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A standardized method for the calibration of thermodynamic data for the prediction of gas chromatographic retention times

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ABSTRACT

A new method for calibrating thermodynamic data to be used in the prediction of analyte retention times is presented. The method allows thermodynamic data collected on one column to be used in making predictions across columns of the same stationary phase but with varying geometries. This calibration is essential as slight variances in the column inner diameter and stationary phase film thickness between columns or as a column ages will adversely affect the accuracy of predictions. The calibration technique uses a Grob standard mixture along with a Nelder–Mead simplex algorithm and a previously developed model of GC retention times based on a three-parameter thermodynamic model to estimate both inner diameter and stationary phase film thickness. The calibration method is highly successful with the predicted retention times for a set of alkanes, ketones and alcohols having an average error of 1.6 s across three columns.

1. Introduction

Predictive modelling of gas chromatographic separations is valuable both for the optimization of separation conditions [1] and in the determination of unknown peaks in chromatograms [2]. The increased interest in comprehensive multidimensional gas chromatography (GC × GC) creates a need for improved tools to aid in optimization and peak identification.

Tools for computer-based optimization of GC × GC separations are required because the true optimization of these separations across the multitude of possible stationary phase and geometry combinations available is time consuming for even experienced users. This arises from the interdependence of the separation conditions in the two dimensions of the GC × GC experiment. Any changes made to one dimension (i.e. column geometry, column chemistry, temperature, or flow) will affect the conditions experienced by analytes in both dimensions of the separation [3]. Accurate predictive modelling tools would prove extremely useful for the rapid development of both GC × GC, and to a lesser extent GC methods.

Predictive modelling also aids in the determination of unknown peaks within chromatographic separations, particularly when used in conjunction with mass spectrometry. Retention data adds another layer of information and confidence to compound identification, particularly for compounds such as structural isomers that would otherwise be difficult or outright impossible to distinguish by mass spectrometry alone. The use of retention data as supplemental information for compound identification has already been demonstrated through the use of linear retention indices to improve the accuracy of NIST library hit tables [4]. Retention indices (RI) form a popular basis for retention modelling techniques due to the ease with which data can be collected and used [5]. Linear retention index (LRI) [6], a variation of the Kovats retention index is one of the more popular forms of retention index as data can be collected in a single temperature-programmed run. As such the LRI is often offered as supporting data when identifying unknown compounds, with the current version of the NIST mass spectral library offering RI values for ~71,000 compounds. A recent review by Zellner et al. [7] highlights the widespread usage of LRI.

While RI data are fast and easy to use, RI values have a dependence on the experimental conditions which leads to variations in the reported RI values for both inter- and intra-laboratory studies [4]. For the roughly 71,000 compounds listed as having RI values in the NIST database there are ~350,000 RI values listed for those compounds, the bulk of which are for standard non-polar stationary phases (100% polydimethylsiloxane or poly(95% dimethyl–5% diphenylsiloxane)). If retention data are used to assist the determination of structurally similar compounds any variation in RI values could lead to inconclusive results or prove useful only for a select set of experimental conditions.

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Table 1
Measured values for column length, experimentally determined column inner diameter, and calculated film thickness for all columns used.

Column	Determined length (m)	Determined inner diameter (mm)	Estimated average film thickness (μm)
30 m × 0.25 mm × 0.25 μm (reference)	29.99	0.248	0.250
30 m × 0.25 mm × 0.50 μm	31.66	0.244	0.567
15 m × 0.1 mm × 0.1 μm	16.40	0.103	0.121
30 m × 0.25 mm × 0.25 μm (>4 years of use)	29.10	0.254	0.253

Within the context of the GC × GC experiment, the application of RI is relatively straightforward for the first separation dimension (^{1}D), but it is not so for the second dimension (^{2}D). Isovolatility curves can be generated from a series of alkanes to estimate ^{2}RI (second-dimension retention index), but this is technically difficult on commercial instruments and can be time consuming [8]. It has also been suggested that alkanes are not an appropriate series of standard molecules for second dimension of a GC × GC experiment [9]. Nevertheless, RI-based approaches remain popular with several new studies conducted within the last few years [10,11] and a recent review by von Muehlen and Marriott [5].

Our research has focused on exploiting predictive models based upon thermodynamic data. This approach has a significant advantage over RI methods, namely accuracy is maintained over a range of instrumental conditions [12], and the errors when converted to RI units are typically a fraction of an RI unit [12]. Various studies have been conducted on the use of thermodynamic models for a variety of analytes [13–18]. Additionally, for GC × GC methods, thermodynamic models perform equally well in the first and second dimensions [19]. Thus, unlike the RI, they are inherently suitable for the prediction of GC × GC separations.

The two downsides to the thermodynamic approach have historically been the time required to collect the data and a method to account for variability in column geometry. These two hurdles have kept thermodynamic approaches academically interesting but of little practical value. Recent work in our laboratory [20] has changed this. Our algorithm has allowed us to reduce the instrument time required to obtain thermodynamic data for a set of ten compounds from 41.6 h to 2.0 h and thus set the stage for the development of a library of thermodynamic data that can be used for predictive models, much like those in place for RI. Briefly, nonlinear fitting techniques are used to estimate the changes in enthalpy and entropy of the analyte at some reference temperature, $\Delta H(T_0)$ and $\Delta S(T_0)$, respectively, as well as the change in its adiabatic molar heat capacity, ΔC_p directly from experimental data from a series of temperature-programmed experiments.

To apply the approach, the column's length, film thickness, and inner diameter are required, bringing the second challenge for applying thermodynamic tools in GC. The vendor-supplied nominal values for column geometry are not precise enough to permit the translation of thermodynamic parameters measured on one column to another column. Small variations in the actual film thickness and column inner diameter result in large errors between the predicted and experimental retention times.

A method to calibrate thermodynamic data and account for variation in column geometry in order to obtain accurate predictions across multiple columns is required. To be practically useful, the method must fulfill several requirements: the experimentation required to calibrate the column must be rapid and compatible with standard commercial GC equipment. The chemicals required should also be both universally available and inexpensive. Herein, we introduce and validate an approach that meets the above criteria and enables the reliable use of thermodynamic data across multiple columns.

2. Experimental

2.1. Chemicals

A Grob mix (Sigma–Aldrich #47304; Oakville, Ontario) consisting of 2,3-butanediol, decane, dicyclohexlamine, 2,6-dimethylaniline, 2,6-dimethylphenol, 2-ethylhexanoic acid, methyl decanoate, methyl laurate, methyl undecanoate, nonanal, 1-octanol, and undecane was used to calibrate the column geometry. The compounds are of varying concentration ranging from 290–530 μg/mL (Sigma–Aldrich).

A second mixture comprised of alkanes, alcohols and ketones was used for the validation of the calibration procedure. n-Alkanes ranging from undecane to tetradecane were obtained from Sigma–Aldrich (Oakville, Ontario). 2-Undecanone, 2-dodecanone, and 2-tridecanone were purchased from Alfa-Aesar (Ward Hill, MA). Primary alcohol standards 1-undecanol, 1-dodecanol and 1-tridecanol were also purchased from Sigma–Aldrich. The standard mixture was prepared at a concentration of 1000 ppm in toluene (Sigma–Aldrich). Methane from the laboratory natural gas supply was used as a dead time marker when needed.

2.2. Instrumental

A Bruker 461 GC (Bruker, Milton, ON) equipped with a split/splitless injector and flame ionization detector was used for all experiments. Injections were performed in split mode with a split ratio of 100:1 and an inlet temperature of 280 °C. The flame ionization detector was maintained at a temperature of 250 °C with a data sampling rate of 100 Hz. 99.999% Helium (Praxair, Edmonton, AB) was used as a carrier gas. All columns used for the study were of a 5% phenyl substituted polydimethylsiloxane stationary phase, specifically SLB5ms (Supleco, Bellefonte, PA). The dimensions of each column used are listed in Table 1.

Except where mentioned, all separations were performed under constant flow conditions. For all 0.25 mm ID columns, the carrier gas flow was set to 1.0 mL min^{-1} and for the 0.1 mm ID column, the carrier gas flow rate was set at 0.29 mL min^{-1}. The separations were initialized at 50 °C, with the oven temperature programmed at ramp rates of 5, 8, 10, 12, 16, and 20 °C min^{-1} to 250 °C. The column inner diameter, column film thickness, thermodynamic estimations, and GC retention time predictions were calculated using custom scripts written in MATLAB 7.10.0 (The Mathworks, Natick, MA).

3. Results and discussion

3.1. Calibration techniques

Calibration of the column is carried out in three steps; first the column length must be determined, followed by the determination of the column inner diameter, and finally the estimation for the stationary phase film thickness. A 30 m × 0.25 mm; 0.25 μm film column was chosen to serve as a reference column for this study. This column was chosen as the reference column due to historical usage of this size of column within our thermodynamic