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Predictions of comprehensive two-dimensional gas chromatography separations from isothermal data

Shukui Zhu[a,*], Sheng He[a], David R. Worton[b,c], Allen H. Goldstein[b]

[a] Key Laboratory of Tectonics and Petroleum Resources (China University of Geosciences), Ministry of Education, Wuhan 430074, China
[b] Department of Environmental Science, Policy & Management, University of California, 151 Hilgard Hall, Berkeley, CA 94720, USA
[c] Aerosol Dynamics Inc., Berkeley, CA 94710, USA

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ABSTRACT

Two-dimensional retention times and peak widths in temperature programmed comprehensive two-dimensional gas chromatography were predicted using a theoretical model developed from experimental data obtained under isothermal conditions. A Matlab program was written to calculate the following parameters: dead time (t_M), elution temperature (T_e), retention time (t_R), hold-up width (w_M) and peak width (w_R). The two-dimensional retention times of a sample mixture that contained n-alkanes and polyaromatic hydrocarbons (PAHs) were predicted and were observed to be in excellent agreement with experimentally determined values. The relative deviation between the model and the experimental data was less than 2 and 7% for the primary and secondary retention times, respectively. The relative deviation of peak width was less than 7 and 10% in the primary and secondary dimensions, respectively. The advantage of this model was its simplicity, informed entirely from experimental data, with no reliance on theoretical parameters. This prediction model would be useful for optimizing GC × GC separation conditions and for confirming compound identifications of components that are chromatographically resolved but that have nearly identical mass spectra.

1. Introduction

Developing the capability to predict retention times in temperature programmed gas chromatography (GC) has attracted a great deal of interest over the last 30 years. As a result many methods have been developed that can predict the retention times of compounds in one-dimensional gas chromatography (1DGC) [1–10]. The ability to predict retention times and peak widths offers several key advantages. Firstly, optimization of GC separating conditions becomes easier and more efficient, especially for the analysis of complex samples. Secondly, predicted retention times provide an important complement for detailed analysis when used in conjunction with mass spectrometry to confirm compound identifications. This is especially important for isomeric compounds which may have differing physical properties allowing them to be chromatographically separated but that have very similar mass spectral fragmentation patterns, which limit definitive identification.

The resolution of 1DGC is often insufficient when analyzing complex samples, even with the use of highly selective stationary phases and high resolution 'narrow-bore' columns. With the introduction of comprehensive two-dimensional gas chromatography (GC × GC), high peak capacity and resolving power have become more readily available [11]. In GC × GC, the peaks eluting from the first column enter a modulator, which continuously traps short portions (e.g. 5 s) of the effluent and rapidly introduces them as sharp pulses onto the second column for additional separation. GC × GC has been successfully applied to resolve the chemical composition of many different types of complex mixtures, e.g., petrochemicals [12], foods [13] and atmospheric aerosols [14].

The capability to do accurate retention time and peak width predictions in GC × GC would be particularly advantageous because determining the optimal column sets and temperature program conditions in GC × GC can be substantially more complicated and time-consuming than 1DGC. Previous work on retention time and peak width predictions of 1DGC are not suitable to GC × GC in their current forms and further theoretical development of them is necessary in order to make them applicable.

Previous studies have taken various approaches to predict separations in GC × GC. For example, Beens et al. calculated two-dimensional retention times using vapor pressure and the enthalpic contribution to the activity coefficient to determine the capacity factor (k) [15]. Western and Marriott depicted GC × GC retention maps by studying the elution of a series of some selected reference compounds [16]. Lu et al. developed a model to predict the resolution of a component pair of interest and optimize the temperature program to give the desired resolution [17].

* Corresponding author. Tel.: +86 15391512571.
E-mail addresses: shukuizhu@126.com, shukuizhu@cug.edu.cn (S. Zhu).

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Zhu et al. determined the GC × GC retention indices under constant inlet pressure conditions from so-called 'isovolatility' curves [18]. Zhao et al. developed a method to calculate the second dimension retention index of GC × GC data using n-alkanes as reference compounds [19]. D'Archivio et al. used a quantitative structure–retention relationship (QSRR) method to predict the retention times of polychlorinated biphenyls (PCBs) in GC × GC [20]. Seeley and Seeley developed a model for approximating the relative retention of solutes in GC × GC by using retention data from standard single-column temperature-programmed separations [21], and then developed a solvation parameter model to predict GC × GC retention diagrams for 54 solutes on four different stationary phase combinations [22]. Bieri and Marriott developed a method producing simultaneously three retention indices for compounds in dual-secondary column GC × GC [23], and then developed a new instrumental approach for determining bidimensional retention indices in GC × GC, which will allow straightforward determination of temperature-variable retention indices of target analytes [24].

In this paper, a simple and novel model to predict GC × GC retention time and peak widths was developed based entirely on experimental retention time data obtained under isothermal conditions. This model was used to 'simulate' a GC × GC chromatogram of n-alkanes and PAHs under temperature programmed conditions and was compared against an experimental separation of the same components obtained using identical chromatographic conditions. Additionally, it can be expanded to predict retention times and peak widths of many other compounds and so can be applied to more complex samples.

2. Theory

2.1. Prediction of two-dimensional retention time

To predict retention times in temperature programmed GC, two critical parameters need to be determined: the dead time (t_M) of the analytical columns and the elution temperature (T_e) of the compounds of interest. A detailed description of the chromatographic theory used here has been described previously [18]. In brief, t_M is the time a non-retained compound spends in the mobile phase, which is also the amount of time the non-retained compound spends on the column. Since compounds used to determine dead time (such as methane) are not retained in the cryotrap, it is difficult to be experimentally determined in the second dimension. In this study the dead time was obtained according to the definition of the capacity factor (k), which is often used to describe the migration rate of an analyte on a column and is related to t_M by:

$$k = \frac{t_R - t_M}{t_M} \tag{1}$$

According to the carbon number law [25], t_M can be determined by measuring the absolute retention time (t_R) for a series of n-alkane homologs analyzed under isothermal conditions according to:

$$\ln\ k = \ln\left(\frac{t_R - t_M}{t_M}\right) = a_1 n + b_1 \tag{2}$$

where n is the n-alkane carbon number and a_1 and b_1 are constants that define the slope and intercept, respectively, of a straight line.

According to thermodynamic theory [26], k for an analyte under isothermal conditions is related to T_e by:

$$\ln\ k = \ln\left(\frac{\alpha}{\beta}\right) - \frac{\Delta H}{RT_e} \tag{3}$$

where β is the phase ratio ($V_{mobile}/V_{stationary}$), $\alpha = \exp(\Delta S/R)$, R is the molar gas constant, ΔH is the change in enthalpy and ΔS is the change in entropy. Although it was defined under isothermal conditions, Eq. (4) was proved to be usable when the temperature changed, and the minor error could be neglected in the scale of usual GC temperatures [27]. By determining the absolute retention time of compounds at two or more different isothermal separation temperatures it is possible to determine values for $-\Delta H/R$ (slope) and α/β (intercept) by plotting $\ln k$ versus $1/T_e$.

Linear temperature programmed gas chromatography is well known to be described by [26]:

$$\int_0^{t_R} \frac{dt}{t_M[1 + \alpha/\beta\ \exp(-\Delta H/RT)]} = 1 \tag{4}$$

Defining r as the oven ramp rate and T_0 as the initial temperature in a temperature programmed run, Eq. (4) can be rewritten as:

$$\frac{1}{r}\int_{T_0}^{T} \frac{dT}{t_M[1 + \alpha/\beta\ \exp(-\Delta H/RT)]} = 1 \tag{5}$$

By substituting the calculated values of α/β and $-\Delta H/R$ into Eq. (5), the T_e and therefore t_R can be determined for separations conducted under temperature programmed conditions.

2.2. Prediction of peak widths

In order to predict the peak widths the hold-up width (w_M) needs to be determined. The hold-up width is the base width of a non-retained analyte. The width factor (p) relates the hold-up width (w_M) to the peak width at the base (w_R) for a series of homologs under isothermal conditions by [28]:

$$p = \sqrt{\frac{w_R^2 - w_M^2}{w_M^2}} \tag{6}$$

By analogy to retention time, the linear relationship between the natural logarithm of p and the carbon number (n) under isothermal chromatographic conditions can be described by [29]:

$$\ln\ p' = a_2 n + b_2 \tag{7}$$

where a_2 and b_2 are constants that define the slope and intercept, respectively, of this relationship. The hold-up width can be determined by measuring w_R for a series of n-alkane homologs analyzed under isothermal conditions.

For a specific compound, under temperature programmed conditions, p and T_e are known to be related by [30]:

$$\ln\ p' = a_3 + \frac{b_3}{T_e} \tag{8}$$

where a_3 and b_3 are constants. By determining the peak width of compounds at two or more different isothermal separation temperatures it is possible to determine values for a_3 (slope) and b_3 (intercept) by plotting $\ln p$ versus $1/T_e$.

Therefore, for any compounds in a temperature programmed GC run, the elution temperature (T_e) can be obtained by Eq. (5) in Section 2.1, and then the base peak width (w_R) can be predicted using Eq. (8).

3. Experimental

3.1. Materials

Retention parameters for the n-alkanes and PAHs were determined through injections of two custom standard mixtures: one containing C_8–C_{40} n-alkanes (Accustandard) and another containing C_8–C_{40} n-alkanes and a range of two to six ring PAHs (Accustandard). These standards were either injected separately or

together. The PAH standard contained 16 PAHs, which were: naphthalene ($C_{10}H_8$), acenaphthylene ($C_{12}H_8$), acenaphthene ($C_{12}H_{10}$), fluorene ($C_{13}H_{10}$), phenanthrene ($C_{14}H_{10}$), anthracene ($C_{14}H_{10}$), fluoranthene ($C_{16}H_{10}$), pyrene ($C_{16}H_{10}$), benzo[a]anthracene ($C_{18}H_{12}$), Chrysene ($C_{18}H_{12}$), benzo[b]fluoranthene ($C_{20}H_{12}$), benzo[k]fluoranthene ($C_{20}H_{12}$), benzo[a]pyrene ($C_{20}H_{12}$), indeno[1,2,3-cd]pyrene ($C_{22}H_{12}$), dibenz[a,h]anthracene ($C_{22}H_{14}$), and benzo[g,h,i]perylene ($C_{22}H_{12}$).

3.2. GC × GC instrumentation and methods

The GC × GC system consisted of a GC (6890 model, Agilent Technologies, Wilmington, DE, USA) equipped with a flame ionization detector (FID) and a time-of-flight mass spectrometer (Pegasus III, Leco Corp., St. Joseph, MI, USA). The GC oven contained two capillary columns that were connected serially by means of a press-fit connector with zero dead volume along with a cold-jet modulator (part of the Pegasus III set-up). Nitrogen and air were used as the cold and hot gases, respectively. The modulation time was 5 s. A detailed description of the cold-jet modulator has been described in a previous publication [31]. A Rxi-5MS column 30 m × 0.25 mm × 0.50 μm (Restek, Bellefonte, PA, USA) and a Rtx-200MS column 1.2 m × 0.10 mm × 0.10 μm (Restek, Bellefonte, PA, USA) were used as the primary and secondary dimensional columns, respectively. The carrier gas was helium (purity ≥99.9995%). The injector temperature was 290 °C and injections were performed in split mode with a split ratio of 30:1. The mass spectrometer was operated at an acquisition rate of 100 spectra per second for a mass range of 35–500 *m/z* using 70 eV electron impact ionization and 1650 V multi-channel plate voltage. The ion-source temperature was 220 °C and the transfer-line temperature was 250 °C. The pressure inside the flight tube was about 10^{-7} Torr.

3.3. Data processing

In order to calculate the parameters outlined in Section 2 (t_M, T, t_R, w_M and w_R), a custom Matlab (Mathworks) program was written, which calculates t_R and w_R values based on isothermal retention time data, e.g., for a series of n-alkane homologs.

4. Results and discussion

4.1. Determination of dead time and hold-up width

According to Eqs. (1) and (7) the dead time (t_M) and hold-up width (w_M) can be calculated by determining the retention times (t_R) and peak widths (w_R) of a series of n-alkane homologs under isothermal conditions. Apparently, three or more data points need to be collected for each analyte. In order to obtain the average value and provide some necessary data for determining the thermodynamic parameters in Section 4.2, the C_8–C_{40} n-alkane standard was injected at 12 different isothermal temperatures (100, 110, 120, 140, 160, 180, 200, 220, 240, 260, 280, and 290 °C). The GC oven was held for 30–90 min at the isothermal temperature before ramping to 330 °C at 10 °C/min.

The resultant retention time data for all 12 isothermal temperatures are shown in Appendix A, Table A.1. This data was analyzed using the Matlab program, which determined values for t_M and w_R that resulted in the best linear fits for $\ln(t_R - t_M)/t_M$ against carbon number (n) for both dimensions. According to these linear regression curves for the C_{13}–C_{17} n-alkanes separated at an isothermal temperature of 140 °C and flow rate of 1.8 ml/min, the dead times (t_M) in both dimensions were determined to be 1.21 min and 0.42 s for the primary and secondary dimensions, respectively. The

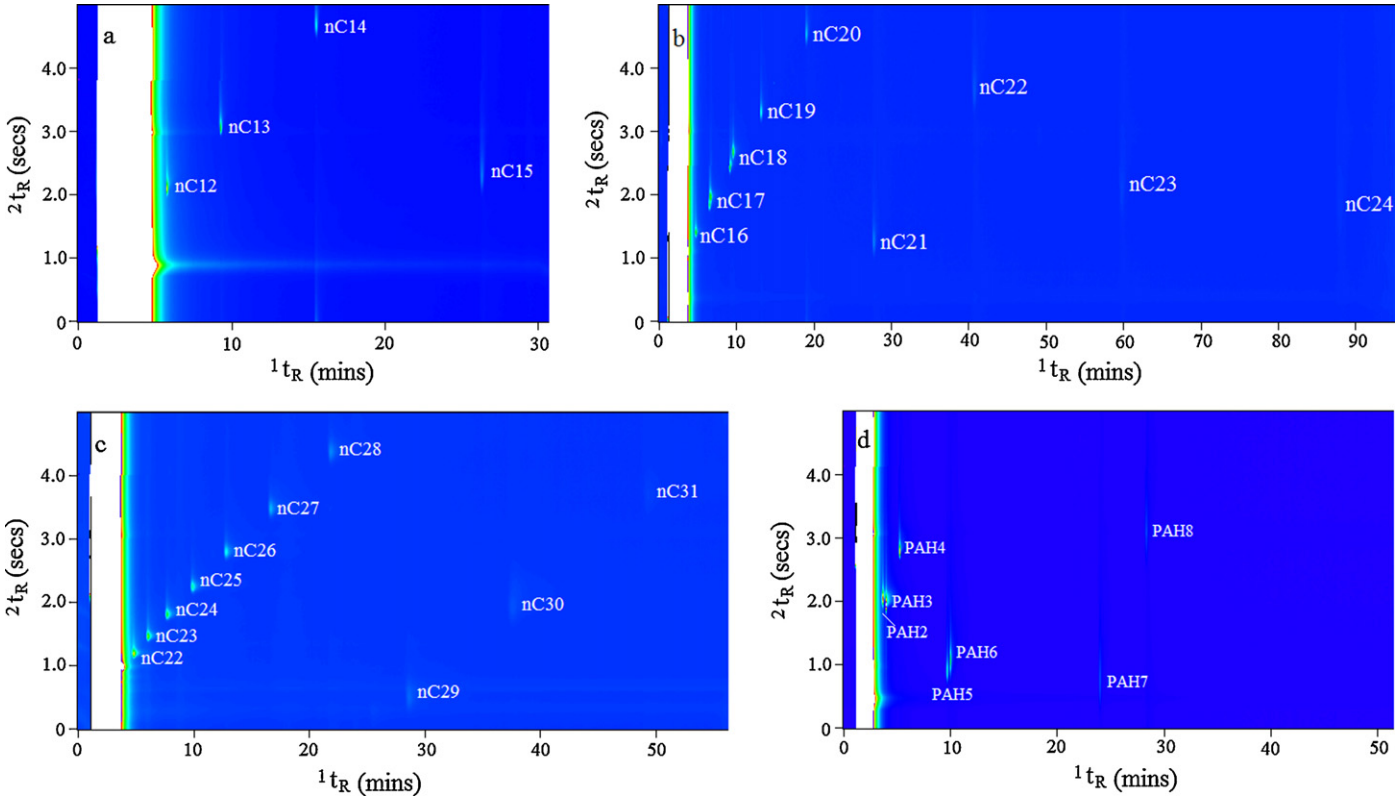

Fig. 1. Example GC × GC chromatograms of n-alkanes and PAHs separated under different isothermal temperature conditions. (a) n-Alkanes, 120 °C (30 min), (b) n-alkanes, 180 °C (90 min), (c) n-alkanes, 240 °C (60 min), and (d) PAHs,180 °C (60 min). *Key*: PAH_2 = acenaphthylene ($C_{12}H_8$), PAH_3 = acenaphthene ($C_{12}H_{10}$), PAH_4 = fluorene ($C_{13}H_{10}$), PAH_5 = phenanthrene ($C_{14}H_{10}$), PAH_6 = anthracene ($C_{14}H_{10}$), PAH_7 = fluoranthene ($C_{16}H_{10}$), and PAH_8 = pyrene ($C_{16}H_{10}$).

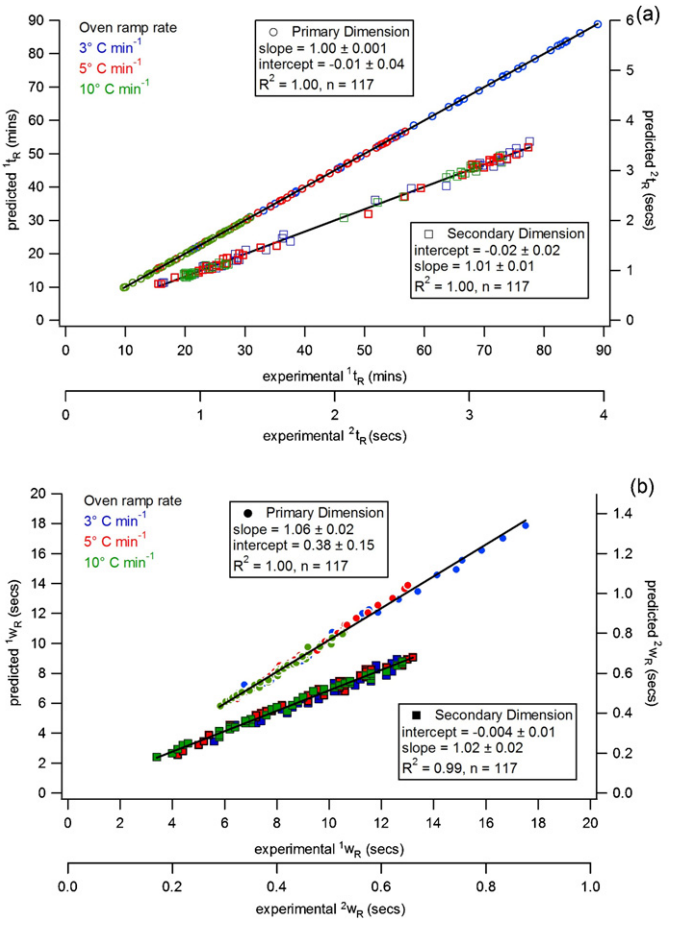

Fig. 2. Comparison of experimental and predicted retention times (a) and peak widths (b) for the C_{12}–C_{40} n-alkanes and 16 PAHs on both the primary and secondary dimension columns.

hold-up widths (w_M) were 5.08 s and 0.09 s for the primary and secondary dimensions, respectively.

4.2. Determination of thermodynamic parameters

According to Eq. (3) the thermodynamic parameters (α/β and $-\Delta H/R$) can be calculated by determining retention times (t_R) under different temperature conditions and plotting $\ln k$ (derived from Eq. (2)) versus T_e. The C_8–C_{40} n-alkanes and PAHs mixture were analyzed at isothermal temperatures of 100, 110, 120, 140, 160, 180, 200, 220, 240, 260, 280, and 290 °C. Several example GC × GC chromatograms are shown in Fig. 1 and the observed retention times are listed in Table A.1. T_e for the individual compounds could be derived from Eq. (5) and then t_R could be easily predicted from the oven temperature program.

Similarly, two-dimensional peak widths could be obtained from the contour plots. According to Eq. (8), a_3 and b_3 could be calculated from a plot of $\ln p$ versus T_e. When T_e is known, two-dimensional peak widths of the individual compounds can be easily predicted.

4.3. Prediction of retention time and peak width of compounds in a temperature programmed analysis

Using thermodynamic parameters determined at isothermal conditions (Section 4.2), the retention time and peak width of compounds in a mixed sample were predicted for a range of different GC oven temperature programs. The initial and final oven temperatures were 40 and 290 °C, respectively. Comparison between

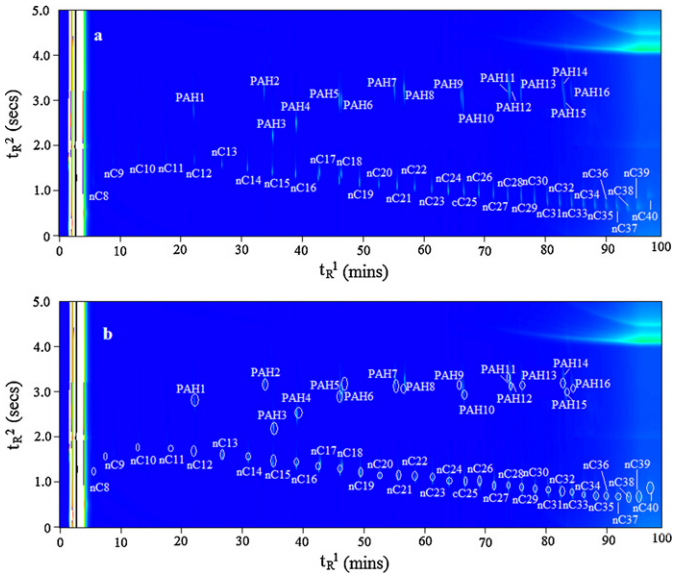

Fig. 3. Comparison of a GC × GC chromatogram of an injection of a standard mixture of C_8–C_{40} n-alkanes and 16 PAHs and the predicted retention times determined from the model developed in this work, (a) GC × GC chromatogram of a standard mixture, (b) overlaid picture of (a) and predicted chromatogram (ellipses). *Key*: PAH_1 = naphthalene ($C_{10}H_8$), PAH_2 = acenaphthylene ($C_{12}H_8$), PAH_3 = acenaphthene ($C_{12}H_{10}$), PAH_4 = fluorene ($C_{13}H_{10}$), PAH_5 = phenanthrene ($C_{14}H_{10}$), PAH_6 = anthracene ($C_{14}H_{10}$), PAH_7 = fluoranthene ($C_{16}H_{10}$), PAH_8 = pyrene ($C_{16}H_{10}$), PAH_9 = benzo[a]anthracene ($C_{18}H_{12}$), PAH_{10} = chrysene ($C_{18}H_{12}$), PAH_{11} = benzo[b]fluoranthene ($C_{20}H_{12}$), PAH_{12} = benzo[k]fluoranthene ($C_{20}H_{12}$), PAH_{13} = benzo[a]pyrene ($C_{20}H_{12}$), PAH_{14} = indeno[1,2,3-cd]pyrene ($C_{22}H_{12}$), PAH_{15} = dibenz[a,h]anthracene ($C_{22}H_{14}$), and PAH_{16} = benzo[g,h,i]perylene ($C_{22}H_{12}$).

the model predictions and the experimental data for the retention times and peak widths are shown in Fig. 2a and b, respectively. The predicted values were in very good agreement with experimental values, with slopes between predicted and experimental values of unity and negligible intercepts. Appendix A, Tables A.2 (retention times) and A.3 (peak widths) list the data and show the relative deviation between the model and experimental data for the 23 n-alkanes and 16 PAHs presented here. The relative deviation in the predicted versus experimental retention times are less than 2 and 7% for the primary and secondary dimensions, respectively. The relative deviation of peak widths is less than 7 and 10% in the primary and secondary dimensions, respectively. The model was further validated by simulating a GC × GC chromatogram of the n-alkane and PAH standard mixture for an oven ramp of 3 °C/min. Fig. 3 demonstrates very good agreement between the experimental and simulated GC × GC chromatograms, providing validation of the theoretical methodology.

5. Conclusions

In this paper a simple and novel method for predicting two-dimensional retention times and peak widths in temperature-programmed conditions was developed, based on experimental data obtained under isothermal conditions. Once constrained by isothermal data the model can predict separations for different chromatographic conditions, e.g., oven ramp rates, relatively easily. To illustrate the application of the model a GC × GC chromatogram separation of n-alkanes and PAHs under temperature programmed conditions was simulated and compared against one obtained experimentally. There was very good agreement between the predicted and experimental values providing validation of the model. While, in this work, the model was only initially applied to 23 n-alkanes and 16 PAHs, it can be expanded to other compounds

and future work will focus on applying this methodology to more complex samples, more typically analyzed by GC × GC.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.chroma.2012.02.032.

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