THE STATISTICAL SIMPLEX METHOD FOR EXPERIMENTAL DESIGN IN PROCESS OPTIMIZATION

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Abstract

Finding optimal operating conditions fast for process systems is a key competitive factor in fine chemicals and pharmaceutical industrial sectors to increase the value added in many stages of a product/process lifecycle. To deal successfully with noise and bias in experimental optimization a statistical characterization of a local optimum that is more amenable for process outputs rather than numbers is discussed. The Kendall's statistic τ is used for characterizing candidate local optima as clusters of *strongly correlated* points. A statistical simplex algorithm that resorts to correlation-based ordering of the simplex vertices is proposed. Results obtained in the optimization of the operating policy for a semi-batch reactor are presented.

Keywords

Process development, Optimization, Simplex method, Nonparametric statistics.

Introduction

Finding optimal operating conditions fast for process systems is a key competitive factor in fine chemicals and pharmaceutical industrial sectors to increase the value added in many stages of a product/process lifecycle, including recipe development, scale-up and run-to-run optimization (Öberg and Deming, 2000). Product customization and reduced time-to-market are features of central concern to speed up process development in order to succeed against an increasing number of alternative products (Tirronen and Salmi, 2003). The drivers for experimental process optimization include compress timeliness to market of new products, increase throughput of projects, accelerate process screening for alternative products, and above all breaking the new bottleneck: *process development* (Harre, Tilstam and Weinmann, 2000).

Three factors: *noise, time and cost*, constitute major stumbling blocks to the design of algorithms for experimental optimization with process data. Process outputs often contain significant quantities of noise, or error, and sampling bias while time and money allows for only a reduced number of experimental runs or trials. Another complicating factor is often the requirement of a "black-box" system behaviour, namely the lack of *a priori* fundamental knowledge (e.g. multiple optima or continuity) about the objective function and its noisy characteristics over the input domain of interest for optimization. The *Simplex* search method proposed by Nelder and Mead (1965) has been successfully used for mathematical functions but has severe difficulties to deal with noise, bias and process discontinuities that are ubiquitous in experimental optimization problems.

This work proposes a *statistical simplex* method based on correlation ordering of the simplex vertices using sampled values of a noisy function. The main difference of the statistical simplex with regards to the Nelder-Mead Simplex is that the ranking of points in the simplex is not based on the sample values of the objective function, but on the Kendall´s τ correlation coefficients calculated for each one of the candidate optima resulting from a reflection, an expansion or a contraction operation in the current simplex. Also, a replication operation is added.

Statistical characterization of a local optimum

The function $g(\boldsymbol{x})$ to be optimized is typically unknown except for the scarce, noisy and biased information $y(\boldsymbol{x}_i), i = 1,2,....$ provided by a sequence of experimental trials. As a result, efficient detection of a local minimum or maximum in the face of output variability demands developing a statistical model for local optima. A robust and quite general assumption about sampled information in the vicinity of a minimum (maximum) is the *local monotonicity* property*:*

> "*Sampled values of the objective function for inputs* $\boldsymbol{x}_i$ *closer to a local minimum (maximum)* $\boldsymbol{x}^*$ *should exhibit a greater degree of positive (negative) correlation than those of inputs that are farther away.*"

In mathematical terms, this assumption requires that, for a given candidate optimum $\boldsymbol{x}^*$, there locally exists a monotonic relationship φ such that:

$$f(\boldsymbol{x}) = \varphi(\|\boldsymbol{x} - \boldsymbol{x}^*\|) \tag{1}$$

It is worth noting that this guiding model for a local optimum does not impose any constraint on the shape of φ in the vicinity of the minimum (maximum) as long as the function is monotonically increasing (decreasing) with respect to the distance from the optimum. Furthermore, beyond the assumption of symmetry with respect to the distance metric $\|\bullet\|$, local optimum characterization is independent of any continuousness assumption for the $g(\boldsymbol{x})$, or its derivatives. Also, there is no assumption about a given noise distribution for $y(\boldsymbol{x}_i), i = 1,2,....$. The only constraint is that the expected value of y, $E(y)$, for a given $\boldsymbol{x}$ is equal to $g(\boldsymbol{x})$.

Sampled data will locally fit the model of optima in Equation (1) to different extents. The existence of a local optimum $\boldsymbol{x}^*$ requires a monotonic association between $x_i = \|\boldsymbol{x}_i - \boldsymbol{x}^*\|$ and $g(\boldsymbol{x}_i)$. Under the influence of noise, we are interested in finding enough evidence to accept or reject the hypothesis of independence, i.e. no correlation between x_i and $y(\boldsymbol{x}_i), i = 1,2,....$, against the alternative that may correspond to a positive or negative correlation, depending if $\boldsymbol{x}^*$ is a local minimum or maximum, respectively. To test for the strength of this relationship between x_i and $y(\boldsymbol{x}_i), i = 1,2,....$, it is tackled here using nonparametric statistical methods that can be applied more broadly since much fewer assumptions about the data set need to be made. A typical non-parametric measure of correlation that can be used for this purpose is the *Kendall's correlation coefficient* τ (Sprent and Smeeton, 2000).

Denoting the ranks of x_i, y_i by r_i, s_i respectively, the Kendall's tau coefficient is defined to measure the strength of the association (correlation) between the ranks of x and y. If such dependency between the ranks exists, then if we arrange the *x*-ranks in ascending order, i.e. so that $r_i = i$, then y-ranks should show, despite noise and bias, an increasing trend when there is positive association (local minimum) or negative association (local maximum). Accordingly, Kendall (1938) proposed that after arranging observations in the increasing order of *x*-ranks, we score each paired difference $s_j - s_i$ for $i = 1,2,...,n-1$ with $j > i$ as +1 if this difference is positive and –1 if this difference is negative. Kendall called these differences *concordances* and *discordances*, respectively, with respect to an expected monotonic trend between the ranks. Denoting the sums of observed concordances and discordances by n_c and n_d respectively, the equation for the sample Kendall's coefficient τ is:

$$\tau = (n_c - n_d) \Big/ \frac{1}{2} n(n-1) \tag{2}$$

Since there exist $1/2\ n(n-1)$ pairs $s_j - s_i$, if all are concordances $n_c = 1/2\ n(n-1)$ and $n_d = 0$, then $t_K = 1$ and monotonic association is perfectly positive. Similarly, if all are discordances, monotonic association is perfectly negative with $\tau = 1$. If the rankings of x and y are independent we do expect a fair mix of concordances and discordances, whence $\tau \approx 0$. When there are not ties in the ranking $n_c + n_d = 1/2\ n(n-1)$, thus it is necessary to calculate only either the concordances or discordances (Sprent and Smeeton, 2000).

A semi-batch reactor example

Consider the chemical reaction system conducted in an isothermal semi-batch reactor, which behaves according to the 'unknown' mechanism:

$$A + B \underset{k_2}{\overset{k_1}{\Leftrightarrow}} I \xrightarrow[k_3]{} C; \qquad B + B \xrightarrow[k_4]{} D \ \text{(order 2.5)}$$

At a given operating temperature, the 'true' kinetic parameters (which are also assumed unknown) have the following *mean* values: $\boldsymbol{k}_1 = 1.1355, \boldsymbol{k}_2 = 5.0, \boldsymbol{k}_3 = 4.5239$ and $\boldsymbol{k}_4 = 3.5880$, which correspond to 'perfect' temperature control. In industrial-size batch reactors, temperature control is often far from perfect because of severe nonlinear behavior and poor modeling. As a result, the final state of each run will show unsystematic variations (see Table 1 below). The reaction system is operated in a semi-batch mode where a stream of pure *B* ($[B]_{\boldsymbol{feed}} = 0.2$ moles per liter) is added to a 1000 liters vessel which initially contains 0.2 moles per liter of *A* and no *B*, and is filled to 50%. The objective is to maximize a productivity index (see Table 1) for the process defined as follows:

$$J(x_f) = (1000 \times ([C]_f \times V_f) / t_f \tag{3}$$

For *safety* reasons in downstream processing, the final concentration of unreacted *B* cannot be greater than 0.0032 moles per liter. Hence, if the remaining *B* has a concentration greater that this maximum the batch must be allowed to continue further until a final time t_f where this threshold is achieved; as a result, the reactor productivity is decreased. Due to a heat extraction constraint the feed addition rate is limited to a maximum value of 12.0 liters min^{-1}, whereas because of production scheduling it is expected that the overall reactor cycle does not exceed 180 min.

Suppose data in Table 1 has been obtained and the optimal solution $\boldsymbol{x}^*$ is hypothesized to be one with a semi-batch period (x_1) of 40 min. and a feed rate (x_2) of 9.5 liter/min. In order to assess for this optimum's degree of fit, let's test for a positive monotonic association between $y(\boldsymbol{x})$ and $\|\boldsymbol{x}-\boldsymbol{x}^*\|$. This relationship is illustrated in Figure 1. To test for the hypothesis that the optimum is $\boldsymbol{x}=(40, 9.5)^{\mathrm{T}}$, the value of τ and its significance need to be calculated. Table 2 provides ranked data from Table 1; the paired ranks are used to calculate the statistic τ for the hypothetical optimum yielding $\tau = -0.4545$ with $n_c = 17$ concordances and $n_d = 49$ discordances.

Table 1. *Sampled data for the example*

Run #	*x*1	*x*2	Tfinal[min]	Index *J*
1	45.0	7.25	102	0.5200
2	50.0	10.00	152	0.4732
3	48.0	8.00	118	0.5099
4	55.0	9.00	156	0.4711
5	38.0	12.00	125	0.5480
6	40.0	9.5	109	0.5221
7	44.0	11.00	139	0.4816
8	54.0	9.20	156	0.4660
9	58.0	8.60	162	0.4435
10	50.0	7.00	112	0.5299
11	52.0	9.60	155	0.4795
12	55.9	9.00	160	0.4400

Testing for the significance of the hypothesis $H_0 : \tau = 0$ against the alternative $H_1 : \tau < 0$ requires a pre-calculated value of the Kendall's τ critical values for $n = 12$ and a chosen significance level $(1-\alpha)\%$ (Hollander and Wolfe, 1999). Tables give nominal 5 and 1 per cent critical values for significance when $n = 12$ in one-tail test as -0.3929 and –0.5455. Corresponding values for $n_d - n_c$ are 26 and 36, whereas an approximated Monte Carlo estimate of the exact one-tail probability *P* of rejecting H_0 when in fact it is true is 0.0396. Since $-0.4545 < -0.3929$, we reject H_0 and accept the postulated optimum with a confidence of 95%, on the other hand the available data does not provide strong statistical support to accept the postulated optimum at $\boldsymbol{x}=(40, 9.5)^{\mathrm{T}}$ with a confidence level of 99%.

Table 2. Ranked data for the example

***x*-rank**	1	2	3	4	5	6	7	8	9	10	11	12
***y*-rank**	10	7	8	5	12	9	6	3	11	4	1	2

Statistical simplex method

Simplex search methods (Nelder and Mead, 1965) resort to an effective device for parsimoniously sampling the input space in the search for an optimizer. A simplex is a set of *n*+1 points in $\Re^n$. Thus, a simplex is a triangle in $\Re^2$, a tetrahedron in $\Re^3$, etc. A non-degenerate simplex is one for which the set of edges adjacent to any vertex in the simplex forms a basis for the space. The simplex search algorithm mainly resorts to three operations: *reflection*, *expansion* and *contraction*. In the statistical simplex method, these operations are based on the correlation coefficient τ for hypothetical optima. Additionally, the statistical simplex algorithm uses a new operation, named *replication*, namely re-measuring the process output for one of the simplex vertices, e.g. the vertex exhibiting the greatest degree of correlation τ.

At the beginning of the *k*th iteration, $k \geq 0$, a non-degenerate simplex Δ_k is given along with its *n*+1 vertices, each of which is a point in $\Re^n$. One of the key issues addressed by the statistical simplex method is how vertices should be ordered. It is assumed here that iteration *k* begins by labeling and ordering the current simplex vertices as $\boldsymbol{x}_{n+1}^{(k)}, \boldsymbol{x}_n^{(k)}, ..., \boldsymbol{x}_1^{(k)}$ such that:

$$\tau_{n+1}^{(k)} \leq \tau_n^{(k)} \leq ... \leq \tau_1^{(k)} \tag{4}$$

where $\tau_i^{(k)}$ denotes the Kendall´s correlation coefficient for a given vertex under the hypothesis that it corresponds to the optimum. Assuming that the search seeks to minimize $g(\boldsymbol{x}_i)$, $\boldsymbol{x}_1^{(k)}$ is referred to as the *best* point or vertex, to $\boldsymbol{x}_{n+1}^{(k)}$ as the *worst* point and to $\boldsymbol{x}_n^{(k)}$ as the *next-worst* point.

Following ordering, the worst point can be reflected as usual:

$$\boldsymbol{x}_r = 2\,\bar{\boldsymbol{x}} - \boldsymbol{x}_{n+1} \tag{5}$$

where $\bar{\boldsymbol{x}} = \sum_{i=1}^{n} \boldsymbol{x}_i / n$ is the centroid of the *n* best point. Evaluate $y(\boldsymbol{x}_r)$ and compute its τ_r. If $\tau_r \geq \tau_1^{(k)}$, then an expansion step is done by computing the expansion point:

$$\boldsymbol{x}_e = 3\,\bar{\boldsymbol{x}} - 2\boldsymbol{x}_{n+1} \tag{6}$$

Evaluate $y(\boldsymbol{x}_e)$ and compute its τ_e. If $\tau_e \geq \tau_r$, accept $\boldsymbol{x}_e$, leave out of the next simplex the point $\boldsymbol{x}_{n+1}^{(k)}$ and terminate iteration. Otherwise, accept $\boldsymbol{x}_r$ as a replacement for $\boldsymbol{x}_{n+1}^{(k)}$ and terminate iteration. Whenever $\tau_n^{(k)} < \tau_r < \tau_1^{(k)}$ a replication of the best vertex $\boldsymbol{x}_1^{(k)}$ is done, accept $\boldsymbol{x}_r$ as a replace for $\boldsymbol{x}_{n+1}^{(k)}$ and the iteration is terminated.

A simplex contraction operation between $\bar{\boldsymbol{x}}$ and the better of $\boldsymbol{x}_{n+1}^{(k)}$ and $\boldsymbol{x}_r$ is carried out if $\tau_r \leq \tau_n^{(k)}$. If $\tau_{n+1}^{(k)} < \tau_r \leq \tau_n^{(k)}$, compute the point corresponding to an outside contraction:

$$\boldsymbol{x}_{oc} = \frac{3}{2}\,\bar{\boldsymbol{x}} - \frac{1}{2}\,\boldsymbol{x}_{n+1} \tag{7}$$

and using the current dataset calculate τ_{oc} (note that this calculation is done without actually sampling the objective function). If $\tau_{oc} > \tau_{n+1}^{(k)}$, accept $\boldsymbol{x}_{oc}$, evaluate $y(\boldsymbol{x}_{oc})$ and terminate iteration. Else perform an inside contraction:

$$\boldsymbol{x}_{ic} = \frac{1}{2}\,\bar{\boldsymbol{x}} - \frac{1}{2}\,\boldsymbol{x}_{n+1} \tag{8}$$

Evaluate $y(\boldsymbol{x}_{ic})$ and compute its τ_{ic}. If $\tau_{ic} > \tau_{n+1}^{(k)}$ accept $\boldsymbol{x}_{ic}$, leave out $\boldsymbol{x}_{n+1}^{(k)}$ and terminate iteration; else replicate the best vertex $\boldsymbol{x}_1^{(k)}$.

The main steps and logic of the statistical simplex method are summarized in Fig. 1. The rationale of *replicating* a previously tried operating condition is to improve the point-wise estimation of the process output for a given input. That is, spending some experimental effort sampling apparently inferior vertices to see if they might actually be better. The replication step gives rise the question of how best choose which vertex in the current simplex for re-measuring the process output.

At first glance, it seems convincing to select the current "best" vertex as proposed above. This is called greedy replication. The balance between exploration and exploitation can be achieved in different ways, though. One alternative to address the exploration/exploitation trade-off in the search for the optimum is resorting to random exploration in the so-called $\varepsilon - greedy$ replication. The idea is simply that with probability $(1-\varepsilon)$ the current best vertex is chosen for replication, whereas with probability ε any of the other vertices in the simplex can be selected for re-measuring the process output.

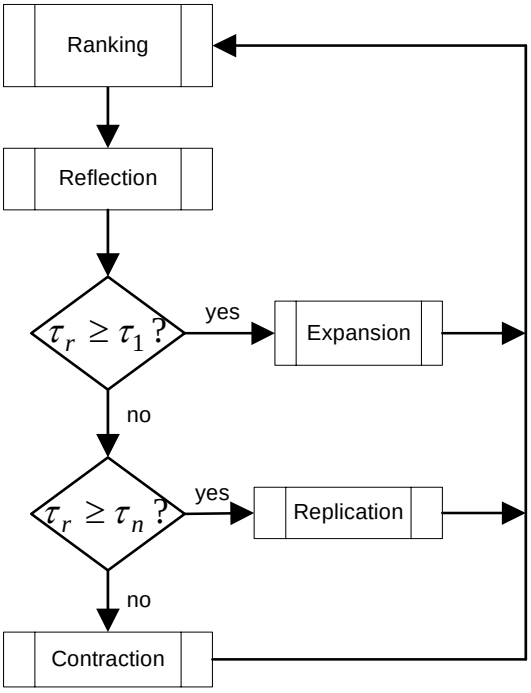

Figure 1. *The statistical simplex method*

A better method is to vary the vertex selection probabilities as a graded function of their corresponding correlation coefficient. The best vertex is still given the maximum selection probability for doing a replication experiment, but other operating conditions, even the worst vertex, are given probabilities which are dependent on their Kendall τ´s. This is called the *softmax* criterion for replication where the probability of selecting the *kth* vertex is defined as:

$$e^{\tau_k / T} \Big/ \sum_{i=0}^{n+1} e^{\tau_i / T} \qquad (9)$$

where T is a positive parameter called the "temperature". High temperatures cause all vertices in the current simplex to be nearly equiprobable for replication. As the temperature is lowered, a vertex with higher τ has greater chances of being selected. In the limit as $T \to 0$, the bias towards pure exploitation is total, i.e., the probability of selecting the best vertex tends to 1, and no room for exploration is left.

As a stopping condition in the search for the optimal condition the following ratio has been chosen:

$$\frac{\bar{g}^{k+1} - \bar{g}^{k}}{\bar{g}^{k+1}} \leq \delta \qquad (10)$$

where $\bar{g}^{k}$ stands for the output average for all the vertices in the *kth* iteration simplex and δ is a small tolerance. In the Table 3 the results obtained for different variants of the Statistical simplex method with $\delta = 0.05$ are provided.

Table 3. Results for the semi-batch reactor

	Final J	***# experiments***
greedy	0.5298	55
(**0.1**)***-greedy***	0.5304	49
softmax	0.5378	46

Final remarks

A direct search method for experimental optimization grounded on a statistical characterization of an optimum has been discussed. The logic for the statistical simplex algorithm is based on the correlation coefficients τ´s for each vertex. A *replication* operation that addresses the exploitation/exploration dilemma is proposed to deal with noise and uncontrollable factors affecting process outputs.

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