SRO_ANN: An integrated MatLab toolbox for multiple surface response optimization using radial basis functions[☆]

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ABSTRACT

SRO_ANN, a MatLab® toolbox for implementing multiple surface response optimization by artificial neural networks (SRO_ANN) is presented. Radial basis functions, a type of artificial neural networks, are applied through an easily managed graphical user interface. A detailed description of the interface is provided, including a simulated and two literature examples which allow one to show the potentiality of the software. The discussed experimental examples correspond to: (1) the maximization of the research octane number (RON) of fuels, influenced by three factors (reaction temperature, operating pressure and low liquid hourly space velocity), and (2) the optimization of the calcification process for diced tomatoes, evaluated through three different responses (calcium content, firmness and pH), which are affected by three factors (calcium concentration, solution temperature and treatment time). The results show that the application of a nonparametric tool can enhance the performance of optimization modeling tasks.

1. Introduction

Multivariate design of experiments (DOE) and optimization of procedures using the response surface methodology (RSM) are issues of high concern for the analytical community. Their implementation is mandatory in analytical chemistry instead of classical univariate procedures for a number of reasons, namely: (1) less effort and resources are required, (2) considerably less experimental points are needed, saving time, energy and cost, (3) global instead of local optima are achieved, (4) possible interactions among affecting factors are considered, and, perhaps more importantly, (5) truly optimal results are achieved [1,2]. DOE and RSM have been proved to be useful for developing, improving and optimizing a wide variety of procedures, not only of analytical concern, but from other real-world applications [3].

The following steps are followed for applying DOE and RSM [2]: (a) identification of the responses, which are affected by controlled and uncontrolled variables (factors), (b) factor screening, in which the original (possibly large) number of factors is reduced to a handful of significant factors, (c) building a response surface design, (d) modeling the design by least-squares or artificial neural networks to explain how the responses are affected by the factors, and (d) optimization, where the optimal combination of factors allowing to reach the best or desired response is obtained. If several responses are being simultaneously optimized following some pre-defined criteria, the desirability function may become a powerful assisting tool [4].

In the present report, a chemometric MatLab® toolbox is presented, developed to perform response surface optimization based on artificial neural networks, and integrated in an easy-to-use graphical interface environment. It has been named SRO_ANN. Calculations and graphical outputs are conveniently managed through graphical user interface (GUI) shells. The software does not require a highly experienced user, but a basic knowledge of the underlying methods is advisable in order to successfully interpret the results.

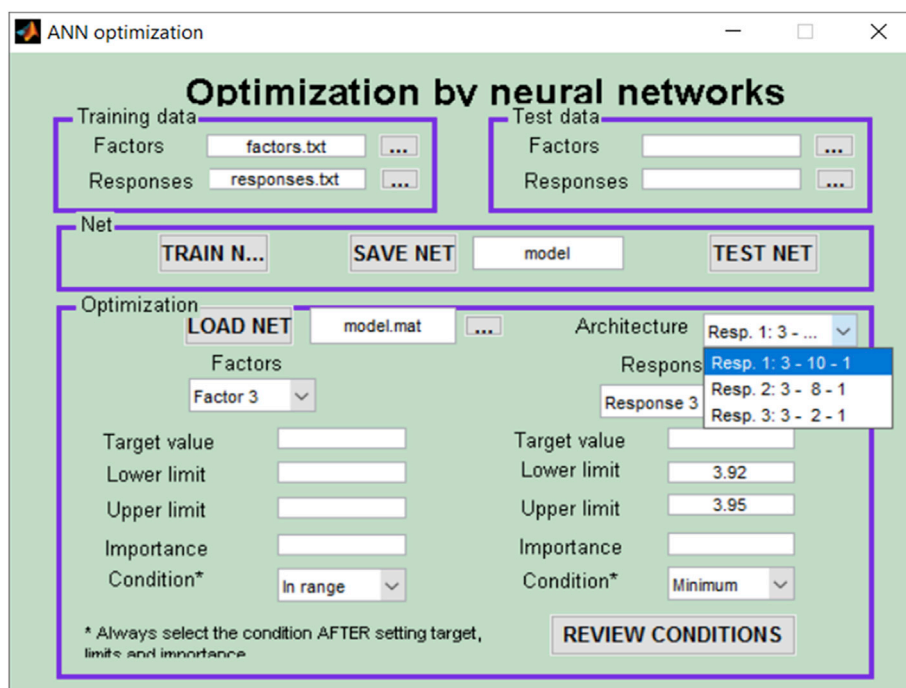A simulated example where classical least-squares solution fails is

Fig. 1. Main window of the SRO_ANN program.

presented, showing the potentiality of the ANN approach for studying a system where the behavior of the response as a function of the influencing factors is known. In addition, selected literature examples were studied for which this toolbox is ideally suited, namely: the maximization of the research octane number (RON) influenced by three factors (reaction temperature, operating pressure and low liquid hourly space velocity) [5], and the optimization of the calcification process for diced tomatoes followed by three responses (calcium content, firmness and pH) which are affected by three factors (calcium concentration, solution temperature and treatment time) [6]. The examples are presented in the order of increasing complexity: the first one pursues the optimization of a single response, whereas the latter implies three responses which should be optimized following different criteria.

The software is freely available and is provided on request via e-mail, including manual and examples. The software itself comes in two formats: (1) a set of open MatLab codes, or (2) a stand-alone compiled version. Please contact the corresponding author.
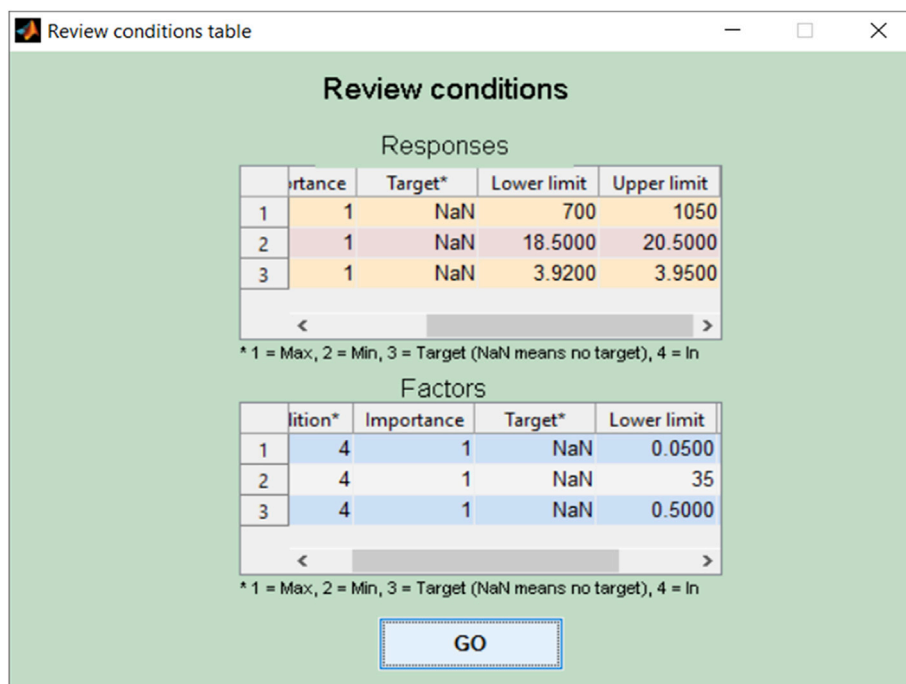

Fig. 2. SRO_ANN window summarizing the selected conditions for optimization for Example #2.

Table 1
Central composite design built to find the optimal conditions of *n*-octane reforming.

Experiment	Factors[a]			Response
	T (ºC)	P (bar)	LHSV (h^{-1})	RON[b]
1	480.00	10.00	1.20	88.6
2	480.00	10.00	1.80	88.1
3	480.00	30.00	1.20	82.3
4	480.00	30.00	1.80	81.2
5	510.00	10.00	1.20	95.3
6	510.00	10.00	1.80	98.5
7	510.00	30.00	1.20	88.7
8	510.00	30.00	1.80	91.2
9	495.00	20.00	1.50	85.2
10	468.00	20.00	1.50	81.3
11	521.00	20.00	1.50	93.7
12	495.00	2.36	1.50	91.5
13	495.00	37.63	1.50	88.3
14	495.00	20.00	0.97	90.5
15	495.00	20.00	2.02	80.8
16	495.00	20.00	1.50	85.7

[a] T(ºC): reaction temperature, P(bar): operating pressure, LHSV(h^{-1}): low liquid hourly space velocity.

[b] RON: research octane number.

Fig. 4. Actual and predicted values for the response RON using both LS and RBF models.

2. Theory

2.1. Response surface methodology

RSM is based on building a mathematical model for each response, in general, by fitting a second-order polynomial expression of the response as a function of the influencing factors. Only in rare cases cubic polynomials have been employed for modeling [7]. The general form of the second-order expression is the following:

$$y = \beta_0 + \sum_{i=1}^{k} \beta_i x_i + \sum_{i=1}^{k} \beta_{ii} x_i^2 + \sum_{1 \le i \le j}^{k} \beta_{ij} x_i x_j + \varepsilon \qquad (1)$$

where *y* represents the response, x_i and x_j the factors, β_0 is the constant term or intercept, β_i, β_{ii} and β_{ij} the coefficients of linear, quadratic and

interacting terms, respectively, and ε is a residual term. Usually, only two-factor interactions are taken into account [2].

The model equation is usually fitted by the least-squares (LS). When the data do not follow a normal distribution or the relationship between factors and response is too complex to be fitted by polynomial functions, artificial neural networks (ANN) can be used as a nonparametric tool for non-linear multivariate modeling [8]. In any case, the model must be able to properly describe the data behavior to make meaningful predictions. When only two factors are optimized, a single graphical view is generated, since the response surface can be represented as a solid surface in a three-dimensional space. On the other hand, when more than two factors are being optimized, several graphical representations may be produced for pairs of them, maintaining the remaining ones at constant values. Additionally, contour maps may be plotted as a complementary visualization strategy, consisting of iso-response lines corresponding to specific values of the response.
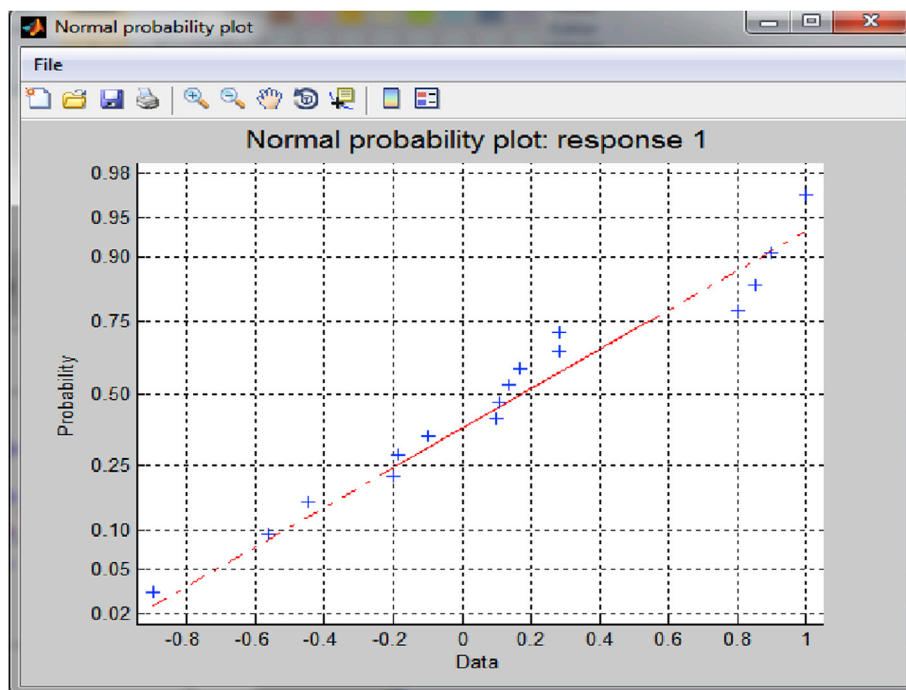

Fig. 3. Normal probability plot for the residuals corresponding to response RON in Example #1.
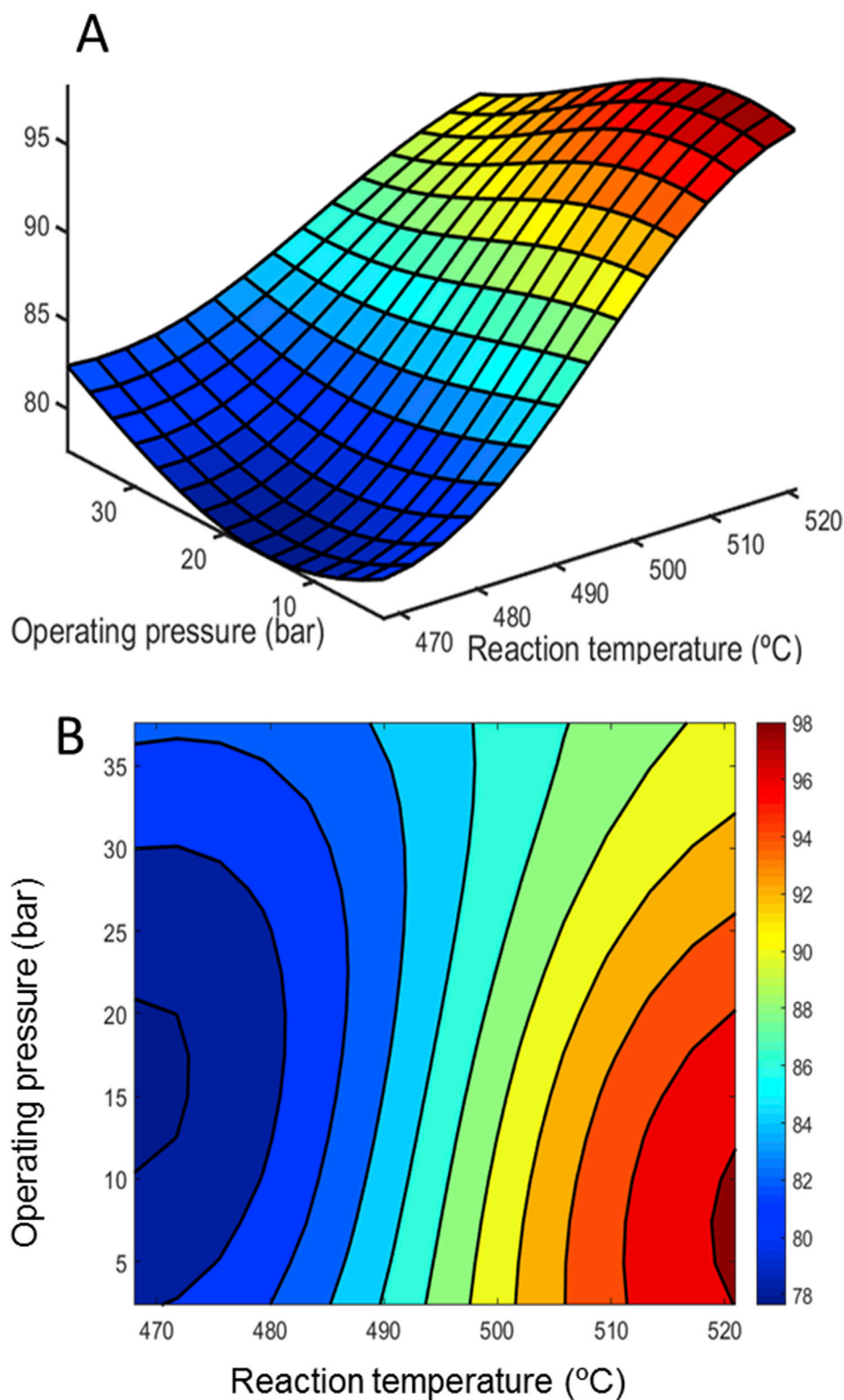
Fig. 5. Response surface (A) and contour plot (B) for the response RON obtained by application of the RBF approach.

2.2. Multiple response optimization: desirability function

The global desirability function (*D*) was proposed by Derringer and Suich in 1980 to optimize multiple responses [9]. The *D* function is based on the idea that the quality of a product or process that has many features is completely unacceptable if one of them is outside of a "desirable" limit.

The object is to find operating conditions that ensure agreement with the criteria of all the involved responses, providing the best value of compromise in the desirable joint response [4]. This is achieved by obtaining a single response which combines the individual ones. Derringer's desirability function allows the analyst to find the factor levels which allow to simultaneously reach the optimal value for all the

Table 2
Box-Behnken design built to find the optimal conditions on a calcification process for diced tomatoes.

Experiment	Factors[a]			Responses[b]		
	Ca (% CaCl$_2$)	Te (ºC)	Ti (min)	CC (µg g^{-1})	F (N g^{-1})	pH
1	0.75	65.00	3.35	2890.3	20.79	4.01
2	1.45	50.00	3.35	7490.2	26.48	3.61
3	0.75	35.00	3.35	1698.1	22.85	3.69
4	0.75	50.00	1.93	1274.3	20.00	4.13
5	0.75	35.00	0.50	804.9	17.75	3.92
6	0.05	50.00	3.35	253.5	14.81	4.33
7	0.75	65.00	0.50	1162.5	21.57	4.33
8	0.05	50.00	0.50	152.0	10.10	4.35
9	0.05	65.00	1.93	390.4	15.40	4.35
10	0.05	35.00	1.93	248.1	12.85	4.20
11	0.75	50.00	1.93	1505.9	23.53	3.85
12	0.75	50.00	1.93	1660.3	24.12	3.77
13	1.45	35.00	1.93	5578.8	24.81	3.75
14	1.45	65.00	1.93	3720.0	23.04	3.86
15	1.45	50.00	0.50	1842.9	20.59	4.00

[a] Ca (% CaCl$_2$): calcium concentration, Te (ºC): solution temperature, Ti (min): treatment time.
[b] CC (µg g^{-1}): calcium content, F (N g^{-1}): firmness.

evaluated variables, including the researcher's priorities during the optimization procedure.

The first step in this procedure consists in obtaining an individual desirability function $d_i(\hat{y}_i)$ for each response $\hat{y}_i(k)$, computed using the fitted models and establishing the optimization criteria. Desirability always takes values between 0 and 1, where $d_i(\hat{y}_i) = 0$ for an undesirable response, and $d_i(\hat{y}_i) = 1$ represents a completely desirable value, i.e., an ideal response. Intermediate values of $d_i(\hat{y}_i)$ indicate more or less desirable responses.

Depending on the adopted optimization criteria, different functions may be built. They vary within an acceptable range of response values given by ($U_i - L_i$), where U_i is the upper acceptable value for the response and L_i is the lower. Thus, if the response has to be maximized, $di(\hat{y}_i)$ can be described by the following equation:

$$d_i(\widehat{y_i}(x)) = \begin{bmatrix} 0 & \text{if } \widehat{y_i}(x) < L_i \\ \left(\dfrac{\widehat{y_i}(x) - L_i}{U_i - L_i}\right)^s & \text{if } L_i \le \widehat{y_i}(x) \le U_i \\ 1 & \text{if } \widehat{y_i}(x) > U_i \end{bmatrix} \qquad (2)$$

where s is a power value or weight, set by the analyst to determine how important it is for $\hat{y}_i$ to be close to the maximum. Equations for minimization and for a target value can also be created [4]. Factor levels may also be included in the optimization procedure, in order to prioritize the use of certain suitable conditions within the experimental region.

Finally, once the n variables (factor and responses levels) are transformed into n desirability functions, they can be combined in a unique function: the global desirability (D), to find out the best joint responses using the following equation:

$$D = \left(d_1^{r_1} \times d_2^{r_2} \times \dots\dots \times d_n^{r_n}\right)^{\frac{1}{\sum r_i}} = \left(\prod_{i=1}^n d_i^{r_i}\right)^{\frac{1}{\sum r_i}} \qquad (3)$$

where r_i is the importance of each variable relative to the others. When D attains a value different to zero, all variables being simultaneously optimized reach a desirable value. On the contrary, D will be zero if just one of the responses is completely undesirable.

2.3. Radial basis functions

Radial basis functions (RBF) are ANN consisting on three layers. The input layer serves to distribute the input variables to the hidden one.

Each of the m neurons of the hidden layer uses a basis Gaussian function as transfer. Suitable parameters (centres and widths) are required for the hidden Gaussian functions [10]. The centres are contained in a $k \times 1$ vector **c**. Both centres and widths are usually considered to be equal for all functions. The output from the mth. hidden neuron, for a given input $k \times 1$ object **s**, is therefore expressed as:

$$\text{out}_i = \exp\left(-\frac{1}{2\sigma^2}\|\mathbf{s} - \mathbf{c}_i\|^2\right) \qquad (4)$$

where $\|\mathbf{s} - \mathbf{c}_i\|$ is the Euclidean distance between **s** and $\mathbf{c}_i$. The input value to the output node is the weighted sum of all the outputs of the hidden nodes, with the response of the output node linearly related to its input. Hence, the RBF network output (out) for an input object **s** is given by:

$$\text{out} = w_0 + \sum_{i=1}^m w_i \exp\left(-\frac{1}{2\sigma^2}\|\mathbf{s} - \mathbf{c}_i\|^2\right) \qquad (5)$$

where w_0 is the bias and w_m is the weight assigned to the mth. hidden output. These weights are adjusted to minimize the mean square error of the net output. Therefore, two sets of parameters (the centres and widths) in the hidden layer, and a set of weights in the output layer are adjusted. RBF has a guaranteed learning procedure for convergence: given the centres of the m basis functions and a set of k training objects with known factor values and target response, the minimum squared error in the prediction of the response is attained when the weights are given by:

$$\mathbf{w} = (\mathbf{H}^T \mathbf{H})^{-1} \mathbf{H}^T \mathbf{r} \qquad (6)$$

where **w** is a vector ($m \times 1$) collecting the weights, **r** ($n \times 1$) is the vector of target response values, and **H** ($n \times m$) is the so-called design matrix, whose elements are calculated as:

$$H(j, i) = \exp\left(-\frac{1}{2\sigma^2}\|\mathbf{s} - \mathbf{c}_i\|^2\right) \qquad (7)$$

We have followed one of the procedures recommended by Orr, where the value of m is tuned by forward subset selection and generalized cross-validation [10]. This avoids overfitting, i.e., the selection of an m value equal to the number of independent training samples.

3. SRO_ANN: program description

Among other interesting features, SRO_ANN involves a single main window, from which all steps required for RBF modeling can be carried out (Fig. 1):

1) Frame labelled "Training data". Two browsers allow one to load in the workspace the files containing the values of factors from the design matrix data and the measured experimental responses. The design information includes factor combinations corresponding to the implemented experimental design (full factorial, central composite, Box-Behnken, Doehlert, optimal, etc.), and should be uploaded as a '.txt' file of size ($n \times k$), where n is the number of experiments and k the number of factors. Responses should be uploaded also as a '.txt' file of size ($n \times r$), where r is the number of responses being analysed. For example, if a central composite design with five central points for two factors and three responses is employed, the design matrix is of size 13×2 ($13 = 2^k + 2 \times k + Nc$, where k is the number of factors and Nc the number of central points), and the response matrix is of size 13×3.
2) Frame labelled "Test data". The browsers allow one to load factor and response values for independent experiments to test the performance of the trained RBF network.
3) Frame labelled "Net". Pressing the "TRAIN NET" button, the RBF can be optimized through the procedure described in Eq. (6). Three plots are displayed in this step: (a) predicted vs. nominal response values,
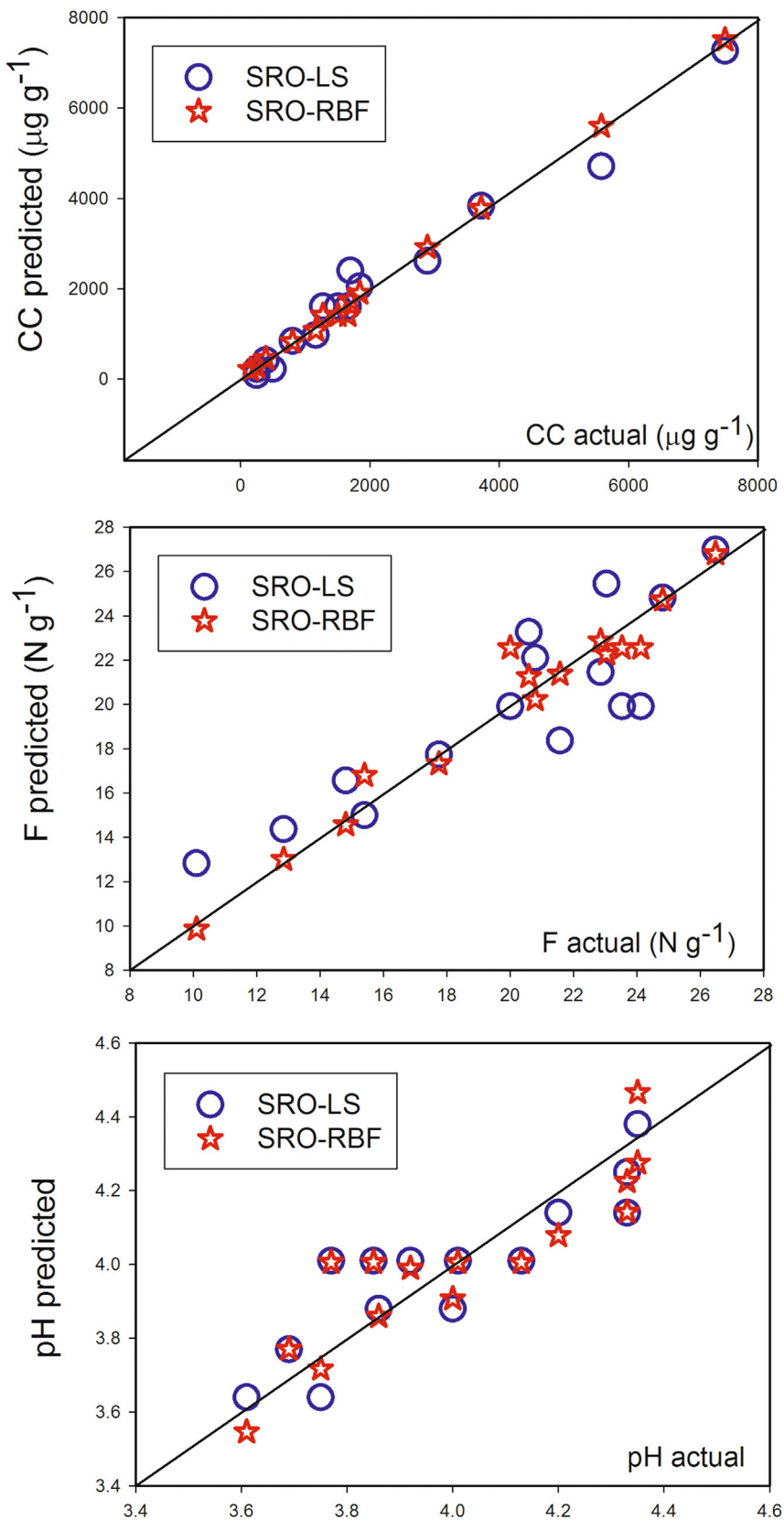
Fig. 6. Nominal and predicted values for the responses CC, F and pH using both LS and RBF models.
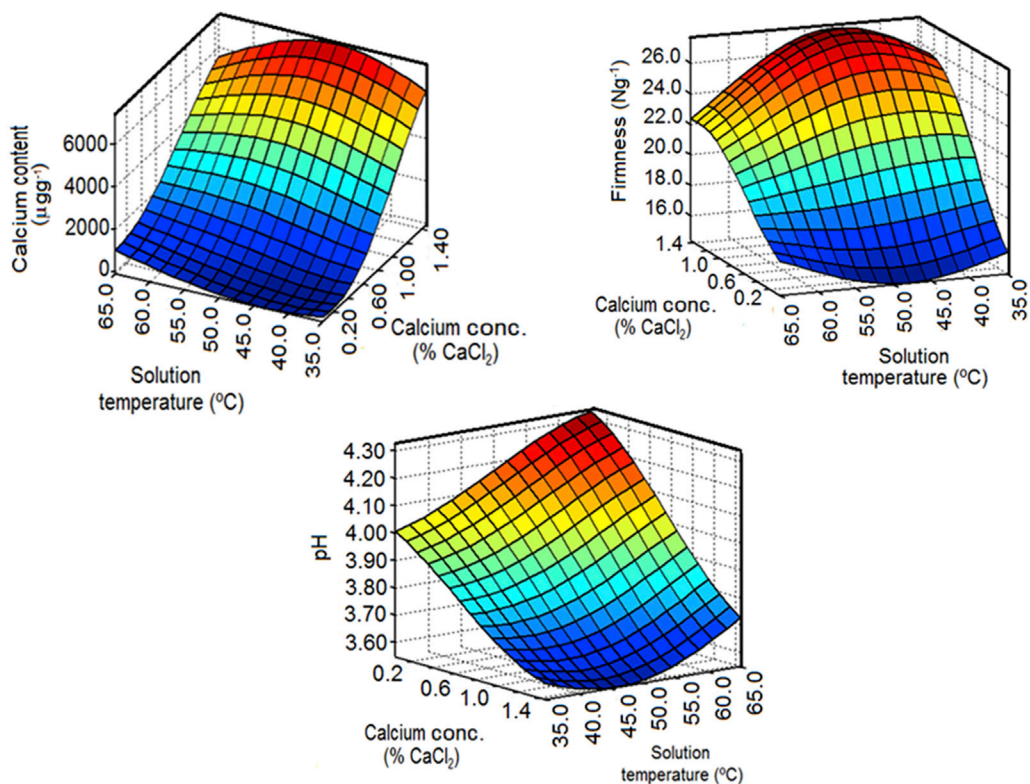
Fig. 7. Response surfaces for CC, F and pH, obtained by means of RBF.

(b) prediction residuals vs. nominal responses, and (c) normal probability plot for the residuals. This latter graph is of great importance when the data are suspected to follow a non-normal distribution and a better fit could be attained using nonparametric tools. Additionally, training results (nominal, predicted and residuals) can be saved as a file 'trairesults.txt' in the working folder where the data are located, and the network architecture is provided in the main screen (number of input, hidden and output neurons for each trained net). The parameters corresponding to the optimized model should be saved to be used for future predictions and for building the response surface with the button "SAVE NET".

The button "TEST NET" allows one to test the performance of the trained network on the independent data set if the latter is available. This experimental verification can be performed comparing response predictions with experimental values. The information should be uploaded in files '.txt' of similar structure than those uploaded for training information. Indicators of the quality of the model can be attained at this stage.

4) Frame labelled "Optimization". First the net parameters should be loaded using the "LOAD NET" button. Then the desirability function is implemented, which is important when there are several responses to be optimized: factors as well as responses can be optimized to find the optimal combination of factors which produce the optimal response according to the criteria set by the experimenter. Information for both factors and responses can be set including the following: minimum, maximum, target or in range. Importance can be assigned to factors and responses as shown in Eq. (3). Then, pressing the button "REVIEW CONDITIONS", a window is displayed summarizing the selected conditions for optimization (see Fig. 2).

Table 3
Criteria used for the optimization of a calcification process for diced tomatoes.

Factors[a], response[b] and *D* value	Optimization criteria	Lower limit	Upper limit	Predicted	
				SRO-LS	SRO-ANN[c]
Ca (%CaCl$_2$)	In range	0.05	1.45	0.40	0.45
Te (°C)	In range	35.00	65.00	35.00	37.14
Ti (min)	In range	0.50	3.35	3.35	2.74
CC (mg g^{-1})	Minimize	700.0	1050.0	8.68	739.26
F (N g^{-1})	Maximize	18.50	20.50	18.898	19.88
pH	Minimize	3.92	3.95	3.82	3.92
D	–	–	–	0.457	0.817

[a] Ca: calcium concentration; Te: solution temperature; Ti: treatment time.
[b] CC: calcium content; F: firmness.
[c] Network architectures: 3-9-1 for CC, 3-4-1 for F and 3-4-1 for pH (number of input, hidden and output neurons).
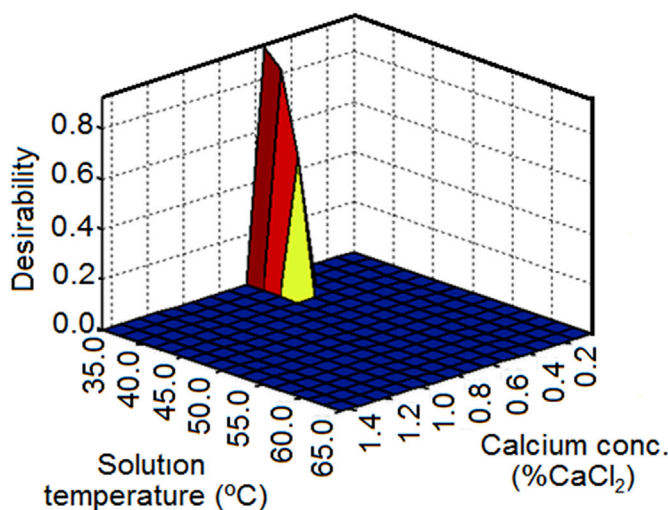

Fig. 8. Desirability surface as a function of calcium concentration and solution temperature, obtained by means of RBF in Example # 2.

When pressing the button 'GO' on the latter window, the results of the optimization are displayed in a table with optimal values for the responses being optimized and their corresponding combination of factors. Additionally, the global desirability function value is presented for the best factor combination, which is relevant for multiple response optimization. Figures are also available showing the response surface or contour plot for user-selected pairs of factors. When more than one response is analysed, the global desirability or individual responses can be selected for plotting.

4. Results and discussion

4.1. Software requirements

The MatLab version of the software only uses MatLab R2012a by MathWorks®. The codes, manual and examples are freely available at www.iquir-conicet.gov.ar/descargas/opt_rbf.rar. The files only need to be copied into a folder declared in the MatLab Path. Alternatively, a stand-alone compiled version is available, including a free version of the MatLab Common Runtime (MCR) program for installation. In this case, after installing MCR, the executable sro_ann.exe file can be copied in any folder from which it can be run. The compiled software version and the MCR program can be freely obtained at the following sites:

https://www.dropbox.com/sh/6xjf4nzk5w8h5at/AAAm5oQbv5txDEI5XdBjNF2ia?dl=0.

https://www.dropbox.com/sh/eqc34ngkzphkvqt/AAAUiqi7aJhVPeCAZXgMihj9a?dl=0.

4.2. Examples

With the aim of showing the usefulness of the approach, one simulated and two literature case-studies are presented. In the simulated example, a response is varied as a function of two factors using a cubic polynomial, allowing to test the ANN approach under controlled conditions.

In the first experimental example, the optimized experimental conditions for the maximization of the research octane number (RON) are sought [5]. The second example corresponds to the optimization of the calcification process for diced tomatoes [6]. The examples are presented in the order of increasing complexity: the first one involves a single response and the second one three different responses with different criteria.

4.2.1. Simulated example

To test the results of the ANN approach in comparison with the LS one, a simulated response r has been created as a function of two factors x_1 and x_2:

$$r = 4 + x_1^3 - 2x_1^2 + x_2^3 - 2x_2^2 \tag{8}$$

This function has a maximum at $x_1 = 0$, $x_2 = 0$, with a value of 4 units. The factor values were dictated by a central composite design with five central replicates, and with extreme values of the factors of -1 and 1 in both cases. Gaussian noise with a standard deviation of 0.05 units was added to all responses.

Classical LS analysis using a second-degree polynomial leads to a residual standard deviation s_{fit} of 0.27 response units, corresponding to a lack-of-fit (LOF) probability of $p = 0.005$, indicating the presence of a significant LOF, although the value of R^2 was 0.9723. Using the estimated polynomial coefficients, the maximum value of r was predicted to be 4.13 units at $x_1 = 0.16$, $x_2 = 0.28$.

On the other hand, training an RBF with the same data using 7 hidden neurons gave considerably better results. The residual standard deviation s_{fit} of 0.057 units indicated a non-significant LOF value with $p = 0.37$ ($R^2 = 0.9992$). Moreover, modeling the response as a function of the

factors using the SRO_ANN software correctly predicted the values of the factors leading to maximum response: $x_1 = 0$, $x_2 = 0$. The maximum value of r was predicted to be 4.02 units, in closer agreement with the analytical solution.

4.2.2. Example #1: modeling and optimization of catalytic naphtha reforming

This case-study was taken from the work reported by F. M. Elfghi [5] concerning three factors affecting the maximum RON that can be obtained by reforming *n*-octane over a Pt—Re bimetallic catalyst. In the present report, we recreated the central composite design (Table 1) and analysed the results by means of surface response optimization through least-squares (SRO-LS) and artificial neural networks (SRO-ANN). Specifically, the interest is focused on the effect of reaction temperature (T, ºC), operating pressure (P, bar) and low liquid hourly space velocity (LHSV, h^{-1}) on the RON value for the corresponding reformed compound. For each experiment, RON was instrumentally measured. The final objective is to determine the factor combination improving the RON value.

The analysis of the SRO-LS results through the ANOVA test demonstrated that a linear model fits the RON response with a residual standard deviation s_{fit} of 3.05 response units, corresponding to a lack-of-fit (LOF) probability of $p = 0.086$, close to the limit of a significant LOF (0.05). The R^2 value was 0.7539, i.e. the model could only explain 75.39% of the variability in the response. Equation (9) is a mathematical expression of the obtained linear model.

$$y = 86.0 + 6.45\,x_1 - 3.93\,x_2 + 0.75\,x_3 \tag{9}$$

here y is the RON response, and x_1, x_2 and x_2 are the factors T, P and LHSV, respectively. Fig. 3 shows the normal probability plot for the residuals. As can be appreciated, the bad SRO-LS results are consistent with the apparent deviation of the residuals from the normality assumption. Notice that a different model was considered in Ref. [5], because of the inclusion of non-significant quadratic and interaction terms in the model expression.

The system was then analysed by means of SRO-ANN using 6 hidden neurons, reaching considerably better results. The residual standard deviation s_{fit} of 2.00 units indicated a clearly non-significant LOF value with $p = 0.431$ and $R^2 = 0.9269$. This better performance of RBF may be attributed to its ability to universally approximate non-linear systems. The improvement in model fit for the response can be seen in Fig. 4, which shows the correlation between actual and predicted values for the response using both models (the RBF results are taken from the output of the presently described program).

Fig. 5A and B shows the response surface and the contour plot for the response RON obtained by the application of the most reliable RBF approach for factor 1 (T, ºC) and factor 2 (P, bar), maintaining factor 3 (LHSV, h^{-1}) at a constant value (its maximum value). The optimal conditions maximizing RON correspond to 521.0 °C, 7.4 bar and 1.7 h^{-1}, rendering a RON value equal to 99.2. In sum, the RBF approach was capable of improving the model fit in comparison to what was obtained by applying LS, leading to reliably optimized results.

4.2.3. Example #2: optimization of the calcification process for diced tomatoes

This example comes from the work performed by Floros et al., 1992 [6], and is based on the optimization of a calcification process for diced tomatoes to produce firm tomato dices without excessive Ca^{2+} uptake. It comprises three factors: calcium concentration (Ca), solution temperature (Te) and treatment time (Ti), and three responses: calcium content ($y_1 = CC$), firmness ($y_2 = F$) and pH (y_3). Table 2 presents the Box-Behnken design used by the authors and recreated in this work for the present study. The three responses were analysed by means of SRO-LS and SRO-ANN. For each experiment, the total calcium content was

determined by atomic absorption spectrometry, the firmness was measured using a multiple blade share cell and computed as maximum share force, and the pH was measured using a pH-meter. The objective is to determine the optimum processing conditions that provide a final product with calcium lesser than 800 μg g^{-1}, maximum firmness, and pH as low as possible.

Using the LS methodology, the ANOVA test indicated that linear models could reasonably fit the responses F and pH, respectively, with residual standard deviations s_{fit} of 2.6 and 0.1 units, and no significant lack of fit ($p = 0.493$ and $p = 0.884$). The R^2 values were 0.880 for F and 0.835 for pH. On the other hand, the CC response showed a high s_{fit} value of 820 units, and significant lack of fit ($p = 0.039$), indicating that the model (linear with interaction between Ca and Ti) did not appropriately fit this response. A number of mathematical transformations were probed, on a trial-and-error basis, to improve this result. It was found that a square root transformation $[(CC)^{1/2}]$ led to a satisfactory two-factor interaction model, with no significant lack of fit ($p = 0.202$) and $R^2 = 0.955$. However, although this mathematically transformed model improves the fit, there appears to be no physico-chemical motivation why the CC response should be subjected to the square root.

Equations (10)–(12) are the mathematical representation of the obtained models:

$$(y_1)^{1/2} = 40.1 + 25.2\,x_1 + 10.1\,x_2 + 10.0\,x_3 - 4.4\,x_1\,x_2 + 10.0\,x_1\,x_3 \quad (10)$$

$$(y_2) = 19.9 + 5.2\,x_1 + 0.3\,x_2 + 1.9\,x_3 \quad (11)$$

$$(y_3) = 4.0 - 0.3\,x_1 + 8.3\,x_2 - 0.1\,x_3 \quad (12)$$

where y_1, y_2 and y_3 are $(CC)^{1/2}$, F and pH, and x_1, x_2 and x_3 are Ca, Te and Ti, respectively. Only the factors that are significant for the responses have been included in the above equations.

Subsequently, the factor combinations and response values were analysed applying SRO-ANN. The residual standard deviation s_{fit} of 533, 1.3 and 0.1 units indicated non-significant LOF p-values of 0.097, 0.965 and 0.983, with R^2-values of 0.977, 0.968 and 0.942, for CC, F and pH, respectively. Beyond the better numeric result for the response CC using RBF, the latter model is preferable since it implies no assumptions as to the mathematical relationship among the variables. The response fitting improvements can be appreciated in Fig. 6, which shows the correlation between actual and predicted values for the responses using both models. Fig. 7 shows the response surfaces for (CC), F and pH obtained by means of the RBF model.

Using the obtained models for each of the responses, the desirability function was applied to find the experimental conditions that minimize CC (the legal limit is below 800 μg g^{-1}) and pH, and maximize F. The obtained solutions, taking into account the models obtained by both approaches were not satisfactory since the predicted values for CC were 1631.7 and 2496.5 μg g^{-1}, respectively, values much higher than 800 μg g^{-1}.

Then, new criteria were set in order to accomplish the requirements, mainly for CC. These new criteria were to minimize CC between 700.0 and 1050.0 μg g^{-1}, maximize F between 18.50 and 20.50 Ng^{-1}, and minimize pH between 3.92 and 3.95. These criteria and the optimum combinations obtained applying both methods are presented in Table 3. The optimal value found for D in the SRO-LS case was 0.457, indicating that 45.7% of the specified criteria could be accomplished. On the contrary, for SRO-RBF case, the D value was significantly higher (0.817), meaning that the criteria were almost fully reached. In addition, higher firmness may be achieved using the RBF approach in comparison with LS, with almost the same calcium content and pH, and employing a lower treatment time. One fact that should be remarked is that both RBF and LS could minimize the pH below the predefined range. Fig. 8 shows the desirability response surface as a function a calcium concentration and solution temperature, obtained by means of LS and RBF. By applying RBF, the models for the three responses could be significantly improved in comparison to LS.

5. Conclusion

In this work, a description of SRO_ANN, a new flexible and freely available MatLab toolbox, is carried out using as a test two literature examples. In this toolbox, modeling with RBF artificial neural networks and optimization with the desirability function have been implemented.

6. Validation

Two independent reviewers, Prof. Adriano de Araújo Gomes, College of Chemistry, Natural Science Institute, Federal University of South and Southeast of Pará, Brazil, and Prof. Manuel Bravo Mercado, Facultad de Ciencias, Pontificia Universidad Católica de Valparíso, Curauma, Chile, have tested the software, and report the following statements.

Report from Prof. de Araújo Gomes: the authors developed the MatLab toolbox "SRO_ANN" in the executable and MatLab GUI versions. Both programs allow the user to load the data in txt format, carry out multiple response optimization using neural networks and generate several useful graphical and statistical parameters outputs. Not least, all this can be done with little effort and without any knowledge about MatLab. I used the program, and it works as described in the user manual.

Report from Prof. Bravo Mercado: the authors have developed a Guided User's Interface (GUI) for optimization of experimental designs based on radial basis-neural networks. I installed the interface in a windows-PC and used with Matlab 2012a. The interface includes a manual and data sets for training analysis. The GUI allows the optimization of one or several experimental responses, using desirability function for the last option. For application, the available functions are very intuitive and the network model can be easily built and validated. The data (only "txt" format) can be loaded directly from the interface, for training or validation purposes. In my opinion, this interface can be easily adapted for academic and research purposes; and, it represents a very interesting alternative to polynomial approaches for experimenters requiring optimization based in experimental design methodology.

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