

Data Assimilation of Membrane Dynamics and Channel Kinetics with a Neuromorphic Integrated Circuit

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Abstract—Techniques of data assimilation (DA) for parameter identification and forecasting in complex dynamical systems offer promising tools for the analysis of neural data and inference of neural function. Here we present experiments using DA to characterize the dynamics of a neuromorphic very large-scale integrated (VLSI) circuit emulating membrane dynamics and channel kinetics in a network of 4 generalized Hodgkin-Huxley neurons coupled through 12 conductance-based chemical synapses. The analog VLSI chip, NeuroDyn, features 384 digitally programmable parameters specifying for all neurons and synapses reversal potentials, conductances, and spline-regressed voltage dependence profile of opening and closing rates of the gating variables. In a set of experiments, we conducted DA on the membrane potentials of neurons recorded on the chip under current injection according to the model structure upon which the chip was designed and the known current input sequence, to arrive at the programmed parameters save for model errors due to analog imperfections in the chip fabrication. In a related set of experiments we extended the DA procedure to map songbird neural dynamics onto the chip by identifying and programming parameters extracted using DA from intracellular neural recordings. Application of the chip to neurological data may help to understand the effects of neuromodulators or neurodegenerative diseases on ion channel kinetics, and may further provide insights into the relationship between molecular properties of neurons and the emergence of different spike patterns or different brain behaviors.

I. INTRODUCTION

In the field of neuromorphic engineering, analysis-by-synthesis is an emerging approach to studying single neurons and neural networks. Formulating a proper model to emulate multiple types of neurons is a critical step of synthesis.

NeuroDyn [1] [2] is an analog very large-scale integrated (VLSI) circuit instantiation of a general model of neural dynamics on a small-scale, 4-neuron 12-synapse network. NeuroDyn features 384 digitally programmable parameters, specifying for each neuron and synapse reversal potentials, conductances, and spline-regressed voltage dependence profile of opening and closing rates of the gating variables. While the implementation of these parameterized characteristics in NeuroDyn provides the capacity to emulate a large variety of neuron and synapse behaviors, it requires tuning over a large number of parameters. A simple calibration and parameter fitting procedure proved adequate to set parameters in the biophysical model approximately to desired

values [1] and even to generate phasic and tonic bursting in an extended Hodgkin-Huxley model formalism [2]. A more powerful method for fine tuning of these parameters, to account for uncertainties in the modeling as well as imprecisions and transistor mismatch in the implemented model, would still be desirable.

Here we investigate the use of data assimilation (DA) methods, which have shown great promise for model estimation and time series prediction in natural systems [3], to systematically map biophysical neural function onto NeuroDyn, facilitating the task of programming its parameters. We find that DA is not only capable of producing accurate predictions when data recorded from the chip is assimilated to the model, but of correctly predicting the waveform information of a songbird HVC neuron within the accuracy of the intrinsic variability of the neuron, despite the considerable difference in complexity of the two systems.

II. NEURODYN MODEL

The Hodgkin-Huxley (H-H) model has long been the standard of biophysical realism in single-unit neural dynamics described by differential equations [4]. NeuroDyn implements an extended form of H-H dynamics with generalized rate-based kinetics in the gating variables. It also provides for rate-based synaptic coupling between neurons, which is not investigated here. Each neuron undergoes membrane dynamics of the form

$$C_{mem} \frac{dV_i}{dt} = -I_{Na} - I_K - I_L - I_{injection} \quad (1)$$

with currents, conductances, and gating variable dynamics of the approximate form

$$I_{Na} = G_{m^3h} g_{Na} (V_m - E_{Na}) \quad (2)$$

$$G_{m^3h} g_{Na} = \frac{\kappa}{V_T} I_g \left(\frac{I_m}{I_{ref}} \right)^3 \frac{I_h}{I_{ref}} \quad (3)$$

$$CV_T \frac{d}{dt} \frac{I_{gate}}{I_{ref}} = I_\alpha \left(1 - \frac{I_{gate}}{I_{ref}} \right) - I_\beta \frac{I_{gate}}{I_{ref}} \quad (4)$$

for Na^+ , with similar usual expressions for K^+ and leak (L) conductances, where I_{gate} stands for either one of the gating variables n , m and h , and where $V_T = kT/q$ is the thermal voltage. However, in contrast to the specific heuristic equations for the opening and closing rates of the kinetics in the gating variables, as arrived at through intricate curve fitting in the original H-H model [4], NeuroDyn permits a more general form regressed as 7-point additive spline sigmoidal functions

$$I_{rate}(V) = \sum_{k=1}^7 I_{bk} I_{\sigma,k}(V) = \sum_{k=1}^7 \frac{I_{bk}}{1 + e^{\pm \kappa (V_{bk} - V)/V_T}} \quad (5)$$

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where the output current I_{rate} denotes either one of the I_α and I_β rates, and V_{bk} are fixed uniformly spaced voltages.

III. DATA ASSIMILATION METHODS

Data assimilation refers to analytical and numerical procedures in which information in measurements is transferred to model dynamical equations selected to describe the processes thought to produce the data. In the absence of measurements or first principles to derive parameters and unknown states in a model, data assimilation provides a method to obtain them systematically.

A. Path Integral Methods of Data Assimilation

We formulate our problem as a path integral realization of a statistical data assimilation procedure [3]. Because measurements and models will always have errors, our data assimilation method formally represents the time evolution of the unknown quantities with probability distributions. State variables of the models evolve in time according to a dynamical rule specified by the values of model parameters.

The vector of states is a D dimensional vector $\mathbf{x}(t)$ defined in an estimation window $[t_0, t_M]$ defined at discrete times. Usually, the measured states $\mathbf{y}(t)$ are noisy and have a dimension L much smaller than D . The goal of data assimilation is to estimate unknown state variables at the end of the estimation window $\mathbf{x}(t_M)$ and the unknown model parameters \mathbf{p} .

Skipping the derivation [3], the probability for the configuration of the state vector at the end of the window given the observations is of the form:

$$P(\mathbf{x}(t_M)|Y(t_M)) = \int dX \exp(-A_0(X, Y)). \quad (6)$$

Here X and Y denote the collection of all state variables $\mathbf{x}(t)$ and set of measurements $\mathbf{y}(t)$ at every time point in the estimation window, respectively. A_0 we call the action by analogy with path integral formalisms used in statistical physics and quantum mechanics [3].

The use of Laplace's approximation [5] to evaluate the integral shifts the numerical difficulty of the problem into one of optimization. In the present case, this involves finding the lowest minimum of the cost function A_0 , a non-convex problem. $\mathbf{x}(t_M)$ and \mathbf{p} are expected values of $P(\mathbf{x}(t_M)|Y(t_M))$ under two conditions. One occurs when the values of $A_0(X_i)$ for distinct saddle paths X_i are widely separated. Another occurs when a saddle path contains correct values of $\mathbf{x}(t_M)$ and \mathbf{p} in conditions where these quantities are known, as is shown to be the case here.

A_0 can be written as a sum of two terms; a measurement noise term and a model error term. When the measurement noise and model error is assumed additive and Gaussian, the action has a particular form:

$$A_0(X|Y(t_M)) = \frac{R_m}{2} \sum_{n=0, l=1}^{M, L} (h_l(\mathbf{x}(t_n)) - y_l(t_n))^2 + \frac{R_f}{2} \sum_{n=0, d=1}^{M-1, D} (x_d(t_{n+1}) - f_d(\mathbf{x}(t_n)))^2 \quad (7)$$

The h_l are measurement operators which operate on the state of the system at every time point $\mathbf{x}(t_n)$. R_m is the inverse variance of the measurement error, and R_f is the inverse variance of the model error. The relative values of R_m and R_f are assigned before the beginning of the optimization procedure.

B. Annealing

The way in which R_m and R_f are weighted relative to one another in the cost function influences the result of minimizing the cost function. Manipulating the cost function by varying these values forms the basis of our annealing method, shown to be effective in state and parameter estimation in archetypal chaotic models such as the Lorenz '96 model [6]. When $R_m \gg R_f$, the measurement error is assumed small while the model error is large. Such an assumption causes the cost function to form minima in the high dimensional landscape defined over the state and parameter space where measured states in the model fit the data closely. The model error is assumed large, so the model is enforced weakly, effectively decoupling parameters and unmeasured states from the data. These are unlikely to be estimated correctly [6].

When $R_m \approx R_f$, both terms contribute equally to the cost function, so minimizing the cost function will tend to satisfy the data while simultaneously enforcing the dynamical map. However, when the model error is forced, by large R_f , to be small, the nonlinearity of the vector field $\mathbf{f}(\mathbf{x})$ manifests itself at the smallest scales in the phase space of the paths X over which we are searching. This results in complicated fine structure seen as multiple local minima [3] in the action, especially when the number of measurements L is too small. It is unlikely that directly minimizing the cost function under this condition will yield good estimates of the system's parameters and state variables.

An annealing method has been developed [6] that uses information available in educated initial guesses about where the minima are to attempt to fit the data and enforce the model simultaneously. In this method, $R_m \gg R_f$ initially. The cost function is then minimized, which is typically easy. Then R_f is increased in magnitude by a factor $\alpha > 1$, and the cost function is minimized again, starting the search for minima at the previous solution. The process is repeated until $R_f \gg R_m$. In this way, the algorithm creeps gradually towards a minimum which fits the data and the model better than other options.

The implementation of the algorithm was accomplished through the use of the open source software package IPOPT (Interior Point OPTimizer) with the linear solver ma57 [7].

IV. EXPERIMENTS AND RESULTS

A. Data Assimilation with Synthetic Data

We applied DA to synthetic data emulating the dynamics of the NeuroDyn chip in Matlab according to the model (1)-(5), given a drive signal $I_{injection}$, to gain insight about what measurements are necessary to accurately estimate unknown states and parameters of the model of the physics on the Neurodyn chip. The results, shown in Fig. 1, suggest that if

the measurement functions h_l are known and the model of the physics on the chip is correct, sufficient measurements can be obtained from the chip for the DA algorithm to correctly estimate all unknown parameters.

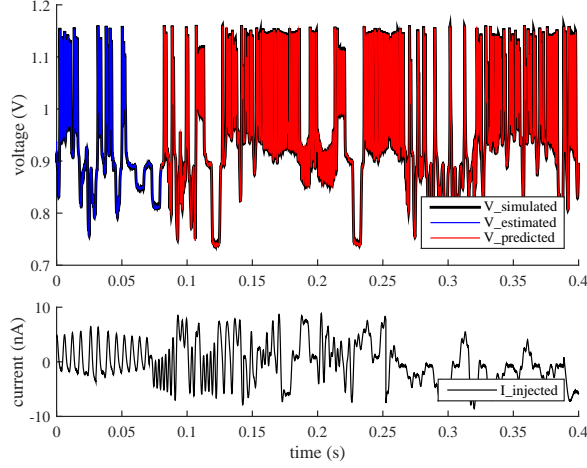


Fig. 1: Estimated (blue), predicted (red), and simulated (black) data of the NeuroDyn model in software. The prediction is obtained by integrating the equations of motion forward using the estimated parameters and configuration of the system at the end of the estimation window. The injected stimulating current protocol (black) is also displayed.

B. Data Assimilation with NeuroDyn

DA can be used as a tool for tuning parameters configured on the chip to values producing biologically realistic dynamics. However, the model of the physics on the chip may be not precise enough, so it is desirable to check for discrepancies between configured parameter values and theoretical parameter values obtained with DA.

Data obtained from the chip yield time series measurements of $[V(t), m(t), h(t), n(t)]$ at a time resolution of 500 kHz. Membrane potential $V(t)$ was measured directly from the chip, while gating variables were measured indirectly by measuring voltage $h_i(\mathbf{x})$ produced by I_{gate} , as given in (4), passing a resistor R_{gate} .

Because the gating variables were measured indirectly, when doing DA we applied known measurement operators h_l to each of the gating variables \mathbf{x}

$$h_i(\mathbf{x}) = I_{ref}R_{gate}x_i + k_i \quad (8)$$

where k_i is a relatively small constant shift in the voltage obtained from indirect measurement of the gating variables x_i . I_{ref} and R_{gate} have values ≈ 10 nA, 1.53 M Ω , respectively.

In our experiments, we apply a complex stimulating current waveform to the Neurodyn chip to elicit waveforms, which when used as data in DA, sample as many of the available degrees of freedom in the model as possible. This is necessary for the data assimilation procedure to produce accurate estimates of the unknown states and parameters.

The results of DA are displayed in Fig. 2. Although the estimate and predictions are good, there is some disagreement

between the theoretical values given the model of the chip and the configured values, shown in table I. This difference is due to a combination of model error, uncertainty in the measurement functions h_l , and numerical limitations of the DA procedure.

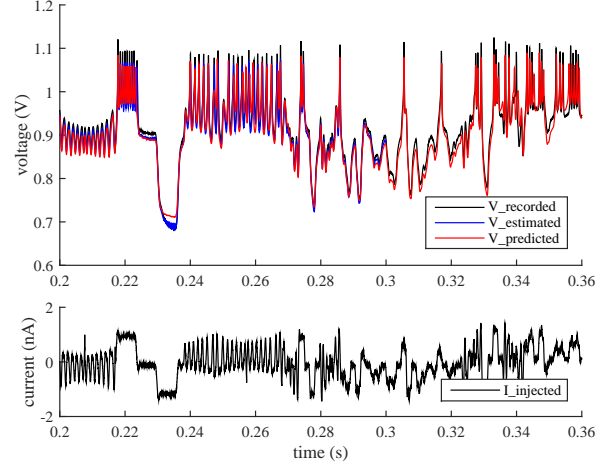


Fig. 2: Estimated (blue), predicted (red), and measured (black) data recorded from the NeuroDyn chip. The estimation and prediction were obtained, and the current injection was applied, under identical conditions as in Fig. 1.

TABLE I: Reference and Estimated Values

Params	Ref	Estimated	Params	Ref	Estimated
g_{Na}	600	294.81	α_{h5}	0	4.3293e-6
e_{Na}	450	408.089	α_{h6}	0	3.0360e-6
g_K	160	100	α_{h7}	0	3.0332e-6
e_K	200	234.401	β_{h1}	0	10
g_L	12	2.60719	β_{h2}	0	2.8240e6
e_L	250	235.877	β_{h3}	0	1.0368
k_{inj}	1	0.0846	β_{h4}	0	3.0750e-5
σ	13.5	15	β_{h5}	41	79.9999
V_{b1}	0.61	0.6117	β_{h6}	25	49.9737
V_{step}	0.123	0.13	β_{h7}	8	48.7581
α_{m1}	0	0.0003	α_{n1}	0	4.9057e-5
α_{m2}	0	0.0001	α_{n2}	0	0.0374
α_{m3}	120	222.943	α_{n3}	0	1.3169e-6
α_{m4}	400	306.742	α_{n4}	0	1.2238
α_{m5}	800	600.001	α_{n5}	18	49.9987
α_{m6}	1023	800.211	α_{n6}	5	1.5156
α_{m7}	1023	809.773	α_{n7}	43	18.9959
β_{m1}	1023	1000.14	β_{n1}	1	0.0414
β_{m2}	1023	1022.93	β_{n2}	0	0.0009
β_{m3}	1023	1023	β_{n3}	0	2.3919
β_{m4}	1023	800	β_{n4}	1	8.3258e-6
β_{m5}	0	9.9998	β_{n5}	0	2.2087e-5
β_{m6}	0	9.9999	β_{n6}	0	0.0067
β_{m7}	0	9.9999	β_{n7}	1	2.6981
α_{h1}	237	120	I_{master}	100	83.5093
α_{h2}	5	1	I_{volt}	232	228.9760
α_{h3}	7	1.0000	V_{offset}	1	0.9913
α_{h4}	6	14.4858	R_{gate}	1.53e+06	1.5373e+6

C. Data Assimilation with Biological Neuron Data

Using the above DA method, we proceeded to assimilate voltage data obtained from zebra finch HVC_I neurons [8] to the model of the physics on the chip. Integrating forward

the state of the model with the obtained parameter set, the resulting waveform matches the recorded voltage data within the intrinsic variability of the neuron. This is displayed in Fig. 3. Although the unresolved discrepancy between chip configured parameters and theoretical parameters obtained from DA presently limits us from configuring the chip to emulate the biological neuron, the result is interesting because to our knowledge an H-H model with only I_{Na} , I_K and I_L has previously been insufficient to describe neurons within the central nervous system such as the nucleus HVC. Credit for such feat may be due to the more flexible implementation of opening rates α and closing rates β in NeuroDyn's highly parameterized model.

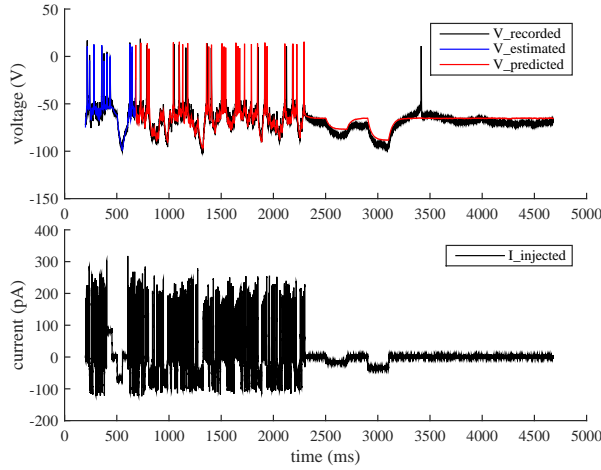


Fig. 3: Estimated (blue), predicted (red), and electrophysiological (black) data recorded *in vivo* from an HVC interneuron (HVC₁) [8] and instantiated onto the NeuroDyn hardware model.

D. Discussion

We have presented a DA procedure capable of tuning the parameters of a model of an analog VLSI chip emulating membrane dynamics and channel kinetics of generalized H-H neurons, and have shown that if all measurement functions h_l are known and the dynamical model of the chip is accurate, we can correctly estimate all of the parameters, many of which enter the equations nonlinearly. We have also shown that given noisy voltage data recorded from zebra finch HVC₁ neurons and the relatively simple extended H-H model of the Neurodyn chip with only two ionic currents, I_{Na} and I_K , the time evolution of an HVC₁ neuron can be accurately predicted.

We also found during DA on synthetic data and chip data that without prior constraints about the range of parameter values, many different parameter sets could be found which produced accurate estimations and predictions of all state variables which could not be distinguished from each other.

Potential discrepancies between theoretical values of parameters estimated using DA and configured parameters on Neurodyn have also been identified. Further work is needed to ascertain whether these discrepancies caused by mismatch

of transistors can be resolved with improvements to the model, measurement functions h_l , and/or refinements to the DA procedure.

The approach presented here targets applications where biophysical detail in modeling neural and synaptic dynamics at the level of channel kinetics is critical. Examples include modeling of the effect of neuromodulators, neurotoxins, as well as neurodegenerative diseases on neural and synaptic function through parameter changes in the channel kinetics. For these and other applications in computational neuroscience, a direct correspondence between the parameters governing the biophysics of neural and synaptic function and those in the implemented computational model, is of great benefit.

V. CONCLUSIONS

Our experiments demonstrate that our methods of data assimilation are not only capable of recovering all the parameters of a dynamical model describing physical processes on Neurodyn, but of correctly predicting the waveform information of an HVC neuron of the zebra finch within the accuracy of the intrinsic variability of the neuron. These results provide a basis for building biologically realistic network models in an integrated analog circuit chip which will form closed-loop interaction between artificial and biological neural networks.

Although we have shown that the extended H-H model implemented on Neurodyn is sufficient for describing one class of interneurons within the nucleus HVC, there is a tremendous diversity of mechanisms in nervous systems. Such mechanisms include other ion channels such as calcium channels, neuromodulators, multi-compartmental dynamics through linear and nonlinear dendritic coupling, and intracellular signalling pathways. In addition, NeuroDyn is not designed for large-scale brain emulation as each chip emulates only 4 neurons, two ion channels and one leaky channel for each neuron. In the near future we will scale up the number of neurons on the chip with increasing biophysical accuracy to form larger artificial neural systems.

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