35th Annual International Conference of the IEEE EMBS
Osaka, Japan, 3 - 7 July, 2013

Blind Deconvolution of Hodgkin-Huxley Neuronal Model

M. Lankarany[1], Student Member, IEEE, W.-P. Zhu[1], Senior Member, IEEE, M. N. S. Swamy[1], Fellow, IEEE, and Taro Toyoizumi[2]

[1]Dept. Electrical and Computer Eng (ECE), Concordia University, QC, Canada
[2]Lab for Neural Computation and Adaptation, Riken Brain Science Institute, Japan

ABSTRACT

Neuron transforms information via a complex interaction between its previous states, its intrinsic properties, and the synaptic input it receives from other neurons. Inferring synaptic input of a neuron only from its membrane potential (output) that contains both sub-threshold and action potentials can effectively elucidate the information processing mechanism of a neuron. The term coined *blind deconvolution* of Hodgkin-Huxley (HH) neuronal model is defined, for the first time in this paper, to address the problem of reconstructing the hidden dynamics and synaptic input of a single neuron modeled by the HH model as well as estimating its intrinsic parameters only from single trace of noisy membrane potential. The blind deconvolution is accomplished via a recursive algorithm whose iterations contain running an extended Kalman filtering followed by the expectation maximization (EM) algorithm. The accuracy and robustness of the proposed algorithm have been demonstrated by our simulations. The capability of the proposed algorithm makes it particularly useful to understand the neural coding mechanism of a neuron.

Index Terms**—** Hodgkin-Huxley model, Blind deconvolution, Kalman filtering, Expectation maximization

1. INTRODUCTION

Neuron, i.e., a specialized cell for receiving, integrating and transmitting information, transforms information from the synaptic input (received from thousands of other neurons) into the membrane potential that includes small (sub-threshold) and large (action potential) fluctuations [1]. Therefore, estimating synaptic inputs of a neuron from its output (membrane potential) can improve the level of our understanding of *information processing mechanism* of a neuron [2]. There are several works in neuroscience which aimed to extract the synaptic input of a neuron (excitatory and inhibitory synaptic inputs separately or the sum of them) from the sub-threshold membrane potential (see [3] and references therein). In addition to the significance of synaptic input in neural coding, the dynamics of ion channels influence on neural coding properties [1]. The recent methods of [2] and [4] are the only works in the literature that are not restricted to sub-threshold recordings of the membrane potential wherein the Hodgkin-Huxley (HH) model is used to represent the behavior of a single neuron and Kalman filtering technique is employed to estimate both ion channels dynamics and synaptic input. It is to be noted that the intrinsic parameters of a neuron are known in [2, 4].

In this paper, we extend the scope of previous works ([2] and [4]) by addressing the problem of reconstructing the hidden dynamics of ion channels and synaptic input (sum of the excitatory and inhibitory) of a single neuron modeled by the HH model as well as estimating its intrinsic parameters, maximal conductances and statistical parameters (standard deviation of channel noise) only from single trace of noisy membrane potential. Since the dynamics, synaptic input and parameters of the HH neuronal model are unknown, the so called *blind deconvolution* of the HH model (although it is not the same as the conventional convolution models) is addressed for the first time in this paper. The blind deconvolution is accomplished via a novel recursive algorithm.

The organization of this paper is as follows. In Section 2, state-space representation of the HH model and the assumptions by which our algorithm works are introduced. Our recursive algorithm is proposed in Section 3. Simulation results are provided in Section 4, and finally in Section 5 concluding remarks are given.

2. PROBLEM STATEMENT

In this paper, we are considering the HH neuron model to represent the dynamics of a single neuron. This model can be stated as follows.

$$C_M \frac{dv}{dt} = -g_{Na} m^3 h (v - E_{Na}) - g_K n^4 (v - E_K) - g_L (v - E_L) + I_{inj}(t) + I_{syn}(t) \quad (1)$$

where (g_{Na}, g_K, g_L) and (E_{Na}, E_K, E_L) denote the maximum conductances and the reversal potentials of the sodium, potassium and leak currents, respectively. I_{syn} is the total synaptic input (excitatory and inhibitory) that a neuron receives and I_{inj} is the intracellularly injected current. m, n

and h, which indicate the dynamics of the HH model, can be determined by the Langevin equation [5].

$$\frac{dq}{dt} = \alpha_q(v)(1-q) - \beta_q(v)q \ , \ q = m, n, h \qquad (2)$$

where $\alpha_q(v)$ and $\beta_q(v)$ are nonlinear functions of voltage (see [4] for details). In view of the limitations of the imaging techniques, it is impossible to measure all the necessary biophysical variables describing a single neuron model. This paper assumes the intercellular electrophysiological recordings by which the membrane potential, v (plus noise) in (1), is the only measurable variable. The objective of this paper is reconstructing the full HH ionic dynamics, $\{n(t), m(t), h(t)\}$, estimating the unknown parameters, $\{g_{Na}, g_K, g_L\}$, and inferring the synaptic input, $I_{syn}(t)$, using solely single trial of membrane potential. This measurement, on the other hand, may contain noise from recording equipment, i.e., known as observation noise that is modeled by the white Gaussian noise [6]. It is to be noted that it is not possible to address this problem using only a single trace of the membrane potential as the observation, because the number of unknowns overwhelm the number of data points. To overcome this problem we need to provide some *a priori* knowledge about the unknown variables. In this paper, it is assumed that, 1- the reversal potentials (E_{Na}, E_K, E_L) have been already measured experimentally, 2- functional form of voltage-dependent ionic inputs, $\alpha_q(v)$ and $\beta_q(v)$, are known, 3- similar to [2], the smoothness of the synaptic input is preserved by a random-walk-type prior and 4- in consistent with [7], the initial values of the maximum conductances are randomly selected from the ±25% neighborhood of the true values to ensure the identifiability of the HH model. Now, to meet our objective based on aforementioned assumptions, we define a state vector $x = [v, n, m, h, I_{syn}, g_{Na}, g_K, g_L]^H$ including the observed state variable, v, augmented by unobserved state variables, $[n, m, h, I_{syn}]$, and system parameters, $[g_{Na}, g_K, g_L]$. Therefore, a state space representation of the HH neuron model can be expressed as follows.

$$\begin{cases} \dot{\mathbf{x}}(t) = F[\mathbf{x}(t)] + BI_{inj}(t) + \boldsymbol{\varepsilon}_S(t) \\ y(t) = C\mathbf{x}(t) + \varepsilon_O(t) \end{cases} \qquad (3)$$

where $C=[1, \mathbf{0}_{1\times 7}]$, $B=C^H$, ε_O (observation noise), $\boldsymbol{\varepsilon}_S$ (system noise) and $I_{inj}(t)$ are mutually independent and uncorrelated. ε_O and $\boldsymbol{\varepsilon}_S$ are modeled by the zero-mean white Gaussian noise of variance σ^2_O and covariance matrix $\Sigma_S = diag([\sigma^2_v, \sigma^2_{syn}, \sigma^2_n, \sigma^2_m, \sigma^2_h, \sigma^2_{Na}, \sigma^2_K, \sigma^2_L])$, respectively. $F[\mathbf{x}(t)]$ is the time-varying transition matrix that can be easily provided from (1) and (2) (see [4, 6] and [8] for details). Let us define $\boldsymbol{\theta} = [\sigma^2_v, \sigma^2_{syn}, \sigma^2_n, \sigma^2_m, \sigma^2_h, \sigma^2_{Na}, \sigma^2_K, \sigma^2_L]^H$ as the statistical parameters of the HH neuronal model. In the next section, we present our proposed recursive algorithm to track (estimate) the state vector $\boldsymbol{x}$ and the statistical parameter $\boldsymbol{\theta}$.

3. PROPOSED ALGORITHM

The main idea behind our proposed recursive algorithm is illustrated in this section. Fig.1 shows the block diagram of this algorithm.

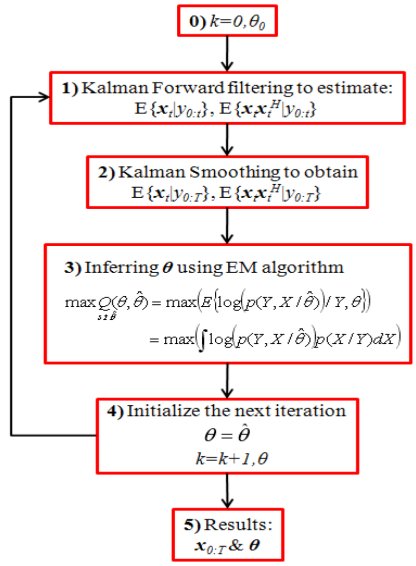

Fig.1. Block diagram of the proposed recursive algorithm.

As can be seen in Fig.1, our recursive algorithm consists of five main steps whose descriptions are given as follows. The algorithm begins with its initial values, θ_0, which can be set to very small values 10^{-6}. In step 1, the extended Kalman filtering (EKF) is employed to accomplish filtering the states $\boldsymbol{x}$ and providing the conditional first and second order statistics, $E\{\boldsymbol{x}_t \mid y_{0:t}\}$ and $E\{\boldsymbol{x}_t\ \boldsymbol{x}_t^{\ H} \mid y_{0:t}\}$ (see [8] for full derivation of EKF for the HH model). Sufficient statistics for the EM algorithm, $E\{\boldsymbol{x}_t \mid y_{0:T}\}$ and $E\{\boldsymbol{x}_t\ \boldsymbol{x}_t^{\ H} \mid y_{0:T}\}$ over whole time, $\{0{:}T\}$, are provided by Kalman smoother, in step 2. The new estimation of the statistical parameters, $\hat{\boldsymbol{\theta}}$, is calculated by the EM algorithm, in step 3, as follows.

$$\max_{s.t.\hat{\theta}} Q(\theta, \hat{\theta}) = \max\left(E\left\{\log\left(p(Y, X/\hat{\theta})\right)/Y, \theta\right\}\right) \qquad (4)$$
$$= \max\left(\int \log\left(p(Y, X/\hat{\theta})\right) p(X/Y) dX\right)$$

where Y and X stand for the observation, $\{y\}_{0:T}$, and states, $\{\boldsymbol{x}\}_{0:T}$, over the whole time. In fact, we want to find new statistical parameters $\hat{\boldsymbol{\theta}}$ such that to maximize the expected joint log likelihood of the observation and the hidden states with respect to statistical parameters $\boldsymbol{\theta}$. Expanding (4), we can write:

$$E\left\{\log\left(p(Y, X/\hat{\theta})\right)/Y, \theta\right\} = E_{p(X/Y,\theta)}\left\{\sum_{t=1}^{T} \log(p(y_t/\boldsymbol{x}_t, \theta)) + \sum_{t=2}^{T} \log(p(\boldsymbol{x}_t/\boldsymbol{x}_{t-1}, \theta)) + \log(p(\boldsymbol{x}_1/\theta))\right\} \qquad (5)$$

Reminding that, $p(y_t/\boldsymbol{x}_t,\boldsymbol{\theta})=N(y_t;C\boldsymbol{x}_t\ ,\sigma^2_O)$ and $p(\boldsymbol{x}_t/\boldsymbol{x}_{t-1},\boldsymbol{\theta})=N(\boldsymbol{x}_t;F[\boldsymbol{x}_t]+BI_{inj}\ ,\Sigma_S)$ where $N(\mu,\sigma^2)$ stands for the normal distribution of mean μ and variance σ^2, and taking the derivative of (5) with respect to Σ^{-1}_S (=$diag(\boldsymbol{\theta})$), we can calculate the new estimation of the Σ_S as follows.

$$\frac{\partial Q(\theta,\hat{\theta})}{\partial \hat{\Sigma}_S^{-1}} = \frac{1}{2}\sum_{t=2}^{T}\left(\hat{\Sigma}_S - \left(\hat{\boldsymbol{x}}_t - A(t)\hat{\boldsymbol{x}}_{t-1}\right)\left(\hat{\boldsymbol{x}}_t - A(t)\hat{\boldsymbol{x}}_{t-1}\right)^H\right) = 0$$
$$\Rightarrow \hat{\Sigma}_S = \frac{\sum_{t=2}^{T}\left(\hat{R}_t(t) - A(t)\hat{R}_{t-1}(t)^H\right)}{T-1} \tag{6}$$

where,

$$\hat{R}_t(t) = \hat{\Sigma}_x(t) + \hat{\boldsymbol{x}}_t\left(\hat{\boldsymbol{x}}_t\right)^H$$
$$\hat{R}_{t-1}(t) = \hat{\Sigma}_{\boldsymbol{x}}^{t-1}(t) + \hat{\boldsymbol{x}}_t\left(\hat{\boldsymbol{x}}_{t-1}\right)^H$$

wherein $\hat{\boldsymbol{x}}_t = E\{\boldsymbol{x}_t \mid y_{0:T}\}$ and $\hat{\Sigma}_x^t(t) = E\{\boldsymbol{x}_t\boldsymbol{x}_t^H \mid y_{0:T}\}$ are the first and second order statistics that have been already calculated in the Kalman smoothing step (see [9] for details). Then, $\boldsymbol{\theta}$ can be easily obtained as the diagonal of the $\hat{\Sigma}_S$. It is to be noted that $A(t)$ in (6) represents the first order derivative of the transition matrix $\boldsymbol{F}$ with respect to the states, $\boldsymbol{x(t)}$ (see [8] for computing $A(t)$).

As our proposed algorithm is recursive, we initialize the next iteration in step 4. The algorithm stops when no considerable changes occur in two consecutive iterations. It is observed in our simulations that the variation of the estimated synaptic input, I_{syn}, is a good candidate as for the stopping criterion. Therefore, our algorithm stops when the variance of the estimated synaptic input changes in two consecutive iterations is less than 5%.

4. SIMULATION RESULTS

Two different types of synaptic input are considered in our simulations to verify the accuracy and robustness of our proposed algorithm. In the first simulation, the synaptic input contains two jumps (see Fig. 2) which do not preserve the smoothness assumption we have previously made. The second simulation is more realistic wherein the synaptic input is generated from Ornstein-Uhlenbeck process (colored noise). For each experiment, the accuracy of our proposed algorithm in estimating the parameters of the HH neuronal model and reconstructing its synaptic input is demonstrated. The simulated data is generated by an HH model whose specifications are: $\{E_{Na}$=55, E_K=-90, E_L=-70$\}^{mV}$, $\{g_{Na}$=32, g_K=10, g_L=0.1$\}^{\mu S/m2}$, $c_M=1^{\mu F/cm2}$ and the rate constants of the ion channel state transitions ($\alpha_q(v)$ and $\beta_q(v)$) are the same as [10]. A zero mean white noise of standard deviation 10 mV is added to the generated membrane potential as the observation noise. All the simulations were carried out by MATLAB and the HH neuron model dynamics are obtained by solving (1) using the "ode15" of MATLAB functions with 0.01 ms as the integration time step while the membrane potential is sampled every 0.1 *ms*. Figures 2 & 5 show the noisy recorded membrane potentials (top) and the true synaptic inputs (bottom) for the first and the second simulation, respectively. Figures 3 & 6 demonstrate the reconstructed versus the true membrane potential (top) and the synaptic input (bottom) of each experiment using the proposed algorithm. Moreover, Figures 4 & 7 indicate the reconstruction of the HH channel dynamics, for each experiment.

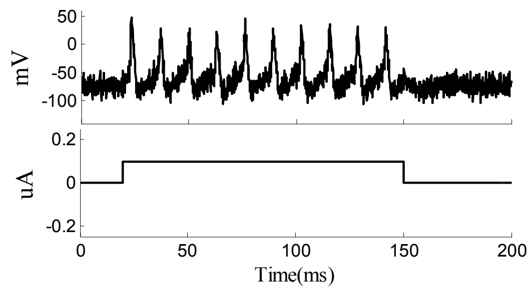

Fig.2. Noisy membrane potential in the first simulation (top) and original synaptic input (bottom).

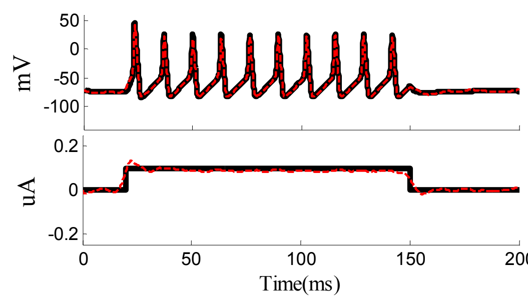

Fig.3. Estimated (red dashed line) versus true (black solid) membrane potential (top) and synaptic input (bottom). The algorithm stops in the 7th iteration. The initial value of $\boldsymbol{\theta}$ (for all variables) is 10^{-6}.

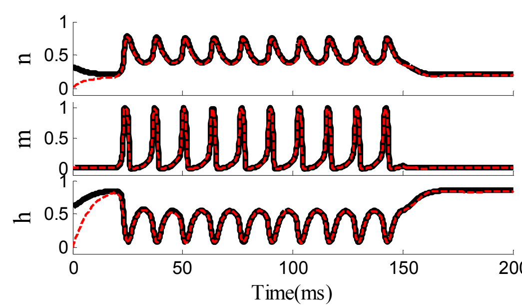

Fig.4. Estimated (red dash line) versus true (black solid) channel dynamics of the HH model. The initial values of *n*, *m*, *h* are zero.

Fig.8 is plotted to show how the parameters of the HH model, the maximum conductances in the first experiment, converge to their true values. As can be seen from Fig.8, all the estimated parameters, g_{Na}, g_K and g_L are accurately converge to their true values.

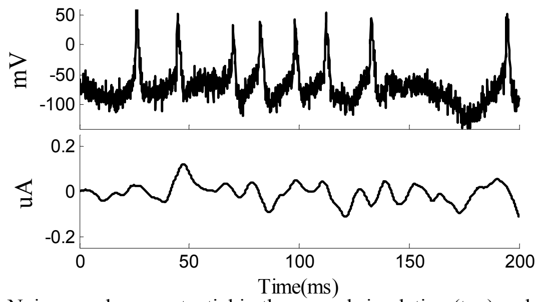

Fig.5. Noisy membrane potential in the second simulation (top) and original synaptic input (bottom). The step current, I_{inj} = 0.06 μA/cm^2, $20ms \leq t \leq 150ms$, is injected to neuron in this simulation.

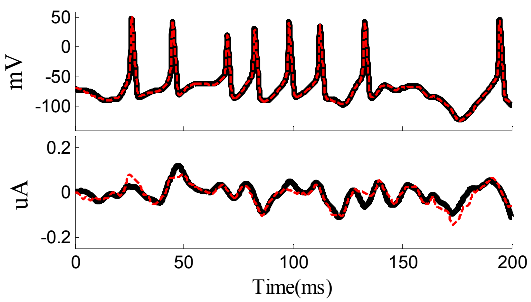

Fig.6. Estimated (red dashed line) versus true (black solid) membrane potential (top) and synaptic input (bottom). The algorithm stops in the 3th iteration. Synaptic input is generate by low pass filtering (0.4/(1-0.9z^{-1})) the white Gaussian noise. The initial value of $\boldsymbol{\theta}$ (for all variables) is 10^{-4}.

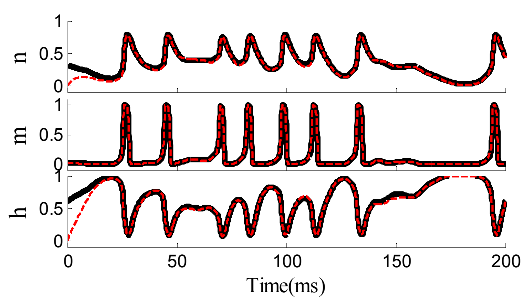

Fig.7. Estimated (red dash line) versus true (black solid) channel dynamics of the HH model. The initial values of *n*, *m*, *h* are zero.

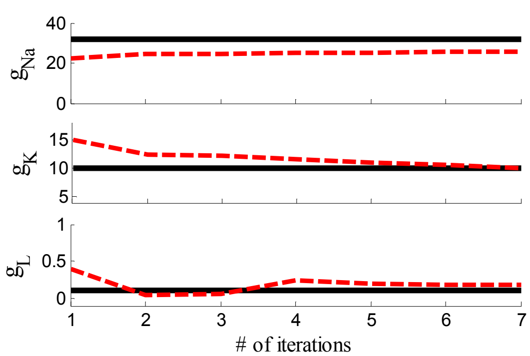

Fig.8 . Estimated (red dash line) versus true (black olid) parameters of the HH model.

As seen in Figures (2-8), the intracellular voltage, *v*, the dynamics of ion channels, {*n*, *m*, *h*}, the synaptic input, I_{syn}, and the intrinsic parameters {g_{Na}, g_K, g_L}, are all estimated with excellent accuracy only from noisy recorded membrane voltage using our proposed algorithm.

5. CONCLUSION

A novel recursive algorithm has been proposed, in this paper, to address the problem of estimating the unobserved dynamics, the synaptic input and the intrinsic parameters of the Hodgkin-Huxley neuronal model. The so called *blind deconvolution* of HH neuronal model has been tackled by employing an extended Kalman filtering followed by an EM algorithm. The robustness and accuracy of this algorithm have been validated by two simulations. The corresponding promising results imply that the proposed algorithm provides a powerful framework for estimating the unobserved dynamics and input of a neuron and therefore, can better reveal how neurons transform information from the synaptic input to the membrane potential. Employing the proposed algorithm to real intracellular recordings builds our future line of research.

REFERENCES

[1] C. Koch, Ed., *Biophysics of Computation.* Oxford University Press, 1999.

[2] Kobayashi. R, Tsubo. Y, Lansky. P and Shinomoto. S, "Estimating time-varying input signals and ion channel states from a single voltage trace of a neuron," *Advances in Neural Information Processing Systems 24 (NIPS 2011),* 2011.

[3] M. Wehr and A. M. Zador, "Balanced inhibition underlies tuning and sharpens spike timing in auditory cortex," *Nature,* vol. 426, pp. 442-446, Nov 27, 2003.

[4] Yina Wei, Ghanim Ullah, Ruchi Parekh, Jokubas Ziburkus, Steven J. Schiff, "Kalman filter tracking of intracellular neuronal voltage and current," in *2011 50th IEEE Conference on Decision and Control and European Control Conference (CDC-ECC),* Orlando, FL, USA, 201 .

[5] R. F. Fox, "Stochastic versions of the Hodgkin-Huxley equations," *Biophys. J.,* vol. 72, pp. 2068-2074, May, 1997.

[6] G. Ullah and S. J. Schiff, "Tracking and control of neuronal Hodgkin-Huxley dynamics," *Physical Review.E, Statistical, Nonlinear, and Soft Matter Physics,* vol. 79, pp. 040901, 2009.

[7] David Csercsik, KatalinM.Hangos, Gabor Szederkenyi, "Identifiability analysis and parameter estimation of a single Hodgkin–Huxley type voltage dependent ion channel under voltage step measurement conditions," *Neurocomputing,* vol. 77, pp. 178-188, 2012.

[8] M. Lankarany, W.P. Zhu and M. N. S. Swamy, "Parameter estimation of Hodgkin-Huxley neuronal model using dual extended Kalman filter," Accepted in *IEEE International Symposium on Circuits and Systems,* China, 2013.

[9] S-V. I. Rosti and M. J. F. Gales, "Generalized linear gaussian models," Cambridge University, Tech. Rep. TR.420, 2001.

[10] Bard Ermentrout and David Terman, Ed., *Foundations of Mathematical Neuroscience.* 2010.