Extracting nonlinear spatiotemporal dynamics in active dendrites using data-driven statistical approach

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Abstract. We propose a data-driven statistical method for extracting nonlinear spatiotemporal membrane dynamics of active dendrites. We employ a framework of probabilistic information processing to extract the nonlinear spatiotemporal dynamics obeying the reaction-diffusion equation from partially observable data. By employing sequential Monte-Carlo method and other statistical methods, membrane dynamics and their underlying electrical properties are simultaneously estimated in the proposed method. Using the proposed method, we show that nonlinear spatiotemporal dynamics in active dendrites can be extracted from partially observable data.

1. Introduction

Recent findings in experimental neuroscience suggest that active dendrites plays an important role in neural information processing such as directional selectivity [1], integration of sensory and motor inputs [2], and so on [3, 4, 5, 6, 7, 8, 9, 10]. For example, recent experimental results showed that active dendritic computation in retinal ganglion cells plays a key role in directional selectivity for visual stimuli [1, 2]. However, the mechanism of active dendritic computation is still unclear, since the spatiotemporal dynamics of active dendrites remains unknown.

Dynamical behaviors in active (nonlinear) dendrites depend on nonlinear ion channels and neuronal morphology and can be described by a reaction-diffusion equation called a nonlinear cable equation, while classical theoretical studies of dendrites have assumed passive (linear) dendrites [11, 12, 13]. Great advances in measurement technology enable us to deal with spatiotemporal data from neural systems including active dendrites as imaging data. However, the observable information in the measurements is quite limited, when compared with the complexity of the entire system of active dendrites.

Some estimation techniques using the state-space modeling approach to extract the spatiotemporal dynamics of the dendrites have been proposed. In some of previous methods, only membrane potentials are estimated while assuming the parameters underlying spatiotemporal dynamics are known [14], and most of the previous methods only estimate linear dynamics in multi-compartment models or nonlinear dynamics in single-compartment models [15], even...
though to reveal the active dendritic computation, it is important to establish methods for extracting nonlinear dynamics for spatiotemporal membrane evolution in multi-compartment models.

In this study, we propose a data-driven statistical method to estimate nonlinear spatiotemporal membrane dynamics of active dendrites in order to extract nonlinear dynamics of dendritic membrane. We employ a data-driven statistical approach to extract the nonlinear spatiotemporal dynamics obeying the nonlinear reaction-diffusion equation from partially observable data. First, we formulate a generalized state-space model of active dendrite that is based on multi-compartment model, and then we derive sequential estimation algorithm for the generalized state-space model. Membrane dynamics and the electrical properties underlying them are simultaneously estimated by using sequential Monte-Carlo method and other statistical methods. Using the proposed method, we show that nonlinear spatiotemporal dynamics in active dendrites can be extracted from partially observable data.

This paper is organized as follows. In section 2, we formulate spatiotemporal dynamics in active dendrites from the nonlinear cable equation and derive a nonlinear state-space model for active dendrites. In section 3, we propose a statistical method for simultaneously extracting membrane responses and membrane properties from partially observable data. In section 4, we show the effectiveness of the proposed method by using multi-compartment models, including the one for hippocampal pyramidal neurons. Concluding remarks are given in section 5. A preliminary version of this work appeared in [16].

2. Theory

In this section, we propose a statistical method for extracting spatiotemporal nonlinear dynamics of active dendrites. As shown in Fig. 1, we consider simultaneous estimation of membrane responses and electrical properties underlying dendritic dynamics from partially observable noisy data. To this end, we formulate a generalized state-space model of dendritic dynamics. We first derive a system model that describes spatiotemporal nonlinear dynamics of dendrite. Next we formulate an observation model that reflects the partially observable situation, as in imaging experiments. Finally we derive a data-driven statistical method for estimating membrane responses including membrane potential and channel variables and underlying parameters such as membrane properties from partially observable data.

2.1. System Model

Here we derive a probabilistic model of membrane potential and channel variables in active dendrites. A nonlinear reaction-diffusion equation for active dendrites is employed to the system model.

2.1.1. Dynamics of Membrane Potential A membrane potential $V(x, t)$ at position $x$ and time $t$ in active dendrite is assumed to obey the following reaction-diffusion equation called nonlinear cable equation [13]:

$$C \frac{\partial V}{\partial t} = - \sum_X g_X m_X N_X (V - E_X) - D \frac{\partial^2 V}{\partial x^2} + I_{ext}(x, t) + \xi(V)(x, t),$$  

(1)

where $m_X$ and $h_X$ show the activation and inactivation for ion channel variables, respectively. Each compartment is assumed to have some kinds of membrane currents $\sum_X g_X m_X^N X^N (V - E_X)$, axial currents $D \frac{\partial^2 V}{\partial x^2}$, external input currents $I_{ext}(x, t)$ and noise current $\xi(V)(x, t)$. The maximal membrane conductances, reversal potentials and membrane capacitance are expressed by $g_{X, x}$, $E_X$ and $C$, respectively.
By discretizing Eq. (1) with respect to space and time, we derive the following equation:

\[ v_{x,t+1} = v_{x,t} - \Delta \sum X g_{x,x} (m_{x,x,t}) M_X (h_{x,x,t}) N_X (v_{x,t} - E_X) - \Delta g_{axial} \sum y (v_{x,t} - v_{y,t}) + \Delta I_{ext,x,t} + \sqrt{\Delta \xi_{v,x,t}}, \]

where time width is set to \( \Delta \) and we put \( C = 1 \) without loss of generality. Each position in the spatially discretized system is called a compartment, and compartments are connected according to neuronal spatial structure as shown in Fig. 2(a).

Based on the statistics of noise, the probabilistic density function of membrane potential is described by a probabilistic model \( p(v_{x,t+1} | v_{x,t}, m_{x,x,t}, h_{x,x,t}) \) that depends on the state of neighboring compartments at preceding time \( \{ v_{x,t} \} \). If the noise is white Gaussian, the probabilistic density function can be described by

\[ p(v_{x,t+1} | v_{x,t}, m_{x,x,t}, h_{x,x,t}) = N(v_{x,t+1} | \mu_{x,t+1}, \sigma_{v}^{2}), \]

where the average is expressed by \( \mu_{x,t+1} = v_{x,t} - \Delta \sum X g_{x,x} (m_{x,x,t}) M_X (h_{x,x,t}) N_X (v_{x,t} - E_X) - \Delta g_{axial} \sum y (v_{x,t} - v_{y,t}) + \Delta I_{ext,x,t}, \) and the variance is expressed by \( \sigma_{v}^{2} \).

2.1.2. Dynamics of Channel Variables In conductance-based models such as the Hodgkin-Huxley model, channel variables \( m_{x,x,t} \) and \( h_{x,x,t} \) obey the following first-order kinetics:

\[ \frac{dm_{x,x,t}}{dt} = \alpha_{mX}(V_{x}) (1 - m_{x,x}) - \beta_{mX}(V_{x}) m_{x,x} + \xi_{mX}(t), \]

\[ \frac{dh_{x,x,t}}{dt} = \alpha_{hX}(V_{x}) (1 - h_{x,x}) - \beta_{hX}(V_{x}) h_{x,x} + \xi_{hX}(t), \]

where \( \alpha_{mX}(V_{x}), \alpha_{hX}(V_{x}), \beta_{mX}(V_{x}), \) and \( \beta_{hX}(V_{x}) \) are functions of membrane potential. By discretizing Eq. (4) and (5) with respect to time, we obtain the probabilistic model of the channel variables: \( p(m_{x,x,t+1} | m_{x,x,t}, v_{x,t}) \) and \( p(h_{x,x,t+1} | h_{x,x,t}, v_{x,t}) \). If the noise is white Gaussian, the probabilistic density function can be described by

\[ p(m_{x,x,t+1} | m_{x,x,t}, v_{x,t}) = N(m_{x,x,t+1} | \mu_{m_{x,x,t+1}}, \sigma_{m_{x,x}}^{2}), \]

\[ p(h_{x,x,t+1} | h_{x,x,t}, v_{x,t}) = N(h_{x,x,t+1} | \mu_{h_{x,x,t+1}}, \sigma_{h_{x,x}}^{2}). \]

Based on probabilistic models (Eqs. (3), (6), and (7)), the system models for all the hidden state vectors \( X_t = \{ v_{x,t}, m_{x,x,t}, h_{x,x,t} \} \) are summarized as \( p(X_{t+1} | X_t) \).
Note that according to neuronal morphology. (b) state-space model of dendrite. Nonlinear spatiotemporal dynamics obeying compartment has passive and active ion channels and is assumed to be connected to neighboring compartments

\[ p(X_{i+1} | X_i) = \int p(X_{i+1} | X_i) p(X_i | Y_{1:t}) dX_i, \]  

where \( p(X_t | Y_{1:t}) \) shows a filtering distribution given the observable data up to the same time \( Y_{1:t} \) as follows:

\[ p(X_t | Y_{1:t}) = \frac{p(Y_t | X_t) p(X_t | Y_{1:t-1})}{\int p(Y_t | X_t) p(X_t | Y_{1:t-1}) dX_t}. \]  

Note that the predictive and filtering distributions can be obtained iteratively by using Eqs. (10) and (11). Using the filtering and predictive distributions, a smoothing distribution \( p(X_t | Y_{1:T}) \) is obtained as follows:

\[ p(X_t | Y_{1:T}) = p(X_t | Y_{1:t}) \int \frac{p(X_{t+1} | X_t) p(X_{t+1} | Y_{1:T})}{p(X_{t+1} | Y_{1:t})} dX_{t+1}. \]
Note that these three distributions have system model \( p(X_{t+1}|X_t) \) and observation model \( p(Y_t|X_t) \). By maximizing the filtering distribution \( p(X_t|Y_{1:T}) \) or the smoothing distribution \( p(X_t|Y_{1:T}) \), we obtain the estimated values for hidden variables \( X_t \).

Since we have assumed the nonlinearity in the generalized state-space model, the integrations in filtering, predictive and smoothing distributions become analytically intractable. In the present study, we employ a sequential Monte-Carlo method \([17, 18, 19]\) to tackle this difficulty and perform the filtering and prediction iteratively.

In addition to hidden variables of \( X_t \), a set of parameters including maximal membrane conductances \( \{g_{X,x}\} \) is unknown. The EM algorithm \([20, 21, 22]\) is employed in order to estimate those parameters underlying the nonlinear spatiotemporal dynamics. In the E-step, expectation of log-likelihood function is calculated

\[
Q(\Theta|\Theta_k) = \langle \log p(\{X_t\}, \{Y_t\}|\Theta) \rangle_{p(\{X_t\}|\{Y_t\},\Theta_k)},
\]

where \( \Theta_k \) shows a set of parameters estimated at step \( k \) of the EM algorithm. In the M-step, we obtain the set of parameters \( \Theta \) that maximizes \( Q(\Theta|\Theta_k) \) as \( \Theta_{k+1} \).

\[
\Theta_{k+1} = \arg \max_{\Theta} Q(\Theta|\Theta_k).
\]

By performing the E-step and the M-step iteratively, we obtain estimated values of parameters by the converged value of \( \Theta_k \).

4. Results

In this section, we evaluate the effectiveness of the proposed method by using simulated data of multi-compartment models with active channels. We assume that each compartment has passive and active channels, and only noisy membrane potentials are partially observable. Using the proposed method, we estimate not only membrane potentials but also other hidden variables such as activation and inactivation variables for active channels for every compartments. We also estimate underlying parameters, including maximal membrane conductances of active channels, which govern the nonlinear spatiotemporal dynamics of dendritic membrane.

Here we consider a compartment model with serially connected compartments and extract true membrane potentials \( v_{x,t} \) and channel variables of sodium current \( m_{Na} \), \( h_{Na} \) and potassium current \( m_{K} \), \( h_{K} \). The estimated time evolution of these hidden variables is shown in Fig. 3(a). We find that true membrane potential at each compartment \( x \) can be estimated accurately. Furthermore, other non-observable hidden variables such as those for sodium channels can be estimated as shown in the bottom figures in Fig. 3(a). Hidden variables for potassium channels can be estimated as well (data not shown). These results show that the proposed method enables us to extract hidden variables underlying nonlinear spatiotemporal dynamics of dendritic membrane. Electrical properties such as maximal membrane conductances should be estimated since they govern nonlinear spatiotemporal dynamics of dendritic membrane potentials and channel variables. The estimated maximal membrane properties of sodium and potassium channels are shown in Fig. 3(b). In Fig. 3(b), we find that estimated maximal membrane conductances converge to true value (dashed line). In these results, we see that the proposed method simultaneously estimates only electrical properties but also membrane potentials and channel variables.

To evaluate the proposed method in a more realistic situation, we extract nonlinear spatiotemporal dynamics in a hippocampal CA1 pyramidal neuron model by the proposed method. We utilize simulated data of action potentials backpropagating from soma to apical dendrites as shown Fig. 4(a). We assume that only noisy membrane potentials in parts of dendritic compartments can be observed. Using this limited data, we simultaneously
Figure 3. Estimation of nonlinear spatiotemporal dynamics in multi-compartment model. (a) True and estimated time courses of membrane potentials $v_{1,t}$ and channel variables $m_{Na,1,t}$ and $h_{Na,1,t}$. Dashed and solid lines show true and estimated time courses, respectively. (b) Estimated maximal conductances of ion channels $g_{Na}$ and $g_{K}$. As iteration of estimation proceeds, the estimated values (solid lines) converge to true values of the maximal conductances (dashed lines).

estimate membrane response and membrane properties. The estimated distribution of membrane potentials is shown in Fig. 4(b). We find that the estimated distribution is similar to the true one, and that underlying parameters can be estimated successfully (data not shown), and that backpropagating action potentials can be reproduced by the proposed method. These results show that the proposed method can extract spatiotemporal nonlinear dynamics of active dendrites from partially observable noisy data.

5. Concluding Remarks
In this study, we have proposed a data-driven statistical method for estimating spatiotemporal membrane dynamics of active dendrites. The generalized state-space model of active dendrite based on the multi-compartment model of dendrites has been derived. A novel spatiotemporal dynamics extraction technique has been realized by using the sequential Monte-Carlo method and the EM algorithm. Using the proposed method, we have shown that inner state of neurons, such as membrane potential and ion channel variables and their underlying parameters, are simultaneously estimated in the multi-compartment model of the hippocampal CA1 pyramidal neuron. These results show that nonlinear spatiotemporal dynamics of active dendrites can be extracted from partially observable data by means of the proposed method.

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Figure 4. Estimation of spatiotemporal dynamics in multi-compartment model with neural morphology of hippocampal CA1 pyramidal neuron. True and estimated distributions of membrane potentials are shown in figures (a) and (b), respectively. Backpropagating action potentials along apical dendrite are simulated and a part of compartments is assumed to be observable for estimation. Maximal values of membrane potentials at each position in active dendrite $v_{x,t}$ are shown.

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