Randomness and variability of the neuronal activity described by the Ornstein-Uhlenbeck model

Lubomir Kostal[1], Petr Lansky[1], Cristina Zucca[2]

[1] *Institute of Physiology, Academy of Sciences of Czech Republic, Videnska 1083, 142 20 Prague 4, Czech Republic*

[2] *Department of Mathematics, University of Torino, via Carlo Alberto 10, 10 123 Torino, Italy*

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Address for correspondence:
Lubomir Kostal
Institute of Physiology, Academy of Sciences of Czech Republic,
Videnska 1083,
142 20 Prague 4,
Czech Republic
tel: +420 2 4106 2276,
fax: +420 2 4106 2488,
e-mail: kostal@biomed.cas.cz

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Abstract

Normalized entropy as a measure of randomness is explored. It is employed to characterize those properties of neuronal firing that cannot be described by the first two statistical moments. We analyze randomness of firing of the Ornstein-Uhlenbeck neuronal model with respect either to the variability of interspike intervals (coefficient of variation) or the model parameters. A new form of the Siegert's equation for first-passage time of the Ornstein-Uhlenbeck process is given. The parametric space of the model is divided into two parts (sub- and supra-threshold) depending upon the neuron activity in the absence of noise. In the supra-threshold regime there are many similarities of the model with the Wiener process model. The sub-threshold behavior differs qualitatively both from the Wiener model and from the supra-threshold regime. For very low input the firing regularity increases (due to increase of noise) cannot be observed by employing the entropy, while it is clearly observable by employing the coefficient of variation. Finally we introduce and quantify the converse effect of firing regularity decrease by employing the normalized entropy.

1 Introduction

Several approaches have been proposed in the literature to model the activity of a single neuron. Such models usually describe the evolution of the membrane potential and they can be either stochastic or deterministic (Gerstner and Kistler, 2002; Tuckwell, 1988). The leaky integrate-and-fire concept is employed very often (for a recent review see Burkitt (2006)). In one of the stochastic versions of this model the membrane potential evolution is described by the Ornstein-Uhlenbeck (OU) process bounded by a firing threshold. Another and simpler model, parallel to the OU process, is the perfect integrator described by a Wiener process with a positive drift. Due to its simplicity many results can be obtained in a closed form while for the OU model only few analytical results are available.

The neuronal firing in both these models is viewed as a first-passage time of the membrane potential through a threshold S. The spike itself is considered to be a point event after which the membrane potential is reset. The spiking activity of the OU and Wiener models is therefore described by the renewal process of interspike intervals (ISIs) T with probability density function $f(t)$. The densities $f(t)$ for different parameter values are mutually compared by calculating the moments of the distribution. The advantage of using the approach based on the moments lies in the possibility of relating statistical characteristics with some key concepts of neuronal coding or neuronal properties. For example, the mean value $E(T)$ describes the neuronal firing from the rate coding hypothesis point of view (Gerstner and Kistler, 2002). The characteristics based on the variance can be related to the variability coding hypothesis (Perkel and Bullock, 1968) and may also provide some information about the metabolic efficiency of the neuronal coding (Laughlin, 2001). Variability, reflected by the coefficient of variation, of ISIs generated by the OU model was recently a topic for a very extensive discussion initiated by Softky and Koch (1993). On the other hand the estimates of higher moments cannot be reliably determined from samples of relatively small size as is normal with the neuronal data. Thus the attempts to use higher moments are not as frequent as using mean and C_V (Han et al., 1998; Lewis et al., 2001; Ruskin et al., 2002; Shinomoto et al., 2002). Besides the approach based on statistical moments, the information-theoretic quantities are employed in analysis of neuronal signal in order to provide an alternative point of view. Recently, for example, the concept of the Kullback-Leibler distance has been utilized in Johnson et al. (2001) and DeWeese and Meister (1999), although for a different purpose than in this paper.

The aim of our paper is to discuss the properties of different firing regimes of the OU model by employing statistical characteristics of the resulting spike trains with respect to the two input model parameters – signal μ and 'noise' σ^2. Besides the mentioned $E(T)$ and C_V we define the normalized entropy (related to the Kullback-Leibler distance), η, as a measure of randomness of the neuronal firing. Among these three characteristics $(E(T), C_V, \eta)$ we concentrate mainly on the differences between C_V and η, i.e., the differences that go beyond the first moment. We continue the work started in Kostal and Lansky (2007) and show, that the notions of variability and randomness describe different qualities of the neuronal firing and that these terms cannot be interchanged generally. We also note at this point, that the relation between η and some recently proposed information measures (Chacron et al., 2001, 2003; DeWeese and Meister, 1999) has been exploited in Kostal and Lansky (2006b). Our current study describes similar phenomena to those obtained in Lindner at al. (2002), though from a different point of view. The approach used here permits a global comparison of the ISI probability densities generated by the model. Further on, working in the parameteric space of the original model gives an opportunity to judge if the features observed in the standardized form can be realized by real neurons.

2 Theory and Methods

2.1 Classification of neuronal firing

One of the most important characteristics of the neuronal firing (besides the firing rate) is its variability. The variability is often described by the coefficient of variation, C_V, which relates standard deviation to the mean value, $C_V = \sqrt{Var(T)}/E(T)$. The C_V is dimensionless and does not depend on the linear scaling of the random variable, $C_V(aT) = C_V(T)$. In this sense the C_V does not depend on the actual $E(T)$ and both these numbers provide separate views on the spiking activity. Nevertheless, $E(T)$ and C_V cannot be used to distinguish between two probability distributions that differ in higher than second moments.

Instead of looking for classifications based on higher moments we offer a conceptually different approach based on the randomness of the firing. The measure of randomness of a random variable T with probability density $f(t)$ is given by the entropy, $h(f)$,

$$h(f) = -\int_0^\infty f(t) \ln f(t)\, dt, \tag{1}$$

see Cover and Thomas (1991) for details. The entropy can be seen as measuring the 'choice' in neuronal firing, i.e., its value decreases as the possible ISI lengths are subject to more constraints. The maximum entropy on $[0, \infty)$ for a fixed $E(T)$ is realized by the exponential distribution, $h(f) = 1 + \ln E(T)$. The particular value of $h(f)$, however, generally depends on $E(T)$. In order to make the entropy independent of the linear scaling (in the same way as C_V) we transform the original random variable T to $\Theta = T/E(T)$. The 'new' variable Θ is dimensionless with mean $E(\Theta) = 1$ and we denote its entropy as 'normalized entropy' $\eta(f)$. The normalized entropy is related to the original entropy of the unscaled variable T as

$$\eta(f) = h(f) - \ln E(T). \tag{2}$$

If the firing is regular, i.e. $f(t) = \delta(t - t_0)$, then $\eta(f) = -\infty$. On the other hand, the value of η is maximized for the exponential probability density function and in that case $\eta(f) = 1$ which identifies maximum randomness of the firing.

Normalized entropy (2) can be related to the Kullback-Leibler (KL) distance, $D(f, g)$, of a general probability density function $f(t)$ to the exponential density, $g(t) = \lambda e^{-\lambda t}$, with the same mean, i.e., with $\lambda = 1/E(T)$

$$D(f, g) = \int_0^\infty f(t) \ln \frac{f(t)}{g(t)}\, dt = 1 + \ln E(T) - h(f). \tag{3}$$

Combining formulas (2) and (3) yields

$$\eta(f) = 1 - D(f, g). \tag{4}$$

Note that for the exponential distribution $C_V = 1$ holds, but the reverse statement is not valid. On the other hand, it follows from the properties of the KL distance (Cover and Thomas, 1991) that $\eta(f) = 1$ if and only if $f(t)$ is exponential density. Thus, for $C_V \neq 1$ it always holds $\eta(f) < 1$. Finally we note, that the (normalized) entropy can be estimated directly from experimental data, see, e.g., Beirlant et al. (1997); Tsybakov and Meulen (1996) for an overview of different methods.

2.2 The models

We assume that the membrane depolarization of a neuron is described by a stochastic process $X = \{X_t; t \geq 0\}$ and a spike is elicited any time the process crosses a constant boundary S from below, under the condition that the process is reset after each spike. The time between two consecutive firings of the neuron is identified with the first-passage time of the stochastic process through a threshold S, $T = \inf\{t > 0 | X_t \geq S, X_0 = x_0 < S\}$.

The OU model describes the membrane depolarization by the stochastic process that fulfills the stochastic differential equation

$$dX_t = \left(-\frac{X_t}{\theta} + \mu\right) dt + \sigma dW_t, \quad X_0 = 0 \tag{5}$$

where $W = \{W_t; t \geq 0\}$ is a standard Wiener process, $\theta > 0$ is the membrane time constant, the constant μ characterizes the net-neuronal input and $\sigma > 0$ is a further constant related with the variability of the neuronal input. Commonly, the constant μ is denoted as the signal and σ^2 as the noise. However, such a distinction may appear to be confusing, because generally, there is dependence between μ and σ^2 (Hanson and Tuckwell, 1983; Lansky and Sacerdote, 2001) and large values of μ imply relatively low values of σ^2 (Ditlevsen and Lansky, 2005). The choice $X_0 = 0$ implies that the resting and resetting potentials are set to zero. The parameters S and θ are the intrinsic parameters of the model while μ and σ^2 depend on the activity of other neurons in a network (Tuckwell and Richter, 1978). The parameters of the process determine two firing regimes, depending on the behavior of the model in absence of noise ($\sigma^2 = 0$). If $\mu\theta > S$ (supra-threshold regime) the neuron is active also in absence of noise and the firing is regular. If $\mu\theta < S$ (sub-threshold regime) the neuron is silent in absence of noise. The intermediate situation corresponds to the threshold regime $\mu\theta = S$.

The Wiener model can be obtained by taking the limit $\theta \to \infty$ in formula (5). The membrane potential is then described by the Wiener process with drift $Y = \{Y_t; t \geq 0\}$, that fulfills the stochastic differential equation

$$dY_t = \mu dt + \sigma dW_t, \quad Y_0 = 0. \tag{6}$$

Due to the properties of the model (6) an additional condition $\mu > 0$ has to be imposed, otherwise T is not a proper random variable, $\mathrm{Prob}(T = \infty) > 0$. From formula (6) follows that the membrane potential always approaches and crosses the threshold linearly for any σ^2. From this point of view, the Wiener model is always operating in the supra-threshold regime.

The ISI probability density of the Wiener model is known in a closed form, and is equivalent to an inverse Gaussian density (Chhikhara and Folks, 1989),

$$f_W(t) = \frac{S}{\sqrt{2\pi\sigma^2 t^3}} \exp\left\{-\frac{(S-\mu t)^2}{2\sigma^2 t}\right\}. \tag{7}$$

The ISI probability density of the OU model is known in a closed form only in the threshold regime $\mu\theta = S$

$$f_{OU}(t) = \frac{2S}{\sqrt{\pi\sigma^2 t^3}} \frac{\exp\left(2t/\theta\right)}{(\exp\left(2t/\theta\right)-1)^{3/2}} \exp\left\{-\frac{S^2}{\sigma^2\theta(\exp\left(2t/\theta\right)-1)}\right\}. \tag{8}$$

In the remaining cases, i.e., $\mu\theta \neq S$, numerical techniques have to be employed. The mean and C_V of the Wiener model follow from formula (7),

$$E(T) = \frac{S}{\mu}, \qquad C_V = \frac{\sigma}{\sqrt{\mu S}}. \tag{9}$$

For the OU model the first two moments can be written in several ways in terms of integrals (Siegert, 1951; Keilson and Ross, 1975) or in terms of series (Tuckwell and Cope, 1980; Ricciardi et al., 1999). Nevertheless these expressions are difficult to handle especially from a numerical point of view.

2.3 Numerical procedures

The method used throughout the paper for the numerical evaluation of the ISI probability density function $f_{OU}(t)$ is based on the integral equation with non-singular kernel derived in (Buonocore et al., 1987; Ricciardi et al., 1999). Furthermore, $E(T)$ can be evaluated using a closed form expression or calculated numerically from $f_{OU}(t)$ together with C_V. Normalized entropy given by formula (2) is estimated numerically by an approximation of the involved integrals using a trapezoidal rule. We explicitly note that a reliable numerical integration is possible because the probability density function can be numerically evaluated with sufficient precision in a sufficiently dense set of points.

A simulation technique for the computation of the entropy does not give reliable results due to the estimation of the density function via histograms that are not smooth and depend on the binning. Kernel density estimators are also not useful here since, even if they give smooth densities they are bin-width dependent.

3 Results and discussion

Throughout the paper we set $S = 10\,\mathrm{mV}$ and $\theta = 10\,\mathrm{ms}$ to make our results biologically plausible and comparable with the previously published studies (La Camera et al., 2004; Inoue et al., 1995; Lansky and Rospars, 1995; Kandel and Schwartz, 1985; Stevens and Zador, 1998; Tuckwell and Richter, 1978). Consequently, the threshold value of neuronal input is $\mu = 1\,\mathrm{mV/ms}$ and any smaller value results the sub-threshold regime independently on the value of σ^2. The maximum value of σ^2 we allow is $\sigma^2 = 40\,\mathrm{mV^2/ms}$ which is within the range of the estimated values from experimental data (Inoue et al., 1995).

3.1 Relations between model parameters and statistical characteristics of the generated ISIs

In order to obtain better insight into the behavior of the OU model we first review the dependence between the two input parameters μ and σ^2 and the two statistical characteristics C_V and $E(T)$ in the sub-threshold and supra-threshold regimes. The Siegert formula (Siegert, 1951) for the mean first-passage time of the OU process is

$$E(T) = \sqrt{\frac{\pi\theta}{\sigma^2}} \int\limits_{-\mu\theta}^{S-\mu\theta} \exp\left(\frac{z^2}{\theta\sigma^2}\right) \left[1 + \operatorname{erf}\left(\frac{z}{\sigma\sqrt{\theta}}\right)\right] dz. \tag{10}$$

Equation (10) can be written as

$$\begin{aligned} E(T) &= \frac{(S-\mu\theta)^2}{\sigma^2}\, {}_2F_2\left(1,1;\tfrac{3}{2},2;\frac{(S-\mu\theta)^2}{\sigma^2\theta}\right) - \frac{\mu^2\theta^2}{\sigma^2}\, {}_2F_2\left(1,1;\tfrac{3}{2},2;\frac{\mu^2\theta}{\sigma^2}\right) \\ &\quad + \frac{\pi\theta}{2}\left[\operatorname{erfi}\left(\frac{\mu\sqrt{\theta}}{\sigma}\right) + \operatorname{erfi}\left(\frac{S-\mu\theta}{\sigma\sqrt{\theta}}\right)\right], \end{aligned} \tag{11}$$

where ${}_2F_2(a_1, a_2; b_1, b_2; z)$ is the generalized hypergeometric function (Abramowitz and Stegun, 1972) and $\operatorname{erfi}(z) = \operatorname{erf}(iz)/i$ is the imaginary error function. This expression is particularly useful for numerical evaluation since the involved special functions can be implemented with sufficient precision.

As shown in Fig. 1 the qualitative dependence of $E(T)$ on σ^2 is monotonous for all values of parameter μ. With decreasing σ^2 the $E(T)$ increases to infinity in threshold ($\mu = 1$) and sub-threshold ($\mu < 1$) regimes and to a constant in supra-threshold ($\mu > 1$) regime as expected intuitively. With increasing σ^2 the mean ISI always tends to zero, which is shown up to 5 ms.

The relation between C_V and σ^2 is shown in Fig. 2. We can see again the different

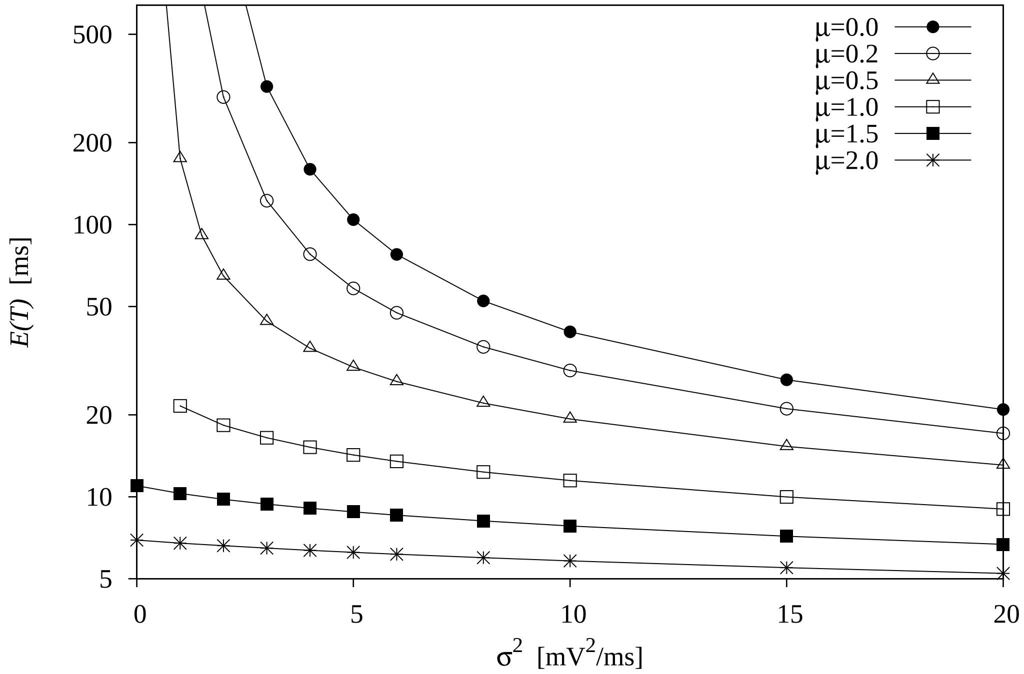

Fig. 1: The dependence of the mean ISI upon the noise σ^2 for different values of μ for the OU model ($S = 10\,\mathrm{mV}$ and $\theta = 10\,\mathrm{ms}$, μ is in mV/ms).

behavior between the two regimes in the OU model. In the supra-threshold regime as $\sigma^2 \to 0$ we get $C_V \to 0$ that means absence of variability, indeed the ISIs are almost constant. In the sub-threshold regime it holds $C_V \to 1$ for $\sigma^2 \to 0$. As expected, the density of T converges to an exponential density and this is illustrated by C_V close to one. With σ^2 increasing we notice the local decrease of C_V. This effect is often denoted as the coherence resonance (Lindner at al., 2002).

In Fig. 3 the dependence between $E(T)$ and C_V is illustrated. The dependency is always plotted for fixed μ and varying σ^2. In the supra-threshold regime as C_V increases $E(T)$ monotonically decreases. On the other hand, in the sub-threshold regime C_V does not determine $E(T)$ uniquely, i.e., it is impossible to determine $E(T)$ and σ^2 only from μ and C_V. However, it is possible to determine μ and C_V from $E(T)$ and σ^2 as Fig. 1 shows. Comparison of Figs. 1, 2 and 3 reveals, that

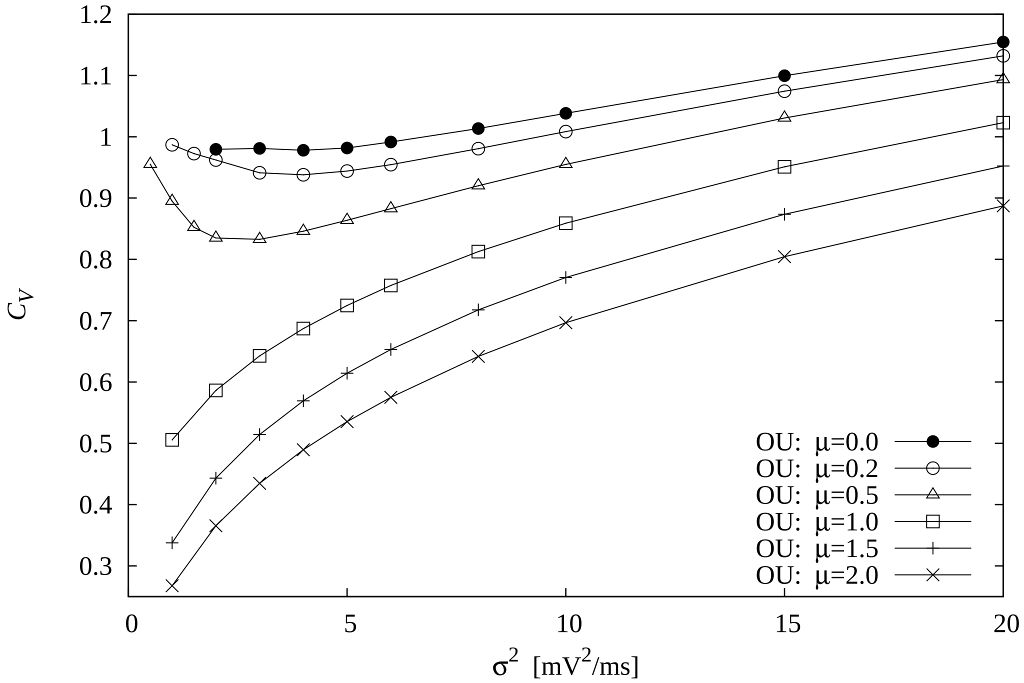

Fig. 2: Coefficient of variation C_V for the OU model in dependency on the noise σ^2 with different values of the input parameter μ (in mV/ms).

knowledge of (almost) any two values in the quadruplet $(\mu, \sigma^2, E(T), C_V)$ uniquely determines the remaining two. The only exception is that $(E(T), \sigma^2)$ cannot be determined from (μ, C_V) due to the coherence resonance effect (local C_V decrease) described later.

3.2 Randomness and moment characteristics of firing

We examine the behavior of randomness by employing the normalized entropy in dependency on the C_V. (Recall that the effect of different $E(T)$ values is removed for both of these measures.) For the Wiener model the normalized entropy can be written in terms of C_V as follows from Kostal and Lansky (2006a)

$$\eta(f_W) = \frac{1}{2} + \frac{1}{2}\ln(2\pi C_V^2) - \frac{3\, e^{1/C_V^2}}{\sqrt{2\pi C_V^2}} K_{\frac{1}{2}}^{(1,0)}(1/C_V^2), \tag{12}$$

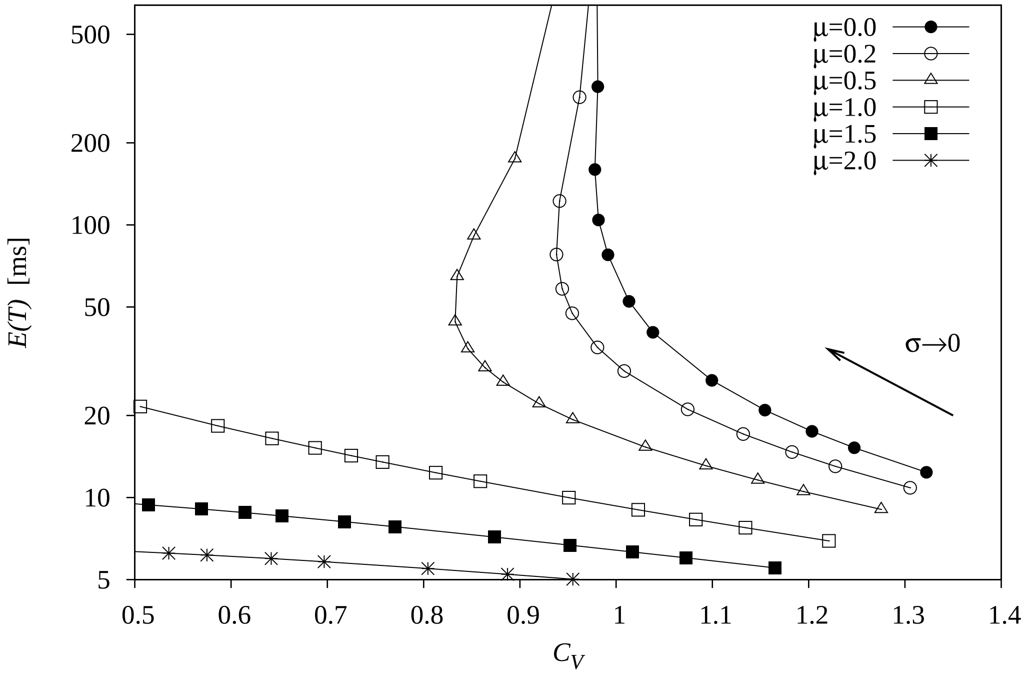

Fig. 3: The mean ISI in dependency on C_V (along the curves from right to left σ^2 decreases) for different values of μ for the OU model ($S = 10\,\mathrm{mV}$ and $\theta = 10\,\mathrm{ms}$, μ is in mV/ms). The maximum value of σ^2 is $40\,\mathrm{mV}^2/\mathrm{ms}$. Note the non-unique relation between $E(T)$ and C_V due to the coherence resonance effect (local decrease in firing variability with increasing input noise) in the sub-threshold regime.

where $K_\nu^{(1,0)}(z)$ is the derivative of the modified Bessel function of the second kind (Abramowitz and Stegun, 1972). For the OU model only numerical procedure is available.

The results are shown in Fig. 4 for the Wiener model and both sub- and suprathreshold regimes of the OU model. We see that maximum randomness does not coincide with maximum variability. (Note, that there are distributions with maximum variability and randomness coinciding, i.e., Pareto distribution, see Kostal and Lansky (2006b) for details). Similarly, we see that $C_V = 1$ does not imply maximum randomness. For the OU model in the sub-threshold regime C_V does not determine the randomness (and thus the shape of the ISI probability density) uniquely if μ is fixed (see Fig. 2). We can deduce from Fig. 4, that there are always two different shapes of the probability density functions with C_V close to unity: one which is very close to the exponential density (maximum randomness) and the second one further away. With small input μ the C_V cannot be made deliberately small regardless of the noise amplitude. As the input in the sub-threshold regime increases the minimal value of C_V, $C_V^{(\min)}$, decreases. Note that around $C_V = 1.25$ the values of η are nearly the same for all sets of parameters of the sub-threshold OU model.

The effect of coherence resonance can be observed in both measures, C_V and η. However, it follows from the picture that the coherence resonance can be reliably observed in randomness only for $\mu > 0.2$. This fact further enhances the difference between variability and randomness, i.e, the increase of regularity (as measured by C_V) does not necessarily imply the decrease in randomness of the spike train. Namely, few sufficiently long ISIs in otherwise 'almost' regular spiking activity result in a high variability although the randomness may be low.

For the case of $\mu \geq 1$ (the threshold and supra-threshold regimes) the behavior of the model is less complicated and all C_V values are obtainable. Furthermore it always holds $\eta \ll 1$, i.e., the ISI probability density is never close to the exponential distribution. The curves $\eta(f_{OU})$ parameterized by the C_V in the supra-threshold regime have a very similar shape and are similar to the Wiener model as expected. For increasing μ the normalized entropy of the OU model converges to the entropy of the Wiener model and the shape of $\eta(f_{OU})$ is less convex. This similarity holds only for small C_V. For $C_V > 1.4$ the randomness of the OU model is always lower than the randomness of the Wiener model.

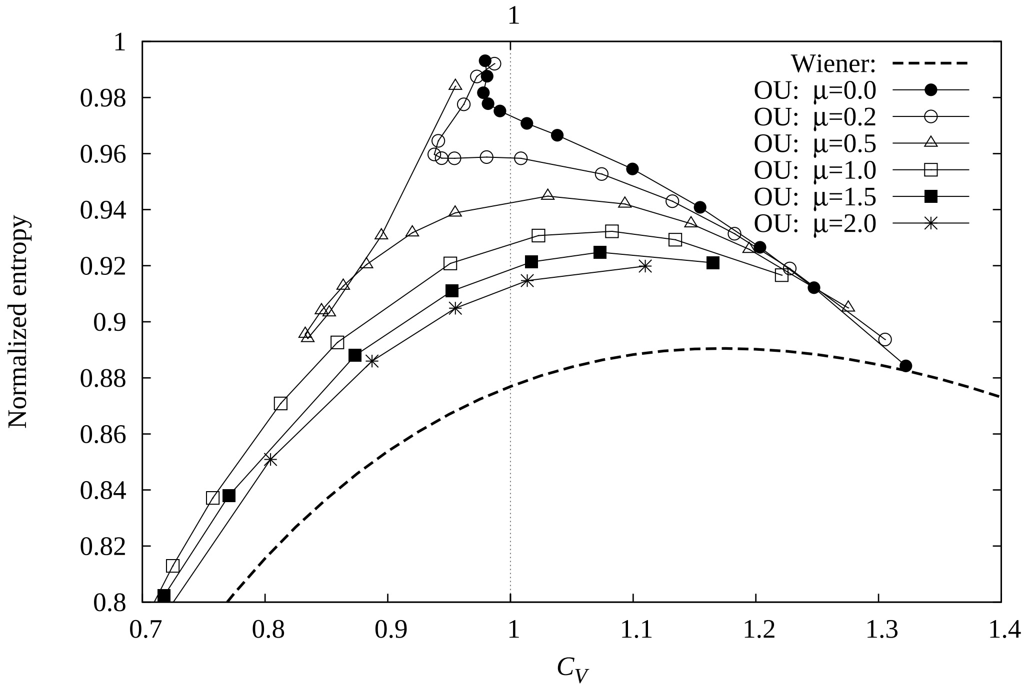

Fig. 4: Normalized entropy in dependency on the coefficient of variation C_V with different values of the input parameter μ ($S = 10\,\mathrm{mV}$ and $\theta = 10\,\mathrm{ms}$). The maximum value of σ^2 is $40\,\mathrm{mV}^2/\mathrm{ms}$. The dashed line represents the normalized entropy of the Wiener model.

3.3 Randomness and input parameters

In this section we explore randomness in the Wiener and OU models with respect to the model parameters (μ, σ^2). The normalized entropy for the Wiener model is given in terms of (S, μ, σ^2) by combining formulas (9) and (12). For the OU model we can write the normalized entropy only in the threshold regime ($\mu = 1$) and we get an expression in terms of the parameters (S, θ, σ^2)

$$\eta(f_{OU}) = \frac{1}{2} + \frac{3}{2}\left[\gamma + \ln\left(\frac{4S^2}{\sigma^2\theta}\right)\right] - \ln\left(\frac{2S}{\sqrt{\pi\sigma^2\theta^3}}\right) - \frac{2}{\theta}E(T) - \ln E(T), \qquad (13)$$

where $E(T)$ is given by formula (11) and $\gamma \approx 0.577$ is the Euler Gamma constant (Abramowitz and Stegun, 1972). For the threshold regime we checked the agreement between η given by formula (13) and its numerical estimation obtained directly from the probability density function.

The results relating randomness to μ and σ^2 are shown in Fig. 5. For $\mu = 0$ the dependence $\eta(\sigma^2)$ is almost linear and decreases rather slowly. The non-linearity is more pronounced for increasing values of μ. For $\mu < 1$ as $\sigma^2 \to 0$ the normalized entropy tends to 1, it means that the probability density function is getting exponential. Then as σ^2 increases the randomness decreases to its local minimum (coherence resonance) and then increases again to its local maximum and it slowly decreases again. On the other hand, for $\mu \geq 1$ the firing gets more regular in the case of $\sigma^2 \to 0$ which is reflected by $\eta \to -\infty$. The local maxima of η occur for higher values of σ^2 with increasing μ.

Though Fig. 5 looks very similar to Fig. 2 there are substantial differences between the measures C_V and η. To demonstrate this we plot the dependence of $E(T)$ on η in Fig. 6 and compare it with a similar plot for C_V in Fig. 3. The behavior of normalized entropy is more complex. The coherence resonance is present in the sub-threshold regime only for $\mu > 0.2$ as already mentioned. Moreover, the relation between $E(T)$ and η is non-unique even in the supra-threshold regime. For each $\mu > 0.2$ we observe a local increase in randomness (and irregularity of the firing) in dependence on $E(T)$ (or σ^2) even though C_V is monotonous in the supra-threshold regime.

4 Conclusions

The normalized entropy as a measure of randomness was introduced. We applied it to the neuronal activity described by the OU and Wiener models. In particular,

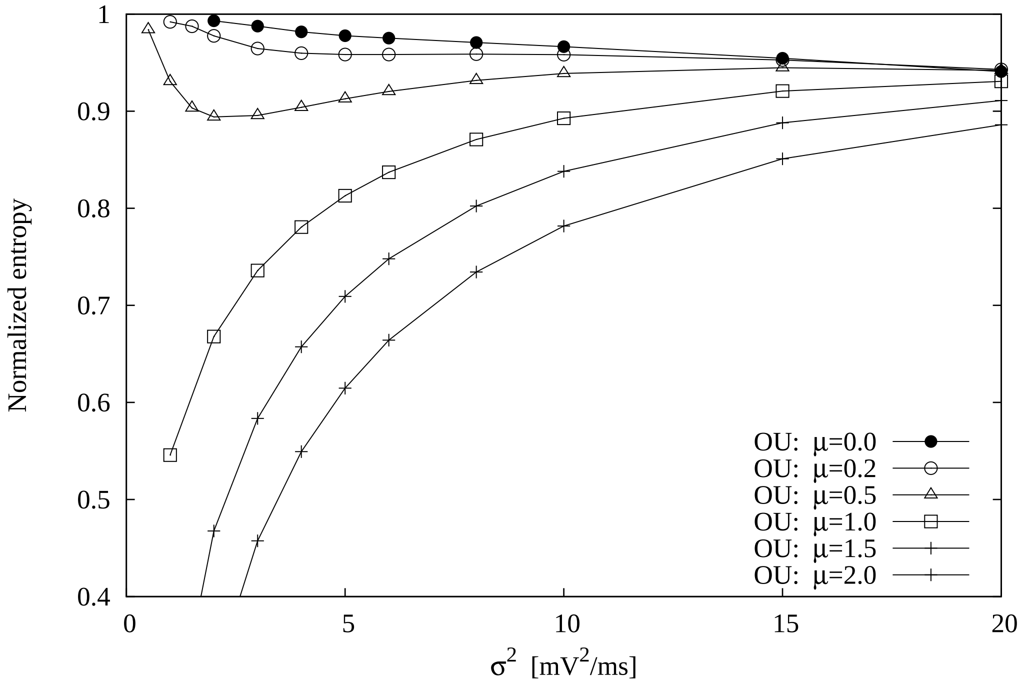

Fig. 5: Normalized entropy as a function of the noise σ^2 for different values of parameter μ of the OU model ($S = 10\,\mathrm{mV}$ and $\theta = 10\,\mathrm{ms}$). Note the similarity with Fig. 2, however, the local decrease in C_V in the sub-threshold regime is not prominent for μ smaller than $0.2\,\mathrm{mV/ms}$.

we described the firing characteristics that go beyond the first statistical moment and analyzed the randomness of the ISIs with respect to the coefficient of variation and the mean ISI (the statistical approach) or with respect to the model parameters (the modeling approach).

The behavior of the OU model is qualitatively different in the sub- and supra-threshold regimes. In the sub-threshold regime C_V does not determine uniquely the shape of the ISI probability density function even if the model parameters (except the input noise) are fixed. For both sub- and supra-threshold regimes we identified such regions of C_V and model parameter values for which the randomness can be considered independent on the neuronal input. Finally we noted that the local

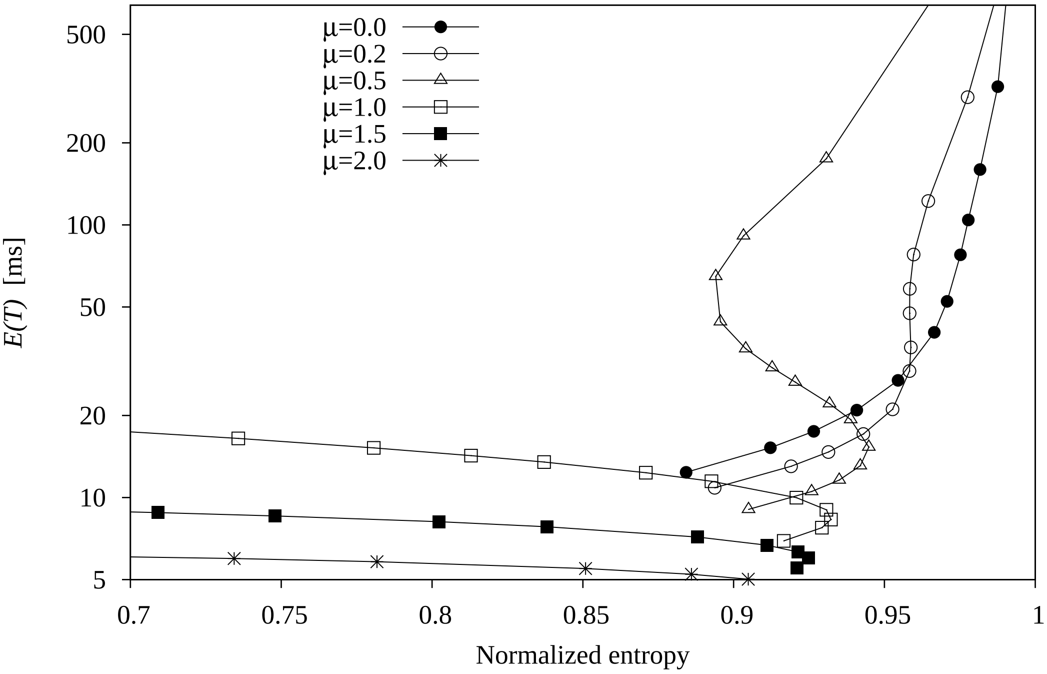

Fig. 6: The mean ISI in dependency on the normalized entropy (compare with Fig. 3). The maximum value of σ^2 is $40\,\mathrm{mV}^2/\mathrm{ms}$. Note the non-unique relationship in the supra-threshold regime and local increase of randomness present for regimes with μ greater than $0.2\,\mathrm{mV/ms}$.

decrease in variability (with respect to the noise) for very low neuronal values input is not reliably observable by employing the normalized entropy of the firing, which demonstrates the key difference between randomness and variability. Moreover, we described the converse effect (the local decrease in regularity of the firing), which on the other hand cannot be observed by employing the notion of variability.

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