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The FitzHugh-Nagumo Model: Firing Modes with Time-varying Parameters & Parameter Estimation

Rose T. Faghih Ketan Savla Munther A. Dahleh Emery N. Brown

Abstract—In this paper, we revisit the issue of the utility of the FitzHugh-Nagumo (FHN) model for capturing neuron firing behaviors. It has been noted (e.g., see [6]) that the FHN model cannot exhibit certain interesting firing behaviors such as bursting. We illustrate that, by allowing time-varying parameters for the FHN model, one could overcome such limitations while still retaining the low order complexity of the FHN model. We also highlight the utility of the FHN model from an estimation perspective by presenting a novel parameter estimation method that exploits the multiple time scale feature of the FHN model, and compare the performance of this method with the Extended Kalman Filter through illustrative examples.

I. INTRODUCTION

Since the seminal work of Hodgkin and Huxley, there has been a continued interest in the dynamical systems viewpoint of a neuron. Hodgkin-Huxley (HH), Hindmarsh-Rose (HR), and FitzHugh-Nagumo (FHN) models are among the most successful dynamical models in computational neuroscience for capturing neural firing behaviors. A detailed explanation of these and several other models can be found in [6]. The HH model consists of four differential equations with a high number of coefficients. Although this model is capable of generating all the behaviors of neuron spiking, it is a highly nonlinear model. The HR model, on the other hand, consists of three differential equations, which are highly coupled, and it can exhibit all the firing modes obtained from the HH model except for biophysically meaningful behaviors [5]. Finally, the FHN model consists of two differential equations, and is simpler than the HH and HR models, though it is unable to exhibit important firing behaviors such as bursting. In fact, it has been noted [5] that without using a reset or adding noise, the FHN model can not exhibit bursting. The focus of this paper is on *low complexity* dynamical models that can exhibit most of the neural firing activities of interest that are possible by well-known dynamical systems models (such as the HH model) but are nevertheless of low complexity. Here, we use the term complexity to refer to the presence of redundancies in the model on top of its capability to capture neural firing behaviors and difficulty in parameter estimation. With this in mind, we propose an extension of the FHN model with time-varying parameters,

where the hypothesis is that the time variations of these parameters are either physiologically programmed within a neuron or are coupled to the output of the typical hormone generating systems that are triggered by the neural firings, e.g. the negative feedback effect of cortisol level on the neurons in the hypothalamus [2]. We also highlight the utility of the FHN model from an estimation perspective. We present a novel parameter estimation method that exploits the multiple time scale feature of the FHN model, and compare the performance of this method with the Extended Kalman Filter (EKF) for the fixed parameter case through illustrative examples. The examples demonstrate that this estimation method outperforms the EKF when the sensor covariance is large or when the sampling rate is low. Then, we extend this method to the case when the spiking threshold is varying slowly and one has more knowledge about the structure of the variations of this threshold. For this case, our method outperforms EKF when the sampling rate is low. Due to space limitations, we keep our discussions brief; for further details refer to [4].

II. THE FITZHUGH-NAGUMO MODEL WITH TIME VARYING THRESHOLD

As mentioned above, a simplified version of the HH model is the FHN model:

$$\frac{dv}{dt} = a(-v(v-1)(v-b) - w + I), \quad \frac{dw}{dt} = v - cw$$

where v is the membrane potential, w is the recovery variable, a and c are scaling parameters, and I is the stimulus current. Moreover, b is an unstable equilibrium that corresponds to the threshold between electrical silence and electrical firing [1]. For appropriate constant parameters, it is possible to generate tonic firing using FHN, where tonic firing is referred to as a firing behavior in which the neuron spikes in a periodic manner.

Considering that conventionally the parameters in the FHN model are kept constant, certain firing behaviors such as bursting can not be obtained using this model[6]. Since I is an external input, it can externally control the firing mode observed in the output (v), and result in firing behaviors such as bursting [8]; on the other hand, the parameters a , b , and c are governed by the mechanisms internal to the neuron, and their variations can be associated to some internal physiological system. In this paper, we consider variations in b because b is the threshold between electrical silence and neural firing, and physiologically, it might be the case that this threshold is varying throughout the day, causing the neurons to switch on and off, and generate bursting.

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Since b can control the firing frequency, we propose that by varying b in FHN, it is possible to obtain firing modes such as bursting. The following is our proposed extension to FHN model, which includes a time-varying threshold:

$$\frac{dv}{dt} = a(-v(v-1)(v-b) - w + I), \quad \frac{dw}{dt} = v - cw, \quad \frac{db}{dt} = g(t)$$

In the following sections, we will show that using this approach, spiking patterns such as tonic bursting and varying frequency neural firing can be obtained. In [4], we showed that other firing patterns such as mixed mode firing and neural firing with non-increasing frequency could also be obtained using this model.

A. Tonic Bursting

Tonic bursting is a firing behavior in which a neuron fires a certain number of spikes and is silent for a certain amount of time. Then, it repeats this pattern in a periodic manner. To simulate tonic bursting using FHN, we keep a , I , and c at constant values 10^5 , 1, and 0.2, respectively, and vary b using a sinusoidal function as observed in Fig. 1. This is one possible way of varying b in order to obtain tonic bursting.

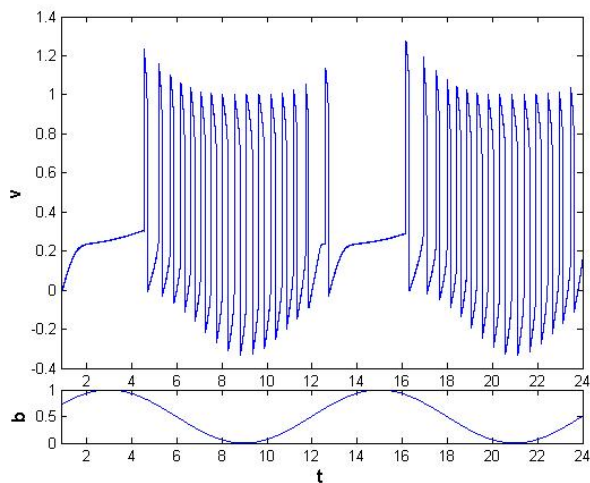


Fig. 1. Tonic Bursting

B. Varying Frequency Neural Firing

Neural firing with varying frequency can also be obtained using FHN. To simulate this firing mode, we keep the parameters a , I , and c fixed at constant values 10^5 , 1, and 0.3, respectively, while slowly varying b using a two-harmonic function as observed in Fig. 2.

III. PARAMETER ESTIMATION

Parameter estimation for the HH, HR and FHN models is usually done using *standard* methods such as Simulated Annealing, Genetic Algorithms, Differential Evolution [3], Adaptive Observer, or Extended Kalman Filter [7]. However,

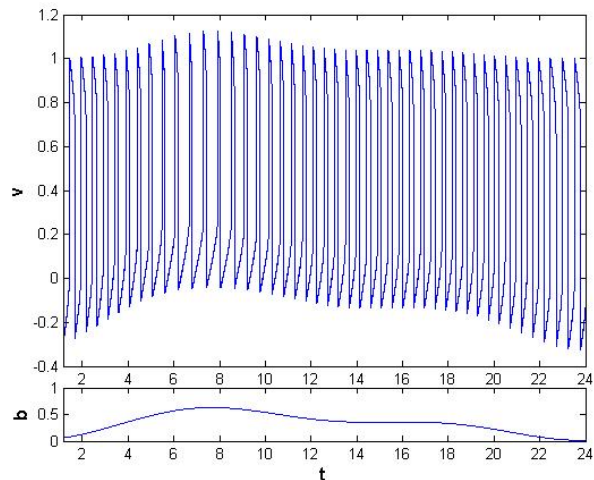


Fig. 2. Varying Frequency Neural Firing

in principle, if the model has a known structure, one could exploit it to formulate a parameter estimation method customized to that model and tune it to get better performance than the standard methods. In the following, we develop one such method for estimating the parameter b for the FHN model by exploiting the fast-slow dynamics of FHN. We will then compare the performance of this method with that of the EKF.

A. Estimating b Using Fast-Slow Dynamics of the FitzHugh-Nagumo Model

Fig. 3 is a representation of the slow and fast manifolds of FHN on the wv -plane and its corresponding behavior with respect to the time-series plot of v . The phase portrait shows that, in case of tonic firing mode, the trajectories switch between *slow scale dynamics* and *fast scale dynamics*. Considering the dynamics of the FHN model, we propose to develop a novel estimation algorithm that exploits the multiple time-scale feature of FHN. To do so, we will start with a time-series plot of membrane potentials v that are firing in a tonic manner, and develop an algorithm to estimate b , which we refer to as the Fast-Slow Dynamics (FSD) estimation algorithm. Since v does not change much when the system is following the slow time scale dynamics of FHN, we will approximate its derivative as zero. $\frac{dv}{dt} = 0 \Rightarrow w = -v(v-1)(v-b) + I$. Then, define f as: $f(v, b, I) = -v(v-1)(v-b) + I$. Let v_2 and v_0 be the values of v that maximize and minimize f :

$$v_0 = \frac{1}{3}(b+1 - \sqrt{b^2 - b + 1}), v_2 = \frac{1}{3}(b+1 + \sqrt{b^2 - b + 1})$$

As observed in Fig. 3, w_2 and w_0 do not exactly correspond to maximum and minimum values of f ; however, we can approximate w_2 and w_0 by plugging in the values of v_2 and v_0 in $f(v, b, I)$, as shown below:

$$w_0 \approx -\frac{2}{27}\sqrt{(b^2 - b + 1)^3} + \frac{2}{27}b^3 - \frac{1}{9}b^2 - \frac{1}{9}b + \frac{2}{27} + I$$

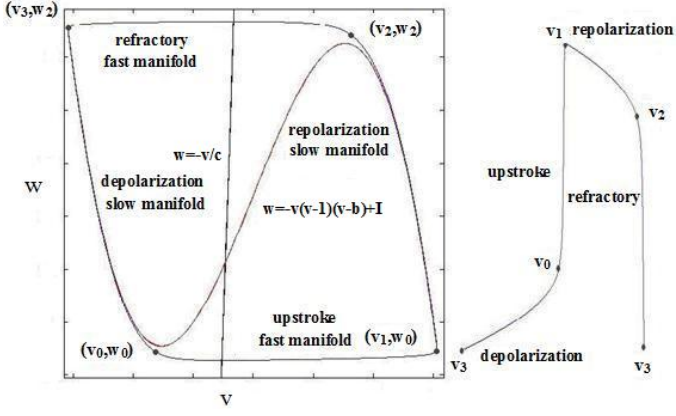


Fig. 3. Phase Portrait (left) and Time-series Plot (right): $a=1369$, $b=0.2$, $I=1$, $c=0.3$

$$w_2 \approx \frac{2}{27} \sqrt{(b^2 - b + 1)^3} + \frac{2}{27} b^3 - \frac{1}{9} b^2 - \frac{1}{9} b + \frac{2}{27} + I$$

Let $h_0(b) = w_0 - I$ and $h_2(b) = w_2 - I$. From the time series data of membrane potentials, it is possible to obtain the maximum and minimum values of v , v_1 and v_3 , respectively. As observed in Figure 3, $f(v_1, b, I) \approx w_0$ and $f(v_3, b, I) \approx w_2$. Hence, we obtain:

$$-v_1(v_1 - 1)(v_1 - b) \approx h_0(b), \quad v_3(v_3 - 1)(v_3 - b) \approx h_2(b)$$

Since there are two equations and one unknown, the system might not have a solution; in cases that the system has a solution, the solution can be obtained using equation (1):

$$-v_1(v_1 - 1)(v_1 - b) + v_3(v_3 - 1)(v_3 - b) = -\frac{4}{27} \sqrt{(b^2 - b + 1)^3} \quad (1)$$

For simplicity in the computation, one can approximate $-\frac{4}{27} \sqrt{(b^2 - b + 1)^3} \approx by - 0.21b^2 + 0.21b - 0.15$. Let $h_b = -v_1(v_1 - 1)(v_1 - b) + v_3(v_3 - 1)(v_3 - b) + 0.21b^2 - 0.21b + 0.15$. Setting $h_b = 0$, two values for b are obtained, and considering that b takes on a value between zero and one, the value of b that satisfies this bound is the desired solution. In the cases that both solutions satisfy the bound, we plug both values of b into equation (1), and the value that minimizes the absolute value of the difference between the two sides of equation (1) is the desired value of b . If a b value is not obtained using this approach, we will find the value of b that minimizes h_b . If this value still does not satisfy the bound, one could plug in values zero and one into equation (1), and the value that minimizes the absolute value of the difference between the two sides of equation (1) is the desired value of b .

Using parameters $a=10^5$, $I=1$, $c=0.3$ for the FHN model, and starting with $b=0.05$ and increasing the b value in 0.05 increments until the system does not have a tonic behavior ($b=0.75$), we estimated b using the method described above, and the error varied between 0.42% and 5.20%.

B. Comparison of Constant b Estimation Algorithm with Extended Kalman Filter

In the previous section, a novel approach for estimating b was proposed. In this section, we compare the b esti-

mates given by the Fast-Slow Dynamics (FSD) estimation algorithm and EKF. In order to compare our estimation method with EKF, process noise and sensor noise were incorporated into the simulations. Let σ_p and σ_s represent the standard deviation in the process noise and the sensor noise, respectively. In order to implement EKF, we discretized the system using Euler forward method with a sampling rate Δ . For this comparison, v was simulated using $a=10^5$, $I=1$, $c=0.3$, $b=0.5$ while adding a zero-mean normal process noise with a standard deviation of 0.1 ($\sigma_p=0.1$), and the sampling rate and sensor noise were varied as discussed in the following three examples. Moreover, we averaged the data for 24 tonic firings to run FSD and implemented EKF while using the actual initial condition values as the initial guess, and an initial covariance estimate of zero.

- 1) A zero-mean sensor noise with $\sigma_s=0.001$ was added to the simulated membrane potentials for $\Delta=10^{-5}$. Using our method, a b estimate of 0.5079 (1.58% error) was obtained. Then, EKF was implemented on the data, and the estimated value of b after one limit cycle was 0.5001 (0.02% error). In this simulation, the sampling rate was very high and the sensor noise was very low, putting EKF in an advantage. However, by increasing the sensor noise or decreasing the sampling rate, our method performed better than EKF.
- 2) By adding zero-mean sensor noise with $\sigma_s=0.01$ to the simulated action potentials, and using $\Delta=10^{-5}$, a b estimate of 0.5253 (5.06% error) was obtained using our method while b estimates for EKF did not converge and varied between 0.1358 and 1.47.
- 3) For $\Delta=10^{-3}$, and a zero-mean sensor noise with $\sigma_s=0.001$, we implemented both FSD and EKF. Using FSD a b estimate of 0.5175 (3.5% error) was obtained, while EKF diverged.

Hence, comparing the two methods, EKF is more sensitive to sampling rate than our method. Moreover, EKF does not converge if the sensor noise covariance is large.

C. Comparison of Time-varying b Estimation Algorithm with Extended Kalman Filter

In this section, using examples, we will illustrate that Fast-Slow Dynamics (FSD) estimation algorithm for constant b can be employed on neural firing data that is generated by time-varying b . We will compare FSD estimation algorithm with EKF for tonic bursting, which can be obtained using a sinusoidal b as described in II-A. For this comparison, process noise and sensor noise were incorporated into the simulations. For this comparison, v was simulated using $a=10^5$, $I=1$, $c=0.3$, $b=0.5$ while adding a zero-mean normal process noise with $\sigma_p=0.1$, and the sampling rate and sensor noise were varied as discussed in the following three examples. We simulated five datasets using this method for each of the following examples, and used the average of these datasets in order to estimate the parameters. In order to run FSD for time-varying b , we found the membrane potential peaks, and broke the data into smaller data sets, in a way that each smaller dataset started at one peak and ended at the following peak (in other words, we break the data points in a way that

each of these smaller datasets goes through the limit cycle once). Then, using our algorithm for estimating constant b , we estimated b for each of these smaller datasets. Then, we associated each of these estimates with the time that the second peak was observed. Let $\lambda = \frac{2\pi}{T}$. Knowing that b was a sinusoid of the form $\alpha \sin(\frac{2\pi}{T}t + \beta) + \gamma$, we found the period by looking at the time series plot of the b estimates, and then using the trigonometric identity, we rewrote this problem as $\alpha \sin(\frac{2\pi}{T}t) \cos(\beta) + \alpha \cos(\frac{2\pi}{T}t) \sin(\beta) + \gamma$, and implemented multiple regression to find the coefficients α , β , and γ . In order to implement EKF, we used the actual initial condition values as the initial guess, and an initial covariance estimate of zero.

- 1) After adding a zero-mean sensor noise with $\sigma_s=0.001$ to data with $\Delta=10^{-5}$, we implemented FSD and EKF. The parameter estimates and the corresponding percent error for each of the parameters is reported in Table I. In reporting the EKF estimate, we ignored the estimates for which the error covariance matrix becomes very high.

TABLE I

COMPARISON OF PARAMETER ESTIMATES OBTAINED BY FSD AND EKF FOR EXAMPLE 1 FOR TIME-VARYING b

	FSD estimate	FSD error	EKF's estimate	EKF's error
$\alpha=0.5$	0.4926	1.48%	0.5	0%
$T=12$	11.933	0.5583%	12	0%
$\cos(\beta)=1$	0.9804	1.9558%	1	0%
$\gamma=0.5$	0.4937	1.26%	0.5	0%

- 2) By adding a zero-mean sensor noise with $\sigma_s^2=0.1$, and using $\Delta=10^{-5}$, we implemented FSD and EKF. The EKF parameter estimates became very noisy; however, the average value of the noisy parameter estimates obtained by EKF had a small error, and here we are reporting the average value of the noisy estimates as the EKF parameter estimate. The parameter estimates and the corresponding percent error for each of the parameters is reported in Table II.

TABLE II

COMPARISON OF PARAMETER ESTIMATES OBTAINED BY FSD AND EKF FOR EXAMPLE 2 FOR TIME-VARYING b

	FSD estimate	FSD error	EKF's estimate	EKF's error
$\alpha=0.5$	0.5708	4.72%	0.5045	0.9%
$T=12$	11.933	0.5583%	12.1461	1.2176%
$\cos(\beta)=1$	0.9944	0.56%	1	0%
$\gamma=0.5$	0.5602	12.04%	0.5062	1.24%

- 3) For $\Delta=10^{-3}$, and a zero-mean sensor noise with $\sigma_s=0.001$, using our method parameter estimates reported in Table III were obtained, while EKF diverged.

Our proposed method could be implemented on other firing patterns such as the varying frequency neural firing pattern by again fitting the estimated values of b using multiple regression. In the cases that b follows two or more different functions as a function of time, one could break the data into two parts at the point that the variations in the function

TABLE III

COMPARISON OF PARAMETER ESTIMATES OBTAINED BY FSD AND EKF FOR EXAMPLE 3 FOR TIME-VARYING b

	FSD estimate	FSD error	EKF's estimate	EKF's error
$\alpha=0.5$	0.4638	7.24%	Diverged	NA
$T=12$	12.029	0.2417%	Diverged	NA
$\cos(\beta)=1$	0.9215	7.8511%	Diverged	NA
$\gamma=0.5$	0.4996	0.08%	Diverged	NA

occurs, and depending on the kind of function b is following linear or multiple regression could be used to fit the b estimates. In [4], we provided illustrative examples of such cases.

IV. CONCLUSION AND FUTURE WORK

The proposed approach in extending the FHN model by varying the parameters of FHN allows for simulating more complex behaviors than the ones that were possible by keeping the parameters constant. In this paper, variations in the threshold between electrical silence and electrical firing were investigated. Then, an estimation algorithm that exploits the fast-slow dynamics of FHN was proposed. For constant b , the proposed parameter estimation algorithm performed better than the EKF when the sampling rate was not very high or when the sensor noise covariance was not very low. For time-varying b , this parameter estimation method performed better than EKF when the sampling rate was low. Another advantage of this estimation method over EKF is that for cases that the structure of b is unknown, discrete b estimates can be obtained using our method to add insight to the underlying structure. On the other hand, EKF can not estimate the coefficients if the underlying structure of b is not known. In our future work, we will extend our model and estimation method to other parameters, and explore the physiological factors determining the parameter variations that lead to variations in neural firing patterns.

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