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Leonardo Tomazeli Duarte, Christian Jutten

Advances in Signal Processing and Image Analysis for Physico-Chemical, Analytical Chemistry and Chemical Sensing
Progrès en traitement des signaux et analyse des images pour les analyses physico-chimiques et la détection chimique

Design of Smart Ion-Selective Electrode Arrays Based on Source Separation through Nonlinear Independent Component Analysis

L.T. Duarte[1]* and C. Jutten[2]

[1] School of Applied Sciences, University of Campinas (UNICAMP), rua Pedro Zaccaria, 1300, Limeira-SP - Brazil
[2] GIPSA-lab, UMR 5216 CNRS, Institut Polytechnique de Grenoble,
11 rue des Mathématiques, BP 46, 38402 Saint-Martin-d'Hères Cedex - France
e-mail: leonardo.duarte@fca.unicamp.br - christian.jutten@gipsa-lab.grenoble-inp.fr

* Corresponding author

Résumé — **Développement de réseaux de capteurs chimiques intelligents par des méthodes de séparation source fondée sur l'analyse de composantes indépendantes non linéaire** — Les réseaux de capteurs chimiques fondés sur la Séparation Aveugle de Sources (SAS) fournissent une solution prometteuse pour palier le problème d'interférence typique des électrodes ion-sélective. Cette nouvelle approche peut rendre plus simple la phase d'étalonnage, surtout en évitant l'utilisation d'un ensemble important de points pour l'ajustage de la méthode de traitement des données. Les premiers travaux sur le problème n'ont considéré que la situation dans laquelle les ions en cours d'analyse ont des valences égales. Motivé par cette limitation, le présent travail vise à développer une technique de SAS qui fonctionne lorsque les ions ont des valences différentes. Dans ce cas, le modèle de mélange résultant appartient à une classe particulière de systèmes non linéaires qui n'ont jamais été étudiés dans la littérature de SAS. La solution proposée est fondée sur un réseau récurrent comme système de séparation et sur une approche de minimisation de l'information mutuelle pour l'estimation des paramètres. La méthode peut être utilisée pour des analyses *off-line*. La validité de notre approche est justifiée par des tests où les paramètres du modèle de mélange ont été obtenus à partir de données réelles.

Abstract — *Design of Smart Ion-Selective Electrode Arrays Based on Source Separation through Nonlinear Independent Component Analysis* — *The development of chemical sensor arrays based on Blind Source Separation (BSS) provides a promising solution to overcome the interference problem associated with Ion-Selective Electrodes (ISE). The main motivation behind this new approach is to ease the time-demanding calibration stage. While the first works on this problem only considered the case in which the ions under analysis have equal valences, the present work aims at developing a BSS technique that works when the ions have different charges. In this situation, the resulting mixing model belongs to a particular class of nonlinear systems that have never been studied in the BSS literature. In order to tackle this sort of mixing process, we adopted a recurrent network as separating system. Moreover, concerning the BSS learning strategy, we develop a mutual information minimization approach based on the notion of the differential of the mutual information. The method works requires a batch operation, and, thus, can be used to perform off-line analysis. The validity of our approach is supported by experiments where the mixing model parameters were extracted from actual data.*

INTRODUCTION

There is a great number of situations in chemical analysis in which the estimation of the concentration and/or the activity of a certain number of ions is desirable. For instance, this problem arises in water quality control [1, 2] and biomedical monitoring [3, 4]. A widely used approach to this problem is founded on potentiometric Ion-Selective Electrodes (ISE), in which the transduction mechanism relates the potential difference in an electro-chemical system with the concentration of a charged chemical specie. The advent of miniaturization has rendered potentiometric sensors a practical and inexpensive option, becoming attractive for a number of applications. Besides the ubiquitous glass-electrode for pH measurement, one may find a growing interest on the detection of other ions [5], such as Na^+ and NH_4^+.

Although attractive, there is an important drawback limiting the use of ISE. Usually, such a device is not selective, *i.e.*, the generated potential at the membrane depends on a given target ion but also on other undesirable ions, which are called interfering ions. While in some situations the interfering process can be negligible, there are cases in which this problem seems to be more accentuated and, as consequence, the measurements acquired by the chemical sensor become uncertain when the concentrations of the interfering ions are high enough.

A first approach to overcome the interference problem is to develop more selective membranes [6]. Alternatively, one may adopt sensors that are not very selective in conjunction with signal processing methods. Therefore, due to the lack of selectivity, at time t, the response $x_i(t)$ of the i-th sensor within the array is a function of the concentrations of all ions present in the solution, that is:

$$x_i(t) = f_i(s_1(t), s_2(t), \ldots, s_N(t)) \qquad (1)$$

where $s_j(t)$ corresponds to the temporal evolution of the concentration of the j-th ion. The goal of the signal processing algorithm is to estimate $s_j(t), j = 1, \ldots, N$. If a set containing samples of the concentrations and of the corresponding sensor responses is available, then the functions f_i can be identified by means of a calibration step ([7, 8] for instance). Nonetheless, there are at least two problems in this approach (usually referred to as supervised approach):

– the acquisition of training samples may be cost and time-demanding;
– this calibration procedure must be performed from time to time due to the sensors drift.

On the other hand, if a set of training samples is not available, the problem is to retrieve the signals $s_j(t)$, $j = 1, \ldots, N$, by solely means of the sensor responses $x_i(t)$. Such a problem has been intensively studied in signal processing since 1990, and is known as Blind Source Separation (BSS) [9, 10]. According to the BSS terminology, the signals $s_j(t)$ are called sources whereas the sensor responses $x_i(t)$ correspond to the mixtures. There is a number of methods for performing BSS. The basis of the majority of these techniques is the Independent Component Analysis (ICA) [11, 12], a powerful data analysis framework that works under the assumption that the sources are statistically independent.

In [13, 14], BSS algorithms have been adopted to face the interference problem in ISE. Despite the promising results obtained in these works, they are only suitable for the cases in which the ions under analysis have equal valences. In the present paper, we propose a novel BSS framework for the case in which the valences are different. It should be emphasized that such a situation is quite different from the approaches [13, 14], since it defines a new class of nonlinear functions that has never been dealt with.

The proposed BSS method is based on a combination of a nonlinear recurrent network as separating system with an ICA-based learning algorithm. We conduct a stability analysis for the separating system which permits us to establish the operation range of the chemical sensor array. Concerning the learning algorithm, we consider a method based on the minimization of the mutual information between the retrieved sources. The paper is organized as follow. We first introduce the BSS problem. Then, in Section 2, we discuss the mixing model associated with the chemical sensor array. After that, in Section 3, we describe the building blocks of our method, starting with a description of the adopted separating system and ending with the ICA method adopted as learning rule. The method works requires a batch operation, and, thus, can be used to perform off-line analysis. In Section 4, we conduct some experiments to assess the performance of our proposal. Finally, we state our conclusions and some perspectives for future works.

1 BLIND SOURCE SEPARATION REVIEW

Let $s_1(t), s_2(t), \ldots, s_N(t)$ represent a set of N source signals. In addition, let $x_1(t), x_2(t), \ldots, x_M(t)$ denote a set of signals that are generated by mixing the source signals. Then, the mixing process can be described in the same way as in Equation (1). We can equally represent the mixing process through a matrix notation, *i.e.*:

$$\boldsymbol{x}(t) = \boldsymbol{F}(\boldsymbol{s}(t)) \qquad (2)$$

where $\boldsymbol{x}(t) = [x_1(t), \ldots, x_M(t)]^T$, $\boldsymbol{s}(t) = [s_1(t), \ldots, s_N(t)]^T$, and the mixing system is represented by $\boldsymbol{F} = [f_1(\boldsymbol{s}(t)), \ldots, f_M(\boldsymbol{s}(t))]^T$. The aim of BSS methods is to provide estimates of the source signals $\mathbf{s}(t)$ by using only the information contained in the mixtures $\mathbf{x}(t)$. Assuming that $\boldsymbol{F}(\cdot)$ is invertible, this problem can be dealt with by defining a separating system $\boldsymbol{G} = [g_1(\mathbf{x}(t)), \ldots, g_M(\mathbf{x}(t))]^T$ such that the signals given by:

$$y(t) = \boldsymbol{G}(\mathbf{x}(t)) \tag{3}$$

are as close as possible to the signals $\mathbf{s}(t)$.

The problem of BSS is ill-posed by nature [10] and, as a consequence, it becomes necessary to make use of some additional information. For instance, each source $s_i(t)$ may be modeled as a random variable, and one may assume that these sources are mutually statistically independent. In this scenario, the mixtures are no longer independent, since all x_i are functions of the same random variables. Therefore, an attempt to retrieve the original sources would be based on the recovery of statistical independence, *i.e.* one could search for a separating system $\boldsymbol{G}(\cdot)$ that provides a vector $\mathbf{y}(t)$ that has, again, statistical independent components. This idea is known as Independent Component Analysis (ICA) [9, 11]. In ICA, the measure of dependence is based only on samples of $\mathbf{y}(t)$. As will become clear in Section 3, this allows one to estimate the parameters of $\boldsymbol{G}(\cdot)$ without requiring a learning database constituted of pairs $(s_i(t), x_i(t))$, $t = 1, \ldots, T$.

A fundamental question in the ICA concerns the separability of the mixing model, *i.e.*, the conditions on the sources and on the mixing system for which the recovering of statistical independence results in source separation. For instance, when the mixing system is linear ($\mathbf{x}(t) = \mathbf{A}\mathbf{s}(t)$, where $\mathbf{A}$ is a $M \times N$ matrix), it was shown [11] that ICA results in source separation when the following conditions are held:

– there is at most one source signal that is Gaussian distributed,
– $M \geq N$, *i.e.*, the number of mixtures is greater than or equal to the number of sources,
– $\mathbf{A}$ is full rank so that its inverse or pseudo-inverse exists.

On the other hand, it has been shown that ICA methods do not work for general nonlinear models [15, 16]. In other words, there are cases in which the recovery of the independence does not guarantee source separation. Fortunately, there are constrained mixing systems as, for example, Post-NonLinear (PNL) mixtures [16] and linear-quadratic mixtures [17], in which the ICA framework is still valid.

Let us now turn our attention to some practical aspects of an ICA method. A first step concerns the definition of the separating system structure $\mathbf{G}(\cdot)$. For a linear mixing process a natural choice is a matrix. However, in a nonlinear scenario, this task becomes tricky since the separating system mapping should be able to invert the action of the mixing system $\mathbf{F}(\cdot)$ but, at the same time, it cannot be too general in order to preserve the separability of the model [15]. A second important point is how to define a statistical independence measure. For instance, the mutual information [18] between random variables can be used, since this measure is always non-negative and takes zero only when the random variables are independent — it should be stressed here that, although based on statistical criteria, there is no need to define the statistical distribution for the sources, since ICA works in a blind fashion. Finally, the development of ICA methods boils down to an optimization problem, *i.e.*, one must design an optimization scheme to adjust the parameters of the separating system $\mathbf{G}(\cdot)$ in order to maximize a measure associated with the independence of the retrieved sources $\mathbf{y}(t)$. Later, in Section 3, we shall discuss how each of these steps can be accomplished in the context of the chemical sensing application envisaged in this paper. A first step in this direction is the modeling of the ISE. This will permit us to define a parametric model for the function $\mathbf{F}(\cdot)$ which in turn is fundamental for a good choice of $\mathbf{G}(\cdot)$. We shall discuss this point in the next section.

2 MIXING PROCESS MODEL

There are basically two ways to design a potentiometric sensor for estimating ions concentrations, either it can be implemented through electrodes or it can be built on a Metal-Oxide-Semiconductor Field-Effect Transistor (MOSFET) by replacing the metallic gate with a membrane sensitive to the ion of interest [19], giving rise to a device called Ion-Sensitive Field-Effect Transistor (ISFET). For both cases, the Nernst's equation can be used for modeling the electrochemical sensor [5]. However, this equation does not predict the interference process which, as discussed later, is paramount when more than one ion is analyzed. For such a situation, a more adequate description is given by an empirical extension of the Nernst's equation: the Nicolsky-Eisenman (NE) model [5, 20]. According to this model the response of the i-th potentiometric sensor within the array is given by:

$$x_i = E_i + \frac{RT}{z_i F} \ln \left(s_i + \sum_{j, j \neq i} a_{ij} s_j^{\frac{z_i}{z_j}} \right) \tag{4}$$

where E_i is a constant, z_i the valence of the i-th ion, R the gas constant, T the temperature in Kelvin, F the Faraday constant and a_{ij} the selectivity coefficients; s_i represents the activity of the i-th ion, which is very close to its concentration for solutions with a small ionic strength [5][(1)].

Note that when the valences of the ions under analysis are the same, the mixing model resulting from Equation (4) becomes a linear mixture followed by a component-wise nonlinear function (logarithm in this case). Actually, this kind of mixing system is a particular case of the class of Post-NonLinear (PNL) models [16], and consequently has the nice property to be identifiable using ICA. In [13], a PNL source separation method was developed for the problem of estimating the concentrations of K^+ and NH_4^+. However, when the valences are different and sensors having different ions as targets are used, the resulting model (4) becomes tougher due to the appearance of a nonlinearity (power relation) inside the logarithm term and, as a consequence, PNL algorithms cannot be used anymore in this new case.

In this work, we focus on a simpler version of the model (4). We assume knowledge on the parameter that multiplies the logarithm term and the constant E_i. For instance, at room temperature, according to (4), the sensibility of a potentiometric sensor per decade is:

$$\text{Ln}(10)RT/Fz_i \approx 59/z_i \text{ mV}^{(2)}$$

The electrodes with such sensibility are said to have a Nernstian response.

Another simplification of the model (4) concerns the number of sources and sensors. Despite the fact that the proposed technique can be extended to high-dimensional scenarios, we will consider only the case with 2 sources (or, equivalently, 2 ions in the solution) and 2 chemical sensors. This assumption is realistic in many practical situations, where one interfering ion is dominant and the others can be neglected. For instance, when analyzing potassium and ammonium, the interference from other ions is so weak that a model based only on these two ions provides a satisfactory result. Moreover, this choice makes possible a theoretical analysis and, thus, a better understanding of the elements of our proposal.

If we consider the two simplifications described in the last paragraphs and a scenario with two ions and with an array of two sensors (each one having a different ion as target), then we obtain the following realistic mixing model $\mathbf{F}(\cdot)$:

$$x_1 = s_1 + a_{12}s_2^k$$
$$x_2 = s_2 + a_{21}s_1^{1/k} \tag{5}$$

where x_i and s_j denote the i-th mixture and the j-th source, respectively. The term k corresponds to z_1/z_2 and we assume that we know it in advance and that it takes only positive integer values. Indeed, in many actual applications, typical target ions are NH_4^+, Ca^{2+}, K^+, etc. Consequently, we always have $k \in \mathbb{N}$. In addition, the sources are supposed positive, since they represent concentrations. Finally, it is assumed that the signals s_1 and s_2 are statistically independent.

3 A SOURCE SEPARATION ALGORITHM FOR THE NICOLSKY-EISENMAN MODEL

In this section, we described the developed BSS algorithm. As discussed in Section 1, the design of a source separation method encompasses:
– the definition of a separating system $\mathbf{G}(\cdot)$ suited to the mixing model (5);
– the derivation of a learning strategy (cost function definition plus optimization technique design).

Our presentation will follow these two steps, and we will start by conducting an analysis of the adopted nonlinear separating system. After that, we shall deal with the problem of adjusting the parameters of this system through an ICA technique.

3.1 The Separating Structure

3.1.1 Invertibility of the Mixing Model

An important point to be addressed before defining a separating system concerns the invertibility of the mixing system (5). In other words, one should verify if it is possible to restore the sources values s_i from the knowledge of x_i and of the coefficients a_{ij}. This can be done by solving Equation (5) for s_1 and s_2. By a simple substitution on this expression, we obtain:

$$x_1 = s_1 + a_{12}(x_2 - a_{21}s_1^{(1/k)})^k \tag{6}$$

After straightforward calculation, including a binomial expansion, Equation (6) becomes:

$$(1 + a_{12}b_0)s_1 + a_{12}\sum_{i=1}^{k-1} b_i s_1^{1-\frac{i}{k}} + (a_{12}b_k - x_1) = 0 \tag{7}$$

where:

$$b_i = \binom{k}{i}x_2^i(-a_{21})^{(k-i)}$$

being $\binom{k}{i}$ defined as $\frac{k!}{i!(k-i)!}$.

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By considering the transformation $u = s_1^{\frac{1}{k}}$ in Equation (7), one can verify that the solution of this expression is equivalent to the determination of the roots of a polynomial of order k and, as a consequence, the number of solutions grows linearly as k increases. With that in mind, we may investigate the nature of these solutions, *i.e.*, if there are solutions that are still nonlinear combinations of s_1 and s_2. The main problem of such an approach is that we need to solve Equation (7), which is a difficult task for high values of k.

In order to gain more insight into Equation (7), we can solve it for $k = 2$. After some calculation, we obtain two sets of solutions, the first one being the expected pair $(\phi_1, \phi_2) = (s_1, s_2)$, while the second one is given by:

$$\phi_1 = \left(\frac{(2a_{12}a_{21}s_2) + (a_{12}a_{21}^2 - 1)s_1^{\frac{1}{2}}}{(1 + a_{12}a_{21}^2)} \right)$$

$$\phi_2 = s_2 + a_{21}s_1^{\frac{1}{2}} - a_{21} \left| \left(\frac{(2a_{12}a_{21}s_2) + (a_{12}a_{21}^2 - 1)s_1^{\frac{1}{2}}}{(1 + a_{12}a_{21}^2)} \right) \right| \tag{8}$$

From (8), one may notice that the mixing model is not invertible, since there is a solution that still consists of a nonlinear mixture of the actual sources. Therefore, the only alternative is to limit the operation of the source separation technique to regions in which the mixing model is locally invertible. In the sequel, we show how this can be done in a systematic way by using a recurrent network as separating system.

3.1.2 A nonlinear Recurrent Separating System

The use of a recurrent network as separating system was developed in the first approaches regarding linear BSS [21]. Its extension to the nonlinear came up in [22], in the context of source separation of linear-quadratic mixtures. The use of this kind of separating system is particularly attractive for the cases in which one desires to counterbalance the action of the mixing system without relying on its direct inversion.

In our case, we adopt the separating structure shown in Figure 1. In mathematical terms, this recursive structure is characterized by the following dynamics:

$$y_1(n+1) = x_1 - w_{12}y_2(n)^k$$
$$y_2(n+1) = x_2 - w_{21}y_1(n)^{\frac{1}{k}} \tag{9}$$

where $[w_{12}\, w_{21}]^T$ are the parameters to be adjusted, and where n is the iteration number. In order to understand how this structure works, we must investigate their equilibrium points. By setting $y_1(n+1) = y_1(n) = y_1$ and
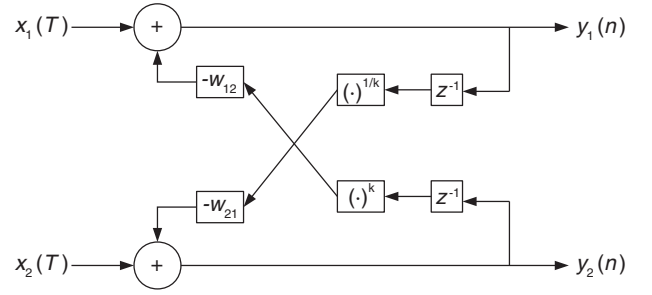

Figure 1

A recurrent separating system for the simplified NE mixing model.

$y_2(n+1) = y_2(n) = y_2$ in (9), one can easily check that, when $[w_{12}\, w_{21}]^T = [a_{12}\, a_{21}]^T$, the equilibrium points correspond to the solutions of (5). In other words, it is possible, by running this network, to achieve the solutions of (7) in a sort of implicit inversion of the considered mixing model.

Evidently, we saw that the mixing model is not globally invertible and, thus, the recurrent network in (9) may converge to points other than the actual sample of the sources, *e.g.* to (8). The next step of our investigation is exactly to verify the conditions to be satisfied so that the equilibrium point associated with the sources is stable and, thus, a potential attractor for the adopted dynamical system.

In view of the difficulty embedded in a global analysis of stability, we consider the study of the local stability in the neighborhood of the equilibrium point $\mathbf{s} = [s_1\, s_2]^T$ based on the first-order approximation of the nonlinear system (9). This linearization can be expressed by using a vectorial notation as follows:

$$\mathbf{y}(n+1) \approx \mathbf{c} + \mathbf{J}|_{\mathbf{y}=\mathbf{s}}\mathbf{y}(n) \tag{10}$$

where $\mathbf{y}(n) = [y_1(n)\, y_2(n)]^T$, $\mathbf{c}$ is a constant vector and $\mathbf{J}|_{\mathbf{y}=\mathbf{s}}$ is the Jacobian matrix of (9) evaluated at $[s_1\, s_2]^T$, which is given by:

$$\mathbf{J}|_{\mathbf{y}=\mathbf{s}} = \begin{bmatrix} \frac{\partial y_1(n)}{\partial y_1(n-1)}|_{\mathbf{y}=\mathbf{s}} & \frac{\partial y_1(n)}{\partial y_2(n-1)}|_{\mathbf{y}=\mathbf{s}} \\ \frac{\partial y_2(n)}{\partial y_1(n-1)}|_{\mathbf{y}=\mathbf{s}} & \frac{\partial y_2(n)}{\partial y_2(n-1)}|_{\mathbf{y}=\mathbf{s}} \end{bmatrix}$$
$$= \begin{bmatrix} 0 & -a_{12}ks_2^{(k-1)} \\ -\frac{1}{k}a_{21}s_1^{(\frac{1}{k}-1)} & 0 \end{bmatrix} \tag{11}$$

It is well known that a necessary and sufficient condition for local stability of a discrete system is that the

absolute values of the eigenvalues of the Jacobian matrix evaluated at the equilibrium point of interest be smaller than one [23]. Applying this result on (11), the following condition of local stability is obtained:

$$|a_{12}a_{21}s_1^{(\frac{1}{k}-1)}s_2^{k-1}| < 1 \qquad (12)$$

This stability condition points out a first constraint of our method, given that we are able to separate only the sources lying in this region. In the context of the chemical sensing problem treated in this work, this condition gives the range in which our chemical sensor array can operate properly.

Another interesting point related to the stability of the recurrent separating system is that it can provide a systematic way of avoiding the convergence to a solution that does not correspond to the actual sources. In order to clarify this idea, let us present an example. Consider the mixing of the sample $\mathbf{s} = [0.5\,1.5]^T$ in a scenario where the parameters in (5) are given by $a_{12} = a_{21} = 0.5$ and $k = 2$. The resulting sample of the mixtures is $\mathbf{x} = [1.625\,1.853]^T$. In Figure 2, we plot the contour lines $x_1 = $ constant and $x_2 = $ constant in the (s_1, s_2) plane. In particular, the contour lines corresponding to the mixtures are highlighted. Obviously, the solutions of Equation (5), or equally the equilibrium points of (9), are given by the intersection of these two contour lines. In this case, we may find two points that solve our problem, which is in accordance with our previous discussion. Finally, we indicate in this same figure the region for which the condition (12) is met. Note that

the point within this region corresponds to the actual source, whereas the spurious solution lies outside and, as a consequence, will never be a potential attractor for the recurrent network (9). Of course, this example is not a proof. However, we observed in our simulations such an approach may indeed be useful to deal with the non-invertibility of the mixing model.

Analogously to Figure 2, it is also possible to analyze the stability boundaries in the (a_{12}, a_{21}) plane, so we can have an idea about the coefficients for which the adopted recurrent network works properly. Indeed, as mentioned before, the stability condition of Equation (12) should be satisfied for each sample. Thus, if s_1 and s_2 are bounded in the intervals $(s_{1_{min}}, s_{1_{max}})$ and $(s_{2_{min}}, s_{2_{max}})$, respectively, then a necessary condition for the stability of all samples can be written as[3]:

$$|a_{12}a_{21}s_{1_{min}}^{(\frac{1}{k}-1)}s_{2_{max}}^{k-1}| < 1 \qquad (13)$$

It is interesting to note that such condition is somewhat related to the degree of nonlinearity of the mixing model given that the point $(s_{1_{min}}, s_{2_{max}})$ is one that suffers the most severe nonlinear distortion[4].

The stability condition (13) provides an important practical information in the context of ISE, namely: given the range of the sources, one can trace the stability boundaries in the (a_{12}, a_{21}) plane, *i.e.* one may know for which selectivity coefficients the adopted recurrent network works properly. For example, suppose that we are interested in detecting the ions in the range 0.001 M-0.5M, where M stands for Mole. Then, the adopted recurrent separating will work properly if the ISE array has selectivity coefficients inside the gray regions shown in Figure 3a (for $k = 2$) and in Figure 3b (for $k = 3$). Note that the area of the stability region becomes smaller as k grows.

3.2 Design of an ICA Learning Algorithm

After defining the structure of the separating system, we can now develop a learning algorithm which, in this work, will follow the guidelines provided by ICA. In short, the unknown parameters of (9) are adjusted so that the statistical independence between the outputs y_i be maximum. The cornerstone of our approach is the notion of the differential of the mutual information, proposed in [24]. In this work, it was proved that a small variation Δ of a given random vector $\mathbf{y}$ results, up to

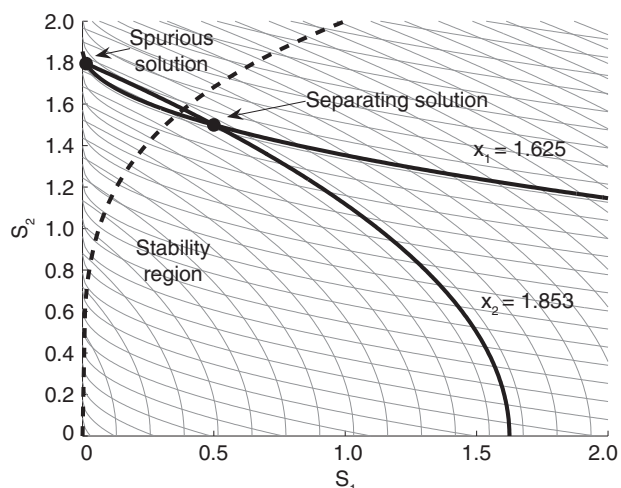Figure 2

Stability boundary (dashed line) and equilibrium points (black dots) of the dynamic (9).

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[3] This is simply a worst-case condition.
[4] Note that the derivative of $s_1^{1/k}$ increases as s_1 decreases whereas the derivative of s_2^k increases as s_2 increases.

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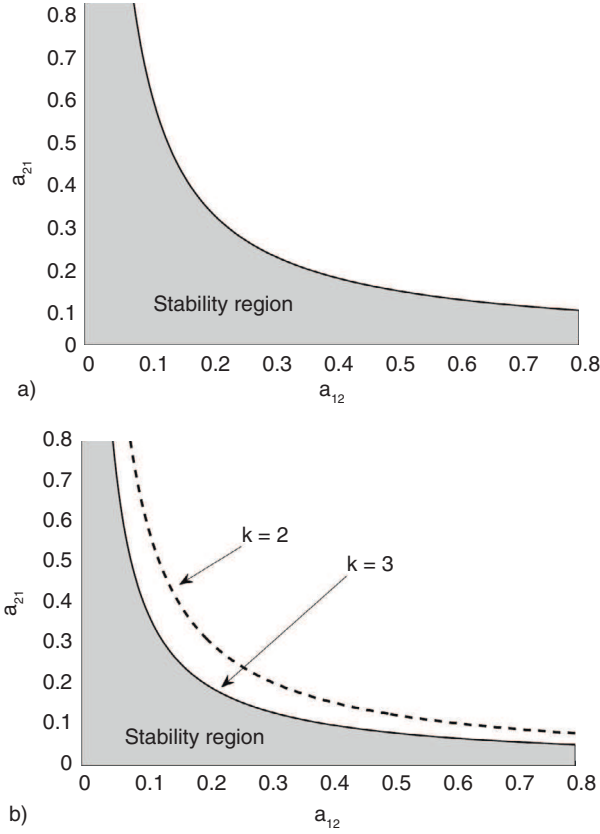
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a)

b)

Figure 3

Stability boundaries in the (a_{12}, a_{21}) plane: an example where the ions lie in the range 0.001M-0.5M. a) Stability region for $k = 2$; b) stability region for $k = 3$.

higher-order terms (expressed by $o(\Delta)$), in the following variation of the mutual information:

$$I(\mathbf{y} + \Delta) - I(\mathbf{y}) = E\{\Delta^T \beta_{\mathbf{y}}(\mathbf{y})\} + o(\Delta) \qquad (14)$$

where $\beta_{\mathbf{y}}(\mathbf{y})$ is the score function difference vector associated with the random vector $\mathbf{y}$. In view of this result, $\beta_{\mathbf{y}}(\mathbf{y})$ can be interpreted as the gradient of the mutual information with respect to $\mathbf{y}$. In mathematical terms, the i-th element of $\beta_{\mathbf{y}}(\mathbf{y})$ is given by:

$$\beta_{y_i}(\mathbf{y}) = \left(-\frac{\partial \log p(\mathbf{y})}{\partial y_i}\right) - \left(-\frac{d \log p(y_i)}{dy_i}\right) \qquad (15)$$

i.e., it is the difference between the i-th component of the joint score function of $\mathbf{y}$ and the marginal score function of y_i. It is not difficult to prove [24] that $\mathbf{y}$ have independent components if, and only if, $\beta_{y_i}(\mathbf{y}) = 0$ for every i.

The result expressed in (14) provides the guidelines for the design of a learning algorithm according to the minimum mutual information idea. The first step is to determine how a small variation of the separating system parameters, denoted by the vector $\Delta\mathbf{w} = [\Delta w_{12} \ \Delta w_{21}]^T$, affects their outputs. Then, the "gradient" of the mutual information with respect to $\mathbf{w}$ is estimated by (14), by substituting the calculated small variations of the outputs in this expression.

In order to determine the variation $\Delta\mathbf{y} = [\Delta y_1 \ \Delta y_2]^T$ related to a small variation $\Delta\mathbf{w}$, one may consider a linearized version of the separating system (9) with respect to $\mathbf{w}$. Considering two sources, this is expressed by:

$$\begin{bmatrix} \Delta y_1 \\ \Delta y_2 \end{bmatrix} = \frac{\partial \mathbf{y}}{\partial \mathbf{w}} \Delta\mathbf{w} = \begin{bmatrix} \dfrac{\partial y_1}{\partial w_{12}} & \dfrac{\partial y_1}{\partial w_{21}} \\ \dfrac{\partial y_2}{\partial w_{12}} & \dfrac{\partial y_2}{\partial w_{21}} \end{bmatrix} \begin{bmatrix} \Delta w_{12} \\ \Delta w_{21} \end{bmatrix} \qquad (16)$$

where the elements of $\frac{\partial \mathbf{y}}{\partial \mathbf{w}}$ are determined in Appendix.

Replacing in (14) Δ by $\Delta\mathbf{y}$, then one readily obtains:

$$I(\mathbf{y} + \Delta\mathbf{y}) - I(\mathbf{y}) = E\left\{\Delta\mathbf{w}^T \frac{\partial \mathbf{y}}{\partial \mathbf{w}}^T \beta_{\mathbf{y}}(\mathbf{y})\right\} + o(\Delta\mathbf{y}) \quad (17)$$

As stated above, the score function difference $\beta_{\mathbf{y}}(\mathbf{y})$ may be interpreted as the gradient of (14). Hence, considering (14) and (17), one may argue that the "gradient" of the mutual information with respect to the parameters $\mathbf{w}$ is:

$$\frac{\partial I}{\partial \mathbf{w}} = E\left\{\frac{\partial \mathbf{y}}{\partial \mathbf{w}}^T \beta_{\mathbf{y}}(\mathbf{y})\right\} \qquad (18)$$

Therefore, it is expected that the following learning rule minimizes the mutual information between the reconstructed sources:

$$\mathbf{w} \leftarrow \mathbf{w} - \mu E\left\{\frac{\partial \mathbf{y}}{\partial \mathbf{w}}^T \beta_{\mathbf{y}}(\mathbf{y})\right\} \qquad (19)$$

where μ denotes the learning rate.

The system given in (9), together with the learning rule (19) form the basis of our source separation framework. From (19), one can note that in a blind (unsupervised) scheme the adaptation is done based only on the data provided by the sensors. This contrasts to supervised processing, where the learning rule requires a set of source samples (learning database) that must be known in advance. This explains why blind methods avoid the need of a training (calibration) stage before the effective use of the measurement system.

3.3 Notes on the Application of the Developed BSS Algorithm in a Practical Scenario

As commented in Section 2, we assume that E_i and $d_i = RT/z_iF$ in Equation (4) are known in advance. Therefore, before applying the developed method on the acquired data, we should conduct the following pre-processing step:

$$x_i = \exp\left(\frac{x_i^* - E_i}{d_i}\right) \qquad (20)$$

where x_i^* denotes the actual response provided by the i-th electrode of the sensor array. It should be stressed that there may be some situations for which a strong deviation between the value predicted by the Nernst equation for d_i and the actual one is observed. This can be due to the sensor aging for example. In these cases, this pre-processing step will introduce a nonlinear effect that is not predicted by Equation (4) and, as a consequence, our proposal becomes useless if the deviation is too high. Fortunately, a discrepancy between the actual value of E_i and the one used in the pre-processing stage is not important as in the case of the parameter d_i. Indeed, when E_i is not exactly known, we can still apply our method but the best we can do is to retrieve each source up to a unknown multiplicative gain. In these cases, a simple two-point calibration can be conducted to cancel the introduced gain.

Another important point that should be emphasized is that our proposal works in an off-line fashion. Actually, in Equation (19), the estimation of $\beta_y(y)$ requires a batch operation.

4 EXPERIMENTAL RESULTS

Aiming to assess the performance of our proposal, we present a set of experiments considering an array formed by a Ca^{2+} ISE and a Na^+ ISE. Therefore, this situation is modeled by Equation (5) where $k = 2$ (considering that the first equation models the Ca^{2+} ISE response). The signals $s_i(t)$, which represent the ions activities, were artificially generated, but the mixtures $x_i(t)$ were obtained using the selective coefficients that were extracted from actual experiments. Concerning the organization of this section, we firstly describe the practical scenarios that provided us the selectivity coefficients used in our tests. After that, we present the results obtained by the developed source separation method.

In all experiments, the quality of each retrieved source is quantified according to Signal-to-Interference Ratio (SIR), which, for each pair source/retrieved signal, is defined as follows:

$$\mathrm{SIR}_i = 10 \log\left(\frac{E\{s_i^2\}}{E\{(s_i - y_i)^2\}}\right) \qquad (21)$$

Thus, $\mathrm{SIR} = 0.5(\mathrm{SIR}_1 + \mathrm{SIR}_2)$ defines a global index. Regarding the estimation of the score function difference vector in (19), we considered the method proposed in [25]. In short, this is a kernel-based method which differs from the classical approaches in two points: the estimation is done over a regular grid and a cardinal spline is used as kernel function. As a consequence, one obtains a faster algorithm than the classical kernel method.
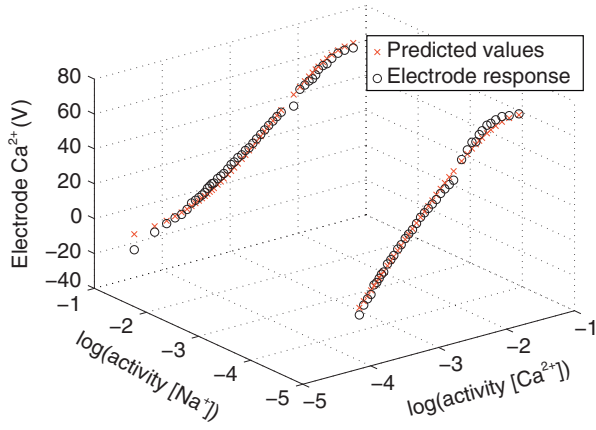
4.1 Scenarios

We consider two distinct scenarios. In the first one, the selective coefficients were obtained through experiments conducted by us[5], in which we started with a fixed concentration of Na^+ and then a solution of $CaCl_2$ was injected. In Figure 4, we present the responses of the electrode Na^+ and of the electrode Ca^{2+} as well as the predicted responses provided by the Nicolsky-Eisenman equation. Note that two experiments are represented in these figures and in both cases, the concentration of Ca^{2+} varies from 10^{-4}M to almost 10^{-1}M. However, in one of them the initial concentration of Na^+ is approximately 10^{-4}M while in the other one this initial concentration is 10^{-1}M. In Table 1, we present the selective coefficients obtained from a regression considering the NE model and also the associated Mean Squared Error (MSE). The total number of regression points in this case was 86.

We also consider a second scenario where the selective coefficients are higher that in the first case. Actually, this allows us to assess the performance of the BSS method in a situation where the interference takes place in the two electrodes. For this second scenario, the values of the selective coefficients, which are presented in the second row of Table 1, were taken from [27].

4.2 Performance of the Developed BSS Method

For the first scenario, we consider a situation in which the activity of the ion Ca^{2+} lies in the interval $[10^{-4}, 10^{-3}]$M, whereas the activity of Na^+ varies between $[10^{-4}, 10^{-1}]$M. In Figure 5, we present the artificial sources generated for this case and also the mixtures generated by Equation (5). Concerning the separation system, a set of 500 samples of the mixtures was considered. The learning rate was set $\mu = 0.003$ and the initial conditions of the recurrent network were

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5 This dataset is publicly available [26].

a)
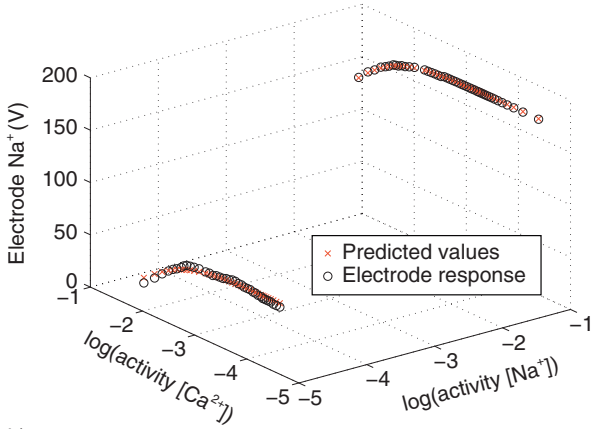
b)

Figure 4

Electrodes responses in the first scenario. a) Ca^{2+} electrode response; b) Na$^+$ electrode response.

TABLE 1

Selective coefficients

	$\log(a_{12})$	$\log(a_{21})$	MSE Ca^{2+}	MSE Na$^+$
Scenario 1	−1.23	−4.03	2.74	1.65
Scenario 2	−0.70	−0.40	–	–

$[y_1(1)\, y_2(1)]^T = [0\,0]^T$. In this situation, the learning algorithm converged after 8 500 iterations. The results of this first case are expressed in the first row of Table 2. Our method was able to provide a very good source separation, as can be seen in Figure 5.

For the second scenario, the Ca^{2+} ion activity varies in $[10^{-4}, 10^{-2}]$M while the Na$^+$ activity is varying in $[10^{-4}, 10^{-1}]$M. The sources and the associated mixtures

a)

b)
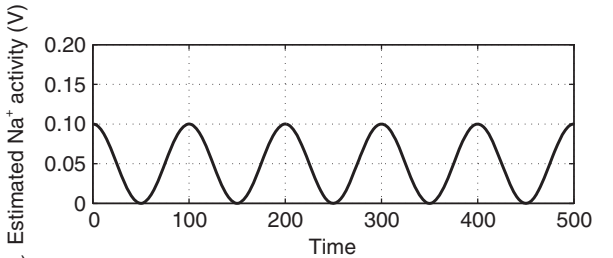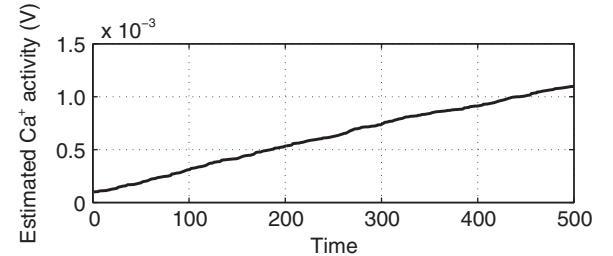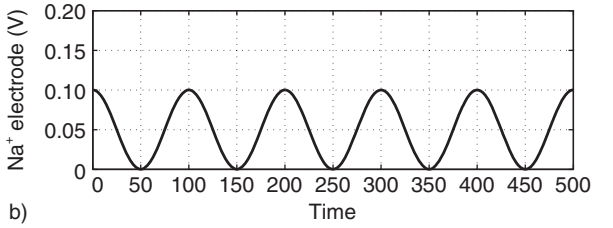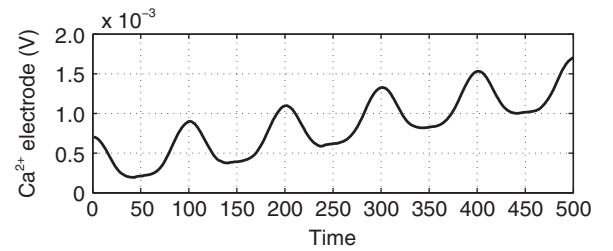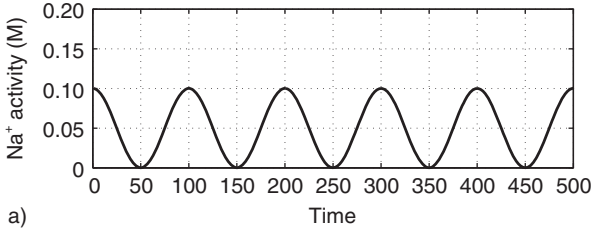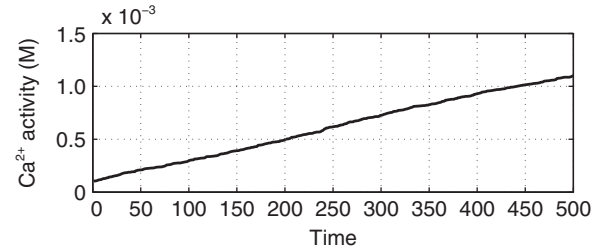
c)

Figure 5

a) Sources, b) mixtures and c) sources estimates for the first scenario (retrieved sources after 8 500 iterations).

TABLE 2

Obtained SIR for both scenarios

	SIR_1	SIR_2	SIR
Scenario 1	56.90	56.35	56.62
Scenario 2	43.77	35.70	39.74

are depicted in Figure 6. Note that in this situation, the interference is important in both electrodes. Again, the number of available samples was 500. The convergence was observed after 600 iterations while the learning rate in this case was set $\mu = 0.01$. As can be checked in the second row of Table 2, our proposal was able to provide good source estimations. This is illustrated in Figure 6, where we show the retrieved sources in a typical situation.

In Figure 7, we present the evolution of the $[w_{12} \; w_{21}]^T$ during the learning algorithm. Note that these parameters indeed converge to the ideal values which are given by selectivity coefficients a_{12} and a_{21}. As discussed in Section 3.2, the adjustment of $[w_{12} \; w_{21}]^T$ is conducted by solely means of the data provided by the sensor array (unsupervised scheme), that is, our method was able to estimate the selectivity coefficients without any calibration step. Of course, as discussed in Section 3.3, if the parameters E_i in Equation (20) are unknown, then a two-point calibration is mandatory. Moreover, even when E_i is known, there would be a scale indetermination for scenarios with a greater number of sources. Actually, this gain indetermination is inherent in ICA/BSS methods [11] and, thus, a two-point calibration would also be required in this case. However, even in these scenarios, BSS methods would avoid a complete calibration step based on a great number of learning samples (calibration points).

4.3 Sensibility to Noise

Although the NE model is widely used for modeling the response of an ISE, there has been reported in the literature that the prediction provided by such a model may deviate from the actual response. In this situation, a more adequate description of mixing model would have to incorporate noise. Hence, we here study the performance degradation of our proposal in a noisy situation.

As discussed in Section 2, our method was developed for a simplified version of the NE model which omits the logarithm term, since we assume that its multiplying factor is known (Nernstian case). Also we discuss in Section 3.3, the inversion of these logarithm functions can be done by simply passing our data through
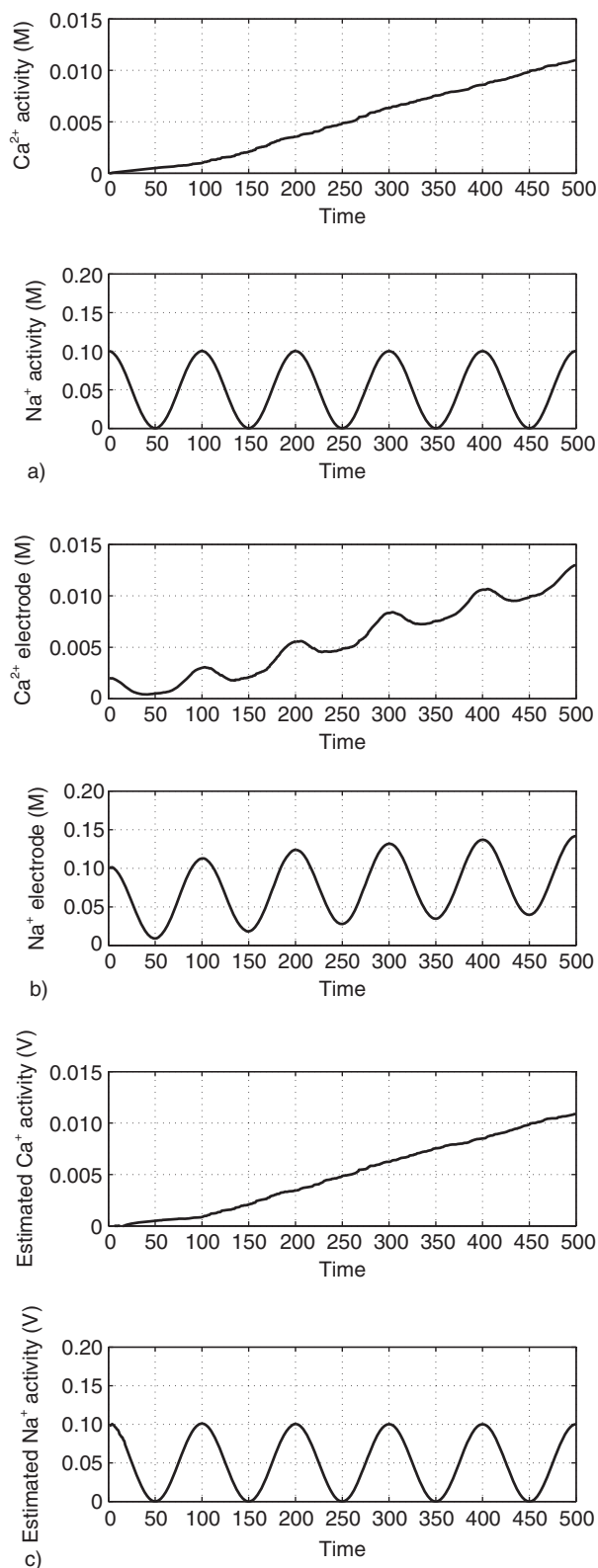
Figure 6

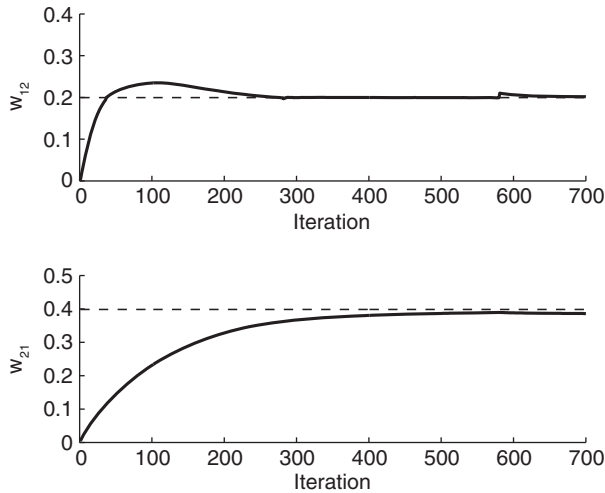a) Sources, b) mixtures and c) sources estimates for the second scenario (retrieved sources after 600 iterations).

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Figure 7

Evolution of the separating system parameters (solid) and
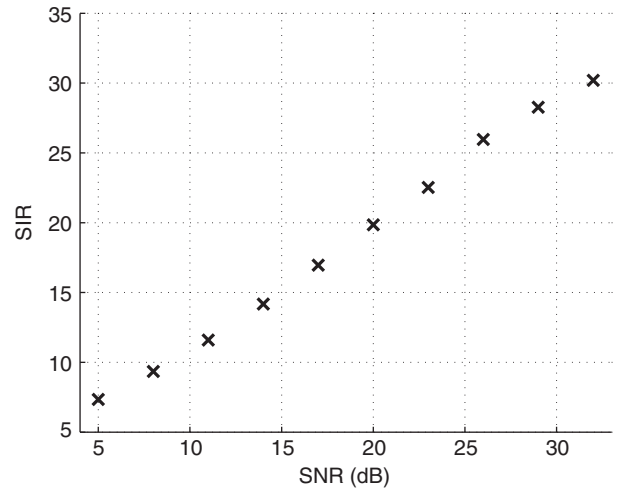the selectivity coefficients (dashed).

Figure 8

Output SIR *versus* input noise (AWGN inside the loga-
rithm term) SNR.

exponential functions. This procedure opens at least two
possibilities for modeling the noise, we consider either an
additive noise inside the logarithm term[6] of the model
(4), or the noise added to the outputs of the logarithm
functions[7]. In the sequel, we provide experiments for
both cases.

In a first step, we considered an Additive White
Gaussian Noise (AWGN) on each sensor of model (5),
which is equivalent to consider an AWGN inside the log-
arithm functions of (4). We tested our method in a sce-
nario in which $k = 2$ and the random sources are
uniformly distributed between $[0.1, 1.1]$. In Figure 8,
where each result represents the average of 30 experi-
ments, we can note that the performance index SIR
increases linearly as the Signal-to-Noise Ratio (SNR)
grows.

We have performed another set of experiments to ver-
ify the influence of the (measurement) noise on our
method with an AWGN outside the logarithm function.
The results of this experiment are shown in Figure 9
(average of 30 experiments). Although the algorithm still
works properly for SNRs higher than 25 dB, the perfor-
mance degradation due to noise is rather stronger than
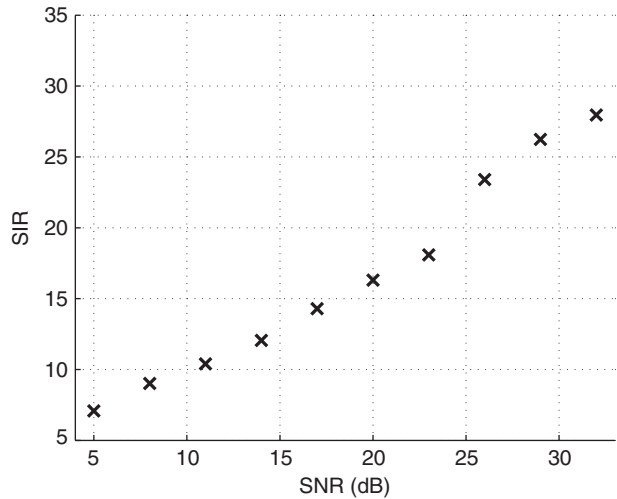the first situation. This case is nothing but the model

Figure 9

Output SIR *versus* input noise (AWGN outside the loga-
rithm term) SNR.

(5) with a log-normal multiplicative noise on each sen-
sor. Indeed, the pre-processing given in Equation (20),
where the additive Gaussian noise is passed through an
exponential function, returns two multiplicative terms,
one of them being the exponential of a Gaussian random
variable which in turn culminates in a log-normal distri-
bution.

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[6] This noise here is associated with model error due to the missing inter-
fering ions.
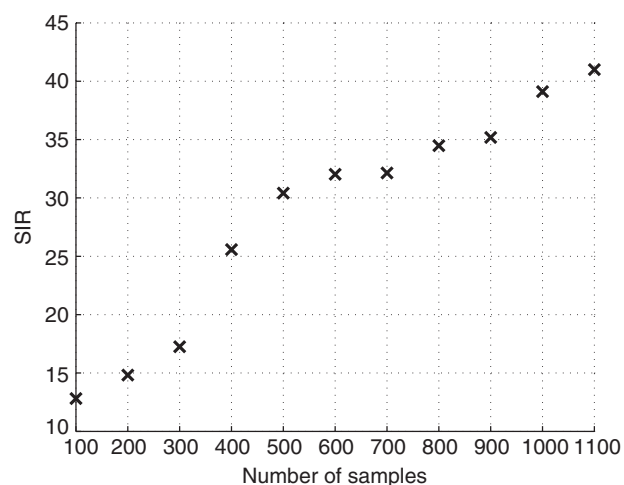[7] The noise here models measurement errors.

Figure 10

Influence of the number of samples.

4.4 Influence of the Number of Samples

We also investigated the performance degradation of our method as the number of available samples decreases. Our motivation for this analysis comes from the fact that in the envisaged chemical sensing application the number of samples is usually small[8]. In this study, we consider a scenario with sources uniformly distributed and $k = 2$. We checked through simulations that good estimations are provided for SIR higher than 20 dB. Therefore, as we can see in Figure 10, where each result represents the average of 20 experiments, the proposed algorithm works properly with a number of samples equal to or greater than 400.

CONCLUSIONS

The objective of this work was to develop a blind source separation method for processing the signals acquired by an array of ion selective electrodes. The motivation behind our study was to overcome the interference problem in the situation in which the ions under analysis have different valences. Our method was built by defining a recurrent network as separating structure and by developing a mutual information approach for its training. A set of experiments using parameters extracted from real experiments and signals artificially generated was

conducted. The obtained results attested that our proposal was able to estimate the source signals (temporal evolution of the activities) as well as the selective coefficients without the need of performing a calibration stage before the measurement.

In additional to the very promising results obtained in this work, there are still several points to be addressed in future works. The first one regards the limitations of the use of an ICA-based source separation. For instance the assumption that the sources are mutually independent in the considered application is equivalent to state that there is no interaction between the ions under analysis. Also, ICA methods present a performance degradation when the number of available samples is small (in our problem, we could check that a proper operation requires more than 300 samples). Finally, two other points could be investigated. First, an investigation about the possibility of incorporating stabilizing elements into our recurrent network so we can increase its operation range in the mixing parameter space. Our motivation comes from the very good results obtained with a stabilized network developed for the separation of linear-quadratic mixtures [28]. Secondly, despite the fact that BSS methods are quite general, they rely on a parametric description of the mixing system. Therefore, we could investigate the gains brought by the development of BSS methods for more precise models than the one offered by the Nicolsky-Eisenman, like the one presented in [29].

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[8] Note here that the number of samples is related to the samples to be processed and not to the calibration points.

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APPENDIX

Calculation of $\frac{\partial y}{\partial w}$

In this appendix, we are interested in the determination of:

$$\frac{\partial \mathbf{y}}{\partial \mathbf{w}} = \begin{bmatrix} \dfrac{\partial y_1}{\partial w_{12}} & \dfrac{\partial y_1}{\partial w_{21}} \\ \dfrac{\partial y_2}{\partial w_{12}} & \dfrac{\partial y_2}{\partial w_{21}} \end{bmatrix} \tag{A1}$$

After the convergence of (9), the mapping performed by the separating system for a given value of $\mathbf{w}$ is given by:

$$\begin{aligned} x_1 &= y_1 + w_{12} y_2^k \\ x_2 &= y_2 + w_{21} y_1^{\frac{1}{k}} \end{aligned} \tag{A2}$$

Therefore, the derivatives in (A1) can be calculated by applying the chain rule property on (A2). For instance, it is not difficult to verify from that:

$$\frac{\partial y_1}{\partial w_{12}} = -\left(y_2^k + w_{12} k y_2^{k-1} \frac{\partial y_2}{\partial w_{12}}\right) \tag{A3}$$

Given that:

$$\frac{\partial y_2}{\partial w_{12}} = -\frac{1}{k} w_{21} y_1^{\frac{1}{k}-1} \frac{\partial y_1}{\partial w_{12}} \tag{A4}$$

and substituting this expression in (A3), one obtains:

$$\frac{\partial y_1}{\partial w_{12}} = \frac{-y_2^k}{1 - w_{12} w_{21} y_1^{\frac{1}{k}-1} y_2^{k-1}} \tag{A5}$$

By conducting similar calculations, one obtains the other derivatives:

$$\frac{\partial y_2}{\partial w_{12}} = \frac{w_{21} y_1^{\frac{1}{k}-1} y_2^k}{k\left(1 - w_{12} w_{21} y_1^{\frac{1}{k}-1} y_2^{k-1}\right)} \tag{A6}$$

$$\frac{\partial y_1}{\partial w_{21}} = \frac{k w_{12} y_1^{\frac{1}{k}} y_2^{k-1}}{1 - w_{12} w_{21} y_1^{\frac{1}{k}-1} y_2^{k-1}} \tag{A7}$$

$$\frac{\partial y_2}{\partial w_{21}} = \frac{-y_1^{\frac{1}{k}}}{1 - w_{12} w_{21} y_1^{\frac{1}{k}-1} y_2^{k-1}} \tag{A8}$$