ELSEVIER

Analytica Chimica Acta 398 (1999) 93–102

ANALYTICA
CHIMICA
ACTA

www.elsevier.com/locate/aca

Novel application and comparison of multivariate calibration for the simultaneous determination of Cu, Zn and Mn at trace levels using flow injection diode array spectrophotometry

Maia Azubel, Facundo M. Fernández, Mabel B. Tudino*, Osvaldo E. Troccoli

Laboratorio de Análisis de Trazas, Departamento de Química Inorgánica, Analítica y Química Física / INQUIMAE, Facultad de Ciencias Exactas y Naturales, Pabellón II, Ciudad Universitaria (1428), Buenos Aires Argentina

Received 09 February 1999; received in revised form 15 April 1999; accepted 23 April 1999

Abstract

Three different calibration approaches: Partial Least Squares, Unfold Partial Least Squares and *n*-way Partial Least Squares are compared in terms of explained variance, root mean square error of calibration and root mean square error of cross-validation. Attention is also focused on the application of genetic algorithms to spectral data as a way to obtain an improvement in calibration accuracy. Influence of initial starting conditions for the genetic algorithms (population size, mutation probability, % initial terms etc.) was investigated by means of factorial experimental designs. A simple flow injection manifold coupled to a diode array spectrophotometer and multivariate calibration were employed in order to determine Ni, Cd, Pb, Cu, Zn and Mn. Calibration was not successful for the three first elements. Rapid determination of the microamounts of Cu, Zn and Mn was performed in the presence of concomitant ions with a sample throughput of 180 samples h^{-1}. Since three metals were simultaneously determined, this corresponds to 540 determinations h^{-1}. The effect of different matrix interferences (Fe, Al, Ca, Mg, Cr, Sr, Co) was studied in natural and synthetic water samples. Chemical masking with NaF was assayed for the interferent ions Fe and Al. The typical recoveries ranged from 91 to 94% with typical relative standard deviation between 5 and 10 %. ©1999 Elsevier Science B.V. All rights reserved.

Keywords: Flow injection; Photodiode array spectrophotometry; Partial least squares regression; Metal ions determination

---

1. Introduction

The determination of heavy metals in water samples is one of the most important issues in environmental monitoring considering the characteristics of bioavailability, persistency and toxicity of these metals even at very low concentrations.

Several analytical techniques are employed for this purpose — i.e. atomic absorption spectrometry (AAS), inductively coupled plasma coupled to atomic emission spectrometry (ICP-AES) or mass spectrometry (ICP-MS), etc. These techniques are sensitive and selective enough for determination but require expensive equipment.

Chemical complexation followed by UV-visible spectrophotometry could be a cheap solution except for the big loss in selectivity. Nevertheless, as Engström and Karlberg have quoted [1]: “if multivariate calibration methods are applied, those complexes formed with a non-selective complexing agent that only differ slightly from metal to metal with respect

---

* Corresponding author. Fax: +54-11-4576-3341
E-mail address: tudino@q3.fcen.uba.ar (M.B. Tudino)

0003-2670/99/$ – see front matter
PII: S0003-2670(99)00375-X

to their spectral characteristics may be used for identification and quantification of individual metal ions.”

Multivariate calibration provides a great advantage keeping the pre-treatment of samples to a minimum and reducing, by the employment of high-speed computers, the time spent in collecting data [2,3].

Several regression methods can be adopted being Principal Component Regression (PCR) and Partial Least Squares Regression (PLS), the most widespread [4,5]. Both of them involve spectral decomposition into latent variables (LV). PCR is based only on spectral decomposition and PLS is based on spectral and concentration matrix decomposition. PLS seems to be a better choice for prediction when there are random linear baselines or, major spectral components (independently varying) which overlap with the spectral features of the analytes [6].

Several authors have described the application of multivariate calibration to UV-Vis spectrophotometry in batch systems [1,5,7–11] using PLS or PCR as algorithm for calibration. However, not much work has been done in real samples and, mostly, synthetic ones have been chosen. Thus, the system performance is observed in a quasi-ideal situation. Only one working group has dealt with PLS-PDA determination of trace metals in both real and synthetic problems [1,11]. Moreover, the enhancement in sample throughput obtained by the use of a simultaneous calibration is not fully exploited in batch procedures as manual pre-treatment of the sample limits the velocity of the whole process.

The combination between a multivariate calibration method and flow injection (FI) offers more precision with the subsequent decrease in the root mean square error of calibration (RMSEC) and cross-validation (RMSECV). A more rapid screening system is also obtained since the tedious batch procedure is replaced by ‘on-line’ operation.

Several papers have been published on the simultaneous FI determinations of metal ions using multivariate calibration and spectral data. Both, major sample components as Ca and Mg [12–14], and minor components (transition metals) [15–18] have been determined. However, these papers involve only binary or ternary mixtures which is not the usual situation in real problems. In these cases more ions are expected to be present, so, it is necessary to develop calibration models for samples involving more than three analytes.

As FIA is a source of dynamic and kinetic information [19], this kinetic information can be employed for regression. A possible approach is to unfold each signal matrix (spectra vs. time) into a single vector (‘unfolding methods’). If this operation is repeated for all the standards, a signal matrix is constructed where each row contains the spectra collected for each standard. After this matrix is built, PLS is performed. A typical signal is shown in Fig. 1.

Another calibration approach suitable for three-way data — as obtained with FI-PDA — could be multiway partial least squares. Since in some cases, multiway methods seem to be more robust and interpretable than unfolding methods [20,21], *N*-way partial least squares (*N*-PLS) [20] was assayed in this work. The potentialities of Unfolding and Multi-Way calibration methods on FI-PDA data haven’t been compared with traditional simultaneous determinations before this study.

If the complete spectrum is used for calibration, wavelengths that may introduce unnecessary information such as noise or non-linearities are processed together with the useful ones. The use of certain wavelengths with better selectivity for prediction can improve results in comparison with the full spectrum methodology [22–24]. Genetic Algorithms (GA) have been used as a powerful tool for wavelength selection and optimization of a given response function [25,26].

In this work, a rapid screening method (180 samples h^{-1}) for the detection of trace levels of Cu, Zn and Mn in the presence of other ions occurring in natural waters is presented. PLS, UNFOLD-PLS and N-PLS are assayed on the datasets. Wavelength selection with GA is also investigated. Figures of merit for the different approaches are compared.

2. Experimental

2.1. Reagents and standards

Metal ion standards were prepared from AAS 1.000 $g\,l^{-1}$ stock solutions (Merck, Darmstadt, Germany). Doubly de-ionized water (DIW, 18 $M\Omega\,cm$) was obtained from a Milli-Q water system (Millipore, Bedford, MA, USA).

A 10^{-3} M solution of the colorimetric reagent (PAR, (4-(2-pyridylazo) resorcinol), (Merck) in bo-

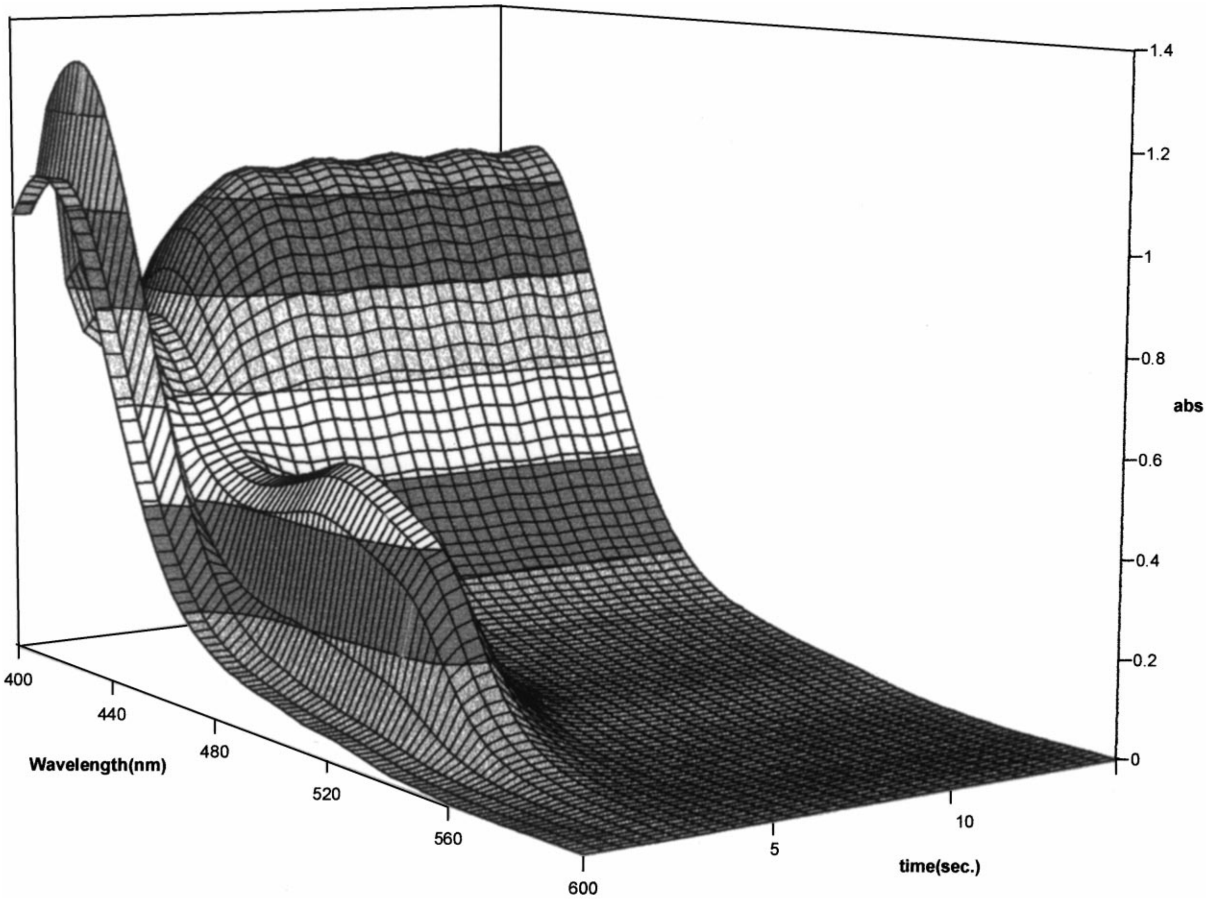

Fig. 1. Typical signal obtained from a FI-PDA system.

rate buffer (0.1 M, pH = 9.2 as recommended [27]) was prepared monthly and stored at 4 °C. Solutions kept at 4°C in the dark during 2 months showed a 3% decrease in absorbance at 406 nm (maximum absorption of the reagent). NaF 0.1 M was added to the PAR solution as a masking agent for Fe and Al (see Interference Study).

Samples were filtered through a 0.22 µm membrane (Millipore) and kept in clean Nalgene flasks (Nalge, Rochester, NY, USA) until analysed.

2.2. Apparatus and flow Injection manifold

The flow injection manifold used is depicted in Fig. 2. An Ismatec 8-roller, 12-channel pump was used (Glattbrugg, Germany). The volume of the injected sample was 120 µl and the reactor coil was 27 cm long and 0.5 mm i.d. (53 µl). A 6-port Cheminert® Valco valve (Valco Instruments, Houston, TX, USA) was employed to inject the sample into the DIW

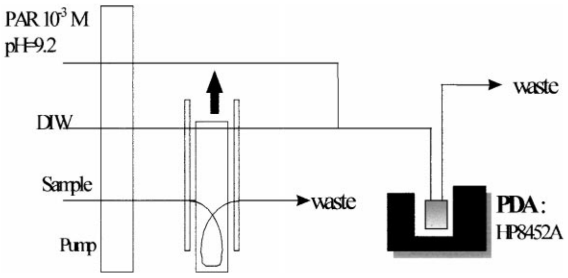

Fig. 2. Schematic flow system. Flow rates are detailed under experimental conditions.

carrier stream. The valve was equipped with an electric actuator triggered simultaneously with the detector. The manifold was assembled with zero dead volume Cheminert® fittings (Valco). All the manifold tubing was made of PTFE (0.5 mm i.d.).

The sample, PAR and carrier flow rates were 0.24, 0.15 and 5.2 ml $\mathrm{min}^{-1,}$ respectively.

The detector was a Hewlett-Packard HP 8452A Diode Array Spectrometer connected to an AT486 PC-compatible computer via an HPIB protocol (Hewlett-Packard, Palo Alto, CA, USA). Data were acquired between 400 and 600 nm (201 absorbance values) for a 10 s. period, sampling each 0.5 s. (0.2 s integration). The spectrophotometer was furnished with a 80 μl, 1 cm optical path flow cell (Hellma, Mülheim/Baden, Germany).

Metal ion concentration in river water samples was validated by flame (Cu, Zn, Mn and Ni) and graphite furnace (Cd, Pb) atomic absorption spectrometry in a Shimadzu 6701 atomic absorption spectrometer equipped with a graphite furnace Shimadzu GFA 6000 and an autosampler Shimadzu ASC 6000.

2.3. Software and data processing

Data acquired with the HP 8452A was transferred to a different computer for processing via a Local Area Network (LAN). A 166 MHz Pentium®-based PC with 32 MB RAM operating under Windows 95™ was employed. Multivariate regression and data processing were carried out with the PLS_Toolbox version 1.5 (Eigenvector Research, Manson, WA, USA). Experimental designs were constructed with Statgraphics 7.0. The ASCII data produced by the HP 8452A (*.wav format) was edited with Excel 7.0 to erase headers and make the conversion to *.dat format. The N-PLS algorithm was obtained from the World Wide Web: http:\\newton.foodsci.kvl.dk\foodtech.

No crossvalidation routine was available for this algorithm, the optimum number of latent variables (LV) was selected according to the increase in explained variance (EV%) produced for each LV added to the model. LV improving less than 2% the explained variance, were discarded.

Data were mean-centered in all cases. In PLS models Venetian Blinds cross-validation was employed and the optimum number of LV was selected at the minimum in the Prediction Error Sum of Squares (PRESS). PLS was assayed both, as PLS1 (one dependent variable) and PLS2 (multiple dependent variables). PLS1 showed better results and was used through this work.

3. Results and discussions

3.1. Optimization of FI conditions

The parameters influencing the degree of mixing and reaction between the metal ions and the PAR reagent were investigated. The flow rate of the carrier and reagent solutions varied between 5.2 and 10.4 ml min^{-1} and 0.15 and 0.30 ml min^{-1}, respectively. Sample loop volumes varied between 80 and 150 μl. Reactor coil lengths varied between 8 and 100 cm. When short reactors were used (<15 cm), a significant loss in sensitivity was observed due to incomplete mixing. The optimum variables were selected as a compromise situation between the highest sample throughput (>100 samples h^{-1}) compatible with the maximum sensitivity at the sub-mg l^{-1} level.

Under the optimized FI conditions, the sequence of sample injection and acquisition of data took 10 s per sample and the saving of data to the PC hard disk took 8 s. This gives a sampling frequency of about 180 samples h^{-1}.

3.2. Feasibility study

A feasibility study was carried out in order to assess the potentialities of the method. Among the analytes of environmental interest, those presenting major differences among their pure spectra, Pb, Cu and Cd, were employed for the study. The experimental design was a 2^3+star factorial design (see Fig. 3). Concentration levels were chosen in accordance with the linear ranges obtained for single analyte experiments and reproducing the expected concentrations in natural waters. Results are shown in Table 1.

Feasibility studies were performed in a ‘batch’ system and a FI system. The latter shows only slight improvement in the number of LV needed to model the data but a great one in the RMSEC and RMSECV error values (see Table 1). This fact is connected to the capability of FIA for highly repetitive measurements.

Table 1
Feasibility study[a]

BATCH PLS	LV%	EV%	RMSECV[b] (mg/l)	RMSEC[c] (mg/l)
Pb(0.15–0.25)mg/l	4	99.19	0.048	0.038
Cu(0.10–0.4)mg/l	5	98.48	0.014	0.010
Cd(0.03–0.1)mg/l	5	99.08	0.017	0.012
FIA				
Pb(0.15–0.25)mg/l	4	98.68	0.009	0.007
Cu(0.10–0.4)mg/l	3	99.44	0.012	0.009
Cd(0.03–0.1)mg/l	5	98.22	0.008	0.004
UNFOLD				
Pb(0.15–0.25)mg/l	6	99.50	0.022	0.004
Cu(0.10–0.4)mg/l	4	99.69	0.018	0.007
Cd(0.03–0.1)mg/l	6	99.02	0.017	0.003
N-PLS				
Pb(0.15–0.25)mg/l	3	96.58		
Cu(0.10–0.4)mg/l	2	99.07		
Cd(0.03–0.1)mg/l	2	82.73		

[a] Data were mean-centered in all cases, and Venetian Blinds cross-validation employed (11 test sets).
[b] RMSECV = Root mean square error in cross-validation.
[c] RMSEC = Root mean square error in calibration.

The best results were obtained with PLS at the maximum of the FI peak. The cross-validation error was of the same magnitude as the calibration error, which demonstrates no overfitting. The obtained errors are in the $\mu g\,l^{-1}$ range which is about 10% of the measured concentrations. Good quality of the regression encourages repeat of the calibration in the presence of more metal ions.

UNFOLD-PLS and N-PLS were also assayed but less satisfactory results were obtained.

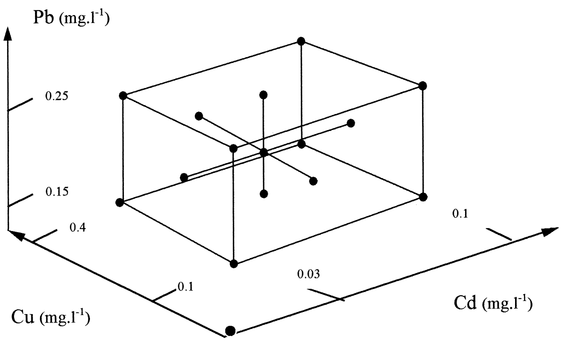

Fig. 3. Experimental design used for the feasibility study.

3.3. Screening of calibration algorithms for 6-analyte data

In order to explore different algorithms for six analytes calibration standards, Continuum Regression [28] (CR) was employed. CR is a continuously adjustable technique which encompasses PLS and includes PCR and MLR. When CR is used, cross-validation must be done to determine both, the optimum number of factors and the technique that produces the optimum model. CR was applied to the spectra at the peak maximum in order to select the best technique for calibration.

Prediction Error Sum of Squares (PRESS) had a minimum at 10 LV with a Singular Value Decomposition (SVD) Power of 1.68. The obtained power is close to a PLS model [29]. This verifies that PLS is the better choice as well as a fast and simple algorithm.

3.4. Calibration with six metal ions

In order to perform calibration with six metal ions, a careful design of calibration standards is needed. On the one hand the number of runs for calibration must be kept to a minimum to avoid an increment of the time

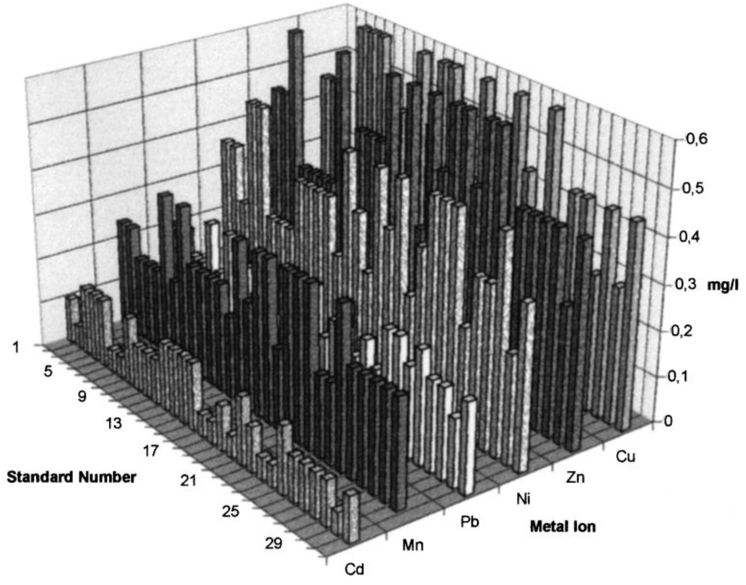

Fig. 4. Experimental design for 6-analyte calibration.

Table 2
Six metals' calibration results

Metal (Concentration range, mg l^{-1})	PLS[a]			UNFOLD PLS[a]			n-PLS
	(EV% & LV) (at min. PRESS)	RMSECV (mg/l)	RMSEC (mg/l)	(EV% & LV) (at min. PRESS)	RMSECV (mg/l)	RMSEC (mg/l)	(EV% & LV) (at min PRESS)
Cu (0.30–0.60)	99.18 (6)	0.026	0.013	99.19 (9)	0.041	0.013	98.03 (10)
Zn (0.30–0.60)	98.31 (5)	0.028	0.018	99.33 (8)[b]	0.032	0.011	97.77 (8)
Mn (0.18–0.36)	97.95 (6)	0.022	0.012	99.44 (12)	0.050	0.006	93.57 (8)
Pb (0.15–0.25)	94.98 (8)	0.031	0.011	97.97(12)[c]	0.058	0.007	93.88 (13)[d]
Ni (0.24–0.48)	92.09 (7)	0.062	0.031	93.66(11)[c]	0.222	0.028	55.56 (6)[d]
Cd (0.05–0.15)	94.32 (11)	0.065	0.010	81.40 (8)[c]	0.049	0.018	48.65 (5)[b]

[a] Data were mean-centered in all cases, and Venetian Blinds cross-validation employed (11 test sets).

[b] LV were selected up to the one that produces less than 1% improvement in the EV%.

[c] Also present a local min. in PRESS at 1 LV

[d] It is a local minimum in PRESS.

of analysis. But on the other, each metal concentration needs to be varied independently which increases the number of experiments.

The experimental design shown in Fig. 4 (Draper-Lin, one block) was used to cover the linear range of concentrations for all the metals. The chosen design allows to make all the measurements in a few hours with a reasonable number of standards (30 standards + blank).

The regression algorithms tested under the feasibility study were applied to the 6-analyte data. Results are given in Table 2. PLS at the peak maximum presents the best calibration results (similarly to the feasibility study). RMSECV and RMSEC values are closer for Cu, Zn, Mn and Pb which indicates that the models are stable (no overfitting). Cu, Zn and Mn determination is performed with good quality of regression. Even though Ni, Cd and Pb showed acceptable explained variances they should not be predicted due to a higher number of latent variables.

As stated above under the feasibility study, no improvement was achieved with UNFOLD-PLS (See Table 2). In order to find out in which situation PLS and UNFOLD-PLS may show different performances,

Table 3
Screening of initial conditions for GA wavelength selection

Pop size	% Initial terms	Mutation rate	PRESS^{-1} (from the best chromosome)
100	80	0.005	136.2
200	30	0.005	186.9
200	80	0.01	143.6
100	30	0.01	144.4

the system was tested in conditions where the FI profile stores kinetic information. Thus, just for exploratory purposes, experiments were carried out in deficiency of ligand as a way to exploit the non-equilibrium conditions in FI.

These experiments show a significant improvement in CVEV for Mn and Ni (5.3 and 9.3%, respectively) with UNFOLD-PLS. Mn and Ni probably show lower reaction rate with PAR [30]. Thus, the inclusion of the tail improves the calibration results.

Calibration results with N-PLS were poor probably because the data obtained did not have a distinctive third mode. This approach was not further employed.

3.5. *Genetic algorithm variable selection*

Genetic Algorithms (GA) were developed by Holland [31] and co-workers in the 1960s and since then much work has been done in the fields of evolutionary computation [32]. GA have been used in the field of Chemometrics for wavelength selection in multivariate calibration. GA use evolution (in a biological sense) as an inspiration for optimization. GAs will not be described here; for an overview see Refs. [32] and [33].

Genetic Algorithms require setting the initial values of several parameters before optimization itself: the initial population size, the mutation rate and the percentage of initial wavelengths employed to build the chromosomes. The experimental design used to select the initial parameters was a Fractional Factorial Design (2^{3-1}) . The reciprocal of the prediction error (PRESS^{-1}) was employed as the response function for exploring the initial conditions. A model with good response implies low prediction error (good predictive ability). The results for the screening of initial conditions are shown in Table 3.

A population size of 200 spectra was selected as the optimum initial population. This population must be high in order to explore more possible solutions during the optimization procedure. Taking into account that the spectra are severely overlapped and probably not every wavelength has further information, the percentage of the initial terms must be low. The optimum value was set at 30%. Also, to assure that good genes ‘survive’ from one generation to another, the mutation rate must be kept low.

Calibration with PLS at the peak maximum after GA wavelength selection makes an improvement in the RMSECV and RMSEC values and decreases the number of LV needed to model the calibration set (Table 4). Even though RMSEC values for Zn are higher, the minimum number of LV obtained with GA generates a simpler model for data analysis. Selected wavelengths are given in Fig. 5.

3.6. *Interference study*

The potential interferent ions that frequently accompany Cu, Zn and Mn in real samples were investigated in a synthetic solution containing several metal ions. A given ion was considered interferent if its presence produces an error above 10% in the determination of Cu, Zn and Mn for a mixture containing 0.45 mg l^{-1} Cu, 0.45 mg l^{-1} Zn, 0.275 mg l^{-1} Mn, 0.2 mg l^{-1} Pb, 0.10 mg l^{-1} Cd and 0.35 mg l^{-1} Ni.

Ca, Mg and Sr showed little effect on the analyte signals. Cr and Co become a serious interference at a concentration of 0.30 mg l^{-1}, since they form strong complexes with PAR. Usually these levels of Cr and Co are not found in natural waters. However if high contents of Cr and/or Co are expected, they must be included in the calibration set. Fe and Al interferences are reduced or even eliminated by masking them with fluoride salts, since they form highly stable complexes with this anion. Masking was achieved by making the colorimetric reagent 0.1 M in NaF. Table 5 shows the concentration ratio at which interferences are tolerated in the determination of the three analysis.

3.7. *Validation*

River water samples were spiked with different analytes. The final concentration (original + spiked) of the analytes was determined by flame or graphite furnace atomic spectrometry and with the proposed methodol-

Table 4
Comparison between PLS with full spectra and spectra after GA optimization

	PLS Full spectra[a]			PLS GA[a]		
	EV & LV (at min. PRESS %)	RMSECV (mg/l)	RMSEC (mg/l)	EV & LV (at min. PRESS %)	RMSECV (mg/l)	RMSECV (mg/l)
Cu (0.30–0.60)mg/l	99.18 (6)	0.026	0.013	99.67 (6)	0.013	0.008
Zn (0.30–0.60)mg/l	98.31 (5)	0.028	0.018	98.04 (3)	0.023	0.020
Mn(0.18–0.36)mg/l	97.95 (6)	0.022	0.012	98.96 (6)	0.014	0.008

[a] Data were mean-centered in all cases, and Venetian Blinds cross-validation employed (11 test sets).

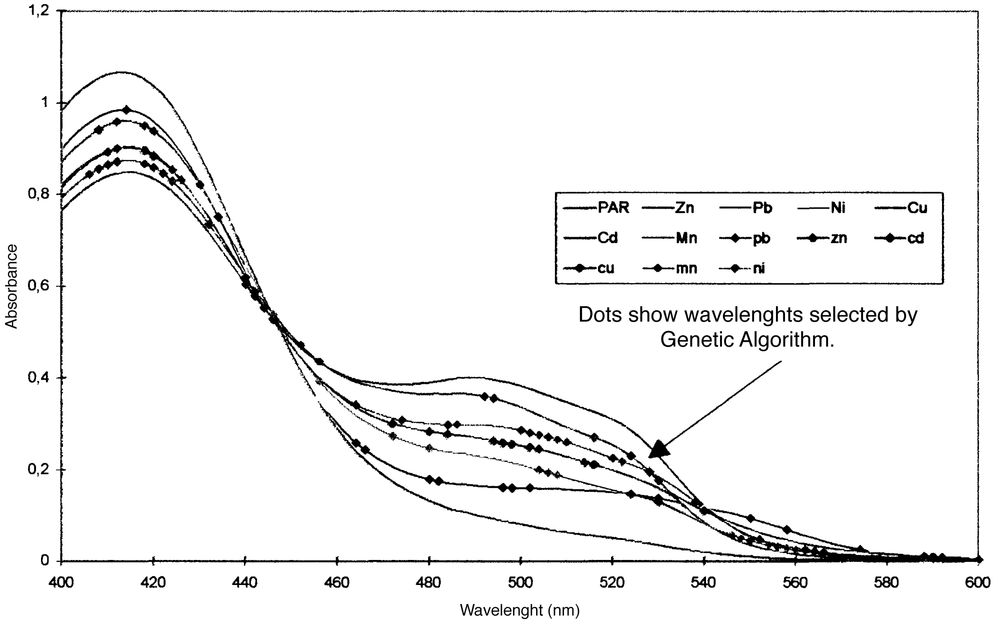

Fig. 5. Spectra of pure metal–PAR complexes at the maximum of the FI peak and variables selected by GAs.[Metal]=5.10^{-5}, [PAR]=1.10^{-3}

Table 5
Interference study. Table shows concentration ratios at which interferents are tolerated

	Interferent						
	Fe^{+3}	Ca	Mg	Cr^{+3}	Al	Sr	Co
Cu	1 : 2	1 : 100	1 : 100	<1 : 1	1 : 50	1 : 50	<1 : 1
Zn	1 : 10	1 : 100	1 : 100	<1 : 1	1 : 50	1 : 50	<1 : 1
Mn	1 : 2	1 : 50	1 : 100	1 : 1	1 : 50	1 : 50	<1 : 1

ogy. From an analytical point of view and in order to establish the performance of the method in real samples the determinations need to be carried out with no spiking. Unfortunately, since the collected samples (surface river waters) showed very low levels of the three analytes (they were not detected even when AAS was employed), we decided to spike them in order to perform the study in the presence of a real matrix and trace them against a referee method. The determination of Ca, Mg, Fe, Al, Co and Cr in the samples showed that they were not at the interfering level. Table 6 shows the results obtained in synthetic samples and spiked river water samples. In most cases, prediction with the GA optimized model improves the results. The mean recoveries for Cu, Zn and Mn were 105, 94 and 104%, respectively. The results are good enough to be used in practice as the analytical figures of merit (i.e. detection limit, precision etc.) are able to attend the expectancies of the regulations for drinkable water.

Table 6
Determination of Cu, Zn, Mn and Pb in real samples

	Synthetic samples ($n=7$) Concentration range (mg l^{-1})	% Recovery		Natural Water Samples[a] ($n=15$) Concentration range (mg/l)	% Recovery	
		Full spectra	GA		Full spectra	GA
Cu	(0.30–0.45)	110	105	(0.29–0.50)	109	105
Zn	(0.30–0.45)	101	101	(0.38–0.59)	89	88
Mn	(0.12–0.30)	94	101	(0.28–0.39)	110	106

[a] Spiked river water (filtered through 0.22 μm Millipore membrane).

Table 7
Analytical figures of merit[a]

	Concentration range (mg l^{-1})	Estimated Detection Limit (mg l^{-1})		Repeatability (RSD%, $n=10$)	
		Full spectra	GA	Full spectra	GA
Cu	(0.30–0.60)	0.126	0.096	3.3	4.0
Zn	(0.30–0.60)	0.094	0.072	2.6	3.7
Mn	(0.18–0.36)	0.058	0.045	8.6	6.6

[a] Detection Limit = 3*$\text{RMSEP}_{\text{Synthetic samples}}$

3.8. Detection limits and repeatability

The study of the theoretical concept of limit of detection (LOD) in multicomponent systems is recent [34]. Its practical applications are limited to a few techniques such as ICP-OES, HPLC-PDA and GC-MS. Some calculations have been reported for direct calibration [21] and inverse calibration methods [35] but, these calculations are not easily performed. In this paper LOD has been calculated in a simpler way: three times the prediction error (RMSEP) obtained for the synthetic test set [1]. Obtained values are listed in Table 7. LODs for Cu and Mn are close to those obtained by AAS. Zn shows a relatively higher value due to its great sensitivity in AAS. LODs are lower when GAs are employed due to the lower prediction error obtained through this approach.

Repeatabilities range between 3.3 and 8.6%, which is good enough for screening. The use of GA slightly impoverishes repeatability because prediction is done with fewer wavelengths.

4. Conclusions

The proposed system allows the determination of three metal ions simultaneously with a sampling frequency of 180 samples h^{-1} and low operating cost. Calibration algorithms that use the complete FI profile (UNFOLD-PLS, N-PLS) give the same information than those that employ only one spectrum. Wavelength selection with GA produces improved detection limits and prediction errors with little effect on repeatability. Best results are obtained with simple PLS at the peak maximum.

Acknowledgements

The authors thank the program of Science and Technology of Buenos Aires University (UBACyT), Fundación Ciencias Exactas and INQUIMAE for financial support.

References

[1] E. Engström, B. Karlberg, J. Chemom. 10 (1996) 509.
[2] N. Porter, B.T. Hart, R. Morrison, Anal. Chim. Acta 281 (1993) 229.
[3] E.V. Thomas, Anal. Chem. 66 (1994) 795A.
[4] H. Martens, T. Naes, Multivariate Calibration, Wiley, New York, 1989.
[5] P. MacLaurin, P.J. Worsfold, P. Norman, M. Crane, Analyst 118 (1993) 617.
[6] Y. Ni, Anal. Chim. Acta 284 (1993) 199.
[7] M. Otto, W. Wegscheider, Anal. Chem. 57 (1985) 63.
[8] M. Vitouchová, L. Jancár, L. Sommer, Fresenius J. Anal. Chem. 343 (1992) 274.

[9] M. Blanco, J. Coello, H. Iturriaga, S. Maspoch, M. Redón, Appl. Spectrosc. 48 (1994) 37.

[10] M. Jimenéz Arrabal, P. Valiente González, C. Caro Gámez, A. Sánchez Misiego, Analyst 119 (1994) 1537.

[11] E. Engström, I. Jönebring, B. Karlberg, Anal. Chim. Acta 371 (1998) 227.

[12] I. Ruisánchez, A. Rius, M.S. Larrechi, M.P. Callao, F.X. Rius, Chemom. Intell. Lab. Syst. 24 (1994) 55.

[13] O. Hernández, F. Jimenez, A.I. Jimenez, J.J. Arias, J. Havel, Anal. Chim. Acta 320 (1996) 177.

[14] F. Blasco, M.J. Medina-Hernández, S. Sagrado, F.M. Fernández, Analyst 122 (1997) 639.

[15] C. Ridder, L. Noergaard, Chemom. Intell. Lab. Syst. 14 (1992) 297.

[16] O. Hernández, F. Jimenez, A.I. Jimenez, J. J Arias, Anal. Chim. Acta 310 (1995) 53.

[17] O. Hernández, F. Jimenez, A.I. Jimenez, J.J. Arias, Analyst 121 (1996) 169.

[18] C. Moreno, M.P. Mánuel-Vez, I. Gómez, M. García-Vargas, Analyst 121 (1996) 1609.

[19] E.H. Hansen, Anal. Chim. Acta 261 (1992) 125.

[20] R. Bro, J. Chemom. 10 (1996) 47.

[21] K.S. Booksh, B.R. Kowalski, Anal. Chem. 66 (1994) 782A.

[22] A. Garrido Frenich, A.D. Jouan-Rimbaud, D.L. Massart, S. Kuttatharmmakul, M. Martínez Galera, J.L. Martínez Vidal, Analyst 120 (1995) 2787.

[23] D.J. Rimbaud, B. Walczak, D.L. Massart, I.R. Last, K.A. Prebble, Anal Chim. Acta. 304 (1995) 185.

[24] F. Navaroo-Villoslada, L.V. Pérez-Arribas, M.E. León-González, L.M. Polo-Díez, Anal. Chim. Acta 313 (1995) 93.

[25] D. Jouan-Rimbaud, D.L. Massart, R. Leardi, O.E. De Noord, Anal.Chem. 67 (1995) 4295.

[26] A.S. Bangalore, R.E. Shaffer, G.W. Small, M.A. Arnold, Anal.Chem. 68 (1996) 4200.

[27] L. Sommer, V. Kubán, M. Langová, Fresenius Z. Anal. Chem. 310 (1982) 51.

[28] M. Stone, R.J. Brooks, J. R. Statist. Soc. B 52 (1990) 337.

[29] B. Wise, N.B. Gallagher, PLS_Toolbox, 1.5, User's Manual, Eigenvector Technologies, Manson WA, 1996.

[30] R.B. Jordan, Reaction Mechanisms of Inorganic and Organometallic Systems, Oxford University Press, New York, 1991.

[31] J.H. Holland, Adaptation in Natural and Artificial Systems, 2nd. edn., MIT Press, Cambridge, MA, 1992.

[32] M. Mitchell, An Introduction to Genetic Algorithms, MIT Press, Cambridge, MA, 1996.

[33] R.E. Shaffer, G.W. Small, Anal. Chem. 69 (1997) 236A.

[34] R. Boqué, F.X. Rius, Chemom. and Intell. Lab. Syst 32 (1996) 11.

[35] A. Lorber, K. Faber, B.R. Kowalski, Anal. Chem. 69 (1997) 1620.