1 **Comprehensive Two-Dimensional Gas Chromatographic Separations**
2 **with a Temperature Programmed Microfabricated Thermal Modulator**

3
4 William R. Collin,^{a,d} Nicolas Nunovero,^{b,d} Dibyadeep Paul,^{c,d}
5 Katsuo Kurabayashi,^{c,d} and Edward T. Zellers^{a,b,d*}

6
7 ^a Department of Chemistry, University of Michigan, Ann Arbor, MI, 48109-1055, USA

8 ^b Department of Environmental Health Sciences, Univ. of Michigan, Ann Arbor, MI 48109-2029, USA

9 ^c Department of Mechanical Engineering, University of Michigan, Ann Arbor, MI, 48109-2125, USA

10 ^d Center for Wireless Integrated MicroSensing and Systems (WIMS²), University of Michigan, Ann
11 Arbor, MI, 48109-2122, USA

12 *for correspondence: ezellers@umich.edu; ph: 734-936-0766; fax: 734-763-8095
13
14

Abstract

Comprehensive two-dimensional gas chromatography (GC×GC) with a temperature-programmed microfabricated thermal modulator (μTM) is demonstrated. The 0.78 cm², 2-stage μTM chip with integrated heaters and a PDMS coated microchannel was placed in thermal contact with a solid-state thermoelectric cooler and mounted on top of a bench scale GC. It was plumbed fluidically coupled through heated interconnects to an upstream first-dimension (¹D) PDMS-coated capillary column and a downstream uncoated capillary or second-dimension (²D) PEG-coated capillary. A mixture of *n*-alkanes C₆–C₁₀ was separated isothermally and the full-width-at-half-maximum (*fwhm*) values of the modulated peaks were assessed as a function of the computer-controlled minimum and maximum stage temperatures of μTM, T_{min} and T_{max} , respectively. With T_{min} and T_{max} fixed at -25 and 100 °C, respectively, modulated peaks of C₆ and C₇ had *fwhm* values <53 ms while the modulated peaks of C₁₀ had a *fwhm* value of 1.3 s, due to inefficient re-mobilization. With T_{min} and T_{max} fixed at 0 and 210 °C, respectively, the *fwhm* value for the modulated C₁₀ peaks decreased to 67 ms, but C₆ and C₇ exhibited massive breakthrough. By programming T_{min} from -25 to 0 °C and T_{max} from 100 to 220 °C, the C₆ and C₇ peaks had *fwhm* values ≤ 50 ms, and the *fwhm* for C₁₀ peaks remained < 95 ms. Using the latter conditions for the GC × GC separation of a sample of unleaded gasoline yielded resolution similar to that reported with a commercial thermal modulator. Replacing the PDMS phase in the μTM with a trigonal-tricationic room temperature ionic liquid eliminated the bleed observed with the PDMS, but also reduced the capacity for several test compounds. Regardless, the demonstrated capability to independently temperature program this low resource μTM enhances its versatility and its promise for use in bench-scale GC×GC systems.

Keywords: GC×GC, microfabricated, micro gas chromatography, thermal modulation, RTIL

1. Introduction

Comprehensive two-dimensional gas chromatography (GC×GC) is often the most effective means of separating complex mixtures of volatile and/or semi-volatile organic compounds (S/VOCs). Examples include the congeners of polychlorinated biphenyls and other polyhalogenated aromatic compounds [1,2], pesticide residues [3,4], hydrocarbon fractions in crude oil [5,6], fatty-acid methyl esters in biodiesel blends [7], and trace-level VOC biomarkers of disease or metabolism in breath and urine [8,9].

In GC×GC a first-dimension (¹D) column is connected through a thermal or pneumatic modulator to a short second-dimension (²D) column with retention selectivity that differs from that of the ¹D column [10-12]. As peaks elute from the ¹D column they are parsed by the modulator into segments and injected in rapid succession into the ²D column such that no mass is lost. This requires very rapid ²D separations. If operated under the proper conditions then the total peak capacity approaches the product of the peak capacities afforded by each dimension [13], which should exceed that provided by a one-dimensional separation column of similar length. In any case, the reductions in peak widths achieved with modulation can improve both the resolution and detectability of the eluting peaks [12,13]. In addition, information about analyte functionality can often be inferred from the structure of the GC×GC contour plot of ¹D vs. ²D retention times (t_R), because analytes within the same class usually occupy segregated bands within the plot [10-12].

Pneumatic GC × GC modulators create peak segmentation by injecting pulses of carrier gas or by redirecting flow at regular intervals across peaks eluting from the ¹D column [14-18]. Values of full width at half maximum ($fwhm$) < 25 ms have been achieved for peaks separated by

GC $\times$ GC with state-of-the-art pneumatic modulation systems [15]. Thermal modulation (TM) entails alternately trapping ^1D peak segments by condensation, typically by bathing a short section of the (typically ^2D) capillary column in a fluid at cryogenic temperatures, and then remobilizing them by removing the fluid and/or applying a jet of hot air, which rapidly raises the temperature for passage of the segment to the ^2D column [19-25]. Values of *fwhm* as low as 20 ms have been reported by use of TM [25].

With TM, the trapping efficiency depends critically on the minimum modulator temperature, T_{min} , the rate at which T_{min} is recovered after each heating cycle, and the analyte vapor pressure, p_v . The efficiency of remobilization, in turn, depends on T_{max} and the rate at which T_{max} is attained after each cooling cycle. For GC $\times$ GC separations of analyte mixtures spanning a large p_v range, there is a tradeoff between maintaining T_{min} low enough to avoid breakthrough of relatively high- p_v components and attaining a sufficiently high T_{max} at a sufficiently high rate to minimize broadening of relatively low- p_v components upon re-injection into the ^2D column.

Several investigators have reported on ways to address this problem by gradually ramping the modulator temperature as a separation proceeds [19, 26-28]. For example, the Marriott group addressed this problem effectively with their longitudinally modulated cryogenic system (LMCS), in which a moveable sleeve around a section of capillary column is cooled with a flow of cryogenic fluid [19]. As the sleeve is moved back and forth along a designated section of one of the columns, peak segments are first immobilized by virtue of the cooling and then remobilized by virtue of the column section returning to oven temperature. By modulating the flow of cryogenic fluid to the sleeve, they were able to gradually increase T_{min} over the course of a temperature programmed separation so as to maintain the difference between T_{min} and the oven

temperature constant [21,23]. This resulted in narrower and more symmetric re-injected peaks and reduced consumption of cryogen, while also avoiding breakthrough of the more volatile components of the mixtures analyzed.

Inspired by this approach, we were interested in incorporating a similar feature into the microfabricated thermal modulator (μ TM) on which we have reported recently [29-33]. First described in 2010 [29,30], this μ TM is cryogen-free and requires much less power to operate than conventional TMs. It consists of a single, Pyrex-sealed Si microchannel with two thermally isolated spiral sections, or stages, each with independent thin-metal-film heaters. The μ TM is mounted on a solid-state thermoelectric cooler (TEC) capable of maintaining T_{min} as low as -35 °C, and it can be heated rapidly to > 250 °C and then cooled again with modulation periods, P_m , as short as 5 s. We have used this device in GC $\times$ GC separations with conventional capillary columns [30,31], and in μ GC $\times$ μ GC separations with microfabricated columns [32] and, most recently, with a polymer-coated, microfabricated optofluidic ring resonator (μ OFRR) as the detector [33].

Recognizing the constraint on the analyte volatility range over which effective μ GC $\times$ μ GC separations could be performed with fixed values of T_{min} and T_{max} , we first explored a passive approach to ramping these μ TM temperatures by placing the device inside the GC oven during a temperature programmed separation [32]. As the oven temperature increased, T_{min} increased because of the reduction in heat dissipation from the TEC heat sink and T_{max} also increased because of the improved efficiency of heating the stages at constant applied voltage. This was marginally effective at reducing peak widths for low p_v analytes as compared to isothermal operation, but the maximum oven temperature was limited to < 100 °C by the temperature sensitivity of the printed circuit boards (PCB) on which the μ TM was mounted.

Furthermore, despite cross-linking the PDMS stationary phase lining the wall of the μ TM channel, loss due to bleed (i.e., decomposition) of the PDMS became notably greater at $T_{max} > 210$ °C, which placed an additional constraint on this operating parameter.

Several commercial stationary phases are now available that have been formulated to exhibit low bleed at temperatures exceeding 350 °C [34-36]. Many of these are siloxane or silylene polymers, which also have low glass transition temperatures. The complexity or proprietary nature of required synthesis or deposition procedures, and/or the need for high-temperature surface pretreatments render the incorporation of such low-bleed stationary phases into microfabricated devices difficult. Recently, a relatively new class of stationary phase coatings, trigonal tricationic room temperature ionic liquids (RTILs), was shown to exhibit a combination of properties that make them attractive candidates for μ TM stationary phases, including high decomposition temperatures, low melting temperatures, low bleed rates at high temperature, high viscosities, and reasonably good retention of non-polar compounds [37,38]. Synthesis is relatively straightforward and although the surface pretreatment is tricky it does not involve high temperatures [32,37]. RTILs of this type have been used in the 2 D column for GC $\times$ GC separations[32,39], and they were, therefore, pursued in this study as phases for our μ TM.

Here, we describe an extension of our previous studies in which we demonstrate the feasibility of incorporating active temperature programming of the μ TM to gradually increase T_{min} and T_{max} values over the course of a GC $\times$ GC separation. Toward this end, we used a bench scale GC, commercial 1 D (non-polar) and 2 D (polar) capillary columns, manual syringe injection, and flame ionization detection (FID). We mounted the μ TM assembly on top of the GC oven and used heated interconnects to couple the μ TM to the 1 D and 2 D columns. Although most experiments used a μ TM with a PDMS wall coating, we also performed preliminary tests with an

RTIL μ TM wall coating, in an attempt to extend the value of T_{max} . After describing the methodology, separations of a simple mixture of alkanes are presented in which the μ TM was cycled between different fixed T_{min} and T_{max} values and then was temperature programmed such that T_{min} and T_{max} were increased over the course of the run. As a practical application, the GC $\times$ GC separation of unleaded gasoline is then demonstrated. A trigonal tricationic RTIL coated μ TM was then evaluated as a substituted for the PDMS stationary phase. The impact of the results on the design and function of a μ TM as a simple replacement for more cumbersome and costly TMs in bench scale GC $\times$ GC is assessed.

2. Experimental methods

2.1 Materials

Solvents and individual test compounds were purchased from either Sigma-Aldrich (St. Louis, MO) or Fisher Scientific (Pittsburgh, PA) in >98% purity. Unleaded regular gasoline was obtained from a local filling station. PDMS was obtained from Ohio Valley Specialty Chemicals (OV-1, Marietta, OH). The RTIL used, tris[2-(6-aminopropylphosphonium-hexaamido)ethyl]amine tris[bis(trifluoromethylsulfonyl)imide], was taken from an existing supply, which was synthesized by a known method [32,37]. It showed a stable melting transition temperature of -27 °C by differential scanning calorimetry upon repeated thermal cycling [32].

2.2 GC Instrumentation

A bench scale GC (6890, Agilent Technologies, Palo Alto, CA) equipped with a split/splitless injector and an FID was used for all experiments. Helium was used as carrier gas. Capillary columns were obtained from Agilent and Restek (Bellefonte, PA) for The PDMS-coated 1 D column was from Agilent (HP-1, 30 m long, 0.250 mm i.d., 0.25 μ m film thickness)

and the PEG-coated ^2D column used for the analysis of gasoline was from Restek (Bellefonte, Pa) (RTX-Wax; 1 m long $\times$ 0.100 mm i.d. $\times$ 0.10 μm film thickness). For most experiments, the ^2D column was replaced with a 0.5-m long segment of uncoated 100- μm id fused silica. For all experiments, the GC oven was operated isothermally at 80 $^\circ\text{C}$. The ^2D column was coiled and held snugly against a Kapton[®] encapsulated resistive-foil heater pad (Omega Engineering, Inc., Stamford, CT) with polyimide tape, and then wrapped with fiberglass insulation to enable heating above the oven temperature. Manual liquid injections from equal-volume-mixtures of the analytes diluted with CS_2 made using a microliter syringe through the split/splitless injection port of the GC (250 $^\circ\text{C}$). The FID was maintained at 300 $^\circ\text{C}$. Note that we chose to operate the columns under the same isothermal (rather than temperature programmed) conditions for all experiments so that any changes in peak parameters could be related unambiguously to the μTM operating conditions.

2.3 μTM Assembly

The two-stage μTM has been described previously [29-33]. The Si chip (13 $\times$ 6 mm) contains a deep-reactive-ion-etched (DRIE) Si $\mu\text{channel}$ with a cross section of 250 (w) $\times$ 140 (h) μm arranged in two convolved square-spiral segments, 4.2 cm (stage 1) and 2.8 cm (stage 2) long, separated by a 1.0 mm long segment of straight channel. A 100- μm thick Pyrex cap is anodically bonded to the top surface of the entire chip to seal the $\mu\text{channel}$. Four meander-line Ti/Pt resistive heaters are patterned on the Pyrex surface; one above each μTM stage and one above the fluidic ports on the rim of the device. Ti/Pt resistive temperature devices (RTDs) are patterned in between heater traces to measure temperature at all four locations. Sections ($\sim$ 2 cm) of deactivated fused silica capillary (250 μm i.d., upstream; 100 μm i.d., downstream) inserted

175 into expansion ports on the chip and sealed with epoxy (Hysol 1C, Rocky Hill, CT) provided
176 fluidic interconnections.

177 The μ TM used for most testing was statically coated with PDMS from a solution that also
178 contained 1% (w/w) dicumyl peroxide as the crosslinking agent using a published procedure
179 [40,41]. The PDMS concentration was adjusted to produce an average (nominal) wall-coating
180 thickness of 0.30 μ m. The PDMS in the μ TM was cross-linked by heating at 180 °C for 1 h
181 under N₂ using the on-chip stage heaters in order to avoid rupturing the capillary-chip union from
182 expansion of the adhesive. An unavoidable consequence of the method is that the connecting
183 capillaries are coated with un-crosslinked PDMS. The RTIL μ TM was also statically coated,
184 following a NaCl surface pretreatment [33]. The RTIL concentration was controlled to yield an
185 average nominal wall-coating thickness of 0.07 μ m. No crosslinking was performed and this
186 method also resulted in RTIL-coated connecting capillaries.

187 The coated devices were epoxied, Pyrex side up, to a custom carrier PCB with a hole cut
188 out beneath the device for thermal isolation. Aluminum wire bonds provided electrical
189 connections off-chip. Importantly, all four RTDs were carefully calibrated by placing the device
190 in the GC oven and measuring resistances at several temperatures with a digital multimeter.

191 In a departure from our previous μ TM mounting schemes [29-33], a small swatch of
192 thermally conductive silicone material (Sil-Pad, Henkel, Chanhassen, MN) was placed against
193 the heater on the Pyrex side of each stage, and held there with a thin film of thermal paste. Two
194 small, square slabs of Si were then coated on both sides with thermal paste and placed on top of
195 the Sil-Pad swatches. The Sil-Pad provided efficient heat transfer while electrically insulating the
196 heater traces from the Si slabs. This sub-assembly was inverted and mounted in a custom-
197 machined aluminum press with the Pyrex surface of the μ TM was facing downward. The TEC

was then situated beneath the μ TM sub-assembly and the press ~~suspended directly above the~~
(TEC) ~~with the top layer of thermal paste in contact with the TEC. A custom machined~~
~~aluminum press~~ was used to lower it onto the TEC in a carefully controlled manner to achieve
intimate contact while avoiding excessive torque that might break the device. The basic
arrangement is similar to that shown in Figure 1a in ref. 29.

The TEC heat sink was fabricated from stainless steel and copper. Since the assembly
was in close proximity to the heated inlet and FID of the GC during testing, a small fan was
placed nearby and a duct was used to direct the flow of room air directly over the TEC heat sink
to aid in cooling. A shallow, rectangular, plastic shroud through which a constant stream of dry
air was passed during operation to prevent atmospheric water condensation was placed over the
 μ TM and secured to the peripheral PCB surface.

2.4 Heated Interconnects

Each of the two interconnect heaters was fashioned from a 0.5-cm i.d., 5-cm long section
of thin-walled brass tubing bent at a 90 ° angle at one end and soldered to a 0.175-mm i.d., 5-cm
long piece of Cu tubing. A base layer of polyimide tape was then applied, followed by a coil of
NiCr heater wire, another layer of polyimide tape, and finally an insulating fiberglass sleeve
(HiLec 210C, Arcade, NY). A fine wire thermocouple (Omega Engineering, Inc., Stamford, CT)
was inserted between the heater and the fiberglass sleeve to monitor the temperature of the
assembly. One end of a press-tight capillary connector was inserted into the open end of the
brass tube and fitted with a length of deactivated fused silica capillary (250 μ m i.d. for the
upstream side and 100 μ m i.d. for the downstream side) that was threaded through the heater
tubing and extended 2-3 cm beyond the Cu end. The other end of the press-tight was used to
connect to the inlet or outlet capillary epoxied to the μ TM chip. Screening tests confirmed the

effectiveness of the heaters in minimizing band broadening associated with sample transfer to and from the μ TM (see Table S1 and associated text in the *Supplementary Information*).

2.5 System Integration

The layout diagram of the GC $\times$ GC set-up is shown in Figure 1a and a photograph of the μ TM assembly mounted on top of the GC is shown in Figure 1b. Figure 1c provides an enlarged view of the μ TM, the proximal brass end of the heated interconnect, as well as part of the plastic shroud over the μ TM. The μ TM assembly was oriented with the top face of the plastic shroud facing downward, and positioned $\sim$ 4 cm from the top of the GC with standoff bolts. The Cu sections of the interconnects fit into holes drilled through the top of the GC oven at a central location. The upstream side of the 1 D column was connected to the split/splitless inlet of the GC and the downstream side was connected to the μ TM through the heated interconnect. The downstream side of the μ TM was connected through the other heated interconnect to the 2 D column which, in turn, was connected to the downstream FID.

2.6 μ TM Temperature Control

Separate programmable power supplies (Model E3647A, Agilent, Palo Alto, CA; Precision 1787B, B&K, Yorba Linda, CA) were used to apply the voltage pulses to the integrated stage heaters, via solid-state relays, required to control the temperature of each μ TM stage. The circuit diagram is presented in Figure S1 of the *Supplementary Information*. A 16-bit multi-functional DAQ card (USB-6212, National Instruments, Austin, TX) was used for signal conditioning and data acquisition. Custom software was written in LabVIEW to drive and monitor the temperature measurements from the RTDs and automatically execute the controlling tasks upon setup of desired set points through a computer graphical user interface (GUI). In order to explore the technical requirements and limitations of the μ TM temperature control, a

mathematical model was constructed and run inside a control feedback loop to simulate the performance of different controllers against the desired temperature profiles. To account for the temperature vs. voltage non-linearity, thermal responses were measured for different applied voltages. The dynamic components of the responses were fitted to a single normalized exponential curve, while the amplitude components were fitted to a second order polynomial curve. With the controller architecture determined, most of the values of the parameters of the system were estimated using the developed model, and then finely tuned with the real device after the system was implemented. The results of this simulation are shown in Figure S2 of the *Supplementary Information*.

To achieve T_{max} , a variable width pulse (55 V for the first stage and 50 V for the second stage) was periodically supplied for a very short time, initially 60 ms. By increasing the pulse width over the course of an analysis cycle, precise control of T_{max} was attained. The offset between the first and second stage heater actuations was held constant at 500 ms. For controlling T_{min} , a proportional-integral-derivative (PID) controller combined with a 200 Hz pulse-width-modulated (PWM) signal (15 V for each stage) was found to provide the best control accuracy and temperature stability. In order to allow for a smooth transition from T_{max} to the desired T_{min} , the PID control was turned on ~500 ms after the end of each T_{max} pulse and was suspended before the next T_{max} pulse was applied.

FID data were collected using ChemStation (Agilent Technologies, Palo Alto, CA) and analyzed using OriginPro 9.1 (OriginLab, Northampton, MA). Contour plots were generated using GC Image (Zoex, Houston, TX).

3. Results and discussion

3.1 Performance as a function of T_{min} and T_{max} .

Figure 2a shows the 2-D contour plot of C_6 – C_{10} with T_{min} and T_{max} fixed at $-25\text{ }^{\circ}\text{C}$ and $100\text{ }^{\circ}\text{C}$, respectively, and with $P_m = 6\text{ s}$. The temperatures of the rims of the device (T_{rim}) were set to $30\text{ }^{\circ}\text{C}$ via the heaters, and they periodically increased to $35\text{ }^{\circ}\text{C}$ with the heating of the proximal modulator stages. Without active heating T_{rim} would reach a value much closer to T_{min} , due to proximity to the TEC, and become a significant cold spot in the fluidic pathway. Unfortunately, increasing T_{rim} further led to an increase in T_{min} due to thermal cross-talk within the device. Thus, heating the rims to $30\text{ }^{\circ}\text{C}$ represented a compromise between the two competing factors.

Efficient trapping and remobilization for C_6 , C_7 and C_8 , was evident from the sharp, well-defined peak profiles obtained, although careful inspection of the plot near C_6 revealed a small degree of breakthrough. Indeed, a characteristic tail in the otherwise sharp modulated C_6 peak was apparent in the raw chromatogram (Figure 2b). The peak profiles for C_9 and C_{10} (Figure 2a), in contrast, were excessively broad and diffuse due to inefficient remobilization of these less volatile compounds, as expected from the low T_{min} and T_{max} values of the μTM . This can be seen quite clearly in the raw chromatogram for C_{10} (Figure 2c): the *fwhm* values of the modulated peaks were $\sim 1.3\text{ s}$, tailing was quite significant, and peaks did not quite return to baseline between modulations.

Under these operating conditions, the modulation number, M_N , which is defined as the number of detectable ^2D peaks per ^1D peak, was 1 for C_6 – C_8 and it was 2 and 4 for C_9 and C_{10} , respectively. Table 1 presents the height and *fwhm* of the largest modulated peak for each compound in Figure 2a. As shown, the C_6 – C_8 peaks were significantly narrower and taller than those for C_9 and C_{10} , consistent with the peak contours. The slightly larger *fwhm* for C_6 , relative

to that for C₇, is ascribed to partial breakthrough of C₆, which has been observed previously with this μ TM design under similar operating conditions [29,30]. That notwithstanding, the results indicate that the fixed, lower-temperature condition is not very effective for compounds less volatile than C₈ ($p_v = 1.9$ kPa). For reference, Table 1 also presents the summed area under all modulated peaks for each compound, and shows the gradual increase in sensitivity with carbon number expected for an FID.

Figure 3a shows the contour plot of the same n-alkanes with the μ TM T_{min} and T_{max} values fixed at 0 and 220 °C, respectively. For this series, T_{rim} was set at 50 °C, and the T_{rim} values were observed to increase to ~55 °C at the inlet or outlet with the periodic heating of the adjacent μ TM stage. The broad ²D peak contours for C₆ and C₇ in Figure 3a are indicative of complete modulator breakthrough. The peaks eluted at slightly shorter t_R values than expected along the ¹D axis and at longer t_R values than expected along the ²D axis; the latter being completely unrelated to their retention on the uncoated ²D column.

The raw chromatogram in Figure 3b shows a short, broad peak for C₆, which reflects the failure of the μ TM to trap this compound. A similar peak profile was observed for C₇. The short, broad modulated peak in the raw chromatogram for C₆ in Figure 3b resulted from the failure of the μ TM to trap this compound (as well as C₇). The sharper profiles for C₈, C₉, and C₁₀ in Figure 3a reflect their efficient trapping and re-injection for this range of modulator temperatures. Comparing the raw chromatogram for C₁₀ in Figure 3c to that in Figure 2c further illustrates this point. Under these μ TM operating conditions, the M_N values for C₆-C₉ did not change from those under the preceding conditions, but the M_N value for C₁₀ decreased from 4 to 2, due to the increase in re-mobilization efficiency. The ¹D t_R values for C₆-C₈ did not change significantly either, despite the breakthrough of C₆ and C₇, but the t_R value of C₉ decreased by

about ~5 s and that for C₁₀ decreased by nearly 30 s, again, due to the improvement in re-mobilization of these less volatile analytes under these conditions. ~~That is,~~ We believe that the longer t_R values for C₉ and C₁₀ observed under the lower-temperature conditions ~~were artifacts of the lower T_{rim} values and associated cold spots within the μ TM. in the , which would have created cold spots~~ residual quantities of these compounds remaining in the μ TM from modulations of prior peak segments.

Consistent with the chromatograms in Figure 3, Table 1 shows that the $fwhm$ values for C₆ and C₇ peaks were 1-2 orders of magnitude larger, and their heights were an order of magnitude smaller, than those of the C₈–C₁₀ peaks. Peak areas were comparable to those under the previous operating conditions. Note also the continuous horizontal line near the baseline of the contour plot in Figure 3a, which is evidence of stationary phase bleed. This is absent from Figure 2a.

Figure 4a shows the 2-D contour plot obtained with the μ TM stage temperatures programmed as shown in Figure 5. Initially, T_{min} and T_{max} were set at –25 and 100 °C, respectively, and held at these values for the first two minutes of the run. Then, they were increased to -10 and 150 °C, respectively, linearly over the next two minutes. Finally, T_{min} and T_{max} were increased to 0 and 220 °C, respectively, over the next six minutes, at which point the run was concluded. All of the alkanes eluted in < 8 min (Figure 4a). The values of T_{rim} were not dynamically controlled, and they did increase with each successive change in T_{min} and T_{max} . Initially set at ~45 °C, T_{rim} increased to ~50 °C over the course of the 10-min separation.

As shown in Figure 5, the actual temperatures achieved by the μ TM, represented by the narrow white and red peaks, agreed quite closely with the programmed μ TM temperature profiles indicated by the yellow lines. Target and actual T_{max} values generally differed by less

than 5 °C. This level of residual imprecision can be related to the RTD data sampling rates. Even at 200 Hz, peak temperatures resulting from the heater pulses, which had durations of 60 to 220 ms, might not be captured at the high heating rates, which ranged from 1,000 to 2,000 °C/s. The return to T_{min} was initially very rapid but required the remainder of the 6-s modulation period to completely cool down to the target value.

Figure 4a shows sharp peak profiles for all of the analytes. The problem of slow re-mobilization of C₉ and C₁₀ under the fixed, lower-temperature modulation conditions, and the massive breakthrough of C₆ and C₇ under the fixed, higher-temperature modulation conditions were eliminated by programming the μ TM temperatures. There was still evidence of partial breakthrough of C₆ (Figure 4b), but no more so than observed for the fixed, lower-temperature case (Figure 2b). The raw chromatogram of the modulated C₁₀ peak in Figure 4c is similar to that in Figure 3c with respect to M_N , peak width, and peak height, despite both T_{min} and T_{max} being lower when C₁₀ eluted in Figure 4c than they were in Figure 3c. Stationary phase bleed became more pronounced toward the end of the separation, as the T_{max} approached 220 °C.

As shown in Table 1, the *fwhm* values for C₆ and C₇ were similar to those for the fixed, lower-temperature case, while those for C₈-C₁₀ were 40-80% larger than for the fixed, higher-temperature case, undoubtedly due to T_{min} and T_{max} values being lower when these peaks eluted. Regardless, all *fwhm* values were < 95 ms, which indicates very good overall performance. The peak areas were significantly larger than in the respective fixed-temperature cases owing to an inadvertent error in injection volume (discovered *post hoc*). This factor accounts for the larger modulated peak heights for C₆ and C₇ for the programmed (vs. lower-temperature) case. For C₈-C₁₀, the peak heights were lower than would be expected after accounting for the peak area

differences, but were qualitatively consistent, again, with the μ TM temperature being lower at the times these analytes eluted.

3.2 Gasoline Separation with Temperature-Programmed μ TM

As a practical demonstration, a sample of unleaded gasoline was analyzed under the same conditions as just described, but with the run extended by 5 min; after the μ TM T_{min} and T_{max} values reached 0 and 210 °C, respectively, they were held at these values from $t = 10$ -15 min (note: T_{max} was not increased further to avoid excessive bleed of the PDMS from the μ TM). The uncoated capillary used downstream from μ TM in the preceding experiments was replaced with the 1-m long PEG 2 D column. The 1 D and 2 D columns were held at 80 and 90 °C throughout the separation.

Figure 6 shows the 2-D contour plot of the gasoline sample. The overall structure of the plot is remarkably similar to that reported by Pedroso et al. [42] for the GC $\times$ GC separation of gasoline with similar 1 D and 2 D column lengths and stationary phases (see Figure 1a in Ref. 39). There are more than 100 distinguishable peaks apparent within the 15-min time period examined. Although a few additional peaks may have eluted later than this [42], no effort was made to capture or identify them. Retention time matching with authentic samples of a subset of 11 known constituents of gasoline, analyzed separately under the same conditions, yielded the list of compounds and associated t_R and $fwhm$ values presented in Table 2. Partial coelution of benzene with another component artificially inflated its assigned $fwhm$ value. Consistent with expectations, among the pairs of alkanes and aromatic compounds with similar 1 D t_R values in Table 2, those with larger 2 D t_R values were broader. On the basis of our data and the assignments reported in ref. 39, we labelled the individual peak contours and the functional

group bands in Figure 6, and then superimposed colored lines to aid in visualization. Neither the broad peak straddling the alkane band at $t_R = 14$ min on the 1D axis nor the clusters of unmodulated and poorly resolved peaks running up the left side of the plot could be identified. The latter, however, undoubtedly include ethanol and light hydrocarbons [42].

For those compounds common to both Figure 6 and Figure 4a, peaks were broader in the former plot due to the addition of a longer, coated 2D column. Still, $fwhm$ values for all identified compounds were < 500 ms, in spite of the low column temperatures employed. Clearly, temperature programming the μTM greatly enhances its performance and expands the complexity of mixtures amenable to $GC \times GC$ separation with this device.

3.3 RTIL Stationary Phase

Figure S3 in the *Supplementary Information* presents 30-s segments of contour plots obtained using the PDMS-coated μTM with $T_{min} = 0$ °C and $T_{max} = 220$ °C in one case and the RTIL coated μTM with $T_{min} = -20$ °C and $T_{max} = 230$ °C in the other. The bleed from the former was quite pronounced, as also seen in Figures 3a and 4a. In contrast, there was no evidence of any bleed from the latter.

The trapping efficiency of the RTIL-coated μTM was then evaluated by analyzing three different sets of samples containing mixtures of homologous alkanes (C_7 - C_{10}), aromatic hydrocarbons (benzene, toluene, ethylbenzene, and 1,2,3-trimethylbenzene), or aliphatic aldehydes (C_5 - C_8) generated in gas sampling bags. For each type of mixture, two different levels of loop-injected mass were tested: ~ 1 ng and ~ 50 ng of each compound. For these tests, T_{min} and T_{max} were set at -20 °C and 230 °C, respectively, P_m was 6 s, a 6-m long PDMS 1D column was used and a 0.5-m long uncoated capillary was used in lieu of a 2D column.

The 1-ng injections of the n-alkanes gave mixed results, as shown in Figure 7a. Partial breakthrough occurred with C₇ and to a lesser extent with C₈ and C₉. Figure 7b shows that with the higher injection masses, however, significant breakthrough occurred for C₇-C₉, while C₁₀ was still apparently captured (and released) efficiently.

The same tests performed with the other two mixtures gave the results shown in Figure S4 of the *Supplementary Information*. For the lower injected mass level of the aromatics, breakthrough was already significant for benzene and toluene, and for the higher injected mass level, breakthrough of ethylbenzene also occurred. The 1,2,3-trimethylbenzene (1,2,3-TMB) profile showed no evidence of breakthrough at either level. Among the aldehydes, breakthrough of pentanal and hexanal was significant at both injected mass levels, breakthrough of heptanal was significant at the higher injected mass level, and although octanal was apparently retained, its profile was very diffuse, indicating that it was not remobilized efficiently, as also observed for C₁₀ in Figure 2.

These results run contrary to our expectations based on retention data reported with this RTIL as a column stationary phase [37], and another study using an even more polar RTIL phases in the ²D column for GC×GC separations (i.e., where the initial segment of the ²D column was thermally modulated) [43]. The nominal thickness of the RTIL, 0.07 μm, was chosen on the basis of exploratory experiments we performed with microfabricated columns wall-coated with this RTIL which indicated that this thickness was suitable. Unfortunately, increasing the RTIL thickness to 0.15 μm did not resolve the problem. Given the polar nature of the RTIL, the lower retention exhibited relative to PDMS is not too surprising, but it indicates that a lower value of T_{min} would be required for effective operation.

4. Conclusions

As shown, the capability for temperature programming this μ TM greatly improves its performance and represents an important step toward expanding the complexity of mixtures that could be analyzed by GC $\times$ GC using this novel, low-resource, low-power modulation device, which requires no additional consumables beyond those required for conventional GC operation. Decoupling the temperature programming of the modulation device from that of the separation columns imparts an additional degree of versatility to the system as well. The utility of μ TM temperature programming was illustrated with a simple mixture of C₆-C₁₀ alkanes, and its practical application was demonstrated by the GC $\times$ GC separation of the components of unleaded gasoline, which is the most complex mixture separation yet performed with a μ TM device.

This study required the adaptation of a conventional benchtop GC to a fully functional GC $\times$ GC system. The challenge of conveying analyte outside of the GC oven for modulation with minimal band broadening ~~from wall adsorption~~ was met by use of simple interconnect heaters applied to the transfer capillaries. The techniques developed for LabVIEW control of the μ TM temperature program were very effective and permitted precise specification of T_{min} and T_{max} values, as well as the rates and durations of the temperature ramps.

The range of temperatures accessible by the μ TM is not inherently limited by the device itself, and reductions in T_{min} could be achieved by adding another stage to the TEC or by improving the efficiency of its heat sink. Increases in T_{max} are constrained only by the thermal stability of the μ TM phase coating. Results obtained with the trigonal tricationic RTIL μ TM coating here were mixed, but the broad liquid range and lack of bleed exhibited are sufficiently compelling in our view to warrant continued pursuit of an RTIL that retains these properties

while also providing greater retention of lighter, less polar compounds, as desired for generalized GC $\times$ GC separations.

Acknowledgements

The authors are grateful to Dr. Sung-Jin Kim for the design of the μ TM and Ms. Amy Bondy for assistance with RTIL synthesis and characterization. Funding for this work was provided by Grant ECCS-1307154 from the National Science Foundation and by a grant from Agilent Technologies. The μ TM devices were fabricated in the Lurie Nanofabrication Facility at the University of Michigan, a member of the National Nanotechnology Infrastructure Network, which is supported by the National Science Foundation.

~~Among the authors, W. Collin designed the experiments, coated the μ TMs, performed all measurements, worked up and analyzed the data, generated the graphics, and drafted the text; N. Nunovero modeled and programmed the μ TM heaters, wrote the LabVIEW control software, and designed and built the interface hardware for all devices; D. Paul meticulously fabricated the μ TMs; K. Kurabayashi supervised the fabrication; E. Zellers guided all aspects of the project, scrutinized and assisted in the design of experiments and the interpretation of the data, and edited the graphics, tabulations, and text.~~

Appendix A. Supplementary data

Supplementary Information associated with this article can be found in the online version, at <http://xxxxxxxxxx>

References

1. Dimitriou-Christidis, P., Bonvin, A., Samanipour, S., Hollender, J., Rutler, R., Westphale, J., Arey, J. S., GC× GC quantification of priority and emerging nonpolar halogenated micropollutants in all types of wastewater matrices: analysis methodology, chemical occurrence, and partitioning, *Environ. Sci. & Technol.*, 2015, 49, 7914-7925.
2. Prebihalo, S., Brockman, A., Cochran, J., Dorman, F. L., Determination of emerging contaminants in wastewater utilizing comprehensive two-dimensional gas-chromatography coupled with time-of-flight mass spectrometry, *J. Chrom. A*, 2015, 1419, 109-115.
3. Nolvachai, Y., Kulsing, C., Marriott, P. J. Pesticides Analysis: Advantages of increased dimensionality in gas chromatography and mass spectrometry. *Crit. Rev. Environ. Sci. & Tech.*, 2015, 45, 2135-2173.
4. Weng, N., Wan, S., Wang, H., Zhang, S., Zhu, G., Liu, J., Yang, Y., Insight into unresolved complex mixtures of aromatic hydrocarbons in heavy oil via two-dimensional gas chromatography coupled with time-of-flight mass spectrometry analysis, *J. Chrom. A*, 1398, 2015, 94-107.
5. Duhamel, C., Cardinael, P., Peulon-Agasse, V., Firor, R., Pascaud, L., Semard-Jousset, G., Livadaris, V., Comparison of cryogenic and differential flow (forward and reverse fill/flush) modulators and applications to the analysis of heavy petroleum cuts by high-temperature comprehensive gas chromatography, *J. Chrom. A*, 2015, 1387, 95-103.
6. Kanateva, A. Y., Kurganov, A. A., Yakubenko, E. E., Application of two-dimensional gas chromatography-mass spectrometry to determination of biodiesel impurities in hydrocarbon fuels, *Petrol. Chem.*, 2014, 54, 459-465.

7. Seeley, J. V., Seeley, S. K., Libby, E. K., McCurry, J. D., Analysis of biodiesel/petroleum diesel blends with comprehensive two-dimensional gas chromatography, *J. Chrom. Sci.*, 2007, 45, 650-656.
8. Ma, H., Li, X., Chen, J., Wang, H., Cheng, T., Chen, K., Xu, S., Analysis of human breath samples of lung cancer patients and healthy controls with solid-phase microextraction (SPME) and flow-modulated comprehensive two-dimensional gas chromatography (GC $\times$ GC), *Anal. Meth.*, 2014, 6, 6841-6849.
9. Weinert, C. H., Egert, B., Kulling, S. E., On the applicability of comprehensive two-dimensional gas chromatography combined with a fast-scanning quadrupole mass spectrometer for untargeted large-scale metabolomics, *J. Chrom. A*, 2015, 1405, 156-167.
10. Eiserbeck, C.; Nelson, R.; Reddy, C.; Grice, K.; "Advances in Comprehensive Two-Dimensional Gas Chromatography (GC $\times$ GC)" in Principles and Practice of Analytical Techniques in Geosciences Edited by K. Glice, Royal Society of Chemistry, 2015, 324-365.
11. Edwards, M., Mostafa, A., Górecki, T., Modulation in comprehensive two-dimensional gas chromatography: 20 years of innovation, *Anal. & Bioanal. Chem.*, 2011, 401, 2335-2349.
12. Dimandja, J. M. D., GC $\times$ GC, *Analytical Chemistry*, 2004, 76, 167-A.
13. Blumberg, L. M., David, F., Klee, M. S., Sandra, P., Comparison of one-dimensional and comprehensive two-dimensional separations by gas chromatography, *J. Chrom. A*, 2008, 1188, 2-16.

14. Adahchour, M., Beens, J., Vreuls, R. J. J., Brinkman, U. T., Recent developments in comprehensive two-dimensional gas chromatography (GC $\times$ GC): I. Introduction and instrumental set-up. *Trends Anal. Chem.*, 2006, 25, 438-454.
15. Mohler, R. E., Prazen, B. J., Synovec, R. E., Total-transfer, valve-based comprehensive two-dimensional gas chromatography. *Anal. Chm. Acta*, 2006, 555, 68-74.
16. Seeley, J. V., Micyus, N. J., Bandurski, S. V., Seeley, S. K., McCurry, J. D., Microfluidic Deans switch for comprehensive two-dimensional gas chromatography, *Anal. Chem.*, 2007, 79, 1840-1847.
17. Poliak, M., Kochman, M., Amirav, A., Pulsed flow modulation comprehensive two-dimensional gas chromatography. *J. Chrom. A*, 2008, 1186, 189-195.
18. Tranchida, P. Q., Salivo, S., Franchina, F. A., Mondello, L., Flow-modulated comprehensive two-dimensional gas chromatography combined with a high-resolution time-of-flight mass spectrometer: A proof-of-principle study, *Anal. Chem.*, 2015, 87, 2925-2930.
19. Marriott, P. J., Kinghorn, R. M., Longitudinally modulated cryogenic system. A generally applicable approach to solute trapping and mobilization in gas chromatography, *Anal. Chem.*, 1997, 69, 2582-2588.
20. Phillips, J. B., Gaines, R. B., Blomberg, J., van der Wielen, F. W., Dimandja, J. M., Green, V., de Boer, J., A robust thermal modulator for comprehensive two-dimensional gas chromatography, *J. High Res. Chrom.*, 1999, 22, 3-10.
21. Haglund, P., Harju, M., Danielsson, C., Marriott, P., Effects of temperature and flow regulated carbon dioxide cooling in longitudinally modulated cryogenic systems for comprehensive two-dimensional gas chromatography, *J. Chrom. A*, 2002, 962, 127-134.

22. Harynuk, J., Górecki, T., New liquid nitrogen cryogenic modulator for comprehensive two-dimensional gas chromatography. *J. Chrom. A*, 2003, 1019, 53-63.
23. Begnaud, F., Debonneville, C., Probst, J. P., Chaintreau, A., Morrison, P. D., Adcock, J. L., Marriott, P. J., Effects of variation in modulator temperature during cryogenic modulation in comprehensive two-dimensional gas chromatography. *J. Sep. Sci.*, 2009, 32, 3144-3151.
24. Libardoni, M., Fix, C., Waite, J. H., Sacks, R., Design and performance evaluation of a two-stage resistively-heated thermal modulator for GC× GC. *Anal. Meth.*, 2010, 2, 936-943.
25. Fitz, B. D., Wilson, R. B., Parsons, B. A., Hoggard, J. C., Synovec, R. E., Fast, high peak capacity separations in comprehensive two-dimensional gas chromatography with time-of-flight mass spectrometry, *J. Chrom. A*, 2012, 1266, 116-123.
26. Gaines, R. B., Frysinger, G. S., Temperature requirements for thermal modulation in comprehensive two-dimensional gas chromatography, *J. Sep. Sci.*, 2004, 27, 380-3888
27. Worton, D. R. , Kreisberg, N. M., Isaacman, G., Tend, A. P., McNeish, C., Górecki, T. , Hering, S. V., Goldstein, A. H., Thermal Desorption Comprehensive Two-Dimensional Gas Chromatography: An Improved Instrument for In-Situ Speciated Measurements of Organic Aerosols, *Aerosol Sci. and Technol.*, 2012, 46:4, 380-393,
28. Libardoni, M., Hasselbrink, E., Waite, J. H., Sacks, R. D., At-column heating and a resistively heated, liquid-cooled thermal modulator for a low-resource bench-top GC×GC, *J. Sep. Sci.*, 2006, 29, 1001–1008.

29. Kim, S. J., Reidy, S. M., Block, B. P., Wise, K. D., Zellers, E. T., Kurabayashi, K.,
Microfabricated thermal modulator for comprehensive two-dimensional micro gas
chromatography: design, thermal modeling, and preliminary testing, *Lab Chip*, 2010, 10,
1647-1654.
30. Kim, S. J., Serrano, G., Wise, K. D., Kurabayashi, K., Zellers, E. T., Evaluation of a
microfabricated thermal modulator for comprehensive two-dimensional microscale gas
chromatography, *Anal. Chem.*, 2011, 83, 5556-5562.
31. Serrano, G., Paul, D., Kim, S. J., Kurabayashi, K., Zellers, E. T., Comprehensive two-
dimensional gas chromatographic separations with a microfabricated thermal
modulator, *Anal. Chem.*, 2012, 84, 6973-6980.
32. Collin, W. R., Bondy, A., Paul, D., Kurabayashi, K., Zellers, E. T., $\mu\text{GC} \times \mu\text{GC}$:
comprehensive two-dimensional gas chromatographic separations with microfabricated
components. *Anal. Chem.*, 2015, 87, 1630-1637.
33. Collin, W. R., Scholten, K. W., Fan, X., Paul, D., Kurabayashi, K., Zellers, E. T.,
Polymer-coated micro-optofluidic ring resonator detector for a comprehensive two-
dimensional gas chromatographic microsystem: $\mu\text{GC} \times \mu\text{GC}$ - μOFRR , *Analyst*, 2016, 141,
261-269.
34. Sigma-Aldrich Product Information Page [http://www.sigmaaldrich.com/analytical-
chromatography/gas-chromatography/columns/slb-gc-capillary/story.html](http://www.sigmaaldrich.com/analytical-chromatography/gas-chromatography/columns/slb-gc-capillary/story.html) (accessed 1-7-
16)
35. Agilent Webinar Transcript
[http://www.agilent.com/cs/library/eseminars/public/Low%20Bleed%20Stationary%20Ph
ase%20for%20GC.pdf](http://www.agilent.com/cs/library/eseminars/public/Low%20Bleed%20Stationary%20Phase%20for%20GC.pdf) (accessed 1-7-16)

36. Restek Product Information Page http://www.restek.com/Landing-Pages/Content/gen_B004 (accessed 1-7-16)
37. Payagala, T., Zhang, Y., Wanigasekara, E., Huang, K., Breitbach, Z. S., Sharma, P. S., Armstrong, D. W., Trigonal tricationic ionic liquids: a generation of gas chromatographic stationary phases, *Anal. Chem.*, 2008, 81, 160-173.
38. Sharma, P. S., Payagala, T., Wanigasekara, E., Wijeratne, A. B., Huang, J., Armstrong, D. W., Trigonal tricationic ionic liquids: molecular engineering of trications to control physicochemical properties, *Chem. Mater.*, 2008, 20, 4182-4184.
39. Joshi, M. D., Anderson, J. L., Recent advances of ionic liquids in separation science and mass spectrometry, *RSC Advances*, 2012, 2, 5470-5484.
40. Reidy, S., Lambertus, G., Reece, J., Sacks, R., High-performance, static-coated silicon microfabricated columns for gas chromatography. *Anal. Chem.*, 2006, 78, 2623-2630.
41. Serrano, G., Reidy, S. M., Zellers, E. T., Assessing the reliability of wall-coated microfabricated gas chromatographic separation columns, *Sens. and Act. B*, 2009, 141, 217-226.
42. Pedroso, M. P., de Godoy, L. A. F., Ferreira, E. C., Poppi, R. J., Augusto, F., Identification of gasoline adulteration using comprehensive two-dimensional gas chromatography combined to multivariate data processing, *J. Chrom. A*, 2008, 1201, 176-182.
43. Delmonte, P., Fardin-Kia, A. R., Rader, J. I., Separation of fatty acid methyl esters by GC-online hydrogenation $\times$ GC, *Anal. Chem.*, 2013, 85, 1517-1524.

Table 1. Peak metrics from modulated chromatograms of C₆ □ C₁₀ n-alkanes for fixed temperature and temperature programmed μ TM operation.^a

Cmpd	Fixed, Lower-Temp.			Fixed, Higher-Temp.			Temp. Programmed		
	<i>fwhm</i> (ms)	height (pA)	area (pA-s)	<i>fwhm</i> (ms)	height (pA)	area (pA-s)	<i>fwhm</i> (ms)	height (pA)	area (pA-s)
C ₆	52	120	13	610	24	16	50	280	23
C ₇	44	270	13	1200	11	15	39	510	22
C ₈	81	170	13	35	390	16	55	400	24
C ₉	560	31	18	44	340	17	79	280	24
C ₁₀	1300	7	22	67	170	18	94	190	25

^aPeak heights and peak *fwhm* values were calculated for the largest modulated peak. Each peak area value represents the sum of the areas of all modulated peaks. See text for values of T_{max} and T_{min} .

Table 2. Peak metrics for the GC×GC contour plot of unleaded regular gasoline shown in Figure 6.^a

No.	Cmpd	¹ D t _R (min)	² D t _R (s)	<i>fwhm</i> (ms)
1	benzene	1.7	0.46	300 ^b
2	C ₇	1.8	0.43	140
3	toluene	2.1	0.79	170
4	C ₈	2.2	0.54	150
5	ethylbenzene	3.0	1.08	200
6	C ₉	3.0	0.72	170
7	<i>m</i> -xylene	3.3	1.35	220
8	C ₁₀	4.6	0.96	190
9	1,2,3-TMB	5.1	1.08	270
10	C ₁₁	8.4	1.51	270
11	naphthalene	11.0	3.81	460

^a Numbers correspond to the peak contours identified by retention time matching in Figure 6. Peak full-width at half maximum (*fwhm*) values were taken from largest modulated peak for a given compound.

^bPartial coelution with an unidentified, untrapped compound inflated the benzene *fwhm* value.

Figure 1. a) Diagram of the GC × GC system; b) photograph showing the inverted μTM assembly, the heated interconnects, and the placement on the top of the GC oven (LEGO figure shown for scale; cooling fan and heater wiring was removed for clarity); c) View of interconnect heaters at their interface with the μTM chip.

649
 650 Figure 2. Modulated separations with (fixed) $T_{min} = -25\text{ }^{\circ}\text{C}$ and $T_{max} = 100\text{ }^{\circ}\text{C}$. a) 2-D contour
 651 plot of the separation of C₆-C₁₀ n-alkanes; b) raw chromatogram for the C₆ peak; c) raw
 652 chromatogram for the C₁₀ peak. Chromatographic conditions: 30 m (l) $\times$ 0.250 mm (id) $\times$ 0.25
 653 μm HP-1 ¹D column; 0.3 μm PDMS coated μTM ; 0.5 m (l) $\times$ 0.170 cm (id) uncoated deactivated
 654 fused silica capillary ²D column; 80 $^{\circ}\text{C}$ GC oven; 2.0 mL/min He carrier gas; FID.

655
 656 Figure 3. Modulated separations with (fixed) $T_{min} = 0\text{ }^{\circ}\text{C}$ and $T_{max} = 220\text{ }^{\circ}\text{C}$. a) 2-D contour plot
 657 of the separation of C₆-C₁₀ n-alkanes; b) raw chromatogram for the C₆ peak; c) raw
 658 chromatogram for the C₁₀ peak. Chromatographic conditions were otherwise the same as in
 659 Figure 2.

Figure 4. Modulated separations with temperature programmed μ TM, $T_{min} = -25$ to 0 $^{\circ}\text{C}$ and $T_{max} = 100$ to 220 $^{\circ}\text{C}$ (see detailed temperature profiles in Figure 5). a) 2-D contour plot of the separation of C_6 - C_{10} n-alkanes; b) raw chromatogram for the C_6 peak; c) raw chromatogram for the C_{10} peak. Chromatographic conditions were otherwise the same as in Figure 2.

666

667 Figure 5. Programmed (i.e. set point) temperatures of T_{max} of μ TM (dashed yellow) and T_{min} of
 668 μ TM (solid yellow) overlaid on the actual temperature excursions of the μ TM stages (red and
 669 white lines) for a ~10-min run.

670

Figure 6. Unleaded gasoline sample analyzed using the μ TM temperature program in Figure 5. Colored lines were added as visual aids to locate the bands corresponding to different groups of compounds, as labelled; each ϕR_i designates a group of alkyl-substituted benzenes (for $i = 4,5$ the band assignments were inferred from Figure 1a in ref. 42). Those compounds identified by retention time matching are numbered: 1, benzene; 2, C_7 ; 3, toluene; 4, C_8 ; 5, ethylbenzene; 6, C_9 ; 7, *m*-xylene; 8, C_{10} ; 9, 1,2,3-trimethylbenzene; 10, C_{11} ; 11, naphthalene. Chromatographic conditions were the same as in Figures 2-4 except that the 2D column was a 1.0 m (l) $\times$ 0.100 mm (id) $\times$ 0.1 μ m RTX-Wax capillary held at 90 $^{\circ}$ C.

683

684

685

686 Figure 7. 2-D contour plots from modulated separations of C_7 - C_{10} *n*-alkanes (numbered 1-4,
 687 respectively) using the RTIL-coated μ TM. a) 1 ng each; b) 50 ng each. The RTIL layer thickness
 688 was 0.07 μ m and the μ TM operating parameters were as follows: $T_{\min} = -20$ $^{\circ}$ C; $T_{\max} = 230$ $^{\circ}$ C;
 689 $P_m = 6$ s. Chromatographic conditions: 6-m (l) $\times$ 0.250 mm (id) $\times$ 0.2 μ m HP-1 1 D column; 0.5-
 690 m (l) $\times$ 0.100 mm (id) uncoated, deactivated fused silica capillary 2 D column; GC oven = 30 $^{\circ}$ C;
 691 1.5 mL/min He carrier gas; FID.

692

693

694

Figure Captions

Figure 1. a) Diagram of the GC $\times$ GC system; b) photograph showing the inverted μ TM assembly, the heated interconnects, and the placement on the top of the GC oven (LEGO figure shown for scale; cooling fan and heater wiring was removed for clarity); c) View of interconnect heaters at their interface with the μ TM chip.

Figure 2. Modulated separations with (fixed) $T_{min} = -25\text{ }^{\circ}\text{C}$ and $T_{max} = 100\text{ }^{\circ}\text{C}$. a) 2-D contour plot of the separation of C_6 - C_{10} n-alkanes; b) raw chromatogram for the C_6 peak; c) raw chromatogram for the C_{10} peak. Chromatographic conditions: 30 m (l) $\times$ 0.250 mm (id) $\times$ 0.25 μm HP-1 ^1D column; 0.3 μm PDMS coated μTM ; 0.5 m (l) $\times$ 0.170 cm (id) uncoated deactivated fused silica capillary ^2D column; 80 $^{\circ}\text{C}$ GC oven; 2.0 mL/min He carrier gas; FID.

Figure 3. Modulated separations with (fixed) $T_{min} = 0\text{ }^{\circ}\text{C}$ and $T_{max} = 220\text{ }^{\circ}\text{C}$. a) 2-D contour plot of the separation of C_6 - C_{10} n-alkanes; b) raw chromatogram for the C_6 peak; c) raw chromatogram for the C_{10} peak. Chromatographic conditions were otherwise the same as in Figure 2.

Figure 4. Modulated separations with temperature programmed μTM , $T_{min} = -25$ to $0\text{ }^{\circ}\text{C}$ and $T_{max} = 100$ to $220\text{ }^{\circ}\text{C}$ (see detailed temperature profiles in Figure 5). a) 2-D contour plot of the separation of C_6 - C_{10} n-alkanes; b) raw chromatogram for the C_6 peak; c) raw chromatogram for the C_{10} peak. Chromatographic conditions were otherwise the same as in Figure 2.

Figure 5. Programmed (i.e. set point) temperatures of T_{max} of μ TM (dashed yellow) and T_{min} of μ TM (solid yellow) overlaid on the actual temperature excursions of the μ TM stages (red and white lines) for a ~10-min run.

Figure 6. Unleaded gasoline sample analyzed using the μ TM temperature program in Figure 5. Colored lines were added as visual aids to locate the bands corresponding to different groups of compounds, as labelled; each ϕR_i designates a group of alkyl-substituted benzenes (for $i = 4,5$ the band assignments were inferred from Figure 1a in ref. 42). Those compounds identified by retention time matching are numbered: 1, benzene; 2, C_7 ; 3, toluene; 4, C_8 ; 5, ethylbenzene; 6, C_9 ; 7, *m*-xylene; 8, C_{10} ; 9, 1,2,3-trimethylbenzene; 10, C_{11} ; 11, naphthalene. Chromatographic conditions were the same as in Figures 2-4 except that the 2D column was a 1.0 m (l) $\times$ 0.100 mm (id) $\times$ 0.1 μ m RTX-Wax capillary held at 90 $^{\circ}C$.

Figure 7. 2-D contour plots from modulated separations of C_7 - C_{10} *n*-alkanes (numbered 1-4, respectively) using the RTIL-coated μ TM. a) 1 ng each; b) 50 ng each. The RTIL layer thickness was 0.07 μ m and the μ TM operating parameters were as follows: $T_{min} = -20$ $^{\circ}C$; $T_{max} = 230$ $^{\circ}C$; $P_m = 6$ s. Chromatographic conditions: 6-m (l) $\times$ 0.250 mm (id) $\times$ 0.2 μ m HP-1 1D column; 0.5-m (l) $\times$ 0.100 mm (id) uncoated, deactivated fused silica capillary 2D column; GC oven = 30 $^{\circ}C$; 1.5 mL/min He carrier gas; FID.