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Parameter estimation of the FitzHugh-Nagumo model using noisy measurements for membrane potential

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This paper proposes an identification method to estimate the parameters of the FitzHugh-Nagumo (FHN) model for a neuron using noisy measurements available from a voltage-clamp experiment. In the presence of the measurement noise, a simple least squares method is employed to estimate the associated parameters involved in the FHN model. Although the available measurements for the membrane potential are contaminated with noises, the proposed identification method aided by wavelet denoising can also give the FHN model parameters with satisfactory accuracy. Finally, two simulation examples demonstrate the effectiveness of the proposed method. © 2012 American Institute of Physics. [http://dx.doi.org/10.1063/1.4729458]

I. INTRODUCTION

The FitzHugh-Nagumo (FHN) model is important for analyzing the dynamical behavior of an excitable neuron and thus identification of this model is particularly valuable for its practical applications. However, in engineering practice, the FHN model cannot be obtained easily. In a voltage-clamp experiment, only the membrane potential variable in the FHN model can be measured with some certain instrument while the associated recovery variable is in effect unmeasurable. As a result, using the available measurements for the membrane potential to estimate the overall parameters in the FHN model is a main objective of this paper. Due to the existence of the unmeasurable variable, the FHN model parameters cannot be estimated in a straightforward manner. The most direct and simplest strategy is the elimination of the unmeasurable variable from the FHN model. To achieve this end, a second order ordinary differential equation is derived from the original FHN model and it only involves the measurable variable, i.e., the membrane potential. With this equation, a simple least squares method is applied to estimate the associated FHN model parameters and its efficient implementation can be realized by a recursive algorithm. However, the measurement noise corrupting the membrane potential is in no doubt amplified during the first and second order derivatives of the noisy measurements. The remedial measure is to filter the noisy measurements by wavelet denoising before they can be used for the parameter estimation. As can be concluded from the simulation examples, the proposed method can give the unbiased effective consistent estimation although the noisy measurements are encountered in its practical applications.

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noises in the measurable variables. Yu and Parlitz\textsuperscript{15} propose a partial synchronization method to identify the chaotic systems with uncertainty. This peculiar method first uses a feedback linearization theory to transform the synchronizing model into a canonical form and then designs a control signal to guarantee the stability of the canonical model.

Different from the foregoing reviewed methods, the main contribution of this paper is to propose a novel method for the parameter estimation of FHN models. According to the characteristics of the state FHN model, it can be further derived as a second order ordinary differential equation merely involving the measurable variable. Based on this differential equation, a quite simple least-squares method\textsuperscript{16} can be applied directly to estimate the involved parameters. In order to improve the applicability of this method, the wavelet denoising technique\textsuperscript{17} with an automatically chosen denoising threshold is utilized to adaptively filter the measurement noise and the noises caused by the derivative to the noisy measurements.

The remainder of this paper is organized as follows. In Sec. II, we derive a parametric second order ordinary differential equation only involving the measurable membrane potential variable. Based on this equation, the simple least squares method is then employed for the estimation of the FHN model parameters and its recursive algorithm is also addressed to circumvent the complex computational loads. Section III gives two classical simulation examples to verify the proposed identification method: one is for the straightforward presence of the equation error and the other is for the measurement noise. The concluding remarks for the proposed method are summarized in Sec. IV.

II. PARAMETER ESTIMATION METHOD

A. The parameterized FHN model

Without loss of generality, the classical parameterized FHN model can be characterized by the following state differential equations with first-order derivative\textsuperscript{1}

\[
\begin{align*}
\dot{x}_1 &= ax_1 + bx_1^3 - x_2 + u, \\
\dot{x}_2 &= dx_2 + ex_1 + f,
\end{align*}
\]  

where \(x_1\) is a measurable membrane potential variable; \(x_2\) is an unmeasurable recovery variable; \(u\) denotes an injected current stimulus; \(a, b, d, e, e, f\) are the unknown parameters to be estimated by only employing the noisy measurements of \(x_1\). The upper and lower differential equations in Eq. (1) describe the dynamical behaviors of \(x_1\) and \(x_2\), respectively. Since \(x_2\) is unavailable in an engineering application, so the most straightforward idea is to eliminate it from the upper equation. To this end, we first take first-order derivative to the upper equation and this operation yields

\[
\dot{x}_1 = (a + d)x_1 + 3bx_1^2x_1 - x_2 + \dot{u}.
\]  

Then, substituting \(\dot{x}_2\) in Eq. (2) with the lower equation in Eq. (1) gives the following second order ordinary differential equation involving only \(x_1\):

\[
\ddot{x}_1 = (a + d)x_1 + 3bx_1^2x_1 + (-e - ad)x_1 - bdx_1^3 - du + f + \dot{u}.
\]  

According to this differential equation, the following parameter equation can then be obtained

\[
z = \sum_{i=1}^{6} y_i \beta_i,
\]  

with the variable definitions

\[
\begin{align*}
z \triangleq \dot{x}_1 - \dot{u}, \quad y_1 \triangleq \dot{x}_1, \quad y_2 \triangleq \dot{x}_1^2x_1, \\
y_3 \triangleq x_1, \quad y_4 \triangleq x_1^3, \quad y_5 \triangleq u, \quad y_6 \triangleq 1,
\end{align*}
\]  

and the parameter definitions

\[
\begin{align*}
\begin{cases}
\theta_1 \triangleq a + d, & \theta_2 \triangleq 3b, & \theta_3 \triangleq e - ad, \\
\theta_4 \triangleq -bd, & \theta_5 \triangleq -d, & \theta_6 \triangleq f.
\end{cases}
\end{align*}
\]  

In Eq. (4), \(z\) and \(y_i, i = 1, 2, \ldots, 6\) are known variables; \(\theta_i, i = 1, 2, \ldots, 6\) are the intermediate parameters relating to the FHN model parameters to be estimated. In Sec. II B, we will address a parameter estimation method based on this specified equation.

B. The least squares method

In order to gather enough experimental data to accurately estimate the parameter \(\theta_i\) defined in Eq. (6), the sampling time instant \(t_k\) is introduced into the defined variables in Eq. (5) as follows:

\[
\begin{align*}
z(k) &\triangleq \dot{x}_1(t_k) - \dot{u}(t_k), \quad y_1(k) \triangleq \dot{x}_1(t_k), \\
y_2(k) &\triangleq \dot{x}_1^2(t_k)x_1(t_k), \quad y_3(k) \triangleq x_1(t_k), \\
y_4(k) &\triangleq x_1^3(t_k), \quad y_5(k) \triangleq u(t_k), \quad y_6(k) \triangleq 1
\end{align*}
\]  

with \(k = 1, 2, \ldots, N\). By collecting the sampled data in Eq. (7) from the time instant \(t_1\) to \(t_N\), the following matrix equation can be given according to Eq. (4):

\[
z^N = H_N \theta,
\]  

where

\[
z^N = \begin{bmatrix} z(1) \\ z(2) \\ \vdots \\ z(N) \end{bmatrix}, \quad H_N = \begin{bmatrix} h^T(1) \\ h^T(2) \\ \vdots \\ h^T(N) \end{bmatrix}, \quad \theta = \begin{bmatrix} \theta_1 \\ \theta_2 \\ \vdots \\ \theta_6 \end{bmatrix}
\]  

with \(h(k) = [y_1(k), y_2(k), \ldots, y_6(k)]^T, k = 1, 2, \ldots, N\).

Due to the existence and effect of the measurement noise in the measurements of \(x_1\), Eq. (8) becomes that

\[
z_m^N = H_N \theta + \epsilon^N,
\]  

where \(z_m^N = [z_m(1), z_m(2), \ldots, z_m(N)]^T\) is the sampled data used for parameter estimation; \(\epsilon^N = [\epsilon(1), \epsilon(2), \ldots, \epsilon(N)]^T\) is an equation error which is supposed to be a time series of white noise. According to Eq. (10), the best possible estimation for \(\theta\) has a least squares solution\textsuperscript{18} as follows:
\[ \hat{\theta} = [H_N^T H_N]^{-1} H_N^T z_N \]  

(11)

With the estimated parameter \( \hat{\theta} \), a solution for the associated parameters in the FHN model can then be given as below

\[
\begin{align*}
\hat{a} &= \hat{\theta}_1 + \hat{\theta}_5 \\
\hat{b} &= \hat{\theta}_2 - \frac{2}{3} \\
\hat{d} &= -\hat{\theta}_5 \\
\hat{e} &= (\hat{\theta}_1 + \hat{\theta}_5) \hat{\theta}_5 - \hat{\theta}_3 \\
\hat{f} &= -\hat{\theta}_6
\end{align*}
\]

(12)

**Remark 1.** From the parameter definitions in Eq. (6), we can see that

- The parameters \( b \) and \( f \) can be uniquely determined from \( \theta_2 \) and \( \theta_6 \), respectively.
- Since the parameter \( d \) can be estimated from either \( \theta_5 \) or \( \theta_8 \) with the given \( b \), so \( \theta \) is redundant for its estimation in Eq. (12), \( \theta_5 \) is used to estimate \( d \) in a simpler form.
- Once \( d \) is estimated, the parameter \( a \) can then be uniquely determined from \( \theta_1 \).
- With the estimated \( a \) and \( d \), the estimation of \( e \) is uniquely relies on \( \theta_1 \).

**Remark 2.** If the equation error \( v^N \) in Eq. (10) is a white noise series, then the estimated parameter \( \hat{\theta} \) in Eq. (11) is an unbiased effective consistent estimator for \( \theta \). However, in a real-world application, \( v^N \) may not always obey a white noise distribution. In that case, a remedial measure is to filter \( v^N \) with the wavelet denoising technique and make the resulting filtered series approximately obey the white noise distribution. From the foregoing strategy, the FHN model parameters can also be estimated from Eq. (11) with the approximate unbiasedness and consistency.

**C. The recursive algorithm**

For the sake of improving the estimation accuracy of the resulting FHN model parameters, the amount of measurement data of the membrane potential is tremendous in practice and thus results in the computation of high-dimensional matrices. As a result, the batch computation method in Eq. (11) might not be preferable and its associated recursive algorithm is more useful. Thus, the associated recursive algorithm for estimating the required parameters is given in the following.0.18,19

1. **Step 1.** Take the following initial values

\[
\begin{align*}
P(0) &= m^2 I_6 \\
\hat{\theta}(0) &= \varepsilon
\end{align*}
\]

(13)

where \( m \) is a sufficiently large positive number and \( \varepsilon \) is a sufficiently small positive vector.

2. **Step 2.** Iterate the following recursive formulas

\[
\begin{align*}
K(k) &= P(k-1) h(k) h^T(k) P(k-1) h(k) + 1^{-1} \\
P(k) &= \left[ I - K(k) h^T(k) P(k-1) \right] , \\
\hat{\theta}(k) &= \hat{\theta}(k-1) + K(k) \left( z_m(k) - h^T(k) \hat{\theta}(k-1) \right)
\end{align*}
\]

(14)

where \( z_m(k) \) is the \( k \)th element in \( z_N^m \).

3. **Step 3.** Stop the iteration in step 2, if the following estimation accuracy is arrived at

\[ \max \left| \hat{\theta}_i(k) - \hat{\theta}_i(k-1) \right| < \varepsilon \]

(15)

where \( \varepsilon \) is an appropriately small positive number. Otherwise, \( k = k + 1 \) and return to step 2.

**Remark 3.** The most popular strategy adopted in the previous proposed methods5–12 is to make the error between the constructed parameter model and the underlying model approach zero asymptotically by designing an appropriate control signal from some Lyapunov function. Different from the foregoing strategy, the proposed method in this paper uses the structural characteristics of the FHN model to estimate its unknown parameters.

**III. NUMERICAL SIMULATION**

**A. The equation error being white noise**

The proposed identification method is tested on the following FHN model without a current stimulus

\[
\begin{align*}
\dot{x}_1 &= x_1 - \frac{1}{2} x_1^3 - x_2 \\
\dot{x}_2 &= -0.8 x_2 + 0.1 x_2 + 0.07
\end{align*}
\]

(16)

In this simulation, we adopt the fourth order Runge-Kutta (RK) method20 to produce \( x_1 \) and \( x_2 \) with the iterative initial value \([0, 0]\). The sampling period \( h \) is chosen as 0.001 s to improve the approximation accuracy in using difference in place of differential. Suppose that the equation error \( v^N \) in Eq. (10) is a Gaussian white noise series with a standard deviation of 0.1. The corresponding simulation data \( z_m^N \) used

**TABLE I. Estimated FHN model parameters from white noise.**

| \( a \) & \( b \) & \( d \) & \( e \) & \( f \) |
|---|---|---|---|---|
| True value | -0.3333 | -0.08 | 0.1 | 0.07 |
| Estimation | 0.98985 | -0.33189 | -0.071425 | 0.099412 | 0.07411 |
for identification are plotted in Fig. 1, where the data length $N$ is taken as 4000.

In the foregoing simulation environment, the proposed least squares recursive algorithm is applied to estimate the FHN model parameters with the initiation $P(0) = 10^5 I_s$ and $\theta(0) = 0.5 x_1$. After the implementation of the least squares algorithm, the estimated FHN model parameters are given in Table I.

According to the estimated parameters in Table I, the four-order RK method is reused to generate $\hat{x}_1$ and $\hat{x}_2$. Then, the resulting estimated variables $\hat{x}_1$ and $\hat{x}_2$ are compared with their respective true variables in Figs. 2 and 3, respectively.

From the graph and table comparisons, we can see that the estimated FHN model parameters have relatively high estimation accuracy despite the presence of the white-noise distributed equation error and thus the resulting estimated parameters are able to meet the requirements for practical applications.

B. The equation error being colored noise

When the measurements for the membrane potential $x_1$ are corrupted with noise, $\hat{x}_1$ and $\hat{x}_2$ are undoubtedly lost in the unlimitedly amplified noises. As a result, the noisy measurements have to be filtered by a denoising technique prior to the application of the proposed method. To demonstrate the above idea, we consider the following FHN model excited by the exogenous current stimulus $u$

$$\begin{align*}
\dot{x}_1 &= x_1 - \frac{1}{3} x_1^3 - x_2 + u \\
\dot{x}_2 &= -0.08 x_1 + 0.1 x_2 + 0.07
\end{align*}$$

(17)

where $u$ is a periodical signal and is taken as $u = A \sin(2\pi ft)$ with $A = 0.4$ A and $f = 0.12$ Hz. The simulation data are also generated by the four-order RK method with the initial value $[0, 0]$ and the step length 0.001. We use the two-period input $u$ to excite the FHN model in Eq. (17) and the corresponding outputs of $x_1$ and $x_2$ are both two-period responses.

Suppose that $x_1^m$, the measurements of $x_1$, is contaminated by the Gaussian white noise with a standard deviation of 0.01. Due to the function of derivative, $\dot{x}_1^m$ and $\dot{x}_1^m$ are both undoubtedly corrupted by the diverse high-orders-of-magnitudes noises. For instance, the magnitude of the corrupting noise in $\dot{x}_1^m$ has climbed up to $10^4$ according to the previous simulation setup. As a result, the equation error $v^N$ cannot obey a white noise distribution any more. For the purpose of application of the proposed method, $\dot{x}_1^m$ should be first filtered by the wavelet denoising technique. The highest frequency can be predicted as 0.5 from the fast Fourier transform of $x_1^m$. Then, the wavelet decomposition level should be chosen as 10 in terms of the sampling period of 0.001 s. In the wavelet denoising, the Daubechies wavelet db8 (Ref. 21) is selected and the associated denoising threshold value can be automatically determined according to the properties of the measurements. By taking derivatives to the filtered measurements $\dot{x}_1^m$, the estimation of $\dot{x}_1$ and $\hat{x}_1$ can be obtained from $\dot{x}_1^m$ and $\dot{x}_1^m$, respectively.

From an iteration of the proposed identification method, the estimated FHN model parameters are listed in Table II.

<table>
<thead>
<tr>
<th>$a$</th>
<th>$b$</th>
<th>$d$</th>
<th>$e$</th>
<th>$f$</th>
</tr>
</thead>
<tbody>
<tr>
<td>True value</td>
<td>-0.3333</td>
<td>-0.08</td>
<td>0.1</td>
<td>0.07</td>
</tr>
<tr>
<td>Estimation</td>
<td>0.98741</td>
<td>-0.33031</td>
<td>-0.078545</td>
<td>0.099275</td>
</tr>
</tbody>
</table>

FIG. 2. Comparison of the membrane potential variable $x_1$.

FIG. 3. Comparison of the recovery variable $x_2$.

FIG. 4. Comparison of the membrane potential variable $x_1$. 

TABLE II. Estimated FHN model parameters from colored noise.
with sufficient accuracy. Based on these parameters, the RK method is adopted to regenerate the estimated state variables and the comparisons with their respective true curves are shown in Figs. 4 and 5.

According to the parameter identification accuracy shown in Table II and the fitting capability of the estimated FHN model illustrated in Figs. 4 and 5, it can be concluded that the proposed method can give satisfactory identification results although the noisy measurements are encountered in practice.

Remark 4. In the simulation, we adopt Daubechies wavelets\(^{21}\) to denoise the measurement noise in the membrane potential. The wavelet category can be chosen for obtaining the output maximum signal-to-noise ratio.\(^{22}\) As for the decomposition level, the signal maximum frequency can be programmed into a MATLAB function `ddencmp()`. Other parameters such as the threshold, soft or hard thresholding can be made by some specified criteria,\(^{17}\) which have been programmed into a MATLAB function `ddencmp()`.

Remark 5. Due to the application of the wavelet denoising technique, the strength of the corrupting noise can be estimated with enough accuracy. As a result, the noise strength will make little influence on the estimation accuracy of the FHN model parameters.

IV. CONCLUSIONS

In this paper, we propose an identification method to cope with the FHN model parameter estimation using the available measurements for the membrane potential. In order to estimate the required parameters, the unmeasurable recovery variable is eliminated from the equation of the membrane potential variable and thus a second order ordinary differential equation only involving the latter variable can be derived. Based on this equation, the simple least squares method is employed to iterate the FHN model parameters. In the simulation, two different noise cases are considered to show the effectiveness of the proposed method. It can, therefore, be concluded that our method can give the satisfactory identification accuracy although the measurement noise is encountered in practice.

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