Advancing GC×GC through integrated sample preparation methods and optimized column formats

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Chapter 6

Comprehensive two-dimensional gas chromatography under high outlet pressure conditions

Summary

The column sets typically employed in comprehensive two-dimensional gas chromatography (GC×GC) suffer from the impossibility to fully exploit the efficiency of both dimensions simultaneously. At the high inlet pressures required to reach the optimum of the first dimension (1D) the linear velocity in the second dimension (2D) is far above optimum. Adding a restrictor at the end of the 2D is a possible approach to adjust the linear velocity profile. Under these high outlet pressure conditions the 2D becomes much slower while the effect on the 1D is limited. The gap in terms of optimum inlet pressures is thus reduced. A programme written in Microsoft Excel was used to calculate the efficiencies of the two dimensions in GC×GC at different outlet pressures. A GC×GC set-up with a restrictor at the end of the 2D was successfully installed. Experiments proved that it is possible to enhance the performance of the columns. For example the experimental plate height of the 2D at the 1D optimum for n-decane improves from 0.33 mm to 0.11 mm by installing the restrictor. The chromatograms obtained for a number of applications also confirmed that the separations achieved at elevated outlet pressure with the same column set with this new method are more efficient than under atmospheric outlet conditions. On the other hand, the considerably longer analysis times are a significant drawback. Alternative procedures which can achieve the same objective at a shorter analysis time are clearly more advantageous.

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6.1. Introduction

Comprehensive two-dimensional gas chromatography (GC×GC) nowadays is the method of choice for the analysis of very complex samples of volatile analytes. The main advantages of the technique are its remarkable resolving power, the unmatched peak capacity and the good sensitivity [1-5].

The standard GC×GC column sets consist of a long, normal-bore first dimension (1D) column and a short, narrow-bore second dimension (2D) column. Thanks to the use of the short narrow-bore column in the 2D very fast second dimension separations can be obtained while providing very high efficiency. This way, the 2D separation of each re-injected time-slice is completed before the injection of the following. However, due to the large difference in column diameter a flow mismatch occurs between the two columns making it impossible to operate both columns at their respective optimum linear velocity at the same time [6]. At low inlet pressures the separation in the 2D is fully exploited, but the carrier gas velocity in the 1D is below optimum. When higher inlet pressures are selected to obtain optimum performance in the 1D, the linear velocity in the 2D is far above optimum. Therefore the potential of the GC×GC column set is not fully exploited.

Stop-flow GC×GC [7-9] was presented as a solution to regulate the carrier gas flows in the two columns independently. In this approach the first dimension flow is periodically stopped for a short time. During these pauses the second dimension separation is performed by delivering the carrier gas into the 2D via an auxiliary inlet. This way, the modulation time and the duration of the separation in the 2D are decoupled and both separations can be performed at their respective optimum. The main limitations of this method are the need for additional hardware and the complexity of the instrumental set-up. Another interesting approach was described by Tranchida et al. [10, 11]. These authors installed a splitter between the two dimensions to reduce the flow of carrier gas entering the 2D. This allows using high gas flow rates to operate the 1D at its optimum while maintaining the velocity in the 2D at a suitable value. On the other hand, splitting the flow unfortunately results in poorer detection limits. The use of wider second dimension columns is also an obvious solution [12, 13]. By increasing the i.d. of the 2D the flow
mismatch is reduced or completely solved. However, with such a column set it is not possible to respect the modulation criterion. In chapter four and five the use of monolithic columns and multiple parallel columns as 2D in GC×GC to resolve the flow mismatch [14, 15]. The advantage of using monoliths is that efficiency and column diameter (and hence flow rate) can be optimized independently. Simultaneously operation of the two dimensions at their optimum was achieved. However, the preparation of appropriate monoliths is rather challenging and the efficiency obtained is not yet comparable to that of standard GC×GC set-ups. The use of a multi-capillary 2D was also found to be an effective solution. By splitting the carrier gas flow between multiple columns, the velocities are positively affected and it is possible to fully exploit both dimensions. The GC×multi-GC set-ups developed gave good results in terms of efficiency and applicability. On the other hand, coupling the 1D to the multi-2D is very complex in practice. Significant improvements in terms of instrumental design would be necessary to simplify the set-up and make it available for routine use.

The common factor used to achieve a better match of the 1D and 2D Van Deemter curves in the split method presented by Tranchida and our multi-capillary option is that both routes basically reduce the linear velocity in the 2D. An alternative approach for this purpose is the use of a restrictor at the end of the 2D. By increasing the outlet pressure the total flow of carrier gas through the system is reduced. Due to the different pressure drops across the two dimensions, the effect is more significant in the 2D than in the 1D.

In this work we will report the theoretical evaluation and practical use of a GC×GC set-up operated under high outlet pressure conditions. The set-up is created by incorporating a restrictor at the end of the 2D. A calculation model is developed and applied to predict the effect of the higher outlet pressure on the efficiency and speed of the system. The GC×GC set-up developed was evaluated through model experiments to verify the possibility to operate the two dimensions at their optimum simultaneously. The analysis of real-life samples is shown to confirm the feasibility for practical use and to compare the performance of our system to that of a standard GC×GC set-up.
6.2. Theory

The influence of pressure and pressure drop on the efficiency of capillary GC columns has been well documented [16]. Two pressure correction factors were introduced to convert the plate height equation for columns with negligible pressure drop to the case with a non-negligible pressure drop [17]. The most important correction factor is the $f_1$ factor given by

$$f_1 = \frac{9(p_0^4-1)(p_0^2-1)}{8(p_0^3-1)^2}$$ (1)

The key parameter in this equation is $P_o$:

$$P_o = \frac{p_{in}}{p_{out}}$$ (2)

Here $p_{in}$ and $p_{out}$ are the pressure at the inlet and the outlet of the 1D or 2D column, respectively. $f_1$ represents the loss in column efficiency due to the carrier gas expansion across the column. The values of $f_1$ range from 1 for zero pressure drop to 1.125 (9/8) for the case with very high pressure drop.

In GC×GC the first column has a very low pressure drop, and here no or hardly any loss of plate height due to carrier gas expansion occurs ($f_1 \approx 1.000$). The 2D column has a high pressure drop and hence the maximum loss in efficiency ($f_1 = 1.125$). A way to minimize this loss is to reduce the ratio inlet to outlet pressure of this dimension. This will not affect the plate height in the 1D because, due to the already high average pressure in this dimension, the pressure drop will remain negligible. Since the full set of mathematical equations to describe the effect of pressure drop is too complex, we applied a numerical approach to evaluate it.

Beens et al. [6] described a programme written in Microsoft Excel® to calculate the efficiency for the two dimensions in GC×GC under isothermal conditions. This software provides a very useful means to optimize the column set and the analysis conditions. In their calculations these authors used atmospheric outlet pressure, the situation encountered when using detectors such as the flame ionization detector (FID). Here this programme was modified and used to estimate...
the linear velocities and efficiencies in the two dimensions of a GC×GC set-up operated at elevated outlet pressures. The respective plate heights are calculated according to the procedures described in [6]. A detailed explanation of the equations used and of the algorithm developed is given in the Appendix. Moreover, in article this chapter is based on information is provided on how free access to this software can be obtained.

If it is assumed that the separation mechanisms in the two columns of the GC×GC set-up are orthogonal and that the separation achieved in the 1D is not lost during the modulation, the peak capacity of a two-dimensional system, \( n_{c,2D} \), is given by [18]:

\[
n_{c,2D} = n_c \times n_c^2
\]  

Here \( n_c \) and \( n_c^2 \) are the peak capacities for the 1D and the 2D, respectively. As the theoretical model used in our software is valid only for isothermal conditions, the peak capacities were calculated using the well-known equation [19]:

\[
n_{c,iso} = \frac{\sqrt{N}}{4R_s} \ln \left( \frac{1 + k_\omega}{1 + k_\alpha} \right) + 1
\]

where \( N \) is the plate number, \( R_s \) is the desired resolution, and \( k_\alpha \) and \( k_\omega \) are the retention factors of the first- and last-eluting peaks, respectively. Assuming isothermal conditions is more or less correct for the 2D due to the fast elution and hence the very limited temperature change in this dimension. On the other hand, \( n_c \) will be somewhat underestimated as in practice the 1D temperature is programmed. Nevertheless, Eq. (4) will provide an accurate representation of the system’s efficiency under different inlet pressure conditions and thus of the potential benefits arising from simultaneous at-optimum operation.
Chapter 6

6.3. Experimental

6.3.1. Chromatographic instrument, materials and methods

All GC×GC experiments were performed on an Agilent Technologies (Santa Clara, CA, USA) 6890 Series GC System equipped with a Focus-CombiPal Autosampler (ATAS GL, Veldhoven, The Netherlands), a split/splitless injector, a LECO (Mönchengladbach, Germany) dual-stage, quad-jet thermal modulator, a secondary oven and an FID. The hydrogen flow for the FID was produced by a hydrogen generator PG-H₂ Series 3 (Schmidlin-DBS AG, Neuheim, Switzerland).

A Rxi-5ms capillary column (length 30 m, i.d. 0.32 mm, film thickness 0.25 µm) from Restek (Bellefonte, PA, USA) was used as the first dimension column. The second dimension column was a DB-17 capillary column (i.d. 0.100 mm, film thickness 0.20 µm) from Agilent Technologies. The length of the ²D was 2 m for the performance evaluation of the standard GC×GC system and 1.5 m for the set-ups with the flow restrictors and in all applications. The restrictors (Figure 1) were prepared by melting the end of the column with a high-temperature hydrogen flame (1800°C) till complete closure and then re-opening it partially to obtain the desired flow by grinding it with sand paper [20].

![Figure 1 – Photographs of a restrictor made at the outlet the ²D capillary column.](image-url)
In all experiments an injector temperature of 250°C and a split ratio of 1:200 were applied and helium was used as the carrier gas. For the construction of the Van Deemter curves injections of 1 µL of the test mixture were performed and isothermal analysis was carried out at different inlet pressures. The primary and secondary oven temperature selected were 120°C and 130°C, respectively. The efficiency of the \( ^1 \text{D} \) and \( ^2 \text{D} \) was assessed by performing the analysis with the modulator off and on, respectively. The two-dimensional applications performed to assess the GC×GC set-ups were performed by direct injection of 0.2 µL of the pure sample. The detailed inlet pressure and oven temperature conditions employed in the different series of experiments are provided below.

6.3.2. Chemicals

P.A. grade n-decane, n-dodecane and n-tetradecane were purchased from Aldrich (Zwijndrecht, The Netherlands). n-Heptane was purchased from Biosolve (Valkenswaard, The Netherlands). The test mixture used to evaluate the GC×GC set-ups was prepared my direct dilution of each compound in n-heptane (1:500). The petrol-derived household cleaning products (white spirit, turpentine and kerosene) were purchased in a local supermarket. The diesel oil was obtained from a local petrol station.

6.4. Results and discussion

6.4.1. Theoretical evaluation

The presence of two distinct optima in GC×GC is caused by the difference in i.d. between the two dimensions. An approach that can be used to solve this issue consists of employing wider \( ^2 \text{D} \) columns [6]. However, with such a column set sufficient modulations across a \( ^1 \text{D} \) peak are difficult to obtain. The important parameter is the modulation criterion:
\[
\frac{t_{r2}}{\sigma_1} \leq 1.5
\]  

where \(t_{r2}\) is the retention time in the 2D and \(\sigma_1\) is the standard deviation of the peak eluting from the 1D. This modulation criterion needs to be fulfilled in order not to compromise the resolution achieved in the 1D during the modulation process. When using narrow 2D columns Eq. (5) is normally respected because \(t_{r2}\) is very short and the low velocity in the 1D leads to wide \(\sigma_1\). With a wider 2D the slow elution in this dimension leads to long \(t_{r2}\) and due to the higher speed in the primary column \(\sigma_1\) becomes narrow. Thus the modulation criterion can only be fulfilled if there is a large length difference between the columns length, e.g. the normal-bore 2D has to be very short. However, in this way not enough plates would be delivered, making this solution unsuitable in practice.

The software described in Section 6.2 was used to calculate the Van Deemter curves obtained with different column sets and evaluate the effects described above (Fig. 2). The length of the 2D column is increased along with its i.d. to maintain the plate number of the 2D constant. As expected, when using a narrow-bore 2D column in combination with a normal-bore 1D column the optima of the two dimensions are rather distant (Figure 1A). The 100 \(\mu\)m 2D reaches its optimum (\(2H_{\text{opt}}\approx0.08\) mm) at an inlet pressure of 128 kPa, i.e. 81 cm/s, but at this pressure the 1D is far below its optimum with a plate height \(1H\) of approximately 0.51 mm, i.e. twice the minimum of the column. The 1D optimum \(1H_{\text{opt}}\approx0.30\) mm is reached at an inlet pressure of 275 kPa, i.e. 11 cm/s. However, at this inlet pressure the 2D exceeds its optimum by far: \(2H\approx0.14\) mm. With wider 2D columns the optimum of the 1D shifts towards lower inlet pressures and simultaneous at-optimum operation becomes possible. A quantitative evaluation of the improvement can be obtained by comparing the peak capacities of the different set-ups. The two-dimensional peak capacity \(n_{c2D}\) for the case illustrated in Fig. 1A was calculated using Eq. (4) for both dimensions and then Eq. (3). The plate numbers were calculated with our computer programme. A resolution of 1.5 was selected. Typical retention factor values encountered in practice were selected, i.e. \(1k_a=0.5, 1k_\omega=60, 2k_a=0.1\) and \(2k_\omega=5\). As shown in Table 1 the calculated total peak capacity increases from less than 7,000 to nearly 9,000 (Table 1).
Figure 2 – Comparison of the calculated GC×GC performance obtained by using wider, longer 2D columns (A) or by installing a restrictor at the 2D outlet (B). Reference set-up (black): (30 m×0.320 mm i.d., 0.25 µm df)×(2 m×0.100 mm i.d., 0.20 µm df), $p_{\text{out}}=100$ kPa. The grey lines refer to a 5 m×0.250 mm i.d. 2D column (A) and $p_{\text{opt}}=500$ kPa (B), respectively. The continuous and the dashed lines represent the 1D and the 2D, respectively. $k_1=5$, $k_2=2$. $T=70^\circ$C.

Table 1 – Calculated GC×GC performance obtained by using wider, longer 2D columns. All parameters are calculated at 2D-optimum operating conditions. 1D: 30 m×0.32 mm i.d., 0.25 µm df. 2D: 0.1 µm df while length and i.d. are changed as described. $k_1=5$, $k_2=2$. $T=70^\circ$C.

<table>
<thead>
<tr>
<th>$t_0$ (s)</th>
<th>$N$</th>
<th>$r'N$ (s⁻¹)</th>
<th>$n_c$</th>
<th>$t_0$ (min)</th>
<th>$N$</th>
<th>$r'N$ (s⁻¹)</th>
<th>$n_c$</th>
<th>$n_{c,2D}$</th>
<th>$2tr/\sigma$</th>
</tr>
</thead>
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<tr>
<td>2×0.100</td>
<td>2.5</td>
<td>23017</td>
<td>9288</td>
<td>44</td>
<td>8.5</td>
<td>58483</td>
<td>114</td>
<td>150</td>
<td>6600</td>
</tr>
<tr>
<td>3×0.150</td>
<td>4.3</td>
<td>23869</td>
<td>5530</td>
<td>45</td>
<td>4.3</td>
<td>80894</td>
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<td>177</td>
<td>7893</td>
</tr>
<tr>
<td>4×0.200</td>
<td>6.6</td>
<td>24262</td>
<td>3688</td>
<td>45</td>
<td>2.8</td>
<td>94061</td>
<td>565</td>
<td>190</td>
<td>8576</td>
</tr>
<tr>
<td>5×0.250</td>
<td>9.4</td>
<td>24437</td>
<td>2610</td>
<td>45</td>
<td>2.1</td>
<td>98260</td>
<td>793</td>
<td>195</td>
<td>8795</td>
</tr>
</tbody>
</table>

$r'N = \frac{N}{t_0}$; $n_c$ is calculated using Eq. (4); $n_{c,2D}$ is calculated using Eq. (3).
However, as a result of the effect described above, the modulation criterion is no longer satisfied already for a 2D column of 150 µm i.d. A modified version of Eq. (3) should now be used that takes into account the loss of peak capacity due to 1D undersampling [21]. This means that under the given conditions the overall peak capacity obtained with this approach will be much lower than the 9,000 peaks calculated, especially for the wider columns, reducing the actual efficacy of this approach significantly.

Calculations similar to those described above were also made to evaluate our increased-outlet-pressure approach. The addition of a restrictor at the end of the 2D was simulated by increasing $p_{out}$. Fig. 1B shows the Van Deemter curves so calculated. By increasing $p_{out}$ from 100 to 500 kPa both optima shift to higher inlet pressures, as expected given the higher outlet pressure. However, this shift is more significant for the 2D than for the 1D: the shifts are 319 kPa and 247 kPa, respectively. As a result the two optima are now closer. This can be explained by considering the pressure drop $\Delta p$ across a standard GC×GC column set. The narrow-bore 2D in such a system acts a restrictor on the 1D leading to a high midpoint pressure between the dimensions $p_{mid}$, i.e. a high outlet pressure for the primary column. As a result, the average pressure in the 2D increases and its optimum moves towards higher $p_{in}$ than in 1D-GC. If a restrictor is added at the detector outlet, this now provides the largest contribution to the $\Delta p$ of the system. An effect similar to the one described above for the 1D now occurs in the 2D, i.e. the average pressure in the 2D increases. As a result $H_{opt}^2$ is reached at more elevated $p_{in}$ values. Obviously the restrictor has a similar effect on the 1D, but as the average pressure in this column is already high, the extent of this contribution is less important (Table 2).

Table 2 – Calculated pressure drops obtained in a GC×GC system operated under different outlet pressure conditions. All parameters are calculated at 2D-optimum operating conditions, expressed as the actual inlet pressure (inlet gauge overpressure + 100 kPa). 1D: 30 m×0.32 mm i.d., 0.25 µm df. 2D: 2 m×0.1 mm i.d., 0.1 µm df. $^1k=5$, $^2k=2$. $T=70^\circ$C.

<table>
<thead>
<tr>
<th>$p_{out}$ (kPa)</th>
<th>$p_{in}$ (kPa)</th>
<th>$p_{mid}$ (kPa)</th>
<th>$^1\Delta p$ (kPa)</th>
<th>$^2\Delta p$ (kPa)</th>
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<td>100</td>
<td>230</td>
<td>218</td>
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<td>118</td>
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<td>300</td>
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<td>361</td>
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<td>500</td>
<td>549</td>
<td>543</td>
<td>6</td>
<td>43</td>
</tr>
</tbody>
</table>
This can be confirmed by comparing the changes of the calculated $\Delta p^1$ and $\Delta p^2$. $\Delta p^1$ decreases from 12 kPa to 6 kPa whereas $\Delta p^2$ is reduced from 118 to 43 kPa. When $p_{\text{out}}=500$ kPa the 2D optimum is reached at an inlet pressure of 450 kPa and at this pressure $H^1$ is 0.44 mm (Fig. 2). The gain in terms of 1D plate numbers is 1,300 and the resulting increase in peak capacity is about 12% (Table 3). The price to pay is the longer analysis time. The main advantage is that the modulation criterion remains always fulfilled. Due to the low $\tilde{u}^1$ the bands eluting from the 1D stay relatively broad, allowing to achieve the several modulations per peak required. As a result the theoretical gain in terms of peak capacity will be achieved in practice.

### Table 3 – Calculated GC×GC performance obtained by installing a restriction at the 2D outlet

<table>
<thead>
<tr>
<th>$p_{\text{out}}$ (kPa)</th>
<th>$2D$</th>
<th>$1D$</th>
<th>$n_{c,2D}$</th>
<th>$2tr/\sigma$</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
<td>$t_0$ (s)</td>
<td>$N$</td>
<td>$\dot{N}(s^{-1})$</td>
<td>$n_c$</td>
</tr>
<tr>
<td>100</td>
<td>2.48</td>
<td>23017</td>
<td>9288</td>
<td>44</td>
</tr>
<tr>
<td>300</td>
<td>4.52</td>
<td>24363</td>
<td>5374</td>
<td>45</td>
</tr>
<tr>
<td>500</td>
<td>6.35</td>
<td>24623</td>
<td>3838</td>
<td>45</td>
</tr>
</tbody>
</table>

$rN = \frac{N}{t_0}$; $n_c$ is calculated using Eq. (4); $n_{c,2D}$ is calculated using Eq. (3)

From the calculations presented here it can be concluded that increasing the outlet pressure moves the optima of the two dimensions closer together, allowing a somewhat better exploitation of the efficiency of a given column set. Unfortunately time will increase as well and other options for increasing the efficiency of separation might be preferred.

### 6.4.2. GC×GC under high outlet pressure conditions

#### Efficiencies vs. inlet pressure

In a first series of experiments the efficiency of a standard column set as a function of inlet pressure was assessed to provide a frame of reference. The efficiencies of
the \( ^1 \text{D} \) and the \( ^2 \text{D} \) were measured by performing isothermal analyses with the modulator off and on, respectively. As expected, the optimum velocities for the two dimensions were obtained at very different inlet pressures (Figure 3A). For example the optimum plate height of the \( ^2 \text{D} \) column for n-decane (0.10 mm) is obtained at 100 kPa inlet pressure, but at this pressure the efficiency of the primary column is very poor with \( ^1 \text{H} \approx 0.69 \) mm. The primary-column optimum \( ^1 \text{H}_{\text{opt}} \) of 0.25 mm is obtained at 310 kPa, but under this flow condition the experimental \( ^2 \text{H} \) is above 0.33 mm. Similar results were obtained for the other test compounds.

Next, the performance of our elevated outlet-pressure set-up was investigated. Initially we explored the use of a T-piece and an auxiliary gas inlet at the end of the column set. This way \( p_{\text{out}} \) could be controlled and tuned as desired. The auxiliary pressure line was connected to a three ports SilFlow Stainless Steel GC splitter (SGE, Ringwood, Victoria, Australia) installed at the end of the \( ^2 \text{D} \). The third port was used to deliver the combined flow to the FID by means of a piece of narrow fused-silica capillary (20 cm×0.050 mm). Using this set-up elevated \( p_{\text{out}} \) values and an accurate control of the flow conditions could be obtained. However, the \( ^2 \text{D} \) peaks were significant broadened with a detrimental effect on the efficiency (data not shown). This was most likely caused by the extra-column volume added by the splitter, which was not negligible for the very narrow, modulated peaks. Thus the decision was made to prepare the restrictors directly on the \( ^2 \text{D} \) column (Fig. 1). This way, the possibility to modulate the operational conditions was sacrificed. On the other hand, the instrumental complexity was greatly reduced and sharp, symmetrical peaks were obtained, preserving the efficiency of the \( ^2 \text{D} \). Note that with these restrictors it is no longer possible to control the outlet velocity. Elevated outlet pressures will be obtained, but the actual outlet pressure will depend on the inlet pressure applied.

Two restrictors with different flow characteristics were prepared and tested. These reduced the average linear velocity by 50% (“wide restrictor”) and 80% (“narrow restrictor”), respectively. Based on the assumption that thanks to the better exploitation a shorter length \( ^2 \text{D} \) column can be used while obtaining the same plate numbers, the \( ^2 \text{D} \) was reduced from the 2 m used for the reference experiments to 1.5 m. Figures 3B and 3C show the results obtained with a carrier gas linear velocity reduced with the wide and the narrow restrictor, respectively. As the theoretical
calculations already predicted, the optima of both dimensions are shifted towards higher inlet pressure values. As can be seen for the $^1$D this effect is stronger than calculated (Fig. 2).

![Graph showing Van Deemter curves for 1D and 2D under different outlet pressure conditions.](image)

Figure 3 – Experimental Van Deemter curves obtained for the $^1$D (●) and the $^2$D (△) of a GC×GC system operated under different outlet pressure conditions. A) Open outlet ($p_{out}$ =100 kPa); B) Restrictor #1 ($t_0=1.8·t_0$); C) Restrictor #2 ($t_0=5.3·t_0$). Every point is the average of 3 repeated injections.

This deviation from theory is most likely caused by the fact that our model considers $p_{out}$ as a constant while with the set-up in use it is a function of $p_{in}$. Nevertheless, the two optima indeed become closer (Fig. 3) as the Van Deemter curves of the $^2$D are much more flat above the optimum. This is not surprising as it is known that at low $\Delta p$ the dependence between $H$ and $u$ is less pronounced [22]. Therefore at the high $p_{in}$ required to achieve the $^1$D optimum also the $^2$D is close to its best efficiency. For n-decane the two optima nearly overlap: at the $^1$D optimum
$^2H$ is 0.11 mm while at the $^2$D optimum the efficiency of the primary column is more than doubled with $^2H\approx0.31$ mm (Fig. 3C). As a result the maximum calculated $n_{c,2C}$ increases from less than 5,500 to 7,000 and then 7,500, for an enhancement of 40%. This in spite of the fact that the $^2$D column is use is even shorter than in the reference set-up. This result clearly shows the potential arising from using this method. For a more retained test analyte (n-dodecane) the effect is similar but somewhat less pronounced (Fig. 3). At the $^1$D optimum $^2H$ is somewhat improved, going from 0.22 mm to 0.15 mm with the second restrictor. If the $^2$D optimal conditions are considered the gain is more significant: $^1H$ goes from over 0.6 mm to 0.4 mm. The resulting gain in terms of $n_{c,2C}$ was 10%, in good agreement with the theoretical results obtained in Section 6.2. It is sensible to assume that for more retained compounds higher $p_{out}$ values are required to achieve simultaneous optimal operation. However, this would lead to even longer analysis times and was therefore not further investigated.

The experimental observations discussed above were in reasonable agreement with the predicted trends and values. There was, however, one observation that was not predicted. For the most retained compound we observed a significant loss of efficiency for the $^1$D: with both restrictors about 85,000 plates were delivered instead of the predicted 100,000. Here we speculate that this artifact could be due to the presence of non-uniformities in the stationary phase. Under elevated column pressures molecular diffusion in the gas phase is slower. Variations of film thickness along the column under these conditions could cause band broadening as a result of the uneven diffusion distances encountered in radial direction. This effect would be expected to be more critical for the more retained compounds, as it was indeed observed experimentally. Another possible explanation could be a slow re-injection of the trapped analytes by the hot jet of the modulator as a result of the high pressure in the $^2$D, in particular for the less volatile compounds. Due to this loss of efficiency in the $^1$D for the heavier, more retained compounds there is no gain in terms of $n_{c,2C}$. However, for the fundamental understanding it is noteworthy to stress that a better employment of the two columns in terms of relative position of their optima is still achieved. Only thanks to this effect a consistent peak capacity is obtained in spite of a shorter $^2$D column and a 15% loss in plate number of the $^1$D.
The results described above confirm that the use of a restrictor at the 2D outlet is a simple yet effective approach to alleviate the GC×GC linear velocity mismatch. Under higher pressure outlet conditions it is possible to achieve a better, simultaneous exploitation of the efficiency of the two dimensions albeit only at the expense of time. The main practical disadvantages of the set-up developed are the limited control and flexibility. A substantial improvement would arise from the possibility to tune $p_{out}$ to optimize the performance according to the specific application and/or sample. However, achieving this without adding even the smallest extra-column volume contribution to the system is challenging. Despite these limitations we decided to verify whether the set-up developed indeed provides the desired enhancement of resolving power in a number of selected typical GC×GC applications. Given the better efficiency shown (Fig. 3), the narrow restrictor was selected and used in all applications.

**Applications**

A number of petrol-derived samples were analyzed to (i) assess the suitability of our set-up for real-life applications and (ii) compare its performance with that obtainable using the same column-set under standard atmospheric outlet conditions. For the latter objective the same samples were re-analyzed after removing the restrictor by cutting 3 cm from the end of the 2D. Figure 4A shows the isothermal analysis of a white spirit sample performed with the restrictor installed. The $t_r$ are rather long thus a modulation time of 10 s was chosen, causing some loss in terms of 1D resolution for the first eluting compounds as a result of the low number of modulations across the very narrow 1D peaks. On the other hand, an efficient two-dimensional separation is obtained. Fig. 4B shows the chromatogram obtained without restrictor using the same isothermal program and a very low inlet pressure selected to achieve a consistent analysis time. Under these conditions the separation obtained on the 2D is comparable but the resolution in the 1D is poorer. With a higher inlet pressure the resolution achieved in the 1D improves and becomes as good as with the restrictor with the advantage of a shorter analysis time (Fig. 4C). However, some peaks that were fully separated in the 2D in the set-up with restrictor are no longer resolved because of the poorer
These results show how the presence of different optima for the two dimensions does not permit to obtain the best separation possible on both dimensions simultaneously. With the restrictor, at the price of time, it was indeed possible to achieve that.

Figure 4 – GCxGC chromatograms of a white spirit sample with the restrictor (A) and at ambient outlet pressure under different flow conditions (B-C). Oven: 50°C (isothermal); offset secondary oven: 5°C; $p_{in}=690$ kPa (A), 35 kPa (B) and 105 kPa (C). The arrows indicate the points of interest in terms of peak resolution under the different conditions employed.

Figures 5A, 6A and 7A show the temperature-programmed chromatograms obtained with the restrictor for turpentine, kerosene and diesel oil samples, respectively. Very good two-dimensional separations were obtained for all samples. Elevated secondary-oven offsets, i.e. 30°C or 40°C, and a long modulation time of 10 s were used to avoid wrap-around. All the 2D peaks obtained are narrow and symmetrical.
Figure 5 – GC×GC chromatograms of a kerosene sample with the restrictor (A) and at ambient outlet pressure under different flow conditions (B-D). Conditions: A) 40°C (2 min) to 150°C at 1°C/min; offset secondary oven: 40°C; $p_{in}$= 620 kPa. B) 40°C (2 min) to 150°C at 1°C/min; offset secondary oven: 40°C; $p_{in}$= 45 kPa. C) 40°C (2 min) to 150°C at 3°C/min; offset secondary oven: 10°C; $p_{in}$= 135 kPa. D) 40°C (2 min) to 150°C at 3°C/min; offset secondary oven: 10°C; $p_{in}$= 405 kPa.
Figure 6 – GC×GC chromatograms of a turpentine sample with the restrictor (A) and at ambient outlet pressure under different flow conditions (B-D). Conditions: A) 40°C (2 min) to 150°C at 1°C/min; offset secondary oven: 30°C; $p_{in} = 620$ kPa. B) 40°C (2 min) to 150°C at 1°C/min; offset secondary oven: 30°C; $p_{in} = 35$ kPa. C) 40°C (2 min) to 150°C at 3°C/min; offset secondary oven: 10°C; $p_{in} = 105$ kPa; D) 40°C (2 min) to 150°C at 3°C/min; offset secondary oven: 10°C; $p_{in} = 315$ kPa.
Figure 7 – GC×GC chromatograms of a diesel oil sample with the restrictor (A) and at ambient outlet pressure under different flow conditions (B-D). Conditions: A) 40°C (2 min) to 150°C at 1°C/min; offset secondary oven: 40°C; $p_{in}=620$ kPa. B) 40°C (2 min) to 150°C at 1°C/min; offset secondary oven: 40°C; $p_{in}=45$ kPa. C) 40°C (2 min) to 150°C at 3°C/min; offset secondary oven: 10°C; $p_{in}=135$ kPa; D) 40°C (2 min) to 150°C at 3°C/min; offset secondary oven: 10°C; $p_{in}=405$ kPa.
The use of a long modulation time is not an issue as with the broad ¹D bands generated at this low speed undersampling does not occur. As a result excellent resolution is achieved in both dimensions. Figures 5B, 6B and 7B show the separations obtained without restrictor using the same temperature programs and a flow which would provide comparable retention times. As expected, at the slow carrier gas velocities so obtained both dimensions perform poorly as they are far below optimum. We then used progressively higher inlet pressures to better exploit the efficiency of the ²D and ¹D columns. Other parameters were also modified according to the methods commonly employed in GC×GC: the secondary-oven offset was reduced to 10°C and the oven-temperature ramp was slightly increased to 3°C/min. The results obtained and all experimental details are shown in Figs. 4-7. As can be seen, when the ²D is optimized the separations in this dimension are consistent with those achieved previously with the restrictor. Moreover, the analysis time is shortened. However, the ¹D separation then is sacrificed. At higher inlet pressure the resolution in the ¹D is improved and the analysis time is even faster, i.e. approximately a factor of 4-5, but the resolution in the ²D is lost. For all samples analyzed the GC×GC separations achieved with the restrictor are much slower but show a better resolution than their counterparts obtained with an open outlet.

The results obtained in the practical applications show that the flow mismatch is not merely a theoretical aspect but it has a concrete, negative influence of the GC×GC performance. The presence of two distinct optima leads to a reduction of the resolving power potentially achievable with the column-set selected. In real-life applications this can result in the impossibility of separating the compounds of interest, especially in the case of highly complex samples. By adding the restrictor it is possible to optimize one dimension while preserving, fully or at least to some extent, the performance of the other. As shown, this can indeed lead to better two-dimensional separations. Hence, if a maximum resolution is desired for a given column set and time is less relevant the use of an outlet restrictor can be advantageous.
6.5. Conclusions

Adding a restrictor at the end of the column set is a simple yet efficient approach to reduce the linear velocity in the \(^2\)D and reduce the GC\times\text{GC} flow mismatch issue. A computer programme written in Microsoft Excel\textsuperscript{®} to calculate the column efficiency for both GC\times\text{GC} dimensions was modified to investigate the effect of elevated \(^2\)D outlet pressures. With the aid of this software it was possible to confirm that under such conditions the optima of the two columns are closer and their performance can be better exploited. The calculations also indicate that the modulation criterion remains satisfied.

Restrictors were manufactured by melting until complete closure and then partially re-opening the end of the narrow-bore \(^2\)D columns. The instrumental set-ups developed gave good results in terms of peak shape and efficiency. Model experiments showed that the Van Deemter curves so obtained for the \(^2\)D are more flat at high velocities than those in standard GC\times\text{GC}. For \(n\)-decane at the \(^1\)D optimum \(2H\) is reduced from over 0.33 mm to 0.11 mm. The two-dimensional chromatograms obtained for a number of petrol-derived samples proved the suitability of the method for real-life applications. When compared to those obtained with the same column set under open outlet conditions, the separations achieved with the restrictors are slightly more efficient yet unfortunately much slower. Therefore this approach, although interesting from the theoretical perspective and indeed effective, is probably not convenient in practice. Alternative procedures which can achieve the same objective at a higher speed are clearly more advantageous.
List of references