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Comprehensive two-dimensional gas chromatography: metrics, potentials, limits

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Abstract

Metrics for evaluation of separation performance of comprehensive two-dimensional gas chromatography (GC×GC) and for quantitative comparison of that performance with similar performance of its 1D (one-dimensional) counterparts are described. The performance improvement can be expressed via reduction in the saturation of a chromatogram or—in the case of the uniform distribution of peaks along the second dimension—via the peak capacity gain due to GC×GC. An order of magnitude peak capacity gain due to the comprehensive GC×GC is possible under optimal conditions. Optimal parameters of the second dimension column as well as the optimal operational conditions for that column and for the modulator in a comprehensive GC×GC are also presented.

Keywords: Comprehensive two-dimensional gas chromatography; Separation capacity; Separation power; Optimization; Saturation

1. Introduction

Since the invention of comprehensive two-dimensional gas chromatography (GC×GC) by Phillips [1] over a decade ago, several alternative structures [2–4] and hundreds of applications of the technique have been described. Little attention, however, has been given in the literature to quantitative evaluation, and to design optimization of the comprehensive GC×GC systems, and to quantitative comparison of these systems with their 1D (one-dimensional) counterparts. This void was addressed in the lecture presented by this author at the 25th International Symposium on Capillary Chromatography in Riva del Garda, Italy, 13–17 May 2002. The content, and the flow of material in this report follows that in the lecture.

A systematic description of metrics of performance of comprehensive GC×GC as well as the treatment of optimization goals, criteria, constraints and solutions requires a space far exceeding one lecture or a single report. The goal for the lecture and for this brief report was to describe optimal solutions and to evaluate their benefits rather than to thoroughly formulate the optimization problem and its treatment. To accomplish this goal within a single report, the problem of optimization and its treatment are only briefly outlined.

In addition to providing a potentially superior separation (see below) of components in an analyte mixture, a comprehensive GC×GC analysis can also reveal a valuable information about the analyte's internal structure represented by a 2D (two-dimensional) pattern of peak distribution in a chromatogram. Even if the analyte's structure cannot be decoded from the peak pattern, the pattern itself can

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be treated as a unique 2D signature of the analyte. In any case, the very presence of a distinctive 2D peak pattern can be a powerful analyte identification tool. Generally, a pattern-based decoding of an analyte structure or a pattern-based analyte identification might not necessarily require a separation of all or even a majority of peaks, and the separation requirements for a pattern-based analysis might be very forgiving. A study of this approach, however, is outside of the scope of this report that treats comprehensive GC×GC only as a technique allowing to achieve an adequate separation of more components of an analyte that it is possible in the case of optimally designed 1D-GC.

2. Metrics

The essence of the system of metrics utilized here was described elsewhere [5,6] along with the discussion of shortcomings of several widely used metrics such as [7] resolution, R_s, separation number, etc. The word *system* emphasizes the fact that all the metrics were constructed as members of the same system, and work very well with each other. This cannot be said about the existing metrics, many of which are not compatible with each other [5]. Following is a brief review of the relevant metrics complimented by the extensions of some of them to comprehensive GC×GC.

2.1. Interaction of solutes with a column

An important metric describing a potential of two solutes, ''a'' and ''b'', of being separated in a given column is the separability,

$$\Delta g = \ln(k_b/k_a) \quad (1)$$

of the solutes where k_a and k_b are retention factors [7] of the solutes at the same temperature, T. (The ratio k_b/k_a is known as the solute selectivity.) Two solutes with a given separability, Δg, at the same temperature, can be made to elute at different temperatures where the difference, ΔT, is such that both solutes elute with the same retention factors, k. The rate:

$$\theta_{char} = dT/dg = \lim_{\Delta g \to 0} \Delta T/\Delta g \quad \text{at} \quad k = 1 \quad (2)$$

is a characteristic thermal constant [6,8] of the solutes in a given column. This quantity is not significantly different for different solutes in different columns. In a complex mixture covering a wide temperature range of several hundreds °C, an average value of θ_{char} is between 30 and 40 °C [9]. This means, for example, that a ramp covering 300 °C range (Fig. 1) covers the separability range of about 10. Generally (Fig. 1) the separability, Δg, of all components in an analyte mixture relative to one reference component represents a convenient dimensionless scale for a horizontal axis of a chromatogram.

2.2. Separation space

The key feature of the system of metrics of separation [5] utilized here is the use of the peaks' standard deviation, σ,—the measure of peak width that can be predicted from parameters of a GC system for any peak shape—as the basic and the only unit of separation. A number, S, of σ-wide intervals (briefly, σ-intervals) between two arbitrary times t_a and t_b is separation capacity of the interval (t_a, t_b). It is important to express the separation capacity, S, of an interval (t_a, t_b) via the separability, Δg, corresponding to the interval. The rate:

$$\mathscr{P}_U = dS/dg = \lim_{\Delta g \to 0} \Delta S/\Delta g \quad (3)$$

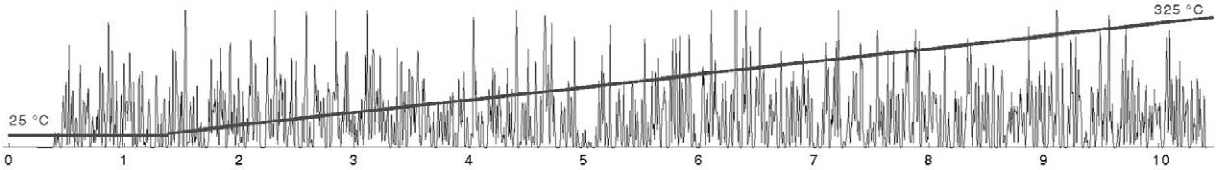

Fig. 1. Computer-generated 1D chromatogram of a 1000-component mixture separated in a column (such as 30 m×0.25 mm) with moderate separation power. A horizontal scale unit corresponds to temperature increase by 33 °C.

is utilized separation power in a given—isothermal or temperature programmed—analysis. Quantity $\mathcal{P}_U$ shows how rapidly S increases with the increase in Δg, and can be found as:

$$\mathcal{P}_U = U\mathcal{P} \tag{4}$$

where

$$\mathcal{P} = \sqrt{N} = \sqrt{L/H} \tag{5}$$

is the separation power of an N-plate column, and U is the utilization [6] (intrinsic efficiency in Ref. [6]) of $\mathcal{P}$ in a given analysis. The highest utilization, $U=1$, takes place when the solutes are well retained [6] ($k \gg 1$). These are the late elutants in an isothermal analysis, and the solutes eluting during a very slow heating ramp ($R \ll \theta_{char}/t_M$, R—heating ramp, t_M—void time) in a temperature programmed analysis [6]. While the high retention is generally favorable for the separation, it is unfavorable for the separation-speed tradeoff [10]. It has been shown elsewhere [6,10] that, in a temperature-programmed analysis with optimal heating rate (about $10\,^{\circ}C/t_M \approx 0.4\theta_{char}/t_M$):

$$U_{opt} \approx 0.8 \tag{6}$$

Because $\mathcal{P}$ is roughly the same for all peaks [6], Eq. (3) implies that the separation capacity, S_{ramp}, of a ramp covering Δg-wide separability range can be found as [6] $S_{ramp} = \mathcal{P}_U \Delta g = U\mathcal{P}\Delta g$. If, as in the case of Fig. 1, the ramp provides a major portion of the net separation capacity, S_{net}, of the analysis then

$$S_{net} \approx S_{ramp} = \mathcal{P}_U \Delta g = U\mathcal{P}\Delta g \tag{7}$$

A chromatogram in Fig. 1 corresponds to a column (such as 30 m × 0.25 mm, 12 m × 0.1 mm, 64 m × 0.53 mm, and other columns with the same ratio, L/d_c, of length, L, to internal diameter, d_c) with a moderate separation power, $\mathcal{P} \approx \sqrt{30\text{ m}/0.25\text{ mm}} \approx 350$, and $\mathcal{P}_U \approx 0.8\mathcal{P} \approx 300$. For the analyte mixture in Fig. 1, $\Delta g = 9$. Hence, $S_{net} \approx S_{ramp} = \mathcal{P}_U \Delta g \approx 2700$. A more accurate evaluation of S_{net} (accounting for S in the initial temperature plateau [6]) yields $S_{net} \approx 3000$. This is equivalent to assuming that $\Delta g = 10$.

2.3. Quality of separation of peaks

The separation, S, of two peaks having retention times $t_{R,a}$ and $t_{R,b}$ is the same as the separation capacity of interval ($t_{R,a}$, $t_{R,b}$). For example, for peaks of any shape, $S=6$ means that there are six σ-intervals between $t_{R,a}$ and $t_{R,b}$. (For adjacent Gaussian peaks that are not very far apart from each other, $R_s = 4S$ [5]. For example, for Gaussian peaks, $S=6$ corresponds to $R_s = 6/4 = 1.5$.)

Let S_{min} be a critical [11], i.e., the lowest acceptable, separation of two adjacent peaks. The peak capacity [5], n_c, of an arbitrary interval having separation capacity S is $n_c = S/S_{min}$, and the net peak capacity [12], $n_{c,net}$, of the entire analysis is:

$$n_{c,net} = S_{net}/S_{min} \tag{8}$$

A revealing metric of quality of separation is saturation, α, of a chromatogram, known from Giddings and Davis [11,13]. This quantity can be found as:

$$\alpha = m/n_{c,net} = mS_{min}/S_{net} \tag{9}$$

where m is a number of components in the analyte mixture. Assuming that in the 1000-component chromatogram ($m=1000$) of Fig. 1, $S_{min}=6$, one has: $n_{c,net} = 3000/6 = 500$, $\alpha = m/n_{c,net} = 1000/500 = 2$. A relationship between the saturation and a quality of separation is illustrated by the data in Table 1.

Table 1
Affect of saturation [11,13], α, on quality of separation

Saturation, α	2	1	0.5	0.2	0.1
Singlets, $e^{-2\alpha}$ (%)	1.8	14	37	67	82
Doublets, $e^{-2\alpha}(1-e^{-\alpha})$ (%)	1.6	8.2	15	12	7.8
Clusters (singlets + doublets + triplets + ⋯), $e^{-\alpha}$ (%)	14	37	61	82	91
Components per cluster (average), e^{α}	7.4	2.7	1.6	1.2	1.1

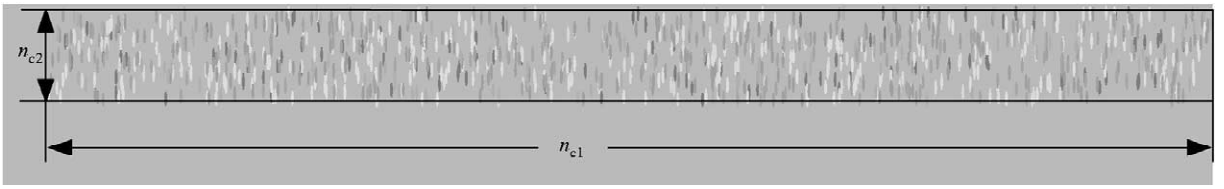

Fig. 2. Comprehensive GG×GC chromatogram of a 1000-component mixture. $\mathcal{P}_1 = 350$ (the same as $\mathcal{P}$ in Fig. 1), $\mathcal{P}_2 = 50$.

2.4. Comprehensive GC×GC

There are many ways to reduce α for a fixed number of components, m, in an analyte mixture. One way (and, some times, the only practical way) is to increase S_{net} in Eq. (9) by increasing the utilized separation power, $\mathcal{P}_U$, Eq. (7), using comprehensive GC×GC (Fig. 2). In that case, quantities Δg, n_c, $\mathcal{P}$, S, U in Eqs. (4) and (7)–(9) can be interpreted as

$$n_c = n_{c,GC\times GC} = n_{c1} n_{c2} \tag{10a}$$

$$S = S_{GC\times GC} = S_1 S_2 \tag{10b}$$

$$U = U_{GC\times GC} = U_1 U_2 \tag{10c}$$

$$\mathcal{P} = \mathcal{P}_{GC\times GC} = \mathcal{P}_1 \mathcal{P}_2 \tag{10d}$$

$$\Delta g = \Delta g_{GC\times GC} = \Delta g_1 \Delta g_2. \tag{10e}$$

3. Potentials

To arrive to specific and representative results, several simplifying assumptions were made. Among them were the assumptions that the columns in both dimensions as well as the thermo-modulator have the same diameter and share the same flow, the separability range, $\Delta g_2 = \ln(k_{last2}/k_{first2})$, in the second dimension can be estimated as $\Delta g_2 = 1$, the analysis is temperature programmed in the first dimension and isothermal in each second dimension run. The time of analysis in the second dimension is critical for the entire system. Using vacuum outlet (with MSD, specially designed TCD, etc.) can, in some cases, substantially reduce the analysis time [14]. Below, the vacuum outlet for a column in the second dimension is assumed. This assumption also simplifies the analysis of the system optimization and leads to simple results (Table 2). It is also assumed that, a modulator has a nearly ideal performance which, in the case of a thermo-modulator, means nearly 100% retention of all solutes during their accumulation, and diminishing retention during their release. The latter might require a cryogenic cooling below the column temperature, T_{col}, during a sample accumulation, and active heating above T_{col} during the sample release. While all these assumptions are reasonable, they are not the only alternatives in designing a GC×GC system. Some assumptions, such as $\Delta g_2 = 1$, require more experimental data.

The potentials of GC×GC were evaluated at optimal conditions corresponding to maximal utilized separation power, $\mathcal{P}_U$, of the whole GC×GC system that can be achieved with the same column in the first dimension running at SOF [15] (speed-optimized flow-rate) and optimal heating rate [10] in both cases. At SOF, a column plate number, N, in Eq. (5) can be estimated as:

$$N = L/d_c \tag{11}$$

Table 2
Parameters of the second dimension column and a thermal modulator

Symbol	L_2	L_{mod}	γ_{mod}	t_{inj2}	t_{anal2}	σ_{M2}	f
Formula 1 (via d_c, L_1)	$d_c^{1/3} L_1^{2/3}$	$1.6 d_c^{2/3} L_1^{1/3}$	$0.5(d_c/L_1)^{1/3}$	$2.5 d_c^{1/3} L_1^{2/3} r$	$5 L_1 r$	$d_c^{1/3} L_1^{2/3} r$	$2/(d_c^{1/3} L_1^{2/3} r)$
Formula 2 (via d_c, $\mathcal{P}_1$)	$d_c \mathcal{P}_1^{4/3}$	$1.6 d_c \mathcal{P}_1^{2/3}$	$0.5/\mathcal{P}_1^{2/3}$	$2.5 d_c \mathcal{P}_1^{4/3} r$	$5 d_c \mathcal{P}_1^{2} r$	$d_c \mathcal{P}_1^{4/3} r$	$2/(d_c \mathcal{P}_1^{4/3} r)$
Value (He/H_2)	0.61 m	2 cm	0.01	8.6 ms/5.1 ms	0.87 s/0.51 s	3.5 ms/2.1 ms	570 Hz/960 Hz

Symbols and comments. Second dimension: L_2, column length; t_{inj2}, injection time; t_{anal2}, analysis time; σ_{M2}, standard deviation of unretained peak; f, data rate. Modulator: L_{mod}, length; $\gamma_{mod} = t_{inj2}/t_{anal2}$, duty cycle. Parameter r: 5.8 ms/m for helium, 3.5 ms/m for hydrogen [18]. All values correspond to 30 m×0.25 mm column in the first dimension.

It can be shown (see Appendix A.1) that optimal retention factor, k_{last2}, of the last elutant in the second dimension is:

$$k_{last2} \approx 4 \quad (12)$$

This, along with requirements for optimal modulation leads to conclusion that (see Appendix A.2):

$$\mathcal{P}_2 = \mathcal{P}_1^{2/3}, \quad \text{and} \quad \mathcal{P} = \mathcal{P}_1\mathcal{P}_2 = \mathcal{P}_1^{5/3} \quad (13)$$

As in the case of a 1D-GC, the whole separation power of a GC×GC is not utilized under optimal conditions. On top of about 80% utilization of $\mathcal{P}_1$ in 1D-GC, there is about 70% (Eq. (A.7) in Appendix A.1) utilization of $\mathcal{P}_2$. The utilization of each dimension further drops due to modulation which lowers $\mathcal{P}_{U1}$ to about 80% of its one-dimensional value (Eq. (A.20) in Appendix A.2) and has about the same effect on $\mathcal{P}_{U2}$. As a result, $U_{opt} = 0.4$ for the entire GC×GC system. This, due to Eqs. (7), (8) and (13) along with the conventions described in Eq. (10) leads to conclusion that the net gain, G_n, in peak capacity due to the addition of the second dimension can be estimated as:

$$G_n = n_{c,net,GC\times GC}/n_{c1,net} \approx 0.5\mathcal{P}_1^{2/3}/S_{2,min} \approx 0.6\mathcal{P}_{1U}^{2/3}/S_{2,min} \quad (14)$$

where $\mathcal{P}_{1U}$ is the utilized separation power of 1D-GC performed with the same column and the same conditions as the ones used in the first dimension of GC×GC. Eq. (14) suggests that

The better is the original 1D-system (high $\mathcal{P}_{1U}$) and the more tolerant is the whole GC × GC system to low separation of adjacent peaks in the second dimension, the greater is the improvement from adding the second dimension

For a chromatogram in Fig. 1 ($\mathcal{P}_{1U} = 300$), $S_{min} = 6$ yields $G_n \approx 4.5$, $S_{min} = 3$ yields $G_n \approx 9$, etc.

To express Eq. (14) in more familiar terms of a peak resolution, R_s, and column plate number, N, we shall notice that if all peaks are Gaussian or nearly Gaussian in the second dimensions then $S = R_s/4$ [5]. Accounting for this relation and for Eq. (5) in Eq. (14) yields:

$$G_n \approx 0.13N_1^{1/3}/R_{s,2,min} \quad (15)$$

where N_1 is a number of plates in the first dimension column, and $R_{s,2,min}$ is the lowest acceptable resolution in the second dimension. For a chromatogram in Fig. 1 ($N_1 = 120\,000$), $R_{s,2,min} = 1.5$ yields $G_n \approx 4.3$, $R_{s,2,min} = 0.75$ yields $G_n \approx 8.6$, etc. (The difference between these results and the results in the previous example comes from the simple number approximations of all parameters and quotients in the last two equations.)

Among other important characteristic of a separation system is its sample capacity [16], detection limit [17] and linear range. It can be shown (see Appendix A.3) that if, like in the case of a thermomodulation, the entire sample is transferred from the first to the second dimension column then the addition of the second dimension, while reducing the sample capacity, changes neither the linear range nor the minimal detectable concentration (MDC) of comprehensive GC×GC.

4. Limits

Optimal parameters of the second dimension column and the modulator are summarized in Table 2. They all follow directly from the above-listed equations combined with the formulae provided in Appendixes A.1 and A.2 below and with conventional formulae know from GC textbooks [11,16,17].

Shown in the previous section, about an order of magnitude gain in peak capacity due to addition of the second dimension is significant, but not overwhelming. The gain can vanish if the system is not optimized. This can happen because of the very demanding requirements (Table 2) to the modulator and to the second dimension column. Implementation of each parameter specified in Table 2 represents a challenge of one sort or another. For example, all formulae in Table 2 are based on the assumption of vacuum at the outlet of the second dimension column. Otherwise, the modulation requirements can, in some cases, lead to substantial reduction in the net system peak capacity, $n_{c,net}$. For example, in the case of a 30 m×0.25 mm column in the first dimension, replacing vacuum with ambient pressure

Fig. 3. GG×GC chromatogram of a 1000-component mixture with a distinctive pattern of peaks. $\mathcal{P}_1 = 350$, $\mathcal{P}_2 = 50$ (the same as in Fig. 2).

at the column outlet in the second dimension would cause about 2-fold reduction in peak capacity gain.

It should also be pointed out that the peak capacity gain does not necessarily reduce the saturation of a chromatogram. This might happen when, due to its distinctive 2D pattern (Fig. 3), the 2D distribution of peaks is substantially not-uniform. As mentioned in Introduction, the revealing of a 2D pattern of peak distribution can be a primary goal of a GC×GC analysis. This approach might have a little concern for the separation of adjacent peaks, and, in that regard, can be substantially different from comprehensive GC×GC if the term comprehensive (i.e., all-inclusive) is understood to emphasize the goal of a satisfactory separation of a majority (or all) adjacent peaks.

5. Conclusion

Under optimal conditions, comprehensive GC×GC can provide an order of magnitude lower saturation of a chromatogram compared to its 1D counterpart based on a column with the same internal diameter and requiring the same analysis time. This improvement, coming from an order of magnitude peak capacity gain, is significant, but not overwhelming, and can vanish if the system is not optimized. Unfortunately, the latter is a real possibility because the optimal conditions described in the report can be very challenging: vacuum outlet in the second dimension column should be used (otherwise, the gain can become twice as low), a thermo-modulator might need to be shorter than 1 or 2 cm, sample introduction time in the second dimension column might not be allowed to exceed several milliseconds, 1 kHz or higher data rate might be required, etc. In addition to that, the peak capacity gain reduces the saturation only if the peak distribution along the second dimension is substantially uniform. These challenges might make it impossible for some implementations of comprehensive GC×GC to provide a higher number of resolved peaks compared to their 1D counterparts. It is hoped, however, that the very fact of clear formulation of the challenges provided in this report can by itself serve as a basis for further developments of the technique of comprehensive GC×GC

Appendix A

A.1. Optimal retention factor, k_{last}, at the end of analysis in isothermal GC

It has been shown elsewhere [6] that, in isothermal GC, the separation capacity, S, of a Δg-wide interval can be found as $S = \mathcal{P}\ln(1+(e^{\Delta g}-1)k_{first}/(1+k_{first})) = \mathcal{P}\ln(1+(e^{\Delta g}-1)k_{last}e^{-\Delta g}/(1+k_{last}e^{-\Delta g})) = \mathcal{P}(\Delta g + \ln((1+k_{last})/(e^{\Delta g}+k_{last})))$ where k_{first} and k_{last} are the retention factors of the first and the last peak in a chromatogram relating as, Eq. (1), $k_{last}/k_{first} = e^{\Delta g}$. In our case of isothermal analysis in the second dimension, $\Delta g = \Delta g_2 = 1$. This reduces the previous expression to:

$$S = \mathcal{P}(1 + \ln((1 + k_{last})/(e + k_{last}))) \quad (A.1)$$

Let $t_{anal} = (1+k_{last})t_M$ be analysis time measured as retention time of the last peak, and $\tau = t_{anal}/t_M$ be the normalized analysis time. A substitution of:

$$k_{last} = \tau - 1 \quad (A.2)$$

in Eq. (A.1) allows to write

$$S = \mathcal{P}(1 + \ln(\tau/(e - 1 + \tau))) \quad (A.3)$$

Eqs. (A.3) and (A.2) illustrate a known fact [6] that increasing the retention of all solutes (via

lowering a column temperature, or increasing amount of stationary phase) increases S. Unfortunately, the rate of increase in S declines with the increase τ. Eq. (A.3) also shows that, as an alternative way, S can be raised by raising $\mathcal{P}$ via increase in the column length at a fixed k_{last} instead of raising k_{last} and, hence, τ. In that case, when column outlet is at vacuum, $\mathcal{P}$ is proportional to $t_M^{1/3}$ [10], and, because τ is fixed,—to $t_{anal}^{1/3}$, i.e.

$$S \sim t_{anal}^{1/3} \tag{A.4}$$

Both ways of raising $\mathcal{P}$ cause an increase in t_{anal}. The preference, therefore, should be given to the way that offers a larger payoff for the same increase in t_{anal}. An analytical solution to this tradeoff does not seem to exist. A numeric analysis of Eqs. (A.3) and (A.4) show that up to k_{last} slightly over 4, raising k_{last} is preferable to raising t_M. After that, raising t_M becomes more effective way of raising S. This suggests that if, in an isothermal analysis, a column outlet is at vacuum and the sample separability range is $\Delta g = 1$ then the column temperature and/or the amount of stationary phase should be arranged in a way leading to:

$$k_{last,opt} \approx 4 \tag{A.5}$$

To evaluate the utilization, U_{opt}, of the separation power of the second dimension column, let us notice that, according to its definition, Eq. (3), the utilized separation power, $\mathcal{P}_U$, is the separation capacity, S, of a unit-wide separability range ($\mathcal{P}_U = S$ when $\Delta g = 1$). This is the case for Eq. (A.1) indicating that, in view of Eq. (4), U corresponding to Eq. (A.1) is:

$$U = 1 + \ln((1 + k_{last})/(e + k_{last})) \tag{A.6}$$

Substitution of Eq. (A.5) in Eq. (A.6) results in

$$U_{opt} \approx 0.7 \tag{A.7}$$

A.2. Optimal separation power in second dimension

Each second dimension run in GC×GC can be preceded by one or more stages of modulation. The latter consists of accumulation of a sample exiting the first dimension column followed by quick release of the accumulated sample. Ideally, the accumulation time is the same as the analysis time, t_{anal2}, in the second dimension. From the data analysis point of view [19], the modulation can be treated as a simple moving-average filtering followed by an ideal sampling. A result of the repetition of the second dimension analyses is a collection of the second dimension chromatograms. In order to construct a 2D-chromatogram from this collection, the second dimension chromatograms should be connected with each other using one of many possible interpolation techniques [19]. The interpolation can also be treated as data filtering. A linear interpolation is equivalent to a simple moving-average filtering similar to one involved in the modulation, and having also accumulation time t_{anal2}. A collection of all filtering processes involved in the first dimension aspect of a final 2D-chromatogram can be treated as a single combined filter. Its net effect can be described by standard deviation, σ_f, of the filter's impulse response. A ratio:

$$a = \sigma_f / t_{anal2} \tag{A.8}$$

depends on the filter composition. For a filter composed of i stages of t_{anal2}-long simple moving-average filters:

$$a = \sqrt{i/12} \tag{A.9}$$

The filtering involved in the sample modulation and in the first dimension data reconstruction broadens the first dimension projections of all peaks, thus reducing the utilization, U_1, of the separation power, $\mathcal{P}_1$, of first dimension. This reveals the following tradeoff between the separation power, $\mathcal{P}_2$, in the second dimension, and the net utilized separation power, $\mathcal{P}_U$, of the entire GC×GC system which, according to Eqs. (4) and (10), can be expressed as:

$$\mathcal{P}_U = U_1 U_2 \mathcal{P}_1 \mathcal{P}_2 = U_{1o} U_{mod} U_2 \mathcal{P}_1 \mathcal{P}_2 \tag{A.10}$$

In this expression, the utilization, U_1, of the first dimension is represented via two components: the stand-alone utilization, $U_{1o} \approx 0.8$, Eq. (6), and the modulation-caused utilization, U_{mod}, in comprehensive GC×GC. With $\mathcal{P}_1$, U_{1o} and U_2 fixed (the latter is $U_2 = U_{2,opt} \approx 0.7$, Eq. (A.7)), $\mathcal{P}_U$ becomes proportional to $U_{mod}\mathcal{P}_2$, i.e.

$$\mathscr{P}_U \sim U_{mod}\mathscr{P}_2 \tag{A.11}$$

Quantity U_{mod} can be found as $U_{mod}=\sigma_{o1}/\sqrt{\sigma_{o1}^2+\sigma_f^2}$ where σ_{o1} is the standard deviation of the peaks in a stand-alone first dimension. According to the previous observations,

$$U_{mod}=\sigma_{o1}/\sqrt{\sigma_{o1}^2+\sigma_f^2}=\sigma_{o1}/\sqrt{\sigma_{o1}^2+a^2t_{ana2}^2} \tag{A.12}$$

$$t_{anal2}=(1+k_{last2})t_{M2}=(1+k_{last2})\mathscr{P}_2\sigma_{M2}=(1+k_{last2})\mathscr{P}_2 rL_2 \tag{A.13}$$

The last transition is based on relation [18]

$$\sigma_M=rL \tag{A.14}$$

where σ_M is the standard deviation of unretained peak, and r is a gas-dependent constant specified in Table 2. Due to Eqs. (5) and (11), Eq. (A.13) can be written as:

$$t_{anal2}=(1+k_{last2})\mathscr{P}_2^3 rd_c \tag{A.15}$$

Turning now to σ_{o1} in Eq. (A.12), we notice first that, during a linear heating ramp covering a wide separability range (Fig. 1), all peaks elute with nearly the same width [6] that can be found as:

$$\sigma_{o1}=\sigma_{M1}/\mu \tag{A.16}$$

where $\mu=$is mobility factor [20] of eluting solutes. Accounting for Eqs. (A.14), (5) and (11), Eq. (A.16) yields:

$$\sigma_{o1}=rL_1/\mu=\mathscr{P}_1^2 rd_c/\mu \tag{A.17}$$

Eqs. (A.15) and (A.17) allow to rewrite Eq. (A.12) as

$$U_{mod}=\mathscr{P}_1^2/\sqrt{\mathscr{P}_1^4+(\mathscr{P}_2/b)^6/2} \tag{A.18a}$$

$$b=(\sqrt{2}a\mu(1+k_{last2}))^{-1/3} \tag{A.18b}$$

Substitution of this expression in Eq. (A.11) yields $\mathscr{P}_U\sim\mathscr{P}_1^2\mathscr{P}_2/\sqrt{\mathscr{P}_1^4+(\mathscr{P}_2/b)^6/2}$. This quantity has a maximum at

$$\mathscr{P}_{2,opt}=b\mathscr{P}_1^{2/3} \tag{A.19}$$

Substitution of this condition in Eq. (A.18) yields:

$$U_{mod,opt}=\sqrt{2/3}\approx 0.816 \tag{A.20}$$

To find a numeric value for b in Eqs. (A.18) and (A.19), we recall [6,10] that at optimal heating rate, $\mu\approx 1/3$. For this value accompanied by Eq. (A.5), and by the assumption that, in Eq. (A.9), $i=2$, Eq. (A.18) for b yields, $b\approx 1.013\approx 1$, allowing to write Eq. (A.19) as:

$$\mathscr{P}_{2,opt}\approx\mathscr{P}_1^{2/3} \tag{A.21}$$

A.3. Linear range of a GC×GC system

Ability of a GC system to detect and measure low concentration solutes is limited by two major factors. On one hand, a column has limited sample capacity—the amount of sample that can be injected in a column without substantially reducing its separation power. On the other hand, there is a background noise in each detector. This limits the low level concentrations that can be detected and measured with required accuracy. Both the column sample capacity and the noise level can be expressed in several ways. The ratio of these two quantities is the linear range of the system.

The sample capacity of a column can be expressed via the largest volume, V_{max}, of a liquefied injected sample zone. The radial depth and the perimeter of that zone are equal to the film thickness, d_f, and to the column diameter, d_c, respectively. Let H and L be, respectively, plate height and length of a column. The limit to the axial width of the injected sample zone can be found from the following consideration. A spatial standard deviation, σ_L, of a non-overloading solute zone at the end of a column can be found as [21] $\sigma_L=\sqrt{HL+\sigma_i^2}$, where σ_i is the axial standard deviation of the injected sample zone. This means that, in order to avoid a substantial loss in the separation, σ_i should be a small fraction of $\sqrt{LH}$. This leads to the conclusion that V_{max}, changes in proportion to $d_c d_f\sqrt{LH}$, i.e.

$$V_{max}\sim d_c d_f\sqrt{LH} \tag{A.22}$$

If (as in the case of the first and the second dimension columns in this report) two columns have the same diameter and flow-rate then their plate heights, H, relate to the diameter, d_c, in approximate-

ly the same way, i.e., $H \sim d_c$. This allows to further simplify Eq. (A.22) as:

$$V_{max} \sim d_c^{3/2} d_f L^{1/2} \quad (A.23)$$

Turning to the noise in a GC system, we should notice that it can have several components (detector noise, chemical noise, etc.). In principal, many of the noise components can be eliminated or substantially reduced. However, a detector electronic noise cannot be reduced below a certain level limited by the white noise (a noise with a fixed spectral density) [22]. If necessary, the data acquired from the detector can be filtered in a data system to eliminate all those spectral components of the white noise that can be eliminated without substantially increasing the widths, σ, of the peaks. The noise level, n_E (expressed as root-mean-square, as ''peak-to-peak'' value, etc.) that will remain after the filtering is inversely proportional to $\sqrt{\sigma}$, i.e.

$$n_E \sim 1/\sqrt{\sigma} \quad (A.24)$$

Quantities V_{max} and n_E can be used to define the linear range of a GC system. The shortest way to do so is to notice that, in the case of a white noise, the random error, ε, of a peak area measurement (by integration) is proportional to $\sqrt{\sigma}$, i.e. [22]:

$$\varepsilon \sim \sqrt{\sigma} \quad (A.25)$$

If necessary, ε can be expressed in units of a sample volume [23], allowing to define a dimensionless linear range, Λ, of a GC system as:

$$\Lambda = V_{max}/\varepsilon \quad (A.26)$$

Eqs. (A.23) and (A.25) allow to write

$$\Lambda \sim d_c^{3/2} d_f L^{1/2}/\sigma^{1/2} \quad (A.27)$$

At high pressure drop (column inlet pressure is much higher compared to outlet pressure as in the case of vacuum outlet), σ can be found as [18]:

$$\sigma = (1 + k) r L \quad (A.28)$$

where k is a solute retention factor (in case of a temperature-programmed analysis, k is measured at the time of the solute elution) and r (Table 2) is a parameter that does not depend on column dimensions. Substitution of this relation in Eq. (A.27) yields:

$$\Lambda \sim d_c^{3/2} d_f/(1 + k)^{1/2} \quad (A.29)$$

The result would be the same if, for example, Λ was defined as the ratio of maximum peak height and the noise level, n_E, Eq. (A.24).

Eq. (A.29) leads to the following observation. In case of a high column pressure drop (and, particularly, vacuum outlet) the linear range of a GC system does not depend on the column length. Therefore, when used with the same detector (appropriately filtered in each case), a GC×GC system using the same column diameter in both dimensions has the same linear range as the stand-alone first dimension has for the peaks with the same retention. This also means that, in the analysis of the same mixture, addition of the second dimension does not change the system MDC (minimum detectable concentration) for any solute that is sufficiently separated in one-dimensional GC and in GC×GC and has the same retention in both cases.

Example. In the case of a 30 m×0.250 mm column in the first dimension, the optimal second dimension column is (Table 2), 0.6 m long—a 50-fold reduction in length. Following are the factors affecting the linear range of GC×GC.

(1) The **sample capacity**, V_{max}, Eq. (A.23), of the short second dimension column (and, hence, of the entire GC×GC) is about seven times lower ($50^{1/2} \approx 7$) compared to that of the first dimension column. (If a stand-alone first dimension was close to the upper limit of its sample capacity then seven times less sample should be injected in case of GC×GC.)

(2) **Peak area measurement error**, ε. The peaks out of the second dimension column are 50 times narrower (Eq. (A.28)) than the equally retained peaks would be in case of the stand-alone first dimension. As a result (Eq. (A.25)), ε, is about seven times lower compared to that in case of the first dimension column.

The **net result**: Λ in Eq. (A.26) is the same in both cases. (End of example.)

Consider now the role of the factor $(1+k)^{1/2}$ in Eq. (A.29). Notice that at the optimal heating rate in the first dimension $k \approx 2$ for all peaks eluting during the ramp [6,10]. On the other hand, second dimen-

sion in comprehensive GC×GC is isothermal with $k>2$ for most of the solutes. For all those solutes, Λ (Eq. (A.29)), is lower compared to Λ in a stand-alone first dimension. Accordingly, MDC for those solutes is higher (worse) in GC×GC compared to MDC in a stand-alone first dimension. This suggests that GC×GC is, typically, unfavorable for Λ and MDC (although, typically, on a minor scale).

Example. For a solute eluting at $k_1=2$ from the first dimension column, and at $k_2=4$—from the second dimension column, there is about 1.3 reduction in Λ $(((1+4)/(1+2))^{1/2}\approx 1.3)$ and 1.3 increase (worsening) in MDC. (End of example)

It is also worth mentioning that the results in this section are based on the assumption of the vacuum outlet at the second dimension column, and the sample conservation in the modulator. Departure from either of these assumptions is unfavorable for Λ and MDC in GC×GC. It can be shown, e.g., that in the case of ambient outlet pressure and low pressure drop, $\Lambda \sim L^{1/4}$. There are also minor factors that might be favorable for Λ and MDC in GC×GC. However, the above analysis suggest that, for the sufficiently separated solutes, there is no reason to expect that GC×GC should be more favorable for Λ and MDC than its first dimension standing alone.

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