31st Annual International Conference of the IEEE EMBS
Minneapolis, Minnesota, USA, September 2-6, 2009

Channel Noise Enhances Signal Detectability in a Model of Acoustic Neuron through the Stochastic Resonance Paradigm

M. Liberti *Member, IEEE*, A. Paffi, F. Maggio, A. De Angelis, F. Apollonio *Member, IEEE*, G. d'Inzeo *Member, IEEE*

***Abstract*—A number of experimental investigations have evidenced the extraordinary sensitivity of neuronal cells to weak input stimulations, including electromagnetic (EM) fields. Moreover, it has been shown that biological noise, due to random channels gating, acts as a tuning factor in neuronal processing, according to the stochastic resonant (SR) paradigm. In this work the attention is focused on noise arising from the stochastic gating of ionic channels in a model of Ranvier node of acoustic fibers. The small number of channels gives rise to a high noise level, which is able to cause a spike train generation even in the absence of stimulations. A SR behavior has been observed in the model for the detection of sinusoidal signals at frequencies typical of the speech.**

I. Introduction

NEURONAL electrical activity relies on the properties of membrane ion channels, whose behavior underlies the basic neuronal features such as action potential (AP) generation, repolarization, adaptation, and accommodation.

Several kinds of ion channels, in terms of activation mechanism (voltage-gated or ligand-dependent) and ionic selectivity, are exhibited in different neurons and different patches of neuron membrane, depending on their functionality [1]. Other significant parameters are the size and the density of the ion channel clusters: in some neuronal areas the channel number is relatively small whereas in areas like nodes of Ranvier the high concentration of channels acts as signal boosters [2]. Therefore, both typology and number of ion channels in different patches of membrane are responsible of specific neuronal functions [3].

The ion channel gating, due to thermal excitation of these protein macromolecules with multiple stable configurations, exhibits stochastic features, which induce random fluctuations in ionic currents. This behavior has been experimentally observed in patch-clamp recordings [4]. The amount of such fluctuations depends again on the number and on typology of ion channels and strongly affects the membrane excitability. In particular, the energy of noisy fluctuations could be high enough to induce spontaneous activity in a silent neuron.

In this work the attention has been focused on acoustic fibers, whose nodes of Ranvier have reduced dimensions (2-8) μm^2 [5] with respect to other neurons such as the motor fibers (> 20 μm^2) [6]. The small number of channels is responsible of a high noise level, which makes the acoustic neuron fire even in the absence of stimulation. Such an amount of noise is probably used by the system to enhance the detection of weak sounds through the paradigm of stochastic resonance (SR) [7]–[9]. Likewise, the channel noise (endogenous noise) could improve the detection of electric signals induced by cochlear prosthesis in those systems where the transduction cells (hair cells) have been damaged [10], [11].

In previous studies [12]–[14], the authors investigated the possibility of both endogenous and exogenous noise [14] inducing a stochastic resonant behavior in models of neurons, fibers and networks.

In this work, the SR phenomenon has been identified in a HH like model [15] representative of an acoustic neuron. The stimulation was a sinusoidal electromagnetic (EM) signal in the acoustic frequency range and the only source of noise was the random gating of the ion channels. The amounts of endogenous noise energy (i.e. channel number), which enhance the detection of the exogenous EM signals, have been found to lie in the typical range of the acoustic fibers (taken into account as the number of channels).

This seems to confirm the hypothesis that such a system is able to employ its internal noise to better detect the exogenous stimuli, which can also be furnished through an EM stimulation, such as in cochlear prosthesis [16], [17].

II. Models and Methods

A. Neuron Model

Moving from the Hodgkin-Huxley model [15], a stochastic neuron model has been setup, taking into account current fluctuations due to random gating of Sodium and Potassium channels. In this model, such two channels have been modeled with finite state machines, whose dynamic behavior is described by a time continuous discrete states Markov processes [18]. The ionic currents are calculated with a stochastic algorithm proposed by Rubinstein [19] based on the extraction of random numbers according to the Monte Carlo method [18]. The whole neuron activity is determined by the following set of differential equations:

$$C_m \frac{dV}{dt} = -I_{Na}(t) - I_K(t) - I_{leak} + I_0,$$

$$I_{Na} = g_{Na} \frac{N_{open}^{Na}(t)}{N_{TOT}^{Na}}(V - E_{Na}),$$

Manuscript received April 7, 2009.

M. Liberti, A. Paffi, F. Maggio, A. De Angelis, F. Apollonio, G. d'Inzeo are with ICEmB @ Department of Electronic Engineering, Univeristy of Rome "La Sapienza", 00184 Rome, Italy (e-mail: liberti@die.uniroma1.it).

$$I_K = g_K \frac{N_{open}^{K}(t)}{N_{TOT}^{K}}(V - E_K),$$

where $N_{open}^{Na}(t)$ and $N_{open}^{K}(t)$ are the instantaneous numbers of open Na and K channels, calculated through the Rubinstein algorithm. The total number of Na and K channels (N_{TOT}^{Na}, N_{TOT}^{K}) in the considered membrane patch are calculated on the basis of the neuron typology. In particular, for the acoustic fibers, N_{TOT}^{Na} and N_{TOT}^{K} can vary from around one hundred to one thousand [11], [20]. Numerical simulations have been performed integrating the differential equations describing the system with a forward Euler method, step-size 1 μs.

Besides Sodium, Potassium, and Leakage currents, the model encompasses the current I_0, accounting for the background level of stimulation coming from the ciliated cells.

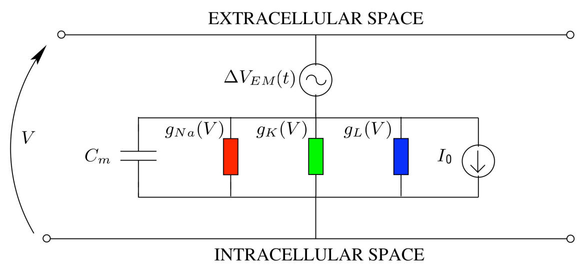

Fig. 1: The chosen HH model with the exogenous signal generator in series with the neuron circuit.

B. *Channel Noise Quantification*

Ion channel stochastic gating induces current fluctuations usually referred to as channel noise [19], [21]. The level of such fluctuations is quantified by the coefficient of variation CV [1], defined as:

$$CV = \sqrt{\frac{1-p}{p}}\frac{1}{\sqrt{N_{TOT}}},$$

which depends on the channel number (N_{TOT}) and the open probability (*p*) of the channel. According to CV definition, the number of ionic channels in the considered patch is in inverse proportion with the amount of noise exhibited by the system.

Channel densities have been fixed to ρ_K=18 channels/μm^2 and ρ_{Na}=60 channels/μm^2, for Potassium and Sodium channel respectively [15], so that different N_{TOT} numbers correspond to different patch areas.

In this work patches from 0.8 to 111 μm^2 have been considered.

C. *Insertion of the Signal in the Model*

The exogenous EM signal has been introduced in the model as an additional voltage over the membrane potential [13]. Looking at the mechanism of interaction, this means that the exogenous stimulation acts directly over the membrane voltage through the additive perturbation $\Delta V_{EM}(t)$. In terms of equivalent electric circuit, the EM stimulus is represented as a voltage generator in series with the membrane capacitor and the ionic conductances, as shown in Fig. 1.

The EM stimulus was chosen as a sinusoidal signal at three different frequencies: 65 Hz, 310 Hz, and 700 Hz, placed in the acoustic sensitivity curve according to Fig. 2. The first frequency is close to the spontaneous firing rate of the considered neuron model (see table I) but corresponds to a quite high sensitivity threshold (Sound Pressure Level-SPL around 35 dB). The other two frequencies are typical of the speech (310 Hz and 700 Hz are representative of the /i/ and /a/ English vowels, respectively, [22], [23]) and are characterized by a very low sensitivity threshold (SPL around 8 dB and 2 dB, respectively).

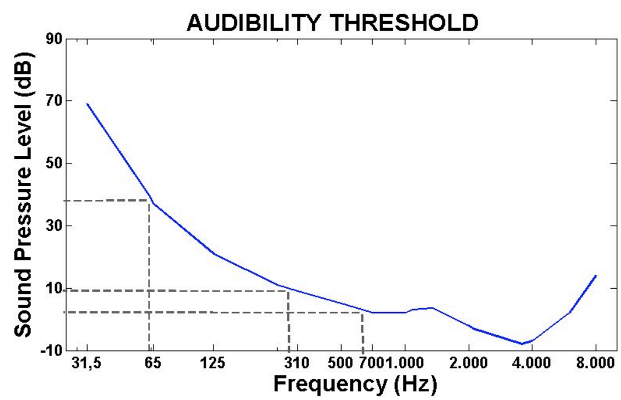

Fig. 2: Audibility threshold curve. The threshold for the three sinusoidal frequencies chosen has been put in evidence.

D. *Evaluation of Signal Detectability*

In order to evaluate the detectability of the EM signal, one should remember that neurons encode information in the output spike rate and timing. This is related to a nonlinear encoding process where every crossing of a voltage threshold corresponds to an AP generation. The presence of a periodic oscillation, like a weak sinusoidal EM signal, may therefore modulate firing activity, which will exhibit a coherent component with the input signal [13]. In our simulations the time course of membrane voltage has been converted in a time series U(t) of standard pulses (width 1 μs and height 1 mV), each correspondent to an AP. This procedure allowed us to remove noisy oscillations on the output membrane voltage, as well as the superimposed EM sinusoidal signal [13]. To quantify the EM signal detectability, the Cross Power Spectrum (CPS) has been evaluated for each noise level. First the normalized cross-correlation $|R_{xy}|$ between U(t) and the EM sinusoidal signal has been calculated, then the Fast Fourier Transform (FFT) of $|R_{xy}|$ has been performed. Finally, an average has been calculated over 100 or 200 runs to reduce standard errors in the estimate procedure. The maximum value of the mean CPS has been taken as a measure of the information transferred from the input signal to the output sequence for each considered noise level.

III. RESULTS

A. Without the EM signal

A single acoustic Ranvier node (130 Na channels and 40 K channels, corresponding to a patch area of 2.2 μm^2) has been simulated in the absence of the EM signal. A sustained neuronal activity has been evidenced also in the absence of stimulation current (I_0=0 $\mu A/cm^2$ in Tab.1), because the channel noise energy related to ionic current fluctuations is sufficient to drive the AP train generation. Tab. 1 shows the mean Inter-Spike-Interval (ISI), standard deviation and CV for increasing stimulation currents, below and above the stimulation threshold for the deterministic solution (I_0=6.3 $\mu A/cm^2$).

Table I
Mean ISI, standard deviation, CV varying I_0

I_0 [$\mu A/cm^2$]	MEAN ISI [ms]	STANDARD DEVIATION [ms]	CV
0.0	20.5	10.0	0.49
2.0	17.0	7.4	0.44
3.0	16.3	6.8	0.42
5.0	15.5	6.4	0.41
6.0	14.4	5.8	0.40
7.0	14.0	5.7	0.41

Despite that all the resulting differences were not statistically significant (*Mann-Whitney Test*), the indication is that firing frequency increases, increasing stimulation current, whereas standard deviation and CV decreases. Such a firing frequency is strictly related to noise intensity due to the small patch area (2.2 μm^2). In a similar way, through the evaluation of the power spectrum of U(t) for different patch areas and thus for several noise intensities, it has been possible to observe a shift in the main frequency peak and an increase of the output power due to the variations of the number of spikes generated for different patch areas (data not shown).

Fig. 3 shows the phase space diagram of the spike trains generated by both the deterministic neuronal model with a stimulation current equal to 6.3 $\mu A/cm^2$ (red line), and the stochastic one (2.2 μm^2 membrane patch area) without a current stimulation (blue line).

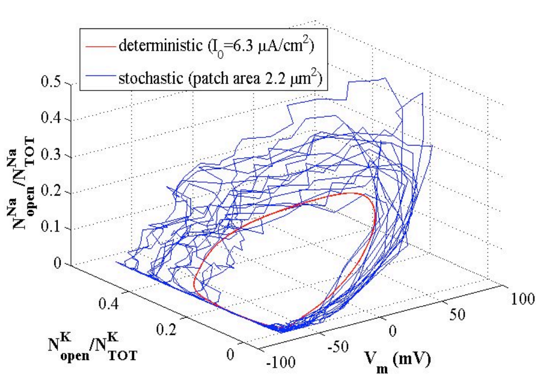

Fig. 3: Phase space diagram of the neuronal model. In red the deterministic solution, in blue the stochastic one (N_{Na}=130, N_K=40 channels).

The phase space diagram reveals how the endogenous noise energy level determined with the chosen membrane patch area is higher than the energy level due to the stimulation current. For this reason, in the following, in order to study the role of channel noise in the EM signal detectability the stimulation current I_0 is set to zero. This is the case where the hair cells should be impaired and the stimulus is applied directly to the fibers.

B. With an EM signal

Fig. 4 shows the PSD of the U(t) sequence for both one unexposed and one exposed cases (310 Hz, 1500 μV)

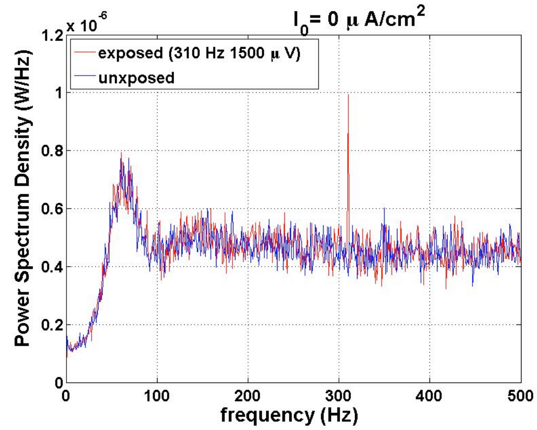

Fig. 4. Comparison between the PSD of U(t) in the presence and in the absence of the EM sinusoidal signal (ΔV_{EM}=1500 μV; f=310 Hz) without stimulation current (I_0=0 $\mu A/cm^2$) and for a well-defined noise level (patch area: A=2.2 μm^2)

The analysis of Fig. 4 evidences how the output power is similar in both cases because the applied EM signal is a subthreshold stimulus. Moreover, due to the presence of a weak EM signal, a 310 Hz component is visible in the spectrum (Fig. 4 red line), coherent with the input signal. This means that the EM signal was encoded in the output spike sequence due to the channel noise.

To investigate the role of endogenous noise in neuronal capability of detecting an exogenous EM signal, the CPS has been evaluated (see section II-C) for various patch areas, corresponding to different noise levels (Fig. 5).

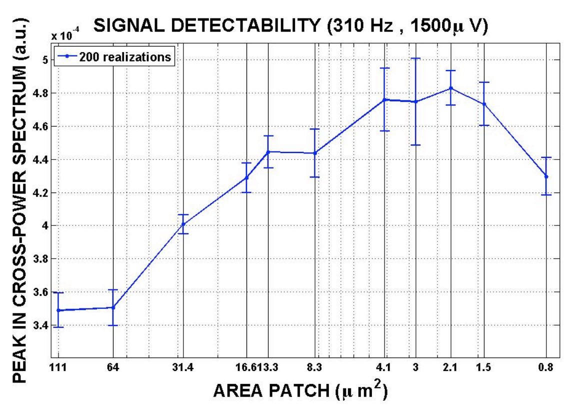

Fig. 5. Mean cross power spectrum of the neuron pulses train U(t) versus channel noise, quantified with the patch areas, without current stimulation and for a sinusoidal EM signal (ΔV_{EM}=1500 μV; f=310 Hz).

The mean CPS, calculated over 200 realizations for the same EM signal of 310 Hz and 1500 μV (Fig. 5), shows a typical bell shaped curve representative of the SR phenomenon.

As evident from the figure, a suitable level of noise exists which optimizes information transfer from input to output and thus enhances the capability of the system to detect the EM input signal. The same kind of results has been obtained with a 700 Hz sinusoidal EM signal varying patch area (data not shown). Instead, with a 65 Hz sinusoidal signal, the maximum of the CPS is out from the patch area range used in this work (see section II – B), probably due to the quite high sensitivity threshold for this frequency (see Fig. 2). Nevertheless, these data confirmed the results obtained in a previous work conducted by the authors [13] where SR has been shown for bigger patch areas.

The obtained results reveal that EM signals detectability varies according to the considered number of ionic channels embedded in the membrane patch. In particular for the two frequencies typical of the speech (310, 700 Hz), the maximum of the CPS is really in correspondence of a well-defined channel noise level (corresponding to a membrane patch from 2 to 8 μm^2), related to a channel number typical of a Ranvier's node of the acoustic fiber.

IV. Conclusion

In this work the SR phenomenon has been investigated in a HH like model representative of an acoustic neuron, in the presence of channel noise. For this purpose stochastic models representing ion channels activity have been introduced into the HH neuron model. An acoustic fiber is characterized by a small number of channels causing significant current fluctuations. The high energy level of such noisy fluctuations is able to excite the neuronal firing without any stimulation current. Signal detectability has been evaluated through the CPS with input stimulation equal to subthreshold sinusoidal electromagnetic (EM) signals at 65 Hz, 310 Hz, and 700 Hz, i.e. in the acoustic frequency range. Results indicate a stochastic resonant behavior consisting in the optimization of the information transferred from the EM input to the neural output for a well-defined level of noise. Such a noise (corresponding to a 2.1 μm^2 membrane patch area) has been found to lie in the typical range of the acoustic fibers, in particular for the 310 Hz and the 700 Hz sinusoidal signals. These results reveal how endogenous noise of acoustic fibers enhances the detection of the exogenous stimuli and must be taken into account in a more accurate design of stimulation parameters of biomedical devices such as cochlear implants.

References

[1] J. A. White, J. T. Rubinstein, and A. R. Kay, "Channel noise in neurons," *Trends in Neurosciences*, vol. 23, no.3, pp. 131-137, 2000.

[2] P. Jung and J. W. Shuai, "Optimal sizes of ion channel clusters," *Europhysics Letters*, vol. 56, no.1 , pp. 29-35, 2001.

[3] M. H. P. Kole, S. Hallermann, and G. J. Stuart, "Single I_h channels in pyramidal neuron dendrites: properties, distribution, and impact on action potential output," *The Journal of Neuroscience,* vol. 26, no.6, pp. 1677–1687, 2006.

[4] E. Neher, and B. Sakmann, "Single-channel currents recorded from membrane of denervated frog muscle fibers," *A Century of Nature: twenty-one discoveries that changed science and the world,* edited by Laura Garwin & Tim Lincoln, 2003.

[5] E. Alajmo, "Otorinolaringoiatria," (2nd ed.), Editor: *Piccin-Nuova Libreria*, 1995.

[6] E. R. Kandel, J. H. Schwartz, and T. Jessel, "Principi di neuroscienze," *Casa Editrice Ambrosiana,* Milano, 2003.

[7] F. Moss, L. M. Ward, and W. G. Sannita, "Stochastic resonance and sensory information processing: a tutorial and review of application," *Clinical Neurophysiology*, vol. 115, no.2, pp. 267-281, 2004.

[8] F. Moss, "Stochastic Resonance from ice ages to the monkey's ear," *In: Weiss GH, editor. Contemporary problems in statistical physics.* Philadelphia, PA:SIAM, pp. 205-253, 1994.

[9] F. G. Zeng , Q. J. Fu, and R. P. Morse, "Human hearing enhanced by noise," *Brain research interactive*, vol. 869, no.1, pp. 251-255, 2000.

[10] C. A. Miller, P. S. Abbas, J. T. Rubinstein, and A. J. Matsuoka, "The neurophysiological effects of stimulated auditory prosthesis stimulation," *Second Quartely Progress Report N01-DC-6-211*, 1997.

[11] H. Mino, "Encoding of information into neural spike trains in an auditory nerve fiber model with electric stimuli in the presence of a pseudospontaneous activity," IEEE *Transaction Biomedical Engineering*, vol. 54, no.3, pp. 360-369, 2007.

[12] M. Giannì, A.Paffi, M. Liberti, F. Apollonio, and G. D'Inzeo: "Channel Noise In A Hodgkin-Huxley Neuron Model: Stochastic Resonance In The Detection Of Electromagnetic Fields," In *Bioelectromagnetics Conference*, Dublin, June 2005.

[13] M. Giannì, M. Liberti, F. Apollonio, and G. D'Inzeo, "Modeling electromagnetic fields detectability in a HH-like neuronal system: stochastic resonance and window behavior," *Biological Cybernetics*, vol. 94, no.2, pp. 118-127, 2006.

[14] A. Paffi, M. Liberti, F. Apollonio, M. Giannì, and G. D'Inzeo, "Effects of Exogenous Noise in a Silent Neuron Model: Firing Induction and EM Signal Detection," in *28th Annual International Conference Of the IEEE Engineering in Medicine and Biology Society*, New York, USA, September 2006.

[15] A. L. Hodgkin and A. F. Huxley, "A quantitative description of membrane current and its applications to conduction and excitation in nerve," *Journal of Physiology,* vol. 117, no.4, pp. 500-544, 1952.

[16] H. Mino, and W. M. Grill, "Effects of stochastic sodium channels on extracellular excitation of myelinated nerve fibers," IEEE *Transaction Biomedical Engineering*, vol. 49, no.6, pp. 527-532, 2002.

[17] B. Moore, "Coding of sounds in the auditory system and its relevance to signal processing and coding in cochlear implants," *Otology & Neurotology*, vol. 24, no.2, pp. 243-254, 2003.

[18] B. Sakmann, and E. Neher, "Single-Channel Recording," Edited by *Plenum Press New York and London*, 1995.

[19] J.T. Rubinstein, "Threshold fluctuations in an N sodium channel model of the node of Ranvier," *Biophysical Journal*, vol. 68, no.3, pp. 779-85, 1995.

[20] F. Rattay, "Basics of hearing and noise in cochlear implants," *Chaos solitons & Fractals*, vol. 11, no.12, pp. 1875-1884, 2000.

[21] H. Lecar, and R. Nossal, "Theory of threshold fluctuations in nerves: relationship between electrical noise and fluctuations in axon firing," *Biophysical Journal,* vol. 11, no.12, pp. 1048-1067, 1971.

[22] R. P. Morse, and E. F. Evans, "Additive noise can enhanced temporal coding in a computational model of analogue cochlear implant stimulation," *Hearing Research*, vol. 133, no.1, pp. 107-119, 1999.

[23] R. P. Morse, E. F. Evans, "Preferential and non-preferential transmission of formant information by an analogue cochlear implant using noise: the role of the nerve threshold," *Hearing Research*, vol. 133, no.1, pp. 120-132, 1999.