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Large Scale Parameter Estimation for Nonlinear Dynamic Systems: Application on Spike-In, Spike-Out Neural Models

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***Abstract*— This paper presents a general method of parameter estimation for large-scale non-linear dynamic models a with particular focus on parameter estimation for spike-in, spike-out neural models. The aim is to provide a convex optimization algorithm for tuning parameters of such a model which enables solving large-scale estimation problem in a linear time. Parameter estimation for a single layer neural network containing hundreds of synapses is addressed and efficiency/performance of the proposed methodology is demonstrated by solving a few examples. It will be also demonstrated that parameters of the model for mapping CA3 output of hippocampus cell into CA1 output, under patch clamp experiment, can be successfully estimated by utilizing the methodology of this paper.**

***Index Terms*—hippocampus, nonlinear dynamical system, parameter estimation for linear dynamical systems, time variant models, spiking neural network, plasticity**

I. Introduction

SPIKE-IN, SPIKE-OUT models for processing neural activities have become a focusing topic in the field of neural engineering and machine learning during last decade. Though modeling spiking activities of the entire brain's neurons is the driving force for creation of these models, neural engineering applications are the other emerging technology which require spiking models for processing, encoding and decoding of brain's spiking signals. Wide variety of neural engineering applications have been developed thus far requiring spike-in, spike-out models; some examples are: 1) neural prosthetic devices to substitute a specific region of the brain which has input-output structure such as those are being developed in research for enhancing or restoring damaged or lost cognitive functionality of the brain (cognitive prosthesis). More specifically, in case of some diseases – anterograde amnesia, stroke, epilepsy, Alzheimer's – or accidents, Hippocampus of the brain will no longer form new long-term memories. To restore the lost functionality of the Hippocampus, mathematical models of the Hippocampus regions are developed to map spiking activities of the Entorhinal Cortex through Dentate Gyrus – input of the hippocampus – to the CA1 which is the output of the Hippocampus [1]. 2) Spiking models are used in the domain of re-animating paralyzed muscles of patients who have spinal cord injury. To achieve this goal, either healthy residual neurons is stimulated or direct electrical stimulation of muscle fibers is performed. In this scenario, activities of the motor cortex is projected to the muscle fibers utilizing the mathematical approach mentioned in the example one. 3) Adaptive biventricular pacemaker with a spiking neural network coprocessor is another application in which optimal pacing intervals for a given heart condition is estimated and provided to the heart. 4) Machine vision for controlling robots and pattern recognition applications in decision making require a brain like models which broadens the spike-in spike-out model application.

The commonality between all these applications is the utilization of bio-inspired mathematical models which receive inputs from real neurons i.e, spike and generate output spikes to the next layer of biological cells.

It is widely accepted that the underlying signal processing capability of a neuron is derived from its capacity to change input sequences of inter-spike intervals into different, output sequences of inter-spike intervals [2,3]. In all brain areas, the resulting input/output transformations are strongly nonlinear, highly dynamic, and may be non-stationary which are due to the inherent nonlinearities, and nonstationarities embedded in the molecular, and cellular mechanisms of neurons and its synapses. The nervous system in macroscopic and microscopic scale is dynamic and has plasticity in short and long term (STP, LTP). Biological evidences show that nervous system responds to sensory and cognitive tasks in less than a few millisecond indicating that neurons operation is based on exact spike timing. Though a significant number of models have been proposed for Spike Time Dependent Processing – STDP – of stimulus, utility of these models has remained limited for neural engineering applications. While the models have represented essential nonlinear dynamic and temporal capabilities of the neuronal systems, their parameter estimation/adaptation for large scale modeling tasks has not been explored and in general application of such models has been limited to small size problems. This is due to the high degree of nonlinear dependency between the input-output of the model and the free parameters of the nonlinear system rendering the parameter estimation of the these systems to be a very challenging task.

Main focus of the current study is to present a methodology for parameter estimation/adaptation of highly temporal, nonlinear, and large scale spike-in-spike-out models.

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Mathematical formulation for estimating and optimization of the model parameters is provided. The proposed method has the property that unknown parameters of the nonlinear dynamic system establishes an affine relationship between state variables and input-output of the model. The presented methodology enables online tuning of the parameter through the time utilizing linear programming approaches (this is not a topic of this paper). A large scale spiking neural network built upon Dynamic Synapse concept is considered as a case study. The Dynamic Synapse Neural Network of this study had 500 synapses consisting of 1000 unknown parameters. The parameters were estimated under two conditions: a) random spike trains provided to the dynamic synapse model with known parameters and output spike train was generated by the model. The task was to reproduce the parameters of the dynamic synapse model employing the same input and output, and b) input-output spiking activities of rat's Hippocampus recorded from CA3-CA1 neurons was modeled and reproduced utilizing the dynamic synapse model and the methodology of the current paper.

II. Parameter Estimation for nonlinear dynamical systems

The presented models for neural processing have the following general structure:

$$\dot{x} = f(x, t, \theta, u), \quad x(t_0, \theta, u_0) = x_0 \tag{1}$$

The equation stated in (1) is a set of nonlinear ordinary differential equations in which $\theta \in \mathbb{R}^{n_\theta}$ is a vector of unknown parameters (e.g. facilitation and depression factors in synaptic transmission models), t is the time, $u \in \mathbb{R}^{n_u}$ is time dependent input spike train, and $x \in \mathbb{R}^{n_x}$ is a time dependent state variables. The nonlinearity embedded in neural process is modeled by f which maps $\mathbb{R}^{n_x} \times \mathbb{R}^1 \times \mathbb{R}^{n_\theta} \times \mathbb{R}^{n_u} \to \mathbb{R}^{n_x}$. In order to estimate unknown parameters of the system, θ, and calculate the state variables, x, there is a need for sufficient number of observations. Some of state variables can be observable, i.e., neuron's membrane potential which their value is known only at the time of firing. Excluding the observable variables, the rest of state variables cannot be observed and represent phenomenological mechanisms of the corresponding synapse or neuron. If number of observable states to be denoted by n_{obs} then there will be $n_{unobs} = n_x - n_{obs}$ unobserved states. The observations can be collected either from weighted summation of the state variables (e.g., a neuron's inputs from multiple synapses) and/or from individual state variables depending on the physical structure of the system. Therefore:

$$y_j(t) = \sum_l w_l^j \, x_l(t)\,, \qquad t = 1, \dots, T, \tag{2}$$

in which x_l is the l^{th} component of the state variables – may or may not be observed – and w_l is known constant weights. Observations only take place at the time of spikes at which the membrane potential exceeds a firing threshold. In this scenario, the equation (2) can be rewritten as following:

$$y_j\left(t_{sp}^i\right) = \vartheta_{thr}, \quad i = 1, \dots, M \tag{3}$$

where ϑ_{thr} is the membrane's firing threshold and i is the time index at which membrane voltage has reached the threshold voltage. Error between the observations and the model presented by equation (1) can be defined as:

$$r_j\left(t_{sp}^i\right) = y_j\left(t_{sp}^i\right) - \vartheta_{thr}, \; i = 1, \dots, N_{sp}, \tag{4}$$

The method of estimating unknown parameters depends on the assumptions and knowledge about the measurement errors. Though in the following sections, least square objective function for error minimization is considered, other objective functions will be also discussed in the future publications.

A. *Solving Nonlinear State Space Model*

In order to find unknown parameters θ, it is assumed that unknown parameters are constant, $\dot{\theta} = 0$, and therefore equation (1) can be reformulated as:

$$\begin{bmatrix} x_1 \\ x_2 \\ \dots \\ x_{n_x} \\ \theta_1 \\ \dots \\ \theta_{n_\theta} \end{bmatrix}^{\bullet} = \begin{bmatrix} f^{(1)}(x, \theta, t, u) \\ f^{(2)}(x, \theta, t, u) \\ \dots \\ f^{(n_x)}(x, \theta, t, u) \\ 0 \\ \dots \\ 0 \end{bmatrix}_{(n_x + n_\theta) \times 1} \tag{5}$$

For simplicity, the equation (5) can be presented in an abstract form which is :

$$\mathbb{X}^{\bullet} = F(\mathbb{X}, t, u), \;\; \mathbb{X} = [x_1, \dots, x_{n_x}, \theta_1, \dots, \theta_{n_\theta}]^{tr} \tag{6}$$

The first step in estimating unknown parameter is expanding the function F around a sample point k using Taylor series (higher order terms are ignored). Therefore:

$$\mathbb{X}_{k+1}^{\bullet} = F_k(\mathbb{X}_k, t, u) + \nabla F_{\mathbb{X}_k} \cdot (\mathbb{X}_{k+1} - \mathbb{X}_k) \tag{7}$$

in which $\mathbb{X}_{\mu \times 1}$ ($\mu = n_x + n_\theta$) represents new state variables i.e. $\begin{bmatrix} x_{n_x \times 1} \\ \theta_{n_\theta \times 1} \end{bmatrix}$ and:

$$\nabla F_{\mathbb{X}_k} = \begin{bmatrix} \frac{\partial f_k^{(1)}}{\partial x_1} & \frac{\partial f_k^{(1)}}{\partial x_2} & \dots & \frac{\partial f_k^{(1)}}{\partial \theta_1} & \frac{\partial f_k^{(1)}}{\partial \theta_2} & \dots \\ & & \dots & & & \\ & & \dots & & & \\ \frac{\partial f_k^{(n_x)}}{\partial x_1} & \frac{f_k^{(n_x)}}{\partial x_2} & \dots & \frac{\partial f_k^{(n_x)}}{\partial \theta_1} & \frac{\partial f_k^{(n_x)}}{\partial \theta_2} & \dots \\ & & \mathbb{0}_{n_\theta \times \mu} & & & \end{bmatrix}_{\mu \times \mu} \tag{8}$$

is the Jacobin of F at step k and $\mathbb{0}$ is a $n_\theta \times \mu$ zero matrix. Please note that linearization is performed with respect to state variables and not variable t.

Equation (7) is the key equation in the simulations; it is a first order linear differential equation which is an approximation for the nonlinear ordinary equation which was expressed by (1). Solution of a linear differential equations is *linear combination* of particular, $P(t)$, and homogeneous, $h(t)$, solutions where particular solution $P(t)$ is the response of the system to its inputs with known initial conditions and

$h(t)$ is the impulse (or zero input) response of the system. Therefore at any step k, the solution of the (7) can be expressed as:

$$\mathbb{X}_{k+1}(t) = P(t) + \theta_1 h_1(t) + \theta_2 h_2(t) + \cdots + \theta_{n_\theta} h_{n_\theta}(t) \quad (9)$$

in which unknown parameters of the system are expressed in a linear weighted summation of homogenous and particular solutions. The particular solution of (7) is found by:

$$P^{\bullet} = F_k(\mathbb{X}_k, t, u) + \nabla F_{\mathbb{X}_k} \cdot (P - \mathbb{X}_k),\ P(0) = \mathbb{X}(0) \quad (10)$$

and impulse (or zero input) response of the equation (7) is:

$$h^{\bullet} = \nabla F_{\mathbb{X}_k} \cdot h \quad (11)$$

The impulse response h should be solved under different initial conditions for each state variables:

$$h_1(0) = \begin{bmatrix} \mathbb{0}_{n_x \times 1} \\ 1 \\ \mathbb{0}_{(n_\theta - 1)\times 1} \end{bmatrix},\ h_2(0) = \begin{bmatrix} \mathbb{0}_{(n_{x+1}) \times 1} \\ 1 \\ \mathbb{0}_{(n_\theta - 2)\times 1} \end{bmatrix},\ \ldots,\ h_{n_\theta}(0) = \begin{bmatrix} \mathbb{0}_{(n_x + n_\theta - 1)\times 1} \\ 1 \end{bmatrix} \quad (12)$$

B. *Optimization*

Parameter estimation in dynamical models is computationally intensive process, since it requires a repetitive numerical solution for the underlying set of differential equations. Efficient and robust methods for solving this problem is important for the development and improvement of the processing models. It is recommended that the reference [6] to be studied for techniques regarding general information about parameter estimation for nonlinear dynamical systems.

The set of equations presented in (9) is an affine transformation with respect to the unknown parameters. The parameters can be estimated after solving the homogenous and particular solution's differential equations stated in (10) and (11). Therefore:

$$\mathbb{X}_{k+1}(t) - P(t) = \left[h_1(t)\ h_2(t) \ldots\ h_{n_\theta}(t) \right] \begin{bmatrix} \theta_1 \\ \theta_2 \\ \ldots \\ \theta_{n_\theta} \end{bmatrix} \quad (13)$$

where $h_i(t)$, and $i = 1, 2, \ldots, n_\theta$ is a $T \times 1$ vector which T is the time duration of simulation. A subset of the state variables $\mathbb{X}$ which presents membrane potential, are observed at the time of spike. The observed value of the states in $\mathbb{X}$ is set to be ϑ_{thr}, because at the time of spike, membrane potential reaches to a firing threshold. Equation (13) can be solved under different constraints depending on how the mathematical model has been formed. Since membrane potential is greater than a threshold voltage at the time of firing so one may reformulate and solve (13) under constraint that $V > \vartheta_{thr}$.

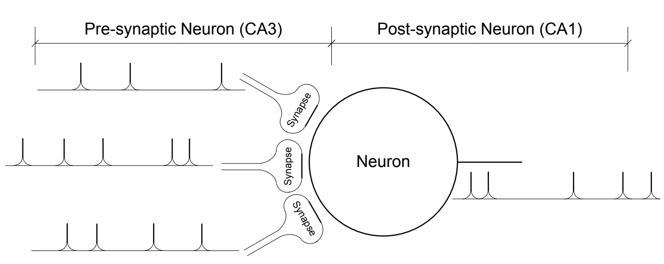

Fig. 1: Connection between multiple synapses and a neuron

TABLE I: PARAMETERS OF THE SYNAPSE MODEL

Symbol	Quantity	Typical value
τ_f	Facilitation time constant	$50 < \tau_f < 500$ mili-second
F_0	Resting facilitation	$0 < F_0 < 1$
ΔF	Facilitation factor	$0 < \Delta F < 1$
τ_r	Vesicle recovery time constant	$100 < \tau_r < 1500$ mili-second
N_{max}	Maximum number of release sites	$1 < N_{max} < 50$
a_2, a_1, a_0	15, 75, 125	$a_2 = 3a$, $a_1 = 3a^2$, $a_0 = a^3$; $a = 5$,

III. CASE STUDY OF DYNAMIC SYNAPSE NEURAL MODEL

A. *Dynamic Model of Synapse and Neuron*

Throughout the rest of this paper a few examples will be considered. A simple case of a single synapse which is connected to a single neuron is described in this section. Dynamic model of synapse which is built upon Facilitation-Depression (FD) model [4] has been used in this article which is defined as:

$$dF/dt = -(F - F_0)/\tau_f + (1 - F) \cdot \Delta F \cdot AP(t - t_{ap}) \quad (14)$$

$$dN/dt = -(N - 1)/\tau_r - F_{t^+} \cdot N \cdot AP(t - t_{ap}) \quad (15)$$

The state variable F describes facilitation dynamics in response to incoming action potentials, APs, and variable N represents the portion of release-ready vesicles. Parameter ΔF controls calcium influx in the presynaptic terminal of a synapse, and it is the main biological factor in modulating synaptic dynamics. Facilitation increase and vesicle release dynamics process are both driven/adjusted by action potentials where the AP time is defined by $AP(t - t_{ap})$. Post Synaptic Potential – PSP – is generated by integrated sum of released vesicles:

$$V^{\cdots} + a_2 V^{\cdot\cdot} + a_1 V^{\cdot} + a_0 V = \sum_{i=1}^{nSynapse} N_{max}^{(i)} \cdot release^{(i)}(t - t_{sp}^{i}) \quad (16)$$

$$release^{(i)}(t - t_{sp}^{i}) = F_{t^+}^{(i)}(t) N^{(i)}(t) AP(t - t_{sp}^{i}) \quad (17)$$

PSP of a single synapse in equation (15) is a non-linear function of synapse state variables – $F_{t^+} \cdot N$ – and it is the interplay of facilitation and vesicle recovery/release that determines the temporal dynamics of the synaptic response. Equation (16) is a third order differential equation which utilizing parameter values shown in Table I, it generates an alpha exponential function. Parameter N_{max} is a post-synaptic dependent factor which represents number of neurotransmitter receptors or simply synaptic strength and $nSynapse$ is the number of synaptic connections. The FD model proposed in equation (14-17) defines the fundamental biological

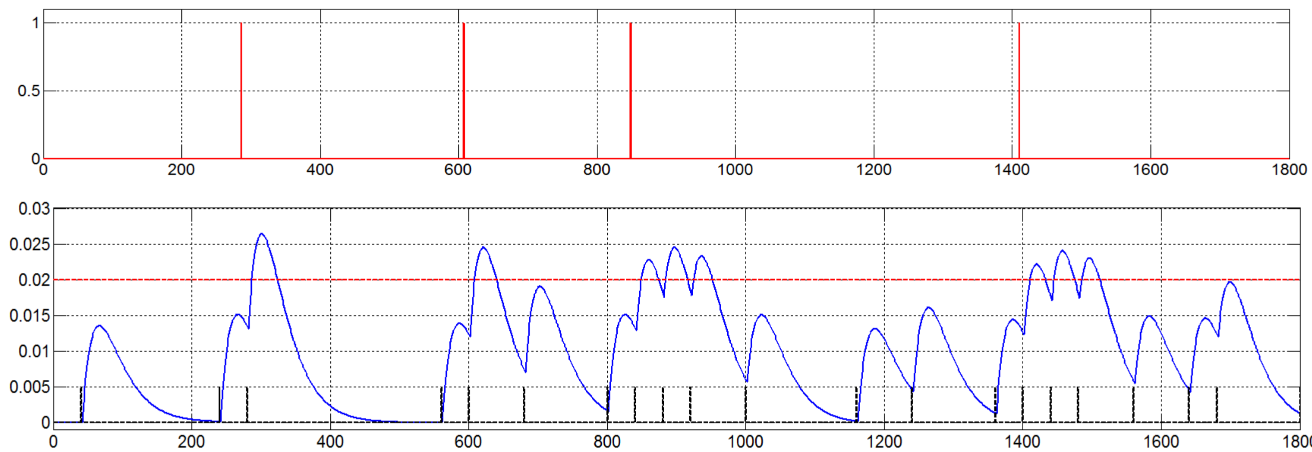

Fig. 2: Blue is the membrane potential, black vertical bars are input action potentials and red vertical bars (top graph) are membrane's action potential (t = 286, 608, 849, 1410 millisecond). The red horizontal is the $\vartheta_{thr} = 0.02$ threshold line. In this example, the simulation parameters are $N_{max} = 0.8$, and $\Delta F = 0.18$.

components shaping synapse temporal dynamics.

Considering the neuron/synapse model introduced by equations (14) through (17), and with applying a minor modification on the state equations, the following state space model is formed:

$$\begin{bmatrix} F \\ N \\ V_1 \\ V_2 \\ V \\ \Delta F \\ N_{max} \end{bmatrix}^{\bullet} = \begin{bmatrix} -(F-F_0)/\tau_f + (1-F)\cdot\Delta F\cdot AP(t) \\ -(N-1)/\tau_r - F\cdot N\cdot AP(t^-) \\ -a_2V_1 - a_1V_2 - a_0V + F\cdot N\cdot N_{max}\cdot AP(t^-) \\ V_1 \\ V_2 \\ 0 \\ 0 \end{bmatrix} \tag{18}$$

in which $V^{\cdot} = V_2$, $V^{\cdot\cdot} = V_2^{\cdot} = V_1$ are state variables of the equation (16). The model expressed by (18) transforms input spike train AP – input to the synapse – into another spike train generated by neuron's membrane. The input, $AP(t)$, is known and given for the simulations. Membrane potential V is partially observed and its value is only known at neuron's firing time; therefore $V(t) = \vartheta_{thr}|_{t=t_{sp}}$. The unknown parameters of the (18) are ΔF, and N_{max} (facilitation factor and synaptic strength respectively) which are supposed to be estimated using the observed data.

To show performance of the algorithm, case study of a single synapse, single neuron was simulated with $\Delta F = 0.18$, and $N_{max} = 0.8$. A random input spike train was produced and provided to the synapse and output spike train was generated when membrane potential exceeded the threshold $\vartheta_{thr} = 20$ milivolt. Figure 2 shows the simulations of the equation (17) when the model parameters are known.

Then it was assumed that N_{max}, and ΔF are unknown so the methodology presented in the sections *II.A* and *II.B* was implemented to find the unknown parameters. The authors leave deriving intermediate equations to the reader however would like to note that the initial conditions required for solving particular and homogenous solutions i.e., equations (9) and (10). The initial conditions are:

$$P(0) = [0\ \ 1\ \ 0\ \ 0\ \ 0\ \ 0\ \ 0]^{trans} \tag{18}$$

$$h_1(0) = [0\ \ 0\ \ 0\ \ 0\ \ 0\ \ 1\ \ 0]^{trans} \tag{19}$$

$$h_2(0) = [0\ \ 0\ \ 0\ \ 0\ \ 0\ \ 0\ \ 1]^{trans} \tag{20}$$

To obtain unknown parameters, the equation (13) has to be formed at each iteration k and solved at the firing times. For

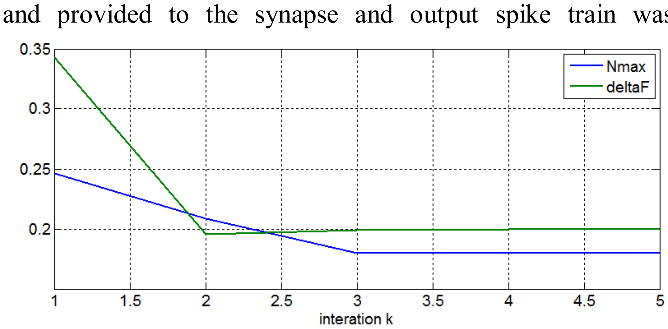

Fig. 3: Parameter optimizationfor single synapse, single neuron: convergence of N_{max} , and ΔF.

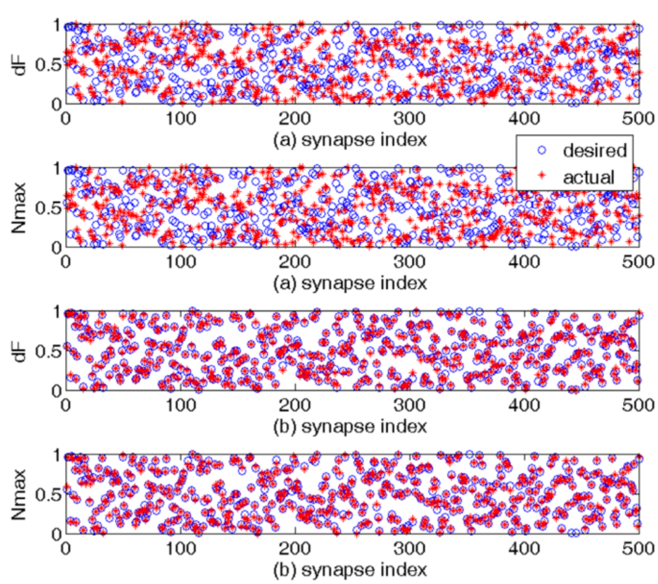

Fig. 4: Training progress of the network with 500 synaptic connections consisting 1000 unknown parameters, a) Desired synapse parameters and initial guess of synapse parameters b) Desired and trained synapse parameters of Type I DSNN with 1500 training samples

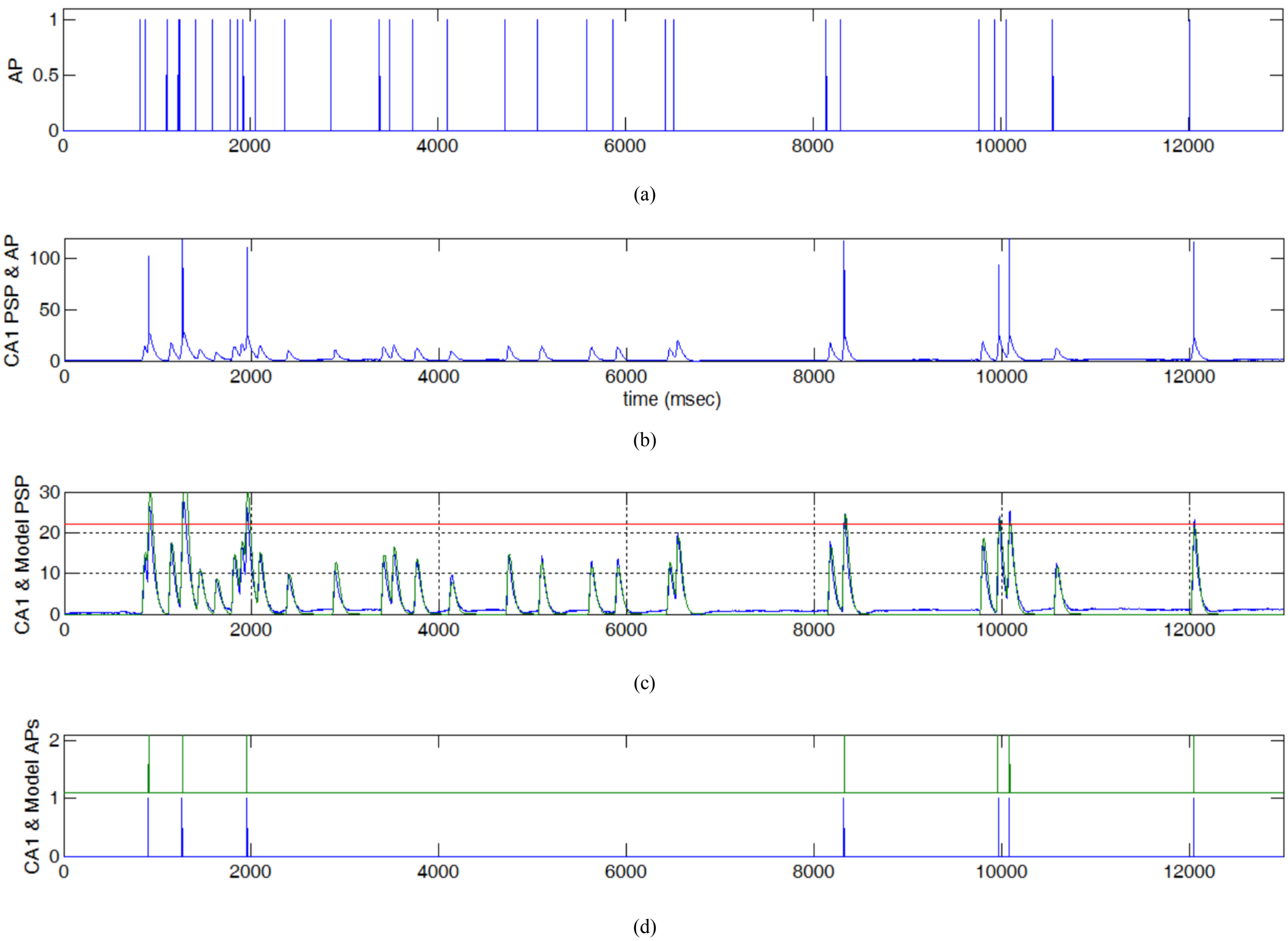

Fig. 5: CA1 PSP dynamics and facilitation-depression model response a) Input spike train to the CA1 pyramidal neuron synaptic pathway, b) Single CA1 neuron PSP response and its AP activity, c) Predictive model of CA1 neuron PSP dynamics plus synapse FD model PSP response, d) Spiking activity of the CA1 neuron plus synapse FD model. The model with only one synaptic connection predicts CA1 neuron spiking activity with an average of 6.6 millisecond jitter accuracy plus firing an extra spike.

the example shown in the Figure 2 we have:

$$\begin{bmatrix} V(286) - P^5(286) \\ V(608) - P^5(608) \\ V(849) - P^5(849) \\ V(1410) - P^5(1410) \end{bmatrix} = \begin{bmatrix} h_1^5(286) & h_2^5(286) \\ h_1^5(608) & h_2^5(608) \\ h_1^5(849) & h_2^5(849) \\ h_1^5(1410) & h_2^5(1410) \end{bmatrix} \begin{bmatrix} \Delta F \\ N_{max} \end{bmatrix}$$

It is worth mentioning that membrane potential is represented by variable V which is the fifth element of space vector $V(t) = \mathbb{X}_{k+1}^5(t)$. In addition, $P^5(t)$ and $h_i^5(t)$ are fifth row of particular and homogeneous solutions. The convergence of the parameter has shown in the Figure 3.

B. *Large-scale Model*

Scalability and repeatability of the presented algorithm were examined using a large-scale simulation. A network consist of a single neuron and 500 synapses was set up and the network parameters were randomly chosen. The output spike train of the neuron was generated using equations (13) through (16) There were 1000 parameters to estimate.

Due to large number of parameters, demonstrating detailed convergence graph in the limited space of the paper won't be feasible. However parameters at the initial step and after the convergence are shown in the graphs of the Figure 4.

The simulation results identify that the convergence to an optimum parameter set is repeatable and scalable. The simulation results also suggest that the neuron membrane potential is a unique function of incoming spike train and synapse parameters. Thus, the parameter convergence progress in predicting synapse parameters corresponds to the

TABLE II: PARAMETERS OF THE MODEL FOR PREDICTION OF CA1 NEURON

Symbol	Quantity	Typical value
τ_f	Facilitation time constant	200 millisecond
F_0	Resting facilitation	0
ΔF	Facilitation factor	0.115
τ_r	Vesicle recovery time constant	200 millisecond
N_{max}	Maximum number of release sites	10.132
a_2, a_1, a_0	15, 75, 125	$a_2 = 3a, a_1 = 3a^2, a_0 = a^3$; $a = 5$

simultaneous improvement of state variables in particular membrane potential prediction and the unknown parameters. The results of simulations show that estimation of unknown parameters of the large-scale model can be accurately converge to the desired value in a significantly less number of iterations.

IV. Modeling and Predicting Hippocampus CA1 Neuron Activities

A single pyramidal cell of the CA1 hippocampus area was excited by injecting APs on its pre-synaptic pathway with a 2-Hz Poisson spike timing. The patch-clamp technique was utilized for recording the somatic membrane potential of the CA1 neuron in response to the spiking train impinging on its Schaffer collateral synaptic pathway. Figure 5.a shows 13 seconds of the CA1 pyramidal neuron membrane potential and its AP activity in response to the impinging spike train. The input-output property of the CA1 cell was modeled by the equation (18) and utilizing the methodology of section $II.A$ and $II.B$. Free parameters of a single synapse model were adjusted to replicate the PSP dynamics of the CA1 cell including its spiking activity. Figure 5.b presents the PSP prediction and spiking activity using (18). The average error in PSP prediction was %9. The model predicts CA1 neuron spiking activity with a 6.6 millisecond accuracy while generating no extra or missing spikes. The parameter adaptation was applied for the whole recording time – 215 seconds – where the recorded neuron's PSP dynamics showed other nonlinear dynamic processes including facilitation regulation and vesicle depression. For a short recording period, adjusting only $(\Delta F, N_{max})$ parameters suffice to build a precise predictive model of the recorded neuron's PSP response whereas a longer period was required to capture other dynamics such as facilitation regulation and vesicle depression.

V. Summary and Conclusions

In this research was presented an algorithm for parameter estimation of a nonlinear dynamic systems with a focus on spike-in, spike-out models. In general, models representing neural mechanisms are highly nonlinear and temporal which makes their parameter estimation to be challenging. Algorithm of this paper transforms nonlinear parameter estimation problem into an affine model in which parameters can be estimated by any linear programming methodologies.

Utility of the proposed algorithm was demonstrated by a few examples. The examples were based on employing facilitation-depression model. Free parameters of a single neuron with a single synapse was estimated to map input spike train into a set of another spike train which was generated by the model. The parameter optimization successfully achieved estimating the unknown parameters of the system in Five iterations. In another example, a larger neural model consisting of 1000 parameters was trained. In the third example, facilitation-depression model and algorithm of this paper were utilized for development of a predictive model for Hippocamus CA1 cell's PSP and its spiking activity.

There are many unknown questions about neural dynamics and the synaptic adaptation mechanisms. The learning algorithm presented in this paper is limited to a single layer dynamic synapse but can be extended to multiple layers or a cascade neural structure as observed in the brain layers. The spike-domain mappings performed in this paper addressed a small subset of possible spike domain mappings observed in the brain. The next question is how the learning and neural model can be modified to perform more diverse neural processes. The authors' future research will focus on applying dynamic synapse modeling in predicting spiking activity of the hippocampus cortical region where it requires a cascade neural structure.

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