An adaptive inverse controller for online somatosensory microstimulation optimization

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***Abstract*—Precise control of neural circuits via microstimulation is an indispensable but challenging objective in neuroengineering. The effect of electrical stimulation is imprecise and has a spatio-temporal blurring. At the neuron level, the effects are obfuscated by the complexity of neural dynamics. This paper proposes an online multiple-input-multiple-output (MIMO) adaptive inverse controller for somatosensory microstimulation. The control of the target firing pattern is achieved by including an adaptive controller before the stimulator whose transfer function is always adjusted to be the inverse of the neural circuit transfer function. In this paper a synthetic neural circuit is built from LIF neurons to model the neural circuit. Considering a Poisson model for the target spike train, we identify the LIF neural model using a Generalized Linear Model (GLM) fitted with a maximum likelihood (ML) criterion. The controller architecture becomes the inverse of the GLM and its parameters are periodically adjusted to ensure that the input to the LIF model approximates the target spike time response. In synthetic data, the results show that this control scheme successfully determines the impulse timing and amplitude of the desired stimuli and drives the dynamic neural circuit output to follow the target firing pattern. With the simulated model, the method is able to preserve the temporal precision of neural spike trains.**

I. INTRODUCTION

Microstimulation is a valuable tool to interface with neural circuits [1], [2]. The rapid advance of microelectrode arrays and electrophysiological recording techniques make it possible to simultaneously stimulate and record the activities of hundreds of neurons at a fine spatiotemporal resolution. This opens up new opportunities for precise control of the neural activity at neural and population levels. Microstimulation has already found a number of medical applications, such as Deep Brain Stimulation (DBS) in the treatment of Parkinson's Disease (PD) [3].

In this paper, we address the following computational problem: how to generate optimal microstimulation patterns so that the output of a neural circuit matches a target neural response. In addition, the system should be on-line and able to track system changes over time.

This work was supported in part by the U.S. National Science Foundation under Grant CNS-0540304, NSF Partnerships for Innovation Program 0650161, and Darpa project N66001-10-C-2008.

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Treating this as a control theory problem, the neural circuit to be controlled will be called the "plant", the control signal is the microstimulation, and the system output are multichannel spike trains. Instead of a conventional fixed feedback controller, which can only work under a stationary assumption or with known dynamics, we apply the adaptive inverse control methodology [4] to drive the unknown dynamic neural circuit. This system will be capable of controlling a time-varying plant, by using an adaptive model of the plant and using the inverse of this plant for control.

This control system has the unique challenge of dealing with spike timing (point process) models, which have different characteristics than typically discrete time continuous level systems Thus the criterion, cannot be the mean-square error (MSE), since the difference operation is not defined for spike trains. Instead, we use an inhomogeneous Poisson assumption for the spiking rate, commonly captured by a Generalized Linear Model (GLM) for neural data [5], and we maximize controller parameters based on a maximum likelihood (ML) model of the firing rate [6]. The GLM forms the base of the plant model and is initially trained offline to capture the function between the microstimulation and the neural response. The inverse controller is trained online by backpropagating the errors through the plant model. The plant model is also continuously adapted online to track any non-stationarity in the plant.

In this paper, we discuss the design of a Multiple-Input-Multiple-Output (MIMO) adaptive inverse control with ML criterion for neural spiking patterns that can be used to precisely control a nonstationary neural circuit to produce target spiking patterns. The method is demonstrated on a *simulated* neural circuit, and the results show that the inverse controller is able to generate the optimal stimulation with the target spike train as the input to the plant, and then precisely control the plant to output the target firing pattern.

II. SYSTEM DIAGRAM

The MIMO control system diagram is illustrated in Figure 1, where the plant (P) represents the neural circuit driven by the microstimulation control signal and produces a spike activity output. The controller (C) takes the target spike train as an input and produces a non-negative time series that represents current delivered by a physical stimulator system. In the simulation, the controller output is low-pass filtered with a Gaussian function to mimic the real microstimulation, and this smoothed signal is sent to the plant.

Theoretically, the adaptive controller transfer function is the inverse of the plant. However, the plant (P) transfer function is unknown so it is modeled offline by the plant model ($\hat{P}$) using adaptive system-identification techniques. For better modeling, the system feedback is applied to periodically adjust the plant model parameters and track dynamical plant changes.

Because the distribution of real spike trains is approximately Poisson, maximum likelihood (ML) is a much better cost function than MSE [6]. The system parameters are adjusted by maximizing the likelihood between the target spike train and the system output.

Optimization causes the adaptive inverse controller (C) to be the maximum likelihood inverse to the plant model ($\hat{P}$) for the given input spectrum. The adaptive algorithm attempts to make the cascade of plant (P), waveform simulator, and adaptive inverse controller (C) behave like a unitary transfer function, i.e. just a perfect wire with some delay. Therefore, if the target spike train is used as the command input of the inverse controller to generate the control signal, we can expect that the control signal is able to drive the plant such that the output spike train follows the target.

With the delay incorporated as shown in Figure 1, the inverse will be a delayed inverse where we set the delay to be half the order of the stimulus filter [4].

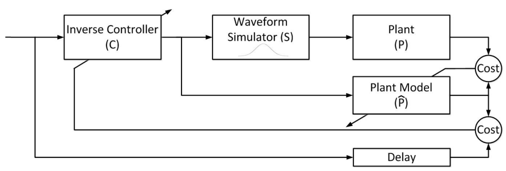

Fig. 1. **The adaptive inverse control system diagram**

A. Plant simulation

In the experiment, the plant is simulated by *a neural Circuit SIMulator* (CSIM). The network consists of 10 fully connected neurons. All neurons are modeled as Leaky Integrate-and-Fire (LIF) units. Neuron parameters [7]: membrane time constant 30ms, absolute refractory period 2ms (excitatory neurons), threshold 15mV (for a resting membrane potential assumed to be 0), reset voltage 14.3mV, constant nonspecific background current 13.5nA, input resistance 1MΩ and input noise 9nA. The postsynaptic current is modeled as an exponential decay $exp(-t/\tau_s)$ with $\tau_s = 3$ms. All neurons fire at a firing rate range (1Hz to 10Hz). This neural circuit has one current input and two spike-train outputs recorded from neuron 1 and neuron 2.

B. Plant model

The generalized linear model (GLM) is applied to model the plant, which estimates the functional relationship between the stimuli and the recorded spike trains of the two plant output neurons. The generalized linear model (GLM) is a powerful framework for modeling statistical relationships in point process data sets [5], which predicts the current number of spikes using the recent spiking history and the preceding stimulus. Two GLMs are trained independently based on maximum likelihood (ML) between the GLM output and the spike trains of the plant output neurons, as shown in Figure 2.

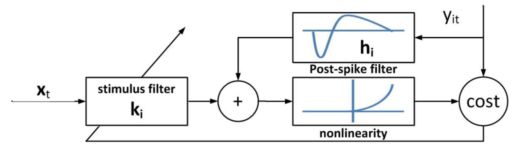

Fig. 2. **The GLM-based plant model contains two GLM model with the same input. x_t is the stimulation input. y_{it} represents the desire spike train recorded from the output neurons O_{it} in the neural circuit.**

Let y_{it} be the spiking activity of neuron i binned at a brief time resolution Δ (5 msec) and indexed by time t which is assumed to be a function of the recent spiking history and the preceding stimulus. Let $\mathbf{x}_t = (x_{t-\tau},...,x_{t-1})$ represent the vector of preceding stimuli up to but not including time t. Let $\mathbf{y}_{it} = (y_{it-\tau},...,y_{it-1})$ be a vector of preceding spike counts up to but not including time t. We posit that $\mathbf{y}_{it}$ is distributed according to a Poisson distribution whose conditional intensity λ_{it} is related to the stimulus and previous spiking history by

$$\lambda_{it} = f(\mathbf{k}_i \cdot \mathbf{x}_t + \mathbf{h}_i \cdot \mathbf{y}_{it} + \mu_i) \quad (1)$$

where $\mathbf{k}$ is a stimulus filter of the neuron, $\mathbf{h}$ is a post-spike filter to account for spike history dynamics and μ is a constant bias to match the neuron's firing rate when there is no input. In the GLM framework, f is an arbitrary invertible function termed a link function. If f is monotonic increasing function, there is a single optimal solution for the parameters. Here we select $f = exp(\cdot)$ for simplicity. In this case, a stimulus preceding time t that closely matches the filter $\mathbf{k}$ increases the average spike rate by a multiplicative gain $exp(\mathbf{k} \cdot \mathbf{x}_t)$. Likewise, if a spike occurs just prior to time t, the convolution of the spike occurrence (a delta function) with the post-spike filter diagrammed decreases the probability of a spike by factor $exp(\mathbf{h} \cdot y_t)$ to mimic more complex inter-spike interval properties such as refractory period or renewal processes.

The probability of observing the complete spike train Y_i is

$$Ł_{\theta_i} = \sum_t y_{it}(\mathbf{k}_i \cdot \mathbf{x}_t + \mathbf{h}_i \cdot \mathbf{y}_{it} + \mu_i) - \Delta \sum_t exp(\mathbf{k}_i \cdot \mathbf{x}_t + \mathbf{h}_i \cdot \mathbf{y}_{it} + \mu_i) \quad (2)$$

where $\theta_i = \{\mathbf{k}_i, \mathbf{h}_i, \mu\}$ and y_{it} is the spike trains recorded from output neuron i. We utilize the standard gradient-ascent algorithms to calculate the maximum likelihood estimate of θ.

C. Inverse controller

We design the inverse controller based on the structure of the GLM-based plant model, as shown in Figure 3. Let $\mathbf{d}_{1t} = (d_{1t+1},...,d_{1t+\tau})$ and $\mathbf{d}_{2t} = (d_{2t+1},...,d_{2t+\tau})$ represent the command inputs that are two target spike trains. According to the assumption of the GLM-based plant model that the y_t is only associated with τ preceding stimulus $\mathbf{x}_t = (x_{t-\tau},...,x_{t-1})$, x_t is estimated by the τ posterior spike trains

$$x_t = f(\mathbf{w}_1 \cdot \mathbf{d}_{1t} + \mathbf{w}_2 \cdot \mathbf{d}_{2t} + \nu) \quad (3)$$

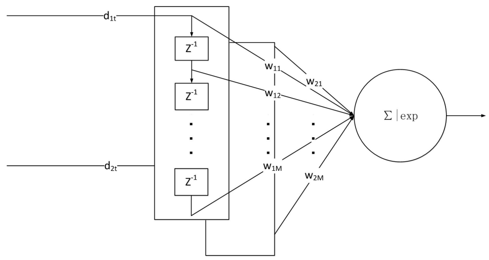

Fig. 3. **The inverse controller**

where $\mathbf{w}_1$ and $\mathbf{w}_2$ are posterior spike train filter of two neurons, ν is a constant bias to match the amplitude of the stimulus. The probability of the observing the desired spike train D is

$$Ł_\phi = \sum_{i=1}^{2}(\sum_t d_{it}(\sum_{m=1}^{M} k_{im} f(\mathbf{w}_1 \cdot \mathbf{d}_{1t-m} + \mathbf{w}_2 \cdot \mathbf{d}_{2t-m} + \nu) + \mathbf{h}_i \cdot \ \mathbf{d}_{it} + \mu_i) \\ -\Delta \sum_t exp(\sum_{m=1}^{M} k_{im} f(\mathbf{w}_1 \cdot \mathbf{d}_{1t-m} + \mathbf{w}_2 \cdot \mathbf{d}_{2t-m} + \nu) + \mathbf{h}_i \cdot \mathbf{d}_{it} + \mu_i)) \quad (4)$$

where $\phi = \{\mathbf{w}_1, \mathbf{w}_2, \nu\}$ and d_{it} is the input/desired spike train of neuron i. We utilize the standard gradient-ascent algorithms to calculate the maximum likelihood estimate of ϕ.

III. THE EXPERIMENT

A. The stimulus

A periodic current stimulation is input to the neural circuit generating the target spike train. The stimulation repeats every 2s and consists of four 500ms subsections of varying amplitude. In each 500ms section, there are two current impulses separated by 60ms with the same amplitude. The impulse amplitudes for the four subsections are 1500nA, 3600nA, 600nA and 150nA, respectively, as shown in Figure 4.

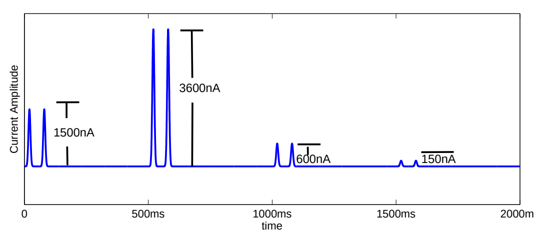

Fig. 4. **The desired periodic stimulation that is used to elicit the target spike trains**

B. The adaptation

The training set is generated by providing 10s of random stimulation (random timing and random amplitude within the safe stimulation ranges) to the plant and the resulting spiking output is recorded, which are used to train the plant model first. Once the plant model is trained, the inverse controller is also initially trained offline with the spiking output. The training of the inverse controller relies on a trained plant model.

After initialization, the target spike train is used as the command input of the inverse controller. The resulting stimulation is feed to both the plant and the plant model. At 2s interval the parameters of the inverse controller are adjusted by maximizing the likelihood between the output of the plant model and target spike trains. To maintain the stability of the system, we update the plant model every 10s with the corresponding output of plant as the desire signal. When the norm of the learning step is less than 10^{-4}, the adaptation is stopped.

C. Results

The tracking performance of the MIMO adaptive controller is shown in Figure 5. The comparison between the target spike train and the plant output spike reveals that even though not every spike in the reference spike train is reproduced, the controller certainly forced the output neurons to fire at a similar pattern and the precision of the spike timing is on average within in the order of 2ms. The cross correlation analysis further illustrates that the output spike train and the desire spike train are highly correlated with a time lag around 1ms, as shown in Figure 6. The cross-correlation curves also reveal the existing of the delay between the desire and the plant outputs.

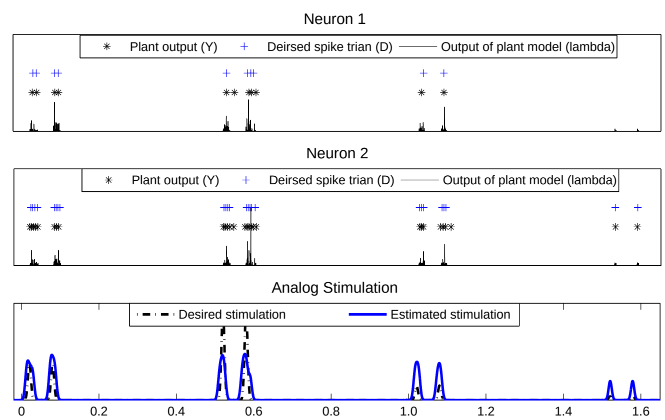

Fig. 5. **The tracking performance of the MIMO adaptive controller. The first two plots show the target spike trains (D), the output of the plant (Y), and the plant model output (λ) of the output neuron O1 and O2, respectively. The bottom plot compares the estimated stimulation that elicit the output spike train and the desired stimulation that elicit the target spike train.**

In addition, in order to investigate the ability of MIMO control system to determine the optimal stimulation, we compare the estimated stimulation and the desired stimulation that elicit the target spike train, as shown in Figure 5. The results reveal that our control system is capable of estimating not only the stimulation timing but also the amplitude varying pattern of the desired stimulation.The dynamics of the neural circuits induces the variance of the stimulation amplitude. However, the impulse width of the estimated stimulus is wider than the desired width. Therefore, future work will improve the design of the waveform simulator by considering the optimal width of the smoothing window or using other strategies.

Furthermore, Kolmogorov-Smirnov (KS) plots based on time-rescaling theorem [8] are applied to assess goodness-of-

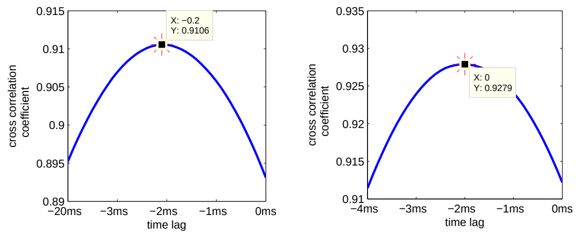

Fig. 6. **The cross correlation between the plant output and the desired spike trains**

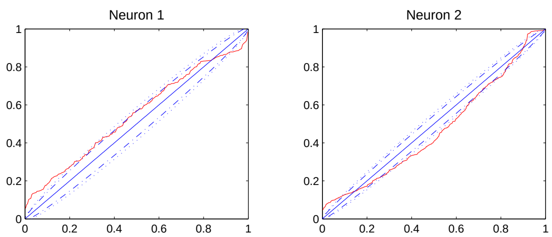

Fig. 7. **A Kolmogorov-Smirnov goodness-of-fit test of the GLM model via time rescaling the spike times and aligning them with target distribution. A diagonal line is ideal; dotted lines show confidence intervals.**

fit for the plant model, as shown in Figure 7, where the 45-degree line represents exact agreement between the modeled rate function and the desire spike train. For two neurons, the GLM-based KS plots fall around the 95% confidence bounds, which indicates that plant model of the rate functions captures the majority of desired spike trains. This result illustrates that the GLM-based plant model is able to identify functional relationship between the control signal and the spike train of the plant output.

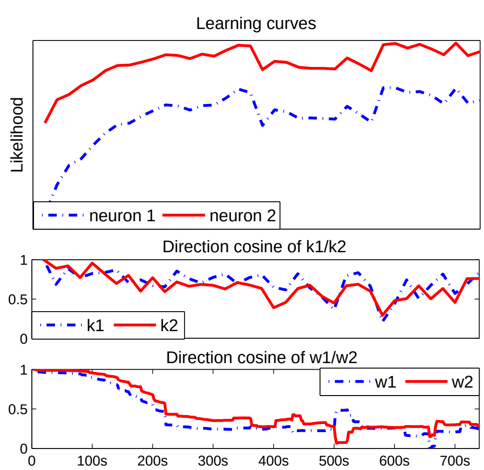

Fig. 8. **The control process of the nonstationary neural circuit. The top plot shows the learning curves of the plant model. The direction cosine evolution of the parameters of the plant model and the controller with respect to their initials are illustrated in the middle plot and the bottom plot, respectively.**

We also investigate the ability of the control system to track the nonstationarity of the neural circuit by looking at the learning curves of the plant model and the evolution of parameter direction cosine, as shown in Figure 8. In the top plot of Figure 8, the learning curve of the plant model increases fast at beginning demonstrating the ability of the GLM-based plant model to learn the plant functional organization progressively with the increase of available data. The nonstationarity of the neuron circuit induces the fluctuations of the learning curve. However, the plant model is able to learn this plant variation by adaptation. The direction cosine evolution of the parameters of the plant model and controller with respect to their initiations are shown in the middle and bottom plot in Figure 8, which illustrate that the plant model and inverse controller converge after the learning process. When the plant functional organization changes, the direction cosine of the plant model keep varying until it captures the new plant function organization. Meanwhile, the controller parameters vary right after the plant model updated, but converge fast to a new state with respect to the current plant model.

IV. Conclusions

In this paper, an MIMO adaptive inverse control system with ML criterion is developed to precisely control the firing pattern of a dynamic neuronal circuit follow the target spike trains. The goodness-of-fit test shows that GLM-based plant model is able to identify functional relationship of the plant between the control signal and the output spike train. According to maximizing the likelihood between the plant model output and the target spike trains, the parameters of the inverse controller is automatically adjusted to generate the optimal stimulation, which successfully drive the plant output follow the target spike trains. The accuracy of the spike timing is roughly 2ms on average. Moreover, the desired pattern of the impulse amplitude and timing is captured by the estimated stimulus that is generated by controller.

Acknowledgement

The authors thank Sohan Seth for useful discussions.

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