



Letter

# On the possible use of ICA to identify synaptic inputs from observations of several neurons

Pando Gr. Georgiev<sup>a,1</sup>, Henry C. Tuckwell<sup>a,b,c,\*</sup>

<sup>a</sup>*Riken Brain Science Institute, Wako-shi, Saitama 351-0198, Japan*

<sup>b</sup>*Department of Mathematics, University of California at San Diego, La Jolla, CA 92093, USA*

<sup>c</sup>*Max-Planck-Institut für Mathematik in the Sciences Inselstr. 22, D-4103 Leipzig, Germany*

Received 22 July 2004; received in revised form 16 August 2004; accepted 18 August 2004

Available online 7 March 2005

Communicated by R.W. Newcomb

---

## Abstract

We consider the problem of separating and determining the time courses of various synaptic input currents from simultaneous recordings of the time courses of membrane potentials, including spikes, of several neurons. Employing a suitable mathematical model, the method involves the differentiation of potentials and the use of ICA to determine the relative strengths of various synaptic inputs. At the same time, the waveforms of these input currents are recovered. We illustrate the application to nonlinear point models with deterministic and stochastic input currents, using a single-component Fitzhugh–Nagumo approximation.

© 2005 Published by Elsevier B.V.

*Keywords:* ICA; Synaptic potentials; Separation; Identification

---

---

\*Corresponding author. Department of Mathematics, University of California at San Diego, UCSD, Gillman Drive, La Jolla, CA 92093, USA. Tel.: +1 858 534 5863; fax: +1 858 452 9848.

*E-mail addresses:* [georgiev@bsp.rain.riken.go.jp](mailto:georgiev@bsp.rain.riken.go.jp) (P.G. Georgiev), [tuckwell@u444.jussieu.fr](mailto:tuckwell@u444.jussieu.fr) (H.C. Tuckwell).

<sup>1</sup>From September 2004: ECECS Department, University of Cincinnati, Cincinnati, OH 45221-0030, USA.

## 1. Introduction

Neurons in mammalian central nervous systems receive many synaptic inputs from various sources, with about 7500 excitatory and 2500 inhibitory inputs per cortical pyramidal cell [15]. The majority of the excitatory inputs arise from other cortical neurons that form a recurrent excitatory network within which are many GABA-ergic inhibitory interneurons. Axons from pyramidal cells synapse not only with other pyramidal cells, but also inhibitory interneurons, which subsequently innervate local pyramidal cells.

In order to observe and understand the dynamical responses of single cells and of neuronal populations, various recording techniques are employed. Intracellular recordings of potential, available for over 50 years, are usually restricted to single neurons but give the most information. Extracellular recordings may record the spiking activity but do not pick up the detail of synaptic potentials which have driven the neuron to spiking. In early studies [6], usually only one electrode was employed and the recordings were usually presumed to be of somatic origin. Recent advances in techniques have enabled measurements to be made of potentials from sites identifiable as dendritic [5] and also from several locations at once. The latter has been achieved with extracellular multielectrode arrays [7,10,14]. The possibility of recording simultaneously the intracellular potentials of two or more locally connected neurons would provide great insight into neural dynamics [8,9]. There are several circuits in both the cerebellum and cerebral cortex where neighboring neurons share common input [2,13] and the identification of the inputs is the problem addressed in this article.

## 2. Theory

In the last 15 years, a method of determining the elements of a set of independent sources or functions from a linear combination of them, now generally known as independent component analysis (ICA), has become widely popular in various engineering and communications applications [3,11]. In its usual formulation, there are  $n$  random signals  $S_k(t)$ ,  $k = 1, \dots, n$ , defined on some time interval and a mixing matrix  $\mathbf{A}$  so that observations are made of the resulting linear combinations  $X_k(t)$  which are components of the vector

$$\mathbf{X}(t) = \mathbf{A}\mathbf{S}(t). \quad (1)$$

With certain algorithms it is required that the  $S_k$ 's are statistically independent, whereas for others uncorrelatedness suffices. Given the observations on  $X_k$  the method of ICA returns an estimate of the matrix  $\mathbf{A}$  and of the signals  $S_k(t)$ . MATLAB programs such as JADE and SOBI are available for the application of the separation algorithms—for example, JADE, which was found most useful for the present application, can be downloaded at the following address: <http://www.tsi.enst.fr/cardoso/Algo/Jade/jade.m>. The reader may obtain a copy of sobi.m

from either of the authors. The ICA method for recovery of the source signals assumes independence of the source signals [4], whereas some blind source separation methods, like SOBI, work for sources which are uncorrelated and colored [1].

The application of ICA is most often to time-varying signals according to an algebraic prescription as in (1) and it has been employed in neurobiology for the analysis of spike trains [12]. The application in this paper is, as far as known to the authors, new, in that it concerns differential (or possibly integro-differential) operators. Thus we may have that  $\mathbf{X}(t)$  is governed, for example, by the first-order system

$$\frac{d\mathbf{X}}{dt} = \mathbf{f}(\mathbf{X}, t) + \mathbf{A}\mathbf{S}(t), \quad (2)$$

although the differential operators could be of any order. Here the coefficient matrix  $\mathbf{A}$  and the signals  $\mathbf{S}$  are unknown and to be estimated. We now suppose that observations  $\hat{\mathbf{X}}$  on  $\mathbf{X}$  are made. (Here and throughout the symbol  $\hat{\phantom{x}}$  indicates an estimate from data.) From these observations, the derivative is obtained numerically as  $d\hat{\mathbf{X}}/dt$  and the quantities

$$\hat{\mathbf{Y}} = \frac{d\hat{\mathbf{X}}}{dt} - \mathbf{f}(\hat{\mathbf{X}}, t) \quad (3)$$

are obtained. Applying the standard ICA algorithms to the new observations  $\hat{\mathbf{Y}}$  enables estimates of the mixing matrix  $\mathbf{A}$  and the signals  $\mathbf{S}$  to be made. We will apply this technique to simulated data from nonlinear model neurons.

### 3. A pair of Fitzhugh–Nagumo model neurons

As a first illustration we consider two neurons which share common inputs as afferent axons synapse with them. To begin with, we consider point models which can be considered to correspond to an averaging of potential over the entire cells. The simplest model system which is capable of reproducing some of the detail of neuronal responses to synaptic input is the linear leaky integrate and fire model [17]. However, spikes are produced somewhat ad hoc in this model as a voltage threshold must be introduced. Hence, we let  $v_1$  and  $v_2$  be the voltage variables for two model neurons in the Fitzhugh–Nagumo approximation [16]. The recovery variables are omitted for small subthreshold responses [18], which makes the system one-dimensional. Assume that there are two main sources of synaptic input which arrive at possibly multiple locations on each neuron's soma-dendritic surface. The current waveforms are  $I_1(t)$  and  $I_2(t)$  from the two sources and the relative strengths are contained in the matrix

$$\mathbf{A} = \begin{pmatrix} a_{11} & a_{12} \\ a_{21} & a_{22} \end{pmatrix}.$$

The dynamical equations for the evolution of the states of the cells are thus

$$\frac{dv_1}{dt} = k_1 v_1 (v_1 - a_1)(1 - v_1) + a_{11} I_1 + a_{12} I_2, \tag{4a}$$

$$\frac{dv_2}{dt} = k_2 v_2 (v_2 - a_2)(1 - v_2) + a_{21} I_1 + a_{22} I_2. \tag{4b}$$

The time courses of  $v_1$  and  $v_2$  are to be obtained by intracellular recording using a multielectrode device. No knowledge of either the current waveforms or the relative strengths of the input currents are known to the experimentalist. Estimates of the input quantities  $\hat{I}_1$  and  $\hat{I}_2$  and of the mixing matrix

$$\hat{\mathbf{A}} = \begin{pmatrix} \hat{a}_{11} & \hat{a}_{12} \\ \hat{a}_{21} & \hat{a}_{22} \end{pmatrix}$$

are to be made.

The parameters were set at  $a_1 = a_2 = 0.1$ ,  $k_1 = k_2 = 0.5$ , throughout. We considered first the case of two non-overlapping wave forms:

$$I_1(t) = 0.5[H(t - 0.2) - H(t - 0.3)], \quad I_2(t) = [H(t - 0.5) - H(t - 0.6)],$$

where  $H$  is the Heaviside unit step function. The initial condition was  $v_1(0) = v_2(0) = 0$  and the coefficient matrix set at

$$\mathbf{A} = \begin{pmatrix} 5 & 1 \\ 2 & 3 \end{pmatrix}.$$

The observations are generated in this case by using a Runge–Kutta routine; the quantities

$$\frac{dv_1}{dt} - k_1 v_1 (v_1 - a_1)(1 - v_1), \tag{5a}$$

$$\frac{dv_2}{dt} - k_2 v_2 (v_2 - a_2)(1 - v_2) \tag{5b}$$

were estimated using the five-point derivative estimator at the  $k$ th point:

$$f'(k) = [f(k - 2) - 8f(k - 1) + 8f(k + 1) - f(k + 2)]/12\delta t, \tag{6}$$

where  $\delta t$  is the time step. The ICA program JADE was found to give more accurate results than SOBI and was used to estimate the mixing matrix and the current waveforms. The returned value was

$$\hat{\mathbf{A}} = \begin{pmatrix} 0.7905 & 0.3162 \\ 0.3162 & 0.9486 \end{pmatrix}, \tag{7}$$

which is in excellent agreement with the columns of  $\mathbf{A}$  (the method of ICA returns an estimate of the mixing matrix  $A$  and that of the signals  $S_k(t)$  up to a permutation and scaling). The waveforms returned by JADE were also in excellent agreement with the source functions through  $\hat{I}_1$  and  $\hat{I}_2$ .

As a more realistic example, we made  $I_1$  a pair of random excitatory postsynaptic potentials and  $I_2$  a random inhibitory postsynaptic potential. These are described by

$$I_1(t) = (A_1[H(t - t_1) - H(t - t_2)](t - t_1)e^{-2.5(t-t_1)} + A_2[H(t - t_3) - H(t - t_4)](t - t_3)e^{-2.5(t-t_3)})(1 + N(t)),$$

$$I_2(t) = A_3[H(t - t_5) - H(t - t_6)](t - t_5)e^{-4(t-t_5)}, \quad (8)$$

where  $0 < t_1 < t_2 < t_3 < t_4$ ,  $t_5 < t_6$ ,  $A_1$ ,  $A_2$  and  $A_3$  are random amplitudes and  $N(t)$  is a small Gaussian noise process. The membrane potentials for the two neurons are shown in the top two frames of Fig. 1; the synaptic input currents are shown in the lower left frame and the estimated input currents are shown in the lower right hand frame (JADE). The currents  $I_1$  and  $I_2$  and their estimates have been drawn on the same graph for convenience because they are well separated in time.

The actual mixing matrix was

$$\mathbf{A} = \begin{pmatrix} 1/2 & 1/20 \\ 1/20 & 3/20 \end{pmatrix}, \quad (9)$$

whereas the value returned by JADE was

$$\hat{\mathbf{A}} = \begin{pmatrix} 3.6362 & 0.09100 \\ 0.36358 & 0.13622 \end{pmatrix}, \quad (10)$$

which is again in excellent agreement with the columns of  $\mathbf{A}$ . It was found that the accuracy of the estimates was greatest when the input pulses were non-overlapping

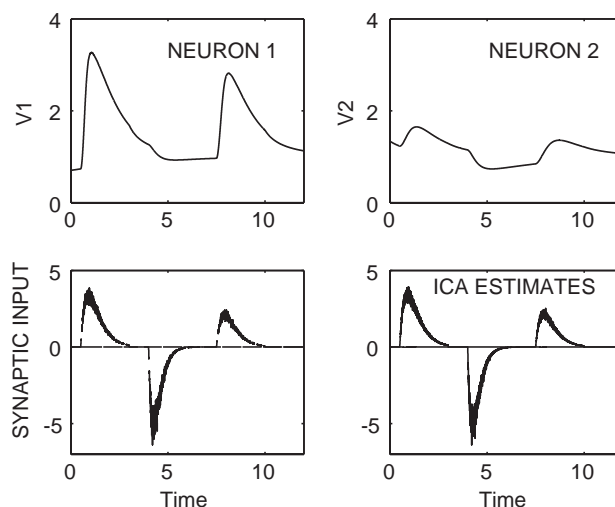


Fig. 1. In the upper two frames, the membrane potentials from two model neurons are shown. In the lower left frame, the input current is depicted as two excitatory and one inhibitory postsynaptic potential. The lower right frame shows the scaled input current estimated from the observed potentials using the ICA method.

with diminishing accuracy as the overlap increased from zero. This arises because the requirement of complete statistical independence is difficult to realize in computer simulations.

#### 4. Conclusions

Neurons in mammalian cerebral cortex receive many synaptic inputs from intracortical and extracortical sources. The recording of membrane potentials from neighboring neurons in conjunction with ICA analysis may provide a method of analyzing in a quantitative way the nature and relative strengths of shared inputs.

#### References

- [1] A. Belouchrani, K. Abed-Merain, J.F. Cardoso, E. Moulines, A blind source separation technique using second order statistics, *IEEE Trans. Signal Processing* 45 (1997) 434–444.
- [2] D.V. Buonomano, Timing of neural responses in cortical organotypic slices, *PNAS* 100 (2003) 4897–4902.
- [3] J.-F. Cardoso, Source separation using higher order moments, *Proceedings of ICASSP*, May 1989, Glasgow, pp. 2109–2112.
- [4] J.F. Cardoso, A. Souloumiac, Jacobi angles for simultaneous diagonalization, *SIAM J. Math. Anal. Appl.* 17 (1996) 161–164.
- [5] R. Cossart, et al., Distribution of spontaneous currents along the somato-dendritic axis of rat hippocampal CA1 pyramidal neurons, *Neuroscience* 99 (2000) 593–603.
- [6] J.C. Eccles, *The Physiology of Nerve Cells*, Johns Hopkins, Baltimore, 1957.
- [7] E. Fernandez, J. Ferrandez, J. Ammermuller, R.A. Normann, Population coding in spike trains of simultaneously recorded retinal ganglion cells, *Brain Res.* 887 (2000) 222–229.
- [8] W. Gerstner, W.M. Kistler, *Spiking Neuron Models*, Cambridge University Press, Cambridge, UK, 2002.
- [9] Y. Hanein, K.F. Bohringer, R.C. Wyeth, A.O.D. Willows, Towards MEMS Probes for Intracellular Recording, *Sensors Update* 10 (2002) 1–29.
- [10] J.L. Johnson, J.P. Welsh, Independently movable multielectrode array to record multiple fast-spiking neurons in the cerebral cortex during cognition, *Methods* 30 (2003) 64–78.
- [11] C. Jutten, J. Herault, Independent Components Analysis Versus Principal Components Analysis, *Signal Processing IV: Theory and Applications*, Elsevier, Amsterdam, pp. 643–646.
- [12] M. Laubach, M. Shuler, M.A.L. Nicolelis, Independent component analyses for quantifying neuronal ensemble interactions, *J. Neurosci. Methods* 94 (1999) 141–154.
- [13] M. Matsumura, et al., Synaptic interactions between primate precentral cortex neurons revealed by spike-triggered averaging of intracellular membrane potentials *in vivo*, *J. Neurosci.* 16 (1996) 7757–7767.
- [14] M.A. Nicolelis, S. Ribeiro, Multielectrode recordings: the next steps, *Curr. Opin. Neurobiol.* 12 (2002) 602–606.
- [15] M.N. Shadlen, W.T. Newsome, Noise neural codes and cortical organization, *Curr. Opin. Neurobiol.* 4 (1994) 569–579.
- [16] H.C. Tuckwell, *Introduction to Theoretical Neurobiology*, vol 2: Nonlinear and Stochastic Theories, Cambridge University Press, New York, 1988, pp. 70–82 (Chapter 8).
- [17] H.C. Tuckwell, *Introduction to Theoretical Neurobiology*, vol 1: Linear Cable Theory and Dendritic Structure, Cambridge University Press, New York, 1988 (Chapter 3).
- [18] H.C. Tuckwell, R. Rodriguez, F.Y.M. Wan, Analytical determination of firing times in stochastic nonlinear neural models, *Neurocomputing* 48 (2002) 1003–1007.