A Systems Identification Approach to Estimating the Connectivity in a Neuronal Population Model

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Abstract— **Mapping the brain and its complex networked structure has been one of the most researched topics in the last decade and continues to be the path towards understanding brain diseases. In this paper we present a new approach to estimating the connectivity between neurons in a network model. We use systems identification techniques for nonlinear dynamic models to compute the synaptic connections from other pre-synaptic neurons in the population. We are able to show accurate estimation even in the presence of model error and inaccurate assumption of post-synaptic potential dynamics. This allows to compute the connectivity matrix of the network using a very small time window of membrane potential data of the individual neurons. The specificity and sensitivity measures for randomly generated networks are reported.**

I. INTRODUCTION

Network models have always generated significant interest when being used to describe different physical phenomenon. They are considered extremely important as they are able to simulate the intereaction between the different individual elements. Network models exist in different mathematical forms such as statistical network models, artificial neural networks, coupled nonlinear dynamic models and are used in a variety of applications ranging from social network analysis to reconstructing the population dynamics of the neurons in the brain.

We focus on the ability of a coupled nonlinear dynamic model [1] to reproduce the spiking of a population of neurons [2] and the problem of computing the unknown coupling coefficients from the observation of the outputs of the individual neurons. Understanding the connectivity in a network of neurons is one of the active problems in computational neuroscience [3]. Accurate identification of synapses in the brain and tracking the changes in the synaptic connections is crucial in the research of brain diseases and in mapping the functional network of the neurons in the brain. There are a variety of methods in published literature that are used to estimate the functional connectivity of the brain. Statistical testing [4], partial directed coherence [5] and correlation measures [6] are a few of the approaches that do not require explicit models. However, these techniques need significantly long windows of time series data. Considering that the synaptic connections vary in time, it is not appropriate to use long time-windows of data. fMRIs have been used in [7] to successfully estimate functional connectivity

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in the hippocampal area of the brain but involve expensive equipment and cannot be implemented in real time. [8] have implemented Kalman filters to estimate the parameters of a coupled nonlinear dynamic model from membrane potential observations. Although this approach does not require large amounts of data to estimate the connectivity parameters, the convergence of the parameter estimates largely depends on the continuous time dynamics of the model used to simulate the neuronal spiking activity. A large group of neuron models involve discontinuities at the time of spikes and with a growing database of hybrid models [9] it is important to develop a technique that is able to produce results with the existing discontinuities.

In this paper we use a network of Izhikevich neurons [10] with linear coupling and exponentially decaying post-synaptic potentials to simulate population dynamics. The nonlinear dynamic model is then re-defined as a linear system with observed and reconstructed variables. We then use system identification techniques (recursive least squares estimation) to compute the connectivity parameters of the linear model. We present accuracy and robustness to noise results for test data generated by the model itself. To validate the ability of the method to produce results in real data we introduce a significant amount of model error by generating data from a population of Hodgkin-Huxley (HH) [11] neurons. The specificity and sensitivity measures are reported for a network of twenty neurons.

II. POPULATION DYNAMICS

In this section we describe the nonlinear dynamic model and the coupling between the individual neurons of the network. We extend the single neuron model, described in [10], to represent the dynamics of a neuronal network. As established in [2] and [12], neurons are connected to each other by synapses. As pre-synaptic neuron fires a post-synaptic potential is generated. The collection of the post-synaptic potentials from all connected pre-synaptic neurons is the synaptic current, that acts as an input to the post-synaptic neuron. Fig. 1 is a block diagram representation of
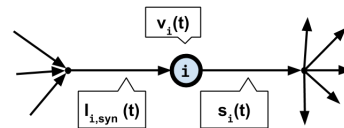

Fig. 1. Block diagram of the ith neuron in a network.

a single neuron in a network where $I_{i,syn}(t)$ is the synaptic current to neuron i, $v_i(t)$ is the membrane potential recording

and $s_i(t)$ is the post-synaptic potential. The differential equations used to model the membrane potential, $v_i(t)$, and the recovery variable, $u_i(t)$ of neuron i in the population is -

$$\dot{v}_i(t) = p_{i1}v_i^2(t) + p_{i2}v_i(t) + p_{i3}[u_i(t) - I(t)] + p_{i4}$$
$$+ I_{i,syn}(t) \tag{1}$$
$$\dot{u}_i(t) = p_{i5}v_i(t) + p_{i6}u_i(t)$$

We model the synaptic current, $I_{i,syn}(t)$ as a weighted sum of the post-synaptic potentials, $s_j(t)$, modeled as decaying exponentials with multiple time constants.

$$I_{i,syn}(t) = \frac{g}{N}\sum_{j=0, j\neq i}^{N} w_{ij}s_j(t), \qquad s_j(t) = \sum_{m=1}^{M}\alpha_m s_{j,m}(t)$$
$$\dot{s}_{i,m}(t) = -\frac{1}{\tau_m}s_{i,m}(t), \qquad m = \{1,..,M\}$$
$$\tag{2}$$

The Izhikevich neuron also employs a discrete reset that is activated on detecting a spike. If $v_i(t)$ crosses the threshold of 30 mV

$$v_i(t) = p_{i7}; \; u_i(t) = u_i(t) + p_{i8}; \; s_{i,m}(t) = s_{i,m}(t) + 1 \tag{3}$$

Eqs.1,2,3 together define the nonlinear dynamic model that generates the spiking pattern observed in a network of neurons. g is a scaling factor that defines the glial strength of the population. N is the total number of neurons in the network. We model the post-synaptic potential as a decaying exponential with two time constants, $\tau_1 = 5ms$ and $\tau_2 = 300ms$. The corresponding scaling coefficients are $\alpha_1 = 0.8$ and $\alpha_2 = 0.2$. w_{ij} is the numerical representation of the connection from the pre-synaptic neuron i to the post-synaptic neuron j. It is quantified as $+1$ if the pre-synaptic neuron is excitatory, -1 for an inhibitory pre-synaptic neuron and 0 if neuron's i and j are not connected. $\boldsymbol{p}_i = [p_{i1},...,p_{i8}]^T$ represents the parameter vector of the individual neuron i and $I(t)$ is the external input current that stimulates all of the neurons in the population.

Fig. 2 shows the membrane potentials (left) of all neurons in the population. It is observed that the spiking activity is irregular. The spike rate of each neuron depends on the characteristics and type of the neuron, as well as the connectivity to the other neurons in the network. The figure on the right represents the states of an individual neuron of the population. The synaptic current input is shown on the top row, membrane potential in the middle row and the post-synaptic potential in the bottom row.

III. CONNECTIVITY ESTIMATION

We re-define the nonlinear model described in the earlier section as a linear autoregressive moving average (ARMA) model. This enables us to then use system identification techniques to estimate the parameters.

A. Linear system (discrete time) :

Computation of unknown parameters in a linear system using a least squares based estimation approach is well es-
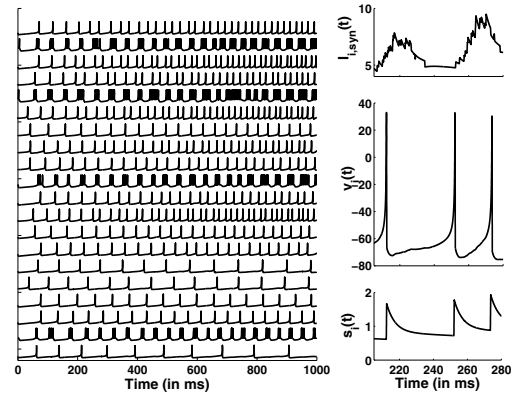

Fig. 2. Population dynamics of a network of 20 neurons (left) and states (synaptic current, membrane potential, post-synaptic potential) of the individual neurons (right)

tablished. This method can be extended to nonlinear dynamic models if the following requirments can be met - (a) the model can be redefined such that it is linear in the parameter space and (b) the redefined inputs and outputs are in terms of observable and reconstructed state variables. In our model of a neuronal population, the membrane potentials of the individual neurons are observed and the synaptic currents are reconstructed from the knowledge of the spike times of the neurons. We assume that the dynamics of the post-synaptic potential are known.

The continuous time variables described in Eqs. 1,2 are discretized and the Euler's forward method is used to approximate the first derivative terms. The constant time-step is chosen as $T = 0.01$. Rearranging the terms and eliminating the unobserved recovery variable, $u_i(k)$, we are able to define the membrane potential as the output of a linear system. The nonlinear term in the equation, $v_i(k)^2$ is treated as a delayed input to the system to maintain causality and linearity.

$$A_i(z)v_i(k) = B_i(z)vs_i(k) + \sum_{j=1, j\neq i}^{N} C_{i,j}(z)s_j(k-1)$$
$$+ D_i(z)I(k-1) + d_i \tag{4}$$

where $vs_i(k) = v_i^2(k-1)$. A, B, C and D can be expressed as FIR filters. Ignoring the T^2 terms, they can be written in terms of the nonlinear model parameter vector, $\boldsymbol{p}_i$ and the synaptic connections, w_{ij}.

$$A_i(z) = 1 + \{-2 - (p_{i2} + p_{i6})T\}z^{-1}$$
$$+ \{1 + (p_{i2} + p_{i6})T\}z^{-2}$$
$$B_i(z) = p_{i1}T - p_{i1}Tz^{-1}$$
$$C_{i,j}(z) = \left[\frac{gT}{N}\right]w_{ij} - \left[\frac{gT}{N}\right]w_{ij}z^{-1} \tag{5}$$
$$D_i(z) = -p_{i3}T + p_{i3}Tz^{-1}$$
$$d_i = -p_{i4}p_{i6}T^2$$

k in Eq. 4 is an integer and represents the index. We use z-transforms to describe the dynamic system where $z^{k_0}x(k) = x(k + k_0)$.

B. Recursive least squares estimation :

Parameter estimation in linear systems is a field that has been extensively researched. There are a variety of existing system identification algorithms that have performed well in tests of accuracy, speed and robustness [13]. However, the performance of such techniques also depend on the dynamics of the system. We tested different system identification algorithms on our model - instrumental variable approach, output error least squares and least squares [14]. We found that the least squares method, implemented as a recursive storage algorithm by considering the membrane potential in between two successive spikes had the best performance with respect to accuracy and robustness.

The linear ARMA system of a neuronal network (Eq. 4) can be written in terms of a parameter vector, $\boldsymbol{\theta}_i$, that contains the coefficients of the FIR filters and a regressor, $\boldsymbol{\varphi}_i(k)$.

$$v_i(k) = \boldsymbol{\varphi}_i(k)^T \boldsymbol{\theta}_i \qquad (6)$$

$$\boldsymbol{\varphi}_i(k) = [vs_i(k), vs_i(k-1), s_j(k-1), s_j(k-2),$$
$$I(k-1), I(k-2), u(k), -v_i(k-1), -v_i(k-2)]^T$$
$$\boldsymbol{\theta}_i = [b_{i,0}, b_{i,1}, c_{i,j,0}, c_{i,j,1}, d_{i,0}, d_{i,1}, d_i, a_{i,1}, a_{i,2}]^T \qquad (7)$$

where $j \in \{1, 2, \cdots, N\}, j \neq i$ and $vs_i(k) = v_i(k-1)^2$. $u(k)$ represents the step input.

The linear model represents the continuous dynamics of the spiking of the neuron, Eqs 1,2. The discrete reset, Eq. 3 in the neuron model means that the system has a discontinuity at the time of spikes. We therefore implement the recursive storage least squares algorithm by computing the parameters over the time window in between two successive spikes, known as the inter-spike interval (ISI) [12]. The estimate is updated over every ISI. This ensures that the discontinuity in the membrane potential does not affect the system identification algorithm.

$$\boldsymbol{q}_{i,s} = \sum_{k=k_{s-1}+\frac{\tau}{T}}^{k_s} \boldsymbol{\varphi}_i(k)\boldsymbol{\varphi}_i(k)^T, \quad \boldsymbol{Q}_{i,s} = \boldsymbol{q}_{i,s} + \lambda \boldsymbol{Q}_{i,s-1}$$

$$\boldsymbol{p}_{i,s} = \sum_{k=k_{s-1}+\frac{\tau}{T}}^{k_s} \boldsymbol{\varphi}_i(k)y_i(k), \quad \boldsymbol{P}_{i,s} = \boldsymbol{p}_{i,s} + \lambda \boldsymbol{P}_{i,s-1}$$

$$\hat{\boldsymbol{\theta}}_{i,s} = \boldsymbol{Q}_{i,s}^{-1}\boldsymbol{P}_{i,s} \qquad (8)$$

where k_s represents the discrete index of the sth spike. Storing the $\boldsymbol{Q}$ and $\boldsymbol{P}$ matrices recursively allows us to include a forgetting factor, λ. By running multiple simulations we found that $\lambda = 0.8$ ensures that the algorithm is robust with respect to noise but is capable of estimating time varying parameters.

The connection parameters, w_{ij} can be coomputed by using the relations defined in Eq. 5.

$$w_{ij} = \frac{(\hat{c}_{i,j,0} - \hat{c}_{i,j,1})N}{gT} \qquad (9)$$

IV. RESULTS

A. Model generated test data :

We first test our method using data generated by the model. Measurements of the individual membrane potentials are corrupted by white noise. We report the accuracy of the method as a function of increasing noise to signal variance. Fig. 3 shows the mean and standard deviation of the absolute relative error of parameter estimates for the entire population (top). The statistics of the distributions for each noise level are computed across different networks (of 20 neurons) with 40% connectivity. 80% of the neurons were excitatory and 20% were inhibitory. Simulations were run for 2000 ms and the final estimates are computed by averaging the parameter convergence results for the last 500 ms. The error is within acceptable levels for noise percentages less than 5%. The convergence of some of the parameters and the mean square error is also shown (bottom). Convergence is achieved in 500ms.
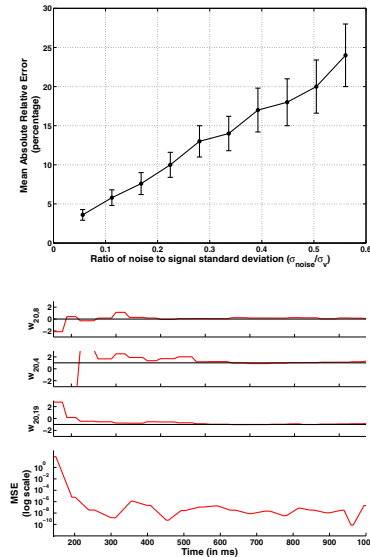

Fig. 3. Mean Absolute Relative Error for varying noise levels and convergence of parameters

B. Identifying connections in a different neuronal model :

In this section we generate membrane potential data from neuronal population models (20 neurons with 40 % connectivity) based on the Hodgkin Huxley neuron [11]. The dynamics of the post-synaptic potentials in the population were the same as that described in Eq. 2. The pre-synaptic neurons are classified as excitatory (80 %) and inhibitory (20 %). Fig. 4 shows the trace of a membrane potential from an HH neuron. The unshaded (white) regions are considered as the ISI data for the recursive storage least squares algorithm, Eq. 8. The time of spike is computed by thresholding, and the spike width is assumed to be 2ms. The bottom subplot shows the actual (blue) and reconstructed (red) post-synaptic potentials (psp). We assume that the psp increases during a spike and then decays exponentially. However, the 'jump' and time constant of the decay are incorrectly assumed to further increase the model error.
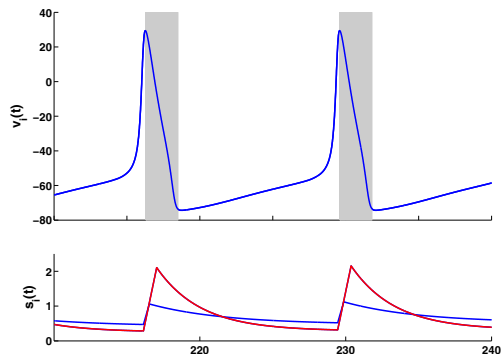
Fig. 4. Observed membrane potential of an individual HH neuron with the spike (unshaded) and reset (shaded) regions. The spike region is used as the ISI data to estimate parameters (Eq. 8)

The results of the estimated connectivity matrix for networks with directed connections are reported. This is representative of a population of neurons in which the presence of a synapse from neuron i to neuron j does not ensure a connection from neuron j to neuron i. Methods that compute the correlation matrix from individual membrane potential measurements are unable to capture this feature of neuronal connectivity. The model error introduces a scaling factor in the estimates. However, the nature of the connection is computed correctly. We normalize the result to be able to compare the actual and estimated connectivity matrix on the same scale. Fig. 5 shows the normalized results compared to the true connections. We use kmeans [15] algorithm in MATLAB to cluster the estimated connections into $\{+1, 0, -1\}$. The clustered results are then used to compute the specificity and sensitivity measures. The means and standard deviations of 1000 simulations with randomly generated networks are reported in Table I.

TABLE I
SPECIFICITY AND SENSITIVITY MEASURES FOR A 20-NEURON NETWORK.

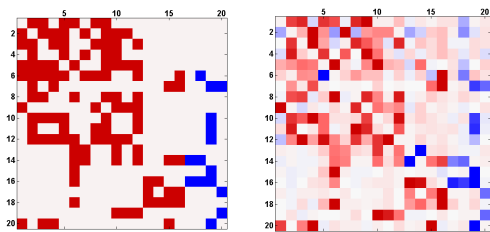| Specificity	Sensitivity
0.93 ± 0.03	0.87 ± 0.05

Fig. 5. True (left) and estimated (right) connectivity shown on the same color scale. Red corresponds to a connection strength of $+1$ and blue represents -1.

V. CONCLUSIONS AND FUTURE WORK

A. Summary

Our ojective was to estimate the connectivity of a neuronal population from observations of membrane potentials of individual neurons. We used linearly coupled Izhikevich neurons to simulate the population dynamics. The nonlinear model was mathematically re-defined as an ARMA system which enabled us to use the least squares algorithm for system identification. We demonstrated the performance of this method in the presence of model error by using it to estimate the connectivity of a network of HH neurons. We established that the technique produces accurate results for a network of twenty neurons and is robust to significant amount of observation noise.

B. Future work

While our method is successful in computing the connections of moderate size networks, it is important to extend this to larger networks (100 neurons). Also, the technique can be adapted to be used with other nonlinear dynamic models with linear coupling, such as extracellular models of groups of neurons. This would enable us to estimate the synaptic strengths in *in vitro* recordings from neuronal tissue.

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