Stochastic FitzHugh-Nagumo model: Distribution of spikes and ISI statistics

Ludovica Aisa

Dipartimento di fisica e astronomia, Alma Mater Studiorum, Università degli studi di Bologna, Via Irnerio 46, Bologna, Italy

Abstract

The purpose of this analysis is to study the distributions of the FitzHugh-Nagumo system's *spikes generation* and the *interspikes interval times* (ISI) statistic affected by two type of stochastic noises: Wiener and Ornstein-Uhlenbeck noises. Their expected distributions are the Poisson distribution for the number of spikes generated by the system in a fixed time interval and Exponential distribution for the ISI. The analysis includes observations varying the temperature which defines the amplitude of the noises. The results are about as expected, which leads to considerations about how the two stochastic noises affects differently the FHN system.

1. Introduction

The FitzHugh-Nagumo model is one of the simplest but effective system that replicates some of the important features of the dynamic of the neuron. It is a 2-dimensional nonlinear differentiable autonomous system, that reproduces the process of excitability of the neuron and the generation of its action potential [1].

1.1. Biological neuron

By biological point of view, the neuron has a polarized membrane that maintains a resting potential, a difference in electrical charge across its surface, with the inside being negatively charged compared to the outside that is positively charged. The polarization in the resting state is maintained by the action of a protein sodium-potassium pump, which transport K+ inside and Na+ outside the membrane, plus the opening of the channel proteins for K+, so that the ions can diffuse through the layer and the closure for the channel of Na+: all these factors leads to the difference concentration of positive ions, mainly sodium ions Na+, between the inside and the outside of the membrane[2].
When a neuron receives a stimulus or input, it can lead to a change in the membrane potential. If the stimulus is strong enough to exceed a certain threshold, it triggers an *action potential.* The action potential is a rapid and transient electrical impulse that propagates along the neuron's membrane. During an action potential, there is a rapid *depolarization* of the membrane. Voltage-gated ion channels in the membrane open, allowing an influx of Na+ positively charged ions, into the neuron. This depolarization continues until a peak membrane potential is reached. Then there is a *repolarization* phase where the membrane potential returns to its resting state. This occurs due to the opening of voltage-gated potassium (K+) channels, allowing an efflux of positively charged potassium ions, and the action of the sodium-potassium pump which restores the negative charge inside the neuron. After repolarization, the membrane potential briefly becomes more negative than the resting potential, known as *hyperpolarization.* This is caused by the delayed closing of potassium channels. The action potential travels along the neuron's axon, which is covered in myelin sheaths that insulate and speed up the conduction of the electrical signal. At the end of the axon, the action potential triggers the release of chemical neurotransmitters into the synapse, which can then transmit the signal to the next neuron or target cell [2].

1.2. Deterministic FHN model

In this analysis the set of differentiable equation chosen to represent the **FHN model** are:

$$\begin{cases} dv = (v - \frac{v^3}{3} - w + I)dt = f_1(v,w)dt \\ dw = \epsilon(v + a)dt = f_2(v,w)dt \end{cases} \tag{1}$$

These equation contains the fast and slow variable (v, w), where v is the fast variable whose dynamics represents excitability while w is the slow one whose dynamics represents accommodation and refractoriness caused by the

hyperpolarization, ϵ is the time scale factor between the fast variable v and the slow variable w. I is a constant bias current which can be considered as the effective external input current and a is a parameter.
In order to study this model the trajectory of the variables should be analyzed in their 2-dimensional phase space $(v, w) \in \mathcal{M}$. The set of equilibrium point correspond to all the fixed point (v^*, w^*), obtained by setting both equations of (1) equal to zero:

$$\begin{cases} w^* = v^* - \frac{v^{*3}}{3} + I \\ v^* = -a \end{cases} \tag{2}$$

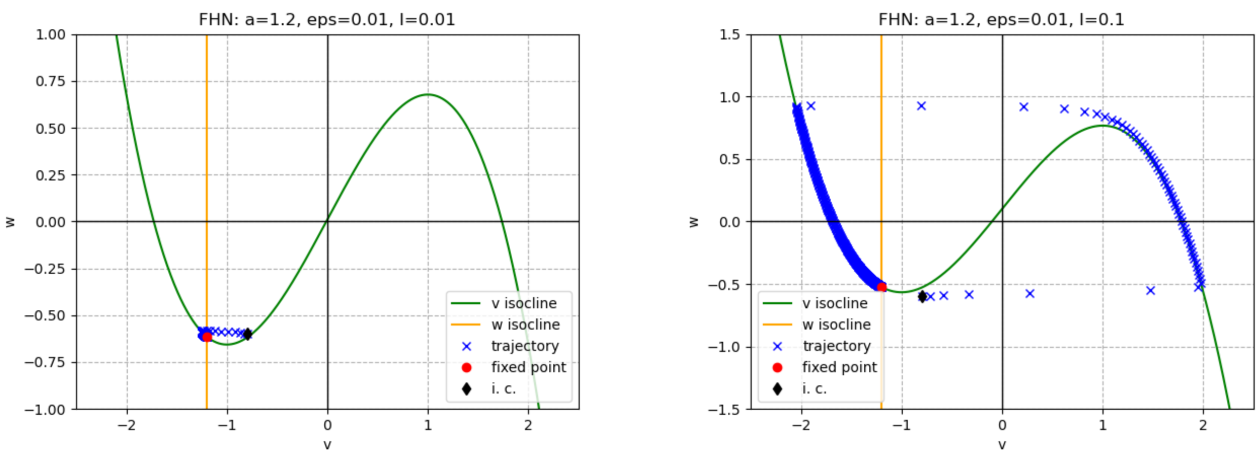
where the equations represent the nullclines of the variables. Generally for the FHN model, according to the values of the parameters there could be one, two or three different fixed point for the system. In this paper the equations are set up to have only one fixed point. The stability of the fixed point can be evaluated through the linearization of the model $\mathbf{F}(v, w) = [f_1(v, w), f_2(v, w)]$ in the neighborhood of the fixed point (v^*, w^*), studying the eigenvalues of the Jacobian matrix in that point [3]. Given Eq.(1), the Jacobian matrix $J\mathbf{F(v,w)}$ is:

$$J\mathbf{F(v,w)} = \begin{bmatrix} 1 - v^{*2} & -1 \\ \epsilon & 0 \end{bmatrix}$$

Through the secular equation $\lambda^2 - \lambda Tr(J\mathbf{F}) + Det(J\mathbf{F})$ the eigenvalues are obtained:

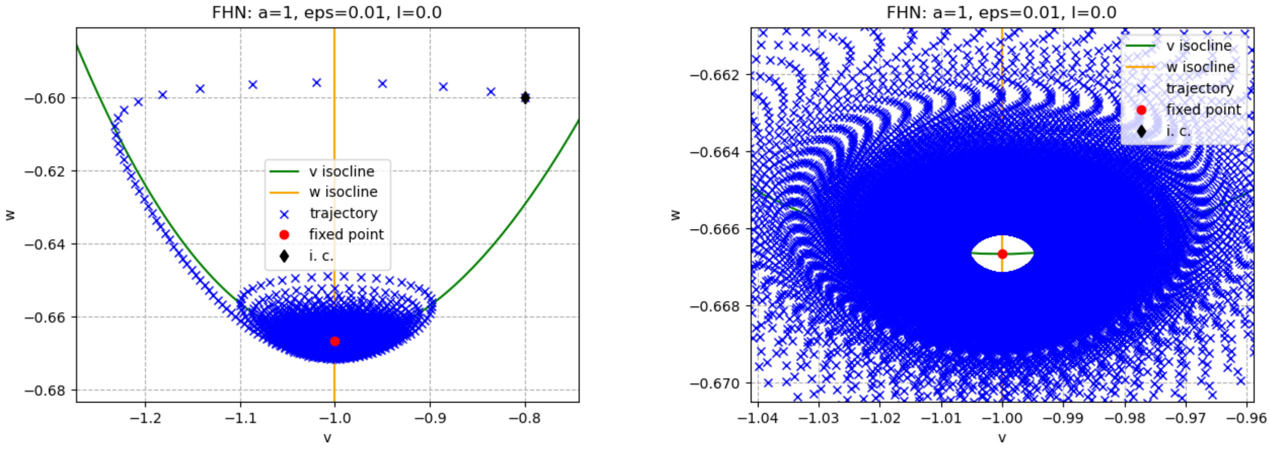
$$\lambda_{1,2} = \frac{+Tr(J\mathbf{F}) \pm \sqrt{Tr(J\mathbf{F})^2 - 4Det(J\mathbf{F})}}{2} \tag{3}$$

In this case the $Tr(J\mathbf{F}) = 1 - v^{*2}$ and $Det(J\mathbf{F}) = \epsilon > 0$. The fact that the determinant is always positive states that the fixed point is a *focus* [3]; when $|v^*| = |a| > 1$ the trace is negative, this means that the focus is attractive and the fixed point is stable, while when $|v^*| = |a| < 1$ the trace is positive, the point is now unstable and the system undergoes to a subcritical Hopf bifurcation with the formation of a cycle limit [4]. When the point is stable and attractive it is called the *excitable regime* of the FHN model, whereas the Hopf Bifurcation occurs in the *tonic spiking regime* [4]. In this paper the excitable regime is chosen to be analyzed by a stochastic point of view.
As it said before, this regime provides an unique fixed point, stable and attractive and in this condition there could be two different paths: the trajectory is directly attracted by the fixed point and it happens in its neighborhood or if the system is excited enough there is a *spike generation*. When a spike occurs the trajectory starts from the initial point and jumps to the right branch of the v-nullcline, then it follows it until the maximum of v then jumps back towards the refractory branch, resuming the asymptotic motion [4].



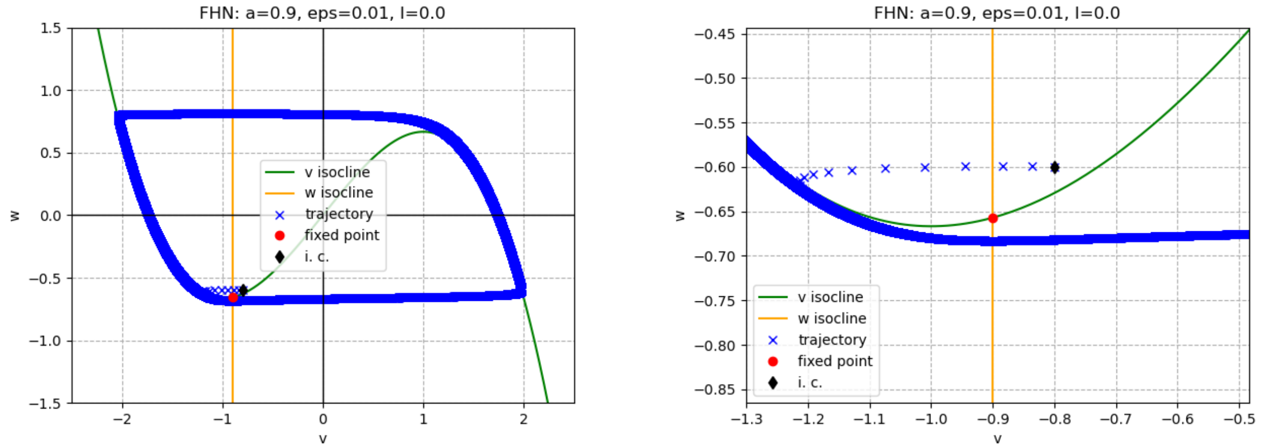
(a) $[v_0, w_0] = [-0.8, -0.6], I = 0.01$ **(b)** $[v_0, w_0] = [-0.8, -0.6], I = 0.1$

Figure 1: Deterministic trajectories $a = 1.2, \epsilon = 0.01$



(a) $[v_0, w_0] = [-0.8, -0.6], I = 0.0$ **(b)** **(a)** detail

Figure 2: Deterministic trajectories $a = 1.0, \epsilon = 0.01$, formation of the limit cycle



(a) $[v_0, w_0] = [-0.8, -0.6], I = 0.0$ **(b)** **(a)** detail

Figure 3: Deterministic trajectories $a = 0.9, \epsilon = 0.01$, formation of the limit cycle, the point is unstable.

1.3. Stochastic FitzHugh-Nagumo

The stochastic FHN model with *white noise* is represented by:

$$\begin{cases} dv = (v - \frac{v^3}{3} - w + I)dt \\ dw = \epsilon(v + a - \gamma w)dt + \epsilon\sqrt{2T\gamma}dW_t \end{cases} \tag{4}$$

where $\sqrt{2T\gamma}$ stands for additive noise with T temperature, γ the dissipative variable and dW_t the differential of the stochastic Wiener process variable. The Wiener process is a Gaussian diffusion process with mean zero and variance t, $\mathcal{N}(0, t)$. To avoid the introduction of energy in the system it was added the dissipative term $-\gamma w$. The Ito integration method is used in order to solve the stochastic system. Calling $X(t) = (v, w)$, $F(X)$ the vector for the deterministic functions and $H(X) = (0, \epsilon\sqrt{2T\gamma})$, the previous system Eq.(4) can be represented as the stochastic equation:

$$dX(t) = F(X)dt + H(X)dW_t$$

$$X_t = X_0 + \int_0^t F(X)dt + \int_0^t H(X)dW_t \tag{5}$$

The first integral in Eq.((5)) is a Riemann integral, the second one is a Stochastic integral that represents fluctuations, and it can be solved through the Ito method: by discretizing the integral and by exploiting its propriety of mean-square integrability it is obtained:

$$\int_0^t H(X)dW_t \approx \lim_{n\to\infty} \sum_{i=1}^{N} H(X(t_{i-1}))(W(t_i) - W(t_{i-1})) \tag{6}$$

where ΔW_t is a random variable sampled from a normal distribution with mean 0 and variance Δt.
Adding white noise to the deterministic FHN model in the excitable regime without spikes can lead to the spikes production due to the deviation from the deterministic trajectory.

This stochastic system is also studied with the application of the Ornstein–Uhlenbeck noise n, that is a correlated process. It is Gaussian and a diffusion process as the Wiener process but with the addition of a negative linear term in its time derivative, so that the resulting system is:

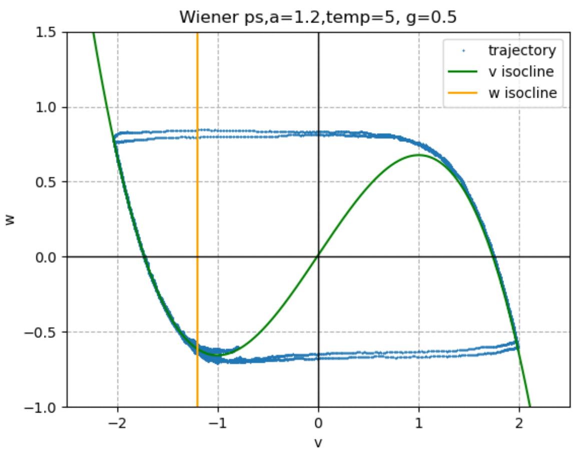
$$\begin{cases} dv = (v - \frac{v^3}{3} - w + I)dt \\ dw = \epsilon(v + a + n)dt \\ dn = -\gamma n dt + T dW_t \end{cases} \tag{7}$$

where T states for the variance and $\gamma = 1/\tau$ where τ is the correlation time, which affects the "memory" of noise $n(t)$: looking at the its time derivative this variable has a dependence on its previous values that its greater as *gamma* decreases. The noise terms for Wiener and O-U process are set in this way in order to match their variances.

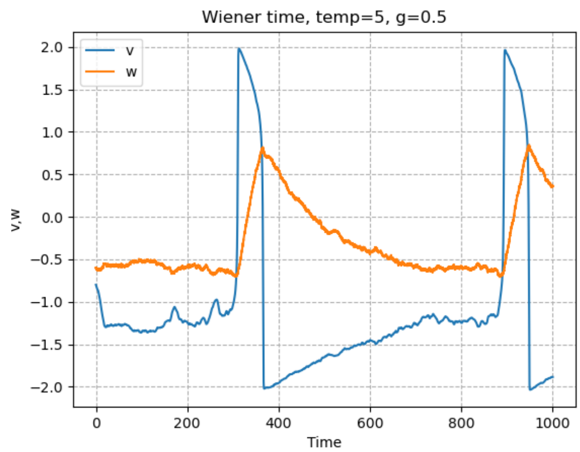
2. Discussion

The parameters $a = 1.2, I = 0.01, \epsilon = 0.01$ are set to perform the *excitable regime* for the FHN model, with a single stable and attractive fixed point. The effect of added stochastic noise is expected to generate random spikes, activating the action potential overcoming the threshold value. Here the threshold is interpreted to be $v = 0$, when the fast variable passes from the *refractory* (left) to the *active* (right) branch. As it was said, the purpose of this analysis is to study the distribution of the number of spike generated due to the effect of stochastic noise and the ISI statistics, the distribution of the *interspike time intervals*, which are the time between one spike and the next. The trajectories have been obtained through the Euler method integration for ODEs and its variation Euler-Marujama for SDEs with the integration time step $dt = 0.01$.

Here 4 5 are an example of the trajectories of equations (4), (7) of the Wiener process and Ornstein-Uhlenbeck correlated process with parameters: $\gamma = 0.5, T = 5$.

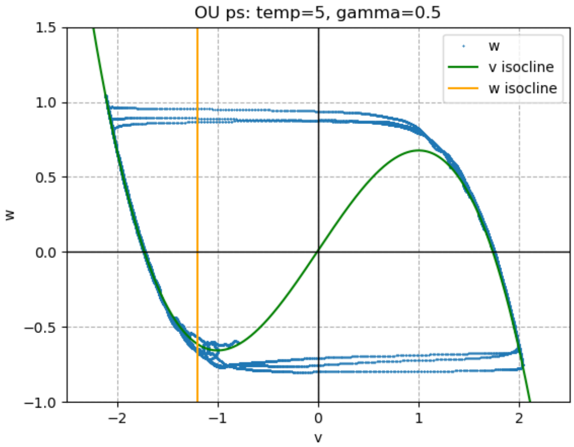


(a) Phase Space

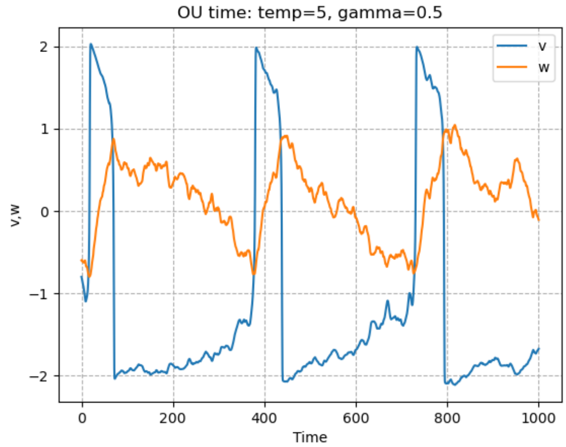


(b) Time series

Figure 4: Wiener Process (4)



(a) Phase Space



(b) Time series

Figure 5: Ornstein-Uhlenbeck Process (7)

Due to the fact that the η noise term affects the slow variable, in Fig.5 it is possible to see how its weight affect the w variable increasing its amplitude.

2.1. ISI statistics

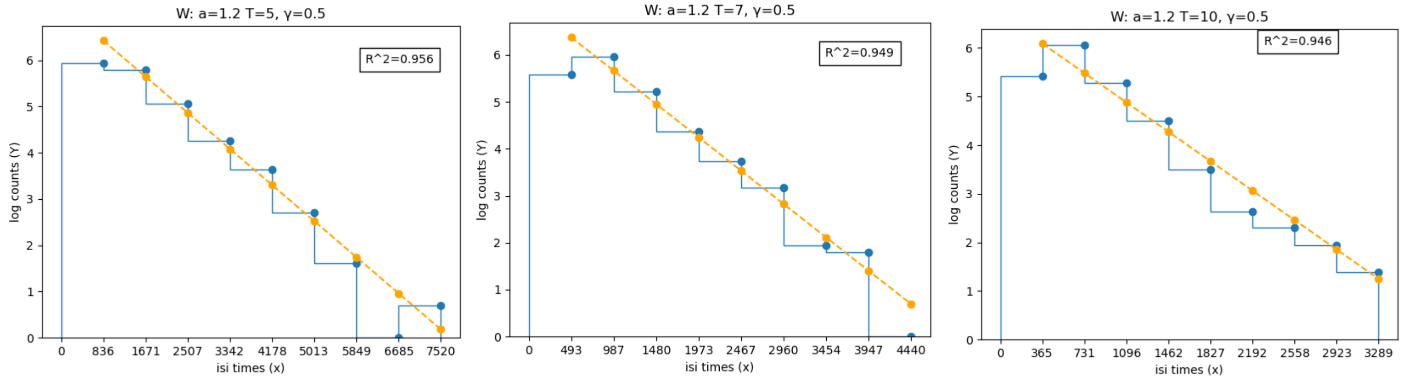
To measure the statistics of the *interspike* time intervals simulations of both trajectories were made with $t = 10.000$ time steps (ms) until the dataset got 1000 values, each time changing the temperature with values $5, 7, 10$. The expected probability distribution is the exponential distribution:

$$y(t) = \lambda e^{-\lambda t} \tag{8}$$

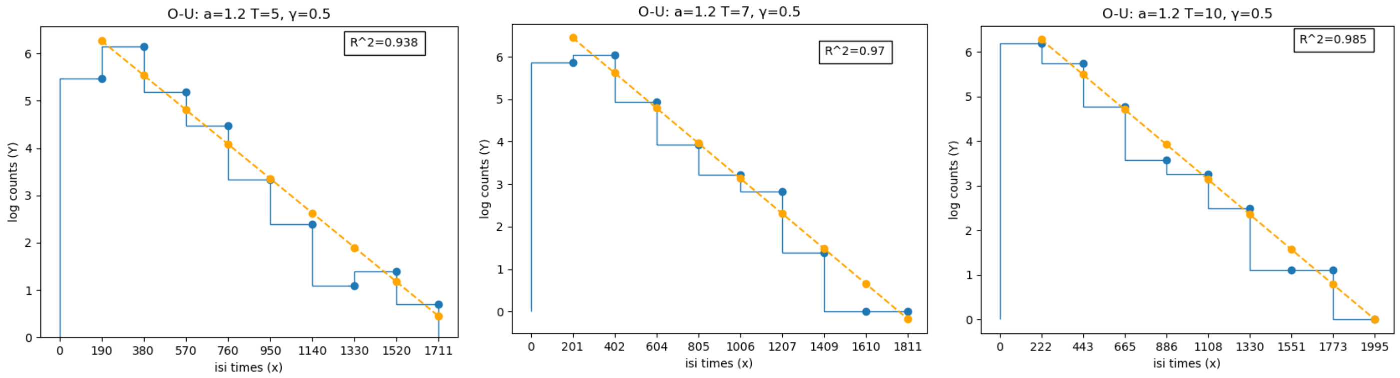
where t represent the time of the interspikes interval and λ is its rate. It is expected that the ISI times decrease in a exponential way, and this similarity should be more evident increasing the temperature.
To compare the dataset with the exponential distribution the Ordinary Least Squares method was implemented **(OLS)** through a linear regression. Applying the logarithm to Eq. (8) the linearization of the model is:

$$\log y = \log \lambda - \lambda t \tag{9}$$

With the OLS method the coefficients ($A = \log \lambda, B = -\lambda$) are obtained minimizing the the sum of squared residuals (SSR) $\sum_i (Y_i - f(x_i))^2$ where of course $f(x_i) = Ax + B$. In Figure(6) are shown the distributions of the datasets with histograms and the linear function $Y = Ax+B$. In addition it is shown the value of the *determination coefficient* R^2, which is a value between 0 and 1 that states how well the model predicts the data, the more is closer to 1 the more our model can be trusted.
The range of the bins of histograms are from zero to the maximum value found in the dataset and the values are distributed in 10 bins. It can be observed that the right bound of the bins decreases as the temperature T increases and that there is a clear difference in this value between the times with Wiener noise and O-U noise. Firstly, this effect can be considered caused by the greater excitation of the noise increasing the temperature that reduces the lenght of the time between two spikes. Secondly, the noise produced by the O-U affects more the FHN system than the Wiener noise, probably because the latter contains the dissipative term that reduces the energy of the system. This results in a lower excitation and thus longer ISI times of the system undergoing Wiener noise rather than O-U process.



(a) Wiener noise



(b) Ornstein-Uhlenbeck noise

Figure 6: Stochastic FHN: the histogram of the ISI times counts in log scale(*blue*), the approximated linear function *(orange)* by OLS method. Three distributions with temperature $T = 5, 7, 10$

Wiener noise (T)	A	B	R^2	O-U noise (T)	A	B	R^2
5	-0.00090	7.2 ± 0.4	0.956	5	-0.0038	7.0 ± 0.4	0.938
7	-0.0014	7.1 ± 0.3	0.949	7	-0.0041	7.3 ± 0.3	0.970
10	-0.0017	6.7 ± 0.3	0.946	10	-0.0035	7.1 ± 0.2	0.985

Here are shown the values of $Y = Ax + B$ with the OLS method with the standard deviation for the B values, the errors of A are negligible. The R^2 values are all close to 1, meaning that the ISI times distribution is really well approximated by the exponential distribution.

2.2. Distribution of the spikes

The expected distribution of the spikes is the Poisson distribution. The Poisson distribution is often used to model the number of events occurring in a fixed interval of time when the following assumptions hold:

- Fixed time: The events must occur within a fixed and finite interval of time or space. In the case of the spikes the time interval was set to 2000t (ms).
- Independence: The occurrence of one event must not affect the occurrence of another event within the same interval. In other words, events must be independent of each other. Moreover, the probability that two or more events happen in a small dt window is negligible w.r.t. the probability that only one event occurs. This is valid for the spikes generation, we know that two spikes cannot occurs together, the system has to be relaxed again, this means that after the spike it has to come back near the equilibrium point before another spike starts. In other words, they are independent. For each temperature $n = 200$ of separate simulations were taken.

- Constant rate: The average rate of event occurrences should be constant throughout the interval. It means that the likelihood of an event happening at any given point in time remains the same. This works for this case too.
- Discrete nature: Since events are discrete and non-negative, the Poisson distribution is appropriate for these types of situations.

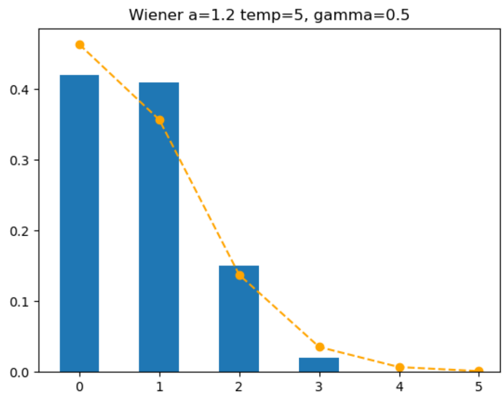
The probability density function is estimated thorough the *maximum likelihood estimation* method (MLE) which is a statistical method used to estimate the parameters of a statistical model by finding the values that maximize the likelihood function. For the Poisson distribution, the ν parameter's estimator correspond to the sample mean of the data.
Poisson distribution:

$$p(n,\nu) = \frac{\nu^n}{n!}e^{-\nu} \tag{10}$$

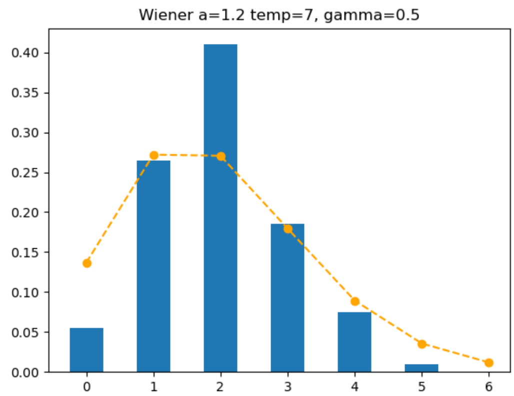
Estimator:

$$\hat{\nu} = \frac{\sum_{i=1}^{n} x_i}{n} \tag{11}$$

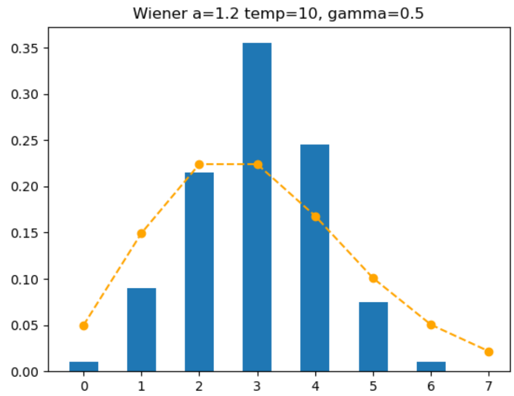
Fig.(7) and Fig.(8) show the distributions of number of spikes in a fixed interval. The Wiener cases are pretty similar to the Poisson distribution while the O-U cases are more centered on the mean value, this is maybe due to the fact that the O-U is able to trigger spikes with some consistency that in the given time window ($2000t$) is around 5 spikes for simulations. It then deviates from the Poisson distribution for "rare" events.



(a) $temp = 5$

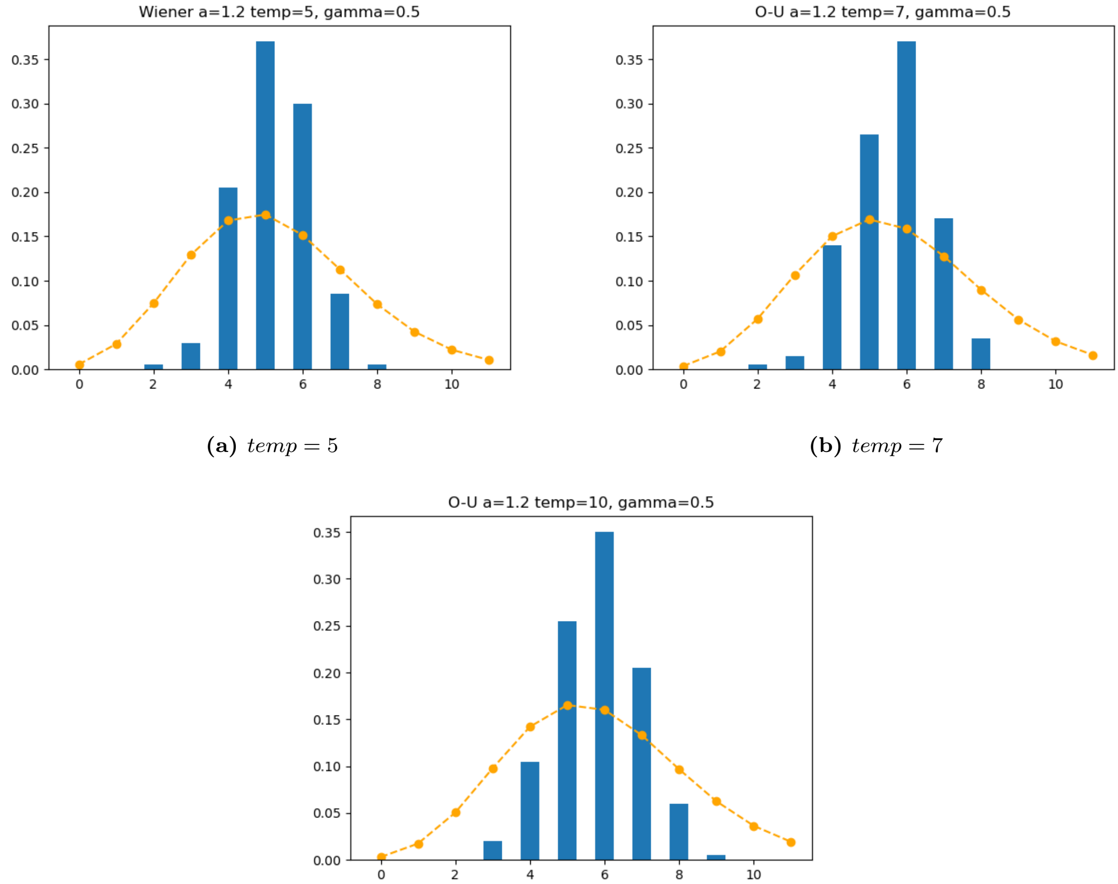


(b) $temp = 7$



(c) $temp = 10$

Figure 7: Poisson distribution of FHN with Wiener Noise



(a) $temp = 5$

(b) $temp = 7$

(c) $temp = 10$

Figure 8: Poisson distribution of FHN with O-U Noise

3. Conclusion

The analysis of the stochastic FitzHugh-Nagumo system under going to Wiener noise and Ornstein-Uhlenbeck noise is strictly dependent of the kind of parameter chosen. Here the values of the temperature were chosen in order to ensure the generation of spikes and comparing the events and ISI distribution with a priori distributions that were chosen for the reasons explained before: the Poisson because is one of the more appropriate for the distribution of rare events and the Exponential for ISI times because the noise's effect easily excites the system and triggers spikes with a certain periodicity that minimize the presence of long interval time between a spike and another. The results are congruent with the expectation but with some deviations due to how differently the two noise affects the FHN system. The Wiener process is an uncorrelated random process and this is evident observing how the ISI statistic is more distributed while the distribution of the number of spike generated is more consistent with the Poisson distribution. On the other hand, the Ornstein-Uhlenbeck process is correlated, its current value at time t depends on the previous one. It is possible to imagine that if its trajectory is far from the equilibrium point the FHN undergoing the O-U noise could be more inclined to keep generating spikes rather than the FHN undergoing the Wiener noise. This can be a reason that explain the behaviour observed in the analysis.

References

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