Characterization of dendrites as nonlinear computation devices

Luis M. Sarro

Dpt. Artificial Intelligence. U.N.E.D.

Abstract

From the spines to the soma, signal processing in the neuron is intrinsically nonlinear. In this paper we present first results of a project whose objective is to identify/characterize dendrites as nonlinear devices in the hope that the resulting model will be of use in bio-inspired connectionist architectures. The methodology used is based on the extension of the Wiener-Volterra formalism to Multiple Input-Multiple Output (MIMO) systems. The project starts by applying the method to a computer model of the Purkinje cell as a guide for the design of real neurophysiological experiments, as well as an aid for the interpretation of results.

Key words:

dendrites, nonlinear system identification, Wiener-Volterra

PACS:

> "What *is the basic computational unit in the brain?... Although to a neuroscientist this question might seem poorly formulated, to a computer scientist it is well-defined. The essence of computation is nonlinearity... The basic unit of any computational system then, is its simplest nonlinear element."*
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> Anthony M. Zador (2000), Nature Neuroscience Supp., Vol. 3, 1167

1 Introduction.

Information processing in the brain takes places in a number of different scales from the single neurons to the brain as a whole, the characteristics of each stage being dictated by the physiology of the intervening units and the architectural implementation of the corresponding scale. The conventional view amongst brain modelers is that the neuron is the basic unit of computation, following pioneering work by McCulloch & Pitts. In the models, the neuron is represented as a non-composite device that performs linear sum of the (possibly) weighted inputs and passes the sum through a static nonlinearity. Nevertheless, in recent years, much attention has been paid to the processing stages within the neuron with the result that new computational capabilities have been discovered in connection with previously neglected parts of the neuron, most significantly, the dendritic tree and spines. These capabilities are associated with the nonlinearities intrinsic to the physiology of the dendrites and spines and most importantly, but not exclusively, with their active properties. This is so because, as exposed in the quote above, the essence of computation is nonlinearity. A composition of linear fuctions, no matter how complicated or deep, is nothing but another linear function. Computation, in a broad sense, cannot therefore be accomplished just with linear units.

In this paper a step-by-step strategy is iniciated in the hope that kowledge about separate computing elements is essential for a thorough understanding of their complex interactions in real neurons. The choice of a computer model as a starting point for the nonlinear analysis of neurons is also inspired by this strategy in a twofold sense: first because a detailed identification of computer models of neurons as nonlinear systems is expected to help us understand

equivalent studies in *in vivo/in vitro* experiments; but also because the differences found between results obtained for models and for real neurons can help improve the models by pointing to the operational differences. In section 2, a brief description of the Wiener-Volterra methodology is sketched; in section 3 the basic properties of the original model of the Purkinje cell used in this paper are summarized; in section 4 the *in silico* experiment designed to obtain the nonlinear properties of the model dendrites is described and, finally, in section 5, Wiener kernels thus obtained are presented and discussed.

2 Wiener-Volterra theory.

We have chosen a classical tool in the field of nonlinear system identification -the Wiener-Volterra functional series expansion- to characterize the nonlinear properties of dendritic trees. From a practical point of view, parallel cascade methods can be an interesting alternative to functional expansion due to their general applicability if *a priori insight of the system structure is available. The full resolution of the neurochemical equations governing the processing of signals in the neuron is not conceivably practical for computing with artificial neurons. There are many applications of the Wiener-Volterra formalism in any of its different flavours to biomedical systems (see e.g. [1], [2] or [3]).*

In its original formulation, the theory only considered single-input systems but was subsequently extended by Marmarelis and Naka to multiple-input/output systems in the context of biological engineering (see [4]). In brief, Wiener [5] showed that, given a causal system S, whose input is x(t) and output y(t), this output can be written as $y(t) = \sum_{n=0}^{\infty} G_n[h_n, x(t)]$ *where* $\{G_i\}$ *is a complete set of orthogonal functionals with respect to a gaussian white-noise input x(t).*

The set of kernels $\{h_i\}$ characterizes the system and each kernel is a symmetric function of its arguments. The first kernel h_1 is nothing but the impulse response of linear systems while higher order (i.e. nonlinear) kernels quantify the nonlinear cross-talk of different portions of the past of the system.

In [5], Wiener expanded the kernels in terms of Laguerre polynomials so that the identification of the system reduced to a problem of coefficient determination. Later Lee and Schetzen [6] showed that the kernels could be obtained directly by means of correlation techniques, which is the approach adopted here. Nevertheless, recent work on Laguerre expansions seems to solve some of the problems associated with the necessity of a gaussian white-noise input that can not always be reliably achieved in all experimental circumstances. The work of Westwick et al. [7] on the sensitivity analysis of kernel estimates tries to asses the validity of this approach.

3 The model neuron

The formalism described above is applied to a model Purkinje cell constructed in GENESIS by De Schutter and Bower,[8] and described further in [9]. In brief, it consists of a compartmental model with active dendritic membrane including ten different types of voltage dependent channels described by Hodgkin-Huxley equations. Ionic channels were differentially distributed over three regions of the cell with Na^+ channels in the soma, fast K^+ channels in the soma and main dendrite and Ca^{2+} channels and Ca^{2+} activated K^+ channels in the entire dendrite. Channel densities were adjusted to reproduce Purkinje cell responses to current injections in the soma or dendrites, as observed in slice recordings.

The model can receive synaptic input from

(1) ***climbing fibers*** *in all compartments of the main and smooth dendrites (with a total delay between the main dendrite and the last smooth dendrite of 0.9 ms)*

(2) ***granule cells*** *in every dendrite with diameter less than 3.17 μm. This represents a total of 1474 synapses (roughly a 1% of the number of real inputs). The difference is compensated for by linearly scaling the firing frequencies and increasing proportionally the membrane surface of each compartment.*

(3) ***stellate cells*** *in both smooth dendritic compartments (two inhibitory synapses of conductance 1.4 mS/cm^2) and small spiny dendrites (one inhibitory synapse of conductance 7 mS/cm^2). This results in a total of 1695 synapses.*

(4) *and* ***basket cells*** *in the soma and main dendrite (20 inhibitory synapses in total with the same kinetics as for stellate cells).*

4 The experiment

The present paper concentrates on the characterization of dendrites as nonlinear systems subject to multiple inputs from granule and stellate cells. The identification of the nonlinear processing capabilities of dendrites under the four kinds of synaptic input sources of the model will be addressed in subsequent research.

In order to apply the Wiener-Volterra formalism we have modified the original model named Purk2M9sA *[8] to switch off asynchronous firing of parallel fiber*

and stellate cell inputs. Climbing fiber and basket cell inputs were kept silent and the original soma was substituted with a passive one.

Granule cell synapses were simulated with a varying number of synaptic inputs located in proximal (b0s01 and b0s02) and distal branches (b3s44 and b3s45) in different experiments. A second set of numerical experiments was performed were proximal and distal branches were simultaneously stimulated in order to obtain second order cross kernels for the intervening synapses. The synaptic locations were distributed in compartments with diameters smaller than 3.17μm and covered the branches homogeneously. The distance to the soma ranges from 8 to 30 compartments (78 to 132 μm from soma) for proximal branches and from 37 to 40 for distal ones (328 to 325 μm from soma). Input in the synapses were independent series of simulated gaussian white noise of zero mean and different variances. Inputs and output at the first dendritic compartment, main[0], were recorded for a total time from 500 to 5000 seconds at time intervals of 1.0×10^{-4} *s. These data were subsequently processed to obtain first and second order self- and cross-kernels. A stabilization period of 5 to 6 seconds was introduced to allow the system to reach stationarity.*

5 Results

In the set of numerical experiments described above we have encountered severe limitations that make it difficult the overall application of the cross-correlation approach to the determination of synaptic Wiener kernels. In the first place, the exploration of parameter space shows that simultaneous stimulation of down to 5 synaptic locations in either branch with gaussian white noise of unit variance drives the system into cyclic production of small scale pseudo-

spikes as shown in figure 1. The precise values of the period and amplitude of the cycles depend on the total power injected in the system through the number of activated synapses and the variance of the white gaussian noise. The kernels in these situations lose their functional meaning.

Below these power levels (i.e. for less than 5 synaptic inputs and variances below unity), the system recovers sensitivity to specific inputs but cross correlations for even first order kernels yield poor statistical results due to the fact that the amplitude of the kernels is of the same order of magnitude of the correlation variance. Figure 2 shows an example of a first order kernel obtained in an experiment with two active synapses on branch b0s01 and gaussian white noise of variance 0.01.

Given the limitations posed to the cross correlation method by limit cycles in the phase space and numerical accuracy in the determination of the kernels we propose a different approach that presents the advantage that can be experimentally validated: a new set of numerical experiments where the same low variance gaussian white noise is simultaneously applied to all the synapses in a given branch while different noise series are applied to different branches. This way, the focus is put on the branches as nonlinear computational devices rather than the synapses themselves.

In the second stage, the Wiener kernels will be expanded in a basis of discrete Laguerre functions whose coefficients can be computed by least square regression, as opposed to the direct cross correlation estimate of the kernels. This technique takes advantage of heuristic knowledge about the expected kernel smoothness. Finally, the variance of the estimated kernels will be assessed following [7].

Luis Manuel Sarro obtained his degree in Physics at the Universidad Complutense de Madrid and started his career as astrophysicist in the Laboratory for Space Astrophysics and Fundamental Physics at Madrid in the field of Solar Physics. In 1998 he obtained his PhD. in Astrophysics and in 2000, he joined the Artificial Intelligence Department at UNED (Madrid) as associate lecturer where he shifted his research interest towards neural network computation and nonlinear information processing in dendritic trees of Purkinje and pyramidal CA1 cells.

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Fig. 1. Repetitive spiking at main[0] recorded for a numerical setup of five activated synapses in branch b0s01 with gaussian white noise of unit variance.

Fig. 2. First order kernel computed for synaptic locus at spine[26] in branch b0s01 obtained with gaussian noise of variance 0.01.

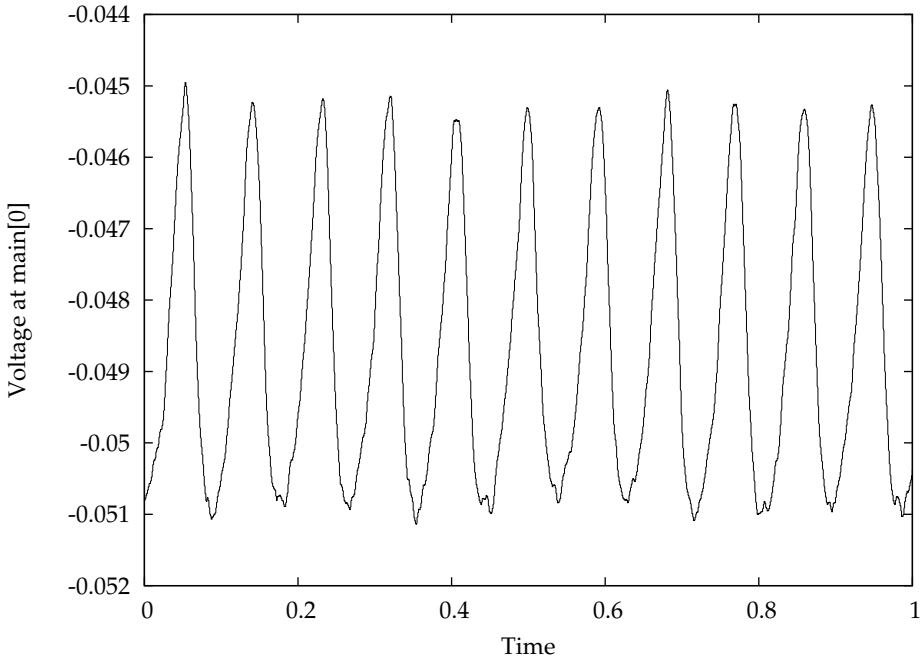
-0.044
-0.045
-0.046
-0.047
-0.048
-0.049
-0.05
-0.051
-0.052
Voltage at main[0]
0
0.2
0.4
0.6
0.8
1
Time

Fig. 1.

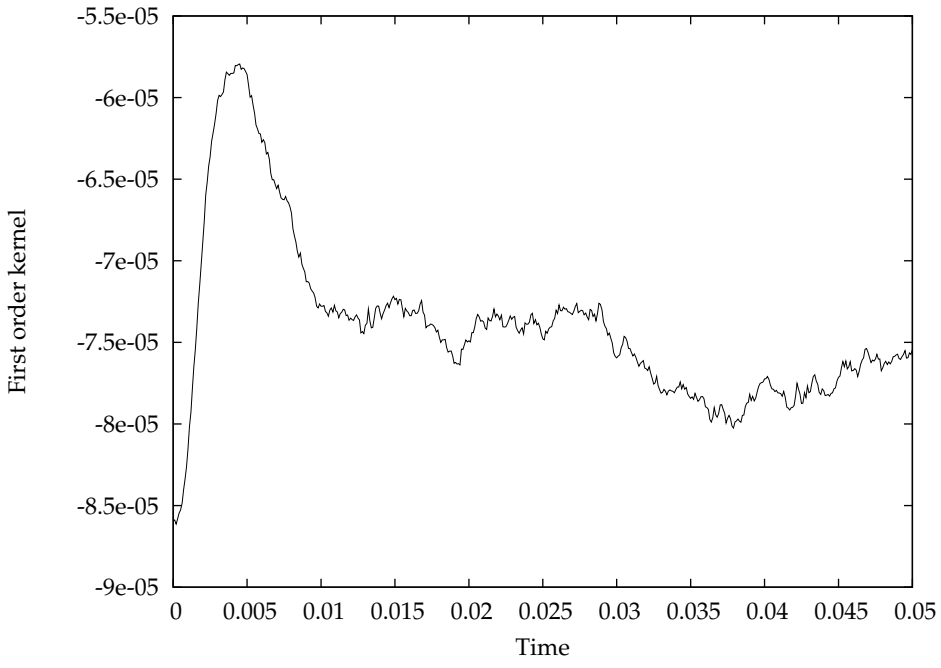
-5.5e-05
-6e-05
-6.5e-05
-7e-05
-7.5e-05
-8e-05
-8.5e-05
-9e-05
First order kernel
0
0.005
0.01
0.015
0.02
0.025
0.03
0.035
0.04
0.045
0.05
Time

Fig. 2.