Talanta 124 (2014) 123–138

Contents lists available at ScienceDirect

Talanta

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

Review

Experimental design and multiple response optimization. Using the desirability function in analytical methods development

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ARTICLE INFO

Article history:
Received 6 November 2013
Received in revised form
21 January 2014
Accepted 23 January 2014
Available online 12 February 2014

Keywords:
Experimental design
Response transformation
Multiple response optimization
Desirability function

ABSTRACT

A review about the application of response surface methodology (RSM) when several responses have to be simultaneously optimized in the field of analytical methods development is presented. Several critical issues like response transformation, multiple response optimization and modeling with least squares and artificial neural networks are discussed. Most recent analytical applications are presented in the context of analytLaboratorio de Control de Calidad de Medicamentos (LCCM), Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional del Litoral, C.C. 242, S3000ZAA Santa Fe, ArgentinaLaboratorio de Control de Calidad de Medicamentos (LCCM), Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional del Litoral, C.C. 242, S3000ZAA Santa Fe, Argentinaical methods development, especially in multiple response optimization procedures using the desirability function.

Contents

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http://dx.doi.org/10.1016/j.talanta.2014.01.034
0039-9140

1. Introduction

Due to the increasing quality requirements of regulatory agencies, the high cost of reagents and the large quantity of variables affecting the analytical process, the procedure of development and validation of analytical methods cannot be considered as a simple task. In this context, the term "optimization" seems to refer to improving the performance of the analytical process, i.e. discovering the conditions at which the best response is obtained [1]. In analytical chemistry, optimization is a critical stage to find the value that each factor must have to produce the best possible response. It must be done assuring a good performance in the analytical methods which are being developed in the laboratory, modified from official or standard methods or obtained from the scientific literature.

In this context, the multivariate design of experiments (DOE) is an important issue because it takes less time, effort and resources than the univariate procedures (which are surprisingly still being used in routine method development), and facilitates the gathering of large quantities of information while minimizing the number of experiments [2]. DOE and the response surface methodology (RSM) have been proved to be useful for developing, improving and optimizing processes [3]. The RSM has been extensively used in analytical applications [4–7], industrial world [8–12] and in bioprocesses [13–16].

As it can be appreciated in the flow chart presented in Fig. 1, DOE and RSM are mostly applied to analytical separations and extraction procedures. After a first screening study, a response surface design is built which provides data that must be generally modeled through the least squares fitting or, exceptionally, by artificial neural networks. When a large number of responses should be optimized (following the appropriate criteria), the desirability function is the most popular tool to be applied [17].

In this review, the role of the DOE in the analytical method optimization stage will be analyzed. Several critical issues will be discussed, especially those which have not been addressed extensively in previous reviews, such as response transformation and multiple response optimization. Finally, some analytical applications are presented in the context of analytical methods development, particularly in multiple response optimization procedures using the desirability function.

2. Aim and methodology of experimental design

A major role of experimental design in analytical chemistry concerns method optimizations, where the main purpose is to discover the experimental conditions which produce the best possible analytical performance [1]. Two stages may be considered in method optimization: (a) a screening step, where many factors are studied to identify those with the significant effects on critical variables, and (b) the optimization, where the factors are further examined in order to determine the best analytical conditions. In addition, experimental design is also used in analytical chemistry to evaluate robustness in method validation (to examine the effects that small changes in the analytical method conditions have on the responses) and to build calibration and validation sets to be used for calibration purposes [18].

Two optimization strategies can be distinguished: the univariate and the multivariate approaches. In the first, only one factor is

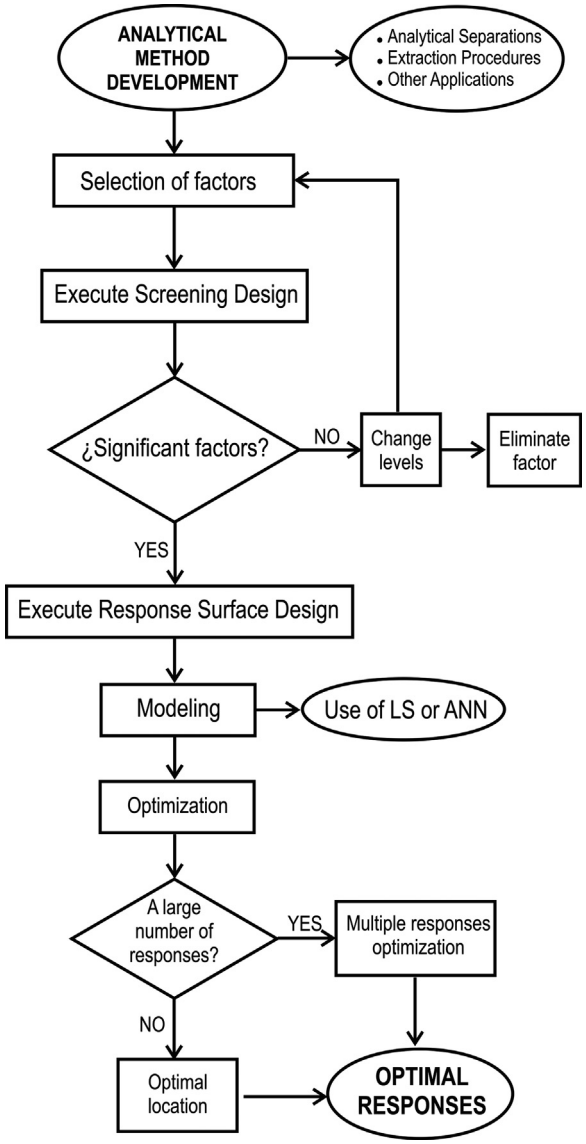

Fig. 1. Flow chart which shows schematically how DOE and RSM are applied in analytical method developments.