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Bayesian estimation of phase response curves

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ABSTRACT

Phase response curve (PRC) of an oscillatory neuron describes the response of the neuron to external perturbation. The PRC is useful to predict synchronized dynamics of neurons; hence, its measurement from experimental data attracts increasing interest in neural science. This paper introduces a Bayesian method for estimating PRCs from data, which allows for the correlation of errors in explanatory and response variables of the PRC. The method is implemented with a replica exchange Monte Carlo technique; this avoids local minima and enables efficient calculation of posterior averages. A test with artificial data generated by the noisy Morris–Lecar equation shows that the proposed method outperforms conventional regression that ignores errors in the explanatory variable. Experimental data from the pyramidal cells in the rat motor cortex is also analyzed with the method; a case is found where the result with the proposed method is considerably different from that obtained by conventional regression.

1. Introduction

Synchronization between neurons is observed everywhere in neural systems (Salinas & Sejnowski, 2001; Varela, Lachaux, Rodriguez, & Martinerie, 2001). For example, the periodic activities seen in EEG are regarded as evidence of synchronicity in the brain. Gray and Singer (1989) proposed a hypothesis that synchronization is essential for understanding the "binding problem" in cognitive neuroscience. Fries (2005) introduced the "communication through coherence" hypothesis, which suggests that coherent oscillations of neurons are important for information transmission in the brain. These hypotheses argue that coherence in neural activities induced by synchronization is not a side effect but essential for understanding brain functions.

To deal with synchronization from the theoretical viewpoint, Kuramoto (1984) developed a theory based on the phase description of an oscillator; see also Ermentrout (1996), Hansel, Mato, and Meunier (1995), Izhikevich (2007), Kopell and Ermentrout (1990), Winfree (2001), and recent surveys (Acebrón, Bonilla, Pérez Vicente, Ritort, & Spigler, 2005; Strogatz, 2000). A key concept of this theory is the phase response curve (PRC), which describes the response of an oscillator to external perturbations. According to the studies by Kuramoto and his successors, the PRC and the network topology are two essential features that determine the synchronicity of an oscillator network. In terms of neural science, neuron's PRCs can be useful for reconstructing the properties of a network consisting of neurons.

Many researchers have recently tried to estimate neuron's PRCs from experimental data (Ermentrout, Galán, & Urban, 2007; Ermentrout & Saunders, 2006; Galán, Ermentrout, & Urban, 2005; Goldberg, Deister, & Wilson, 2007; Gutkin, Ermentrout, & Reyes, 2005; Netoff et al., 2005; Ota, Nomura, & Aoyagi, 2009; Preyer & Butera, 2005; Tsubo, Takada, Reyes, & Fukai, 2007). Noise in the PRC measurements is often very large, and sophisticated statistical techniques are necessary for efficient estimation. A typical method used in these studies is fitting the data with a linear combination of trigonometric functions. Ota and co-workers (Aonishi & Ota, 2006; Ota, Omori, & Aonishi, 2009) introduced a Bayesian procedure wherein PRCs are assumed to be smooth functions. The Bayesian approach has the advantage of easily introducing prior information on PRCs as well as on the measurement process.

A common weakness of the previous studies is that they neglect the errors in the PRC explanatory variables. They also neglect the correlation between errors in the explanatory and response variables; the significance of this correlation is discussed in Section 2.2. This study is devoted to developing a new method that can deal with these errors and the correlation through a systematic use of Bayesian methods. Unlike previous Bayesian methods (Aonishi & Ota, 2006; Ota et al., 2009), our method does not require an assumption that the timing of a perturbation represented as a phase,

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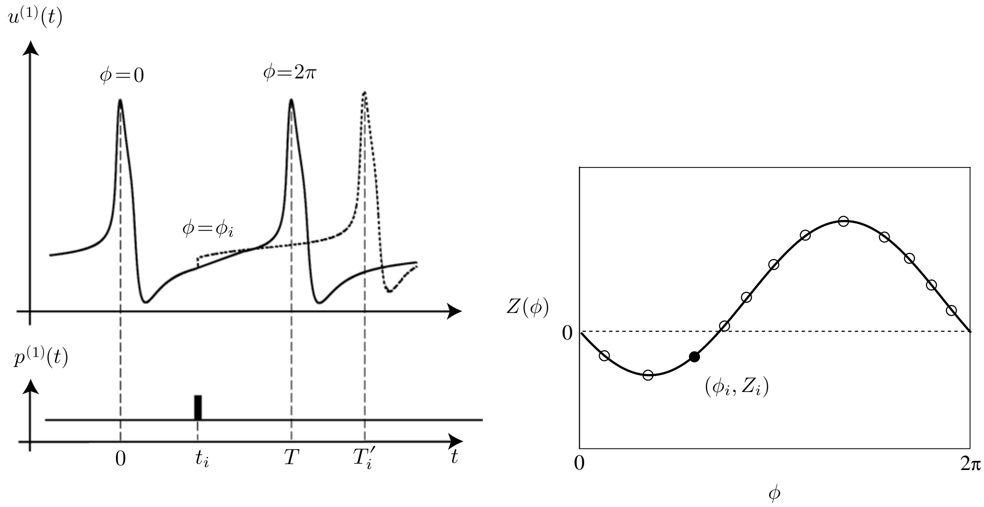

Fig. 1. Measurement of a phase response curve. A trial with a perturbation at $t = t_i$ is illustrated in the left panel. The solid curve indicates the voltage for the neuron without perturbation, while the dotted curve indicates the voltage with perturbation. Each point (ϕ_i, Z_i) in the right panel corresponds to a trial with timing t_i. The PRC is defined by interpolating these points.

later defined as ϕ_i in (1), is known exactly. Using the proposed procedure, we successfully improved the estimation precision for PRCs in examples of simulated data. The proposed method is also applied to experimental data from the pyramidal cells in the rat motor cortex.

The role of errors in explanatory variables for regression has been considered in the literature on statistics (Amari & Kawanabe, 1997; Berry, Carroll, & Ruppert, 2002; Caroll, Ruppert, Stefanski, & Crainiceanu, 2006; Cheng & Ness, 1999; Fuller, 1987). The correlation between errors in the explanatory and response variables is also treated in some textbooks, for example, Cheng and Ness (1999), but it seems a less known subject; its appearance in the present problem of estimating PRCs will be interesting in terms of statistical science.

The Bayesian model proposed in this paper is nonlinear and non-Gaussian; a standard way to treat such a model is with Markov chain Monte Carlo (MCMC) methods (Gelman, Carlin, Stern, & Rubin, 2003; Gilks, Richardson, & Spiegelhalter, 1995; MacKay, 2003; Robert & Casella, 2004). For the current problem, however, a direct application of standard MCMC methods is difficult due to the slow convergence of MCMC. To deal with this difficulty, we introduce the replica exchange Monte Carlo (REM) method (Geyer, 1991; Hukushima & Nemoto, 1996; Iba, 2001). The REM is widely used in statistical physics and biomolecular simulations, and also applied to statistical inference (Geyer & Thompson, 1995; Huelsenbeck & Ronquist, 2001; Jasra, Stephens, & Holmes, 2007). Using the REM, the difficulty is reduced, and we can get results within a reasonable amount of time.

The proposed method for PRC estimation is useful for any kind of nonlinear oscillator that permits the phase description. Although our current interest is in applications for brain science, this method can also be used in other fields of biology, chemistry, and physics.

The organization of this paper is as follows: in the next section, we define the PRC and discuss the properties of the correlation between errors in the explanatory and response variables. In Section 3, we propose a Bayesian model where we consider both the correlation of errors and smoothness of PRCs. In Section 4, we discuss how to estimate the PRC from data using the REM. In Sections 5 and 6, we test the proposed procedure with artificial data generated using the Morris–Lecar equation (Morris & Lecar, 1981) and data from a real experiment.

2. Phase response curve

2.1. Definition of the phase response curve

First, we define the PRC of a neuron from an operational viewpoint. We assume that the activity of a neuron is periodic and that the period is T. The solid curve in the left panel of Fig. 1 represents the voltage time-series for the neuron. We consider a set of trials indexed by i. The neuron is assumed to fire at the origin $t = 0$. For the ith trial, a perturbation is added at time $t = t_i$. The neuron then fires again at time $t = T_i'$ as shown by the dotted curve in Fig. 1. We repeat this procedure a number of times and plot the points $(\phi_i, Z_i),\ i = 1, \dots, n$, defined by

$$\phi_i = 2\pi \frac{t_i}{T}, \qquad Z_i = 2\pi \frac{T - T_i'}{T}. \tag{1}$$

The curve $Z(\phi)$ interpolating these points is the phase response curve (PRC) of the neuron and is shown by the solid curve in the right panel of Fig. 1.

Next, we discuss a connection to the theory of dynamical systems. Let us represent the state of a neuron by the vector $\mathbf{u} = (u^{(1)}, \dots, u^{(m)})$, whose first component $u^{(1)}$ corresponds to the voltage of the neuron. An equation that describes dynamics of the neuron is assumed as

$$\frac{\mathrm{d}\mathbf{u}}{\mathrm{d}t} = \mathbf{F}(\mathbf{u}) + \mathbf{p}(t), \tag{2}$$

where the vector $\mathbf{p}(t) = (p^{(1)}(t), \dots, p^{(m)}(t))$ represents external perturbation. Hereafter, the vector field $\mathbf{F}(\mathbf{u})$ is assumed to have a stable limit cycle. If the perturbation $\mathbf{p}(t)$ is sufficiently small, Eq. (2) is reduced to

$$\frac{\mathrm{d}\phi}{\mathrm{d}t} = \frac{2\pi}{T} + \mathbf{Z}(\phi) \cdot \mathbf{p}(t), \tag{3}$$

where a point on the limit cycle is indicated by the phase variable $\phi \in [0, 2\pi)$ (Kuramoto, 1984). Eq. (3) suggests that a neuron is characterized by the function $\mathbf{Z}(\phi) = (Z^{(1)}(\phi), \dots, Z^{(m)}(\phi))$.

When the perturbation $\mathbf{p}(t)$ is added to the first component $u^{(1)}$ only and the functional form of $p^{(1)}(t)$ is Dirac's delta function $\delta(t - t_i)$, Eqs. (2) and (3) correspond to the experiment defining PRCs from the operational viewpoint. Thus, we can identify the function in Eq. (3) with a PRC $Z(\phi)$ defined from the operational viewpoint. The vector function $\mathbf{Z}(\phi)$ in Eq. (3) can be regarded as a