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Using computer modeling to predict and optimize separations for comprehensive two-dimensional gas chromatography

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Abstract

In order to fully realize the separation power of comprehensive two-dimensional gas chromatography (GC × GC), a means of predicting and optimizing separations based on operating variables was developed. This approach initially calculates the enthalpy (ΔH) and entropy (ΔS) for the target compounds from experimental input data, and then uses this information to simultaneously optimize all column and runtime variables, including stationary phase composition, by comparing the performance of large numbers of simulated separations. This use of computer simulation has been shown to be a useful aid in conventional separations. It becomes almost essential for GC × GC optimization because of the large number of variables involved and their very complex interaction. Agreement between experimental and predicted values of standard test samples (Grob mix) using GC × GC separation shows that this approach is accurate. We believe that this success can be extended to more challenging mixtures resulting in optimizations that are simpler and transferable between GC × GC instruments.

Keywords: GC × GC; Computer modeling; Retention indices; Comprehensive GC; 2D-GC

1. Introduction

The power of comprehensive gas chromatography (GC) × GC, as developed by Phillips and Liu [1], lies in the peak capacity improvement over conventional GC. GC × GC associates retention times on two different columns with each component of a sample mixture. The flow sequence is injector, column one, modulator, column two, and detector. The output of the first column is “sliced” into many of these time increments each of which is refocused onto column two. The purpose of the second column is to achieve an orthogonal separation as compared to the first column, resulting in separation along two axes, each with unique selectivity. A plot $1t_R$ (slice number) versus $2t_R$ spreads the peaks onto a two-dimensional surface. Detector response can be plotted in the third dimension.

Significant simplification and cost savings could be achieved if GC × GC could be used with inexpensive, universal detection methods, such as flame ionization detection (FID), at least for routine analyses. However, calibration of such an instrument for a complex mixture by the traditional means of injection of pure components in pure form becomes a larger problem, as this technique is often employed for the most complex separations. A possible solution may lie in characterization of a complex mixture using GC × GC–TOF-MS (time-of-flight mass spectrometry) instrumentation, then “downloading” the method to less expensive instrumentation using a less complex detector. This alternative presents two new challenges, however. First, the method must now be carefully optimized to insure separation because instrumentation such as GC × GC-FID has no capability to identify unresolved components. This leaves the possibility of method development on GC × GC–TOF-MS then transferring the method to less expensive instrumentation such as GC × GC-FID for routine use. Thus, a mathematical algorithm is required to translate the GC × GC–TOF-MS settings for use with other detectors that differ in operating parameters.

Optimization and translation are more difficult for GC × GC than ordinary one-dimensional GC irrespective of the detector issue. The mathematical algorithms that describe GC are well known, and are also easy to apply in the one-dimensional case. Although the theory remains the same for GC × GC, application becomes more difficult. For example, one expects simple

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improvement in one-dimensional GC by increasing column length. In contrast, for GC × GC, the situation is much less clear. Increasing the length of the second column will decrease the flow rate in both columns, thus changing both t_1 and t_2 and separation quality. Likewise, switching column two output pressures from vacuum (GC × GC–TOF-MS) to 1 bar (FID) changes the modulator pressure and hence the flow rate and retention times for both columns one and two. Even minor retention time shifts have the potential to affect major changes to the two-dimensional chromatogram since each time slice may now collect different components from column one. Thus, a component may completely disappear from one time slice and reappear in another. Not only does this confound identification by t_1 and t_2, but it also changes the separation task of column two. This behavior is not unique to column length or outlet pressure changes, but a possible consequence of several variable changes. Thus, as a general rule even minor parameter changes, such as changing from GC × GC–TOF-MS to FID, will have complicated effects on the chromatogram.

Optimizing stationary phase variables in GC × GC presents special opportunities. With one-dimensional columns [2], stationary phase composition is optimized by adding and subtracting components (polymer functionalities). GC × GC optimization presents the same opportunity (or opportunity) but also allows choice of column (one or two) for the addition/subtraction. The significant difference in the two columns will ordinarily be temperature. Thus, from a theoretical point of view, an important advantage of GC × GC is the exploitation of this difference. Computer simulation permits optimization by simultaneously adjusting the temperature programs and phase compositions for the two columns, thus making maximum use of the additional variables associated with GC × GC.

Modulation rate (or time) is an important additional variable, which is the period of time the output of column one is stored before releasing it onto column two. Standard practice is to choose a modulation period that is longer than the retention time of any component on column two. Column two dimensions are usually chosen so that component retention times are only a few seconds. Other approaches have been used, however. Truong et al. [3], for example, have shown that improvement of sensitivity by a factor of 80 is possible by choosing time slices to include entire peaks. From a simulation standpoint, it is easy to choose a variable modulation rate that optimizes the performance in each part of the chromatogram. This complexity has yet to be achieved in practice, however. In any event, modulation rate joins the more than 10 variables that must be optimized for a given GC × GC application.

Other researchers have attempted to develop predictive modeling procedures to address this separation. Their approaches typically utilize empirical-fit procedures based on either Kovats indices [4,5] or by calculation retention indices based on GC × GC retention data [6]. Additional predictive modeling efforts based on calculations of flow rates given various GC × GC columns configurations and the impart on the resulting separations have also been presented [7,8].

The approach used for this work uses calculated thermodynamic retention indices (ΔH and ΔS), and has been termed computer-assisted stationary phase design, or CASPD, in a previous publication [2]. For extension into comprehensive GC × GC, CASPD2d simulates GC × GC separations as a function of the many variables involved. The result of each simulation is automatically compared with previous output so that the process can proceed toward an optimized set of variables as previously reported in the one-dimensional version, CASPD. The input data consists of the adjusted retention time of each component on each stationary phase under two different temperature programs. This small amount of required input data can come either from one-dimensional or GC × GC instrumentation. Sufficient input data could be achieved rapidly using GC × GC–TOF-MS instrumentation. CASPD2d can then optimize variables for both GC × GC–TOF-MS and GC × GC-FID instrumentation including peak identification for the latter.

2. Experimental

All separations (conventional and GC × GC) were performed using an Agilent Technologies (Little Falls, DE, USA) 6890N gas chromatograph with a split/splitless injection port and a flame ionization detector. The GC system was fitted with a thermal modulator system from LECO (St. Joseph, MI, USA) which uses cryogenically cooled nitrogen and heated air jets to modulate the effluent of column one onto column two. Instrument control and data processing was via ChromaTOF-MS GC × GC (LECO) for the modulated separations and ChemStation (Agilent Technologies) for the conventional separations. All separations used helium as the carrier gas and purification of the carrier as well as the FID gasses was accomplished using a multiple-stage sorbent trap (Restek, Bellefonte, PA, USA). All injections were Grob mix (Restek, catalog no. 35000 and CS-5024) for all analyses with an injection volume of 1.0 μL, using a 7683 autosampler (Agilent Technologies), and a spilt ratio of 10:1. Constant pressure regulation was used for all analyses.

In order to obtain the thermodynamic retention indices for each analyte on each stationary phase, a conventional separation of the Grob mix was performed at two different oven temperature programs (different elution temperatures). The column hold up time (dead time) was also determined for each column by injection of methane at 100 °C. Dead times were verified after all analyses to ensure that no change in linear velocity had developed during the course of data collection. All columns were measured to determine the actual length. Internal diameters (i.d.) and stationary phase film thickness (d_f) were as listed from the manufacturer (Restek).

Initial experiments were run using the intended first dimension column, which was polydimethylsiloxane (Rtx-1). Column dimensions were 30 m (nominal) × 0.25 mm i.d., 0.25 μm d_f Retention times for the target analytes on this column were entered into the modeling program as described below, along with the experimental parameters (column dimensions, pressure, temperature program, dead time, etc.). The modeling program then calculated the indices (ΔH, ΔS) for each component. This procedure was then repeated using a 14% cyanopropylmethyl/14% phenylmethylpolydimethylsiloxane (Rtx-1701).