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MINIMIZING THE TIME FOR GAS CHROMATOGRAPHIC ANALYSIS

SEARCH FOR OPTIMAL OPERATIONAL PARAMETERS BY A SIMPLEX METHOD

JÓZSEF HOLDERITH*, TIBOR TÓTH and ANDRÁS VÁRADI**

Eötvös Loránd University, Department of Chemical Technology, H-1088 Budapest (Hungary)

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SUMMARY

We present an experimental approach based on the simplex algorithm to find those conditions of gas chromatography that give acceptable resolution in minimal time.

The simplex method was modified to give an opportunity for the experimentist to choose from alternatives in a heuristic way, making the search more flexible.

The utility of this procedure was demonstrated by minimizing the analysis time for a mixture of methylbenzenes.

INTRODUCTION

In gas chromatographic (GC) separations it may be important to find the optimal compromise between peak resolution and the time of analysis. Optimization procedures usually aim at finding either the minimal time necessary for acceptable resolution or a maximal resolution within a given period of time.

At present no adequate mathematical model of GC analysis is available to describe precisely the complex effect of all the operational parameters on the retention time and especially peak resolution. Theoretical determination of retention time and resolution of high-speed chromatography is impeded by the limits of validity of the general plate-height expression[1]. For the demonstration of the effect of column temperature and flow-rate of the carrier gas on height equivalent to a theoretical plate (HETP) a three-dimensional graphic presentation has been developed[2] in which HETP points are situated on the surface of a cone and the parameters of the optimal HETP value belong to the lowest point of the cone. The procedure, however, requires numerous measurements at different flow-rates and column temperatures.

The role of pressure and particle size has been emphasized in the determination of the optimal speed and resolution[3]. Another procedure described for the calculation

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* Present address: Eötvös Loránd University, Laboratory of Chemical Cybernetics, H-1088 Budapest, Hungary.
** Present address: Enzymology Department, Institute of Biochemistry, Hungarian Academy of Sciences, H-1113 Budapest, Hungary.

of retention time and resolution, in linear temperature programs, permits prediction and subsequent optimization of a given separation by temperature-programmed GC[4]. This method may be computerized, and two test runs have been shown to be enough in determining the optimal program rate at a given flow-rate and initial temperature. These authors have indicated[4] that the calculated resolution differs significantly from the measured value, owing to the neglected temperature dependence of HETP.

Optimization by real-time computer control has been published[5]. A computer, in addition to calculating and controlling the operational parameters in question, seeks the desired optimal condition by an iterative approach.

A direct computational procedure has been reported[6] for minimizing the retention time. This method, however, considers only the column length and the linear gas velocity as parameters.

Maximal resolution in a given time may be approximated by "length–temperature time normalization chromatography"[7].

If the peaks hardest to separate are followed by other peaks, the optimization is much more complicated[8].

In the present paper, we describe a simple experimental procedure for determination of the values of operational parameters at which the peak separation is sufficient in a minimal time. The approach is based on the simplex method[9] commonly used for planning of experiments. The theory of simplex planning has been extensively reviewed[10,11].

THE OPTIMIZING PROCEDURE

During optimization each experiment is characterized by the value of operational parameters k (called factors), *i.e.* by one point of the k-dimensional factor space. It may occur that some of the factors have only certain discrete values. Because certain points of the factor space can then be set on the instrument, these points are designated as realizable points. The limiting conditions —usually of the inequality type— referring to the factors are designated as permitted points. The permitted and realizable points determine the chromatogram, and the different values of its qualitative characteristics. These values could be the total analysis time, the peak resolution of pairs in question, peak asymmetry factors, etc. Those points of the factor space that meet the requirements of the qualitative characteristics are designated as acceptable points.

The aim of optimum seeking is to find the acceptable points of the realizable and permitted ones to which the minimal analysis time belongs.

Strategy of optimization

To make it easily understandable, the procedure is described in paragraphs, the numbers of the paragraphs corresponding to the serial numbers of the block diagram (Fig. 1). The unnumbered triangles represent stages in the procedure where the researcher has an opportunity to choose intuitively which route to follow.

In our strategy the experimental results are included in tables. Each table has $k + 1$ lines: each line belongs to a given experiment; the first k column contains the factors; qualitative characteristics and analysis time are indicated within further columns. In the experiment shown in line i the value of factor j is indicated as V^i_j.

Fig. 1. Block diagram of the optimizing procedure. The numbers refer to the paragraphs in the text. The unnumbered triangles refer to opportunities of intuitive choice.

(1) First, take the initial simplex. Recently Yarbro and Deming[12] have dealt with questions concerning selection and preprocessing of factors for simplex optimization.

The common feature of the method for simplex searching is that only in the first step $k + 1$ experiments can be done without any calculation. In the further steps the coordinates of the new experimental points are calculated from the coordinates of earlier simplex vertices, by moving one vertex along an axis of projection.

The starting point of the axis of projection is the vertex to be moved to which zero value of step size parameter h belongs. Another point of the axis is the gravity centre of the $k - 1$ dimensional simplex; value $h = 1$ refers to this point. Consequently, the image pair of the original simplex is associated with $h = 2$. On the other hand, $0 < h < 1$ gives a shrunken simplex in the same position as the original one; $1 < h < 2$ forms an image-positioned, shrunken simplex; and $h > 2$ forms an image-positioned, elongated simplex.

(2) Give $h = 2$ value to the step-size parameter.

(3) In the table the lines of our experimental data should be organized in the order of increasing analysis time: $t_i < t_{i+1}$ relations should be done for each $i = 1, \ldots, k$.

If the difference between two analysis times is not significant their sequence can be determined incidentally or according to their "distance" in the limiting conditions. So, in our view, the worst vertex goes into the last line $(k + 1)$ of the table.

(4) Move the last vertex, *i.e.* calculate the coordinates of the centre of gravity:

$$\overline{V}_j = \frac{1}{k} \sum_{i=1}^{k} V_j^i; \quad j = 1, \ldots, k \tag{1}$$

Next, calculate the coordinates of the new vertex:

$$V_j^0 = (1 - h) \cdot V_j^{k+1} + h \cdot \overline{V}_j \tag{2}$$

Do this first for the factors with discrete values.

If the value obtained by calculation cannot be realized (set), then we choose either of the two nearest realizable values and the values of further coordinates are calculated.

In the neighbourhood of the optimum we choose the nearest realizable value that corresponds to a smaller h value as calculated by eqn. 2 and the further coordinates are calculated with this h value.

Remark: Our strategy is applicable without any modification when instead of the arithmetic mean the weighted average is used for calculation of $\overline{V}_j$ in this step:

$$\overline{V}_j = \sum_{i=1}^{k} g_i V_j^i; \quad \sum_{i=1}^{k} g_i = 1; \quad j = 1, \ldots, k \tag{3}$$

(5) If the new vertex is not permitted, then turn to paragraph 11, 13 or 14.

(6) Carry out the experiment and write the data into the temporary line V^0 of the table.

(7) If the new vertex is not acceptable, then turn to paragraph 11, 13 or 14.

(8) When the analysis time belonging to the new vertex is longer than the previous time corresponding to the moved vertex in the last line, turn to paragraph 11 or 14.

(9) Put the line representing the new vertex into the place of the moved one in the last line of the table.

(10) If the last vertex is better than any of the previous ones, *i.e.* $t_{k+1} < t_{i\ max.}$ ($i = 1, \ldots, k$), then turn to paragraph 2 or 12.

(11) Choose a value of step-size parameter in the interval $0 < h < 1$ and turn to paragraph 4.

(12) If the repeated application of steps 11 and 13 results in the shrinkage of the simplex size, the search will be too slow. In this event, give value $h > 2$ to the step-size parameter and turn to paragraph 3.

(13) Take the value of step-size parameter in the interval $1 < h < 2$ and turn to paragraph 3 or 4.

(14) Put the last ($k + 1$st) line into the first line of the table and all the other lines will move down by one line.

The vertex that the simplex will be definitively "centered around" is considered now as an optimal point showing an accuracy governed by the actual size of the simplex in question.

APPLICATION OF THE PROCEDURE TO THE GC SEPARATION OF METHYLBENZENES

Using a multi-component mixture of methylbenzenes we were searching for optimal values of the following operational parameters: Δp, pressure drop of carrier

gas (measured by a U-tube mercury manometer); PR, rate of linear temperature program starting at sample injection; and IT, the initial temperature of the program.

Limiting conditions were as follows. Low and high temperatures were 50 and 140°; the pressure drop was limited to 4 kg/cm²; the program rate of temperature increase was in the range 0–30°/min; the rates could be selected in steps of 2°/min (i.e. 16 realizable values in the range mentioned); the value of peak separation[13] was higher than 0.5.

Our measurements were made on a JEOL-810 gas chromatograph. The column used for the process described was 3 mm × 2 m stainless steel packed with a mixed liquid phase of 5% di-isodecyl phthalate (Applied Science Labs., State College, Pa., U.S.A.) and 5% Bentone-34 (Applied Science Labs.) coated on 60–80 mesh Chromosorb W AW HMDS (Johns-Manville, Denver, Colo., U.S.A.).

Table I summarizes the operational parameters, the retention time of the last peak, the two limiting peak separation values, i.e. to p-xylene and m-xylene, 1,3,5-trimethylbenzene and 1,2,4-trimethylbenzene, for each analysis, as well as data used in the calculation of the operational parameters of the next experiment.

TABLE I

VALUES OF EXPERIMENTAL PARAMETERS AND DATA ON THE STEPS FOR THE SEARCHING PROCEDURE

Experiment No.	PR_r (°C/min)*	IT (°C)	Δp (Torr)	$t_{R max}$ Peak 9	PS Peaks 5,6	PS Peaks 8,9	h	PR_c**	Generation of simplex
1	4	60	265	26.65	0.622	0.580			Initial
2	6	70	265	20.42	0.502	0.551			simplex
3	4	70	524	17.47	0.794	0.740			
4	6	60	524	15.83	0.772	0.718			
5	6	73	610	13.57	0.762	0.699	2	6	4, 3, 2, 1
6	6	65	840	12.47	0.767	0.640	2	4.7	5, 4, 3, 2
7	8	62	792	11.59	0.740	0.643	2	8	6, 5, 4, 3
8	8	80	1194	8.01	0.613	0.514	3	8	7, 6, 5, 4
9	8	65	1274	9.31	0.660	0.505	2	8.7	8, 7, 6, 5
10	10	73	1333	7.45	0.582	0.461***	2	10	8, 9, 7, 6
11	6	78	1413	8.36	0.574	0.470***	2	6.7	6, 8, 9, 7
12	6	73	1226	9.75	0.664	0.534	1.4	7	6, 8, 9, 7
13	8	80	1622	6.88	0.512	0.393***	2	8.7	8, 9, 12, 6
14	8	71	1153	8.85	0.661	0.531	0.8	7	8, 9, 12, 6
15	10	71	1188	7.98	0.637	0.510	2	10	8, 14, 9, 12
16	10	89	1020	6.74	0.554	0.551	2.7	9.7	15, 8, 14, 9
17	10	89	1115	6.07	0.546	0.537	2	10.7	16, 15, 8, 14
18	12	86	1021	6.57	0.551	0.555	2	12	17, 16, 15, 8
19	12	105	916	5.52	0.404***	0.577	2	11.3	17, 18, 16, 15
20	12	93	1011	6.06	0.503	0.554	1.3	10.7	17, 18, 14, 15
21	14	89	1078	5.88	0.507	0.515	2	12.7	20, 17, 18, 14
22	12	94	1115	5.77	0.482***	0.512	2	12	21, 20, 17, 18
23	16	90	958	5.80	0.506	0.520	2	15.3	18, 21, 20, 17
24	14	91	1015	5.92	0.502	0.524	1.2	14.4	23, 21, 20, 18

* PR_r, program rate realized.
** PR_c, program rate calculated from eqn. 2.
*** Values are non-acceptable.

In Fig. 2 the peak separation values belonging to hardest-to-separate pairs, as well as the retention time of the last peak (1,2,3-trimethylbenzene), are plotted as the function of the steps of the procedure.
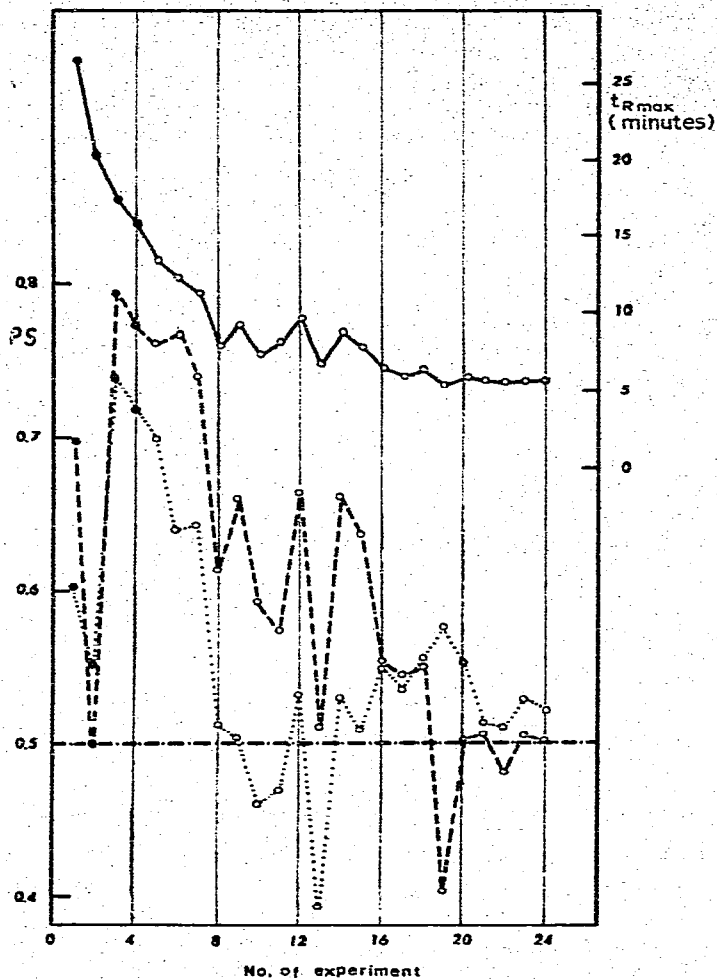

Fig. 2. The peak separation (*PS*) values belonging to the hardest-to-separate pairs and the retention time of the last peak as a function of the steps of the optimizing procedure. — — —, Peak separation value for *p*- and *m*-xylene; ······, peak separation values for 1,3,5- and 1,2,4-trimethylbenzene; ————, retention time of the last peak (1,2,3-trimethylbenzene); —·—·—·, acceptable level.

For comparison, Fig. 3a shows a chromatogram of an experiment belonging to a vertex of the initial simplex (Experiment 1 in Table I). Fig. 3b shows another chromatogram belonging to a vertex of the final simplex (Experiment 23 in Table I). This systematic approach decreased the time of analysis dramatically while retaining sufficient peak separation.
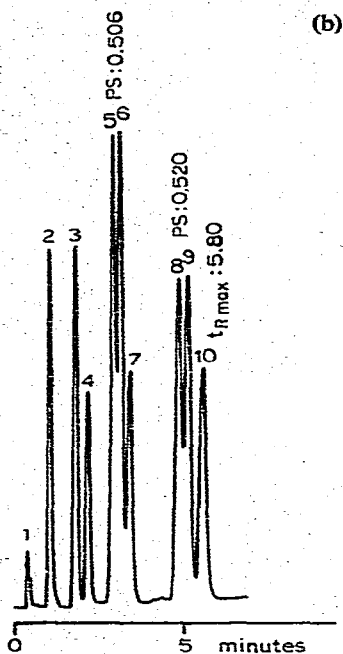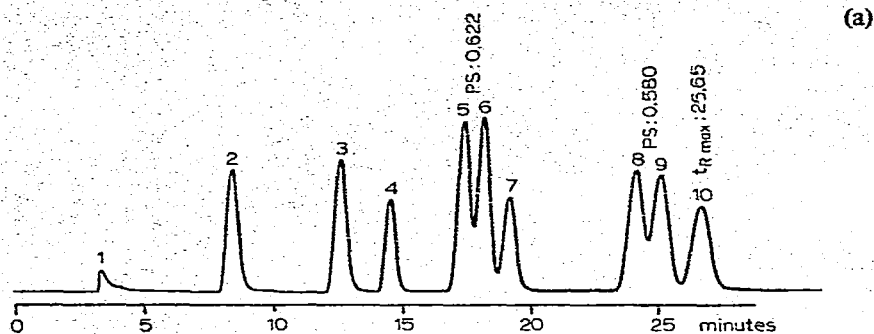
Fig. 3. a, Initial (Experiment 1 in Table I) and b, optimized (Experiment 23 in Table I) analysis of methylbenzenes by GC. 1, Solvent (CS_2); 2, benzene; 3, toluene; 4, n-nonane (internal standard); 5, p-xylene; 6, m-xylene; 7, o-xylene; 8, 1,3,5-trimethylbenzene; 9, 1,2,4-trimethylbenzene; 10, 1,2,3-trimethylbenzene.

NOTE ADDED IN PROOF

After submission of the present paper for publication, an article on the same topic appeared[14].

A part of the present work had been published in ref. 15.

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