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A screen-printed voltammetric electronic tongue for the analysis of complex mixtures of metal ions

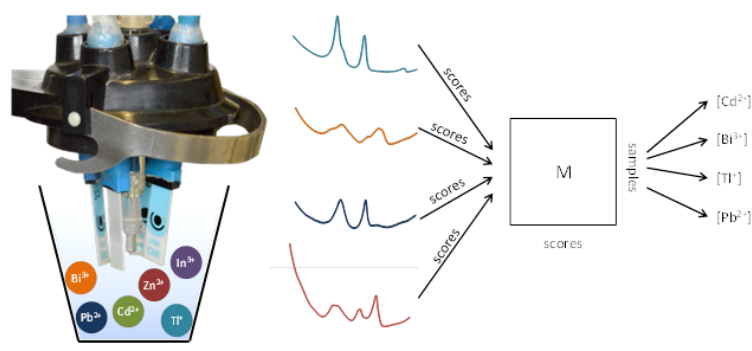
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Graphical abstract



Highlights

- Analysis of a complex mixture of metal ions at ppb level by a voltammetric electronic tongue.
- Four screen-printed modified electrodes: SPCE-CNF, *ex-situ*-SbSPCE-CNF, GSH-SPCE-CNF and Cys-SPCE-CNF are considered.
- Generation of distinct signatures with each sensor and metal ions.
- Use of PLS model for voltammetric data processing.

ABSTRACT

A voltammetric electronic tongue was constituted by four screen-printed modified electrodes: a carbon nanofiber modified electrode, an *ex-situ* antimony film electrode prepared from carbon nanofiber modified electrode, and two carbon nanofiber electrodes chemically modified with Cys and GSH. The tongue was successfully applied to the analysis of a complex mixture of metal ions (4 analytes and 2 interferences) by differential pulse anodic stripping voltammetry. Each sensor was firstly studied for the determination of each metal separately confirming that all electrodes showed differentiated response for the metals. The obtained voltammetric signals provided by the sensor array were processed by Partial Least Squares regression (PLS) to resolve the overlapped nature of the obtained multimetal stripping measurements. This PLS model was built considering a hierarchical model in order to reduce the large amount of data. The method was applied to synthetic mixtures of Cd(II), Pb(II), Tl(I), and Bi(III) in the presence of Zn(II) and In(III) at the levels of $\mu\text{g L}^{-1}$ and successfully validated with correlation coefficients of both calibration and prediction higher than 0.9 obtained from predicted *vs.* expected concentration graphs. Moreover, the simultaneous determination of Cd(II), Pb(II), Tl(I), and Bi(III) in the

presence of Zn(II) and In(III) in a spiked tap water was also satisfactory achieved, providing comparable results to those obtained by ICP-MS.

Keywords: voltammetric electronic tongue, screen-printed electrodes, modified electrodes, metal determination, stripping voltammetry, partial least square regression

1. INTRODUCTION

Heavy metals are natural components of the earth crust and can be released to the environment from both natural and anthropogenic sources such as forest fires, volcanic eruptions, sea spray, biogenic aerosols, mineral extraction, metal processing and incineration of pharmaceutical products, batteries, plastics and electrical goods among others [1,2]. In contrast to other toxic substances, heavy metals are no biodegradable. This fact increases the risk to human health that represent human or anthropogenic contributions to air, water, soil and food by modifying their speciation [3]. This risk is even higher due to heavy metals tend to bioaccumulate and biomagnificate [4,5]. Some heavy metals are essential for the human life in small concentrations. However, most of these metals are harmful when they are found at higher concentrations, being lead, cadmium, arsenic and mercury the most toxic. Heavy metals can be incorporated to the human body through the air, water, food or skin adsorption [4]. Therefore, monitoring heavy metals is very important both for human health and environment. In the last years different techniques were applied for the determination of heavy metals, being atomic absorption spectroscopy, inductively coupled plasma mass spectrometry or inductively coupled plasma atomic emission spectroscopy the most representative ones [6–8]. Nevertheless, these techniques require long times of analysis, expensive instruments

and trained personal. A faster and cheaper alternative that requires simple and portable instrumentation is given by electroanalytical techniques, which present excellent detection limits, sensitivity to the presence of different metals species and ability to multielement determination [9].

In voltammetric measurements of metal ions the electrode usually works as a single-electrode sensor which allows the simultaneous determination of several metal ions when non-overlapped peaks are obtained, i.e. the determination of Zn(II), Cd(II), Pb(II) and Cu(II) with the classical hanging mercury drop electrode [10,11]. However, when the solution contains a complex mixture of metal ions with intricate voltammetric responses (overlapped peaks, different interactions between metals...) the use of a single- electrode sensor does not allow its resolution. To solve these more complex systems a good strategy can be the use of several electrodes grouped in arrays of sensors with low selectivity that present a cross-response performance, giving rise to a multi-sensor array or (bio)electronic tongue, in which each electrode is different searching for a multivariate response [12–15]. Although the use of voltammetric tongues for electroanalytical purposes requires a larger amount of samples for calibration and the use of a multichannel potentiostat, these disadvantages can be overcome if the achieved information is better than that provided by a single sensor.

An essential aspect of any electronic tongue is data analysis. In particular, voltammetric tongues generate large amounts of data, which makes necessary a first step in order to preprocess and compress them prior to building the chemometric model. This preprocessing usually focuses on making data independent from units, removing redundant information or enhancing signal-to-noise ratio. In order to build the model different multivariate chemometric tools such as principal component analysis (PCA), partial least squares regression (PLS) or artificial neural network (ANN) have been used

to maximize the information achieved from the voltammetric data set using the sensor array, that a priori are difficult to analyse [12,16,17].

The use of arrays of voltammetric sensors has recently enabled an application very much desirable from the industrial sector, which is the use of electronic tongue systems to monitor and to detect defects during production of beverages and food [12]. In addition, sensor arrays are also useful in other research fields such as environmental analysis or bioanalysis [14,18–21]. In particular, voltammetric electronic tongues have been recently applied for metal ion determination in simple metal mixtures [22–25]. Nevertheless, to the best of our knowledge no more than 3 different metals were considered.

To ensure the desired cross-response of the electrode array the combination of different sensors modified following different strategies can be useful. In this sense, electrodeposition of metal films onto electrode surfaces [26,27] or chemical modification by electrografting with aryl diazonium salts [28] are two modification processes well known that can lead to sensors presenting a very different voltammetric response.

Nowadays, the screen-printing technology is well established for the production of sensors for electrochemical purposes. This technology allows the mass production of quite reproducible single-use devices with accessible and low cost character that usually incorporate a three-electrode configuration (working, reference and counter) on the same strip. Moreover, recent advances in this technology also allow the production of devices with different designs and the use of different inks (carbon, gold, silver, platinum...) that can include nanomaterials too [26,29–33]. In fact, the use of carbon-based nanomaterials, and in particular carbon nanofiber (CNF), as substrates for

electrode modifications has been reported to provide sensors with a better analytical performance due to their enhanced real surface area [34,35].

Thus, the coupling of SPEs with a voltammetric electronic tongue presents an attractive option for the determination of complex mixtures of heavy metal ions.

In this respect, this study presents a voltammetric electronic tongue which employs an array of sensors constituted by a carbon nanofiber modified screen-printed electrode (SPCE-CNF), an *ex-situ* antimony film electrode prepared from carbon nanofiber modified screen-printed electrode (SbSPCE-CNF), and two chemically modified sensors in which Cys and GSH were immobilized on aryl diazonium salt monolayers anchored to the surface of a carbon nanofiber modified screen-printed electrode (Cys-SPCE-CNF and GSH-SPCE-CNF, respectively) to consider for the first time the multivariate analysis of a really complex metal ion mixture including Cd(II), Pb(II), Tl(I), In(III), Zn(II), and Bi(III) in natural water samples. The electrochemical responses obtained from anodic stripping voltammetry (ASV) were used as departure information and the data treatment was performed with appropriate PLS model.

2. EXPERIMENTAL SECTION

2.1. Chemicals and Solutions.

All chemicals were of analytical grade and used without additional purification. Sb(III) 1.000 mg L⁻¹ atomic absorption standard solution was provided from Merck (Darmstadt, Germany). Potassium ferrocyanide K₄[Fe(CN)₆]·3H₂O, 2-(N-morpholino)-ethanesulfonic acid (MES), nitric acid, hydrochloric acid, sodium acetate, acetic acid and glutathione (GSH), in the reduced form, with purity greater than 99% were purchased from Merck. *N*-hydroxysulfosuccinimide (sulfo-NHS), *N*-(3-

dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride (EDC), 4-aminobenzoic acid (ABA), sodium nitrite, methanol, perchloric acid, sodium monophosphate, potassium dihydrogen phosphate, and L-cysteine (Cys) with purity greater than 99% were provided by Sigma-Aldrich (St. Louis, MO, USA). Potassium ferricyanide $K_3[Fe(CN)_6]$ was supplied by Panreac (Barcelona, Spain). Zn(II), Cd(II), Pb(II), Tl(I), In(III) and Bi(III) stock solutions 10^{-2} mol L⁻¹ were prepared from $Pb(NO_3)_2 \cdot 4H_2O$, $Cd(NO_3)_2 \cdot 4H_2O$, $Zn(NO_3)_2 \cdot 4H_2O$, $TlCl$, $In_2(SO_4)_3 \cdot 5H_2O$ and Bi(III) 1000 mg L⁻¹ atomic absorption standard solution respectively supplied by Sigma-Aldrich. Ultrapure water (Milli-Q plus 185 system, Millipore) was used in all experiments.

Tap water sample was collected in the laboratory from the local water distribution network, managed by Agbar Company (Barcelona; <http://www.agbar.es/eng/home.asp>) and mostly using water coming from Llobregat River.

2.2. Instrumentation.

An Autolab System PGSTAT12 (EcoChemie, The Netherlands), in a multichannel configuration, using GPES Multichannel 4.7 software package (EcoChemie) was used to perform differential pulse anodic stripping voltammetric (DPASV) measurements. The voltammetric cell was constituted by an Ag|AgCl|KCl (3 mol L⁻¹) reference electrode (to which all potentials are referred) provided by Metrohm (Switzerland), the four working screen-printed electrodes (SPEs) modified with CNF, Sb film, Cys and GSH respectively, and a carbon counter electrode from one of the SPEs as a common counter electrode. The working SPEs were prepared from commercial carbon nanofiber modified screen-printed disk electrodes (ref. 110CNT, DS SPCE) of 4 mm diameter supplied by Dropsens (Oviedo, Spain). Four flexible cables ref. (CAC, DropSens) were used to connect the SPEs to the Autolab System (Figure 1).

For pH measurements, a Crison micro pH 2000 pH-meter was used.

All measurements were carried out without oxygen removal and at room temperature (20 °C).

Inductively coupled plasma mass spectrometry Perkin-Elmer model Elan 6000 (USA) was used for ICP-MS measurements.

2.3. Preparation of modified SPEs.

2.3.1. Carbon nanofiber modified screen-printed electrode (SPCE-CNF): SPCE-CNF can be used as it is commercially acquired without any previous treatment before measurements.

2.3.2. Ex-situ antimony film electrode (ex-situ-SbSPCE-CNF): The SPCE-CNF, the auxiliary and the reference electrodes were immersed into a plating solution containing 0.01 mol L⁻¹ HCl and 50 mg L⁻¹ of Sb(III). An $E_d = -0.50$ V was applied during 300 s with solution stirring, followed by a rest period (without stirring) of 20 s. This methodology was previously tested showing a very high repetitivity and reproducibility [36].

2.3.3. Glutathione modified electrode (GSH-SPCE-CNF): GSH was immobilized on aryl diazonium salt monolayers anchored to the surface of SPCE-CNF [35]. Briefly, firstly the aryl diazonium salt is generated by adding 2 mmol L⁻¹ of NaNO₂ to a cooled solution of 73 mmol L⁻¹ of ABA in 1 mol L⁻¹ HCl. After mixing for 30 min in an ice bath, the electrochemical grafting process was conducted by the application of 15 cycles of cyclic voltammetry from 0 V to -1 V at 0.2 V s⁻¹. For the covalent immobilization of GSH via carbodiimide coupling, 10 µL of a 35 mmol L⁻¹ sulfo-NHS and 26 mmol L⁻¹ EDC solution in 0.1 mol L⁻¹ MES buffer (pH 4.5) were dropped onto the functionalized

SPE and left for 1h. Finally, the activated carboxyl groups reacted overnight with the amine terminal groups of GSH (2.9 mg/100 μ L GSH solution in MES buffer) at 4 °C.

This methodology was previously tested showing a very high repetitivity and reproducibility[35].

2.3.4. Cysteine modified electrode (Cys-SPCE-CNF): Cys was immobilized on aryl diazonium salt monolayers anchored to the surface of SPCE-CNF. For the preparation of the Cys-SPCE-CNF the GSH-SPCE-CNF above mentioned procedure was implemented, using Cys instead of GSH.

2.4. Voltammetric measurements.

Stripping voltammetric (DPASV) measurements using SPCE-CNF, *ex-situ*-SbSPCE-CNF, GSH-SPCE-CNF and Cys-SPCE-CNF were performed by applying with stirring a deposition potential (E_d) of -1.4 V during a deposition time (t_d) of 120 s followed by a rest period (t_r) of 5 s. Voltammograms were obtained by scanning the potential from -1.4 to -0.3 V, using a step potential of 5 mV, pulse amplitudes of 50 mV and pulse times of 50 ms.

In order to eliminate the remaining bound metals from the electrodes a cleaning step was performed between measurements by applying a conditioning potential (E_{cond}) of -0.3 V for 15 s in 0.1 mol L⁻¹ HClO₄ for *ex-situ*-SbSPCE-CNF, GSH-SPCE-CNF and Cys-SPCE-CNF electrodes and 0 V for 15 s in 0.1 mol L⁻¹ HNO₃ for SPCE-CNF electrode. On the other hand, the array of electrodes was completely replaced by a new set every 20 measurements to ensure their optimal performance.

Linear calibration plots for the separate determination of considered metal ions were obtained by increasing metal ion concentrations in 0.1 mol L⁻¹ acetate buffer solution at pH 4.5.

In order to allow the simultaneous analysis of Zn(II), Cd(II), Pb(II), Tl(I), In(III) and Bi(III) a total set of 57 samples ranging from 0 to 200 $\mu\text{g L}^{-1}$ were prepared from appropriate dilution of stock solutions. The total set of samples was distributed among training and test subsets. The training subset was formed by 45 samples (79%) distributed in a 6 factor central composite design whereas the test subset was formed by 12 samples (21%) located in the centre of the cubes faces (Figure 2a). In addition, control samples (replicates of the central point of the experimental design) were inserted every 10 measurements.

Furthermore, 3 replicates of a spiked tap water sample with the six considered metal ions distributed in the range of the calibration curve were employed to test the suitability of the four-sensor array for the analysis of Zn(II), Cd(II), Pb(II), Tl(I), In(III) and Bi(III) in natural samples.

2.5. Sample preparation.

Water samples collected from the local water distribution network were firstly acidified (pH 4.5) and then spiked with 70 $\mu\text{g L}^{-1}$ of Zn(II), In(III) and Bi(III), 80 $\mu\text{g L}^{-1}$ of Cd(II) and Tl(III) and 90 $\mu\text{g L}^{-1}$ of Pb(II). Total metal ion concentrations were further determined by ICP-MS.

2.6. Data processing.

Prior to building the PLS model a preprocessing step was performed on each voltammogram. With this purpose, an orthogonal signal correction (OSC) [37] was performed in order to remove variations to the data that are not relevant to the model (noise, baseline...). OSC was performed on calibration data and then applied to the validation data and natural samples data.

In order to reduce the large amount of data generated for each sample (4 sensors x 555 current values) a hierarchical model was considered [38]. In this sense, the data set was separated in 4 blocks corresponding to the 4 sensors and PLS was performed on each block. Scores values obtained for each block were used as new descriptors and PLS was performed again (Figure 2b).

Pre-processing of the data matrices, variable selection and construction of PLS model were made using Matlab[®][39] with PLS-toolbox[40].

3. RESULTS AND DISCUSSION

3.1. Voltammetric calibration data.

Firstly, individual calibration of Zn(II), Cd(II), Pb(II), Tl(I), In(III) and Bi(III) ions by DPASV was carried out on each SPCE-CNF, *ex-situ*-SbSPCE-CNF, GSH-SPCE-CNF and Cys-SPCE-CNF respectively. The optimized application [25,34,35] of an E_d of -1.4 V with stirring during a t_d of 120 s followed by a t_r of 5 s without stirring allows, at each of the four electrodes, the determination of all metal ions in the considered concentration range. In order to build the calibration curves, ten standard concentrations of the considered metal ions were used. Comparable voltammetric responses for Zn(II), Cd(II), Pb(II), Tl(I), In(III) and Bi(III) were obtained using SPCE-CNF, *ex-situ*-SbSPCE-CNF, GSH-SPCE-CNF and Cys-SPCE-CNF at identical experimental

conditions. Figure 3 shows, as an example, the individual voltammetric responses obtained for each metal ion on SPCE-CNF. The individual responses on the other electrodes can be found in the supplementary material (Figure S1). Table 1 summarizes the sensitivities calculated from the slope of the calibration lines of each metal ion at the four modified SPEs and the correlation coefficients, as well as the limits of detection (LOD) considered as 3 times the standard deviation of the intercept over the slope of the calibration curve of the target ions, and the limits of quantification (LOQ) calculated as 10 times the previous ratio for all six metals. It should be pointed out that LOQ was designed as the lowest value of the linear concentration range. Very good linear responses of the peak area *vs.* concentration were achieved for Zn(II), Cd(II), Pb(II), Tl(I), In(III) and Bi(III) until a concentration level close to $200 \mu\text{g L}^{-1}$ for all considered metal ions at the four modified SPEs. Regarding the obtained sensitivities it can be stated that: i) using SPCE-CNF, Cd(II) was the metal ion presenting better sensitivity; ii) Pb(II) was the most sensitive metal using both GSH-SPCE-CNF and Cys-SPCE-CNF; iii) using *ex-situ*-SbSPCE-CNF, Cd(II) and also Zn(II) showed better sensitivity; and iv) the best sensitivity for In(III) and Bi(III) were achieved on SPCE-CNF. The LODs of the six metal ions in the four modified SPEs ranged from 2.6 to $16.8 \mu\text{g L}^{-1}$ depending on both the metal ion and the modified SPE (Table 1) and the LOQ varied from 8.7 to $56.1 \mu\text{g L}^{-1}$ depending again on both the metal ion and the modified SPE (Table 1). These LODs and LOQs values are on the same order than previous reported modified electrodes [26,27,29,35].

Moreover, taking into account the guidelines for drinking water quality [41], the proposed sensors seem to be perfectly suitable for the detection of heavy metals ions in environmental water.

Therefore, the obtained calibration data indicate that the four modified SPEs could be completely appropriate for the analysis of Zn(II), Cd(II), Pb(II), Tl(I), In(III) and Bi(III) at trace levels in environmental samples. Moreover, the cross-response of the selected sensors was stated. Thus, the use of the four modified SPEs as an electrode array configuration instead of as single sensors could introduce some discrimination power to elucidate a mixture of the different metal ions.

3.2. Multimetal Stripping Voltammetric Measurements.

The stripping voltammetric performance of several mixtures of Zn(II), Cd(II), Pb(II), Tl(I), In(III) and Bi(III) was studied using SPCE-CNF, *ex-situ*-SbSPCE-CNF, GSH-SPCE-CNF and Cys-SPCE-CNF working as an electrode array inside the concentration range 0-200 $\mu\text{g L}^{-1}$ to identify potential interactions between the considered metal ions. As an example, Figure 4a shows four stripping voltammograms recorded using *ex-situ*-SbSPCE-CNF (random concentrations). Complex voltammograms with an important overlapping effect were observed hindering not only the straight determination of the different metals of the mixture but also the direct assignment of the oxidation peak potential of each considered metal in the intricate voltammograms. Nevertheless, from separate metal stripping measurements and in general terms, the overlapped peaks from -1.4 V to -0.9 V could be attributed to Zn(II), Cd(II) and Tl(I) whereas the peaks related to Pb(II) and In(III) would be those shown from -0.9 V to -0.55 V and finally the peak close to -0.4 V would be assigned to Bi(III). Figure 4b shows, as an example, a comparison of the stripping voltammograms of 100 $\mu\text{g L}^{-1}$ Zn(II), Cd(II), Tl(I), Pb(II), In(III) and Bi(III) provided by Cys-SPCE-CNF (thin line), *ex-situ*-SbSPCE-CNF (dashed thin line), GSH-SPCE-CNF (dashed thick line) and SPCE-CNF (thick line). Some significant differences in metal peak potentials and shapes can be clearly

perceived in the stripping voltammetric response of the sensor array depending on both the metal ion and the modified SPE used. This fact confirms that the information provided by the electrode array is significantly better than that obtained from a single electrode. Thus, despite the intricate signal origin, in a next step, the voltammetric data set of metal ion mixtures provided by the sensor array will be proposed to be used to calibrate Zn(II), Cd(II), Tl(I), Pb(II), In(III) and Bi(III) with a suitable PLS model that may consider any overlapping to assist us in the better determination of the studied metal ions.

3.3. Calibration and validation of PLS model in metal mixtures.

For the voltammetric electronic tongue study a total set of 57 metal mixtures samples (45 corresponding to the training set and 12 to the test set) with concentrations ranging from 0 to 200 $\mu\text{g L}^{-1}$ were prepared and voltammetric stripping measurements were performed simultaneously on SPCE-CNF, *ex-situ*-SbSPCE-CNF, GSH-SPCE-CNF and Cys-SPCE-CNF. It should be pointed out that, although it has already been proven that these electrodes can be used for a large set of measurements [35,36], to ensure the optimal performance of the sensor array, all the electrodes were replaced every 20 measurements. In addition, due to the large amount of samples considered, the measurements were carried out in two consecutive days. However, control samples inserted between measurements corroborate the use of different electrode units in different days does not affect the voltammetric stripping response.

Prior to building the PLS models, each sensor signal was processed by OSC (1 component determined by the amount of Y block variance explained by the first latent variable) and the resulting data were mean centred. The effect of OSC is that undesired

variations of experimental data (eg, noise, baseline) are removed from the signal whereas variance attributed to target ions is retained. Because of the large amount of information generated (4 voltammograms for each sample), a hierarchical model was considered. In this sense, PLS-2 was performed on each working electrode processed signal, score values were combined in a new data matrix and PLS was performed again, but now in the modality of PLS-1 (Figure 2b).

As it was previously mentioned, Zn(II), Cd(II) and Tl(I) peaks are overlapped in the left side of the voltammogram (from -1.4 V to -0.9 V) whereas Pb(II) and In(III) peaks appear from -0.9 V to -0.55 V and Bi(III) corresponds to the peak near -0.4 V. For this reason, although individual models were performed for each metal, PLS-2 models considering only Zn(II), Cd(II) and Tl(I), only Pb(II) and In(III) or only Bi(III) were performed on each sensor. The number of latent variables, pre-established by cross-validation (venetian blinds method), was selected considering the predictive ability for each metal ion separately and varied from 1 to 6 in the hierarchical step and from 2 to 3 in the final step depending on the considered metal.

Another important aspect to be considered is the number of electrodes to be used in each PLS model. In this sense, it was observed that adding two electrodes with similar sensitivities to the model increases the number of variables, and therefore the complexity of the model, but does not improve its performance. The electrodes used in the PLS model built for each metal are shown in Table 2. It should be pointed out that the inclusion of samples measured in different days on different units does not influence the building of the PLS model.

Good PLS models were obtained for Pb(II), Cd(II), Tl(I) and Bi(III) but not for In(III) and Zn(II). However, the presence of these metals in the sample does not hinder the calibration of PLS models for Pb(II), Cd(II), Tl(I) and Bi(III). The global performance

of the models built is shown in Figure 5 and Table 3. As it can be seen, calibration curves are close to the ideal one, with slopes and correlation values close to 1 and intercept values close to 0. Root mean square errors (RMSE) for calibration were also calculated and are shown in Table 3.

The predictive ability of each model was evaluated with the test subset. As it can be seen in the comparison graphs of predicted vs. expected concentration (Figure 5), test samples (white symbols) are always in the variation range defined by the training set (black symbols). RMSE for prediction, 6.64 for Pb(II), 11.01 for Cd(II), 8.71 for Tl(I) and 14.8 for Bi(III), were all comparable to those obtained for calibration. It should be pointed out that, despite of the increased complexity of the considered system (4 analytes and 2 interferences), the obtained RMSEs values for prediction are similar to those reported by previous voltammetric electronic tongues for metal ions determination [22–25].

These results suggest that the combination of SPCE-CNF, *ex-situ*-SbSPCE-CNF, GSH-SPCE-CNF and Cys-SPCE-CNF as a sensor array could be used for the simultaneous determination of Cd(II), Pb(II), Tl(I) and Bi(III) in the presence of Zn(II) and In(III) in natural samples.

3.4. Application to the analysis of real samples.

At the view of the above results, a sensor array formed by SPCE-CNF, *ex-situ*-SbSPCE-CNF, GSH-SPCE-CNF and Cys-SPCE-CNF was considered for the determination of Cd(II), Pb(II), Tl(I) and Bi(III) in the presence of Zn(II) and In(III) in real samples and its applicability was tested on a spiked tap water. Then, voltammetric stripping measurements of three replicates of the determination of the tap water by means of the

electronic tongue were carried out in the above mentioned conditions and voltammetric signals that behave equally to the training and test sets were obtained.

Cd(II), Pb(II), Tl(I) and Bi(III) concentrations were calculated from the previously calibrated PLS models. A good concordance of all metal ion concentrations between all replicates inferred by the obtained RSD(%) (Table 4) was achieved, especially in the case of Cd(II) and Pb(II). The obtained results, shown in Table 4, were also compared to those obtained by ICP-MS. In order to evaluate the agreement between each metal ion concentration obtained from both techniques, a two-tailed t-test (equal variances) was performed for each sample and it was concluded that the results obtained by the electronic tongue and ICP-MS were statistically similar for a confidence level of 95%.

Therefore, these good results confirm the applicability of the combination of SPCE-CNF, *ex-situ*-SbSPCE-CNF, GSH-SPCE-CNF and Cys-SPCE-CNF in a sensor array with a suitable PLS model for the simultaneous determination of Cd(II), Pb(II), Tl(I) and Bi(III) in the presence of Zn(II) and In(III) in real samples, being an interesting and cheaper alternative to more conventional techniques such as ICP-MS.

4. CONCLUSIONS

In this work, a voltammetric electronic tongue based completely on screen-printed electrodes has been successfully applied for the first time for the analysis of a complex mixture of metal ions in natural samples (4 analytes in the presence of 2 interferences). This electronic tongue was constituted by four sensors that have been modified following different strategies: SPCE-CNF, *ex-situ*-SbSPCE-CNF, GSH-SPCE-CNF and Cys-SPCE-CNF.

Firstly, the voltammetric performance of each metal on each electrode was studied and a cross-response between them was stated. Although the voltammetric response of the

metal mixture of each sensor is very complex due to the presence of overlapped signals, the combination of the four modified SPEs as an electrode array configuration instead of as single sensors introduces some discrimination power that allows to elucidate the mixture of the considered metal ions. In this sense, in the present study, the simultaneous quantification of Cd(II), Pb(II), Tl(I) and Bi(III) in the presence of Zn(II) and In(III) was successfully carried out by combining the voltammetric responses from the four electrodes with chemometric tools. Hence, obtained DPASV data were processed by a PLS model that was built considering a hierarchical model in order to reduce the large amount of data. Good results, both for training and testing, inferred by correlation coefficients evaluated from predicted *vs.* expected concentrations were obtained. Moreover, the simultaneous determination of Cd(II), Pb(II), Tl(I) and Bi(III) in the presence of Zn(II) and In(III) in an spiked tap water was also satisfactory achieved, providing comparable results to those obtained by ICP-MS.

The reported results demonstrate that the use of the presented sensor array combined with the construction of an appropriate PLS model is suitable for the simultaneous quantification of Cd(II), Pb(II), Tl(I) and Bi(III) in the presence of Zn(II) and In(III) in environmental samples.

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Vitae

Clara Pérez-Ràfols graduated in Chemistry with highest honors at the University of Barcelona (UB) in 2014 and received her Master's degree in Analytical Chemistry in 2015, also from the University of Barcelona. She is currently doing her Ph.D. in the area of Analytical Chemistry and Environment in the UB, focusing on the development of sensors and voltammetric electronic tongues for the simultaneous determination of several metal ions. She has published 6 research works in indexed journals.

Núria Serrano was born in 1977. She is temporary Senior Lecturer at the Department of Chemical Engineering and Analytical Chemistry, University of Barcelona (UB), Spain. In 2007 she completed the Ph.D. at the same University. As a postdoctoral researcher, she worked for one year at the Department of Chemistry (Masaryk University, Brno) in 2010; and she spent nine months at the Sensors and Biosensors group (Autonomous University of Barcelona, Bellaterra) in 2013. Her research is mainly focussed on the development of sensors and voltammetric electronic tongues, based on screen-printed electrodes, for the determination of heavy metals. She has participated in 9 competitive research projects, has supervised 2 Ph.D. Theses and has published more than 40 research works in indexed journals.

José Manuel Díaz Cruz was born in 1965. Since 1995 he is Associate Professor of the Department of Chemical Engineering and Analytical Chemistry of the University of Barcelona (UB), Spain, where he had obtained the Ph.D. degree in 1992. In 1993 worked for one year in the Department of Physical and Colloid Chemistry (Wageningen University, The Netherlands). His main research contributions have been in the field of electroanalytical chemistry, studying: i) the interactions of metal ions with macromolecular ligands, colloidal particles and sulphur-containing compounds; ii) the influence of adsorption phenomena in voltammetric measurements; iii) the application

of chemometric methods to electroanalytical data and iv) the development of sensors based on screen-printed electrodes. He has participated in 22 competitive research projects, has supervised 8 Ph.D. Theses and has published more than 120 research works in indexed journals.

Cristina Ariño was born in 1956. Nowadays, she is Associate Professor of the Department of Chemical Engineering and Analytical Chemistry at the University of Barcelona (UB), Spain. She obtained the Ph.D. degree in 1986 and was appointed Associate Professor in 1987. She has participated in more than 20 competitive research projects, has supervised 8 Ph.D. Theses and has published more than 120 research works in indexed journals. Being her research contributions in the field of electroanalytical chemistry, studying: (i) the interactions of metal ions with macromolecular ligands, particles, and sulfur-containing compounds; (ii) the influence of adsorption phenomena in voltammetric measurements; (iii) the application of chemometric methods to voltammetric data concerning solution equilibria; (iv) development and applications of sensors based in screen-printed technology; and (v) the possibilities of screen printed electrodes in amperometric detection. She has also contributed in teaching electroanalytical courses in different master programs from the Faculty of Pharmacy of the University of Concepción (Chile), from the Faculty of Chemistry of the University of Santiago de Chile (Chile) and in different editions of an European Joint Master in Quality in Analytical Laboratories.

Miquel Esteban (1955) is Professor at the Department of Chemical Engineering and Analytical Chemistry, University of Barcelona (UB), Spain. He obtained the Ph.D. at UB, and was appointed Associate Professor in 1984 and Full Professor in 1993. Stays abroad: Institut für Angewandte Physikalische Chemie (Kernforschungsanlage, KFA, Jülich, Germany) in 1986; Department of Physical and Colloid Chemistry (Wageningen

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Caption to figures

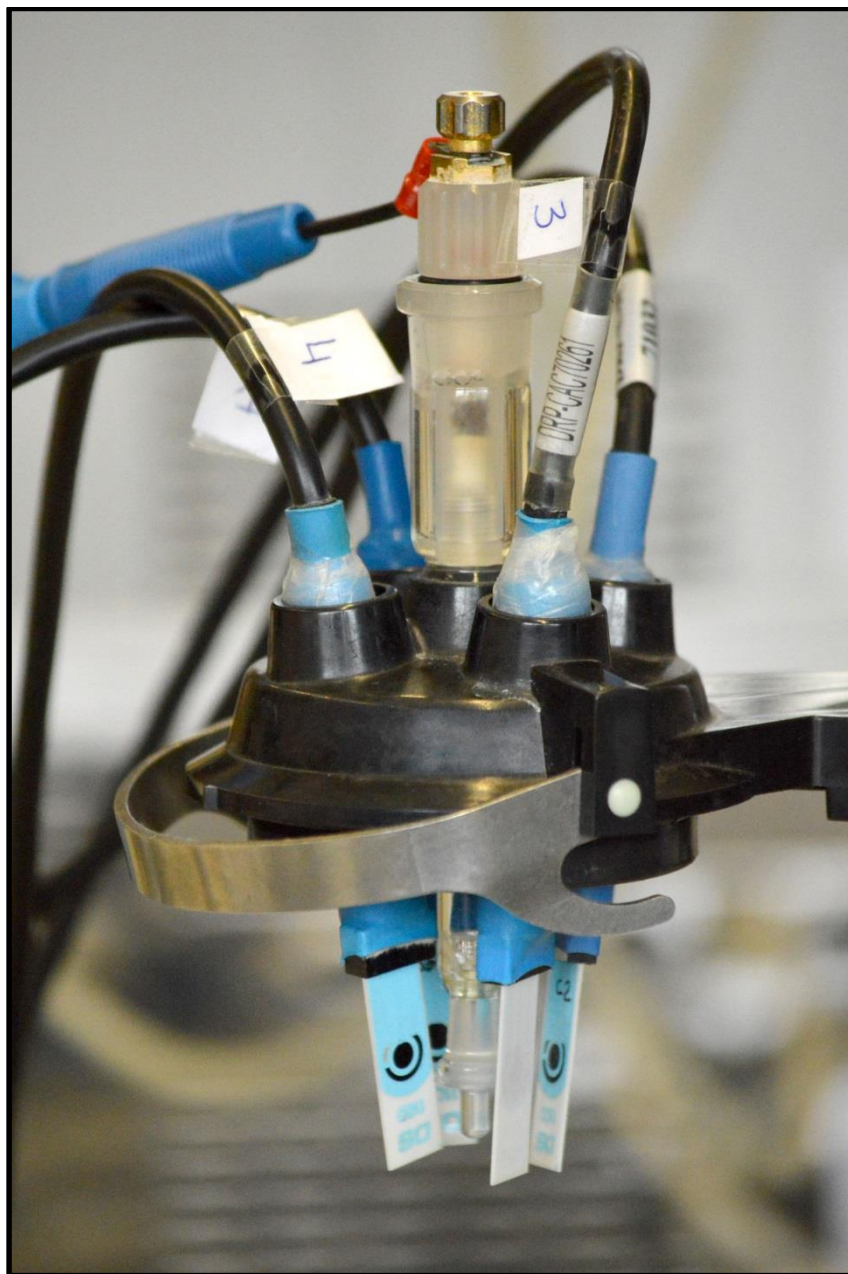


Figure 1. Experimental setup for simultaneous stripping voltammetric measurements with four different screen-printed electrodes. A) DRP-CAC connectors. B) Screen-printed electrodes. C) Ag/AgCl reference electrode. D) Carbon auxiliary electrode.

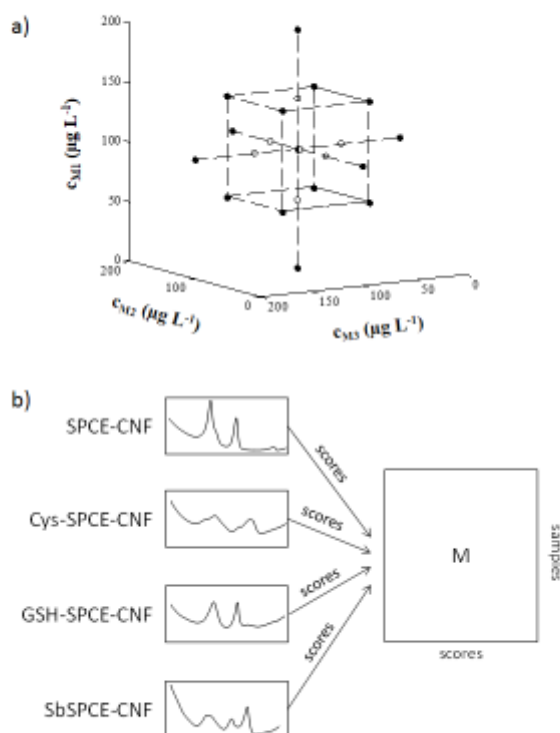
Figure 2

Figure 2. a) Experimental design used for training (●) and testing (○) subsets. M_1 , M_2 and M_3 represent any possible combination of 3 metals among Zn(II), Cd(II), Tl(I), Pb(II), In(III) and Bi(III). b) Hierarchical PLS model performed on the data set obtained with the voltammetric electronic tongue. Scores values from each sensor are used as descriptors in a new data matrix, M .

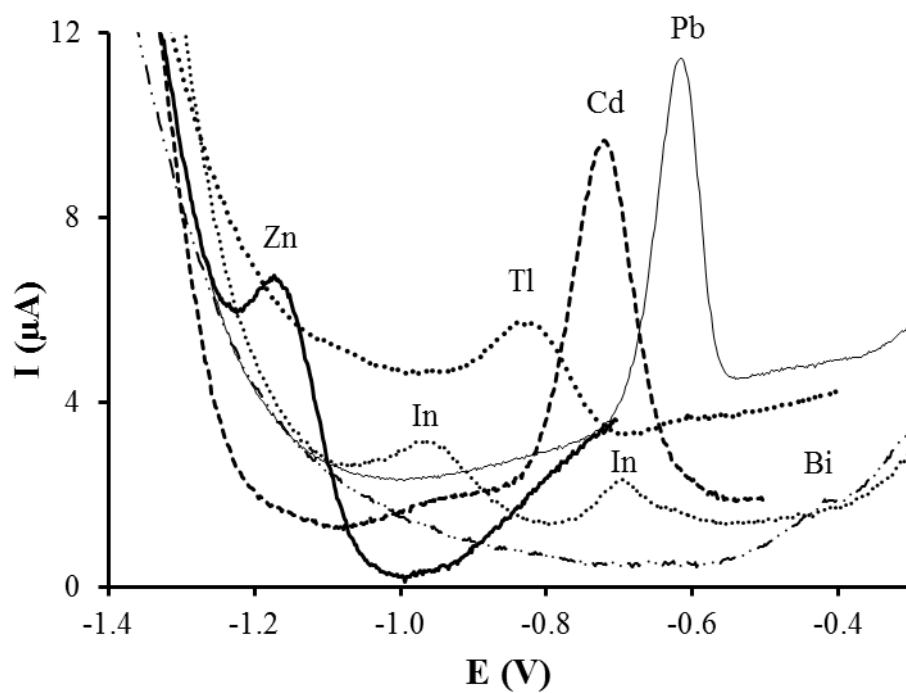


Figure 3. Individual DPASV voltammograms of a solution containing $120 \mu\text{g L}^{-1}$ of Pb(II), Zn(II), Cd(II), Tl(I), In(III) and Bi(III) recorded on SPCE-CNF applying a E_d of -1,4 V during 120 s at acetate buffer pH 4.5.

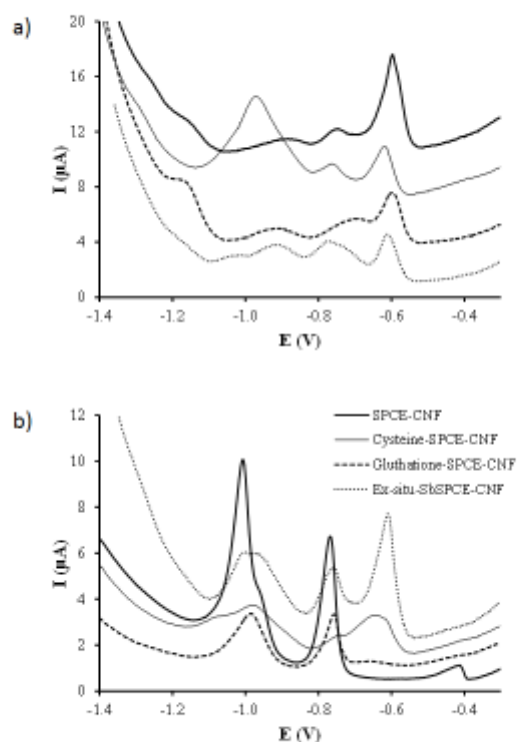
Figure 4

Figure 4. a) DPASV voltammograms on *ex-situ*-SbSPCE-CNF and applying a E_d of -1,4 V during 120 s at acetate buffer pH 4.5 of a solution containing 142 $\mu\text{g L}^{-1}$ Zn(II), Pb(II), In(III) and Bi(III) and 58 $\mu\text{g L}^{-1}$ Cd(II) and Tl(I) (thick line), 142 $\mu\text{g L}^{-1}$ Cd(II), Tl(I), In(III) and Bi(III) and 58 $\mu\text{g L}^{-1}$ Zn(II) and Pb(II) (thin line), 142 $\mu\text{g L}^{-1}$ Zn(II), In(III) and 58 $\mu\text{g L}^{-1}$ Cd(II), Pb(II), Bi(III) and Tl(I) (dashed thick line), 142 $\mu\text{g L}^{-1}$ Tl(I) and In(III) and 58 $\mu\text{g L}^{-1}$ Zn(II), Cd(II), Pb(II) and Bi(III) (dashed thin line). b) DPASV voltammograms of 100 $\mu\text{g L}^{-1}$ Zn(II), Cd(II), Tl(I), Pb(II), In(III) and Bi(III) on Cys-SPCE-CNF (thin line), *ex-situ*-SbSPCE-CNF (dashed thin line), GSH-SPCE-CNF (dashed thick line) and SPCE-CNF (thick line) applying a E_d of -1,4 V during 120 s at acetate buffer pH 4.5.

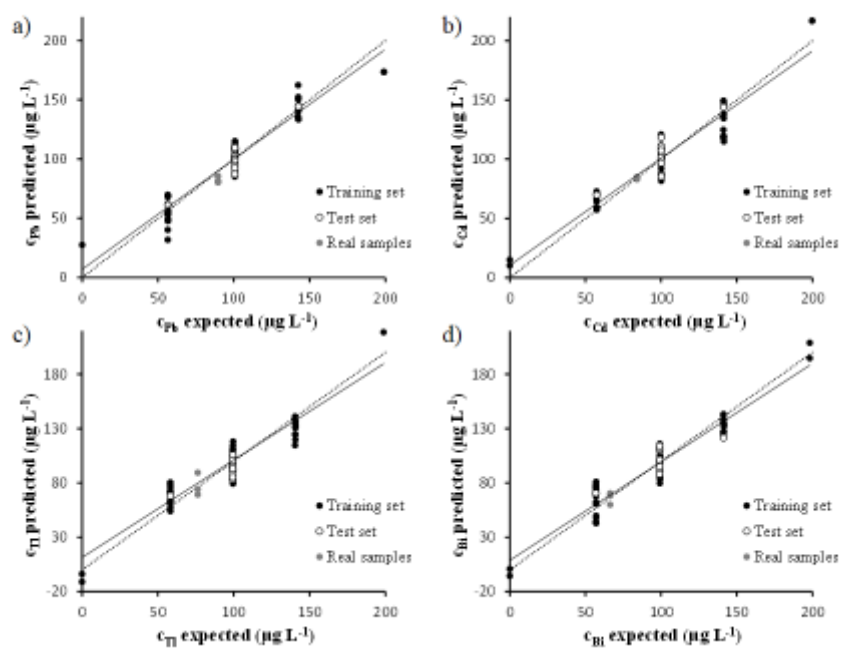
Figure 5

Figure 5. Comparison graphs of predicted vs. expected concentrations for a) Pb(II), b) Cd(II), c) Tl(I) and d) Bi(III) for training set (●), test set (○) and real samples (*). Dashed line represents theoretical diagonal line ($y=x$).

Table 1. Calibration data for the separate determination of Zn(II), Cd(II), Pb(II), Bi(III), In(III) and Tl(I) on the multisensor array formed by

	Zn(II)	Cd(II)	Pb(II)	Bi(III)	In(III)	Tl(I)
SPCE-CNF						
Sensitivity (a.u. $\mu\text{g}^{-1}\text{L}$)	3.75 (0.06)	5.45 (0.05)	4.59 (0.03)	0.40 (0.01)	2.80 (0.03)	2.73 (0.03)
R^2	0.999	0.999	0.999	0.996	0.999	0.999
Linear range ^a ($\mu\text{g L}^{-1}$)	16.9 – 198.3	11.3 – 200.0	8.7 – 200.8	56.1 – 200.7	10.0 – 200.4	21.7 – 274.9
LOD ($\mu\text{g L}^{-1}$)	5.1	3.4	2.6	16.8	3.0	6.5
GSH-SPCE-CNF						
Sensitivity (a.u. $\mu\text{g}^{-1}\text{L}$)	1.71 (0.04)	0.62 (0.01)	3.27 (0.03)	0.240 (0.005)	0.47 (0.01)	0.97 (0.02)
R^2	0.998	0.999	0.999	0.998	0.998	0.998
Linear range ^a ($\mu\text{g L}^{-1}$)	24.5 – 198.3	11.6 – 200.0	10.8 – 200.8	29.1 – 200.7	26.4 – 200.4	41.8 – 274.9
LOD ($\mu\text{g L}^{-1}$)	7.4	3.5	3.2	8.7	7.9	12.5
Cys-SPCE-CNF						
Sensitivity (a.u. $\mu\text{g}^{-1}\text{L}$)	2.19 (0.05)	1.43 (0.01)	3.48 (0.03)	0.196 (0.005)	0.277 (0.004)	1.08 (0.03)
R^2	0.997	0.999	0.999	0.998	0.999	0.998
Linear range ^a ($\mu\text{g L}^{-1}$)	26.3 – 198.3	10.9 – 200.0	10.3 – 200.8	38.0 – 200.7	18.2 – 200.4	57.8 – 274.9
LOD ($\mu\text{g L}^{-1}$)	7.9	3.3	3.1	11.4	5.5	17.4
Ex-situ-SbSPCE-CNF						
Sensitivity (a.u. $\mu\text{g}^{-1}\text{L}$)	2.26 (0.03)	2.42 (0.02)	0.85 (0.01)	0.157 (0.002)	0.75 (0.01)	1.10 (0.02)
R^2	0.999	0.999	0.999	0.999	0.999	0.999
Linear range ^a ($\mu\text{g L}^{-1}$)	14.9 – 198.3	10.7 – 200.0	13.2 – 200.8	17.2 – 200.7	21.0 – 200.4	28.5 – 274.9
LOD ($\mu\text{g L}^{-1}$)	4.5	3.2	4.0	5.2	6.3	8.6

SPCE-CNF/ GSH-SPCE-CNF/ Cys-SPCE-CNF/ *Ex-situ*-SbSPCE-CNF modified electrodes at E_d of -1.4 V using a t_d of 120 s at pH 4.5.

^aThe lowest value of the linear range was considered from LOQ

Table 2. Selection of sensors used in the PLS model for each metal

	Cd(II)	Pb(II)	Tl(I)	Bi(III)
SPCE-CNF	x	x	x	x
GSH-SPCE-CNF	x		x	x
Cys-SPCE-CNF	x	x		
<i>Ex-situ</i>-SbSPCE-CNF	x	x		

Table 3. Main parameters obtained for the fitted regression lines for the comparison between predicted vs. expected values for the training subset of samples and the different metal ions (intervals calculated at the 95% confidence level).

Metal	Slope	Intercept ($\mu\text{g L}^{-1}$)	Correlation	RMSE ($\mu\text{g L}^{-1}$)
Cd(II)	0.90 (0.05)	10 (5)	0.951	12.1
Pb(II)	0.93 (0.04)	8 (4)	0.931	10.7
Tl(I)	0.90 (0.05)	10 (5)	0.927	12.3
Bi(III)	0.92 (0.04)	8 (4)	0.949	11.8

RMSE: root mean square error

Table 4. Total concentrations of Cd(II), Pb(II), Tl(I) and Bi(III) determined in tap water samples by DPASV on the multisensor array formed by SPCE-CNF/ GSH-SPCE-CNF/ Cys-SPCE-CNF/ *Ex-situ*-SbSPCE-CNF modified electrodes and by ICP-MS.

		Cd(II)	Pb(II)	Tl(I)	Bi(III)
DPASV	c ($\mu\text{g L}^{-1}$)	84.1	83.4	77.6	66.1
	RSD (%)	1.1	3.6	13.6	8.4
ICP-MS	c ($\mu\text{g L}^{-1}$)	84.2	89.6	76.3	66.4
	RSD (%)	0.6	0.6	0.6	0.4

n=3 for RSD (%)