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Review

Efficiency through combining high-performance liquid chromatography and high resolution gas chromatography: progress 1995–1999

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Abstract

Progress during the last 5 years in on-line LC–GC and related techniques is reviewed. In normal-phase LC–GC, the wire interface proved to have advantages over the loop type interface. Further investigations on the solvent evaporation process in an uncoated precolumn under conditions of an early vapour exit revealed that the rules for the transfer by the retention gap techniques must be modified. For reversed-phase LC–GC, approaches with a phase transfer compete with direct evaporation. Eluents were extracted into a bed of Tenax located in a programmed-temperature vaporiser and thermally desorbed. Direct evaporation is possible when a hot vaporising chamber is used and solvent/solute separation occurs in a separate compartment, a coated precolumn possibly in combination with packed beds. As a future strategy, LC–GC transfer techniques should be adjusted to those of large volume injection and involve a single device. It is believed that on-column injection/transfer is the choice. This requires that concurrent evaporation in LC–GC is performed by the on-column interface.

Keywords: Reviews; Liquid chromatography–gas chromatography; Interfaces, LC–GC; Injection methods; Programmed-temperature vaporiser; Large-volume injection; Retention gap

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1. Introduction

Food control, searching for possibly toxic components, contaminants, or adulteration, is an example where commonly two tasks are combined: trace analysis in complex matrices and the need for analysing large numbers of samples. Trace analysis calls for efficient clean-up in order to reduce interfering material. The large number of samples requires methods which can largely be automated. On-line LC–GC well responds to both.

1. HPLC offers the best separation power in liquid phase available, i.e. effective sample clean-up.
2. On-line detection enables to cut sharp fractions.
3. On-line transfer is essential for obtaining low detection limits: all the solute material contained in the HPLC fraction reaches GC.
4. The procedure is fully automated.
5. On-line coupling provides high accuracy: (i) reproducibility is high; (ii) losses, e.g., by incomplete separation of liquid phases after an extraction, are ruled out; (iii) there is no contamination from external sources, such as rotary evaporators.

2. Recent progress

During the last 5 years, several excellent reviews have been published [1–5]. This review concentrates on progress in transfer techniques published since 1995.

2.1. Transfer techniques for NPLC–GC

The large majority of LC–GC applications still involves normal-phase HPLC (NPLC). Numerous new applications have been described [6–11], which confirms the advantages of the technique. Most NPLC–GC work involves classical transfer either by fully concurrent eluent evaporation with the loop type interface (Fig. 1) or by partially concurrent evaporation with the on-column interface (Fig. 2), both from the eighties and well described by other reviews (e.g. [12]).

2.1.1. Wire interface

The wire interface was introduced for fully concurrent evaporation [13]. Eluent evaporation is performed in a vaporising chamber (Fig. 3) consisting of a short section of 0.32 mm I.D. fused-silica capillary thermostatted at 250–350°C in, e.g., a detector base block. Shooting of liquid resulting from violent evaporation is prevented by an inserted piece of 0.22 mm O.D. wire of some 4 cm in length. The vapours are driven through a short (ca. 1.5 m) retaining precolumn; since sample evaporation occurs in a hot chamber, there is no need for an uncoated precolumn.

The eluent is introduced by the LC pump, i.e. in speed-controlled manner. The transfer valve has a configuration corresponding to that introduced by Cortes [14]. The carrier gas flow is interrupted during transfer. It is introduced through a second switching valve, kept free of solvent, and fed into the GC through a T-piece positioned just above the vaporising chamber. Vapours are discharged by overflow [15], i.e. by an oven temperature building up a vapour pressure sufficiently high for the concurrent discharge through the vapour exit.

The wire interface was preferred to the loop type interface for the following reasons:

1. better retention of the most volatile components

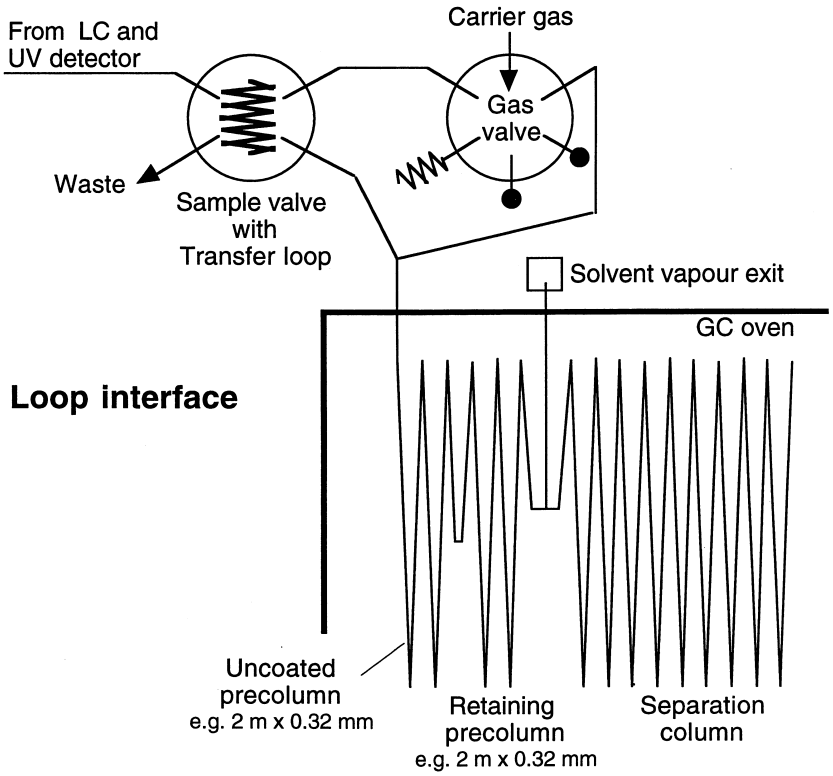

Fig. 1. Loop type interface for LC–GC transfer involving concurrent eluent evaporation. Discharge of the eluent vapours by overflow.

(slightly lower oven temperatures provide substantially more efficient phase soaking);
2. avoidance of mixing within the sample loop [16];
3. flexibility for the adjustment of the fraction volume (the cuts are determined by times, not by loop volume).

2.1.2. Retention gap technique

If the sample contains components which are more volatile than can be retained by a retaining precolumn (concurrent evaporation), commonly the retention gap technique is used, employing solvent trapping in an uncoated precolumn. This technique is more than 15 years old, but recently received some substantial modifications. Vreuls and co-workers [17,18] as well as Boselli and co-workers [19–22] further investigated the process of solvent evaporation in the uncoated precolumn under conditions of partially concurrent solvent evaporation. Some observations, particularly occasional high losses of volatile material, could not be explained by the classical theory postulating that solvent evaporation exclusively takes place at the rear of the flooded zone.

2.1.2.1. Modified working rules

The new evidence required some modifications of current teaching.

1. At carrier gas flow rates above about 50 ml/min, as they are normal when an early vapour exit is used, the capacity of a 10 m×0.53 mm I.D. uncoated precolumn to retain sample liquid should be assumed to be around 250 μl, rather than 80–100 μl. At such high gas flow rates, the sample layer is thicker.
2. The solvent vapour exit should be closed as late as possible because closure reduces the flow rate to a few millilitres and causes the residual liquid to spread to a roughly three times longer flooded zone. This also means that not the whole length of the uncoated precolumn can be exploited for the primary spreading process.

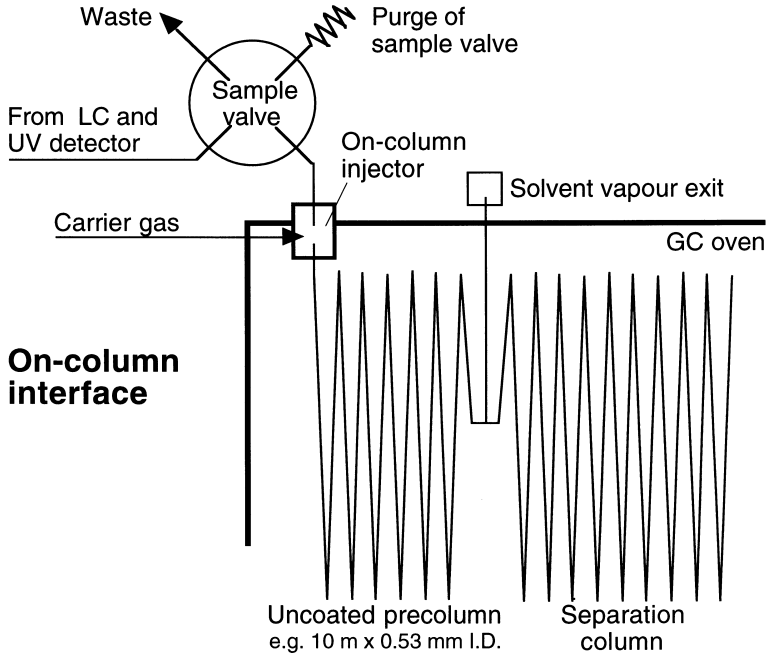

Fig. 2. On-column interface, mostly used for the transfer of wetting liquids by the retention gap technique (partially concurrent evaporation).

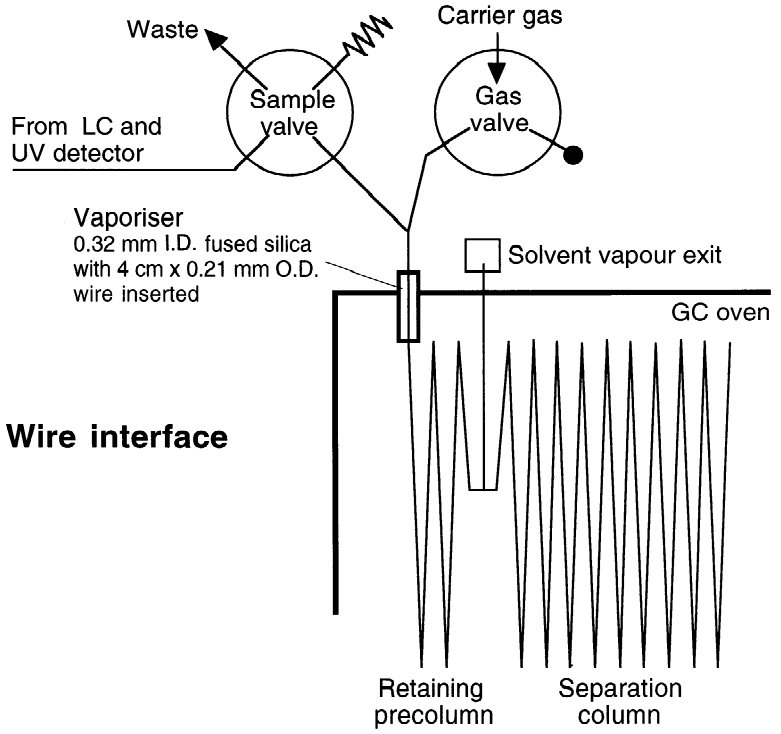

Fig. 3. Wire interface for concurrent evaporation of organic eluents.

3. If the retention gap technique is used with solvent trapping, the retaining precolumn is unnecessary since the sample (solvent) film exerts far higher retention power than the stationary phase. Previous attempts to do without a retaining precolumn failed for a different reason: since the 0.53 mm I.D. uncoated precolumns were combined with 0.32 mm I.D. retaining precolumns, the retaining precolumn acted as a restriction. It reduced the gas flow rate and, thus, compelled to lower the flow rate of the introduced liquid. This helped avoiding important plug formation: plugs of liquid in the uncoated precolumn cause a strong pressure drop and transfer much of the solvent evaporation from the rear of the flooded zone (where it should be for solvent trapping) to its front.
4. Hankemeier et al. [17] reported that the introduction of ''pre-solvent'', i.e. of pure solvent, before injection or transfer of the sample helps reducing losses of volatile components. The improvement was impressive, but the issue requires some further experimenting. In our work, we have never seen such severe losses to begin with. Furthermore, the concept that a layer of pure solvent can be placed downstream of the sample layer has been shown to be unrealistic: liquid introduced later tends to overrun the liquid deposited previously [23].

These findings substantially improve the retention gap technique. The higher capacity of the uncoated precolumn enables the transfer of enlarged fractions: 1000 μl can be transferred with merely 75% concurrent evaporation. The explanation of the sometimes massive losses of volatile solutes with partially concurrent evaporation enables to improve the system: there is no need for a retaining precolumn. A restriction in the vapour outlet is equally effective. Furthermore, for this aspect, helium is preferable to hydrogen because inlet pressures are higher, providing more force to advance the liquid.

2.1.2.2. Closure of the vapour exit

When the wire interface is used, the solvent vapour exit is closed about 1 s after the end of the transfer. The loop type interface solved the problem of finding the suitable moment by monitoring the carrier gas inlet pressure: the exit closes automatically upon a predetermined pressure drop. However, so far, there was no such signal for automated closure when the retention gap technique techniques were applied. Usually the flame method was used: the effluent was lit; solvent vapours enlarge the flame and turn it yellow. The end of solvent evaporation was determined visually and, hence, the closure time set 2–3 s earlier for the subsequent runs.

Hankemeier et al. [24] proposed monitoring the carrier gas flow rate (pressure-regulated system). The vapours generated upon solvent evaporation partly substitute the carrier gas, i.e. reduce the carrier gas flow rate. Return towards the level observed before transfer indicates the end of solvent evaporation. However, since the volatile solutes are released together with the last solvent, closure occurs slightly too late. A retaining precolumn is required to retain the solutes over this period. Furthermore, particularly if helium is used as carrier gas, admixture of solvent vapours with easily three times lower viscosity may result in substantial increase of the total flow rate, i.e. under certain conditions the helium flow rate does not change.

Hyötyläinen et al. [25] detected evaporation inside the precolumn by temperature measurement on the outer capillary wall. Solvent evaporation consumes substantial amounts of energy, which results in cooling by several degrees. Hence passage of the rear end of the flooded zone at a given point is detectable by a temperature drop. This signal can be used for closing the vapour exit: it enables closure before the end of solvent evaporation, i.e. no retaining precolumn is needed. It also helps optimization of the conditions for a given proportion of concurrent evaporation.

2.1.2.3. Filter for retaining non-evaporating by-products

In the rare cases, HPLC fractions contain non-evaporating material at concentrations disturbing the performance of the uncoated precolumn, a vaporiser may serve as a filter (Fig. 4): the sample is evaporated in the hot, packed chamber above the precolumn. Temperature of the chamber is selected such that also the solutes are vaporised. As for on-column injection, oven temperature is kept below the pressure-corrected solvent boiling point. The same solvent trapping as with on-column injection is ob-

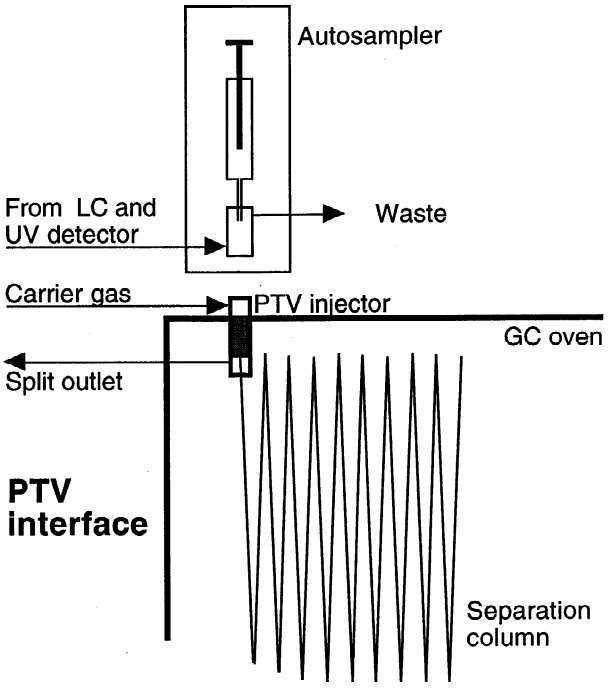

Fig. 4. Coupling of LC to GC through PTV solvent splitting using an autosampler as interface.

tained, the layer of liquid now being formed through recondensation. The system is similar to the vaporiser/precolumn solvent split interface described below. So far, the technique proved useful for large volume on-column injection [26], but has never been used for on-line LC–GC.

2.1.3. Programmed-temperature vaporiser as interface

So far, almost exclusively on-column methods were used for transfer into GC. They show best performance for highly volatile as well as the most high boiling sample components and are quantitatively reliable.

In large volume injection, programmed-temperature vaporising (PTV) injection is a valuable alternative to on-column injection. Performance is inferior, but it tolerates substantially more non-evaporating by-products, which is an important feature for direct injection of extracts.

Gerstel introduced a PTV-based LC–GC interface as a modular system [27] (Fig. 5). The LC effluent passes through a flow cell from which an autosampler syringe picks up the fraction. Then the flow cell turns away and the autosampler performs a speed-controlled PTV solvent split injection.

It is difficult to predict the future importance of LC–GC transfer through a PTV injector. Tolerance towards non-evaporating by-products is less relevant than for general large volume injection since LC preseparates with an efficiency which usually delivers sufficiently clean fractions for on-column injection. Furthermore, the on-column interface with a vaporiser (Fig. 4) is an alternative with better performance. On the other hand, PTV injectors are available in many laboratories, inviting to enter on-line LC–GC through the same door.

2.1.4. Two-dimensional pre-separation

Increasingly complex preseparations are performed in liquid phase. LC–LC with heart cutting was used for the analysis of sterol dehydration products, the first step isolating the hydrocarbons from a large amount of oil, the second separating between various groups of olefins (finally separated by GC) [28].

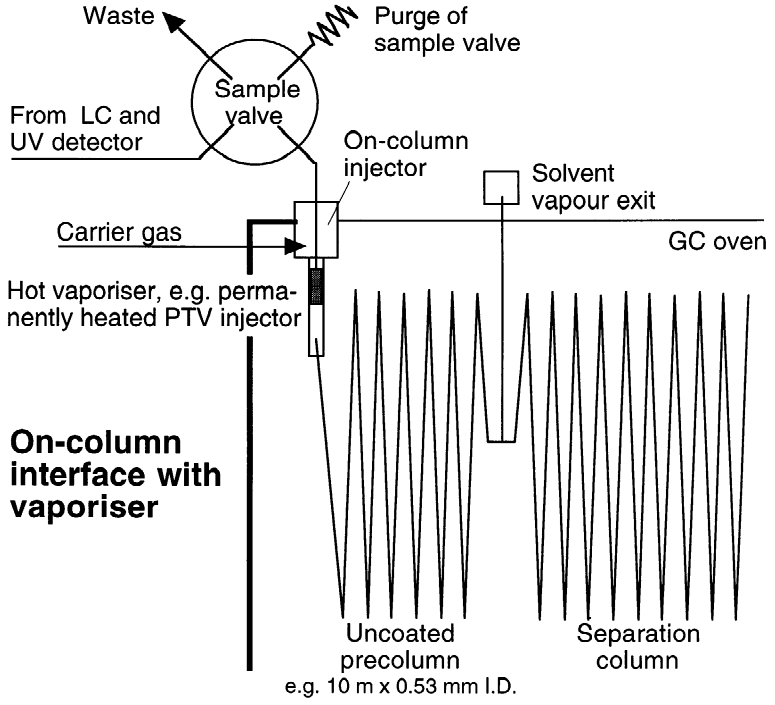

Fig. 5. On-column interface with a vaporising chamber above the uncoated precolumn acting as a filter retaining non-evaporating by-products, here shown as a PTV injector mounted to the bottom of an on-column injector (system Fisons/CE Instruments).

When the mobile phase of the first step is not compatible with the second step, it must be evaporated in-between. This was achieved with a small packed bed from which the eluent was evaporated under vacuum [29]. This system was used for the analysis of mineral oil polyaromatic hydrocarbons in foods: the first NPLC column isolated the hydrocarbons from raw food extracts (primarily fat), while the second separated the polyaromatic hydrocarbons into classes according to ring number [30]. Alternatively, the effluent from the first column was fed into an uncoated and a retaining precolumn through a loop type interface and the solute material reconcentrated in a cold trap [31]. The latter system was used to combine Size Exclusion Chromatography (SEC) and NPLC for the characterisation of mineral oil fractions.

2.1.5. Miscellaneous

Jongenotter et al. [32] developed a method for determining pesticides in olive oil by gel permeation chromatography coupled to GC. A fraction of 1.3 ml volume was transferred by concurrent solvent evaporation. To avoid losses of the early eluted components, co-solvent trapping was used (*n*-nonane in methyl acetate). It is the first time that a method has been elaborated in such detail with this technique. Stability of the transfer was improved by using the on-column interface, i.e. with gas discharge instead of overflow, since this prevented shooting liquid. This also broadened the range of suitable temperatures.

Lanuzza et al. [33] described various LC–GC methods for the analysis of edible oils, including a technique for combining the transfer of two LC fractions from a preseparation into the same GC analysis. A modified loop type interface was used.

3. Transfer techniques for water-containing phases

Transfer of water-containing phases into GC was of interest either aiming at an on-line water analysis

(unattended continuous control) or at on-line RPLC–GC.

3.1. Automated water analysis

Automated water analysis is still dominated by the Dutch, who even offer three entirely different approaches. The method from the Brinkman/Vreuls' group (e.g. [34]) is probably the most sensitive because of its high enrichment capacity. Up to 10 ml of water is extracted onto a solid-phase extraction (SPE) cartridge, the packing dried by a gas stream and desorbed with 100 μl of ethyl acetate. A 4×10 mm I.D. drying cartridge containing silica was added to the system for on-line removal of residual moisture. It is regenerated by heating and purging with nitrogen [35]. On the basis of this SPE approach, Jahr [36] developed a method for the determination of phenols in water.

Goosens et al. [37] optimised on-line liquid–liquid extraction with a phase separator for automated analysis of various types of water samples.

Mol et al. [38] as well as Louter et al. [39] presented reviews on trace analysis in aqueous samples with on-line enrichment. Mol et al. also perfectioned extraction of aqueous samples into open tubular traps coated by a thick film of a silicone stationary phase. The capillary was geometrically deformed in order to enhance radial dispersion and increase the extraction rates up to a few ml/min [40]. The water was displaced by a gas stream and the solutes desorbed with hexane. Transfer into GC involved PTV injection in solvent split mode.

3.2. On-line RPLC–GC

On-line RPLC–GC deals with water-containing phases which can usually be kept free of salts, hence enable direct evaporation, and which are more difficult to extract because of the stronger solvation by the organic components in the mobile phase.

3.2.1. Transfer via phase switching

Hyötyläinen et al. [41] applied on-line liquid–liquid extraction of the mobile phase into an organic solvent before transfer by the loop type interface. Morphine and its derivatives were determined in urine. On-line silylation was applied to facilitate GC analysis. In RPLC–GC, on-line derivatization is of particular importance because derivatization before RPLC is usually impossible.

Goosens et al. [42] described a method for on-line RPLC–GC with direct introduction of wetting mixtures of acetonitrile/water (up to 16% water) into GC by the retention gap technique. The relatively high retention power of the Carbowax-deactivated precolumn was overcome by thermostatting above the column temperature in a separate GC oven. An anion-exchange membrane in a kind of sandwich separator was used for on-line removal of the ion-pair reagent applied in the preceding RPLC (yield of 99.9%).

Herraiz et al. [43,44] used a PTV injector for coupling RPLC to GC. Fractions of more than 2 ml were transferred at flow rates of around 1.5 ml/min through a Tenax-packed 1 mm I.D. injector liner at 21°C, driven by helium at a flow rate of 800 ml/min. The GC column was removed during this time. Since the sample cannot be evaporated at this rate, transfer is primarily based on solid phase extraction (SPE). Desorption occurred thermally after remounting the column (a technique analogous to SPE-thermal desorption (SPE-TD)), described by Vreuls and coworkers [45,46]. The method was used for the analysis of edible oil components [47–49] and flavours [50]. Unfortunately, no data has been published on the recovery of the LC–GC transfer (extraction into Tenax). From the peak sizes it must be assumed that only a few percent of the material reaches GC [51]. The authors stress the high reproducibility of the transfer process, but if most of the solute material is lost, the quantitative aspects of this method should be reconsidered.

3.2.2. Transfer via direct evaporation

Water-containing eluents can be transferred without phase switching when the following points are respected.

1. The mobile phase is free of salts.
2. Vaporisation is performed in a packed insert.
3. Sample evaporation and solvent/solute separation occur in different compartments.
4. The vaporiser is at a temperature far above the eluent boiling point in order to transfer the large amount of heat consumed at a sufficient rate.
5. Solute retention cannot occur by solvent trapping.

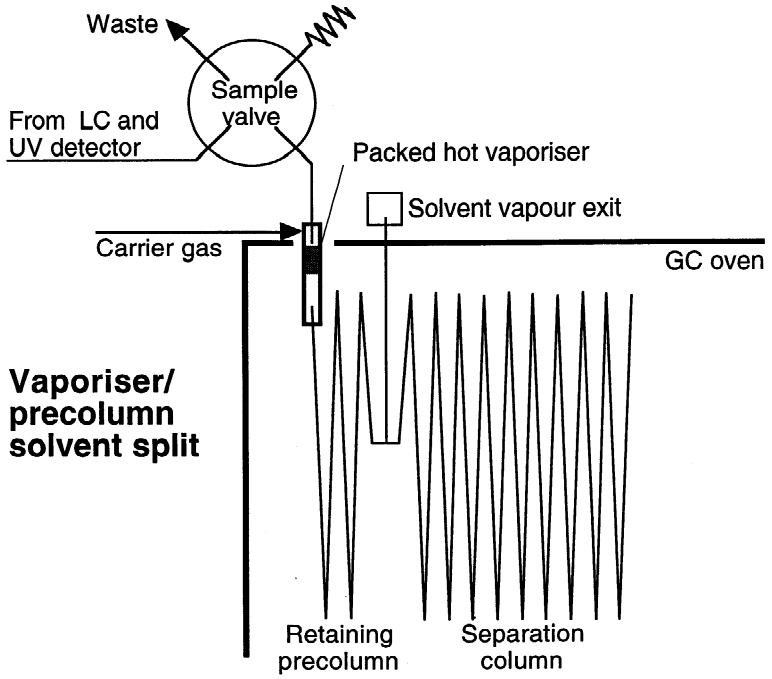

Fig. 6. Vaporiser/precolumn solvent split interface. When used for non-wetting mobile phases, vapours are discharged through a retaining precolumn.

Transfer through a vaporiser/pre-column solvent split system (Fig. 6 [52]) involves vaporisation in a 1 mm I.D. packed chamber typically at 250–350°C and release of the vapours through a retaining precolumn thermostatted in the column oven and a vapour exit. It enables direct transfer into GC without an upper limit of the water content and has been successfully used for two RPLC–GC applications by Hyötyläinen et al. [53,54].

The drawback of precolumn solvent splitting without solvent effects is the loss of solutes up to fairly high boiling points since the temperature of the precolumn must be sufficiently high to prevent recondensation of water. This aspect can be greatly improved upon by adding a packed bed of up to several adsorbents to the retaining capillary pre-column (Fig. 7). Since desorption from this packing requires high temperatures, a PTV injector was installed in the vapour outlet. For desorption, the gas flow is reversed, entering the packing with highest retention power and passing through the retaining precolumn into the separation column [55]. The name ‘‘swing system’’ expresses this change of flow direction. While the precolumn solvent splitting system was restricted to the analysis of methyl esters above C_{18}, the swing system also retains methyl octanoate (100 μl methanol–water, 1:1).

4. Outlook

LC–GC transfer and auxiliary techniques have been substantially refined during the last five years. The applications confirm the expectation that these are the most powerful chromatographic methods for complex analyses presently available. On the other hand, only few laboratories routinely use LC–GC. If an analysis presupposes on-line LC–GC, it is still widely taxed ‘‘not feasible’’. It is not used even when much time could be saved, following the motto of modern working style: *there is no time for saving time*.

If we analyse animal feed or foods of animal origin on mineral oil from wastes, e.g. used motor oil, by LC–GC (Fig. 8), a less efficient method must be developed in parallel for other laboratories. If this

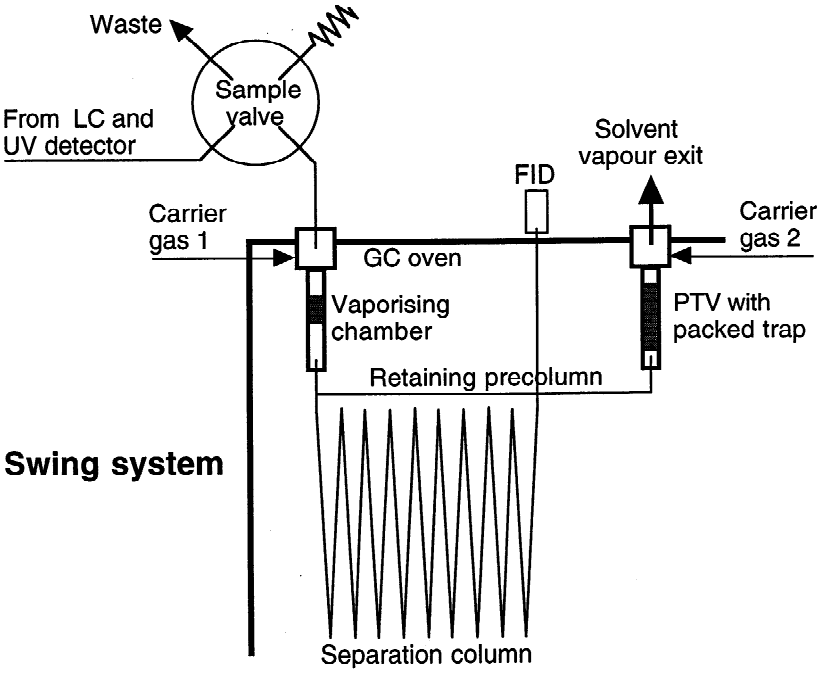

Fig. 7. Swing system for better retention of the volatile solutes.

is not feasible, the analysis cannot be performed all together.

4.1. Requirements for a better acceptance of LC–GC

4.1.1. Introduction through large volume injection

On-line LC–GC has the reputation of being complex. Broader use could be facilitated by simplifying the access. The most promising access is through large volume injection.

1. Fractions obtained from HPLC preseparation can be transferred off-line using large volume injection. In this way, the usefulness of the approach can be evaluated for a possible later justification of the effort and costs to start up an on-line system.
2. Large volume injection and on-line transfer involve the same principles. Hence large volume injection functions as a learning step.
3. Off-line transfer by large volume injection proved to be a useful complementary technique also for laboratories widely applying on-line LC–GC.

For instance, the confirmation of the identity of components analysed in LC or LC–GC involves the collection of the relevant LC fractions into, e.g., small autosampler vials. As concentrations are usually low, there are the options of reconcentrating this phase to a few microlitres followed by splitless injection, or of directly injecting a few 100 μl. Such off-line transfer turned out to be an excellent tool for comprehensive analysis of migrates, e.g., from the internal coating of food cans or tubes [56].

4.1.2. Adjustment of on-line transfer techniques

If the approach to on-line LC–GC is through large volume injection, the techniques involved should be the same. As proposed by David et al. [26], even the instruments could be largely the same, with modules being added to turn them into on-line analysers with LC suitable for LC–GC. The only dedicated instrument marketed so far, the Dualchrom 3000 from Fisons/CE Instruments, offered, in fact, many more features than just timing of the transfer.

A single injector/interface should be sufficient for as many applications as possible. We do not believe that the PTV interface is the best choice. On-column techniques show better performance, and contamina-

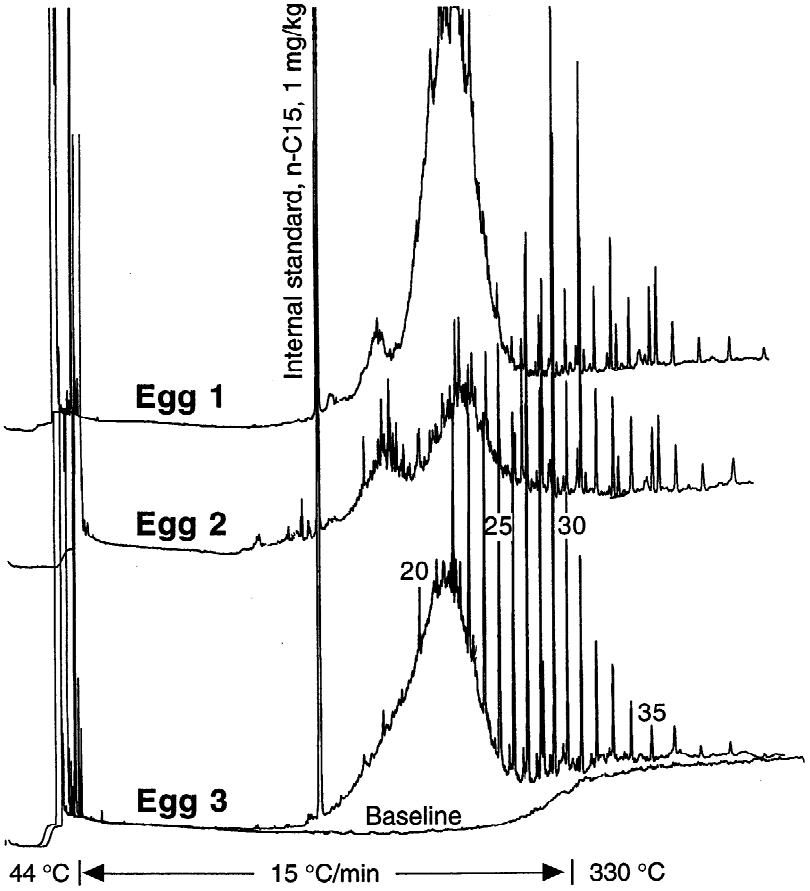

Fig. 8. LC–GC-flame ionization detection chromatograms of mineral oil material in eggs: unresolved humps of branched and cyclic paraffins. Olefins and aromatics (as well as fat and other egg components) were removed by LC. The *n*-alkanes are largely of natural origin. Egg 1 contained 22 mg/kg of saturated mineral oil paraffins, egg 2, 15 mg/kg and egg 3, 20 mg/kg, with at least two different molecular weight ranges. Most eggs and animal body fats are contaminated with such material. There is the suspicion that at least part of these paraffins is from waste oils, such as used motor oils, added to animal feed through used edible oils. 10 mg of crude fat extract from egg yolk injected onto four 25 cm×2 mm I.D. NPLC columns packed with silica gel in series, with pentane at 330 μl/min as mobile phase. The first two columns were backflushed with 2 ml of dichloromethane after each run. A 660 μl fraction was transferred to GC through the wire interface using a 1.5 m×0.53 mm I.D. retaining precolumn. The problem of analysing animal feeds and foodstuffs from animal origin are the large amounts of interfering natural olefins which must be removed by HPLC.

tion of the column inlet is not a serious problem when LC fractions are analysed.

Present on-line transfer with the retention gap technique is the same as used for large volume on-column injection; a transfer line from LC replaces the syringe. There is, however, no large volume injection based on concurrent solvent evaporation with the loop type interface, nor is the wire interface easily connected to an autosampler. Since concurrent evaporation of organic solvents is the by far most frequently used technique for on-line LC–GC, this is the gap to be filled.

4.1.2.1. On-column injection/transfer onto retaining precolumn

Concurrent solvent evaporation involving transfer through the on-column interface was shown in 1986 [57]. The loop type interface was preferred at that time because of its simplicity and robustness. In particular, it ruled out excessively fast transfer with

the consequence of overloading the precolumn and backflow into the injector and the gas supply. At that time, flow restrictions were severe because no solvent vapour exit was used.

With an open solvent vapour exit beyond a 1–2 m precolumn (Fig. 9), gas flow rates are in the range of several hundreds of ml/min, safely discharging the vapours from many hundreds of μl/min of liquid (3–10 μl/s). This well fits large volume injection as well as on-line LC–GC. As the vapours are diluted with carrier gas, lower oven temperatures can be used, which improves the retention of the volatile components.

When flooded zones are kept sufficiently short, injection/transfer may occur directly onto the retaining precolumn. With the commonly used separation columns, initial bands of 20–40 cm in length can be tolerated. This simplifies the system and avoids the use of possibly active uncoated precolumns. Performance for volatile solutes was better than that obtained with the loop type interface [58].

4.2. On-column interface

If a single injector/LC–GC interface should be selected, the on-column injector offers the following advantages.

1. The retention gap technique provides the best retention for the volatile solutes (solvent trapping).
2. On-column techniques provide the best conditions for the analysis of high boiling and labile solutes.
3. Concurrent evaporation directly on retaining precolumns of 1–2 m in length is possible.
4. A permanently hot vaporising chamber can be

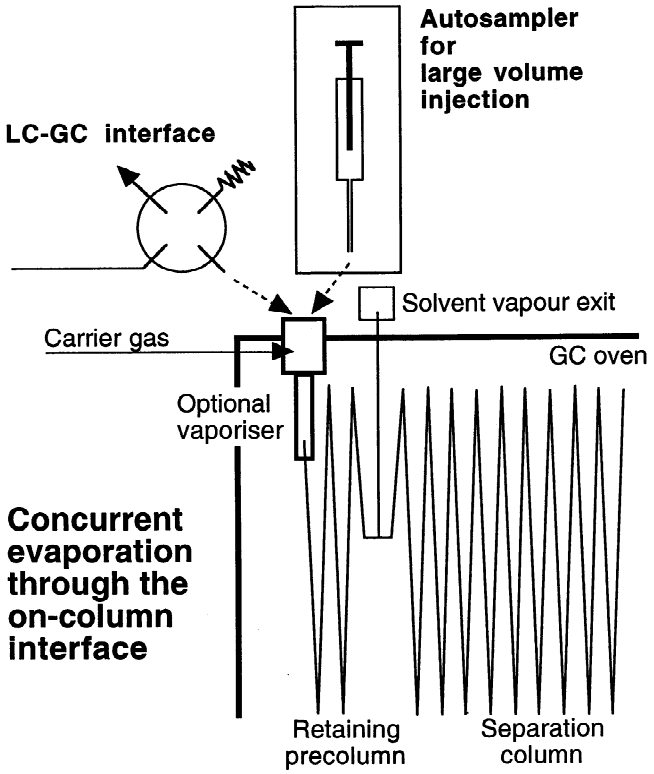

Fig. 9. Concurrent evaporation with the on-column interface for large volume injection as well as on-line LC–GC.

added as a filter for retaining non-evaporating by-products.

If technical performance and efficiency are the deciding criteria, on-line LC–GC and related techniques have a bright future. However, it presupposes appropriate education and the recognition that chromatography requires experts.

References

[1] J.J. Vreuls, G.J. de Jong, R.T. Ghijsen, U.A.Th. Brinkman, J. AOAC Int. 77 (1994) 306.
[2] K. Grob, J. Chromatogr. A 703 (1995) 265.
[3] L. Mondello, G. Dugo, K.D. Bartle, J. Microcol. Sep. 8 (1996) 275.
[4] E.C. Goosens, D. de Jong, G.J. de Jong, U.A.Th. Brinkman, Chromatographia 47 (1998) 313.
[5] L. Mondello, G. Dugo, K.D. Bartle, LC–GC Int., Jan. 98, 26.
[6] A.L. Baner, A. Guggenberger, J. High Resolut. Chromatogr. 20 (1997) 669.
[7] Ch. Droz, K. Grob, Z. Lebensm. Unters. Forsch. 205 (1997) 239.
[8] G.R. van der Hoff, R.A. Baumann, P. van Zoonen, U.A.Th. Brinkman, J. High Resolut. Chromatogr. 20 (1997) 222.
[9] F. Lanuzza, G. Micali, Riv. Ital. Sostanze Grasse 74 (1997) 509.
[10] M. Lechner, B. Reiter, E. Lorbeer, Fett/Lipid 101 (1999) 171.
[11] K.M.L. Holden, K.D. Bartle, S.R. Hall, J. High Resolut. Chromatogr. 22 (1999) 159.
[12] K. Grob, On-Line Coupled LC–GC, Hüthig, Heidelberg, 1991.
[13] K. Grob, M. Bronz, J. Microcol. Sep. 7 (1995) 421.
[14] H.J. Cortes, J. Chromatogr. 626 (1992) 3.
[15] K. Grob, M. Biedermann, J. Chromatogr. A 750 (1996) 11.
[16] K. Grob, A. Artho, P. Le Donne, J. High Resolut. Chromatogr. 15 (1992) 71.
[17] Th. Hankemeier, S.P.J. van Leeuwen, R.J.J. Vreuls, U.A.Th. Brinkman, J. Chromatogr. A A811 (1998) 117.
[18] E.M. Kristenson, J. Dallüge, C. Espiga, R.J.J. Vreuls, in: P. Sandra, A.J. Racksraw (Eds.), Proceedings (CD-ROM) 20th Int. Symp. on Capillary Chromatography, Riva del Garda, May 1998.
[19] E. Boselli, B. Grolimund, K. Grob, G. Lercker, R. Amadò, J. High Resolut. Chromatogr. 21 (1998) 355.
[20] B. Grolimund, E. Boselli, K. Grob, R. Amadò, G. Lercker, J. High Resolut. Chromatogr. 21 (1998) 378.
[21] E. Boselli, K. Grob, G. Lercker, J. High Resolut. Chromatogr. 22 (1999) 149.
[22] E. Boselli, K. Grob, G. Lercker, J. High Resolut. Chromatogr. 22 (1999) 327.
[23] K. Grob, M.-L. Riekkola, Chromatographia 18 (1984) 197.
[24] Th. Hankemeier, S.J. Kok, R.J.J. Vreuls, U.A.Th. Brinkman, J. Chromatogr. A 811 (1998) 105.
[25] T. Hyötyläinen, K. Grob, M.-L. Riekkola, J. High Resolut. Chromatogr. 20 (1997) 657.
[26] B. Grolimund, E. Boselli, K. Grob, R. Amadò, G. Lercker, J. High Resolut. Chromatogr. 21 (1998) 378.
[27] F. David, A. Hoffmann, P. Sandra, LC–GC Eur. September 1999, 550.
[28] K. Grob, A.M. Giuffré, M. Biedermann, M. Bronz, Fat Sci. Technol. 96 (1994) 341.
[29] S. Moret, K. Grob, L.S. Conte, J. High Resolut. Chromatogr. 19 (1996) 434.
[30] S. Moret, K. Grob, L.S. Conte, Z. Lebensm. Unters. Forsch. 204 (1997) 241.
[31] J. Blomberg, E.P.C. Mes, P.J. Schoenmakers, J.J.B. van der Does, J. High Resolut. Chromatogr. 20 (1997) 125.
[32] G.A. Jongenotter, M.A.T. Kerkhoff, H.C.M. van der Knaap, B.G.M. Vandeginste, J. High Resolut. Chromatogr. 22 (1999) 17.
[33] F. Lanuzza, G. Micali, G. Calabrò, J. High Resolut. Chromatogr. 19 (1996) 444.
[34] K.K. Verma, A.J.H. Louter, A. Jain, E. Pocurull, J.-J. Vreuls, U.A.Th. Brinkman, Chromatographia 44 (1997) 372.
[35] Th. Hankemeier, A.J.H. Louter, J. Dallüge, R.J.J. Vreuls, U.A.Th. Brinkman, J. High Resolut. Chromatogr. 21 (1998) 450.
[36] D. Jahr, Chromatographia 47 (1998) 49.
[37] E.C. Goosens, D. de Jong, G.J. de Jong, U.A.Th. Brinkman, J. High Resolut. Chromatogr. 20 (1997) 325.
[38] H.G.J. Mol, H.-G.M. Janssen, C.A. Cramers, J.J. Vreuls, U.A.Th. Brinkman, J. Chromatogr. A 703 (1995) 277.
[39] A.J.H. Louter, J.J. Vreuls, U.A.Th. Brinkman, J. Chromatogr. A 842 (1999) 391.
[40] H.G.J. Mol, H.-G. Janssen, C.A. Cramers, U.A.Th. Brinkman, J. Microcol. Sep. 7 (1995) 247.
[41] T. Hyötyläinen, H. Keski-Hynnilä, M.-L. Riekkola, J. Chromatogr. A 771 (1997) 360.
[42] E.C. Goosens, I.M. Beerthuizen, D. de Jong, G.J. de Jong, U.A.Th. Brinkman, Chromatographia 40 (1995) 267.
[43] F.J. Senorans, M. Herraiz, J. Tabera, J. High Resolut. Chromatogr. 18 (1995) 433.
[44] F.J. Senorans, G. Reglero, M. Herraiz, J. Chromatogr. Sci. 33 (1995) 446.
[45] J.J. Vreuls, U.A.Th. Brinkman, G.J. de Jong, K. Grob, A. Artho, J. High Resolut. Chromatogr. 14 (1991) 455.
[46] A.J.H. Louter, J. van Doornmalen, J.J. Vreuls, U.A.Th. Brinkman, J. High Resolut. Chromatogr. 19 (1996) 679.
[47] F.J. Senorans, J. Villen, J. Tabera, M. Herraiz, J. Agric. Food Chem. 46 (1998) 1022.
[48] M.L. Ruiz del Castillo, M. del Mar Caja, M. Herraiz, G.P. Blanch, J. Agric. Food Chem. 46 (1998) 5128.
[49] J. Villen, G.P. Blanch, M.L. Ruiz del Castillo, M. Herraiz, J. Agric. Food Chem. 46 (1988) 1419.
[50] G.P. Blanch, M.L. Ruiz del Castillo, M. Herraiz, J. Chromatogr. Sci. 36 (1998) 589.
[51] K. Grob, J. High Resolut. Chromatogr. 18 (1995) 665.

[52] K. Grob, M. Biedermann, J. Chromatogr. A 750 (1996) 11.
[53] T. Hyötyläinen, K. Grob, M. Biedermann, M.-L. Riekkola, J. High Resolut. Chromatogr. 20 (1997) 410.
[54] T. Hyötyläinen, K. Jauho, M.-L. Riekkola, J. Chromatogr. A 813 (1998) 113.
[55] E. Pocurull, M. Biedermann, K. Grob, J. Chromatogr., in press.
[56] M. Biedermann, K. Grob, P. Böhler, H.R. Widmer, Mitt. Gebiete Lebensm. Hyg. 89 (1998) 529.
[57] K. Grob, Ch. Walder, B. Schilling, J. High Resolut. Chromatogr. Chromatogr. Commun. 9 (1986) 95.
[58] M. Biedermann, K. Grob, F. Munari, in: P. Sandra, A.J. Rackstraw (Eds.), Proceedings (CD-ROM) 20th Int. Symp. on Capillary Chromatography, Riva del Garda, May 1998.