Eur. Phys. J. B **45**, 391–397 (2005)
DOI: 10.1140/epjb/e2005-00187-2

**THE EUROPEAN
PHYSICAL JOURNAL B**

# Resonant activation in a stochastic Hodgkin-Huxley model: Interplay between noise and suprathreshold driving effects

E.V. Pankratova[1,a], A.V. Polovinkin[2], and E. Mosekilde[3]

[1] Mathematical Department, Volga State Academy, Nizhny Novgorod, 603600, Russia
[2] Radiophysical Department, Nizhny Novgorod State University, Nizhny Novgorod, 603950, Russia
[3] Department of Physics, The Technical University of Denmark, 2800 Kongens Lyngby, Denmark

Received 8 October 2004 / Received in final form 3 March 2005
Published online 6 July 2005 – © EDP Sciences, Società Italiana di Fisica, Springer-Verlag 2005

**Abstract.** The paper considers an excitable Hodgkin-Huxley system subjected to a strong periodic forcing in the presence of random noise. The influence of the forcing frequency on the response of the system is examined in the realm of suprathreshold amplitudes. Our results confirm that the presence of noise has a detrimental effect on the neuronal response. Fluctuations can induce significant delays in the detection of an external signal. We demonstrate, however, that this negative influence may be minimized by a resonant activation effect: Both the mean escape time and its standard deviation exhibit a minimum as functions of the forcing frequency. The destructive influence of noise on the interspike interval can also be reduced. With driving signals in a certain frequency range, the system can show stable periodic spiking even for relatively large noise intensities. Outside this frequency range, noise of similar intensity destroys the regularity of the spike trains by suppressing the generation of some of the spikes.

**PACS.** 87.10.+e General theory and mathematical aspects – 05.40.-a Fluctuation phenomena, random processes, noise, and Brownian motion

## 1 Introduction

Investigations of neuronal models subjected to different types of perturbations have received significant attention in the last years [1]. It is widely acknowledged that signal processing in neural systems takes place in a noisy environment. Hence, it is of interest to understand the statistical properties of stochastic neuronal systems. Investigation of the influence of noise on spike generation in the presence of some external forcing signals is particular important, because noise plays a significant role in the detection, transmission and encoding of such signals.

Recently, it has been demonstrated that the response of neurons to a weak periodic forcing can be optimized by a certain level of noise (the phenomenon of stochastic resonance (SR)), and that the signal-to-noise ratio in this case has a maximum for an optimal noise intensity [2–7]. It has also been shown that even without an external signal a similar behavior can be observed (the phenomenon of coherence resonance (CR)), where the presence of noise reveals an inherent oscillatory tendency in the system [8–11]. In some systems this may be associated with a nearby supercritical Hopf bifurcation [8,12], for other systems CR can be interpreted as the response to noise excitation near the bifurcation of a periodic orbit [9].

Both of the above resonant phenomena (SR and CR) point to the possible beneficial effects of noise on the dynamics of nonlinear systems. Recent experiments on the cricket cercal sensory system have shown that the frequency of the subthreshold driving also plays a crucial role [13]. A range of frequencies exists in which the signal transduction of the neurons is most effective. This phenomenon, called frequency sensitivity in weak signal detection, was proposed to result from a resonance between the intrinsic oscillation and the signal [14].

By examining the principal neuromodulatory features of noisy subthreshold oscillations it has recently been demonstrated that even small parameter variations can profoundly alter the neuron's output [15–17]. In particular, it has been shown that due to the selective stimulus-dependent modulation of the oscillation frequency and the spiking probability it is possible to optimize the encoding sensitivity to various sensory modalities.

However, all of the above effects were observed for the case of subthreshold forcing, when the driving signal alone is insufficient to produce a response from the neuron (i.e., to generate a spike). This situation seems to apply most directly to cases where the neurons are unable to adapt their response thresholds to changes in the external

---

[a] e-mail: `pankratova_e.v@mail.ru`

driving. But it is well known that many sensory neurons do have adaptive capabilities [18]. Thus, the opposite case of strong driving signals is equally important.

As demonstrated by several authors [19–21], if the amplitude of the external driving is suprathreshold, the presence of noise has a detrimental effect on the encoding process: Noise always impairs the information transmission. An exception are neuronal arrays, where noise, as recently shown by Stocks [22,23], can significantly enhance the information transmission, and the effect of suprathreshold stochastic resonance can be observed.

It is in this context that the problem of optimally matched parameters of the external signal arises. Here, the term "optimal parameters" relates to aspects such as the detection of the external information, its subsequent encoding, signal transmission, and so on. In the present paper we focus on the first characteristic and analyze the effect of noise on the time of external signal detection, i.e. on the time of appearance of the first spike. Signals of various shapes and durations can obviously serve as stimuli of a neuronal system. For simplicity, we consider a single neuron subjected to a strong periodic forcing and study the delay of the system's response in dependence on both the driving frequency and the noise intensity.

We observe that the effect of frequency selection also exists in the case of suprathreshold driving and that it takes the form of a resonant activation effect [24,25]: The mean time of appearance for the first spike has a minimum as a function of driving frequency. Thus, less time is needed for the appearance of a response for a certain range of driving frequencies. Moreover, for small enough noise intensities this time changes weakly in the near-resonance region where the standard deviation of the escape time also has a minimum. Both of these facts suggest, that the ability to detect signals by a neuron can be significantly improved when the frequency of the signal falls in a particular range.

In a couple of recent studies [26,27] the phenomenon of noise-delayed decay has been described. In this case the escape time becomes larger with increasing noise intensity. We show that this phenomenon can also be observed for the neuron model, but that the delay due to the noise can be minimized within a certain frequency range.

Finally, we briefly show that similar effects are observed not only for the time of appearance of the first spike, but also for the sequence of subsequent spikes. With driving signals in a certain frequency range, the system can show stable periodic spiking even for relatively large noise intensities. Outside this frequency range, noise of similar intensity destroys the regularity of the spike trains by suppressing the generation of some of the spikes. A study of this phenomenology, which is directly related to the information processing in neuronal systems, is currently in progress.

We emphasize that the phenomena considered in the present paper are qualitatively different from the well-known SR and CR effects [27] and that they arise for a range of forcing amplitudes where these effects cannot occur [23].

## 2 The model

The dynamic equations for the Hodgkin-Huxley model [28] to be considered in this paper are identical to those used by Keener and Sneyd [29]:

$$\begin{aligned} C_m\dot{v} &= -G_{\mathrm{K}}n^4(v-v_{\mathrm{K}}) - G_{\mathrm{Na}}m^3h(v-v_{\mathrm{Na}}) - \\ &\qquad - G_L(v-v_L) + s(t) + \xi(t), \\ \dot{m} &= \alpha_m(1-m) - \beta_m m, \\ \dot{h} &= \alpha_h(1-h) - \beta_h h, \\ \dot{n} &= \alpha_n(1-n) - \beta_n n. \end{aligned} \tag{1}$$

Here, $v$ measures the deviation of the membrane potential from its equilibrium value ($V = V_{eq} + v$) in units of mV, $m$ and $h$ are the activation and inactivation variables of the sodium current, and $n$ is the activation variable of the potassium current. The parameters $G_{\mathrm{Na}} = 120$ mS/cm$^2$, $G_{\mathrm{K}} = 36$ mS/cm$^2$, and $G_L = 0.3$ mS/cm$^2$ are the maximal conductances for the sodium, potassium and leakage channels, respectively, and $v_{\mathrm{Na}} = 115$ mV, $v_{\mathrm{K}} = -12$ mV, and $v_L = 10.6$ mV are the corresponding reversal potentials. The capacity of the membrane is $C_m = 1\ \mu$F/cm$^2$. The specific voltage-dependent functions $\alpha$ and $\beta$ proposed by Hodgkin and Huxley were, in units of (ms)$^{-1}$, [29]:

$$\alpha_m = \alpha_{m_0}\frac{v_1 - v}{\exp\left(\frac{v_1-v}{\vartheta_{m_1}}\right) - 1}, \qquad \beta_m = \beta_{m_0}\exp\left(\frac{-v}{\vartheta_{m_2}}\right), \tag{2}$$

with $\alpha_{m_0} = 0.1$ (mV ms)$^{-1}$, $v_1 = 25$ mV, $\vartheta_{m_1} = 10$ mV, $\beta_{m_0} = 4$ (ms)$^{-1}$, and $\vartheta_{m_2} = 18$ mV.

$$\alpha_h = \alpha_{h_0}\exp\left(\frac{-v}{\vartheta_{h_1}}\right), \qquad \beta_h = \frac{\beta_{h_0}}{\exp\left(\frac{v_2-v}{\vartheta_{h_2}}\right) + 1}, \tag{3}$$

with $\alpha_{h_0} = 0.07$ (ms)$^{-1}$, $\vartheta_{h_1} = 20$ mV, $\beta_{h_0} = 1$ (ms)$^{-1}$, $v_2 = 30$ mV, and $\vartheta_{h_2} = 10$ mV.

$$\alpha_n = \alpha_{n_0}\frac{v_3 - v}{\exp\left(\frac{v_3-v}{\vartheta_{n_1}}\right) - 1}, \qquad \beta_n = \beta_{n_0}\exp\left(\frac{-v}{\vartheta_{n_2}}\right), \tag{4}$$

with $\alpha_{n_0} = 0.01$ (mV ms)$^{-1}$, $v_3 = 10$ mV, $\vartheta_{n_1} = 10$ mV, $\beta_{n_0} = 0.125$ (ms)$^{-1}$, and $\vartheta_{n_2} = 80$ mV.

Neuronal systems can be stimulated by a number of different signals from the external world. Here, we consider the case where the neuron is subjected to a strong periodic signal $s(t) = A\sin(2\pi ft + \varphi)$, and define $s(t)$ to be suprathreshold if a response is observed from the system even in the noise-free case. Besides such deterministic signals, there are numerous noise sources [31]. The occurrence of many uncorrelated synaptic events will deliver a total current to the neuron, which may be expected to approximately approach a Gaussian distribution at the soma [30,31]. Accordingly, the total noise input $\xi(t)$ to the neuron can be modeled as a white Gaussian noise with zero mean $\langle\xi(t)\rangle = 0$ and the correlation function $\langle\xi(t)\xi(t+\tau)\rangle = D\delta(\tau)$ and added to the system (1) as an additive fluctuating current.

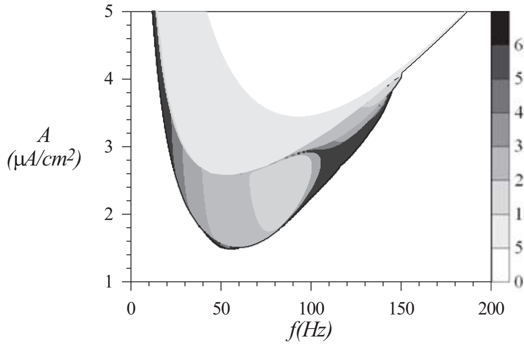

**Fig. 1.** Firing and non-firing regions for the deterministic case for $\varphi = 0$. The region above the bold black curve corresponds to suprathreshold signals. Here, the time needed for the appearance of the response (in ms) is marked according to the gray scale shown to the right. Sinusoidal driving with the amplitude $A = 4\ \mu\text{A/cm}^2$ within the frequency range $f \in [16 \div 149\ \text{Hz}]$ is suprathreshold. Note the dramatic increase of the required amplitude at low driving frequencies.

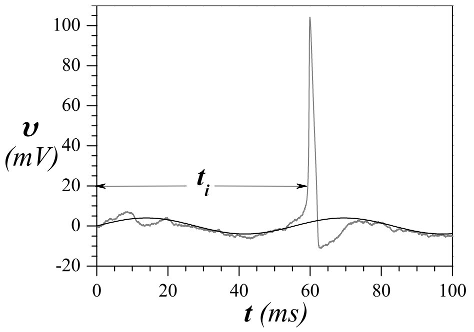

**Fig. 2.** Calculation of the escape time $t_i$ from the first crossing of the detection boundary at 20 mV by the membrane potential $v$. The applied periodic modulation is shown as a black line. Values of the parameter set are: $A = 4\ \mu\text{A/cm}^2$, $f = 18$ Hz, $\varphi = 0$, and $D = 0.5$.

In the absence of stochastic inputs, the region of response from the system for $\varphi = 0$ is illustrated in Figure 1. The minimum threshold value of the driving amplitude required for spike generation is seen to be $\sim 1.5\ \mu\text{A/cm}^2$ and to occur around 60 Hz. In the following, investigations of the influence of noise on the behavior of the nerve system subjected to a signal of amplitude $A = 4\ \mu\text{A/cm}^2$ will be presented.

In our simulations we assume that the initial conditions for each realization are the same, namely that the system is in its stable equilibrium point (the rest state) $(v_0, m_0, h_0, n_0)$ at the initial time $t_0$. In the following, we will refer to the mean time of appearance for the first spike as the mean escape time (MET). As illustrated in Figure 2, MET is obtained by averaging the time of the first passage [32] of the boundary $v = 20$ mV over an ensemble of $N$ noise realizations [3]:

$$T = \langle t \rangle = \lim_{N \to \infty} \frac{1}{N} \sum_{i=1}^{N} t_i. \tag{5}$$

Here, $t_i$ is the appearance time of the first spike for the $i$th realization. This parameter characterizes the delay of the system's response, and has a non-zero value even in the deterministic case because of the non-instantaneous neuronal response. Noise can increase the escape time and lead to an additional delay of the signal detection.

We have also considered the mean square deviation of the escape time

$$\sigma = \sqrt{\langle t^2 \rangle - \langle t \rangle^2} \tag{6}$$

that allows us to detect the region, where the most effective noise suppression occurs. The second moment $\langle t^2 \rangle$ is defined in a manner analogous to equation (5).

Further, assuming that the driving signal initially grows so that the dynamical threshold decreases, we take $\varphi = 0$ in the sinusoidal driving term. In this case all characteristics have been obtained as the ensemble average over many realizations of the noise, see equations (5) and (6). If the input initial phase $\varphi$ is unknown from the experiment then an additional phase-averaging may be performed

$$T_\varphi = \langle T \rangle_\varphi \,. \tag{7}$$

Here, the variable $T$ inside the brackets is the ensemble averaged escape time as defined by equation (5). Following [3], the phase-averaged standard deviation of the escape time may be calculated from

$$\sigma_\varphi = \langle \sigma \rangle_\varphi = \left\langle \sqrt{\langle t^2 \rangle - \langle t \rangle^2} \right\rangle_\varphi \,, \tag{8}$$

where the inner brackets denote the average over the ensemble of the noise realizations and outer brackets indicate the average over the initial phase $\varphi$.

## 3 Main results

In the following analysis we focus on the time of generation for the first spike and, in particular, on the role of noise in the response ability of our system. However, let us start by demonstrating a couple of relatively long voltage traces containing several periods of an external driving. Here, the manifestation of similar effects for another characteristic time of neuronal activity known as the interspike interval, is possible. Such a generalization allows us not only to illustrate the phenomena observed in the following but also to show their significance in the different stages of external signal processing, such as detection, encoding and its subsequent transmission. The study of the influence of noise on the interspike interval in the presence of suprathreshold external signal, including queries of reliability and precision of signal processing, is currently in progress.

Figure 3 presents the temporal variation of the membrane potential in the absence of noise and when noise of two different intensities, $D = 0.1$ and $D = 1$, is added. Parameters of the periodic driving are: $A = 4\ \mu\text{A/cm}^2$, $f = 140$ Hz, and $\varphi = 0$. With these parameters our system is subjected to a suprathreshold signal (Fig. 1)

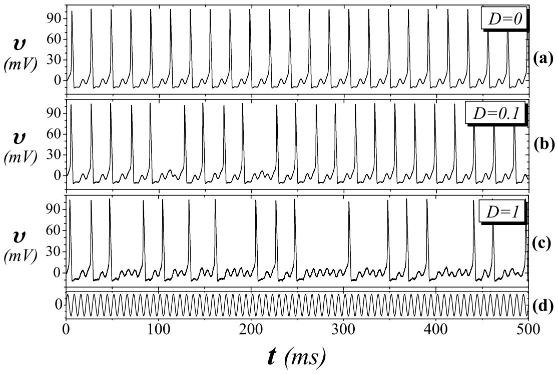

**Fig. 3.** Voltage profiles induced by an external suprathreshold periodic signal of amplitude $A = 4\ \mu\text{A/cm}^2$ for different values of the noise intensity: (a) $D = 0$, (b) $D = 0.1$, and (c) $D = 1$; $f = 140$ Hz. Note, the characteristic phenomenon of spike skipping as the noise intensity increases. The corresponding periodic modulation is shown in (d).

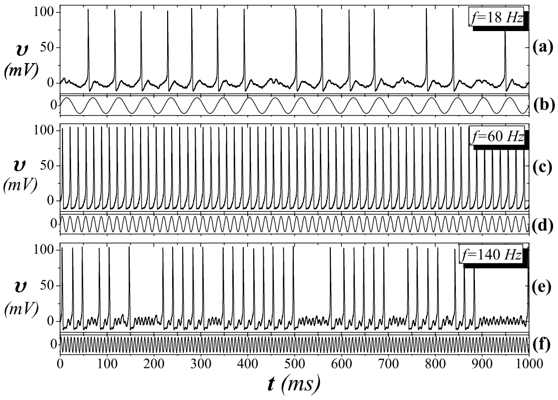

**Fig. 4.** Voltage profiles induced by an external suprathreshold periodic signal with $A = 4\ \mu\text{A/cm}^2$ for different frequencies: (a) $f = 18$ Hz, (c) $f = 60$ Hz, and (e) $f = 140$ Hz. The corresponding periodic modulations are shown in (b), (d), and (f), respectively. $D = 0.5$. The phenomenon of spike skipping is practically absent for $f = 60$ Hz. For $f = 140$ Hz, only about 23% of the potential spikes are realized.

and, as a consequence, a periodic chain of spikes is observed. Note, however, that due to the finite response time and the refractive period that follows each spike, only 1/3 of the potential spikes are realized. In the presence of noise a disruption of this periodicity occurs and the skipping of spikes increases with increasing noise intensity. This destructive role of fluctuations in the presence of a suprathreshold signal is well-known and it has been demonstrated both experimentally [13] and in computational models [19,21] by several authors.

The idea of the present analysis is to demonstrate that the negative influence of noise can be effectively suppressed. With this aim the influence of noise on the process of spike generation is presented in Figure 4 for three different values of the driving frequency $f = 18$ Hz, $f = 60$ Hz, and $f = 140$ Hz with $D = 0.5$. All three signals are suprathreshold (Fig. 1) and, in the deterministic case induce regular periodic spike generation. As illustrated in Figure 3, noise suppresses the generation of some spikes, but this effect is observed only for low and high frequencies. In a certain frequency range around $f = 60$ Hz, the system demonstrates stability to noise: A periodic chain of spikes, as for $D = 0$, is observed, and each period of the forcing signal produces one spike.

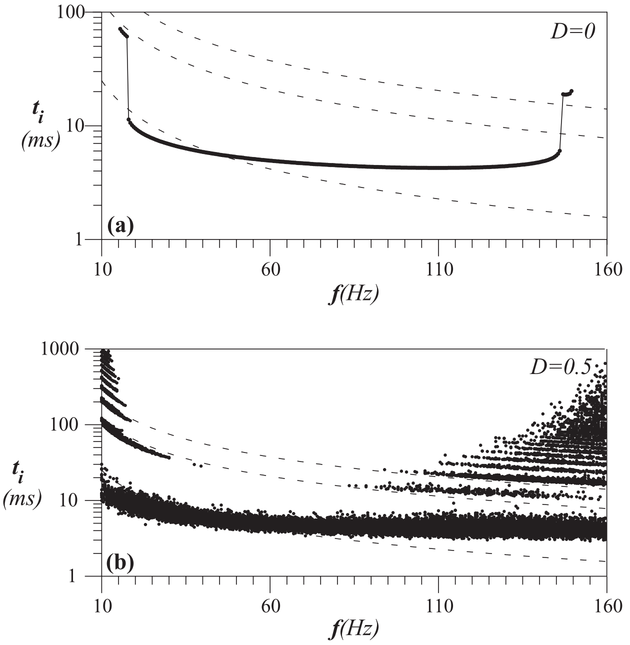

**Fig. 5.** Bifurcation plot of realized escape times versus driving frequency for the deterministic case $D = 0$ (a) and for $D = 0.5$ (b). Dashed lines correspond to the following functions (bottom-up): $t_q = 0.25/f$, $t_q + T_s$, and $t_q + 2T_s$, where $T_s = 1/f$ is the period of sinusoidal driving.

The above examples allow us to understand the role of fluctuations in the process of spike generation in a broader perspective. Let us now return to the main subject of the present paper, to the examination the response ability of our system, and consider the appearance time for the first spike (escape time) in the simultaneous presence of a suprathreshold signal and noise.

Figure 5 shows computed values of the escape times as function of the driving frequency for $D = 0$ (a) and $D = 0.5$ (b), respectively. Since excitations generally occur in the first quarter part of the forcing period $t_q = 1/4f$, during which the driving signal increases to its highest value, we have plotted $t_q$ along with values of $t_q$ shifted by one and two periods as dashed curves in the diagrams for the realized escape times. Due to the delayed response of the system, the dashed curves do not coincide with the computed escape times as defined in Figure 2. If the frequency of the periodic driving is low (but $f > 18$ Hz), then the speed at which the signal changes in the input of the system is smaller than in the output. For such frequencies the escape times and the time of excitation only differ slightly from one another in comparison with $t_q$. At high frequencies (but $f < 146$ Hz), on the other hand, the periodic signal changes quickly, and the escape times noticeably differ from the times of excitation

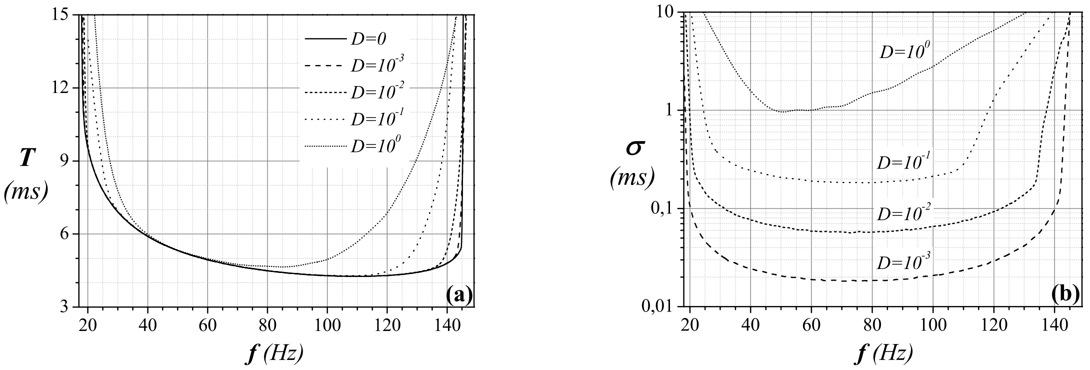

**Fig. 6.** Mean escape time (a) and standard deviation (b) as functions of the driving frequency for $A = 4\ \mu\mathrm{A/cm}^2$.

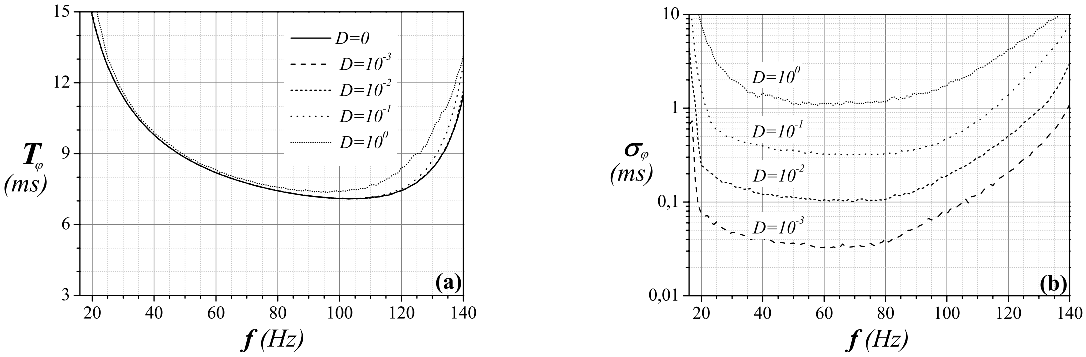

**Fig. 7.** Phase-averaged mean escape time (a) and standard deviation (b) as functions of the driving frequency for $A = 4\ \mu\mathrm{A/cm}^2$.

that occur close to $t_q$. Here, several quarters of a period of the sinusoidal driving can be passed before the membrane potential reaches the value $v = 20$ mV. For the frequencies near the boundaries of the suprathreshold region ($f \in [16 \div 18$ Hz) or $f \in (146 \div 149$ Hz]), the system cannot respond within the first period of the driving. Signals with these frequencies may be detected only during the second, third etc., period.

By inducing the skipping of spikes, noise destroys the regular structure. However, it can easily be seen from Figure 5b that a frequency band exists where the influence of noise is minimal. In the interval $f \in (30 \div 80$ Hz), even relatively large values of the noise intensity leave the system's response nearly unaffected, while outside this frequency range noise leads to a multimodal distribution of the escape times. Here, the system's response is sensitive to noise, and fluctuations play an essential role.

Let us now focus on the ensemble-averaged escape times and consider the dependence of the mean escape time (MET) on the frequency of an external periodic forcing. The existence of a frequency range, where MET displays a minimum is illustrated in Figure 6a. Note, that a similar effect of resonant activation has recently been observed by Pankratov et al. [25] for a system with a metastable state subjected to a strong periodic driving.

From Figure 6a we can estimate, that the minimum of MET occurs in the range $F_T$: $f \in (90 \div 120$ Hz). Near the left boundary of $F_T$ a merging of curves in the resonant regions for small noise intensities $D$ is observed. Here the curves tend to the limit of the deterministic case $D = 0$. Thus, the deterministic escape time gives a good estimate for the time of spike generation in a certain range of frequencies and noise intensities.

The mean-square deviation of the escape time in dependence of the driving frequency for $A = 4\ \mu\mathrm{A/cm}^2$ is illustrated in Figure 6b. Inspection of the figure shows that the standard deviation of the escape time also demonstrates a resonance-like behavior, and that the minimum of this characteristic is in $F_\sigma$: $f \in (60 \div 90$ Hz). Consequently, the effect of noise is significantly reduced in a frequency interval slightly below the region of the fastest response $F_T$. This is one of our main results. It implies that signal detection will be more effective in the frequency range that corresponds to the overlap of the regions $F_T$ and $F_\sigma$ (near $f = 90$ Hz). Here, the most optimal combination of the response time and the noise suppression occurs.

All of the above results have been obtained for zero initial phase of the external forcing. The phase exercises a significant influence on the generation time of the response from the system. However, in some situations information about the phase of the driving signal is not accessible from the experiment, and phase averaged characteristics have to be used. Hence, we will now consider the phase-averaged MET, Figure 7a, and the phase-averaged standard deviation of the escape time, Figure 7b.

As we can see from Figure 7a, this additional averaging leads to an increase of the escape times for all investigated driving frequencies. Qualitatively, however, the phase-averaged MET displays a similar behavior as in

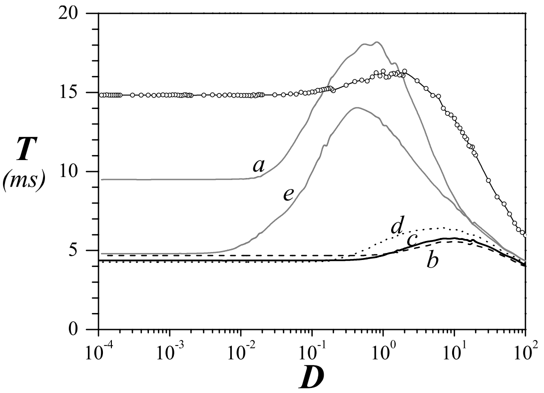

**Fig. 8.** Mean escape time as function of noise intensity for different values of the driving frequency: (*a*) $f = 20$ Hz, (*b*) $f = 70$ Hz, (*c*) $f = 90$ Hz, (d) $f = 110$ Hz, and (*e*) $f = 140$ Hz; $A = 4\ \mu\text{A/cm}^2$. Line with circles corresponds to the case of phase-averaged MET for $f = 20$ Hz.

Figure 6a. Thus, a robustness of the resonant activation effect to the phase averaging procedure is observed.

Further, let us fix five values of driving frequency: (i) near the left end of suprathreshold region: $f = 20$ Hz, Figure 1; (ii) within the region $F_\sigma$: $f = 70$ Hz, Figure 6b; (iii) $f = 90$ Hz; (iv) within the region $F_T$: $f = 110$ Hz, Figure 6a; (v) near the right end of suprathreshold region: $f = 140$ Hz.

The behavior of the mean escape time for noise intensities in the range $D \in [10^{-4}; 10^2]$ is presented in Figure 8. All curves on this figure have a resonant-like shape, and the range of noise intensities can be separated into three regions where different types of behavior for MET exist.

Below a certain value of the noise intensity, the system is weakly sensitive to changes of $D$. Here the curves in Figure 8 are nearly horizontal. This means that the fluctuations are suppressed by the strong external signal and that the necessary time for the generation of a response in the system for the considered noise intensity deviates only weakly from the escape time in the absence of noise.

With further increase of the noise intensity a growth of the MET is observed. Here, noise leads to a delay in the external signal detection. Such an increase of the escape time due to the effect of fluctuations was previously observed in potential systems by Mantegna et al. [26,27], and is known as the phenomenon of noise-delayed decay (NDD). To our knowledge, Figure 8 is the first example of NDD in excitable systems.

When the maximal delay of the system's response is reached, the role of the inverse probability current degrades [27], and further increase of the noise intensity decreases the mean escape time. Such a behavior is usual for thermal activation processes: Noise destroys metastable states that in the absence of noise would exist infinitely long time.

Here it is worth noticing that even in the absence of noise the system will be firing for a certain frequency range, because it is subjected to a suprathreshold signal. In this case noise prevents the escape, and the system needs more time to detect the input signal. It is easy to see from Figure 8 that near the boundaries of the considered frequency range ($f = 20$ Hz and $f = 140$ Hz that corresponds to curves (*a*) and (*e*), respectively), larger noise induced delays occur. Here, MET can be significantly increased by fluctuations in comparison with the deterministic case: ≈ 294% for $f = 140$ Hz and ≈ 193% for $f = 20$ Hz. By contrast, the choice of the driving frequency within the suprathreshold region ($F_T$ or $F_\sigma$) can help minimize the delay of an input signal detection. In particular, near the minimum of $\sigma$, for $f = 70$ Hz (curve (*b*)), the increase of MET does not exceed ≈ 19%. But the response time for small $D$ here is not the smallest: $t_{D=0} \approx 4.7$ ms. As argued above, signal detection will be more effective in the frequency range that corresponds to the overlap of the two regions $F_T$ and $F_\sigma$ ($f = 90$ Hz, for example). Here, the most effective combination of the response time ($t_{D=0} \approx 4.4$ ms) and the noise suppression (≈33%) exists (see curve (*c*) in Fig. 8).

A similar behavior of the phase-averaged escape time was also obtained. Here, the effect of noise-delayed decay is not so well pronounced (line with circles in Fig. 8). Moreover, for some frequency values the complete disappearance of the effect was observed. This additional averaging procedure minimizes the role of fluctuations (the increase of MET does not exceed ≈ 10% for $f = 20$ Hz), but, at the same time, leads to an increase of the system's mean response time for both small and large values of the noise intensity in comparison with curve (*a*) in Figure 8.

## 4 Conclusions

A stochastic Hodgkin-Huxley model was used as a vehicle to investigate the effect of noise on the response of an excitable system in the presence of a suprathreshold periodic driving signal. In this situation, noise is known to have a detrimental effect on the information transfer. However, we showed that this destructive effect exhibits new types of resonant phenomena, related to the delay in the neuronal response and the refractive period following a spike. In particular, the negative influence of noise can be significantly minimized for a certain parameter values. We have demonstrated the phenomenon of resonant activation, namely, MET has a minimum as a function of the frequency of the external forcing. It was shown that near the resonance region the system is weakly sensitive to changes of the noise intensity (for small $D$), i.e., small deviations of the membrane potential only change the time of spike generation slightly in this frequency range. In addition, the standard deviation of the escape time exhibits a minimum here. This is the range that is most useful for signal detection.

The effect of noise-delayed response was also observed. Noise increases the system's response time for all frequencies of the strong driving: The MET has a maximum as a function of noise intensity. But we have shown that the choice of a certain frequency range makes it possible to minimize the delay in signal detection. The influence of the phase-averaging procedure was examined for all of the above mentioned effects. It was shown that resonant activation effect displays a robustness to this procedure. In contrast, the effect of noise-delayed response demonstrates high sensitivity to the phase averaging and, for some frequency values, can practically vanish.

We have also shown, that the destructive influence of noise on the interspike interval can be reduced. With driving signals in a certain frequency range, the system can show stable periodic spiking even for relatively large noise intensities (in comparison with the threshold value). Outside this frequency range, noise of similar intensity destroys the regularity of the spike trains by suppressing the generation of some of the spikes. Thus, the results obtained in the present paper are significant not only for the detection of external information, but also within the context of its further processing by the nerve cell.

The authors would like to thank Professor Vladimir N. Belykh for helpful discussions and suggestions. E.V.P. and A.V.P. acknowledge support from the Russian Foundation for Basic Research (projects N 03-02-17543 and N 05-01-00509). E.V.M. also acknowledges support from the Danish Natural Science Foundation.

## References

1. E.R. Kandel, J.H. Schwartz, T.M. Jessell, *Principles of Neural Science* (Appleton and Lange, Norwalk 1991)
2. J. Douglass, L. Wilkens, E. Pantazelou, F. Moss, Nature **365**, 337 (1993); A. Longtin, J. Stat. Phys. **70**, 309 (1993); J.J Collins, C.C. Chow, T.T. Imhoff, Nature **376**, 236 (1995); D.R. Chialvo, A. Longtin, J. Müller-Gerking, Phys. Rev. E **55**, 1798 (1997)
3. L. Gammaitoni, P. Hänggi, P. Jung, F. Marchesoni, Rev. Mod. Phys. **70**, 254 (1998)
4. V. Anishchenco, F. Moss, A. Neiman, L. Schimansky-Geier, Uspekhi Fizicheskikh Nauk **169**, 7 (1999)
5. W.C. Stacey, D.M. Durand, J. Neurophysiol. **83**, 1394 (2000); W.C. Stacey, D.M. Durand, J. Neurophysiol. **86**, 1104 (2001)
6. F. Liu, Y. Yu, W. Wang, Phys. Rev. E **63**, 051912 (2001); F. Liu, B. Hu, W. Wang, Phys. Rev. E **63**, 031907 (2001); D.T.W. Chik, Y. Wang, Z.D. Wang, Phys. Rev. E **64**, 021913 (2001)
7. Y. Sakumura, K. Aihara, Neural Processing Lett. **16**, 235 (2002)
8. A.S. Pikovsky, J. Kurths, Phys. Rev. Lett. **78**, 775 (1997)
9. A. Neiman, P.I. Saparin, L. Stone, Phys. Rev. E **56**, 270 (1997); S.-G. Lee, A. Neiman, S. Kim, Phys. Rev. E **57**, 3292 (1998)
10. B. Lindner, L. Schimansky-Geier, Phys. Rev. E **60**, 7270 (1999)
11. D.E. Postnov, S.K. Han, T.G. Yim, O.V. Sosnovtseva, Phys. Rev. E **59**, 3791 (1999); Phys. Rev. Lett. **83**, 1771 (1999)
12. V.A. Makarov, V.I. Nekorkin, M.G. Velarde, Phys. Rev. Lett. **86**, 3431 (2001); I.Z. Kiss, J.L. Hudson, G.J.E. Santos, P. Parmananda, Phys. Rev. E **67**, 035201 (2003)
13. J.E. Levin, J.P. Miller, Nature **380**, 165 (1996)
14. W. Wang, Y. Wang, Z.D. Wang, Phys. Rev. E **57**, R2527 (1998); Y. Yu, W. Wang, J. Wang, F. Liu, Phys. Rev. E **63**, 021907 (2001)
15. H.A. Braun, H. Wissing, K. Schäfer, M.C. Hirsch, Nature **367**, 270 (1994)
16. M.T. Huber, J.C. Krieg, M. Dewald, K. Voigt, H.A. Braun, BioSystems **48**, 95 (1998); H.A. Braun, M.T. Huber, M. Dewald, K. Schäfer, K. Voigt, Int. J. Bif. and Chaos **8**, 881 (1998)
17. H.A. Braun, M.T. Huber, N. Anthes, K. Voigt, A. Neiman, X. Pei, F. Moss, BioSystems **62**, 99 (2001)
18. G. Somjen *Neurophysiology - the Essentials* (Williams and Wilkins, Baltimore 1983)
19. M. DeWeese, W. Bialek, Nuovo Cimento D **17**, 733 (1995); A.R. Bulsara, A. Zador, Phys. Rev. E **54**, R2185 (1996)
20. X. Pei, L. Wilkens, F. Moss, Phys. Rev. Lett. **77**, 4679 (1996)
21. M.T. Huber, H.A. Braun, Proceedings of SPIE **5110**, 332 (2003)
22. N.G. Stocks, in Stochastic Processes in Physics, Chemistry and Biology, edited by J.A. Freund, T. Poschel, Lecture Notes in Physics, Vol. 557 (Springer-Verlag, Berlin 2000), pp. 150–159
23. N.G. Stocks, Phys. Rev. Lett. **84**, 2310 (1999); N.G. Stocks, Phys. Rev. E **63**, 041114 (2001)
24. C.R. Doering, J.C. Gadoua, Phys. Rev. Lett. **69**, 2318 (1992); P. Jung, Phys. Rep. **234**, 175 (1993)
25. A.L. Pankratov, M. Salerno, Phys. Lett. A **273**, 162 (2000); A.N. Malakhov, A.L. Pankratov, Adv. Chem. Phys. **121**, 357 (2002)
26. R.N. Mantegna, B. Spagnolo, Phys. Rev. Lett. **76**, 563 (1996).
27. A.N. Malakhov, N.V. Agudov, Phys. Rev. E **60**, 6333 (1999); N.V. Agudov, B. Spagnolo, Phys. Rev. E **64**, R035102 (2001)
28. A.L. Hodgkin, A.F. Huxley, J. Physiol. (London) **117**, 500 (1952)
29. J. Keener, J. Sneyd, *Mathematical Physiology* (Springer Verlag, Berlin 1998)
30. Z.F. Mainen, T.J. Sejnowski, Science **268**, 1503 (1995)
31. F. Liu, W. Wang, X. Yao, Biol. Cybern. **77**, 217 (1997)
32. L.A. Pontryagin, A.A. Andronov, A.A. Vitt, Zh. Eksp. Teor. Fiz. **3**, (1933) 165 [translated by J.B. Barbour and reproduced in *Noise in Nonlinear Dynamics*, edited by F. Moss, P.V.E. McClintock (Cambridge University Press, Cambridge, England 1989), Vol. 1, p. 329]