Microchemical Journal 92 (2009) 58–67

Contents lists available at ScienceDirect

Microchemical Journal

journal homepage: www.elsevier.com/locate/microc

Review article

Chemometric tools in electroanalytical chemistry: Methods for optimization based on factorial design and response surface methodology

César Ricardo Teixeira Tarley [a,*], Gustavo Silveira [a], Walter Nei Lopes dos Santos [b], Geraldo Domingues Matos [c], Erik Galvão Paranhos da Silva [c], Marcos Almeida Bezerra [d], Manuel Miró [e], Sérgio Luis Costa Ferreira [c]

[a] Universidade Federal de Alfenas, Departamento de Ciências Exatas, Alfenas, MG 37130-000, Brazil
[b] Universidade do Estado da Bahia, Departamento de Ciências Exatas, Salvador, BA 41195-001, Brazil
[c] Universidade Federal da Bahia, Instituto de Química, Salvador - BA 40170-290, Brazil
[d] Universidade Estadual do Sudoeste da Bahia, Departamento de Química e Exatas, Jequié, BA 45206-190, Brazil
[e] University of the Balearic Islands, Department of Chemistry, Faculty of Sciences, Palma de Mallorca, Illes Balears, Spain

ARTICLE INFO

Article history:
Received 3 November 2008
Received in revised form 10 February 2009
Accepted 10 February 2009
Available online 21 February 2009

Keywords:
Full factorial design
Central composite design
Doehlert design
Box–Behnken designs
Response surface methodology
Electroanalytical methods

ABSTRACT

The aim of this paper is to give a brief overview of chemometric techniques based on factorial designs and response surface methodologies used in the optimization of electroanalytical methods. Chemometric techniques have several important advantages over one-way optimization for analytical applications, including a relatively low cost, a reduced number of experiments, and possibilities to evaluate interactions among variables. These techniques also enable the selection of optimal experimental conditions, helping to avoid trivial mistakes during optimization. Despite these facts, chemometric techniques have rarely been applied to electroanalytical data, especially in comparison with their use in spectroscopy. The application of chemometric methods in electroanalytical chemistry has been mostly used for solving overlapping signals, multivariate calibration methods, model identification and optimization of analytical procedures. This review is focused on the latter applications and overviews the role of full or fractional factorial designs (first-order designs), as well as second-order designs, such as central composite, Doehlert and Box–Behnken designs, for optimization of electroanalytical methods. A discussion of chemometric-related advantages is also given for stripping analyses, flow injection systems with amperometric detection, differential pulse voltammetry, square wave voltammetry and electrochemical sensor preparation.

Published by Elsevier B.V.

Contents

* Corresponding author. Tel.: +55 35 3299 1483; fax: +55 35 3299 1262.
E-mail address: ctarleyquim@yahoo.com.br (C.R.T. Tarley).

0026-265X/$ – see front matter. Published by Elsevier B.V.
doi:10.1016/j.microc.2009.02.002

1. Introduction

Chemometric tools have been frequently applied to analytical method optimization problems. Among their advantages is the reduction in the number of required experiments, resulting in lower reagent consumption and considerably less laboratory work. Thus, they are faster to implement and more cost-effective than traditional univariate approaches. These methods enable the simultaneous study of several control factors and the development of mathematical models that permit assessment of the relevance and statistical significance of factors being studied. They also facilitate the evaluation of interaction effects between factors. Two types of variables exist in multivariate designs, including: (i) responses (qualitative or quantitative) and (ii) factors, which can be firstly screened by full factorial or fractional factorial designs to get knowledge of those with significant effects on the analytical response. After determining these significant factors, the optimum operation conditions are attained by using more complex experimental designs, such as a Doehlert matrix (DM), Central Composite designs (CCD) or Box–Behnken designs (BBD) [1–3].

Multivariate statistical methods require that the user establishes minimum and maximum values for each factor, defining the experimental domain to be investigated during the optimization procedure. Combinations of the different factor levels for performing actual experiments are then determined based on which multivariate techniques are capitalized.

1.1. First-order model

Designs that be can used in the maximum first-order model are commonly used in exploratory studies when a large number of factors need to be considered or screened. Essentially, this method is used in an attempt to detect factors that exhibit large main effects and to discard from further study any factors with no noticeable effects. The crucial assumption here is that all interactions are negligible, including two-factor interactions. This may not always be realistic, but as a first approximation this is nevertheless a very valuable method. Yet, in some cases, it may be helpful to know the two-factor interactions that each main effect is aliased [4].

1.1.1. Full and fractional factorial design

Full and fractional factorial designs are the most popular first-order designs owing to their simplicity and relatively low cost. They are very useful for preliminary studies or in initial optimization steps, while fractional designs are almost mandatory when the problem involves a large number of factors. Both allow free interaction with data, the ability to make comparisons, seek similarities, differences, trends, etc. They can also be used to determine simple response surfaces that are linear with respect to all of the investigated factors. Only the first stage in a multivariate investigation, where a linear response surface is determined, will be mentioned. For a two-factor case, the response surface is given by the linear model [5,6] as detailed below:

$$\hat{y} = b_0 + b_1x_1 + b_2x_2 + b_{12}x_1x_2 \quad (1)$$

If the interaction term is negligible, then the response surface is planar. The more important the interaction term, the greater is the degree of twisting that the planar response surface experiences.

1.1.2. Plackett–Burman design

Experimental designs of this type exhibit an extremely high degree of confounding. This is not surprising when one considers that a full eleven-factor, two-level design would require 2.048 (2^{11}) individual experiments, involving 11 main effects, 55 second-order interactions, and no fewer than 1.981 further interactions of orders ranging from 3 to 11. Because they are so highly confounded, Plackett–Burman designs cannot be used to evaluate individual main effects and interactions between them, although they are of great value in screening experiments, as mentioned previously. In these experiments, a comparatively large number of factors may have an influence on the response. Thus, it is of value to distinguish those that have an effect from those that do not.

Projections of two-level designs can be used to investigate main effects and interactions of the factors retained, although these cannot support a fully quadratic model, which require at least three levels. However, there are also economical three-level designs that can be used for screening when a second-order fit is desirable. They can be used as initial building blocks for some small, second-order designs.

1.2. Higher order models

There are many cases where the linear model is not sufficient to represent the experimental data adequately. In this case, more experiments can be performed in addition to those of factorial design and the results can be used to determine a quadratic response surface [5,6]

$$\hat{y} = b_0 + b_1x_1 + b_2x_2 + b_{11}x_1^2 + b_{22}x_2^2 + b_{12}x_1x_2 \quad (2)$$

which has curvature and can be used to predict factor levels that produce maximum or minimum response values.

After calculating the model coefficients and their standard errors, an ANOVA is applied to verify the quality of model, that is, the actual fitting to the data. Random execution of experiments is of concern so that an accurate estimation of experimental error is obtained. The regression step does not require user intervention, so it is not described here, and the reader is referred to basic sources on the subject to learn how the computer carries out the calculation. The validation of tentative models using ANOVA is detailed, as this task requires several decisions on the part of the researcher. These decisions concern as to which models are adequate to represent the data and which models should be rejected because they suffer from significant lack-of-fit to the data [7].

1.2.1. Central composite design

A central composite design (CCD) [8] combines a two-level full or fractional factorial design with additional points (star points) and at least one point at the center of the experimental region. This point is selected to obtain several properties, such as rotatability or orthogonality, in order to fit the quadratic polynomials. The CCD is a better

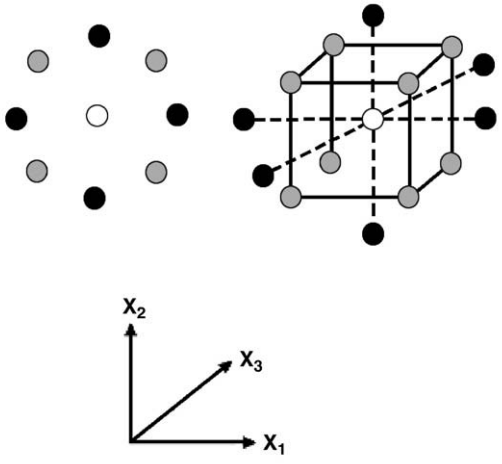

Fig. 1. Central composite design for two and three factors. The gray dots form the square or cubic part (the runs of the 2^2 and 2^3 factorial). The black dots represent the star portions.