Comparison of data processing techniques for dynamic potentiometric data in resolving the double mixtures of chemically similar analytes.

Dmitry Kirsanov[1]*, Xavier Cetó[2]*, Maria Khaydukova[1], Yulia Blinova[1], Manel del Valle[2], Vasily Babain[3], Andrey Legin[2]

1 Chemistry Department, St. Petersburg State University, Universitetskaya nab. 7/9, Mendeleev Center, 199034 St. Petersburg, Russia

2 Sensors and Biosensors Group, Department of Chemistry, Universitat Autònoma de Barcelona, Edifici Cn, 08193 Bellaterra, Barcelona, Spain

3 Khlopin Radium Institute, 2nd Murinsky prospect 28, St. Petersburg, Russia

* two authors equally contributing,

d.kirsanov@gmail.com

xavier.ceto@uab.cat

Abstract

Data processing techniques are very important part of the multisensor systems. Complex analytical tasks like e.g. resolving the mixtures of two components with very similar chemical properties require special attention. We report on application of non-linear (artificial neural networks, ANN) and linear (projections on latent structures, PLS) regression techniques to the data obtained from the flow cell with potentiometric multisensor detection of lanthanides neighbouring in Periodic System of the Elements (samarium, europium and gadolinium). Quantification of individual components in mixtures is possible with reasonable precision if dynamic components of the response are incorporated thanks to the use of an automated sequential injection analysis system. An average absolute error in prediction of lanthanides with PLS was around $1 \cdot 10^{-4}$mol/L, while the use of ANNs allows for lowering prediction errors down to $2 \cdot 10^{-5}$mol/L in certain cases. The suggested protocol seems to be useful for other analytical applications where simultaneous determination of chemically similar analytes in mixtures is required.

1 Introduction

There are a number of analytical applications that require quantitative analysis of mixtures, where the constituents have very similar chemical nature. As an example, one can consider lanthanides determination in various technological solutions or in PUREX (Plutonium-Uranium Extraction) process raffinate of spent nuclear fuel reprocessing. Being close neighbors in Periodic System of elements lanthanides have closely similar chemical properties and the task of their simultaneous determination can be effectively handled with “heavy” instrumental methods, such as e.g. ICP-MS (inductively coupled plasma mass spectrometry). However, these ICP-based methods are usually hard to implement in on-line mode and they require significant amount of consumables, skilled personnel and long sample preparation. There is a need for simple and inexpensive methods that could allow for simultaneous quantification of several chemical substances of very analogous properties. One of the reasonable alternatives for existing “heavy” methods could be electrochemical sensors. There are a lot of reports in literature on the development of potentiometric sensors for selective determination of lanthanides, such as cerium [1, 2], samarium [3, 4], europium [5, 6], etc., but the pH working range reported in these papers is usually around 4-8 pH units. It is not quite clear what are the ions promoting sensor response at these pH level, since Me^{3+} are only present in strongly acidic media. Besides that the reported selectivity values of such sensors are usually rather high ($\log K_{M,RE} < -2$) even in the presence of neighboring lanthanides, and this is quite surprising taking into account very similar ionic radii and chemical properties of lanthanides. The authors of these papers usually do not discuss the nature of such outstanding performance. In most of the cases the measurements are performed in individual solutions of the lanthanides. There are reasonable doubts if the reported data can be extrapolated to the real performance of the sensors in complex mixtures. One of the possible ways for development of fast and inexpensive methods for lanthanides detection is an employment of a multisensor system approach [7]. The main idea of this approach (also called an electronic tongue) is to measure the samples with an array of chemical sensors with high cross-sensitivity towards variety of analytes and to process the resulted unresolved analytical signal from this array by means of multivariate statistics techniques [8]. As an output from this system one can have both qualitative and quantitative chemical information depending on the scope of the study and on the methods employed. This type of systems was recently successfully applied for simultaneous determination of rare earth metals (RE) concentrations in complex

mixtures simulating spent nuclear fuel reprocessing media [9]. As a further extension of this approach it seems reasonable to try an application of such a system in a flow cell conditions. Besides the obvious advantage of simple automation this type of measurement implementation has another important issue – a possibility of dynamic potentiometric measurements, i.e. one can track the evolution of the sensor response in time and this kinetic information can be used in data processing. The shape of the sensor response curve in a time domain can contain valuable chemical information about the sample and this information is lost when only stationary signal of sensor is employed for processing. It was shown that this approach is quite viable in other applications [10-12]. However, dynamic potentiometric data are more complex in nature compared to the ordinary potentiometric signals and pose a certain challenge from the data processing point of view. One of the possible divisions of chemometric techniques (however quite artificial) is to distinguish linear (e.g. principal component analysis (PCA), projections on latent structures (PLS)) and non-linear (e.g. artificial neural networks (ANN), support vector machines (SVM)) methods. Both these data processing groups are in use in the multisensor systems field. Furthermore, in [13] a wide literature survey was performed which revealed that most of the papers devoted to electronic tongues are mainly dealing with only three data processing techniques: PCA, PLS and ANN. This confirms these methods are being powerful and reliable for extracting valuable chemical information from multisensor system's experimental data. When quantitative chemical analysis is in sight both linear and non-linear regression methods can be employed.

This paper is devoted to the comparison study of the linear and non-linear regression techniques applied to the dynamic potentiometric data from double mixtures of chemically similar lanthanide ions. As linear methods three different PLS modes were implemented: ordinary PLS with stationary potentiometric signals as input variables, PLS with the whole response curves unfolded over time axis and multi-way PLS (nPLS) with time axis as a third dimension in data (samples X sensors X time). As non-linear methods, different approaches based on Artificial Neural Networks (ANNs) were evaluated including the use of steady state signal and the compression of the dynamic profile employing the *windowed slicing integral* (Int) method [14].

2 Experimental

2.1 Sensor preparation

The sensor array employed in this study consisted of eight polymeric PVC-plasticized sensors described previously [9]. Briefly each sensor membrane contained 33% wt. of poly(vinylchloride) (PVC), around 65% wt. of *o*-nitrophenyloctyl ether (NPOE) as a solvent-plasticizer (both PVC and NPOE were Selectophore grade from Fluka), and 1-2% of membrane active compounds. The latter were various neutral ligands adopted from liquid extraction systems plus chlorinated cobalt dicarbollide (CCD) as a cation-exchanger. All sensor membranes contained 50 mmol/kg of a neutral ligand and 10 mmol/kg of CCD. The following neutral ligands were employed for sensor preparation [9]: s1 (tetraphenylmethylendiphosphine dioxide), s3 (phenyloctyl-N,N-di-i-butylcarbamoylmethylen phosphine oxide), s4 (1,9-Bis-(diphenylphosphynyl)-2,5,8-trioxanonane), s7 (1,6-Bis-(benzylphenylcarbamoyl)-3-benzo-2,5-oxahexane), s8 (1,9-Bis-(diphenylcarbamoyl)-2,5,8-trioxanonane), s9 (N,N,N',N'-tetraoctyldiamide of diglycolic acid), s11 (N, N'-Diethyl-N, N'-di-p-tolyldiamide of dipicolinic acid), s14 (5,11,17,23-tetra(diethylcarbamoylethoxymethylcarboxamido)-25,26,27,28-tetrapropoxycalix[4]arene). Sensor membranes were prepared according to the standard procedure: weighted amounts of membrane components were dissolved in freshly distilled tetrahydrofuran (THF) and poured in a flat-bottomed teflon beaker and left overnight for solvent evaporation. Disks 4 mm in diameter and 0.5 mm thick were cut from the parent membranes and covered on one side with a suspension of fine graphite powder in PVC-cyclohexanone mixture. After drying for 24 hours the membranes covered with solid electric contact composition were mounted in the flow cell and fixed in the channel with clamping plastic bodies. On the top of each body there was a gold spot to provide electric contact. Thus the sensor design employed in this study was similar to the coated wire type. The resulting sensors were encoded as s1, s2,…, s8 in the order of appearance above. The whole construction made of the sensors mounted in the flow cell is shown in the Fig. 1.

<FIGURE 1>

The flow cell was developed in the framework of FP6 WARMER project and was produced by MedbrytSp. z o.o(Warsaw). This flow cell consists of poly(methylmethacrylate) segments (PMMA) that can be hermetically attached to each other to produce the flow cell with necessary number of sensors. For this study we used

nine segments, eight for polymeric sensors and one for Ag/AgCl reference electrode (MedbrytSp. z o.o). Reference electrode was mounted in the middle of the flow path to minimize electric resistance of the system. The inner diameter of the flow path was 1 mm.

2.2 Potentiometric measurements

Potentiometric measurements were performed in a sequential injection system (SIA) providing the automated operation and generation of RE metal mixtures, plus the measuring and data acquisition stages. The SIA system was formed by two differentiated parts: the fluidic system and the measurement system [15, 16].

The first part was the fluid system which consisted of an automatic microburette (Crison 2030 microburette, Crison, Spain) equipped with a 5mL syringe (Hamilton, Switzerland), a holding coil (5m×1mm i.d. PTFE tubing, Bioblock, France), a 8-way Hamilton MVP valve (Hamilton, Switzerland) and a 7mL Perspex mixing cell (home built) with a magnetic stirrer. The multiport valve is connected to the burette with holding coil placed in between. The burette is fed through a carrier solution reservoir. By commanded sequence, the common port of the valve may access any of the other ports which led to sample, standard stock solutions, mixing chamber or sensor array by an electrical rotation. All the elements were connected together using low pressure liquid chromatography connectors.

The second part was the measurement system that comprised the sensor array, a reference electrode (miniaturized silver/silver chloride electrode with a double junction) and an 8-channel signal conditioning circuit connected to the data acquisition analog inputs (National Instruments NI6221 Multifunction DAQ, TX, USA). EMF readings were recorded with 0.1 sec resolution in time domain.

The whole system was controlled by a PC using a virtual instrument developed in Labview [15], where the other active elements were commanded through RS-232 communication lines.

2.3 Samples

We analyzed the response of the multisensor array in flow conditions in RE double mixtures. Three types of double mixtures were analyzed: Sm-Eu, Sm-Gd, Eu-Gd. The motivation for this choice was immediate vicinity of these elements in the Periodic

system of the elements. The concentrations of cations A (primary ion) were changed in the range from $2.44 \cdot 10^{-7}$ to $1 \cdot 10^{-3}$ M, while the content of cations B (interfering species) was varied in the range from $1.25 \cdot 10^{-4}$ to $1.25 \cdot 10^{-3}$M; example of special distribution along the experimental space can be seen in Fig. 2. These concentration ranges are generally relevant to the technological solutions of spent nuclear fuel reprocessing process [17]. The pH values of all solutions were fixed at 2 by nitric acid addition.

<FIGURE 2>

2.4 Data processing

One of the main ideas of this research is to make use of the dynamic part of potentiometric sensor array response in flow measurement conditions. The shape of the response curve can contain useful chemical information which could help to analyze the content of individual lanthanides in mixtures. The Fig. 3 shows the typical view of the sensor responses curves in time. Traditionally in potentiometry and potentiometric multisensor systems only one *emf* value for each sensor is used for data processing – that from the plateau when sensor readings are already equilibrated (e.g. at the 50th second of measurements in the Fig.3). In this study we employed the whole response curve for processing, i.e. instead of the one thermodinamical equilibrium *emf* value we used the whole transient signal (as an example consider 0-50 seconds interval in the Fig.3). It can be seen that the slopes and the amplitudes of the signals are different for different sensors and this additional information can be potentially useful for data processing, in the sense that kinetics in the response may help in the final resolution.

<FIGURE 3>

Both linear (partial least squares, PLS) and non-linear (artificial neural networks, ANN) algorithms were applied for data processing. PLS processing was done with The Unscrambler 9.7 software (CAMO, Norway), while the rest of the chemometric processing was done by specific routines in MATLAB7.1 (MathWorks, Natick, MA) written by the authors, using Neural Network toolbox (v.4.0.6).

The details on the PLS algorithm are widely available in literature, see e.g. [18]. Three different modes of PLS calibration were employed: 1) ordinary PLS with a single *emf* value for each of the sensors (data matrix 42 samples *X* 8 sensors), for this purpose three last points in the response curve over 100 seconds were averaged, 2) PLS with the *emf* reading unfolded along the time axis (data matrix 42 samples X 3208 variables

(8 sensors X 401 time values)), 3) nPLS with the three way array (42 samples X 8 sensors X 401 time values). Initial data were mean centered in sample direction before the PLS processing. Regression models were validated with two different techniques: full cross-validation and classical test set with 11 samples randomly selected. RMSE (root mean square error) values were calculated for all validation protocols.

The first step in building the ANN model is selecting the topology of the neural network used. Given the difficulties to predict the optimum configuration in advance, this consist in a trial-and-error process where several parameters (training algorithm, number of hidden layers, number of neurons, transfer functions, etc.) are fine-tuned in order to find the best configuration that optimizes the performance of the neural network model [19].

For this proposal, a systematic study of the number of neurons in the hidden layer and combinations of functions in both hidden and output layers were tested. In our case, we varied the number of neurons in the hidden layer between 1 and 12, and evaluated the use of combinations of four different transfer functions (i.e. *logsig*, *purelin*, *tansig* and *satlins*) both in the hidden and output layers.

For the selection of the optimal topology, ANN models were trained with 74% of the data, using the remaining 26% (testing subset) to characterize the accuracy of the quantification model and obtain unbiased estimation of model fitness. Subsequently, comparison graphs of predicted vs. expected concentrations for the two determined species were built to easily check the performance of the ANN model. After this step the best configuration was chosen taking into account which topology gave better slope, intercept and correlation coefficient values (i.e. close to ideal values of 1, 0 and 1, respectively).

For the dynamic treatment, the transient response of each sensor was first compressed employing the *windowed slicing integral* (Int) method [14], and then extracted coefficients were used as inputs of the Artificial Neural Network (ANN) model; specifically, the values corresponding from 2.6s to 12.5s, compromising a total of 100 values. The initial points were discarded since it was only carrier signal, while the inclusion of longer recording time does not reflect in any improvement in the model behavior; then, only this profile was further compressed employing Int method.

3 Results

As a first approach to the problem we determined the sensitivities of the sensors in the individual lanthanide solutions. Sensitivity values (mV/dec) were calculated for the linear parts of the calibration curves in the range 10^{-5} – 10^{-3} M of lanthanide in nitric acid with pH 2. The results are shown in the Fig. 4. As can be seen there is a rather subtle difference in the sensor responses towards samarium, europium and gadolinium, which is obviously due to the fact that these lanthanides are closest neighbors in the Periodic system of the elements. However, when comparing the response patterns of e.g. sensor 3 and sensor 7 one can see that the direction of the sensitivity change is different with the growth of lanthanide atomic number. These small differences together with multivariate data processing approach give a chance to resolve the complex mixtures where these metals are present simultaneously.

<FIGURE 4>

At the next stage of the experiment we analyzed three types of lanthanides double mixtures with the potentiometric sensor array in the flow cell. The data from the instrument were arranged into the matrices and processed with PLS and ANN approaches. Let us first consider the results of three different modes of PLS processing.

3.1 Linear PLS regression

The Table 1 shows the metrics of the regression models constructed with the potentiometric data in lanthanide double mixtures Sm-Eu, Sm-Gd, Eu-Gd. Only the validation related numbers are shown for brevity.

<TABLE 1>

It can be seen that three different linear PLS approaches produce very similar results. No substantial difference can be observed in parameters of the regression models constructed with stationary *emf* values, whole response curve and 3 way data array. In general linear PLS models are able to quantify the content of lanthanides in double mixtures with errors around $1 \cdot 10^{-4}$mol/L. This means the concentrations below 10^{-4}mol/L cannot be reliably measured with the developed multisensor system and PLS modeling and the working range of the array in this case is 10^{-4} – 10^{-3}mol/L of lanthanides. From the chemical point of view it would be reasonable to expect that the lowest prediction errors will be observed for the mixtures Sm-Gd, since these elements are further away

from each other in Periodic system than all other combinations. However, the variation in RMSE values does not support this suggestion. Another interesting observation is that RMSE values for two different validation modes (full cross-validation and independent test set) do not differ significantly, although cross-validation is widely criticized for the tendency to produce over-optimistic results since it employs the same samples for modeling and validation [20, 21]. This is not the case with the data set under study.

3.2ANN results

As it was done in the case of PLS models, two types of ANNs models were built, employing the stationary *emf* values and employing the dynamic components of the signal. However, the modeling of the dynamic profile required a preprocessing step for reducing the large dimensionality of the input data prior to building the ANN model [22]. As stated, in this case, reduction of the large data generated for each sample was achieved by means of *windowed slicing integral* (Int) method [14], which allowed the reduction of signals from each sensor down to 10 coefficients without any loss of relevant information; attaining a compression ratio of 90%. Then, the obtained coefficients were used to build a model that allows the prediction of the double mixtures concentrations.

Table 2 summarizes the results obtained with the different models for the testing subset. As can be seen, reasonably good prediction is attained for all the cases with regression parameters close to the ideal values. Additionally, it can be observed that better performance was attained when using the dynamic potentiometric profile. This fact can be explained by the incorporation of the whole response profile and the usage of richer departure information by the model. Slight difference in dynamic response profiles for different RE thus may contribute positively to the precision of the models.

<TABLE 2>

3.3 Comparison of linear and non-linear methods

As shown in Tables 1 and 2, in both cases (linear and non-linear methods), satisfactory trend is obtained for the different mixtures. However, despite the low and similar RMSE values obtained between the different modeling methods, somewhat better results were obtained with the use of ANNs, and more specifically with the incorporation of the dynamic profile into the modeling stage. While average error in prediction with PLS was

around $1 \cdot 10^{-4}$mol/L, the use of ANN allows for lowering this error down to $2 \cdot 10^{-5}$mol/L in certain cases. These results are consistent with the expected ones and with the previous experience in similar cases [23]. Compared with PLS, ANN is more flexible modeling methodology, since both linear and non-linear functions can be used (or combined) in the processing units, thus they suit well for use with non-linear sensor responses (Fig. 2). This also allows for more complex relationships between a high-dimensional descriptor space and the given retention data, and may lead to better predictive power of the resulting ANN model compared with other linear methods. The employment of the dynamic potentiometric profile does not add to the precision of PLS models while non-linear ANNs accept this additional information readily and prediction power of the ANN models increase almost for all of the studied mixtures. It must be pointed out however, that the results obtained in this study cannot be considered as a general rule. The choice of the processing protocol must be done individually for each particular case.

Conclusion

In certain cases a severe lack of sensor selectivity among chemically similar analytes can be compensated with multisensor methodology and careful choice of data treatment procedures. We have demonstrated here a successful application of potentiometric sensor array for quantitative resolution of several RE double mixtures. Particular challenge of this application is in almost identical chemical properties of samarium, europium and gadolinium ions, thus a design of sharply selective ligands for these metals is hardly possible. Nevertheless their individual analysis in mixtures can be performed by means of “cheap-and-dirty” potentiometric sensor array with sequential injection analysis methodology. A careful approach for data treatment allows for extraction of useful analytical information from unresolved signals of sensors. The established protocol can be of certain use in other applications requiring individual analysis of similar substances in mixtures (e.g. amino acids, polyphenolic compounds, etc.).

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References

[1] H.A. Zamani, M.R. Ganjali, M. Adib, Sensor Actuat. B-Chem., 120 (2007) 545-550.
[2] A.K. Singh, P. Singh, Anal. Chim. Acta, 675 (2010) 170-180.
[3] S. Mittal, H. Sharma, A. Kumar, Sensors, 4 (2004) 125-135.
[4] E. Naddaf, H.A. Zamani, Anal. Lett., 42 (2009) 2838-2852.
[5] M.R. Ganjali, N. Davarkhah, H. Ganjali, B. Larijani, P. Norouzi, M. Hossieni, International Journal of Electrochemical Science, 4 (2009) 762-771.
[6] M.R. Ganjali, F. Faridbod, P. Norouzi, M. Adib, Sensor Actuat. B-Chem., 120 (2006) 119-124.
[7] A. Bratov, N. Abramova, A. Ipatov, Anal. Chim. Acta, 678 (2010) 149-159.
[8] M. del Valle, Electroanal., 22 (2010) 1539-1555.
[9] D. Kirsanov, M. Khaydukova, L. Tkachenko, A. Legin, V. Babain, Electroanal., 24 (2012) 121-130.
[10] A.V. Legin, A. . Rudnitskaya, K.A. Legin, A.V. Ipatov, Y.G. Vlasov, Russ J Appl Chem, 78 (2005) 89-95.
[11] D. Calvo, A. Durán, M. del Valle, Anal. Chim. Acta, 600 (2007) 97-104.
[12] R. Cartas, A. Mimendia, A. Legin, M. del Valle, Electroanal., 23 (2011) 953-961.
[13] P. Oliveri, M.C. Casolino, M. Forina, Chapter 2 - Chemometric Brains for Artificial Tongues, in: L.T. Steve (Ed.) Advances in Food and Nutrition Research, Academic Press, San Diego, US, 2010, pp. 57-117.
[14] X. Cetó, F. Céspedes, M. del Valle, Electroanal., 25 (2013) 68-76.
[15] A. Durán, M. Cortina, L. Velasco, J. Rodríguez, S. Alegret, M. del Valle, Sensors, 6 (2005) 19-29.
[16] A. Mimendia, J.M. Gutiérrez, L.J. Opalski, P. Ciosek, W. Wróblewski, M. del Valle, Talanta, 82 (2010) 931-938.
[17] Advanced Separation Techniques for Nuclear Fuel Reprocessing and Radioactive Waste Treatment, Woodhead Publishing Ltd, Cambridge, UK, 2011.
[18] S. Wold, M. Sjöström, L. Eriksson, Chemometr. Intell. Lab., 58 (2001) 109-130.
[19] M. del Valle, Chapter 30 Potentiometric electronic tongues applied in ion multidetermination, in: S. Alegret, A. Merkoçi (Eds.) Comprehensive Analytical Chemistry, Elsevier, 2007, pp. 721-753.
[20] K.H. Esbensen, Multivariate Data Analysis - in practice, CAMO Sosftware, Oslo, 2002.
[21] K.H. Esbensen, P. Geladi, J. Chemometr., 24 (2010) 168-187.
[22] X. Cetó, F. Céspedes, M. del Valle, Microchim. Acta, 180 (2013) 319-330.
[23] A. Mimendia, A. Legin, A. Merkoçi, M. del Valle, Sensor Actuat. B-Chem., 146 (2010) 420-426.

Table 1. The parameters of PLS regression models in prediction of individual lanthanide content in double mixtures.

Mixture, element	*Slope*	*Offset ($mol \cdot L^{-1}$)*	*R^2*	*RMSECV*	*RMSEV test set ($mol \cdot L^{-1}$)*
		PLS stationary data			
Sm-Eu					
Sm	0.892	$1.4 \cdot 10^{-5}$	0.896	$1.1 \cdot 10^{-4}$	$8.5 \cdot 10^{-5}$
Eu	0.967	$2.4 \cdot 10^{-5}$	0.961	$8.0 \cdot 10^{-5}$	$6.0 \cdot 10^{-5}$
Sm-Gd					
Sm	0.949	$9.4 \cdot 10^{-6}$	0.942	$8.4 \cdot 10^{-5}$	$8.8 \cdot 10^{-5}$
Gd	0.967	$2.3 \cdot 10^{-5}$	0.954	$8.7 \cdot 10^{-5}$	$5.7 \cdot 10^{-5}$
Eu-Gd					
Eu	0.972	$5.6 \cdot 10^{-6}$	0.961	$6.9 \cdot 10^{-5}$	$7.9 \cdot 10^{-5}$
Gd	0.926	$5.1 \cdot 10^{-5}$	0.927	$1.1 \cdot 10^{-4}$	$7.5 \cdot 10^{-5}$
		PLS dynamic response			
Sm-Eu					
Sm	0.906	$1.3 \cdot 10^{-5}$	0.906	$1.1 \cdot 10^{-4}$	$1.1 \cdot 10^{-4}$
Eu	0.959	$2.5 \cdot 10^{-5}$	0.966	$7.5 \cdot 10^{-4}$	$8.9 \cdot 10^{-4}$
Sm-Gd					
Sm	0.959	$6.1 \cdot 10^{-6}$	0.954	$7.5 \cdot 10^{-5}$	$9.0 \cdot 10^{-5}$
Gd	0.971	$2.5 \cdot 10^{-5}$	0.958	$8.4 \cdot 10^{-5}$	$6.1 \cdot 10^{-5}$
Eu-Gd					
Eu	0.947	$1.0 \cdot 10^{-5}$	0.963	$6.7 \cdot 10^{-5}$	$6.1 \cdot 10^{-5}$
Gd	0.963	$3.1 \cdot 10^{-5}$	0.933	$1.1 \cdot 10^{-4}$	$5.9 \cdot 10^{-5}$
		nPLS dynamic response			
Sm-Eu					
Sm	0.891	$1.3 \cdot 10^{-5}$	0.897	$1.1 \cdot 10^{-4}$	$1.1 \cdot 10^{-4}$
Eu	0.971	$2.2 \cdot 10^{-5}$	0.969	$7.0 \cdot 10^{-5}$	$7.0 \cdot 10^{-5}$
Sm-Gd					
Sm	0.941	$9.4 \cdot 10^{-6}$	0.936	$8.6 \cdot 10^{-5}$	$9.1 \cdot 10^{-5}$
Gd	0.971	$2.2 \cdot 10^{-5}$	0.953	$8.6 \cdot 10^{-5}$	$7.1 \cdot 10^{-5}$
Eu-Gd					
Eu	0.957	$7.0 \cdot 10^{-6}$	0.961	$7.3 \cdot 10^{-5}$	$7.4 \cdot 10^{-5}$
Gd	0.937	$4.5 \cdot 10^{-5}$	0.927	$1.0 \cdot 10^{-4}$	$6.5 \cdot 10^{-5}$

Table 2. The parameters of ANN regression models in prediction of individual lanthanide content in double mixtures.

Mixture, element	***Slope***	***Offset ($mol \cdot L^{-1}$)***	***R^2***	***RMSEV, test set ($mol \cdot L^{-1}$)***
		ANN with stationary data		
Sm-Eu				
Sm	0.861	$1.12 \cdot 10^{-5}$	0.865	$3.31 \cdot 10^{-5}$
Eu	0.984	$-2.74 \cdot 10^{-5}$	0.994	$4.91 \cdot 10^{-5}$
Sm-Gd				
Sm	1.061	$3.94 \cdot 10^{-6}$	0.692	$6.45 \cdot 10^{-5}$
Gd	0.962	$2.28 \cdot 10^{-5}$	0.987	$4.70 \cdot 10^{-5}$
Eu-Gd				
Eu	1.028	$-1.27 \cdot 10^{-6}$	0.813	$4.45 \cdot 10^{-5}$
Gd	0.993	$1.04 \cdot 10^{-5}$	0.980	$5.69 \cdot 10^{-5}$
		Int-ANN dynamic model		
Sm-Eu				
Sm	0.985	$4.43 \cdot 10^{-6}$	0.898	$3.02 \cdot 10^{-5}$
Eu	1.016	$-1.36 \cdot 10^{-5}$	0.995	$2.89 \cdot 10^{-5}$
Sm-Gd				
Sm	0.994	$6.00 \cdot 10^{-6}$	0.954	$2.04 \cdot 10^{-5}$
Gd	0.954	$2.11 \cdot 10^{-5}$	0.991	$4.22 \cdot 10^{-5}$
Eu-Gd				
Eu	1.048	$3.11 \cdot 10^{-6}$	0.816	$4.54 \cdot 10^{-5}$
Gd	0.964	$4.93 \cdot 10^{-6}$	0.989	$4.56 \cdot 10^{-5}$

FIGURES

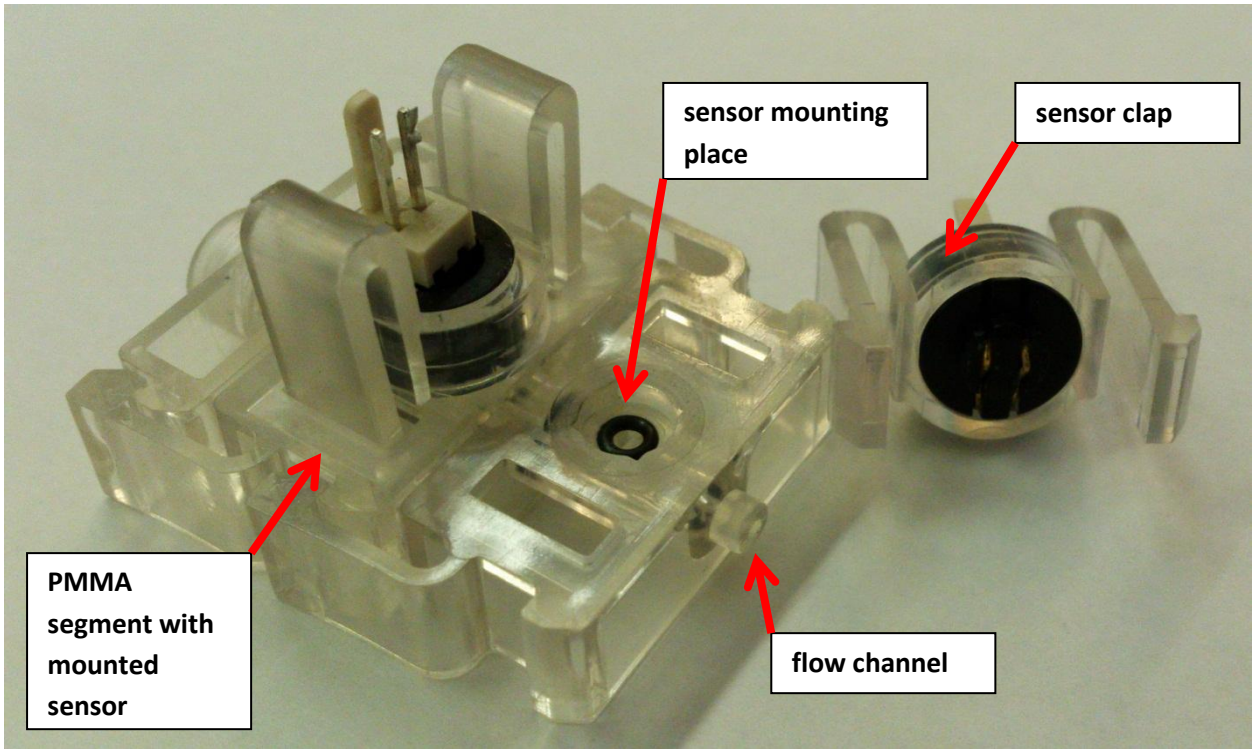

Figure 1. Overview of the flow cell.

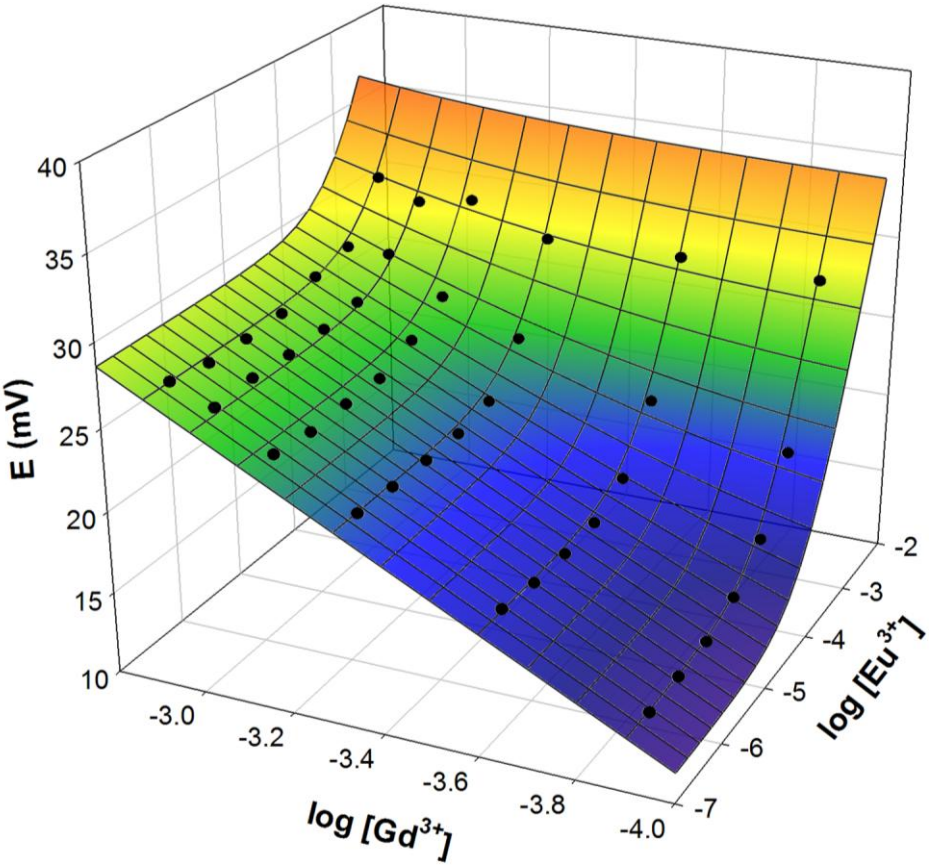

Figure 2. 3D response surface plot corresponding to selectivity experiments of sensor 4 employed in the array, showing their cross-response features with marked slope for Eu^{3+}, and clear interference by Gd^{3+}.

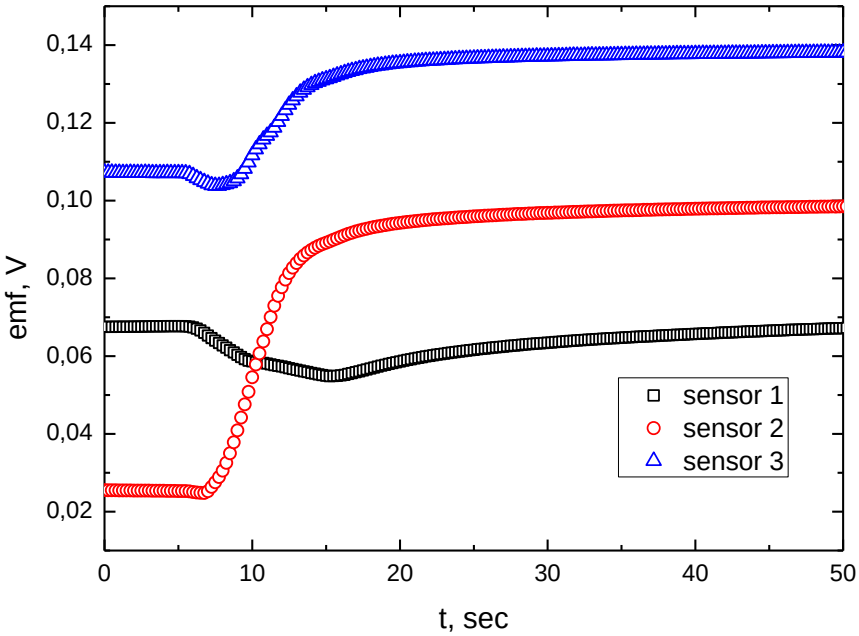

Figure 3. Typical view of the sensor response curves in lanthanide mixtures.

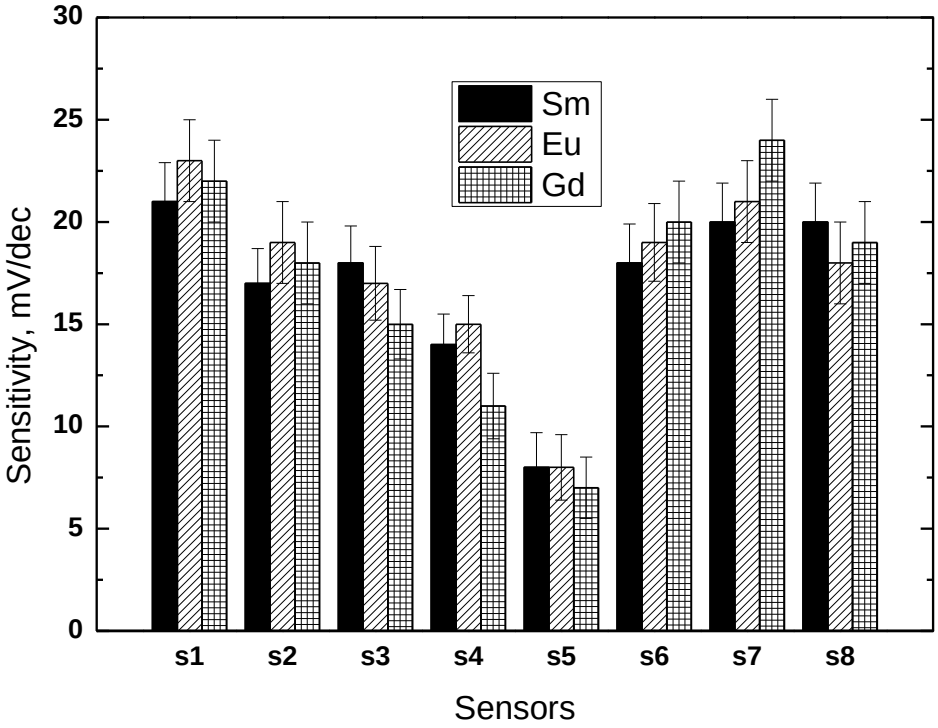

Figure 4. Lanthanide sensitivities of the sensors.