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# Decomposition of neural systems with nonlinear feedback using stimulus–response data

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**Abstract**

The need often arises in many modeling studies of physiological systems with feedback, for separate characterization of the feedthrough and feedback components using stimulus–response data from the entire system. For instance, the hippocampal formation consists of multiple feedback connections which are difficult to identify experimentally. This paper investigates the application of adaptive estimation techniques in the context of the Volterra–Wiener approach to decompose unobservable subsystems from the overall feedback system data. Computer simulation studies have demonstrated its effectiveness over the traditional approach which employs nonlinear systems analysis in the frequency domain. This approach can be used to indirectly characterize the unobservable feedback basket cells in the hippocampus utilizing experimental stimulus–response data from dentate granule cells. 

## 1. Introduction

Feedback is ubiquitous in physiological systems in general and in neural systems in particular. Direct experimental observation in the form of stimulus–response data is usually possible for the overall feedback system. In many instances, experimental manipulation (e.g., pharmacological or surgical intervention) allows the direct experimental observation of stimulus–response data from the feedthrough component alone (i.e., open-loop experiment by disabling the feedback pathway). However, it is rarely feasible to record stimulus–response data directly from the feedback pathway alone

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and, thus direct modeling of the feedback component alone is not usually possible. In these cases, the only way of modeling the feedback component alone is indirectly, through system decomposition using the direct measurements from the overall system and the feedthrough component. This task is mathematically and computationally complicated in the presence of nonlinearities, with no effective methodologies currently available for its pursuit.

This paper presents an effective methodology for accomplishing this task when the feedthrough component is nonlinear and the feedback component is either linear or nonlinear of a specific type. The method is placed in the general Volterra context for the representation of system nonlinearities and employs adaptive estimation techniques to obtain estimates of the feedback component. We expect that this approach can be extended later to a broader class of nonlinear feedback components, as well as more complex model configurations with multiple or nested feedback loops.

The use of adaptive estimation techniques enables the characterization of neuronal network components that are not experimentally observable. The input–output properties of experimentally observable neuronal networks are represented by kernels of the Volterra functional series [1,10–12]. which are determined by random impulse train stimulation of network afferents while simultaneously recording the activity of the output neurons. Kernel representation of these experimentally observable systems enables the methodical identification of experimentally unobservable subsystems (decomposition) using adaptive estimation. The adaptive estimation approach seems to overcome the limitations of the previously used decomposition method that is based on nonlinear systems analysis in the frequency domain [3,6,9,17].

It is hoped that this approach will enable the systematic network analysis and decomposition of the hippocampal formation which consists of five major cell populations. These cell populations are serially organized (Fig. 1B) in a multiple cascade configuration, i.e. the output of one cell population provides the input to another cell population. Each major cell population is further modulated by smaller subsystems of cells which provide a variety of feedback or feedforward connections. While many of the cell populations can be identified experimentally, other smaller subsystems (e.g., feedback) are difficult to record from and cannot be directly identified. This gives rise to the requirement of effective decomposition methods.

As an example, consider the application of the adaptive estimation approach to the study of the granule cells of the dentate gyrus (Fig. 1B) which are modulated by multiple feedback connections known as basket cells. While the granule cells are relatively easy to record from, the basket cells are not, but play a very influential role in memory and learning. However, the dynamic properties of the basket cells can be derived through decomposition of those systems that we can experimentally record from. Simultaneous recording of the granule cell output (including feedback inhibition) during random impulse train stimulation (RITS) at the perforant path is defined as the *overall system*. Recording of the granule cell output *without* the feedback inhibition during RITS is also possible by pharmacologically blocking the basket cells. This system is subsequently described as the *feedthrough subsystem*. Characterization of these two systems enables the decomposition of the *feedback subsystem* using adaptive estimation techniques.

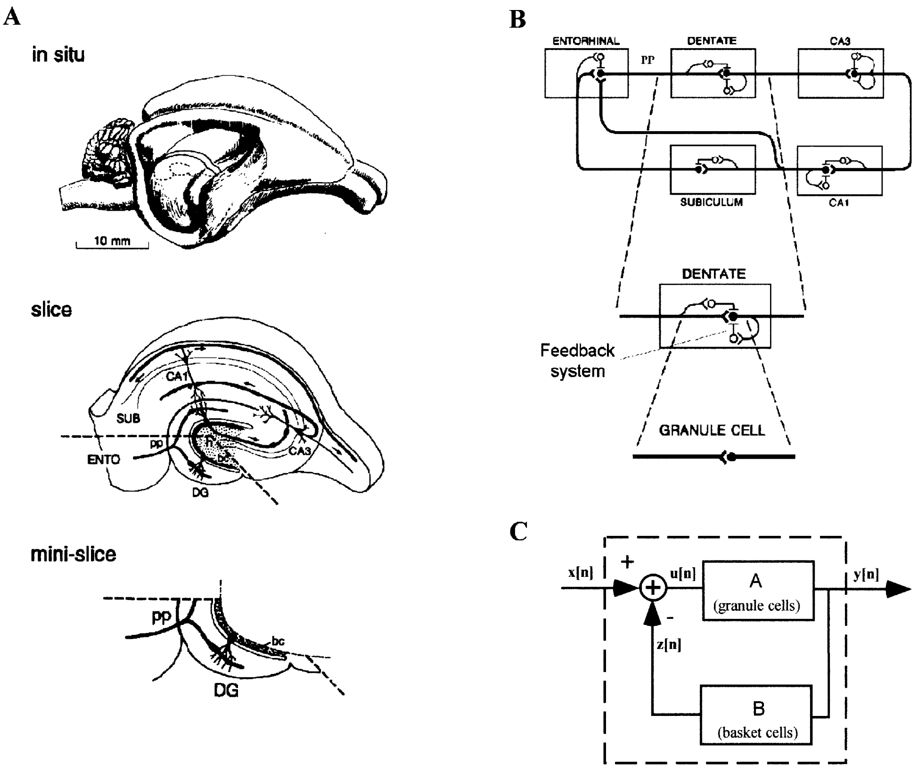



Fig. 1. The hippocampal formation. (A) Illustrations of three preparations which are used to obtain nonlinear response properties for the dentate granule cells of the hippocampus. (B) The corresponding box diagrams of the idealized intrinsic circuitry for each preparation. (C) Feedback model of the dentate gyrus

The adaptive estimation approach alleviates many of the limitations associated with decomposition in the frequency domain using nonlinear systems analysis [4,17]. Successful decomposition using nonlinear systems analysis is highly sensitive to errors in the kernel estimates of observable systems. Conversely, successful decomposition using the adaptive estimation method is less sensitive to errors in the kernel estimates and is performed entirely in the time domain. Initial studies conducted on simulated nonlinear systems with linear and nonlinear feedback in the presence of noise has shown that the adaptive approach is far more effective than nonlinear systems analysis in the frequency domain for feedback decomposition.

## 2. Methodology

Adaptive estimation algorithms have been used extensively to obtain estimates of unknown parameters according to an error minimization criterion. The most basic form of adaptive estimation is the least-mean-squares (LMS) method, which is based on the steepest descent algorithm and enables the adjustment of the unknown parameter values of a system from sample to sample in order to minimize the output mean-square-error (MSE) [7,18]. Many other adaptive estimation algorithms exist, most of them based on gradient descent methods for minimization of an error function.

The application of the Volterra approach to nonparametric modeling of neural systems has been studied extensively in recent years [2,12,13,16,17]. The general input–output relation of any discrete-time, stable, nonlinear time-invariant system may be described by the discrete-time Volterra series:

$$y[n] = k_0 + \sum_{m_1=0}^{M} k_1(m_1)x(n-m_1) + \sum_{m_1=0}^{M}\sum_{m_2=0}^{M} k_2(m_1,m_2)x(n-m_1)x(n-m_2) + \cdots, \tag{1}$$

where $x(n)$ denotes the input and $\{k_i\}$ denote the Volterra kernels of the system. The kernels describe the dynamics of a system at each order of nonlinearity. The kernels for a real biological system can be estimated from input–output data using a variety of techniques [8,10,11,14,15].

This paper is concerned with modeling the dentate gyrus of the hippocampus. This system may be represented by the feedback model of Fig. 1C where the feedthrough subsystem A represents the granule cells and the feedback subsystem B represents the inhibitory feedback interneurons, e.g. basket cells.

While the granule cells of the dentate gyrus are reasonably easy to record from, it is very difficult to record from the feedback interneurons known as basket cells. However, if we can characterize the overall system and the feedthrough subsystem A, then the feedback subsystem B may be indirectly characterized through decomposition. The overall system may be characterized through random impulse train stimulation (RITS) and recording the output of the granule cells which includes the effect of the feedback interneurons. The feedthrough subsystem may be isolated by blocking the feedback inhibition pharmacologically and characterized through RITS.

If input–output data for the overall system and the feedthrough subsystem can be experimentally obtained, then the feedback subsystem may be characterized through decomposition using adaptive estimation. If the feedthrough subsystem A ($a_1$, $a_2$) and the overall system are nonlinear, then the general expressions for the noise-free signals in Fig. 1C are:

$$y[n] = \sum_{m_1=0}^{M} a_1(m_1)u(n-m_1) + \sum_{m_1=0}^{M}\sum_{m_2=0}^{M} a_2(m_1,m_2)u(n-m_1)u(n-m_2) + \cdots, \tag{2}$$

$$z[n] = \sum_{m_1=0}^{M} b_1(m_1)y(n-m_1)$$
$$+ \sum_{m_1=0}^{M} \sum_{m_2=0}^{M} b_2(m_1, m_2)y(n-m_1)y(n-m_2) + \cdots, \tag{3}$$

$$u[n] = x[n] - z[n], \tag{4}$$

where $(a_1, a_2, \dots)$ and $(b_1, b_2, \dots)$ are the Volterra kernels of the subsystems A and B, respectively. If we choose a quadratic error function:

$$C = \tfrac{1}{2}e^2, \tag{5}$$

where $e = y - \hat{y}$ is the error to be minimized between the output model prediction $y$ and the actual output observation $\hat{y}$, then the unknown feedback kernels can be determined by minimization of $C$ using the gradient steepest descent method.

The first-order feedback kernel (Eq. (6)) may be estimated by means of the iterative expression based on gradient descent:

$$b_1^{(j+1)} = b_1^{(j)} - \gamma e(n)\frac{\partial e(n)}{\partial b_1(m)}, \tag{6}$$

where $j$ is the iteration index and $\gamma$ is a specified adaptation constant. The partial derivative in Eq. (6) can be expressed in terms of the chain rule as:

$$\frac{\partial e(n)}{\partial b_1(m)} = \frac{\partial y(n)}{\partial u(n)}\frac{\partial u(n)}{\partial z(n)}\frac{\partial z(n)}{\partial b_1(m)} = -\left[a_1(0) + 2\sum_{i=0}^{M} a_2(i, 0)u(n-i)\right]y(n-m). \tag{7}$$

Likewise, the second-order feedback kernel (Eq. (8)) may be estimated as

$$b_2^{(j+1)}(m_1, m_2) = b_2^{(j)}(m_1, m_2) + \gamma e(n)\frac{\partial e(n)}{\partial b_2(m_1,m_2)}, \tag{8}$$

where $j$ is the iteration index and $\gamma$ (is a specified adaptation constant. The partial derivative in Eq. (8) can be expressed in terms of the chain rule as

$$\frac{\partial e(n)}{\partial b_2(m_1, m_2)} = \frac{\partial \hat{y}(n)}{\partial u(n)}\frac{\partial u(n)}{\partial z(n)}\frac{\partial z(n)}{\partial b_2(m_1, m_2)}$$
$$= \left[a_1(0) + 2\sum_{m} a_2(0, m)u(n-m)\right]y(n-m_1)y(n-m_2). \tag{9}$$

Note that the feedthrough kernels must be known (or previously estimated by open-loop data) for this algorithm. These unknown kernel values are updated until the error function is reduced below a certain specified threshold. Note that the values of $u(n)$ used in the iterative expressions (7) and (9) are also continuously updated at each iteration according to Eq. (4).

## 3. Illustrative example

This approach was tested and validated using simulated data generated from the feedback system of Fig. 2. The feedthrough subsystem A is composed of the cascade of a linear filter with impulse response, $g(m)$ followed by a quadratic static nonlinearity: $(\bullet) + \alpha(\bullet)^2$. The feedback subsystem B is likewise composed of the cascade of a linear filter with impulse response f(m) and a quadratic static nonlinearity: $(\bullet) + \beta(\bullet)^2$. Although the feedthrough and the feedback subsystem is a second-order Volterra system when viewed in isolation, the overall system is an infinite order Volterra system in the closed-loop conditions.

The chosen impulse response functions $g(m)$, feedthrough, and $f(m)$, feedback, are shown in Fig. 3. The nonlinear feedthrough subsystem and the nonlinear overall system are simulated separately for a Poisson process input with mean rate of $\lambda = 0.10$ and 2000 data points (about 200 spikes), for two cases: linear feedback ($\beta = 0$) and nonlinear feedback ($\beta = 0.2$).

From the input–output data of the feedthrough subsystem, we estimate the kernels $a_1$ and $a_2$ using a kernel estimation technique based on artificial neural networks [15]. Comparison of the kernel estimates to the actual kernels (Figs. 4 and 5) shows that the feedthrough first- and second-order kernel estimates are very accurate.

Once the kernel estimates for the feedthrough subsystem are computed, adaptive estimation of the feedback kernels can be performed using the overall system input–output data. For linear feedback, the decomposition result using adaptive estimation is compared to the actual feedback kernel as well as the result using the frequency-domain approach in Fig. 6. The adaptive decomposition result was computed using 1000 iterations with an adaptation constant $\gamma = 0.001$. From the result of Fig. 6, it is evident that the adaptive estimation technique is far more accurate than the frequency-domain technique.

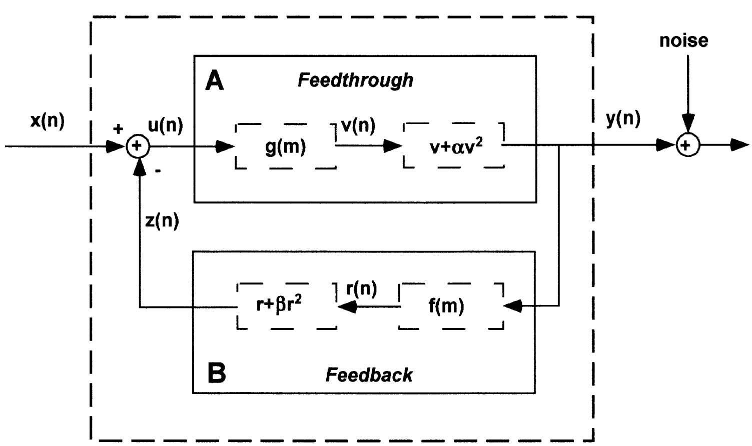



Fig. 2. Simulated feedback system with feedthrough subsystem A and feedback subsystem B.

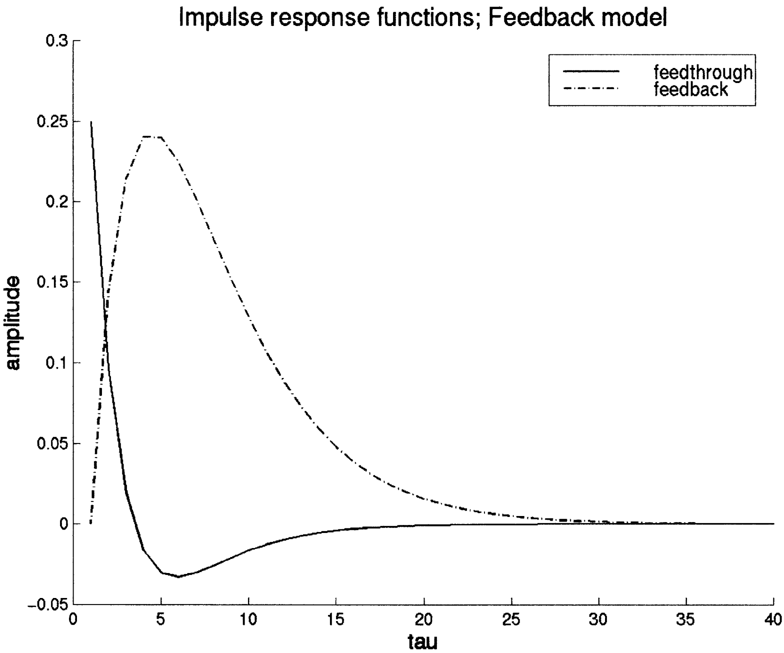



Fig. 3. Impulse response functions of the linear filters of the simulated system.

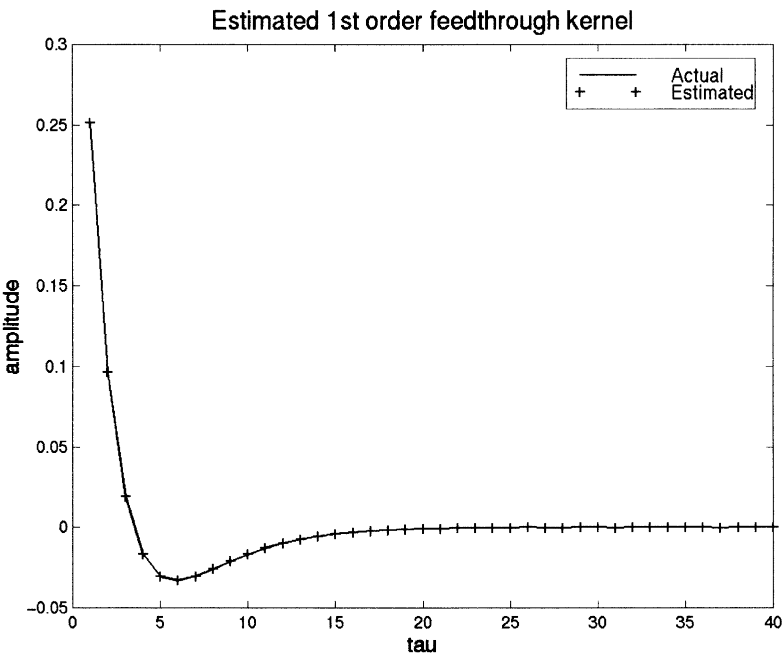



Fig. 4. Exact and estimated first-order kernel of the feedthrough subsystem.

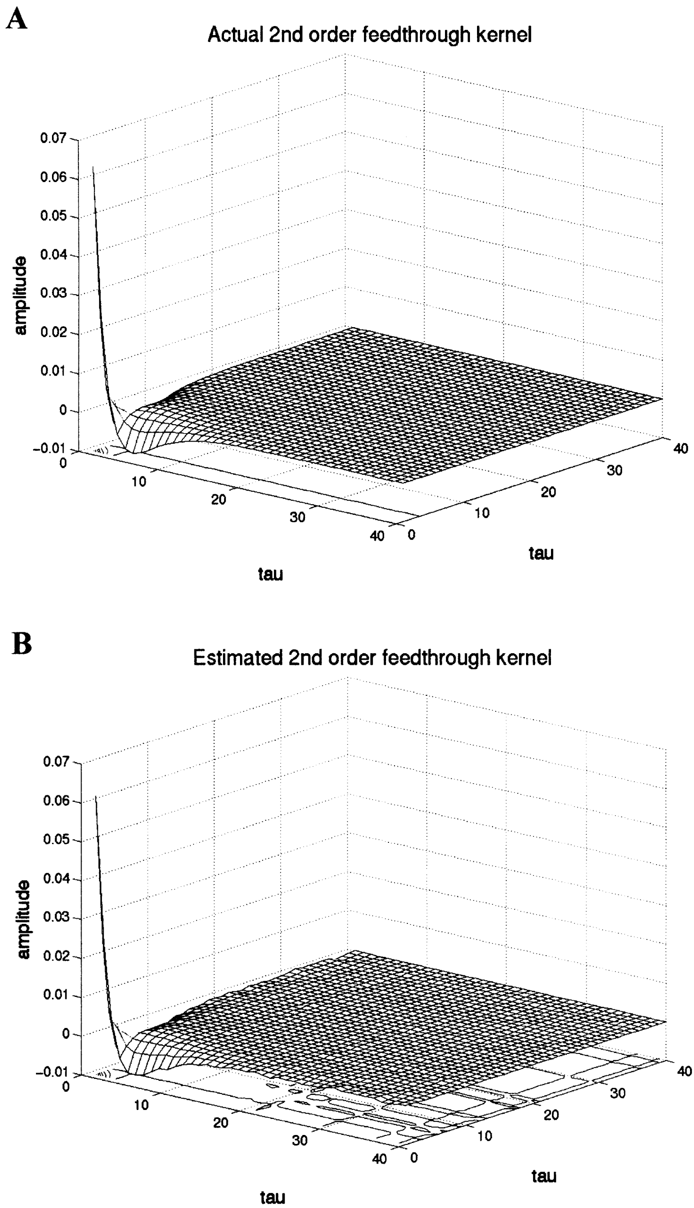



Fig. 5. (A) Actual second-order kernel of the feedthrough subsystem. (B) Estimated second-order kernel of the feedthrough subsystem.

To examine the robustness of the adaptive estimation approach in the presence of output-additive noise, we add Gaussian white noise to the output for a signal-to-noise ratio of 0 dB. The obtained results from the noisy data are shown in Fig. 7 and demonstrate the robustness of the proposed approach.

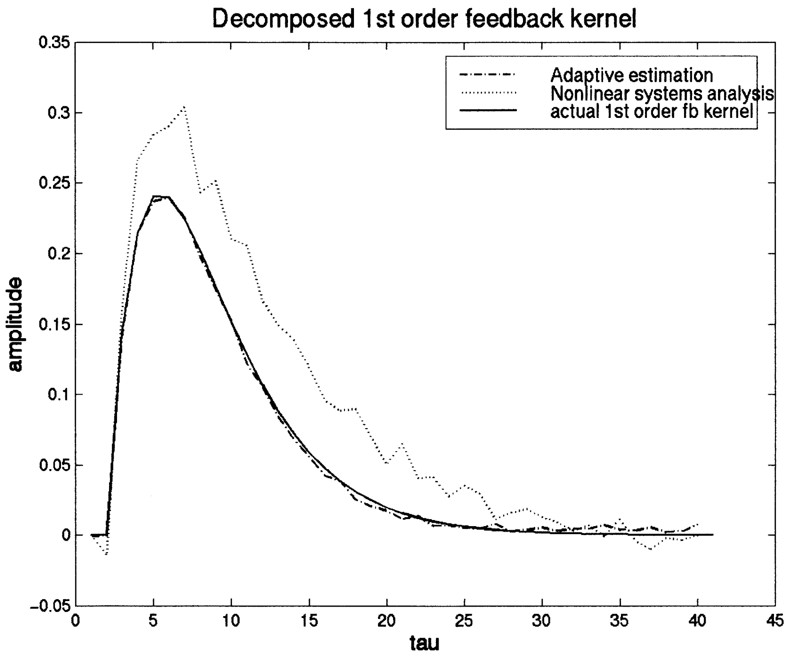



Fig. 6. Decomposed first-order feedback kernel using adaptive estimation vs. frequency-domain technique, along with the actual first-order feedback kernel.

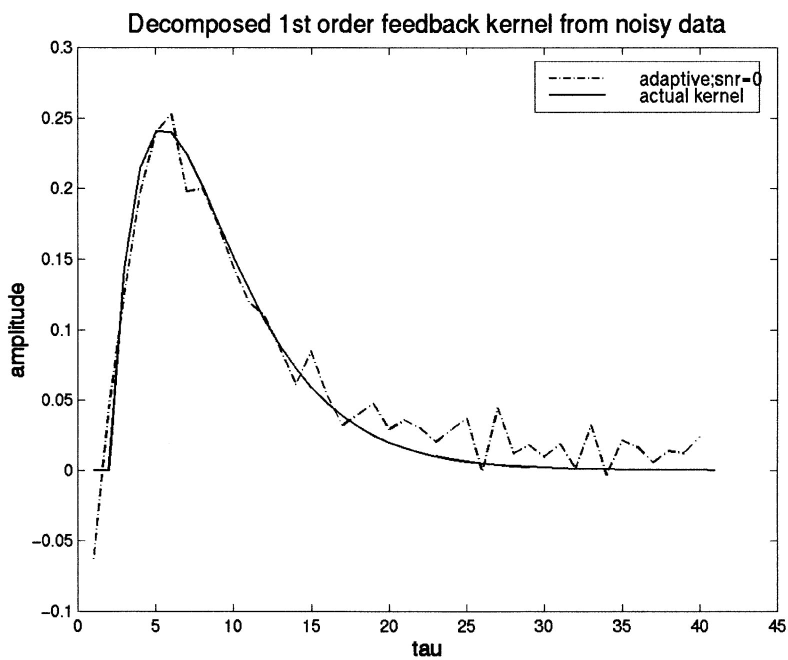



Fig. 7. Comparison of actual first-order kernel to adaptive result with noisy data.

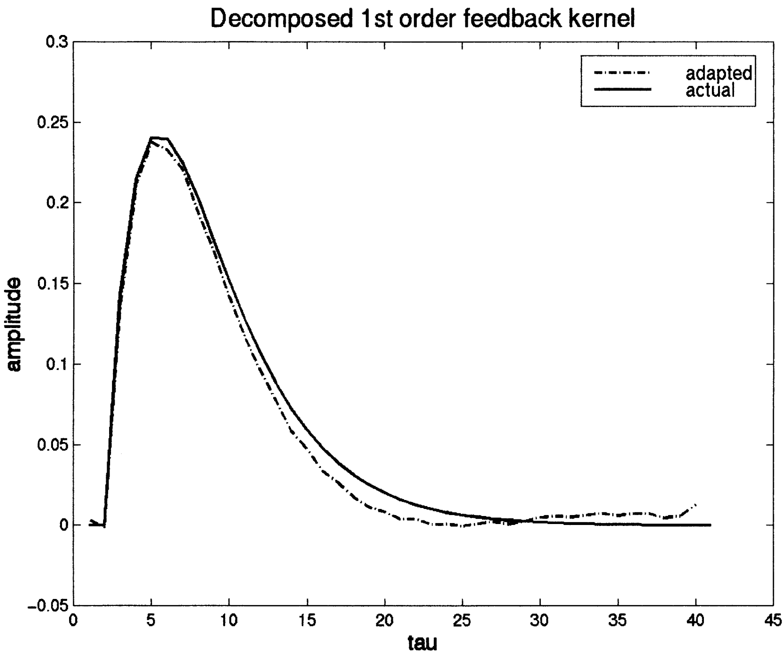



Fig. 8. Decomposed first-order feedback kernel vs. actual first-order feedback kernel for the nonlinear feedback case.

In the nonlinear feedback case ($\beta = 0.2$), we seek to recover the quadratic coefficient $\beta$ (Fig. 2) in addition to the first-order feedback kernel,using adaptive estimation. Using the chain rule for the system of Fig. 2, we derive the following iterative chain rule:

$$f_1(m)^{(j+1)} = f_1(m)^{(j)} - \gamma e(n) \frac{\partial e(n)}{\partial f_1(m)}, \tag{10}$$

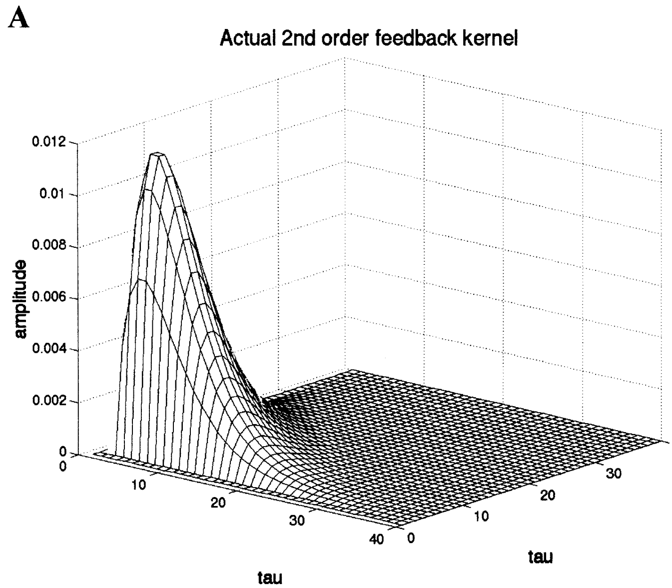
where

$$\frac{\partial e(n)}{\partial f_1(m)} = \frac{\partial y(n)}{\partial u(n)} \frac{\partial u(n)}{\partial z(n)} \frac{\partial z(n)}{\partial r(n)} \frac{\partial r(n)}{\partial f_1(m)}$$

$$= -\left[ a_1(0) + 2 \sum_{i=0}^{M} a_2(i,0) u(n-i) \right] [2\beta r(n) + 1] y(n-m) \tag{11}$$

and

$$\beta^{(j+1)} = \beta^{(j)} - \mu e(n) \frac{\partial e(n)}{\partial \beta}, \tag{12}$$



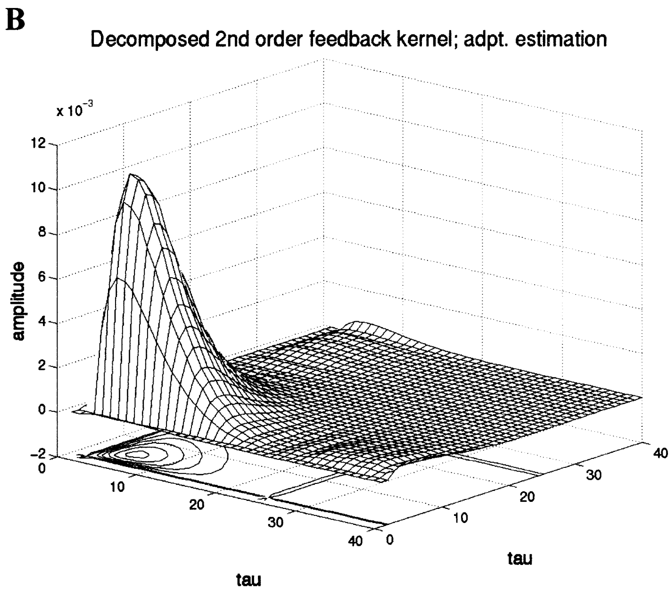




Fig. 9. (A) Actual second-order kernel of the feedback subsystem. (B) second-order feedback kernel constructed from decomposed first-order feedback kernel and the trained $\beta$ coefficient.

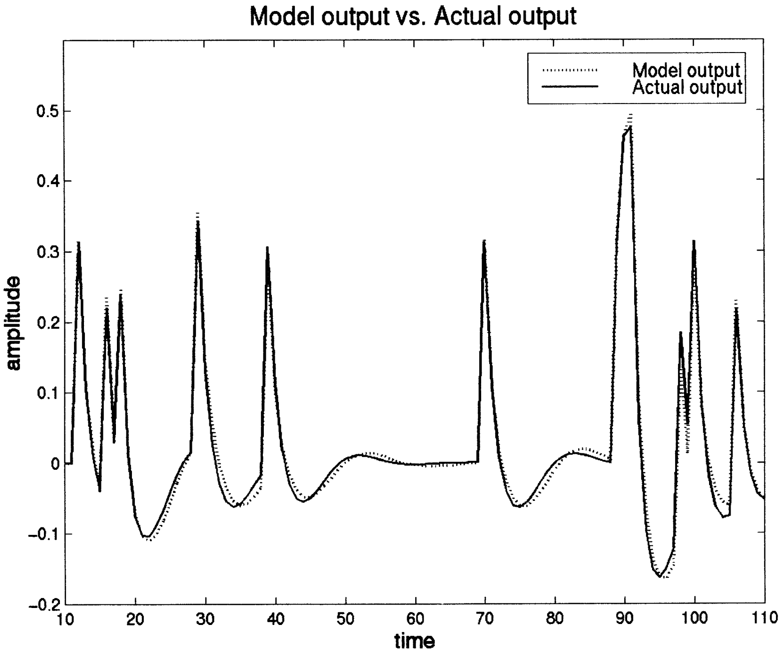



Fig. 10. Model predicted output (dotted) vs. the actual system output (solid) for nonlinear feedback case.

with

$$\frac{\partial e(n)}{\partial \beta}=\frac{\partial y(n)}{\partial u(n)}\frac{\partial u(n)}{\partial z(n)}\frac{\partial z(n)}{\partial \lambda}$$
$$= -\left[a_1(0)+2\sum_{i=0}^{M} a_2(i,0)u(n-i)\right]r(n)^2. \tag{13}$$

Note that $\mu$ is, in general, a different adaptation constant.

The first-order feedback kernel shown in Fig. 8 along with the exact kernel, demonstrates the efficacy of this approach.

The obtained estimate of the quadratic coefficient $\beta$ is 0.1895 (versus the exact value $\beta = 0.2$). The result was computed using 1000 iterations with adaptive constant $\gamma = 0.008$ in Eq. (10) and $\mu = 0.01$ in Eq. (12). However, the nonlinear feedback case required 5000 data points (500 spikes), which was larger than the data record used in the linear feedback case (by a factor of 5).

From the decomposed first-order feedback kernel and the trained $\beta$ coefficient, a second-order feedback kernel was constructed. Comparison of the constructed second-order feedback kernel (Fig. 9B) to the actual second-order feedback kernel (Fig. 9A) show that the constructed kernel is very similar in time course but slightly smaller in amplitude.

Another illustration of the efficacy of this approach is given in Fig. 10, where a segment of the model predicted output is shown along with the actual output.

## 4. Discussion

The development of an adaptive estimation approach for feedback decomposition was necessitated by limitations of the previously proposed method of nonlinear systems analysis in the frequency domain [4]. The adaptive estimation approach yields more accurate results and is more robust in the presence of noise.

One fundamental difference between the two approaches is that kernel estimates are required for both the feedthrough subsystem and the overall system for nonlinear systems analysis, but only the feedthrough kernels are required for adaptive estimation. In nonlinear systems analysis, it was also observed that the poor accuracy of feedback decomposition was primarily attributed to inaccurate overall system kernel estimates due to higher-order nonlinearities [5]. Thus, the adaptive estimation method yields more accurate results because only the feedthrough kernel estimates are required, along with the overall system input–output data.

Another source of error in feedback decomposition is the frequency transformations for nonlinear systems analysis. The latter requires multi-dimensional discrete frequency transforms for each kernel estimate involved in the decomposition process. Small estimation errors associated with each discrete frequency transform can be magnified to larger errors due to divisions used in this approach. Conversely, adaptive estimation is performed entirely in the time domain with an iterative procedure. While this requires a slightly longer computation time, the results have demonstrated higher accuracy and greater robustness to noise.

The initial studies show that the adaptive method produced better decomposition results for the feedback case than the nonlinear systems analysis method in the frequency domain. While adaptive estimation typically requires longer computation time due to the employed iterative procedures, this approach overcomes many of the limitations associated with the frequency domain approach. It is expected that the adaptive estimation approach can be used to decompose different configurations in the hippocampus. Not only can it be applied to feedback systems but the concept can be extended to analyze more complicated configurations including nested feedback, parallel, and cascade systems. Application of this approach to experimental data is currently under way.

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## References

[1] T.W. Berger, J.L. Eriksson, D.A. Ciarolla, R.J. Sclabassi, Nonlinear systems analysis of the hippocampal perforant path-dentate projection. III. Comparison of Random Train and Paired Impulse Stimulation, J. Neurophysiol. 60 (1988) 1095–1109.

[2] T.W. Berger, P.T. Harty, B. Barrionuevo, R.J. Sclabassi, Experimental basis for an input/output model of the hippocampal formation, in: V.Z. Marmarelis (Ed.), Advanced Methods of Physiological System Modeling, Vol. 3, Plenum Press, New York, 1994, pp. 112–128.

[3] M.B. Brilliant, Theory of the analysis of nonlinear systems, Technical Report 345, Research Laboratory of Electronics, Massachusetts Institute of Technology, 1958.
[4] M. Chian, V. Marmarelis, T. Berger, Characterization of unobservable neural circuitry in the hippocampus with nonlinear systems analysis, 4th Joint Symposium on Neural Computation Proceedings, vol. 7, 1997, pp. 43–50.
[5] M.T. Chian, Decomposition of neuronal function using nonlinear systems analysis, Master's Thesis, Dept. of Biomedical Engineering, University of Southern California, 1996.
[6] D.A. George, Continuous nonlinear systems, Technical Report 355, Research Laboratory of Electronics, Massachusetts Institute of Technology, 1959.
[7] E.C. Ifeachor, B.W. Jervis, Digital Signal Processing: A Practical Approach, Addison-Wesley, Wokingham, UK, 1993.
[8] M.J. Korenberg, Identifying nonlinear difference equation and functional expansion representations: the fast orthogonal algorithm, Ann. Biomed. Eng. 16 (1988) 123–142.
[9] B.R. Kosanovic, Theoretical and experimental decomposition of neuronal structures, Master's Thesis, Dept. of Electrical Engineering, University of Pittsburgh, 1992.
[10] H.I. Krausz, Identification of nonlinear systems using random impulse train inputs, Biol. Cybernet 19 (1975) 217–230.
[11] Y.W. Lee, M. Schetzen, Measurement of the Wiener kernels of a non-linear system by cross-correlation, Int. J. Control 2 (1965) 237–254.
[12] P.Z. Marmarelis, V.Z. Marmarelis, Analysis of Physiological Systems: The White Noise Approach, Plenum, New York, 1978.
[13] V.Z. Marmarelis (Ed.), Advanced Methods of Physiological System Modeling, vol. II, Plenum, New York, 1989.
[14] V.Z. Marmarelis (Ed.), Advanced Methods of Physiological System Modeling, vol. III, Plenum, New York, 1994.
[15] V.Z. Marmarelis, X. Zhao, Volterra models and three-layer perceptrons, IEEE Trans. Neural Networks 8 (1997) 1421–1433.
[16] M. Schetzen, The Volterra and Wiener Theories of Nonlinear Systems, Robert E. Krieger Publishing Company, Malabar, FL, 1989.
[17] R.J. Sclabassi, B.R. Kosanovic, G. Barrionuevo, T.W. Berger, Computational methods of neuronal network decomposition, in: V.Z. Marmarelis (Ed.), Advanced Methods of Physiological System Modeling, Vol. III, Plenum Press, New York, 1994, pp. 55–86.
[18] B. Widrow, M.E. Hoff, Adaptive switching circuits, WESCOM Conv. Rec., Pt. 4 (1960) 96–140.

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