t_1 < t_0$ the PSPs may also be excitatory.

Note further that in the case $F(t_1) = 1$ the neuron never fires (except for a possible initial firing). We shall therefore assume $F(t_1) < 1$ throughout.

At each point in time the future of the process depends on the history of the process only through the length of the interval from the last preceding PSP. At the epoch S_n this interval is equal to t_1, if V_n has been affected by a PSP. Thus these

S_n's constitute points where the process regenerates.

We shall prove the existence of limiting distributions for the sequences $V_1, V_2, \dots$ and $S_1, S_2, \dots$ by means of the theory of regenerative processes. The theory was formulated by Feller [12] and Smith [13]. In the paper we use results from [13] in the formulation of Stidham [14]. We adhere to the notation of [14].

3. The regenerative process $V_1, V_2, \dots$.

In this section we show that $V_1, V_2, \dots$ is a regenerative process with the affected V_n's as renewal points.

Let M be the set of indices for the affected V_n's, i.e.

$$n \in M \iff \exists \; r \geqq 1: S_{n-1} < T_r < S_n \;,$$

and let $0 = n_0 < n_1 < n_2 < \dots$ be the ordered elements of M. Define

$$N_i = n_i - n_{i-1} \,, \quad i = 1,2,\dots$$

and define m_i by the relation

$$m_i = m \iff T_{m-1} < S_{n_{i-1}} < T_m, \quad i = 1,2,\dots \;,$$

where we take $T_0 = 0$.

N_i will be the length of the i'th cycle and X_{m_i} will be the interval during which firing number n_{i-1} occurs. It follows from figure 1 and section 2 that $T_{m_{i-1}} < S_n < T_{m_i}$ for $n_{i-1} \leqq n < n_i$, i.e. all V_n in cycle i will start during X_{m_i} and we have the relation

$$X_{m_i} > t_1 + t_0(n - n_{i-1} - 1) \quad \text{for} \quad n \leqq n_i \tag{3.1}$$

As initial conditions we assume that X_1 starts at time $-t_1$ and is strictly greater than t_1 with distribution

$$P\{X_1 \leq t\} = \frac{F(t)-F(t_1)}{1-F(t_1)}.$$

Note that this implies $m_1 = 1$ and

$$\sum_{j=1}^{m_{i+1}-1} X_j = S_{n_i}. \tag{3.2}$$

With this notation we can write

$$V_n = t_0 \quad \text{for } n \notin M$$

and

$$V_{n_i} = X_{m_i} - t_1 - t_0(N_i - 1) + \sum_{j=m_i+1}^{m_{i+1}-1} X_j + t_1, \quad i = 1,2,\ldots \tag{3.3}$$

and we can prove

Theorem 1. $V_1, V_2, \ldots$ is a regenerative process with renewal sequence $N_1, N_2, \ldots$.

Proof: Let $1 \leq s < n$ and take A a Borel set.

For $n_{i-1} < n \leq n_i$ we have from (3.1) and (3.2)

$$P\{V_n \in A | n_{i-1} = s, \{V_m, m < s\}\}$$

$$= P\{t_0 I\{n<n_i\} + I\{n = n_i\}(X_{m_i} - t_0(N_i - 1) + \sum_{j=m_i+1}^{m_{i+1}-1} X_j) \in A |$$

$$\sum_{j=1}^{m_i-1} X_j = S_s, X_{m_i} > t_1 + t_0(n-s-1)\}$$

$$= P\{t_0 I\{n-s< N_1\} + I\{n-s = N_1\}(X_{m_1} - t_0(N_1 - 1) + \sum_{j=m_1+1}^{m_2-1} X_j \in A |$$

$$\sum_{j=1}^{m_1-1} X_j = S_0,\ X_{m_1} > t_1 + t_0(n-s-1)\}$$

$$= P\{V_{n-s} \in A | X_1 > t_1 + t_0(n-s-1)\} = P\{V_{n-s} \in A | N_1 \geqq n-s\},$$

since $m_1 = 1$. This justifies the use of the terms cycle etc. in the preceding paragraphs.

Note that the regenerations take place, when the interarrival time between two consecutive PSP's exceed t_1.

Since the process is regenerative we can compute all relevant asymptotic quantities from the first cycle. Hence in the rest of the paper we shall write $N = N_1 = n_1$ and $R = m_2 - 2$, i.e. N is the length of the first cycle and $R+1$ is the number of PSPs affecting V_N. Moreover, X shall denote the generic element of the i.i.d. sequence $X_2, X_3, \ldots$.

With this notation we have

$$t_1 + (N-1)t_0 < X_1 < t_1 + Nt_0 \ .$$

and from this follow

(i) $\quad P\{N = n,\ X_1 \in A\} = P\{X_1 \in A \cap]\, t_1 + (n-1)t_0 < X_1 < t_1 + nt_0 \,[\,\}$ (3.4)

(ii) $\quad EX^k < +\infty \iff EN^k < +\infty$

(iii) $$\sum_{i=1}^{\infty} P\{N = n\} = \sum_{n=1}^{\infty} P\{t_1 + (n-1)t_0 < X_1 < t_1 + nt_0\}$$

$$\doteq P\{X_1 > t_1\} = 1. \qquad (3.5)$$

4. The limiting distribution of $V_1, V_2, \ldots$.

We can now prove

Theorem 2. If $P\{X > t_1\} = p > 0$, $EX < +\infty$ and the distribution of N is aperiodic, then

(i) the sequence $V_1, V_2, \ldots$ has a limiting distribution for $n \to \infty$

and

(ii) $$\lim_{n\to\infty} P\{V_n \leq t\} = \left(1 - \frac{1}{EN}\right) I\{t_0 \leq t\} + \frac{1}{EN} G_1 * G_2(t), \tag{4.1}$$

where $G_1(t)$ has density

$$g(t) = \frac{1}{p} \sum_{m=0}^{\infty} f(t + t_1 + mt_0) I\{0 < t \leq t_0\}$$

and $G_2(t)$ has Laplace transform

$$\phi(u) = \int_{t_1}^{\infty} e^{-ux} dG_2(x) = \frac{e^{-ut_1} p}{1 - \int_0^{t_1} e^{-ux} f(x)\,dx} .$$

Proof: Assertion (i) follows from [14], Theorem 2, if $P\{N < +\infty\} = 1$, and that obtains by (3.5).

To prove (ii) we note that for A a Borel set the same theorem yields

$$\lim_{n\to\infty} P\{V_n \in A\} = \frac{1}{EN} \sum_{j=1}^{\infty} P\{V_j \in A,\ N \geq j\} = \frac{1}{EN} E \sum_{j=1}^{N} I\{V_j \in A\}.$$

and from (3.3) follows

$$\lim_{n\to\infty} P\{V_n \in A\} = \frac{1}{EN} E \sum_{j=1}^{N-1} I\{t_0 \in A\} + \frac{1}{EN} E\, I\{V_N \in A\} \tag{4.2}$$

$$= \frac{EN-1}{EN} I\{t_0 \in A\} + \frac{1}{EN} P\{V_N \in A\} .$$

Thus it suffices to find the distribution of V_N. By (3.3) we have

$$V_N = X_1 - t_1 - (N-1)t_0 + \sum_{i=2}^{R+1} X_i + t_1, \tag{4.3}$$

where $X_1 - t_1 - (N-1)t_0$ and $\sum_{i=2}^{R+1} X_i$ are independent since N is determined by X_1.

From (3.4) follows

$$P\{X_1 - t_1 - (N-1)t_0 \leq t\} = \sum_{n=1}^{\infty} P\{t_1 + (n-1)t_0 < X_1 < t_1 + (n-1)t_0 + t\}$$

$$= \frac{1}{p}\sum_{n=0}^{\infty} P\{t_1 + nt_0 < X < t_1 + nt_0 + t\} .$$

To compute the distribution of $\sum_{x=2}^{R+1} X_i + t_1$ we note that

$$\{R = r\} = \bigcap_{i=2}^{r+1} \{X_i \leq t_1\} \cap \{X_{r+2} > t_1\} .$$

Hence

$$P\{R = r\} = (1-p)^r p \qquad r = 0,1,\ldots, \tag{4.4}$$

since $X_2, X_3, \ldots$ are i.i.d., and we have

$$E\, e^{-u \sum_{i=2}^{R+1} X_i} = E\, E\left(e^{-u \sum_{i=2}^{R+1} X_i} \mid R\right)$$

$$= E \prod_{i=2}^{R+1} E\left(e^{-uX_i} \mid X_i \leq t_1\right) = E(E\, e^{-uX} \mid X \leq t_1)^R$$

$$= E\left(\frac{\int_0^{t_1} e^{-ux} f(x)\,dx}{1-p}\right)^R = \frac{p}{1 - \int_0^{t_1} e^{-ux} f(x)\,dx} ,$$

since R has the geometric distribution (4.4).

Hence the distribution of V_N is given by the convolution of G_1 and G_2 defined in (ii), because of the independence of $X_1 - t_1 - t_0(N-1)$ and $\sum_{i=2}^{R+1} X_i + t_1$.

This completes the proof.

Remark 1. The limiting distribution for $V_1, V_2, \ldots$ has a continuous part for $t > t_1$ and a point probability in t_0 with

$$\lim_{n \to \infty} P\{V_n = t_0\} = 1 - \frac{1}{EN} .$$

Corollary 1. Let V have the limiting distribution of $V_1, V_2, \ldots$. Then

(i) $EV^k < +\infty$ for $k = 1,2,\ldots$

$$\text{(ii)} \quad EV = \frac{EX}{pEN} \tag{4.5}$$

and

$$\text{(iii)} \quad \operatorname{Var} V = (EN - 1)\left(\frac{EX}{pEN} - t_0\right)^2 + \frac{1}{EN}\left(\operatorname{Var}(X_1 - t_0 N) + \frac{1-p}{p} E(X^2 | X \leqq t_1) + \left(\frac{1-p}{p} E(X | X \leqq t_1)\right)^2\right) \tag{4.6}$$

Proof: To prove (i) we note that (4.2) entails

$$EV^k = \frac{EN-1}{EN} t_0^k + \frac{1}{EN} EV_N^k \quad . \tag{4.7}$$

We have

$$EV_N^k = E\left(X_1 - t_1 - t_0(N-1) + \sum_{i=2}^{R+1} X_i + t_1\right)^k$$

$$\leq 2^{k-1}\left(E(X_1 - t_1 - t_0(N-1))^k + E\left(\sum_{i=2}^{R+1} X_i + t_1\right)^k\right) < +\infty$$

since

$$0 < X_1 - t_1 - (N-1)t_0 < t_0$$

and

$$0 \leq \sum_{i=2}^{R+1} X_i < Rt_1 ,$$

where $ER^k < +\infty$ by (4.4).

To compute EV and $\operatorname{Var} V$ we note that

$$E\left(\sum_{i=2}^{R+1} X_i + t_1\right) = -\phi'(0) = t_1 + \frac{\int_0^{t_1} xf(x)\,dx}{p} = t_1 + \frac{(1-p)E(X|X \leq t_1)}{p}$$

$$\operatorname{Var}\left(\sum_{i=2}^{R+1} X_i\right) = \phi''(0) - (\phi'(0))^2 = \frac{\int_0^{t_1} x^2 f(x)\,dx}{p} + \left(\frac{\int_0^{t_1} xf(x)\,dx}{p}\right)^2 \tag{4.8}$$

$$= \frac{1-p}{p} E(X^2|X \leq t_1) + \left(\frac{1-p}{p} E(X|X \leq t_1)\right)^2$$

and

$$E(X_1 - t_1 - t_0(N-1)) = E(X|X > t_1) - t_1 - t_0(EN-1).$$

Therefore by (4.7)

$$EV = \frac{EN-1}{EN} t_0 + \frac{1}{EN}(E(X|X > t_1) - t_1 - t_0(EN-1) + t_1 + \frac{1-p}{p} E(X|X \leq t_1))$$

$$= \frac{EX}{pEN}$$

and

$$\operatorname{Var} V = (EN-1)\left(\frac{EX}{pEN} - t_0\right)^2 + \frac{1}{EN} \operatorname{Var} V_N$$

$$= (EN-1)\left(\frac{EX}{pEN} - t_0\right)^2 + \frac{1}{EN}\left(\operatorname{Var}(X_1 - t_0 N) + \operatorname{Var} \sum_{i=2}^{R+1} X_i\right)$$

and (iii) follows by substitution of (4.8) for $\operatorname{Var} \sum_{i=2}^{R+1} X_i$.

It follows from (i), that $\operatorname{Var}(X_1 - t_0 N)$ exists even if $\operatorname{Var} X = +\infty$. In this case we have $EXN = +\infty$, i.e. X and N have an "infinite positive correlation".

Note that $\operatorname{Var}(X_1 - t_0 N)$ can be computed from (3.4), when the distribution F is known.

Note further that $EX < +\infty$ entails the existence of a stationary version of the process with distribution given by (4.1), see [14], Theorem 2. The condition that $N_1, N_2, \ldots$ be aperiodic ensures that this stationary distribution is also limiting distribution for the sequence $V_1, V_2, \ldots$. The renewal sequence $N_1, N_2, \ldots$ is aperiodic, if $P\{ t_1 < X < t_1 + t_0\} > 0$. This follows immediately from the relation $\{N = 1\} = \{t_1 < X_1 < t_1 + t_0\}$.

The limiting distribution for the interspike intervals of the pacemaker gives an appropriate description of system behaviour if decoding is "instant", that is if the interspike intervals are decoded one by one. In the next section we derive a central limit theorem for the partial sums of interspike intervals. The limiting mean arrival rate is (of course) the same as above, but the variances differ in general, since the interspike intervals are in most systems dependent. The partial sums describe "time averages" of the system and do apply if information is averaged over long time intervals.

5. The limiting distribution of $S_1, S_2, \ldots$.

In this section we discuss the asymptotic distribution of $S_n = \sum_{i=1}^{n} V_i$. In the terminology of [13] $S_1, S_2, \ldots$ is a cumulative process relative to the sequence $N_1, N_2, \ldots$. We can therefore apply Theorem 9 of [13] to get the following

Theorem 3. If $\operatorname{Var} X < +\infty$ and $P\{X > t_1\} = p > 0$, then

$$\frac{S_n - n\frac{EX}{pEN}}{\sigma\sqrt{n}} \xrightarrow{L} N(0,1) \quad \text{for } n \to \infty,$$

where

$$\sigma^2 = \frac{1}{EN}\left(\frac{EX^2}{p} + \frac{(EX)^2 EN^2}{p^2 (EN)^2} - \frac{2EXEX_1N}{pEN}\right) \tag{5.1}$$

Proof. Let

$$Z = \sum_{i=1}^{N} V_i - N\frac{EX}{pEN} .$$

To apply Theorem 9 of [13] we have to verify

$$EZ = 0,$$

$$\operatorname{Var} Z = \sigma^2 EN$$

and

$$E\tilde{Z}^2 < +\infty$$

where $\tilde{Z}$ is the variation process. We have

$$Z = X_1 + \sum_{i=2}^{R+1} X_i - N\frac{EX}{pEN} ,$$

and

$$EZ = E(X|X > t_1) + \frac{1-p}{p} E(X|X \leq t_1) - \frac{EX}{p} = 0$$

$$\operatorname{Var} Z = \operatorname{Var}(X_1 - N\frac{EX}{pEN}) + \operatorname{Var} \sum_{i=2}^{R+1} X_i$$

$$= \mathrm{Var}\, X_1 + \left(\frac{EX}{pEN}\right)^2 \mathrm{Var}\, N - 2\,\frac{EX}{pEN}\,\mathrm{Cov}(X_1, N) + \mathrm{Var} \sum_{i=2}^{R+1} X_1$$

$$= \frac{EX^2}{p} + \frac{(EX)^2 EN^2}{p^2 (EN)^2} - \frac{2EX}{pEN}\, EX_1 N.$$

Moreover

$$\tilde{Z} < X_1 + \sum_{i=2}^{R+1} X_i + N\,\frac{EX}{pEN} \leqq X_1 + Rt_1 + N\,\frac{EX}{pEN}.$$

Hence $E\tilde{Z}^2 < +\infty$, since X_1 and N have second moments by the assumption $\mathrm{Var}\, X < +\infty$ and R has moments of all orders.

This completes the proof.

Remark 2. Note that Theorem 3 obtains also in the periodic case.

Remark 3. It is not essential for the results in section 4 and 5 that the process starts just after a regeneration at time 0. If this is not the case we will have a delayed regenerative process and the asymptotic results remain unchanged.

Remark 4. In many actual nervous systems, including the muscle receptor organs of the crayfish, a negative serial correlation is observed between consecutive interspike intervals. Hence, one might expect $\mathrm{Var}\, V < \sigma^2$. It is, however, in general not possible to state anything about the relative size of $\mathrm{Var}\, V$ and σ^2. In example 1 we show situations with $\mathrm{Var}\, V < \sigma^2$ and $\mathrm{Var}\, V > \sigma^2$, respectively.

6. Applications.

Example 1: Phaselocking.

As mentioned in the introduction, pacemaker systems are vulnerable to phaselocking. This phenomenon is known to occur in situations where the arriving train of action potentials is sufficiently "regular". To illustrate this we take X to have a Γ-distribution with mean $\frac{1}{\lambda}$ and a variance $\frac{1}{s\lambda^2}$. Note that by varying s, we obtain spike trains with the same mean, but with different levels of "regularity". The Γ-distribution fits certain of the actually observed spike trains in the "accessory neurons" providing the inhibitory input to the stretch receptors of the crayfish [9].

From (3.2) we get

$$P\{X_1 \in A,\ N = m\} = \frac{1}{p} \int_A g(x,m)\,dx,$$

where

$$g(x,m) = \frac{(\lambda s)^s x^{s-1}}{\Gamma(s)} e^{-\lambda s x} I(t_1 + t_0(m-1) < x < t_1 + t_0 m)$$

and

$$p = \int_{t_1}^{\infty} \frac{(\lambda s)^s x^{s-1}}{\Gamma(s)}\,dx .$$

From (4.5), (4,6), and (5.1) follow

$$EV = \frac{1}{\lambda\gamma_s},$$

$$\operatorname{Var} V = \frac{1}{\lambda^2\gamma_s}\left(\frac{s+1}{s} - \frac{1}{\gamma_s} + 2(\lambda t_0)^2\tau_s - 2\lambda t_0\rho_s + 2\lambda t_0 - 2(\lambda t_0)^2\gamma_s + 2(1-\lambda t_0\gamma_s)\frac{1-I(s+1,z_0)}{I(s,z_0)}\right),$$

and

$$\sigma^2 = \frac{1}{\lambda^2\gamma_s}\left(\frac{s+1}{s} - \frac{1}{\gamma_s} + \frac{2\tau_s}{\gamma_s^2} - \frac{2\rho_s}{\gamma_s}\right)$$

where

$$I(r,z) = \int_z^\infty \frac{x^{r-1}}{\Gamma(r)} e^{-x} dx \text{ (the incomplete gamma function ratio)},$$

$$\gamma_s = \sum_{m=0}^\infty I(s,z_m), \qquad \rho_s = \sum_{m=0}^\infty I(s+1,z_m),$$

$$\tau_s = \sum_{m=0}^\infty (m+1)\, I\,(s,z_m), \quad \text{and} \quad z_m = \lambda s(t_1 + mt_0), \quad m = 0,1,\ldots .$$

For the special case $s = 1$, i.e. Poisson input, we get

$$Ee^{-uV} = \frac{\lambda + ue^{d(\lambda + u)}}{\lambda + ue^{t_1(\lambda + u)}}$$

and

$$EV = \lambda^{-1}(e^{\lambda t_1} - e^{\lambda d}) \tag{6.1}$$

$$\sigma^2 = \text{Var } V = \lambda^{-2}(e^{2\lambda t_1} - e^{2\lambda d}) - 2\lambda^{-1}(t_1 e^{\lambda t_1} - de^{\lambda d}),$$

where $d = t_1 - t_0$.

The relation (6.1) was derived in [1] for $t_0 = t_1$ by a different method. Note that for $s = 1$, $V_1, V_2, \ldots$ are i.i.d. and henceforth have the same distribution as V. This also explains the equality of σ^2 and $\text{Var } V$.

In figure 2, $1/EV$ is shown as a function of λ for selected values of s and for $t_1 = t_0$ and $t_1 = 0.8t_0$. For $t_1 = t_0$ we have the model of the stretch receptors suggested by Fenstad et al. [1], while the case $t_1 = 0.8t_0$ is included to illustrate certain theoretical aspects of phaselocking.

For regular input $(s=\infty)$ an extreme degree of phaselocking occurs, and the frequency curve contains large "paradoxical segments", where increased inhibition causes higher output frequencies (see also [7] and [8]). It is seen that as the "irregularity" of the spike train increases, i.e. s decreases, the paradoxical segments gradually disappear. Note that for $t_1 < t_0$ (figure 2b), the "average" effect of the PSPs may be both inhibitory and excitatory depending on λ. Note also that for certain intervals of λ, the response of the pacemaker for high s-values is equal for $t_1 = t_0$ and $t_1 = 0.8t_0$. This illustrates the locking of the output spikes to the input spikes.

The stretch receptors show phaselocking behaviour if they receive (artificial) regular input. However, under physiological conditions, there appears to be specific neuronal mechanisms which cause the system to operate with a level of "irregularity" high enough to avoid paradoxical segments ([9,16]). However, it might be expected that this way of obtaining "smooth" frequency-curves incurs certain costs, for instance unappropriate levels of variation in interspike interval lengths in the stretch receptor. Although the nature of the decoding mechanism is only fragmentarily known, the two measures of variation, Var V ("shortterm") and σ^2 ("longterm"), should provide relevant information. Table 1 shows the values of these measures for $t_0 = t_1 = 1$ and selected values of s and λ. It is seen that for moderately strong inhibition, the variation in interval length is fairly low. Thus, variation does not appear to be a serious obstacle to the "use" of irregularity as a means to avoid phaselocking.

Note from Table 1 that depending on λ, $\mathrm{Var}\,V > \sigma^2$ or $\mathrm{Var}\,V < \sigma^2$, i.e. there is no general "order" of these measures. We also observe that in the middle of the paradoxical segments, high s-values imply low values of variation, while the variation may increase as a function of s around the "jumps" between the paradoxical segments.

Example 2: Summation of excitation and inhibition.

In many neuronal systems, the summation of inhibition and excitation has been observed to obey the following rules (for references, see [1]): a). The frequency reduction caused by the inhibition is approximately proportional to the inhibitory frequency. b). For a constant inhibitory frequency, the frequency reduction is almost independent of the excitatory drive, i.e. the sensitivity of the neuron to changes in excitation is not changed during inhibition.

Granit, Kernell, and Lamarre [17], suggested that this kind of behaviour would occur in certain systems where the inhibition hyperpolarized the neuron without any concomitant shunting of the excitatory currents. Fenstad et al. [1] showed experimentally that the stretch receptors of the crayfish obeyed the above mentioned summation principles, and argued on the basis of intracellular recordings that the inhibitory process works in the way suggested by Granit et al. As mentioned earlier, their description of the inhibitory process lead to the model discussed here with $t_1 = t_0$. Fenstad et al. [1] computed the expected output frequencies under Poisson arrival of the PSPs. These frequencies fitted the experimentally observed frequencies well, except at the lowest levels of excitatory drive.

Under the experimental conditions studied by Fenstad et al. (and probably under many normal physiological conditions) the input to the stretch receptors appears to be better described by gamma distributions more regular than the Poisson process [9]. Using the expressions from example 1, it is seen that with these "improved" input distributions the frequency reduction caused by the inhibition follows the discussed summation principles almost perfectly, (see figure 3, s = 4). Thus, to our opinion, the system provides an illustrative demonstration of how this kind of summation of excitation and inhibition can arise.

In Figure 3b, the behaviour of some model neurons with $t_1 < t_0$ is shown. Note that for low values of t_1 ($\approx$ high reversal potential) the inhibition is very efficient at low levels of excitatory drive.

Figure 1. Idealized electrophysiological activity in a neuron which could be represented by the models discussed here. W_0: resetting membrane potential. W_r: reversal potential. W_T: firing threshold. S_i: firings in the neuron. V_i: interspike intervals in the neuron. T_i: arrival times for the PSPs (marked with arrows). X_i: interarrival times for the PSPs.

Figure 2. Values of 1/EV ("firing frequency") in the model neuron as a function of the frequency (λ) of the PSPs. The interarrival intervals for the PSPs are assumed to be independent and Γ-distributed with mean λ^{-1} and variance $(s\lambda^2)^{-1}$. The curves correspond to different values of the parameter s. In 2a, $t_1 = t_0$ and in 2b, $t_1 = 0.8t_0$.

Figure 3. Values of 1/EV ("firing frequency") in the model neuron as a function of the excitatory drive $(1/t_0)$. The interarrival intervals for the PSPs are assumed to be independent and Γ-distributed with mean λ^{-1} and variance $(s\lambda^2)^{-1}$. The broken lines correspond to different values of the parameters s and t_1. (For $1/t_0 \to \infty$, it can be shown that 1/EV converges towards $\lambda(t_1/t_0 - \frac{1}{2})$, i.e. the frequency reduction caused by the inhibition is proportional to λ). The fully drawn lines represent the response predicted from the summation principles discussed in example 2.