Simultaneous titration of ternary mixtures of Pb(II), Cd(II) and Cu(II) with potentiometric electronic tongue detection

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Abstract

An automatic titration method is reported to resolve ternary mixtures of transition metals (Pb^{2+}, Cd^{2+} and Cu^{2+}) employing electronic tongue detection and a reduced number of pre-defined additions of EDTA titrant. Sensors used were PVC membrane selective electrodes with generic response to heavy-metals, plus an artificial neural network response model. Detection limits obtained were ca. 1 $mg \cdot L^{-1}$ for the three target ions and reproducibilities 3.0% for Pb^{2+}, 4.1% for Cd^{2+} and 5.2% for Cu^{2+}. The system was applied to contaminated soil samples and high accuracy was obtained for the determination of Pb^{2+}. In the determination Cd^{2+} and Cu^{2+}, sample matrix showed a significant effect.

Keywords: Electronic tongue; simultaneous titration; sensor array; transition metals; ion selective electrodes; artificial neural networks.

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1. Introduction

The use of chemometrics in chemistry has increased with the rapid technological development of the past decades. Significant improvements have been achieved in chemical equipment, accompanied by much faster and more powerful desktop computers. Analytical chemistry is one of the disciplines in which there was always interaction with chemometrics, especially in areas like curve fitting and statistical control. Currently, the development of new analytical instruments and the emergence of more complex and multi-causal problems have produced measures that demands new and more effective data analysis methods; this has opened many new options for advanced data treatment, especially when generated data is already of multivariate type. It is for these reasons that there is, every day more, a demand for the use of tools like pattern recognition, multivariate calibration, mathematical mixture resolution and/or some of the new directions that chemometric methods are taking [1].

Titrimetries correspond to one of the more traditional areas of analytical chemistry, and they also have improved upon the application of chemometric techniques; in 1998, Lindberg and Kowalski suggested the use of Partial Least Square (PLS) calibration for the determination of mixtures of acids with pKa (dissociation constant) lower than 4 [2]. In another example, an Artificial Neural Network-Back Propagation (ANN-BP) model was applied to potentiometric titration data for the resolution of polybasic acid mixtures by Shamsipur et al. [3]. The integration of Principal Component Analysis (PCA) with ANNs has been reported as satisfactory approach to resolve mixtures of acids (p-coumaric, sinapinic, vanillic, and isovanillic acids) [4] and drugs (ibuprofen, indomethacin and naproxen) [5].

Electronic tongues (ETs), are a new paradigm in analytical chemistry, being nothing more than a multi-sensor system with cross-responses and using advanced mathematical procedures for signal processing, based on pattern recognition and/or multivariate data analysis; ETs are a good example of integration between chemometrics and electroanalysis. With their use, an important advantage is the generation of multivariate data, that afterwards also makes possible the interpretation of complex compositions, the resolution of mixtures, the deconvolution of the contributions from primary species and their interferents, or even, to distinguish between spurious responses and the true ones [6]. ET systems are mainly applied in

solving qualitative problems in food industry [7-9], but also, their virtues can be exploited in the quantification of a wide variety of analytes in fields such as medical [10, 11], environmental [12-14] and also food and beverages [15, 16].

Titrimetries are established techniques in use for many years; yet today they are very successfully used in water analysis, for example, in the complexometric titration of calcium and magnesium (water hardness). In the case of mixtures of metals with very close metal-ligand formation constants, the conventional methods of endpoint detection are not effective. To solve this problem, specific strategies are used, such as indirect titration or addition of masking agents, among others, but this is satisfactory only for binary mixtures of a few analytical systems.

An innovative idea in this situation is to use an ET as end point detection method in the titration resolving mixtures of two or more components. The pioneers in this sense were Calvo et al. [17]; in this work, the authors showed the abilities of an ET formed by an array of ion-selective electrodes as end-point detection method in the complexometric titration of mixtures of alkaline earth metals. The present work aims to use an electronic tongue formed by ion-selective electrodes and ANNs as data processing method for resolving ternary mixtures of heavy metals Pb^{2+}, Cd^{2+} and Cu^{2+}.

2. Experimental

2.1. Reagents and solutions

The reagents used in the formulation of the eight ISE membranes that formed the array are listed below: *S,S´*-methylenebis(*N,N*-diisobutyldithiocarbamate), tert-butylcalix[4]arene-tetrakis(*N,N*-dimethylthioacetamide), 1,3-bis(*N*-benzoylthioureido)-benzene, *N,N´,N´*-tetrabutyl-3,6-dioxaoctane di(thioamide), *o*-xylylene bis(*N,N*-diisobutyldithiocarbamate), tetrabenzyl pyrophosphate, [2,2']-furildioxime monohydrate and trioctylphosphineoxide were employed as ionophores; the plasticizers: *o*-nitrophenyloctyl ether (NPOE), dioctyl sebacate (DOS), (10-hydroxydecyl) butyrate (ETH 264), bis(1-butyl-pentyl) adipate (BBPA) and dibutylphtalate (DBP); the additive: potassium tetrakis(4-clorophenyl)borate (KTpClPB) and the polymer poly(vinyl chloride) (PVC) all purchased from Fluka (Buchs, Switzerland).

Membranes were deposited (solvent casted) over a carbon-base solid contact to form each ion-selective electrode. The materials used to prepare the solid electrical contact were the epoxy resin components: Araldite M, Araldite M hardener, Araldite M accelerator (all from Fluka), and graphite powder (BDH, Dorset, UK) as conductive filler. Other reagents employed for preparing buffer or stock solutions were imidazole (Fluka), ethylenediaminetetraacetic acid disodium salt (EDTA) (from Panreac, Barcelona, Spain), tetrahydrofuran (THF, from Merck, Darmstadt, Germany) and nitrate salts of the metals of interest (Fluka). Certified standard metal solutions (1000 $mg \cdot L^{-1}$, used for Flame AAS, Fluka) were the reference materials used in the study. All other reagents were of high purity, analytical grade, pro-analysis or equivalent. The solutions were prepared with deionised water (Milli-Q, Millipore, Molsheim, France).

2.2. Apparatus

An automatic titration system with multichannel potentiometric detection, developed in-house [17], was used in this work. The system consisted of a Crison 2030 automatic microburette (Crison, Barcelona, Spain), fitted with a 10 mL syringe (Hamilton, Bonaduz, Switzerland), controlled by a computer. The measurement system comprised the ISE array, a Ag/AgCl double-junction reference electrode (Thermoelectron 900200, Beverly, MA) and a 8-channel signal conditioning circuit connected to a National Instruments NI6221 Multifunction DAQ (Austin, TX). The system was PC-controlled using a QuickBasic program (Microsoft, Redmond, WA).

For the buffer preparation, a Crison 2002 pH meter with a combination pH electrode (Ingold P/N 10/402/3092, Urdorf, Switzerland) was used. As reference method for determining metal concentrations, flame atomic absorption spectrometry (Varian absorption spectrometer, Model 1275, Santa Clara, CA) was chosen.

2.3. Sensor array

For building the sensor array, there were used commercial formulation membranes [18-23] or others developed in our group [24]. The ion selective electrodes (ISEs) were constructed in asymmetric configuration with a solid electrical contact made from a conductive composite [25, 26]. Table 1 describes the formulation of potentiometric membranes employed in this work.

Table 1. Formulation of the ion-selective membranes employed in the construction of the potentiometric sensor array.

Sensor	PVC (%)	Plasticizer (%)	Ionophore (%)	Ref.
Pb^{2+} (1)	37.2	NPOE (49.6)	*S,S´*-methylenebis(*N,N*-diisobutyldithiocarbamate) (11.2) [a]	[21]
Pb^{2+} (2)	33.0	NPOE (65.6)	tert-butylcalix[4]arene-tetrakis(*N,N*-dimethylthioacetamide) (1.0)[a]	[22]
Pb^{2+} (3)*	33.0	DOS (61.5)	1,3-bis(*N*-benzoylthioureido)benzene (5.0) [a]	[24]
Cd^{2+}	34.0	ETH 264 (65.0)	*N,N´,N´*-tetrabutyl-3,6-dioxaoctane di(thioamide) (1.0)	[18]
Cu^{2+}	57.2	NPOE (34.3)	*o*-xylylene bis(*N,N*-diisobutyldithiocarbamate) (6.9) [a]	[21]
Generic (1)	34.2	BBPA (62.6)	tetrabenzyl pyrophosphate (2.3) [a]	[19]
Generic (2)	32.0	DBP (62)	[2,2']-furildioxime monohydrate (4.0) [a]	[23]
Generic (3)	37.7	NPOE (54.9)	trioctylphosphineoxide (5.2) [a]	-

[a] The formulation included potassium tetrakis(4-clorophenyl)borate as additive.
* Ionophore not commercially available.

2.4. Sensors characterization

For the cross-response characterization of the ISEs vs. the three metals considered, there were determined the sensitivity, selectivity coefficient and detection limit of each prepared electrode, according to IUPAC methodology. The activity coefficients of ions in solution were calculated with the Debye-Hückel formalism. The fixed interference method were used to determinate the selectivity characteristics.

2.5. Titration procedure

The titration procedure applied was proposed by Calvo et al. [17], in which a fixed and limited number of titrant additions was used; the motivation in this is to achieve quick procedures with lesser experimental complexity. Just 5 additions of 2 mL of EDTA 0.020 M were employed and the potentials between ISEs and the reference electrode, after 20 s homogenization, recorded. As titration media, a pH of 6 was selected, accomplished adding 5 mL of 0.25 M imidazole buffer to 25 mL of each sample, originally acidic. Generated data per sample and per sensor were 5 potential readings after each addition, plus the initial potential. Therefore, the total input data per sample were 6 (potential readings)×8 (ISEs)= 48 input vector.

Additional samples to those needed for the multivariate calibration process were prepared in order to determine the main performance characteristics of the proposed method: detection limit, accuracy and precision. The LD for each ion was calculated as the concentration with signal equivalent to three times the standard deviation of five blanks. The precision was determined in repetitivity conditions, calculated for each ion through five replicate samples with intermediate range concentration of Pb^{2+}, Cd^{2+} or

Cu^{2+}. The accuracy was estimated using standard solutions of FAAS for the three metals (supplied by Fluka).

2.6. Building of the ANN response model

The multivariate calibration process was based on an Artificial Neural Network (ANN) as response model. A stock of 50 standard solutions (mixtures of Pb^{2+}, Cd^{2+} and Cu^{2+}) were used for the calibration process, prepared manually from individual stock solutions, with random concentrations of the 3 metals and considering the titrant consumption (EDTA) did not exceed the total volume of the burette, 10 mL in this case (Fig. 1). Samples were divided in two subsets: 33 samples were used for training (model building) and the other 17 in the model external validation (to determine its predictive ability). The samples were distributed randomly, but with the precaution that the maximum and minimum concentrations were included in the training subset, this is to prevent the model to perform any extrapolation.

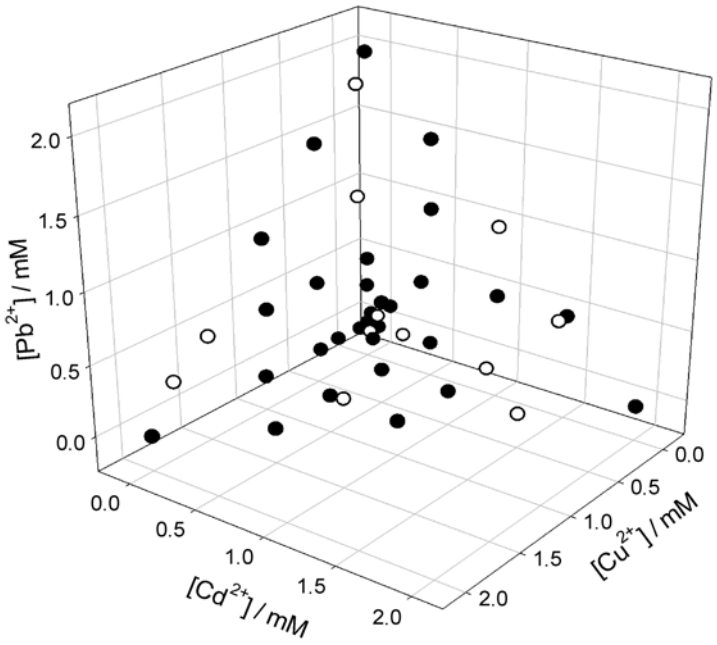

Figure 1. Composition of standards solutions used in the training (●) and external validation (○) process; concentration range selected was between 0.002 mM and 2.0 mM for Pb^{2+}, Cd^{2+} and Cu^{2+}.

To define the architecture of the ANN to be tested, certain configuration characteristics were initially fixed based on our previous experience with ETs formed by potentiometric sensors. These included the number of input neurons, 48, equal to the

input vector dimension (8 sensors×6 readings); the number of output neurons, which was three (the number of target ions); the transfer function of the input layer, which was linear (*purelin*) and a single hidden layer of neurons used in the general layout. The learning strategy used was *Bayesian Regularization*, and the parameters used for learning conditions were: *learning rate* (α=0.1) and *momentum* (β=0.4).

The number of neurons in the hidden layer and the transfer functions used in the hidden and output layer were optimized by systematic evaluation in order to obtain the best performance. The number of neurons in the hidden layer were varied between 3 and 12; 4 transfer functions were assayed on each layer (*logsig:* log-sigmoidal, *tansig:* hyperbolic tangent sigmoid, *purelin:* linear and *satlins:* saturated-linear (112 total configurations tested).

The goodness of fit of the model was determined in function of the smaller values of RMSE (root mean squared error) obtained for the training samples, and the prediction abilities using linear regression of the graphs of obtained (y) vs. expected (x) concentration with slope of 1, intercept of 0 and correlation coefficient close to 1 for the three ions.

2.7. Software

The readings were acquired by using custom software developed by the authors in Microsoft QuickBasic Version 4.5. Neural network processing was developed with MATLAB 7.0 (Mathworks, Natick, MA, USA), using its Neural Network Toolbox (v. 3.0). The graphs were made with Sigma Plot 11 (Systat Software Inc, California, USA).

3. Results and Discussion

3.1. Preliminary characterization

The electrodes forming the array used in the ET were characterized in parallel against the three metals considered, Pb^{2+}, Cd^{2+} and Cu^{2+}. Table 2 summarizes the values of detection limit, sensitivity and potentiometric selectivity coefficients obtained. The sensitivity of all sensors was close to the Nernstian behavior for the primary ion (29.6

mV/dec at 25ºC) if considering the confidence intervals. In ET applications one of the most important conditions is the need of cross-response of the sensor array [27]. Clear evidence of the presence of cross-sensitivity are the values of slopes obtained; for all ISEs these were greater than 20 mV/dec for two or more of the target ions, except for the Pb^{2+} (2) ISE, if considering the confidence intervals. This can be confirmed with the experimentally obtained potentiometric selectivity coefficients; in most of the ISEs, the logarithm of these are higher than -1.5, suggesting important interference (i.e. cross-response). When the ISEs were in contact with the primary ion alone, the detection limits were lower than 7.2 ± 1.4 µM, an acceptable concentration level for the proposed titrimetric application.

Table 2. Response characteristics of the ISEs forming the sensor array.

Sensor	Sensitivity (mV/dec)			$\log K^{pot}_{J,K}$			LD (µM)	Linearity Range (M)
	Pb^{2+}	Cd^{2+}	Cu^{2+}	Pb^{2+}	Cd^{2+}	Cu^{2+}	For primary ion	
Pb^{2+} (1)	29.79±2.4	12.78±3.4	28.87±3.4	-	-3.6	+0.7	0.36 ± 0.11	1.3×10^{-6} – 1.0×10^{-2}
Pb^{2+} (2)	30.42±3.3	14.48±2.2	14.11±3.1	-	-2.9	-1.4	0.19 ± 0.09	3.0×10^{-6} –1.0×10^{-2}
Pb^{2+} (3)	29.91±3.7	5.34±3.3	27.74±2.9	-	-1.8	-0.8	1.10 ± 1.9	4.1×10^{-6} – 1.0×10^{-2}
Cd^{2+}	11.31±3.0	29.15±2.7	18.27±3.9	-2.4	-	-2.1	7.2 ± 1.4	0.7×10^{-5} – 1.0×10^{-1}
Cu^{2+}	20.73±4.1	7.56±4.1	29.95±2.8	-0.8	-4.3	-	0.12 ± 0.13	0.8×10^{-6} – 1.0×10^{-1}
Generic (1)	28.3±3.1	19.6±3.5	21.9±3.2	-	-1.5	-1.1	2.5 ± 2.1 [(a)]	1.7×10^{-5} – 1.0×10^{-2}
Generic (2)	21.1±2.8	15.8±4.0	24.8±3.8	-2.1	-2.4	-	0.42 ± 0.19 [(b)]	6.2×10^{-7} – 1.0×10^{-1}
Generic (3)	24.8±2.7	27.9±2.8	20.4±2.1	-0.7	-	-0.9	3.0 ± 1.2 [(c)]	1.2×10^{-5} –1.0×10^{-2}

Primary ion considered: [(a)] Pb^{2+}, [(b)] Cu^{2+}, [(c)] Cd^{2+}

The need for use of advanced data treatment to solve the proposed analytical problem may be observed in Fig. 2. Illustrative titration curves were constructed using the recorded potential between ISE-Generic (3) and the reference electrode after 20 s homogenization next to the titrant addition. A clear turning point was observed for individual solutions of Pb^{2+}, Cd^{2+} and Cu^{2+} with equivalent concentration of 9.0 mM. When an equimolar mixture with 9.0 mM as total concentration of the three elements was titrated, a superposition of the three reactions is observed, making difficult the conventional determination. What is happening is the overlapping of the three concurrent equilibria, which in turn hinders the occurrence of any clearly singular point, making difficult the conventional titrimetric determination.

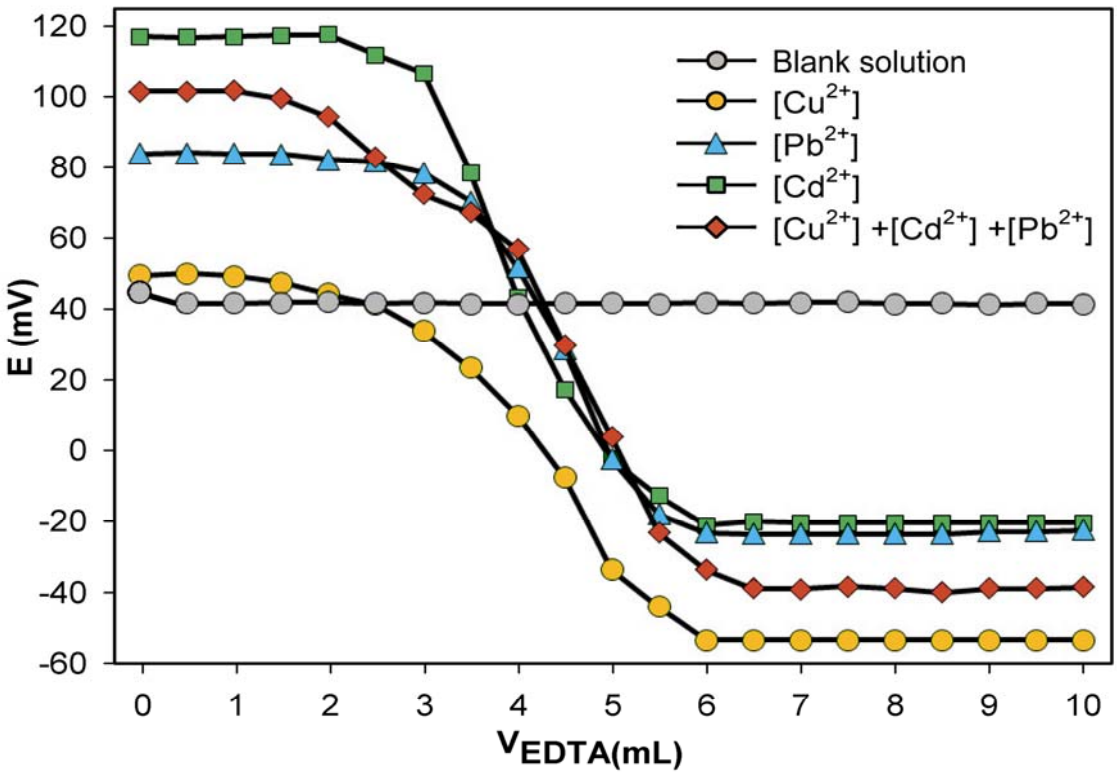

Figure 2. Potentiometric titration curves for different Pb^{2+}, Cd^{2+} and Cu^{2+} individual solutions and one mixture of three components, measured using the ISE-generic (3) as indicator electrode.

3.2. Building of the ANN response model

The training methodology used to determine the topology of the ANN was described in section 2.6. The best architecture was obtained for 48 neurons in the input layer, 6 in the hidden layer and 3 in the output layer, the transfer functions selected were *purelin* and *logsig* for the hidden and output layers respectively. In Fig. 3, a summary of the optimization process is shown, where the selection of the number of neurons in the hidden layer is performed according to obtaining minimum modeled errors (RMSE) plus correct behavior in the obtained/vs./expected results comparison graphs.

The predictive ability of the model was assessed using regression analysis with external validation samples; in Fig. 4, the comparative plots and other parameters of the final model are shown. The results obtained for this set of samples with the optimized model indicate very good correlation for the three ions considered, with worst R^2 =0.975; the ranges of slope and intercept also demonstrate correct behaviour, as they included the ideal values (slope 1 and intercept 0).

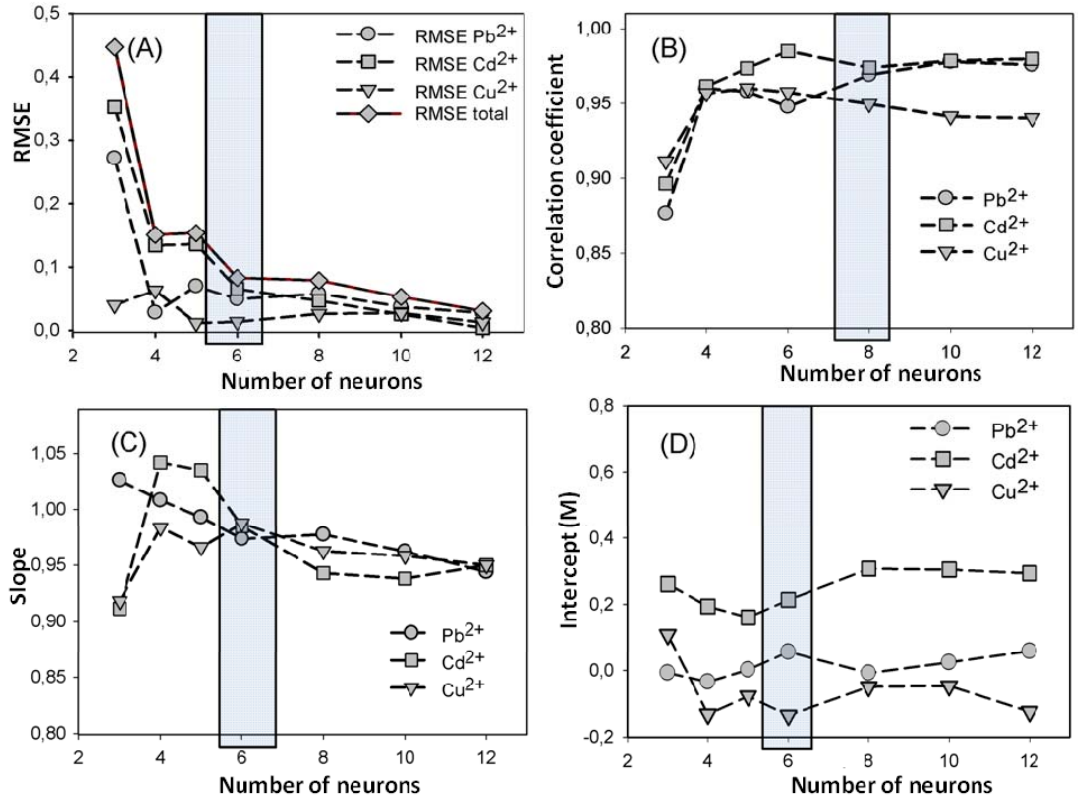

Figure 3. Selection of the optimal number of neurons in the hidden layer for the ANN model using *logsig* and *purelin* transfer functions for hidden and output layers respectively. (A) RMSE values, (B) correlation coefficients, (C) obtained slopes and (D) intercepts for the comparison regression between obtained vs. expected concentrations.

3.3. Determination of the performance characteristics of the method

The principal analytical properties of the method were determined: detection limit, precision and accuracy. The obtained results are shown in Table 3, the detection limits and precision are adequate for the proposed application. The accuracy was checked by comparing the concentration obtained with the proposed titration method vs. values assigned to the certified reference standards used; these verifications demonstrated that the proposed system is unbiased in metals determination.

Table 3. Performance characteristics of the proposed method.

Ion	LD (mg L^{-1})	RSD (%)	Accuracy (mg·L^{-1})	
			Obtained	Expected
Pb^{2+}	0.89	3.0	53.0 ± 1.6	50.0 ± 2.0
Cd^{2+}	1.20	4.1	46.5 ± 1.9	50.0 ± 2.0
Cu^{2+}	1.14	5.2	54.1 ± 2.8	50.0 ± 2.0

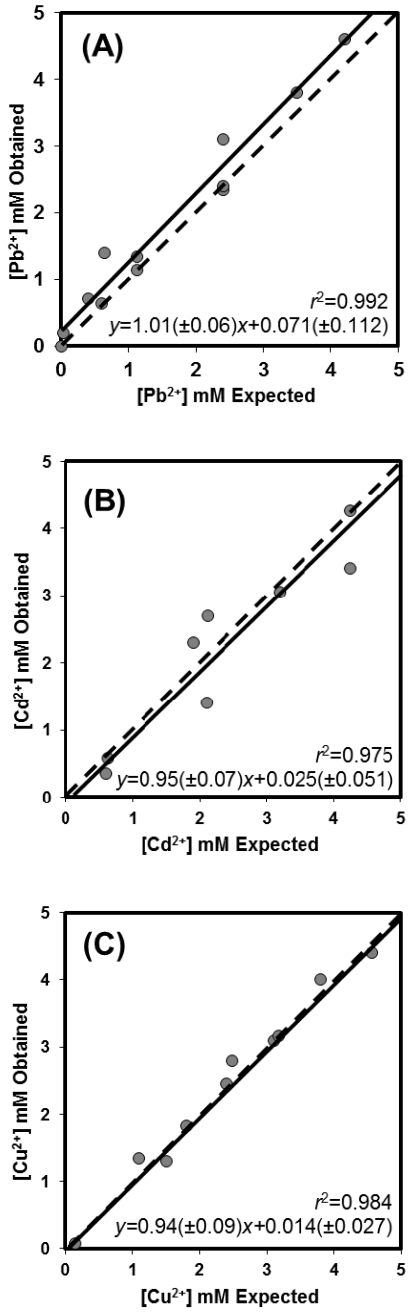

Figure 4. Modeling performance achieved for the optimized ANN with samples from the external test set: (A) Pb^{2+}, (B) Cd^{2+} and (C) Cu^{2+}. The dashed line corresponds to ideality, and the solid line to the regression of the comparison data. Uncertainty intervals were calculated at the 95% confidence level.

3.4. Application of the sensor array in real samples.

After application with synthetic samples, and to demonstrate its complete applicability, the method was applied in real samples. Six samples of motor road soil were taken for the analysis; the sample treatment was performed according to the procedure described in [28]. Due to the low content of target ions in soil extracts, the

samples were doped with standard solutions of Pb^{2+}, Cd^{2+} and Cu^{2+} with concentration of 10 mM. The results obtained with the proposed system were compared with the reference method using the Flame Atomic Absorption Spectrometry technique.

The comparative plots of results obtained by both methods are shown in Fig. 5, comprising the three analytes. The overall statistical comparison showed noticeable agreement, with significant correlations for the three ions, acceptable intercepts, close to 0 and slopes close to 1, considering the complexity of the sample matrix. Although comparisons passed the statistical test for the Cd^{2+} and Cu^{2+}, these ions showed higher dispersion (lower correlation coefficient) and a relatively high slope, respectively. One of the possible explanations for the results obtained is the great complexity of the matrix of the soil samples; also, these poorer results were obtained for the ions with fewer electrodes in the sensor array and therefore with less resolution capability.

The results obtained by the two methods were also compared by a paired sample Student's *t* test. The calculated *t*-statistics were $t = 0.04$ for Pb^{2+}, $t = 0.21$ for Cd^{2+} and $t = 1.63$ for Cu^{2+}. In all cases the values of *t* calculated were below the tabulated critical value $t^* = 2.57$ (for 5 degrees of freedom and 95% confidence level). These facts corroborate the results of the regression analysis performed above, with some higher discrepancies for Cu^{2+} than for the other metals, although still within tolerance limits defined by the statistical significance. General conclusion derived is that the proposed system and the reference method provide comparable results for the determination of $Pb^{2+}/Cd^{2+}/Cu^{2+}$ mixtures at the 95% confidence level. In general terms, it can be stated that better results may be achieved by increasing the number of electrodes for Cd^{2+} and Cu^{2+} in the electronic tongue.

4. Conclusions

In this paper, a simultaneous titration analysis for the resolution of ternary mixtures of $Pb^{2+}/Cd^{2+}/Cu^{2+}$ metals at the mM level was established with good prediction ability in spiked samples. The fixed volume titration method with an array of sensors and analyzing the obtained data with multivariate methods (ANN) allowed us to solve with acceptable accuracy mixtures of Pb^{2+}, Cd^{2+} and Cu^{2+} in samples of complex matrix. This performance, almost unreachable with the employment of conventional

titrimetric procedures, can be extended to other systems with different components, using other multivariate methods such as Partial Least Square (PLS) and to give solution to different problems of environmental, clinic and industrial field.

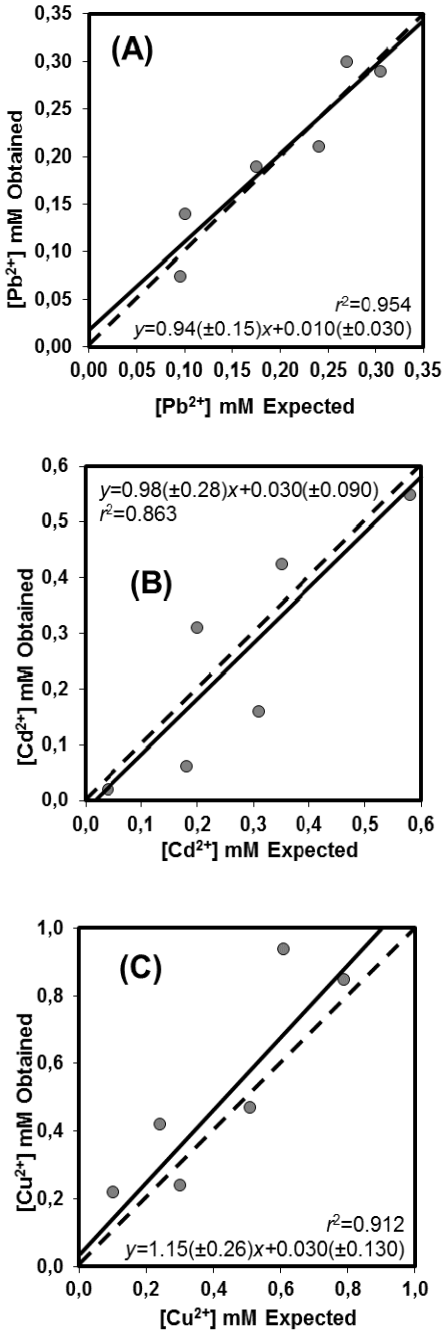

Figure 5. Correlations between obtained and reference concentrations of Pb^{2+} (A), Cd^{2+} (B) and Cu^{2+} (C) for the spiked soil samples. The dashed line corresponds to ideality, and the solid line to the regression of the comparison data. Uncertainty intervals were calculated at the 95% confidence level.

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