On an Intrinsic Stochastic Fitzhugh-Nagumo Model

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Abstract

The Fitzhugh-Nagumo model for excitable systems with a high excitation parameter solves the question of self-oscillatory and self-adaptivity in these systems. This is not the case in systems with low excitation parameter. An intrinsic stochastic model that accounts for endogenous fluctuations is proposed. This model solves the question of self-oscillatory and self-adaptivity in systems with low excitation parameter.

Keywords: Intrinsic stochasticity; Self adaptivity; Self-Oscillatory; Fitzhugh-Nagumo model

Introduction

A first model that describes an excitable membrane was proposed by Hodgkin and Huxely (HH) [1]. This model solved the question of self-oscillatory in an excitable system that is oscillations between resting and ring membrane potentials, through external inputs from ion channels (or extrinsic noise).

Indeed the system undergoes intrinsic noises from randomness coherent with the processes of opening and closing the ion channels. This had been suggested in recent works [2,3]. A simple model that maintains the main aspects of the HH model equation had been proposed by Fitzhugh [4] and, Arimoto and Nagumo [5] (FHN). It reads

\[
\frac{du}{dt} = u(u-a)(1-u) - v + \varepsilon (bu - v) \tag{1}
\]

where \(u\) is the membrane potential and \(v\) is the recovery current [6-8]. In the equation (1), \(0 < \varepsilon \ll 1\), \(a\) is the refractory parameter, \(0 < a < 1\), and \(b\) is the excitation parameter [9-13]. In case of a high excitation parameter \(b\), \(b > \frac{(1-a)^4}{4}\), the eqn. (1) shows an excitable system with a single equilibrium state which is a stable spiral [14-18]. In this case the phase portrait in the \(uv\)-plane shows spiral trajectories. That is in an FHN system with one stable equilibrium state, the question of self-oscillatory was also solved as in the HH model. Consequently, high excitation is sufficient for self-oscillatory and self-adaptivity [3] in excitable systems.

Numerous studies of the effects of induced-noises in a stable FHN system, coherent to input resonances, had been carried out in the literature [6-18]. In these works induced-noises had been considered either in the activation potential or in the recovery current equations. The phase portrait for stochastic FHN systems shows an induced limit cycle solution. Further, intrinsic stochasticity had been introduced in FHN systems empirically apart from some works [18], where two mechanisms had been suggested. Also, everywhere in the literature it had been assumed that the stochastic noise is Gaussian. We think that, after a recent review in this area [13], the effect of intrinsic stochasticity on a bistable FHN system had not been carried out yet in the literature. This is the case that will be considered here. The mechanism suggested, accounts for endogenous fluctuations in both the activation potential and the recovery current in the absence of external resonances. Which is completely a new mechanism?

We shall present for an approach that an intrinsic stochasticity is induced by the fluctuations in the activation potential and in the recovery current due to the successive opening and closing of channels. Indeed these fluctuations enhance activation near the equilibrium states. This will be clarified later on in theorem 2.1.

In an excitable system with a low excitation parameter \(b\), where \(b < \frac{(1-a)^4}{4}\), the FHN equation describes a bistable medium where these two stable equilibrium states are \(u_{1}^e, v_{1}^e\) and \(u_{2}^e, v_{2}^e\). In this case the question of self-oscillatory is not evident by the simple equation (1). It needs further investigations different from those existing in the literature for a FHN system with one stable equilibrium state. The analysis of eqn. (1) shows that when the system starts from near the state of zero potential \(u_{1}^0\) (resting state), then \(u\) evolves towards the state \(u_{1}^e\) (ring state) stimulated by the recovery current, with \(v < 0\). While if the initial potential is greater than \(a\) then the solution of (1) evolves towards \(u_{1}^e\) whatever the behavior of the recovery current. In this case, it was claimed in the literature that the system will return to the state \(u_{1}^e\) through a long excursion [12]. We think that this do not hold due to the fact that; as the equilibrium states \((0,0)\) and \((u_{1}^e, v_{1}^e)\) are hyperbolic then an FHN system attains these states asymptotically. On the other hand the numerical solution of the eqn. (1) by using Runge-Kutta method does not confirm this statement. In section 3, it will be shown that the solution of eqn. (1) evolves towards \(u_{1}^e\) and does not return to \(u_{1}^0\). Thus the FHN model with low excitation parameter is not self-adaptive or self-oscillatory.

We think that the system returns to \(u_{1}^0\) if it is affected by a great stimulus that may arise from endogenous fluctuations (intrinsic noise). Indeed the duration of the potential components in different levels may depend on the strength of the stimulus for intensities near the threshold value. This is accompanied by a long duration of each level (or stage). The duration accounts for the latent period, ring, overshooting, depolarization and hyperpolarization periods. The successive repetition of this sequel may lead to fluctuations in the current. Alternatively, fluctuation in the potential may be argued to the random alteration of the nerve tissue from being a passive conductor to be an active one. Or, fluctuations may be argued to the low threshold of

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excitability of a nerve tissue. We may think that a model that describes the time evolution of an excitable medium may not be deterministic. Due to excitability, a FHN system may undergo fluctuations, so that we may write

\[ u < u^0 + \delta u \equiv u + \delta u, ~ v < v^0 + \delta v \equiv v + \delta v, \]  

(2)

where \( \langle \ldots \rangle \) is an ensemble average over the space of all realizable fluctuations in FHN systems, namely

\[ \langle \ldots \rangle \int_{-\infty}^{\infty} \ldots dm, \]  

(3)

and \( dm \) is the measure endowed by this space. We mention that a similar analysis had been carried out for a discrete ensemble of FHN elements [13,14].

In eqn. (2), \( \delta u \) and \( \delta v \) are the fluctuation about the average with \( < \delta u > = < \delta v > = 0 \). Hereafter, fluctuations are assumed to be smooth that is \( \delta u(t) \) and \( \delta v(t) \) are taken to be continuously differentiable functions.

The Model

By substituting eqn. (2) into eqn. (1) and by conserving only terms quadratic in \( \delta u \), we get [15]

\[ \frac{\text{d} u}{\text{d} t} = -u^3 + (1 + a)u - v + \frac{\text{d} \delta u}{\text{d} t}, \]  

(4)

\[ \frac{\text{d} v}{\text{d} t} = -v^2 - \alpha v + \sigma \frac{\text{d} \delta v}{\text{d} t}, \]  

(5)

By averaging both sides of (1) over the ensemble, we have

\[ \frac{\text{d} u}{\text{d} t} = -u^3 + (1 + a)u - v + \frac{\text{d} \delta u}{\text{d} t} = e (\delta u - \delta v), \]  

(6)

and

\[ \frac{\text{d} \delta u}{\text{d} t} = \sigma \frac{\text{d} \delta v}{\text{d} t} - \sigma \frac{\text{d} \delta w}{\text{d} t} + \sigma \frac{\text{d} \delta v}{\text{d} t} = e (\delta u - \delta v), \]  

(7)

In eqns. (4) and (5) terms in \( (\delta u)^2 \) and higher were neglected. By the same way the equations for \( u \) and \( v \) are given by

\[ \frac{\text{d} \delta \tau}{\text{d} t} = -6 \delta \tau^2 + (1 + a)\tau - \sigma \delta \tau - (1 + a - 3\tau) \leq (\delta \tau)^2 \geq 0 \]  

(9)

\[ \frac{\text{d} \delta \tau}{\text{d} t} = \sigma \delta \tau - \sigma \delta \tau - 2 \sigma \delta \tau = -2 \sigma \delta \tau, \]  

(10)

In the eqn. (6), we need to find \( < \delta u > \). To this end we con ne ourselves to the case when the fluctuations in the membrane potential and in the recovery current are decorrelated (decoupled) \( < \delta u \delta v > = 0 \). By setting \( \sigma_1(t) = < \delta u > \) and \( \sigma_2(t) = < \delta v > \) and by using the eqns. (4) and (5), we find closed form equations for \( \sigma_1(t) \), namely

\[ \frac{\text{d} \sigma_1(t)}{\text{d} t} = -2 \sigma_1(t) \sigma_1(t) + \sigma_1(t) \sigma_2(t), \]  

(11)

and in the eqn. (8) initial conditions are taken \( \sigma_0(t) = 0, i = 1,2 \), b is the activation parameter, practically \( \sigma_0(t) = 0 \). We mention that the case when \( < \delta u \delta v > = 0 \) will be considered in section 4. The eqn. (8) integrates to

\[ \sigma_1(t) = \sigma_1(0) e^{t}, \]  

(12)

From the eqn. (9), we and that \( \sigma_1(t) = 0, \) when \( t \rightarrow \infty \). Also, at the equilibrium states \( u = 0 \) and \( u = u^*, \) where in section 1, weand that

\[ p(0) = -a, \]  

(13)

or

\[ p(0) = -a, \]  

(14)

Consequently the equilibrium states are unchanged due to fluctuations. Thus in the assumption made in the above, the FHN with intrinsic stochasticity is given by

\[ \frac{\text{d} \sigma}{\text{d} \tau} \sigma = f(\sigma) + q(\sigma) \sigma, \]  

(15)
According to when \( u^{(n)}(1+a)/3 \) or \( u^{(n)}(1+a)/3 \), respectively. We consider the in eqn. (11) where by using the Grown walls lemma it solves to
\[
\pi[0] = (1+a)\sigma(t_0) + a+b e^{x^2} \quad \pi[0] = b(1+a)\sigma(t_0) + e^{x^2}
\]
\[
(a + 3\sigma(t_0) + \lambda(\lambda + e^2 + be = 0
\]
A similar result holds for in eqn. (12).

From the second eqn. (13) a periodic solution exists when
\[
0 < \sigma(0) - \frac{(a + e)(a + b)}{2 + a + 2a^2 - 3b} < 2\sqrt{he}
\]

The above equation determines the initial variance of fluctuations in the membrane potential that induce an oscillatory behavior.

After this theorem, we find that an oscillatory solution holds for a sufficiently small initial value of the variance in fluctuations, namely \( \sigma(0) \).

In the next section we shall find numerical solutions of eqn. (10) and show that numerical results do con rm the above theorems.

### Numerical Results

Our aim here is to solve the eqn. (10) for initial conditions \( \pi(0) = u_0, \pi(0) = \nu_0 \) and hereafter the bar on the variables will be omitted for simplicity. In the first eqn. (10) \( \nu(t) \) is replaced by the formal equation;
\[
\nu(t) = e^{-\frac{1}{2}pt} \int_{0}^{t} u(t_1) e^{x^2} + \nu(0)
\]

We will present for a method for finding approximate analytic solutions of the initial conditions (10) [16]. A comparison between this method and some well-known ones is done in some cases. The reason for adopting this method is that it can be applied to find numerical solutions for some well-known ones is done in some cases. The reason for adopting this method is that it can be applied to find numerical solutions for equations with fluctuations in eqns. (15,19). It is based on using the following steps.

Inspecting the equilibrium points of equations. We have shown that in the case where the fluctuations in the membrane potential and the recovery current is decorrelated, the equilibrium points are not changed due to fluctuations. That is these equilibrium states are; \( u_0, \nu_0, 0 \) and \( u_0, \nu_0, \nu_0, 0, \nu_0, u_0 \).

By dividing the first eqn. (10) by \( (u_0 - u_0) \) and then by integrating formally to get
\[
\nu(t) = \frac{u_0 + u_0}{u_0 + u_0} P(u,v,t) = \frac{f(u,v) + q(u,v)\sigma(t)}{a(u - u_0)}
\]
where \( f(u,v), q(u,v) \) and \( \sigma(t) \) are given in eqn. (10).

In an analog to the discritization made for finding the fixed point numerically, the eqns. (1) and (2) are written in the form ( for \( n \geq 1 \))
\[
u(t) = e^{-\frac{1}{2}pt} \int_{0}^{t} u(t_1) e^{x^2} + \nu(0)
\]

For \( n = 0, u_0 = 0 \). For more details [16].

Now we give some numerical solutions of eqn. (1) for initial conditions \( u_0, a \) and \( \nu_0, 0 \). Numerical results for the membrane potential calculated by using Runge-Kutta method and by using the method presented in this section for the second approximation, namely \( u_0(t) \) when \( \sigma(0) = 0 \) that is in the absence of fluctuations. The results are solid and dotted curves respectively. The specific values of the parameters are given in the legend. The two solutions show the same qualitative behavior for the potential. That is the potential \( u(t) \) reaches \( u_0 \) when \( t \to \infty \) and \( u(t) \) does not return to the state \( u = 0 \), which does not agree with what claimed [12] (namely the claim that \( u(t) \) reaches \( u_0 \) and returns to \( u = 0 \) after a long excursion).

### Fluctuations-Coupling Effects

Here, we consider the effects of coupling between the fluctuations in the membrane potential and the recovery current, namely when \( \delta \theta \theta = \sigma(0) = 0 \). From the eqn. (4) and (5) the formal equations for \( \sigma(t) \) are given by
\[
\frac{d\sigma(t)}{dt} = H \frac{\sigma(t)}{\sigma(t)} H = \begin{pmatrix} \frac{2p(\pi)}{2} & -2 & 0 \\ be & p(\pi) - e & -1 \\ 0 & 2be & -2e \end{pmatrix},
\]
where \( p(x) = -3x^2 + 2(1+a)x - a \). It is worth noticing that, in this general case, the FHN intrinsic stochastic model is given by the equations in eqn. (21) and equation
\[
\frac{d\pi(t)}{dt} = \int (\pi(x) + \pi(x))\sigma(t) \frac{d\sigma(t)}{dt} = e^{b\pi - \nu}
\]

These five equations have to be solved with initial conditions namely for \( u(0), v(0), \sigma(0), \sigma(0), \sigma(0) \), and \( \sigma(0) \).

By iteration, the solution of eqn. (21) can be written as
\[
\sigma(t) = \left(1 + \int H(t_1)dt_1 + \int H(t_1)\int H(t_2)dt_2 dt_1 + \right) \sigma(0)
\]

Here we notice that the matrices \( H(t_1) \) and \( H(t_1) \) do not commute, that is the commutator
\[
[H(t_1), H(t_2)] = \int H(t_2)dt_2 - \int H(t_2)dt_2 - \int H(t_2)dt_2 dt_1 = \int H(t_2)dt_2 \rho + n!. \n\]

The eqn. (23) be written in the form
\[
\sigma(t) = \rho(\exp(\int H(t_1)dt_1)) \sigma_0
\]
Now as
\[
H(t_1) = H_1 = \begin{pmatrix} -2a & -2 & 0 \\ be & e - a & -1 \\ 0 & 2be & -2e \end{pmatrix},
\]
\[
H_1 = \rho(\exp(\int H(t_1)dt_1)) \sigma_0
\]

By using Zassenhaus formula [17] for non-commutative matrices
\[
\rho(t) = \exp(H_1 t) \exp(\theta H_1) \exp(-C_2 / 2!) \exp(C_3 / 3!) \sigma_0
\]
\[
C_2 = [\theta H_1, \theta H_1] = \theta t[H_1, \theta H_1] = \theta t[H_1, H_1] + \frac{1}{2} [\theta H_1, \theta H_1], \theta = \int (\int \rho(\pi(t))dt)
\]

By considering the norm of the commutators \( ||C|| = \max ||C|| \), where \( \lambda_1 \) is the eigenvalues of the matrix \( C \), if \( \lambda_1 < 4 ||\pi(\theta)\|b\| \) and \( \lambda_1 < 2||\pi(\theta)\|b\| \). To carry out numerical computations we use the eqn. (27) by neglecting \( C_3 \) and higher limiting calculations for \( t < (9/4)(b+1+a) \) as \( ||\pi(t)|| < (t+1+a)^3/3 \). Numerical
results for the membrane potential, recovery current, mean square of the fluctuations in the potential and recovery current and the mean of the correlated fluctuations in both are displayed in the same initial conditions as respectively.

Conclusions

We have constructed an intrinsic stochastic FHN-model, for systems with low excitation parameter that accounts for endogenous fluctuations. A closed form for the set of equations for the ensemble averages of the membrane potential, recovery current and variances in their fluctuations had been given in eqns. (22) and (21). Theoretical proofs had shown that a system, which is described by this model, is self-adaptive and self-oscillatory. Numerical results had been carried out by including fluctuations effects and they confirmed the theoretical predictions. Consequently this model conserves the main features as in an excitable system with high excitation parameter. The model presented, accounts for fluctuations about the mean and it may be considered as a simple model for describing smooth-noisy systems.

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