

# Estimating inputs and an internal neuronal parameter from a single spike train\*

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**Abstract**— Because neurons are integrating input signals and translating them into timed output spikes, examining spike timing may reveal information about inputs, such as population activities of excitatory and inhibitory presynaptic neurons. Here we construct a state-space method for estimating not only such extrinsic parameters, but also an intrinsic neuronal parameter such as the membrane time constant from a single spike train.

## I. INTRODUCTION

A series of spike times recorded from cortical neurons *in vivo* looks random, but is originally determined by input signals coming from other neurons. Mathematical methods have been developed for inferring the activities of presynaptic excitatory and inhibitory neuronal populations from a recorded spike train. However, most of the former studies were constructed under an unrealistic assumption that the population activities are constant over time [1-3]. Recently, we introduced a state-space model into this inference method to allow for temporal fluctuation in the population activities of presynaptic neurons [4].

The method of input inference can be constructed by inverting a generative model, which represents the forward neuronal transformation from inputs to spikes. In our previous study, we have chosen a standard leaky integrate-and-fire (LIF) model as a generative model and assigned typical parameters that were conventionally adopted. However, the input inference may crucially depend on the choice of a forward generative model and its parameter such as the membrane time constant of a neuron. Thus it is most desirable to estimate not only input parameters, but also a neuronal model parameter from a single spike train (Fig.1).

Here we extend the state-space method to make it possible to estimate both extrinsic input parameters and an intrinsic neuronal parameter. The estimation method is tested with synthetic data.

## II. GENERATIVE MODEL

### A. Leaky integrate-and-fire model

As a forward generative model that mimics the neuronal transformation from inputs to output spike times, we adopt a standard LIF model, given by

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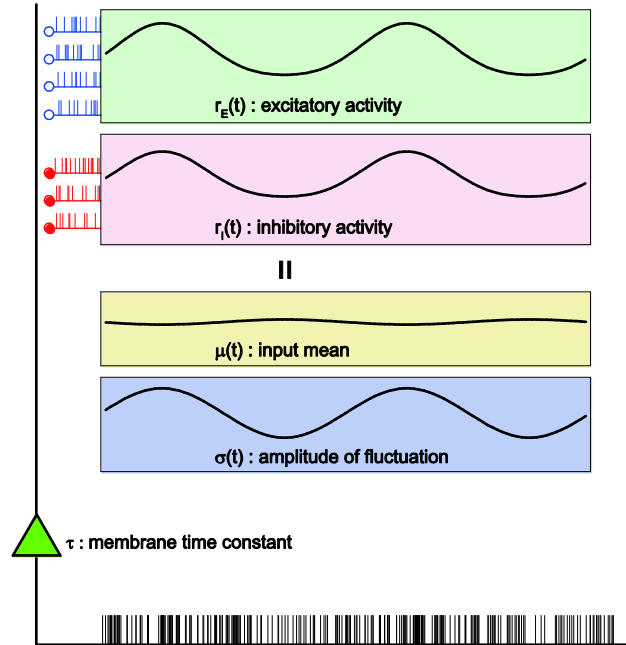


Figure 1. The parameters to be estimated: Input mean  $\mu(t)$ , the amplitude of the fluctuating input  $\sigma(t)$ , and the membrane time constant  $\tau$ .

$$\tau \frac{dV(t)}{dt} = -V(t) + RI(t), \quad (1)$$

if  $V(t) > V_{TH}$ , then fire and  $V(t) \rightarrow V_{RESET}$ ,

where  $\tau$ ,  $V_{TH}$ ,  $V_{RESET}$ ,  $R$ , and  $I(t)$  represent the membrane (leak) time constant, threshold potential, resetting potential, membrane resistance, and input current, respectively. We set some parameters at standard published values:  $V_{TH} = 20$  mV [5-7],  $V_{RESET} = V_{TH} - 6$  mV [8,9], and  $R = 40$  M $\Omega$  [6]. The membrane time constant  $\tau$  is considered largely dependent on the neuronal characteristics, which differ significantly between neurons, in particular pyramidal neurons and interneurons [6,7,10-13]. Because the membrane time constant crucially determines the neuronal firing characteristics, we leave this parameter to be determined by data.

## B. Ornstein-Uhlenbeck process

We assume that the membrane potential  $V(t)$  is subject to small abrupt increment or decrement in response to excitatory or inhibitory spike inputs, respectively. If such postsynaptic potentials occur randomly in time, the input current can be approximated as a diffusion process with a mean drift  $\mu$  and temporally uncorrelated fluctuation  $\sigma_\xi(t)$  [14-16],

$$I(t) = \mu + \sigma_\xi^\xi(t), \quad (2)$$

where  $\xi(t)$  is white noise satisfying the ensemble statistics  $\langle \xi(t) \rangle = 0$  and  $\langle \xi(t)\xi(t') \rangle = \delta(t-t')$ . If the uncorrelated fluctuation  $\xi(t)$  is Gaussian, the membrane potential obeys the Ornstein-Uhlenbeck Process (OUP), and the interspike interval (ISI) is given as the first-passage time of the OUP [16-18].

With the knowledge of typical amplitudes of excitatory and inhibitory postsynaptic potentials, the mean drift  $\mu$  and the fluctuation amplitude  $\sigma$  can be related to the population activities of excitatory and inhibitory inputs,  $r_E$  and  $r_I$ ,

$$\begin{aligned} R\mu / \tau &= a_E r_E - a_I r_I, \\ (R\sigma / \tau)^2 &= a_E^2 r_E + a_I^2 r_I, \end{aligned} \quad (3)$$

where  $a_E$  and  $a_I$  are the unitary excitatory and inhibitory postsynaptic potentials, respectively [15,17].

## III. BAYESIAN INFERENCE

### A. State-space model

The probability that a neuron generates output spikes at times  $\{t_j\} \equiv \{t_0, t_1, t_2, \dots, t_n\}$  can be obtained with the above-mentioned generative model, given the extrinsic input parameters and an intrinsic neuronal parameter. Here, we construct a method of estimating the time varying input parameters  $\mu = \mu(t)$  and  $\sigma = \sigma(t)$ , and the membrane time constant  $\tau$ , given the output spike times  $\{t_j\}$ . The Bayesian posterior distribution of the parameters is given by

$$P(\Lambda | \{t_j\}) = \frac{P(\{t_j\} | \Lambda)P(\Lambda)}{P(\{t_j\})}, \quad (4)$$

where  $\Lambda$  represents the parameters  $(\mu(t), \sigma(t), \tau)$ .

We give the prior distribution for extrinsic and intrinsic parameters in a factorized form,

$$P(\Lambda) = P(\mu(t), \sigma(t))P(\tau). \quad (5)$$

For the prior distribution of the extrinsic input parameters  $\mu(t), \sigma(t)$ , we incorporated their tendency to vary slowly by penalizing the large gradient,

$$\begin{aligned} P_\gamma(\mu(t), \sigma(t)) &= P_\gamma(\{\mu_j\}, \{\sigma_j\}) \\ &\propto \prod_{j=1}^n \exp \left[ -\frac{(\mu_j - \mu_{j-1})^2}{2\gamma^1 s_j} - \frac{(\sigma_j^{-1} - \sigma_{j-1}^{-1})^2}{2\gamma^2 s_j} \right] \end{aligned} \quad (6)$$

where  $\mu_j$  and  $\sigma_j$  respectively represents the input parameters at the time of the  $j$ th spike  $\mu(t_j)$  and  $\sigma(t_j)$ , and  $\gamma \equiv (\gamma^1, \gamma^2)$  is a set of hyperparameters representing the degree of their constancy. This prior distribution represents input parameters exhibiting a random walk, and thus the variance should be rescaled with the  $j$ th ISI,  $s_j \equiv t_j - t_{j-1}$ .

Initial values of input parameters,  $\mu_0, \sigma_0$ , were set to the values estimated through the method of moments [1] on the assumption that input parameters are constant over time.

The membrane time constant  $\tau$  has been considered to range over 5–40 ms [6,7,10-13]. This range can be used to formulate a prior distribution of  $\tau$ ; we assigned an exponential distribution given by

$$P(\tau) = \frac{1}{\zeta} \exp \left( -\frac{\tau}{\zeta} \right), \quad (7)$$

where we have taken  $\zeta = 20$  ms, thus allowing for the above-mentioned range of possible time constant.

In estimating the probability of having spikes under temporally varying input parameters  $\mu(t)$  and  $\sigma(t)$ , we approximate these parameters being constant during each ISI as follows:

$$P(\{t_j\} | \Lambda) = \prod_{j=1}^n P(s_j | \mu_j, \sigma_j, \tau), \quad (8)$$

It should be noted that the constant input parameters do not mean that the input current was constant; on the contrary, the input current fluctuates rapidly in given amplitude  $\sigma_j$ , representing bombardment of a huge number of input spikes from presynaptic populations of neurons.

### B. Choice of hyperparameters

In our previous study, we have selected hyperparameters that specify the degree of temporal modulation of input mean and variance under the Empirical Bayes method, or a principle of maximizing the marginal likelihood function with the Expectation Maximization (EM) algorithm [19,20]. However, this computation turned out to be highly complex and only feasible with up to hundreds of spikes even for the two hyperparameters [4]. A major cause for this limitation is the need to solve a complex integral equation to estimate the ISI distribution function for any given set of input parameters  $(\mu, \sigma)$  [21,22]. Here, we further want to estimate the membrane time constant  $\tau$  in addition to these two input parameters. Accordingly, the marginalization integral

becomes even more complex, and the computational complexity of this marginalization is beyond our available computational capacity. In the present study, we empirically choose the hyperparameters comparable with that have been chosen by the former study, leaving the hyperparameter selection an open issue.

### C. Posterior distribution of the intrinsic parameter

The posterior distribution of the membrane time constant  $\tau$ , given the data  $\{t_j\}$  can be computed by marginalizing the posterior distribution

$$P(\tau | \{t_j\}) = \prod_{j=1}^n \iint d\mu_j d\sigma_j P(\{\mu_j\}, \{\sigma_j\}, \tau | \{t_j\}). \quad (10)$$

We carry out the marginalization integral over all possible values of  $\{\mu_j\}$  and  $\{\sigma_j\}$  by Kalman filtering and smoothing algorithm [4,23].

## IV. RESULTS

We assess the estimation methods by examining synthetic data obtained with several values of the membrane time constant.

### A. Synthetic data

We generated synthetic data by simulating neuronal spiking with the LIF model given nonstationary input parameters comprising the mean and fluctuation of input current. We have simulated three LIF models possessing time constant,  $\tau = 10, 20,$  and  $40$  ms. The other parameters of the LIF model were chosen to match those that were incorporated into the estimator.

The temporally fluctuating input parameters, the mean input  $\mu(t)$  and the amplitude of uncorrelated fluctuation  $\sigma(t)$ , were chosen as

$$\begin{aligned} \mu(t) &= \mu_0 + \delta\mu \sin(2\pi t/T), \\ \sigma(t) &= \sigma_0 + \delta\sigma \sin(2\pi t/T - \phi). \end{aligned} \quad (11)$$

with the phase shifted by  $\phi = \pi/2$ . We have chosen the means  $\mu_0, \sigma_0$  and fluctuation amplitudes,  $\delta\mu, \delta\sigma$  so that the resulting firing rates vary in the range of  $40 \pm 20$  spikes/sec.

### B. Estimation

We applied our state-space model to three kinds of spike trains derived from the above-mentioned simulations. The inference of the input parameters is demonstrated by the maximum *a posteriori* (MAP) paths, by denoting as  $\hat{\mu}(t)$  and  $\hat{\sigma}(t)$ . It is observed that the method gives reasonable estimates for the input parameters for each case (Fig.2).

Regarding the estimation of the membrane time constant  $\tau$ , we demonstrate how a prior distribution of  $\tau$  (7) is transformed into a posterior distribution (10), given a spike

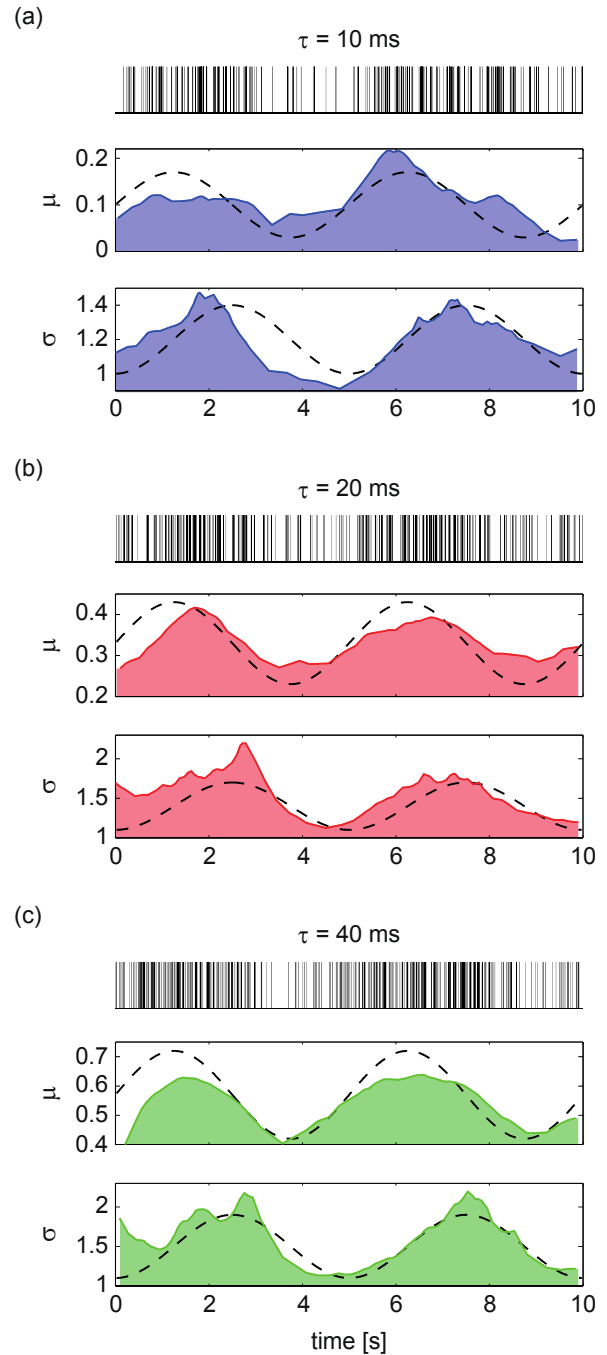


Figure 2. Estimation of input parameters. Three spike trains depicted in raster are derived from neurons of different membrane time constants, (a)  $\tau = 10$  ms, (b)  $\tau = 20$  ms, (c)  $\tau = 40$  ms. The dotted lines represent input parameters, and the color-shaded areas represent the estimated values.

train. In Fig.3, the posterior distribution functions for three kinds of spike trains are plotted together with the prior distribution given by the exponential function of the mean  $\zeta = 20$  ms. It is observed that the wide prior distribution is concentrated to a narrow range in accordance of the original membrane time constant used for the data generation.

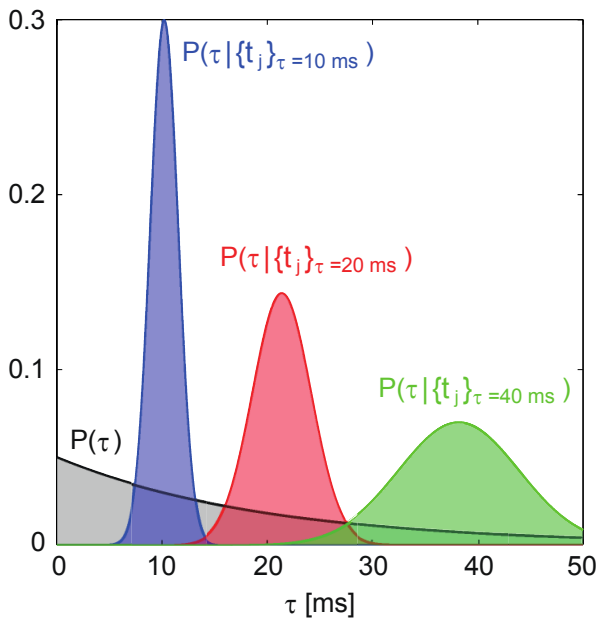


Figure 3. The prior and posterior distribution functions of the membrane time constant  $\tau$ . The prior distribution (7) is depicted in a black line and dark-shaded area. The posterior distributions are depicted in color lines and color-shaded areas. They are respectively obtained from three spike trains in Fig.2.

## V. DISCUSSION

A state-space model for estimating both extrinsic inputs and an intrinsic neuronal parameter has worked successfully with regard to synthetic data. However, there are still unfinished problems. Firstly, the method should be tested with data generated by mismatched models. Our model covers the entire parameter range of the LIF model, allowing for the different membrane time constant, but does not cover the more realistic models containing more timescales and conductance-based models. Secondly, it would be worthwhile to test a particle filter for maximizing marginal likelihood, though it is not trivial if this helps. Thirdly, the method should be eventually applied to real biological data. In particular, it would be most interesting to examine the cases in which extrinsic parameters such as  $\mu$  and  $\sigma$  are shared by different neurons, while the intrinsic neuronal parameters  $\tau$  are different between neurons.

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