

# Dynamic Nonlinear Modeling of Interactions between Neuronal Ensembles using Principal Dynamic Modes

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**Abstract**—We present a novel methodology for modeling the interactions between neuronal ensembles that utilizes the concept of Principal Dynamic Modes (PDM) and their associated nonlinear functions (ANF). This new approach seeks to reduce the complexity of the multi-input/multi-output (MIMO) model of the interactions between neuronal ensembles – an issue of critical practical importance in scaling up the MIMO models to incorporate hundreds (or even thousands) of input-output neurons. Global PDMs were extracted from the data using estimated first-order and second-order kernels and singular value decomposition (SVD). These global PDMs represent an efficient “coordinate system” for the representation of the MIMO model. The ANFs of the PDMs are estimated from the histograms of the combinations of PDM output values that lead to output spikes. For initial testing and validation of this approach, we applied it to a set of data collected at the pre-frontal cortex of a non-human primate during a behavioral task (Delayed Match-to-Sample). Recorded spike trains from Layer-2 neurons were viewed as the “inputs” and from Layer-5 neurons as the outputs. Model prediction performance was evaluated by means of computed Receiver Operating Characteristic (ROC) curves. The results indicate that this methodology may greatly reduce the complexity of the MIMO model without significant degradation of performance.

## I. INTRODUCTION

MODELING of neuronal ensemble activity remains one of the great engineering challenges in the study of neural function and the design of advanced neuroprostheses. Early work using “integrate-and-fire” models was useful in the exploratory phase but it reached soon its limits of utility because it represents a drastic simplification of the actual dynamics encountered in the nervous system. At the same time, it became evident that detailed approaches of the Hodgkin-Huxley mold are too cumbersome to be useful in the context of large-scale neuronal ensembles or networks. The approach introduced by Hopfield-type neural networks and perceptron-type artificial neural networks created, for a

while, considerable excitement and a fair amount of creative work, but led eventually to the sobering realization that these formulations were not necessarily a good or meaningful representation of the dynamics of actual neural networks. This gave rise to intensified and ongoing efforts to find new or hybrid approaches that meet the dual challenge of fidelity to actual neural function and feasibility rooted in reasonable model parsimony. We have participated in this collective effort by exploring the use of parsimonious forms of Volterra-type models which offer the requisite flexibility to represent actual neural function with adequate fidelity but have been viewed heretofore as prohibitively cumbersome. Our results to date have offered considerable promise in achieving reasonable parsimony and predictive capability for the dynamic nonlinear MIMO models that are required for satisfactory representation of actual neural systems [1, 4-8].

The developed modeling methodologies have been tested with actual experimental data from the hippocampus of rodents performing specific behavioral tasks [2], whereby the causal relationship between the recorded activity of neuronal ensembles in the CA3 region of the hippocampus and neuronal ensembles in the CA1 region is quantified with a MIMO model. Validation of these models has been attempted so far with the testing of specially designed hippocampal prostheses (essentially a CA3-to-CA1 “neural bypass”) and through the demonstrated efficacy of designed spatio-temporal patterns of multi-unit neurostimulation [6]. The hippocampus is a region of the brain responsible for the formation of new long-term memories. We seek to redress clinical conditions in which part of the hippocampal intrinsic trisynaptic circuit is damaged, which often occurs as a result of stroke (selective loss of CA1 neurons), epileptic activity (preferential damage to CA3), or head trauma (preferential damage to hilar neurons). Alzheimer’s Disease and other forms of dementia are also associated with loss of neurons throughout the hippocampal formation.

The obtained results to date have provided evidence of the validity and efficacy of this MIMO modeling approach in the rat hippocampus [5-8]. Notwithstanding the success of these efforts, the challenge remains with regard to the practical “scaling up” of this approach to large populations of neurons. The ensembles to date are comprised of a limited number of neurons (up to 32 input neurons and 16 output neurons). If the numbers of input/output neurons rise into the hundreds, then the complexity of the MIMO model begins to test our current computational capabilities. Considerable efforts have been dedicated to exploring rigorous ways to compact the MIMO models further without compromising performance. The work presented herein is part of this effort and concerns the use of the concept of

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Principal Dynamic Modes (PDM) that has been recently introduced by our group and applied successfully to various physiological systems [3].

In the PDM modeling approach, we seek to determine a set of basis functions (the PDMs) that represent the most efficient “coordinate system” for the representation of all the Volterra kernels of a given system. Over the last 10 years, we have developed and tested a methodology by which the PDMs of a given system can be obtained from input-output data. Static nonlinear functions associated with the PDMs (termed ANF: associated nonlinear functions) complete the model. This approach has been shown to provide considerable benefits in terms of model compactness in several diverse applications [3] and it is explored here in the context of MIMO modeling of neuronal ensembles.

This paper presents some initial results of exploratory efforts in PDM-based MIMO modeling of neuronal ensemble activity using data from a small number of neurons (4 inputs and 4 outputs) in the pre-frontal cortex of non-human primates. These results appear to hold great promise with regard to the potential modeling efficiency in this particular context, although the actual test of scaling up to numerous input/output neurons is still to come.

## II. METHODOLOGY

As mentioned above, we seek to obtain parsimonious representations of MIMO Volterra-type models that have the demonstrated ability to represent arbitrary dynamic nonlinear transformations of spatio-temporal input-output data (i.e. spike-trains from multiple neurons of neuronal ensembles). We have already developed an effective methodology for the estimation of Volterra kernels using Laguerre expansions [3]. To reduce further the complexity of the resulting MIMO model, we seek to determine the PDMs of the given system from the estimated kernels. This is accomplished through a three-step procedure: (1) we perform eigen-decomposition on all the second-order kernels and retain only the “significant” eigen-vectors by applying a selection criterion on the respective eigen-values; (2) we construct a rectangular matrix composed of all the first-order kernels and all the selected “significant” eigen-vectors of the second-order kernels weighted by the corresponding eigen-values; and (3) we perform singular value decomposition (SVD) of this rectangular matrix and select the “significant” singular vectors by applying a selection criterion on the respective singular values. The selected singular vectors are the PDMs of this MIMO model.

## III. RESULTS FROM EXPERIMENT DATA

The data were collected in the lab of Dr. Deadwyler at Wake-Forest University from layers 2 and 5 of the pre-frontal cortex of non-human primates (NHP) that were trained to remember a displayed (and immediately removed) image and later re-select this image by moving a cursor on the screen to match it among several images presented after random delays (i.e. a Delayed-Match-to-Sample task). When the correct image is selected, the animal is rewarded.

During this task, the neuronal activity is recorded at the layer-2 and the layer-5 of the pre-frontal cortex (PFC).

We analyzed the data around the response-presentation phase of the correct Match responses in 4 Layer-2 (input) and 4 Layer-5 (output) neurons. The spikes were binned with 10 msec binwidth. The peri-event mean-firing-rate was between 0.25 and 20 spikes per second. We estimated the 1<sup>st</sup> and 2<sup>nd</sup> order kernels using Laguerre expansions with  $\alpha = 0.25$ ,  $L = 5$ ,  $M = 51$ , and  $Q = 2$ . We followed the previously described procedure for the selection of the PDMs of this MIMO model. Four PDMs were deemed significant in this specific system. An illustrative example of the obtained four PDMs over 50 trials (NHP 1357, session 8017) is shown in Fig. 1. These PDMs can be used as a basis of functions to represent all the kernels of this MIMO model.

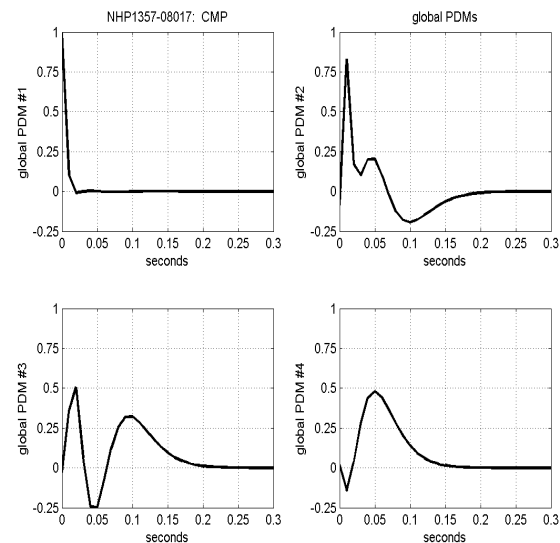


Fig. 1. The four PDMs of the MIMO model obtained from the data of NHP1357 for the first 50 trials of session 8017.

To construct the MIMO model of this system (see Fig. 2), we must determine the ANFs associated with the PDMs.

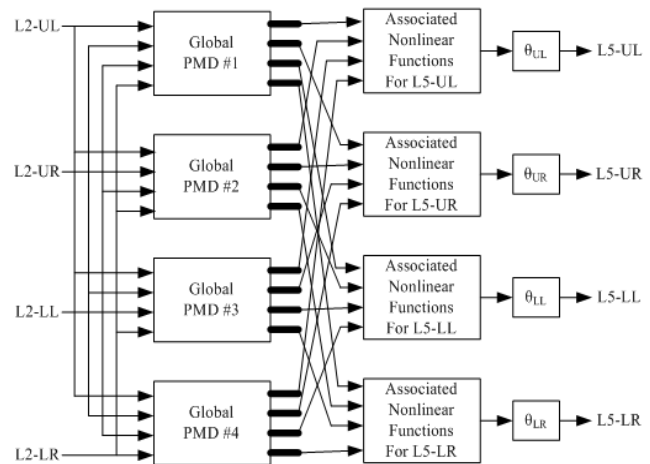


Fig. 2. Block diagram of the MIMO model using 4 global PDMs with four layer-2 input neurons and four layer-5 output neurons. UL: upper-left unit, UR: upper-right unit, LL: lower-left unit, LR: lower-right unit.

In order to determine the 16 ANFs of this PDM-based MIMO model (equal to the product of the number of inputs times the number of PDMs) for each output, we form the ratio of the histogram of PDM outputs leading to output spikes to the histogram of all PDM outputs in the data. As an illustrative example, Fig. 3 shows the obtained ANFs for one (UL: upper left) of the 4 output neurons in layer-5 of PFC. Note that the ordinate values of the ANFs can be interpreted as the individual contribution of each input-PDM “channel” to the probability of firing of the respective output neuron. We observe in Fig. 3 that most of these ANFs make relatively small contributions to output firing and a few make significant contributions to output firing for high values of the abscissa (which represents the PDM output for the respective input-PDM channel). This observation is utilized later to reduce further the complexity of the model.

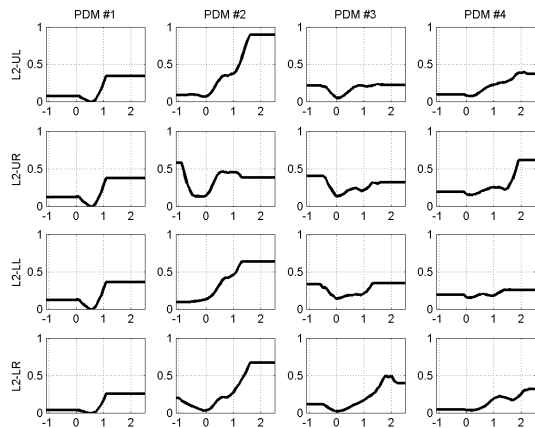


Fig. 3. The 16 ANFs for one (UL) of the output neurons in layer-5 of PFC.

Since the total number of ANFs for each output is the product of the number of PDMs times the number of inputs, it is evident that the complexity of the MIMO model will increase **linearly** (i.e. proportionally) with increasing number of inputs (for each output) -- and **not quadratically** as is the case in the current second-order MIMO model. It is obvious that this represents a major practical advantage of the PDM approach in terms of scaling up the MIMO model to large numbers of inputs and outputs.

It was indicated above that we can reduce further the number of required ANFs in the MIMO model by “pruning” the ones that have no significant impact on the output firing. Upon examination of the ANFs in Fig. 3, we observe that some have shapes that are relatively flat (i.e. the ratio  $R$  of the maximum to the minimum value is close to 1). Thus, we may practically ignore the ANFs that have small  $R$  value (i.e. setting them to zero in the PDM model). To apply this pruning procedure algorithmically, we have to set a threshold value for  $R$  in all ANFs, below which an ANF is considered insignificant. The top panel of Fig. 4 shows the total number of remaining ANFs for all four output neurons (the maximum number of ANFs is 4 outputs x 4 PDMs x 4 inputs =64). The rate of decrease of the total number of “active” ANFs with increasing  $R$  is about the same for all inputs. The bottom panel of Fig. 4 shows the probability of true-positive prediction by the pruned PDM-based MIMO

model for the respective output neuron over various threshold values of  $R$ . The probability of true-positive prediction increases up to a certain point and then declines (for  $R > 3$ ). Based on these results, we chose in this example the threshold value:  $R = 3$ . The total number of “active” ANFs reduces from 64 to 23 for  $R = 3$ . The remaining ANFs of the pruned PDM model are shown in Fig. 5 for each of the four output layer-5 neurons.

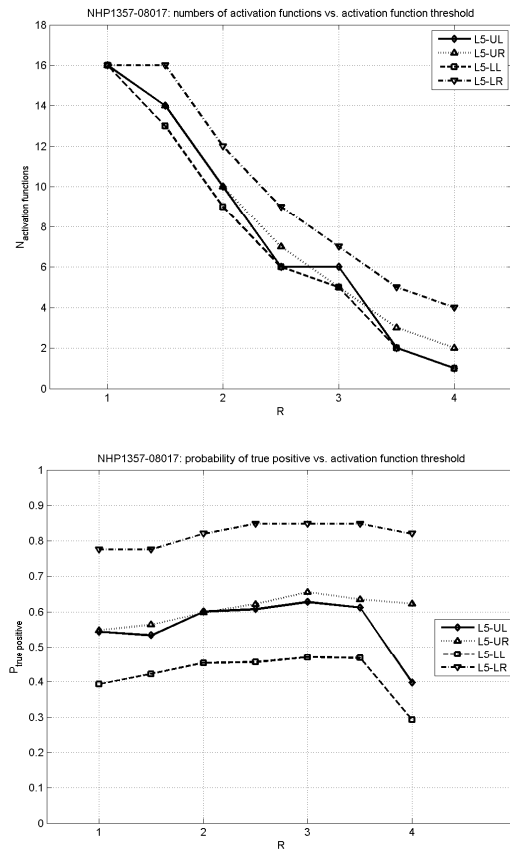


Fig. 4. The total number of remaining ANFs (top) and the probability of true- positive predictions (bottom) vs. various threshold values of  $R$  for the four output neurons of layer-5 in the PFC.

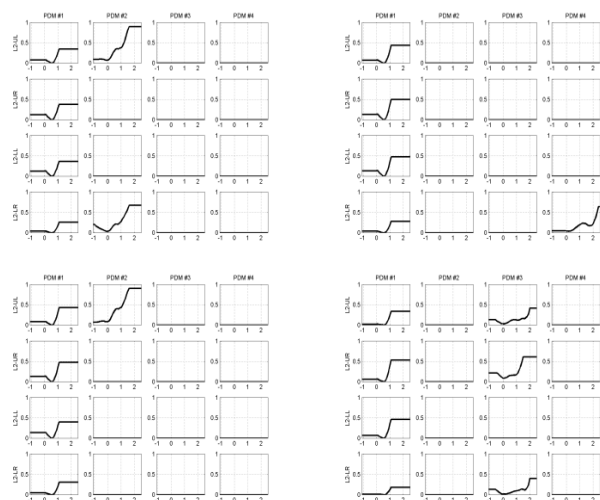


Fig. 5. The pruned ANFs of the PDM-based MIMO model for the four Layer-5 output neurons when the threshold  $R = 3$  is used for pruning.

Using these pruned ANFs, we can predict the output spikes for each of the four layer-5 output neurons for any given activity of the four layer-2 input neurons. The performance of the PDM model is evaluated by means of the receiver operating characteristic (ROC) curves. Assuming maximum spike jitter of one bin, we define a true-positive prediction when the predicted spike is within one bin from the actual output spike – otherwise, we have a false positive prediction. Consecutive true positives are counted separately only when there are also consecutive actual spikes – otherwise, they are counted as one true positive. The right column of Fig. 6 shows the resulting ROC curves for the four output neurons of this example, obtained from the pruned PDM model with the ANFs shown in Fig. 5. The ROC curves obtained by means of the full MIMO model including all the Volterra kernels (a model of much greater complexity) are shown in the left column of Fig. 6. The ROC curves are comparable, giving credence to the notion that the PDM modeling approach may indeed offer a more parsimonious alternative for practical MIMO modeling of neuronal ensembles.

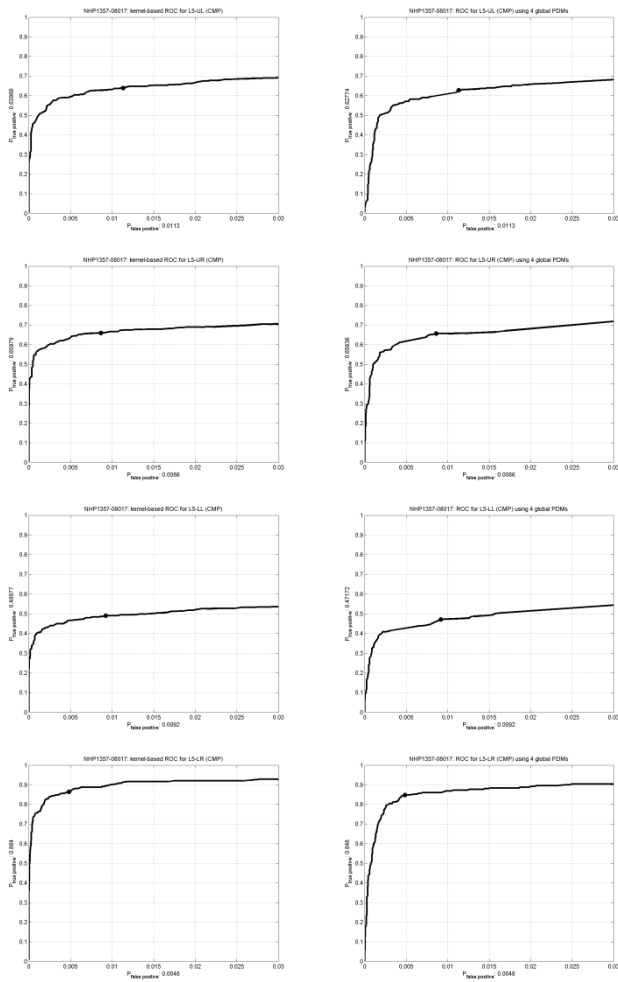


Fig. 6. The ROC curves obtained from the full MIMO model including all the Volterra kernels (left column) and from the PDM-based MIMO model with the pruned ANFs of Fig. 5 (right column) for the four output neurons.

#### IV. DISCUSSION AND CONCLUSION

We have presented a new methodology for modeling the nonlinear interrelationships between neuronal ensembles with Volterra-equivalent models that retain representational efficiency (i.e. model compactness) and provide excellent predictive capability. This methodology is based on the concept of Principal Dynamic Modes (PDMs) and their associated nonlinear functions (ANFs) that has been recently developed and applied successfully to various physiological systems [3]. The obtained multi-input/multi-output (MIMO) models are dynamic and nonlinear, but their complexity increases *only linearly* with increasing number of inputs (for each output), while the complexity of their Volterra-type counterparts increases faster (e.g. quadratically for a second-order MIMO model). This fact has critical practical implications in the scaling up of the MIMO models of neuronal ensembles to accommodate hundreds (or even thousands) of input-output neurons in the future.

Preliminary results of the application of this methodology to data collected from cortical neurons of Layer 2 (inputs) and Layer 5 (outputs) in the pre-frontal cortex of a behaving non-human primate corroborated the basic premise of the advocated approach by demonstrating significant reduction in the complexity of the PDM-based MIMO model without any significant degradation in predictive performance. If this result becomes confirmed by additional studies involving larger numbers of input-output neurons, then we will have at our disposal a practical methodology that can yield PDM-based (Volterra-type) MIMO models incorporating large numbers of input-output neurons with ordinary computational means.

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