2015 International Symposium on Nonlinear Theory and its Applications
NOLTA2015, Kowloon, Hong Kong, China, December 1-4, 2015

Verification of parameter estimation techniques from spike train data

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Abstract—The inverse problem of estimating parameters from spike trains needs a stochastic approach to find most likely solutions. Since the brain exhibits complicated dynamics that is difficult for the model to reproduce, the modeling errors are inevitable. In our recent study, we proposed a Bayesian framework to estimate two model parameters in a segment-wise fashion and then to merge the segmental estimates into a single estimate. The segmental Bayes compensated the modeling errors caused by the mismatch between the brain and the model. The previous study, however, has not yet been properly validated, because it was applied to experimental data, the true parameter values of which are unknown. The aim of this paper is to evaluate the segmental Bayes using simulated spike data, for which the true parameter values are known. The performance evaluation confirmed that the segmental Bayes outperforms other approaches. It also has a strong robustness against non-stationarity of the spike data. We thus conclude that the segmental Bayes provides a useful tool in neuroscience to estimate parameters from spike trains.

1. Introduction

Multiple electrodes have become a standard tool in neuroscience research that enables simultaneous measurement of a population of neuronl activities in a brain region. Such measurement data provide important analysis challenges that must be resolved to understand the brain functions. The parameter estimation is one of the indispensable ones, because some parameters can not be experimentally measured but are needed to construct computational models of the brain. Although the computational models are of extensive use in neuroscience, they usually face two challenges: first, non-stationarity of the brain activities and, second, insufficiency of the computational model in space and time compared with the brain. The first difficulty arises from the fact that most models assume stationarity in the neuronal dynamics. By contrast, the neuronal firings in the real brain shows different dynamics from time to time. The second difficulty is due to the fact that the computational model is typically composed of a far smaller number of the neuronal elements and connectivities compared to the real network of the brain. These difficulties inevitably cause modeling errors and thus cause inaccurate solutions of the inverse problem for estimating model parameters from the spike data [1, 2].

In our recent study [1], we proposed a stochastic approach to reduce the modeling errors by allowing the parameter values to be varied in time segments. In this segment-wise approach, the parameters were firstly estimated segment by segment. This relaxes the condition of the parameter search and thus enables to capture the complicated firing dynamics of experimental spike data. The segmental estimates were then integrated by a hierarchical Bayesian framework, resulting in a single estimate. As a consequence, the segmental Bayes has been shown to minimize the fitting error between experimental and simulation data in the feature space. Our approach, however, has not yet been properly validated because the true parameter values of the experimental data were not known. To further demonstrate its usability, validation of the previously developed approach is desired. By adopting the same task of estimating two conductance values in the inferior olive network model, this study utilizes simulated spike data as the test data. The simulation data are suitable for the validation purpose, because the true parameter values are known. The present study confirmed that the segmental Bayesian inference provides smaller estimation errors than the conventional Bayesian inference, which finds the estimates once across the entire spike data, or the minimum error method [2], which directly finds the closest match in the feature space. Robustness of the segmental Bayesian approach against highly non-stationary dynamics of the spike data is also demonstrated. It thus provides an effective approach to resolve the inverse problem even when the model is an imperfect representation of the experimental data.

2. Methods

2.1. Simulation model

The simulation data was generated using the neuronal model developed in the previous study [2]. The model consisted of 3×3 neurons, each of which was connected to its four neighbouring neurons via gap junctions (g_c). Each neuron was composed by the soma, dendrite and spine compartments. All compartments received excitatory (g_e) and inhibitory (g_i) inputs from *Gaussian* noise generators. The two parameters of interest, g_i and g_c, were varied in the range of [0–1.5 mS/cm^2] with an increment of 0.05 mS/cm^2.

2.2. The segmental Bayesian inference

In this section, we briefly describe the segmental Bayesian framework to estimate the two parameters, g_i and g_c, from neuronal spike trains. The detailed formulas are described in our previous paper [1]. The firing dynamics were characterized by a feature vector (FV) composed of sixty seven features, *e.g.*, firing rate, local variation, cross-correlation, auto-correlation, and minimal distance. The FV was transformed into lower-dimensional space using principal component analysis (PCA). Likelihood function was estimated on the simulation (SIM) data using the Gaussian mixture model in the 3-dimensional PCA space. Finally, the conductance values $g = (g_i, g_c)$ can be determined from the feature vector y by maximizing the posterior probability $P(g|y)$ in accordance with the Bayes' theorem:

$$P(g|y) \propto P(y|g)P(g) \tag{1}$$

where $P(y|g)$ and $P(g)$ are the likelihood and prior of parameter values g, respectively.

The main point of our proposed framework is introduction the neuronal constraint, which deals with the estimation errors caused by the modeling errors, to the Bayesian inference. To minimize such errors, we divided the spike data of each neuron into small time-segments, applied the Bayesian inference to estimate g_i and g_c for every segment, and then merged the segmental estimates into a single estimate for each neuron (Figure 1). Here, the variance of neuronal constraint was optimized so as to maximize the model evidence value.

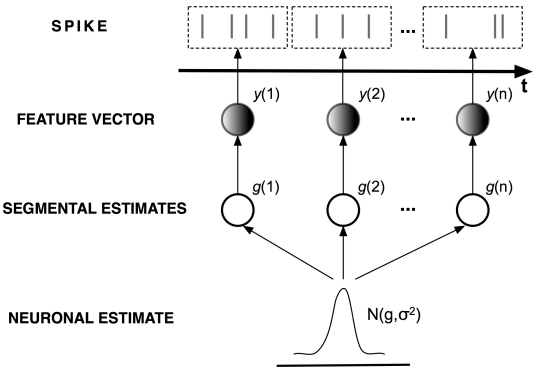

Figure 1: A schematic diagram of the segmental Bayesian inference.

2.3. Simulating non-stationarity in test data

The basic idea of the segmental Bayes is to deal with non-stationary dynamics of the experimental spike data. Such non-stationarity arises typically from high-dimensional spatio-temporal system. Unfortunately, our mathematical model was not complicated enough to produce such non-stationary dynamics. Figure 2 shows the firing rate extracted from spike trains of representative 13 experimental (EXP) and 9 SIM neurons. While exhibiting a comparable mean firing frequency (around 1Hz), the SIM neurons tend to fire periodic and stable in time, as well as there is not much different in firings among those neurons (STD of firing frequency across time and neurons, 0.23 and 0.30, respectively). By contrast, firing frequency of EXP neurons vary strongly in both time and space (0.28 and 0.68). This example indicates that the present simulation failed to precisely reproduce the non-stationarity of EXP data, and thus was not suitable for testing the segmental Bayes.

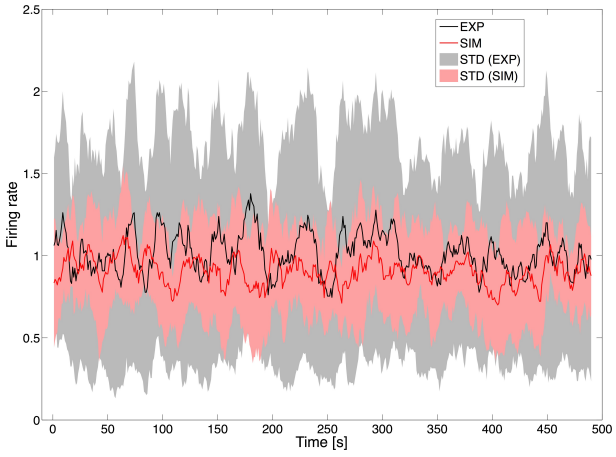

Figure 2: Firing rate averaged over 13 EXP (black trace) and 9 SIM (red trace) neurons. Shaded area represents standard deviation across neurons.

We thus propose a simple method to simulate non-stationarity in the test data as follows. Suppose that the test spike data was selected at a parameter value $g = (g_i, g_c)$, from which we generate 500s spike trains. Unlike the simulation of the forward model in which the parameter value was fixed, the value of g in the simulation of test data was adjusted in every 10s. The adjusting values of g was randomly chosen from the normal (*Gaussian*) distribution $N(g, \sigma^2)$ with the mean g and the variance σ^2. Here, σ can be regarded as a parameter to control the level of non-stationarity in the test data. Then, the PCA scores $\boldsymbol{y}$ of the test data is evaluated as mentioned previously. We conventionally define the standard deviation of the first PCA score of $\boldsymbol{y}$ as the non-stationary level. It is worth noting that simulating non-stationarity in the test data is independent to the construction of the forward model.

3. Results

3.1. Effect of the neuronal constraint

Figure 3 are pseudo-color representation of the posterior probability of g_i and g_c estimated for a representative SIM neuron by the Bayesian inference under the relaxed

neuronal constraint (Figure 3A). The estimates were diffused broadly probably because of the fluctuations of the segmental estimates. By contrast, the g_i and g_c of the same spike data estimated by Bayesian inference under the optimized neuronal constraint were localized at the true value (0.75, 0.75) (Figure 3B).

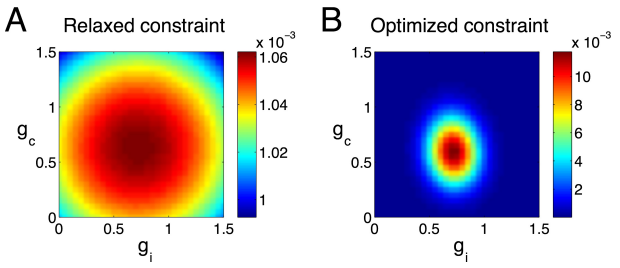

Figure 3: Posterior estimates of a representative SIM neuron with relaxed (A) and optimized (B) neuronal constraint.

3.2. Non-stationarity level of the test data

Figure 4 shows spike trains of 9 simulation neurons at a representative model parameter $g = (g_i, g_c) = (0.7, 0.7)$ before (Figure 4A) and after (Figure 4B) the manipulation process described in 2.3. The firing dynamics of the test data significantly fluctuate: dense at certain times and sparse at others, showing a clear improvement of the non-stationarity.

Figure 4: Spike trains of representative simulation neurons before (A) and after (B) the non-stationarity manipulation.

We also investigate the dependence of non-stationary level of the test data on the parameter σ. Figure 5 indicates that increasing the variance parameter σ monotonically improved the non-stationarity of the test data. The amount of improvement evaluated with $\sigma = 0.3$ (2.77 ± 0.8) and $\sigma = 0.5$ (3.31 ± 1.01) were about 113% and 155%, respectively, compared to that evaluated with $\sigma = 0.1$ (1.3 ± 0.38).

3.3. Parameter estimation for the test data

For each test data, we applied three different approaches to estimate the parameter values (g_i and g_c). They are the

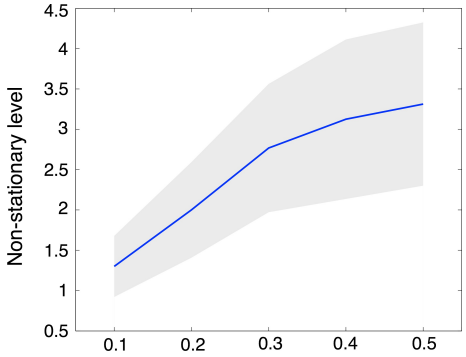

Figure 5: Dependence of non-stationary level on the parameter σ ([0.1–0.5]). Solid and shaded area, mean and standard deviation over 100 trials at each σ.

segmental Bayes, the non-segmental Bayes, which finds the estimates once across the entire spike data, and minimum error method, which determines the estimate as the closest match in the PCA space [3]. The test data sets were generated by a random set of 100 parameter values $g = (g_i, g_c)$ for varied parameter σ in the range [0.1–0.5].

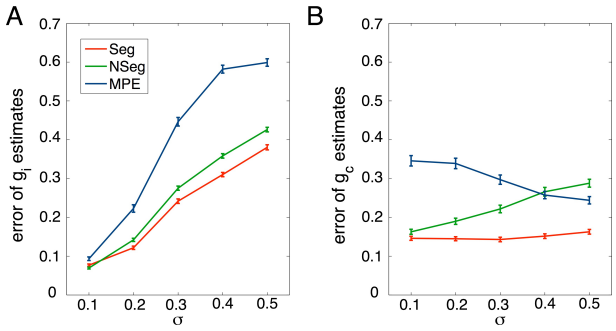

Figure 6: Estimation errors of g_i (A) and g_c (B) by three different approaches: Segmental Bayes (Seg, red trace), Non-segmental Bayes (NSeg, green trace) and minimum error method (MPE, blue trace). Error bars are standard deviations across 100 trials.

Figure 6 shows the absolute differences between the estimated and true parameter values of g_i (Figure 6A) and g_c (Figure 6B), independently. Segmental Bayes outperformed both non-segmental Bayes and minimum error method for g_i and g_c estimation in all non-stationarity levels. These results are consistent with our view that the segmental Bayes minimizes errors in g_i and g_c estimates because of the non-stationary firing dynamics. For the two comparative approaches, there is a tendency that increasing the non-stationary level of the test data decreased the accuracy of both g_i and g_c estimation, whereas it is less clear for the segmental Bayes (Figure 6B). It is notable that g_i errors for all three approaches were higher than those of g_c. This situation is opposite to our findings in [3] and probably due

to the effect of non-stationarity in the test data.

Finally, we tested the superiority of the segmental Bayesian inference over the two comparative approaches in terms of the combined estimation error (Euclidean distance between the true and estimated values in the (g_i, g_c) space). The magnitude of the estimation error was smaller for the segmental Bayesian inference (Figure 7) than that for non-segmental Bayes and minimum error method across the three non-stationary levels, and the statistical significance of the error was largest ($p = 4.6E-10$ and $p = 2.3E-24$ by t-tests between Seg-NSeg and Seg-MPE, respectively), moderate ($p = 6.9E-5$ and $p = 1.3E-23$) and minimum ($p = 0.5$ and $p = 1.1E-14$) for $\sigma = 0.5$, $\sigma = 0.3$ and $\sigma = 0.1$ values, respectively, corresponding to the degree of the non-stationarity of the test data sets. These findings confirm that segmental Bayesian inference performs much better than the other methods in cases of highly non-stationary spike data.

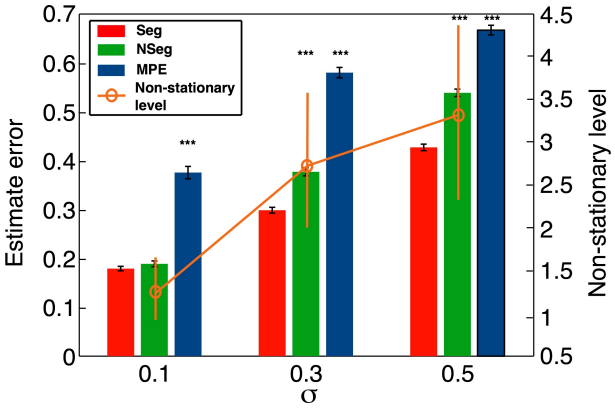

Figure 7: Superiority of segmental Bayesian inference (Seg, red columns) over two other methods (NSeg, green columns and MPE, dark blue columns) at three non-stationary levels of test data sets. The non-stationary level of the test data (orange trace) are from the results of Figure 5. Asterisks represent the significance level by t-tests between Seg-NSeg and Seg-MPE. $***p < 0.0001$.

4. Conclusions

The goal of our studies was to resolve the inverse problem of estimating two model parameters (g_i and g_c) from spike train data. The fact that there is a huge mismatch between the model and the brain, as well as the non-stationarity of the firing dynamics of real neurons inevitably cause the modeling errors and, consequently, the estimation errors. The segmental Bayes developed in our previous study [1] aimed to compensate for these errors by allowing segmental fluctuations of the parameter estimates in the neuronal constraint based. The segmental Bayes has been shown to perform better than the non-segmental Bayes and the minimum error method. It significantly improved the fitting between the simulation and experimental data in the feature space. However, the estimation accuracy has not yet been properly evaluated, because the true values for g_i and g_c were unknown in the experiment conditions.

In this paper, we attempted to verify the segmental Bayes approach using simulated spike data as the test data sets. Due to a rather low complexity of the model, the simulation data used for constructing the forward model is not suitable for the verification purpose. We thus manipulated the non-stationarity in the test data by adjusting the parameter values during the simulation. Since the true values of g_i and g_c were known in the test data, it was straightforward to evaluate the estimation errors. The two important findings in our previous study were confirmed from this study. First, segmental Bayes significantly reduces the estimation errors compared to the two comparative methods. Second, it is also robust to the non-stationarity of the spike data. These results suggest that segmental Bayes is highly recommended for estimating the model parameters from spike data of real neurons that usually exhibits highly non-stationary dynamics. In conclusion, we argue that the segmental Bayesian inference is a useful tool to resolve the inverse problem even in the presence of the imperfectness of the model.

Acknowledgments

The authors would like to thank Dr. Okito Yamashita, Dr. Masa-aki Sato, Dr. Mitsuo Kawato and Dr. Keisuke Toyama from the Advanced Telecommunications Research (ATR) institute for their supports to this study. HH was supported by Grant-in-Aid for JSPS Research Fellows. ITT was supported in part by Grants-in-Aid for Scientific Research (C) (No. 23560446) from MEXT of Japan.

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