Microchip Thermal Gradient Gas Chromatography

Anzi Wang

Brigham Young University - Provo

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Microchip Thermal Gradient Gas Chromatography

Anzi Wang

A dissertation submitted to the faculty of Brigham Young University in partial fulfillment of the requirements for the degree of Doctor of Philosophy

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December 2014

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ABSTRACT

Microchip Thermal Gradient Gas Chromatography

Anzi Wang
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Although the airbath oven is a reliable heating method for gas chromatography (GC), resistive heating is needed for higher analytical throughput and on-site chemical analysis because of size, heating rate and power requirements. In the last thirty years, a variety of resistive heating methods were developed and implemented for both benchtop and portable GC systems. Although fast heating rates and low power consumption have been achieved, losses in column efficiency and resolution, complex construction processes and difficulties experienced in recovering damaged columns have also become problematic for routine use of resistively heated columns. To solve these problems, a new resistively heated column technique, which uses metal columns and self-insulated heating wires, was developed for capillary gas chromatography. With this method, the total thermal mass was significantly less than in commercial column assemblies. Temperature-programming using resistive heating was at least 10 times faster than with a conventional oven, while only consuming 1–5% of the power that an oven would use. Cooling a column from 350 °C to 25 °C with an air fan only required 1.5 min. Losses in column efficiency and peak capacity were negligible when compared to oven heating. The major trade-off was slightly worse run-to-run retention time deviations, which were still acceptable for most GC analyses. The resistively heated column bundle is highly suitable for fast GC separations and portable GC instruments.

Fabrication technologies for microelectromechanical systems (MEMS) allow miniaturization of conventional benchtop GC to portable, microfabricated GC (μGC) devices, which have great potential for on-site chemical analysis and remote sensing. The separation performance of μGC systems, however, has not been on par with conventional GC. Column efficiency, peak symmetry and resolution are often compromised by column defects and non-ideal injections. The relatively low performance of μGC devices has impeded their further commercialization and broader application. This problem can be resolved by incorporating thermal gradient GC (TGGC) into microcolumns. Negative thermal gradients reduce the on-column peak width when compared to temperature-programmed GC (TPGC) separations. This unique focusing effect can overcome many of the shortcomings inherent in μGC analyses. In this dissertation research, the separation performance of μGC columns was improved by using thermal gradient heating with simple set-ups. The analysis time was ~20% shorter for TGGC separations than for TPGC when wide injections were performed. Up to 50% reduction in peak tailing was observed for polar analytes, which significantly improved their resolution. The signal-to-noise ratios (S/N) of late-eluting peaks were increased by 3 to 4 fold. These results indicate that TGGC is a useful tool for bridging the performance gap between μGC and benchtop GC.

Keywords: gas chromatography, resistive heating, metal capillary column, low thermal mass, fast separation, microchip, thermal gradient, peak focusing, resolution.
ACKNOWLEDGEMENTS

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<th>Full Form</th>
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<tbody>
<tr>
<td>BTX</td>
<td>Benzene, toluene and xylene</td>
</tr>
<tr>
<td>CVD</td>
<td>Chemical vapor deposition</td>
</tr>
<tr>
<td>DDPID</td>
<td>Deviation derivative proportional-integral-derivative</td>
</tr>
<tr>
<td>DRIE</td>
<td>Deep reactive-ion etching</td>
</tr>
<tr>
<td>EDP</td>
<td>Ethylenediamine pyrocatechol</td>
</tr>
<tr>
<td>FID</td>
<td>Flame ionization detector</td>
</tr>
<tr>
<td>GC</td>
<td>Gas chromatography</td>
</tr>
<tr>
<td>GC × GC</td>
<td>Comprehensive two-dimensional gas chromatography</td>
</tr>
<tr>
<td>GC/MS</td>
<td>Gas chromatography/mass spectrometry</td>
</tr>
<tr>
<td>IR</td>
<td>Infrared</td>
</tr>
<tr>
<td>ITGC</td>
<td>Isothermal gas chromatography</td>
</tr>
<tr>
<td>LiGA</td>
<td>Lithography, electroplating and molding</td>
</tr>
<tr>
<td>LTCC</td>
<td>Low temperature co-fired ceramic</td>
</tr>
<tr>
<td>LTM</td>
<td>Low thermal mass</td>
</tr>
<tr>
<td>MEMS</td>
<td>Microelectromechanical system</td>
</tr>
<tr>
<td>MOX</td>
<td>Metal oxide</td>
</tr>
<tr>
<td>PAH</td>
<td>Polycyclic aromatic hydrocarbon</td>
</tr>
<tr>
<td>PC</td>
<td>Preconcentrator</td>
</tr>
<tr>
<td>PCB</td>
<td>Printed circuit board</td>
</tr>
<tr>
<td>PDMS</td>
<td>Polydimethylsiloxane</td>
</tr>
<tr>
<td>PID</td>
<td>Proportional-integral-derivative</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Description</td>
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<tr>
<td>--------------</td>
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</tr>
<tr>
<td>PMMA</td>
<td>Polymethylmethacrylate</td>
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<tr>
<td>PTFE</td>
<td>Polytetrafluoroethylene</td>
</tr>
<tr>
<td>PWM</td>
<td>Pulse-width modulation</td>
</tr>
<tr>
<td>RSD</td>
<td>Relative standard deviation</td>
</tr>
<tr>
<td>RTD</td>
<td>Resistance temperature detector</td>
</tr>
<tr>
<td>SAM</td>
<td>Scanning acoustic microscope</td>
</tr>
<tr>
<td>SD</td>
<td>Standard deviation</td>
</tr>
<tr>
<td>SEM</td>
<td>Scanning electron microscope</td>
</tr>
<tr>
<td>SN</td>
<td>Separation number</td>
</tr>
<tr>
<td>S/N</td>
<td>Signal-to-noise ratio</td>
</tr>
<tr>
<td>SOF</td>
<td>Speed-optimized gas flow rate</td>
</tr>
<tr>
<td>SPME</td>
<td>Solid phase microextraction</td>
</tr>
<tr>
<td>SVOC</td>
<td>Semivolatile organic compound</td>
</tr>
<tr>
<td>TCD</td>
<td>Thermal conductivity detector</td>
</tr>
<tr>
<td>TGGC</td>
<td>Thermal gradient gas chromatography</td>
</tr>
<tr>
<td>TPGC</td>
<td>Temperature-programmed gas chromatography</td>
</tr>
<tr>
<td>VOC</td>
<td>Volatile organic compound</td>
</tr>
<tr>
<td>µFID</td>
<td>Microfabricated flame ionization detector</td>
</tr>
<tr>
<td>µGC</td>
<td>Microfabricated gas chromatography</td>
</tr>
<tr>
<td>µPC</td>
<td>Micropreconcentrator</td>
</tr>
<tr>
<td>µTAS</td>
<td>Micro total analysis system</td>
</tr>
<tr>
<td>µTCD</td>
<td>Microfabricated thermal conductivity detector</td>
</tr>
<tr>
<td>µTGGC</td>
<td>Microfabricated thermal gradient gas chromatography</td>
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1 INTRODUCTION*

1.1 OVERVIEW OF HEATING METHODS IN GC

More than sixty years have passed since the principle of gas chromatography (GC) was first demonstrated by James and Martin.\(^1\) In the early years of GC, a number of column heating methods were investigated. Many of them were based on fluid convection with vapor bath,\(^1\) oil bath,\(^2\) or air bath oven.\(^3\) Using these methods, heat was transferred by convection from the heating source (i.e., electric heater) to the column immersed in a fluid. The vapor bath controlled the column temperature by adjusting the pressure of the vapor from a boiling liquid (e.g., ethylene glycol). This method was abandoned because a vapor is restricted to a narrow temperature range, and changing the vapor in the entire container is tedious. A flammable vapor also presents an undesirable safety issue for the laboratory.\(^4\) Oil baths use high-boiling-point oils as thermostats, and they offer wider operating temperature ranges than vapor baths. However, columns can be ruined by any small leak that allows oil inside the column. Changing the column in an oil bath is messy and inconvenient. The air bath oven for GC was introduced in the mid-1950s. Compared with oil and vapor, air has lower thermal mass, it is cleaner and more convenient to handle, and it has no upper temperature limit of operation. More importantly, an air bath oven heats both packed and open-tubular columns more uniformly than other heating approaches. With these advantages, the air bath oven became the standard heating method for GC in the 1960s. The performance of the air bath oven is so reliable and robust that even today it is a component of most benchtop GC systems.

Heating methods based on radiation have also been reported. Gaisford et al.\textsuperscript{5} designed a microwave oven that generated constant electromagnetic field strength. The column was coiled and heated by a microwave-absorbing material which concentrically covered the oven. Because the oven itself was not heated, the power consumption was lower than for an air bath oven, and the heating rate was considerably higher. A GC system employing microwave heating has been commercialized.\textsuperscript{6} Walte et al.\textsuperscript{7} developed an infrared (IR) radiation oven for GC. The heating source was an IR lamp positioned inside or outside the column assembly. Heating rates as high as 1000 °C/min were achievable. For radiation heating methods, uniform heating of the column requires constant radiation strength on the column assembly as well as constant absorption of the radiation, which is difficult to achieve. This possibly explains the limited use of radiation-based heating methods in GC instrumentation.

Resistive heating relies on the use of electrically conductive solid material as the heating source. The heating element is placed in close contact with the column, or it can be the column itself. Heat is transferred mainly by conduction. Although the first use of resistive heating for GC dates back to the 1950s,\textsuperscript{8-11} these methods were replaced by the air bath oven during the 1960s. Resistively heated capillary columns were re-introduced in the 1980s, and have been steadily improved. These methods offer fast heating and cooling rates, low power consumption, and small assembly size at the same time. These features make resistive heating preferable for miniaturized/portable GC and GC/MS instruments.\textsuperscript{12-14} Resistive heating modules have also been adapted for use in recent benchtop GC models to increase the speed of analysis.\textsuperscript{15-16} The following sections compare the differences between oven heating and resistive heating, and describe different resistive heating methods for GC columns and their applications in GC analysis. Pros and cons of each method are critically discussed.
1.2 COMPARISON BETWEEN OVEN HEATING AND RESISTIVE HEATING

1.2.1 Requirements for column heating techniques

Column heating is critical for gas chromatographic separation because the solute (analyte) partition coefficient, $K$, is dependent on absolute column temperature, $T_c$:

$$K = \frac{\rho_S RT_c}{p^o \gamma^o M_S}$$  \hspace{1cm} (1.1)

where $\rho_S$ and $M_S$ are the density and molecular mass of the stationary phase, respectively, $R$ is the gas constant, and $p^o$ and $\gamma^o$ are the saturated vapor pressure and activity coefficient of the solute, respectively.\(^\text{17}\) This relationship can also be expressed as:

$$\log k = \frac{a}{T_c} + b$$  \hspace{1cm} (1.2)

where $k$ is the retention factor, and $a$ and $b$ are constants.\(^\text{17}\) As suggested by Eq. (1.2) and general GC practice, the retention time is reduced by approximately 50% with a 15–25 °C column temperature increase. This equation also indicates several effects that column temperature has on separation. First, for a given sample, column and carrier gas flow, the analysis time (i.e., the elution time of the last peak) is determined by the temperature program. A fast temperature ramp is often desired for fast analysis. Moreover, a non-uniform temperature profile along the column may result in peak broadening and peak symmetry distortion. Even a small cold spot on the column or a slight drift in the ramping rate can compromise the chromatographic performance. Last, but not least, because the values of $a$ and $b$ are different for different compounds, resolution can be significantly affected by column temperature control. To
achieve good separation while maintaining a high analysis throughput, the column heating technique should meet the following technical requirements:

(1) The temperature should be constant along the whole column length.

(2) The temperature profile of each program step should be linear.

(3) Temperature fluctuation or overshooting should be minimized during the ramp.

(4) Maximum heating and cooling rates should be high enough to achieve a short analytical cycle time.

(5) The heating process should be reproducible.

With the rapid development of GC technology in the last thirty years, a number of new interests regarding column heating have arisen, including lower power consumption, reduced system size, faster heating and cooling, and secondary program for multidimensional GC. These practical needs continue to strengthen the motivation for developing new heating techniques for GC.

1.2.2 Practical values of temperature programming rates for fast GC

A trade-off between peak capacity and analysis time is always involved in method development for fast GC. Low heating rates result in high peak capacity, but inevitably increase the analysis time. A considerable portion of the GC run is wasted when over-separation of analytes occurs. On the other hand, using a temperature program that is too fast can produce coeluting analytes due to poor peak capacity. In extreme scenarios, the temperature ramp may end before the elution of any compounds, causing inefficient use of the column. To achieve adequate separation of target analytes in the shortest possible time, the proper selection of
heating rates is dependent on other parameters, including carrier gas flow rate and column
ing length/diameter. Blumberg et al.\textsuperscript{19-21} introduced the concepts of speed-optimized gas flow rate
\((SOF)\) and optimal heating rate \((R_{T,\text{opt}})\), which can be used as default parameters for fast GC
analysis. Here, \(SOF = f_{\text{gas}}d_c\) where \(f_{\text{gas}}\), in mL/(min mm), is determined by the carrier gas type
(10 for hydrogen and 8 for helium) and \(d_c\) is the column internal diameter in mm.\textsuperscript{22} \(R_{T,\text{opt}}\) is
usually 10 °C per void time,\textsuperscript{20} which is determined by the selected flow rate and column
dimensions. Table 1.1 gives some examples of optimal GC parameters and corresponding
calculated analysis times and peak capacities. When the column length is in the range of 1–5 m,
high \(R_{T,\text{opt}}\) values necessitate the use of resistive heating. Such fast temperature programming
rates significantly reduce the analysis time, while the loss in peak capacity is not as dramatic.
Therefore, a short column is preferred if acceptable separation performance can be obtained at
the optimal heating rate. If a change in column dimensions is not possible, using a higher-than-
optimal flow rate and, consequently, a new optimal heating rate would allow faster analysis on a
column that is longer than needed. In either situation, heating rates of 50–800 °C/min are
common.

\textbf{Table 1.1.} Default GC parameters and calculated separation performance for fast analysis.\textsuperscript{a}

<table>
<thead>
<tr>
<th>Column length (m)</th>
<th>(SOF) (mL/min)</th>
<th>Void time (min)</th>
<th>(R_{T,\text{opt}}) (°C/min)</th>
<th>Normalized peak capacity</th>
<th>Normalized analysis time</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.8</td>
<td>0.0134</td>
<td>746</td>
<td>31.6</td>
<td>4.3</td>
</tr>
<tr>
<td>3</td>
<td>0.8</td>
<td>0.0568</td>
<td>176</td>
<td>54.8</td>
<td>18.1</td>
</tr>
<tr>
<td>5</td>
<td>0.8</td>
<td>0.116</td>
<td>86</td>
<td>70.7</td>
<td>37.1</td>
</tr>
<tr>
<td>10</td>
<td>0.8</td>
<td>0.313</td>
<td>32</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

\textsuperscript{a}Carrier gas was helium and column internal diameter was 0.1 mm. Void time was calculated at
50 °C.
Figure 1.1 is a schematic of a modern air bath oven. The oven cavity is made of metal for fast temperature equilibration. It is covered by thermal insulation material to reduce heat loss. The heat source is usually a bare resistive metal wire positioned at the back of the oven. The wire is electrically heated during a temperature program. The capillary column is suspended in the middle of the oven space by a metal rack. A metal heater shield is placed between the resistive wire and the column to block heat radiation that may result in non-uniform heating. A fan behind the resistive wire produces convective air flow, which minimizes any temperature gradients inside the oven. Air vents at the backside are opened for cooling when the program is over. A resistance temperature detector (RTD) reads the temperature near the column, providing feedback for temperature control.

While the air bath oven offers uniform and reproducible column heating, its drawbacks are becoming more and more significant. First, fast GC analysis is difficult to perform with a conventional oven. Under normal operating voltage (120 V), the average heating rate for the entire GC analysis temperature range (50–450 °C) is between 30 and 60 °C/min. Even with higher voltage/current and reduced oven space, 80 °C/min is about the limit. Cool down after running a sample takes approximately 5 min. As a result, typical routine GC analysis requires 20 min or more for one sample. Slow heating and cooling are due mainly to the large total thermal mass of the oven. Second, the power consumption of the air bath oven excludes the possibility of employing it in portable instruments, which are usually battery operated. Last, but not least, the bulky size of the oven raises the manufacturing and maintenance costs of GC systems. Therefore,
there is a need for new column heating technologies, which should be inexpensive, capable of rapid heating/cooling, and feasible for field applications.

![Figure 1.1. Schematic of an air bath oven in a modern GC instrument.](image)

1.2.4 Resistive heating

For resistive heating methods, heating materials (e.g., heating wire) are placed in close contact with the column for good heat conduction, which results in considerably faster heating and cooling than can be achieved with an air bath oven. The elimination of the oven also reduces the thermal mass and the size of the column assembly. Moreover, heat loss is significantly less
due to the smaller surface area, which conserves the power used for heating. These advantages are essential for fast GC separation as well as miniaturized/portable instrumentation.

Figure 1.2. Different types of resistive heating designs for capillary GC columns. (A) Direct resistive heating with conductive film, (B) resistive heating with coaxial heater, (C) resistive heating with collinear wire, and (D) resistive heating with external solid fixture.

Various designs have been proposed and successfully used for resistive heating of GC columns. They can be categorized into four different types. The direct resistive heating design (Figure 1.2A) uses the column itself as the resistive heater. Such columns are either made of metal (e.g., stainless steel) or coated with metal (e.g., aluminum) or conductive paint. The
coaxial design (Figure 1.2B) features a tubular heater through which the column is threaded. In the collinear design (Figure 1.2C), the heater, in most cases a resistive wire, runs parallel to the column. Other methods employ external fixtures (e.g., cylinder as in Figure 1.2D) for column heating. Details of each type of method are discussed in the following sections.

1.3 RESISTIVE HEATING TECHNIQUES FOR PACKED GC COLUMNS

Despite the recent increasing interest in resistive heating and its advantages over oven heating, the former is not a new technology. Resistively heated GC columns were reported as early as 1957. The column consisted of an electrically conductive material (e.g., stainless steel) that could be directly heated with electrical current, although heating rates were not reported. Dal Nogare et al. employed this method for column heating when they demonstrated the advantages of temperature-programmed GC (TPGC). To increase the column temperature during GC analyses, large electric currents were passed directly through the U-shaped packed stainless steel GC column (Figure 1.3A). Heating rates as high as 200 °C/min were obtained, far beyond the ability of other contemporary heating methods such as the oil bath or tube furnace. The main issue with this heating method was the difficulty of finding an insulation material that was durable enough for frequent column change and gas-tight connection. The low resistance of stainless steel also required a high-current, low-voltage power supply. To avoid the drawbacks of direct resistive heating, the column was wrapped with insulated resistive heating wire (Figure 1.3B), which provided linear temperature ramp rates ranging from 2.5 °C/min to 30 °C/min. The so-called “general elution problem” was successfully addressed by PTGC with resistive heating. Wire wrapped GC columns were also employed in early commercial GC instruments, such as the
PerkinElmer Model 222 GC, to eliminate significant thermal lag characteristics of early temperature-programmed ovens. After the introduction of open-tubular columns by Golay in 1956, packed columns were gradually replaced as numerous improvements in column materials, stationary phases and GC detectors for open-tubular columns were made during the 1960s and 1970s.

**Figure 1.3.** Resistively heated packed GC columns. (A) Current was passed directly through the column and (B) the column was heated with resistive heating wire.
1.4 RESISTIVE HEATING TECHNIQUES FOR CAPILLARY GC COLUMNS

Very little effort was made for resistive heating of capillary columns before the mid-1980s for several reasons. First, the air bath oven was improved and became a reliable heating method for regular temperature programming. Second, separation represented only a small part of the total analysis time before the introduction of computer-assisted data processing and advanced instrumentation.29 Shortening the analysis time by fast column heating would not be significant. It was not until the 1980s that the advantages of resistive heating for capillary columns were re-emphasized by Lee et al.30 Since then, numerous designs of resistive heating for capillary GC columns have been proposed.

1.4.1 Direct resistive heating

Because fused silica is an insulator, direct resistive heating of fused silica capillary columns requires a coating of conductive material on the column surface. In 1985, Phillips et al.31 made a thermal modulator for multiplex gas chromatography by painting a short section of fused silica capillary column with electrically conductive paint, which was intended for use in repairing the window defogger of automobiles. By passing an electric pulse through the paint film, the modulator was heated rapidly to release analytes from the stationary phase as a modulated chemical signal. In the next few years, multiplex gas chromatography evolved into comprehensive two-dimensional gas chromatography (GC × GC), and the conductive paint method was used in an early design of the thermal modulator. Later, Jain and Phillips used this method for fast temperature programming32 and temperature gradients33-34 to obtain high-speed
separations. Extremely high heating rates (>1000 °C/min) allowed compounds to be separated within seconds. However, there were some problems associated with use of conductive paint. To evenly heat the capillary, the conductive film must be of uniform thickness along the column, requiring a tedious multi-step coating process. The thin coating was also subject to breakage after repetitive heating cycles.

In 1986, Lipsky et al. developed an aluminum-clad fused silica GC column for high temperature GC applications. By immersing the capillary tubing into molten aluminum, a uniform Al layer, with thickness of tens of microns, was formed on the fused silica. This column was intended to replace polyimide-coated columns for high temperature analyses, because polyimide has a maximum operating temperature of 370 °C. Later, Yost and Hail demonstrated direct resistive heating of the commercialized Al-clad columns. Each column was covered with a Nextel braid for electric insulation and wound around a Teflon spool to form a compact probe-style assembly (Figure 1.4). The two ends of the column were connected to a DC power supply. The column temperature was determined from the resistance of the column and the pre-calibrated resistance–temperature curve. Compared with external temperature sensors which only sample the temperature at certain points, use of the column itself as an RTD provided a more representative average temperature of the column. An average heating rate above 500 °C/min and a cooling rate above 160 °C/min were achieved using a 2.3-m column by direct resistive heating; the power consumption was less than 2% of a conventional oven. Drawbacks observed during the experiment included difficulty in making the low resistance measurement and potential hot/cold spots along the column due to varied coating thickness. A similar metal film-coated capillary column was reported by Cates et al. in the 1980s.
Figure 1.4. Al-clad column assembly. The column was wound around a Teflon spool and inserted into a metal shaft, which was connected to the GC/MS interface.

Although direct resistive heating of aluminum-clad GC columns was never commercialized, a similar resistively heated nickel-clad fused silica GC column is now commercially available (VICI). A nickel layer is formed on the surface of bare or polyimide-coated fused silica columns by electroplating. Each column is then coated with extra polyimide insulation, coiled into a bundle, and covered with aluminum foil. The resistance of the nickel coating serves as the temperature sensor. Because nickel has a resistance change rate approximately five times higher than that of aluminum, temperature sensing based on resistance measurement is more accurate for nickel-clad columns than aluminum-clad ones. This direct resistive heating method can achieve heating rates as high as 800 °C/min as well as sub-
minute cooling times for 5-m columns from 360 °C to 40 °C, while peak power consumption is around 70 W. Depending on whether the column was nickel-clad or wrapped with nickel wire for resistive heating, a separation number loss of approximately 1–4% was observed, respectively, compared to oven heating, which is negligible for most GC applications. The authors suggested several factors contributing to the decrease in column efficiency, including air gap interference, coating thickness variation, and column mounting procedure.

Direct resistive heating of stainless steel capillary columns has also been reported. In 2007, Reid et al. used diaphragm valves and extremely fast temperature programming to achieve peak widths on the order of tens of milliseconds. In their experiments, a 2.3-m stainless steel column was directly heated by connecting to a variable autotransformer. Because the temperature ramp was too fast (e.g., 240 °C/s for a sub-second GC separation), heating rates were determined from chromatographic data rather than by using a temperature sensor. A slightly different method was introduced by Xu et al. The stainless steel column was directly heated by a DC current with pulse-width modulation (PWM) and deviation derivative proportional-integral-derivative (DDPID) control. The modulated DC current provided a time lag for thermal equilibrium of the hot spots, thus attenuating any potential thermal gradients formed on the column during the program. The column was threaded into a glass fiber tube and connected to a fused silica transfer line for insulation. While fast and reproducible heating was achieved, no efficiency loss data were provided by the authors. An example of a commercial GC system that uses a self-heated metal column is zNose. A 1-m stainless steel column is temperature-programmed at rates as high as 20 °C/s by passing a current through it. This system is a sensor-like device and is used for ultrafast separations. A complete analysis cycle, including sampling, separation, data acquisition and re-equilibration, takes ~3 min.
Although direct resistive heating methods add minimum thermal mass to the system and, thus, achieve fast heating/cooling rates and low power consumption simultaneously, some drawbacks also exist. All direct resistive heating methods for fused-silica columns require a coating process, which increases the cost of the column assembly. Conductive films (walls) usually have varied thickness, and are subject to abrasion/scratching during daily use, creating non-uniformly heated regions and reduced column efficiency. A difference in thermal expansion between the capillary and the conductive film may result in mechanical instability. Moreover, it is difficult to recover the column when the conductive layer fails. These factors may continue to be major concerns in the future for designing new direct resistive heating methods.

1.4.2 Resistive heating with fixtures

Instead of being directly heated, capillary columns can be heated with external solid fixtures without any column modification. This approach was used in commercial GC systems many years ago. In 1962, PerkinElmer introduced the Model 226 gas chromatograph, which featured a “solid-state” oven for column heating. The capillary column was coiled inside a metal disk, and the disk was resistively heated by another disk-shaped heating block (Figure 1.5). This system could achieve a heating rate of 50 °C/min with reproducibility comparable to some modern GC ovens. Sides et al. incorporated a resistive column heater in their air monitoring apparatus design. The column was wrapped around a cylindrical solid support, and a heating coil or mat was attached to the inner surface of the cylinder (Figure 1.6). An air fan was also placed inside the cylinder for cooling. The authors reported a heating rate of 210 °C/min from 50 °C to at least 120 °C and less than 2 min cooling time from 180 °C to 50 °C. However, due to the
thermal mass of the cylindrical support, the power consumption (not reported in the patent) was most likely considerably higher than direct resistive heating. A wrap-around design also appeared in the work by Maswadeh et al. The GC oven was a thin aluminum ring (3.8 cm × 2.5 cm × 0.64 cm) with two grooves (Figure 1.7), one in the inner circumference and the other in the outer circumference. A short fused-silica capillary column naturally formed a coil in the inner groove, whereas a heating wire was wound in the outer groove. A small air fan was mounted below the ring oven for cooling. The typical power consumption was under 20 W when using a 1-m column. However, to accommodate longer columns, a larger ring had to be used, which increased the thermal mass and caused thermal gradients. Roques designed a resistively heated column assembly with a spirally and tightly coiled capillary column sandwiched between two sheets of fiberglass cloth. The column was heated using a flat heater which contained a resistive metal filament or carbon film. A heating rate of 60 °C/min resulted in a power consumption of 21 W, whereas a heating rate of 300 °C/min required 91-W power. The main drawback of this method was the manufacturing process, which involved tedious manual scribing of a groove, followed by coiling of the column in the groove.

Methods of resistive heating with fixtures have been applied in commercial GC instruments. A micro GC system (Thermo Scientific) with exchangeable column cartridge uses a column that is coiled in a printed circuit board (PCB), which has patterned heating elements on both top and bottom sides. The maximum rate of temperature programming is 240 °C/min, allowing very fast separation. The power consumption is less than 100 W for one GC channel. However, the maximum operating temperature is limited to 180 °C, which is not high enough for analysis of semivolatiles. This is probably due to the limited thermal stability of circuit board material.
Figure 1.5. Resistively heated column from PerkinElmer Model 226 GC. (A) Column assembly on a heating block and (B) spiral column sandwiched between aluminum plates.
Thermal mass is a major concern for most fixture-based resistive heating approaches. The mass of materials used for support of the column and heater is usually determined by the geometry of the column-heater assembly. A densely coiled column has low surface area and, therefore, requires less materials for housing compared to larger column assemblies. The power consumption is also lower due to lower thermal mass and less heat loss from the surface. However, column loops inside the bundle experience a thermal lag when the ramp is fast, which could compromise the chromatographic performance. Because of this tradeoff, it is hard to find a universal column arrangement suitable for all applications.

Figure 1.6. GC column wrapped on a cylindrical support that was heated by a heating coil inside the cylinder.
Figure 1.7. Ring-shape GC oven made of aluminum. (A) Assembly with column wrapped inside and heating wire wrapped outside and (B) cross-section of the assembly.
1.4.3 Resistive heating with coaxial and collinear heaters

An early collinear heating design was described in a patent by Norem\textsuperscript{53} soon after Golay introduced the open tubular column. In his design, glass tubing containing three evenly spaced, identical bores was employed as the column assembly (Figure 1.8A). One of the bores served as the separation column, while the other two housed an RTD and a heating wire. Although there were no experimental data reported for this method, it is obvious that the low thermal mass and closely bundled design would offer fast heating and low power consumption. Some potential drawbacks are also obvious: manufacturing of tubing with multiple bores is complex, and the connections between the column and external devices (e.g., GC inlet and detector) would require special fittings.

In the early 1970s, Dubsky\textsuperscript{54} tested an in-column coaxial resistive heating approach for step programmed GC, which relied on rapid step changes in the column temperature. Columns made of metal or nylon were heated by squalane coated rectangular stainless steel wire inserted inside the column (Figure 1.8B). Although the author did not report the heating rate, a step change of temperature used in his experiments most likely corresponded to a temperature ramp of approximately 10 °C/s. The in-column wire heating method would be inconvenient for manufacturing, installation and maintenance. Furthermore, the irregular cross-section geometry would also negatively affect the separation performance.

Overton et al.\textsuperscript{55-56} introduced their own collinear and coaxial resistive heating designs in the mid-1990s for portable GC applications and fast separations. In their collinear design, a resistive alloy heating wire, a temperature sensor wire and a fused-silica column were threaded into a polytetrafluoroethylene (PTFE) tube. In their coaxial design, the heating wire was replaced
Figure 1.8. Resistive heating methods with heating wire inside the capillary. (A) Column, heating wire and temperature sensor in a multi-bore capillary and (B) in-column coaxial heating with squalane coated metal wire.
by a resistive alloy tube, which housed both the column and the sensor wire. The coaxial heater was different from the conductive film used in direct resistive heating methods in that it was not deposited on the column and, thus, not vulnerable to breakage from thermal expansion. In both designs, the heater, the sensor and the column were in intimate contact with each other, allowing fast heat transfer and accurate temperature measurement. Overton’s collinear heating design has been employed in a commercial miniaturized GC instrument (microFAST GC, ASI).\textsuperscript{57} The column assembly consists of two 1-m columns with different stationary phases, an insulated heating wire and an RTD wire, all housed in a fiberglass sleeve. Such low thermal mass configuration provides heating rates as high as 1500 °C/min with average power below 100 W.

A method similar to Overton’s coaxial heating design appeared in a patent filed by Rounbehler et al.\textsuperscript{58} The column was inserted into a metal sheath with an inner diameter slightly larger than the outer diameter of the column. The metal sheath was covered with a woven glass sleeve for insulation, and the column assembly was coiled around a holder with minimal contact. This technique was then commercialized as a resistively heated column add-on for conventional GC instruments by Thermedics Detection under the names of “Flash GC” and “EZ Flash.” The EZ Flash module could heat a column at rates up to 1200 °C/min with 96-V power supply, while cooling only took approximately 30 s.\textsuperscript{59} The metal sheath was compatible with 5-m or 10-m fused-silica capillary columns. After Thermedics was acquired by Thermo Scientific, the EZ Flash module was modified to accommodate columns with a broad range of lengths and diameters.

Mustacich et al.\textsuperscript{60-61} demonstrated another collinear heating technique in which the capillary GC column, RTD wire and insulated heating wire were woven together as a bundle using ceramic fibers (Figure 1.9). The bundle was then coiled to form a small torus and covered
with foil. Such a tightly packed design significantly reduced heat loss and, thus, power consumption. For example, heating an 18 m × 0.32 mm fused-silica column at a rate of 60 °C/min only required 23 W (1.3 W/m). This column assembly was commercialized as a low thermal mass (LTM) column by RVM Scientific and employed in several field-deployable GC/MS instruments. In 2008, Agilent acquired RVM and now markets the retrofit column module. This add-on brings cooling and equilibration time down to less than one minute for short columns.

Recently, Tienpont et al. reported a micro-GC device using a coaxial heating jacket for the capillary column. The column was inserted into a polyimide tube over which a thin metal wire was densely braided. The braid was covered by a second layer of polyimide for insulation. The whole GC system could be powered by a 150-W battery. While the operating temperature range and power consumption were not reported, only a low heating rate of 5 °C/min was used. Amirav et al. used a standard fused-silica column and coaxial metal tubing to construct a low thermal mass fast GC/MS system. Analysis cycle times as short as 1 min were obtained by using a high flow rate (35 mL/min), a high heating rate (600 °C/min) and a supersonic molecular beam.

As seen from the descriptions above, both coaxial and collinear heating designs have been successfully commercialized and utilized in benchtop instruments as well as in portable devices. Coaxial heaters tend to offer more even thermal distribution due to the circumferential contact between the heater and column. On the other hand, a tubular heater with thickness variation or bends might create uneven heating in certain regions, reducing the column efficiency. While heating wire is usually more robust and uniform in geometry compared with coaxial heaters, collinear assemblies are subject to less uniform temperature profiles along the column.
Figure 1.9. LTM column assembly. (A) Column coil covered with metal foil, (B) cross-section view of the torus, and (C) column, sensor and heating wire bundled together with ceramic fiber.
1.5 APPLICATIONS OF RESISTIVELY HEATED GC COLUMNS

1.5.1 Fast temperature programming using conventional GC instruments

In general, the major goal of GC method development is to minimize the analysis time while still achieving the desired resolution for accurate qualitative and quantitative analysis. Resistive column heating hardware greatly increases the speed of temperature programming and cooling, thus offering the possibility of high throughput analysis. van Lieshout et al.\textsuperscript{68} assessed the performance of the first commercial resistive GC column module, the Flash-2D GC, for the analysis of hydrocarbons. The reduction in analysis time was much more significant than the decrease in resolution. Dallüge et al.\textsuperscript{59} used the same column module for fast screening of polycyclic aromatic hydrocarbons (PAHs), pesticides and herbicides. The combination of high heating rates (e.g., 500 °C/min) and regular heating rates (e.g., 100 °C/min) in a single temperature program ensured a short analytical run as well as sufficient resolution for target analytes. Williams et al.\textsuperscript{69} employed a Flash GC column for rapid (<90 s) forensic screening. Sloan et al.\textsuperscript{70} incorporated an LTM column in a benchtop GC for analysis of a drug mixture. A negative temperature program was used to maintain the resolution of the critical pair, while the high heating rates cut the analysis time in half compared with oven heating. The detection of biomarkers from bacterial spores using a resistively heated GC column was also reported by Smith and MacDonald.\textsuperscript{71} The analytical column was ramped from sub-ambient temperature to 300 °C at 164 °C/min. Pyridine generated from thermal degradation of Bacillus spores was separated from environmental contaminants in less than 2 min, indicating an analytical throughput of more than 20 samples/h. Analyses of other samples including essential oils,\textsuperscript{72-74}
pesticides, pharmaceutical solvents and cow’s milk were demonstrated using resistively heated columns. For many routine GC analyses, it is practical to improve the existing optimized methods with resistively heated columns to obtain higher analytical throughput.

1.5.2 On-site analysis using portable GC/MS

On-site analysis offers several advantages over conventional laboratory assays. First, it reduces the risk of sample contamination, decomposition and loss during storage and transport. Second, the total analysis time is shortened by in situ sample preparation and detection, thus allowing fast emergency response as well as real-time monitoring. Portable gas chromatography–mass spectrometry (GC/MS) is desirable for field applications involving volatiles and semivolatiles, as it combines instrument portability with high sensitivity and selectivity characteristic of GC/MS. Resistively heated GC columns are preferred in portable GC/MS systems due to their small size, low power consumption and fast temperature response.

Fast analysis time is particularly critical for detection of extremely toxic chemicals, because they can be associated with terrorist attacks or hostile military activities, which require immediate response to reduce potential casualties. Smith et al. compared the performance of two different field-based GC/MS systems for on-site analysis of chemical warfare agents. An LTM column assembly (RVM Scientific, now Agilent Technologies) was employed in both systems for fast temperature programming. The air-sampler based system was limited to a column heating rate of 30 °C/min due to the battery capacity, and its analytical throughput was approximately 3 samples/h. The solid phase microextraction (SPME) based system provided 10 samples/h throughput, as the column was heated at 120 °C/min using a 100-W AC power supply.
Contreras et al.64 demonstrated the use of a battery operated hand-portable gas chromatograph-toroidal ion trap MS for fast identification of chemical warfare agents including sarin, VX and mustard gas. The same type of LTM column was used in this instrument, with a typical heating rate of 120 °C/min. The total time for sample analysis, data acquisition and column cool-down was approximately 5 min. Using this instrument to analyze degraded products of VX has been recently reported.81

Portable GC/MS with resistively heated columns are also suitable for applications when sample transportation is difficult or not desired. A variety of samples including volatile organic compounds (VOCs) in water,82-83 odor emissions of plants84, indoor air contamination,85 adhesives and paints,86 food products,87 and essential oils88 have been successfully addressed. The results of these studies indicate that portable GC/MS enables researchers to perform fast and accurate quali-quantitative tests in fields such as environmental science, food science, industrial hygiene, and health science.

1.6 ADVANTAGES AND DRAWBACKS OF RESISTIVE HEATING IN GC

Considerable work has been done in the last thirty years on resistive heating technology for GC analysis. Below are the major benefits obtained from resistive column heating:

(1) Fast temperature programming and column cool-down are readily achieved with resistive heating. Depending on the sample type, the analysis time for many GC separations can be reduced by a factor of 3–5 with temperature ramps higher than 100 °C/min. It is even possible to achieve separations that are 10 times faster than those accomplished with oven heating if critical pairs can still be resolved at very high heating rates. Sub-minute
cooling and equilibration times further increase the analytical throughput and allow steeper negative temperature programs.

(2) Reduction in size and power consumption facilitates miniaturized and portable GC instruments that can perform a variety of field analyses, including ambient air monitoring, industrial exposure measurements, chemical warfare agent detection, and explosives screening. Some resistive heating methods allow the column to be coiled into a 2-in or 3-in bundle, which can easily fit into a hand-portable GC or GC/MS device for on-site analysis. Low thermal mass column assemblies require less than 2 W/m to heat up and, thus, can be powered by a rechargeable battery pack. Minimizing the power consumption becomes critical when hours of continuous instrument operation are desired.

(3) The manufacturing cost of GC instruments should be reduced by replacing oven heating with resistive heating. Elimination of the air bath oven greatly reduces the materials used, since fabrication of a resistive column bundle or fixture only utilizes a small mass of metal heater and insulation.

(4) Integration of resistive heaters on microfabricated GC columns provides the possibility for producing low-cost, fast-response, low-power, remote controlled, lab-on-a-chip GC sensors. Potential applications of these devices include point-of-care diagnosis, hazardous chemical detection, and air-quality monitoring.

Although all four types of resistive heating techniques have commercialized formats, the air bath oven still remains the dominant and standard column heating method today. The wide usage of next generation column heating techniques is hindered by several drawbacks:

(1) Most resistive heating methods are more or less subject to uneven heating. Hot spots, cold spots and longitudinal/radial temperature gradients result in efficiency and resolution
loss, irreproducible retention times, peak shape distortion or even damage to the column coating.

(2) Many resistively heated columns are associated with complex manufacturing processes, such as weaving insulation materials and manually coiling the column to a specific geometry or arrangement. Production of resistively heated GC instruments in large scale is impeded by fabrication steps that cannot be easily automated or standardized.

(3) Recovering a plugged or broken column is difficult or even impossible. This factor might seem trivial, but is often encountered in practical use. When using an air bath oven, a plugged column can be dismounted, cut and reinstalled, and a broken column can be fixed by connecting the two sections with a deactivated quartz tube. In contrast, for a resistively heated column bundle in which the column, heater, temperature sensor and insulation material are assembled together, isolating the column would be impractical. Therefore, development of new resistive heating column techniques in the future should focus on achieving oven-like uniform heating, reducing manufacturing complexity and costs, and offering the capability of column change/recovery. By resolving the few remaining technical obstacles associated with resistive heating column technology, miniaturization of all GC related instruments is expected.

1.7 OVERVIEW OF MICROFABRICATED GC

Microfabricated gas chromatography (µGC) systems consist of components based on micro-electro-mechanical systems (MEMS), which can include micropreconcentrators (µPCs), micropumps, microcolumns, and microsensors. µGC systems hold promise for field applications,
as they feature fast analysis time, low power consumption and easy portability. The first MEMS-based μGC system was reported by Terry et al. in 1979. The system featured a microfabricated solenoid sample valve, a 1.5-m-long wet-etched separation column, and a microfabricated thermal conductivity detector (TCD). All three major components were integrated on the same wafer. Although this device only achieved ~1000 theoretical plates, it opened up an entirely new area for GC and inspired numerous μGC designs and applications in the following thirty-five years. Today, μGC has emerged as a hot area where researchers from engineering and chemistry fields collaborate with each other to improve the performance of μGC components and develop prototype devices for demanding on-site applications. The following sections review the μGC designs and fabrication methods found in the recent literature.

1.7.1 μPCs

In order to detect trace analytes in gaseous samples taken from the environment, preconcentration is often required for μGC applications. A preconcentrator (PC) is usually a flow channel filled with adsorbent materials which selectively adsorb target analytes. After an adequate amount of sample passes through the adsorbents, the PC is heated, during which the trapped analytes are desorbed into the column and carried to the detector at a higher concentration. Compared with conventional PCs (e.g., a tube or capillary filled with adsorbents), MEMS-based μPCs provide much lower power consumption and superior heat transfer rate during the desorption step. Therefore, considerable research effort has been put into fabricating μPCs that can be integrated with microcolumns and microsensors on the same chip.
The first μPC was reported by Manginell et al. in 2000. In their design, a 1-µm-thick silicon nitride mask was deposited on a silicon wafer, followed by deposition of a Ti/Pt metal trace as a desorption heater. The sampling channel was fabricated by etching a trench through the wafer from the other side until it reached the nitride layer. Adsorbent material was then spray coated onto the channel surface. As shown in Figure 1.10, the thin layer of Si₃N₄ allowed extremely fast heating (40 °C/ms) of the adsorbent, which could create a ~200-ms-wide (full width at half maximum) injection pulse into the GC column. Maintaining a temperature of 200 °C on the heater only required a power input of 0.1 W. The primary drawback of this device was the low sample capacity, which resulted from the limited thickness of the adsorbent layer. Kim et al. reported a similar type of μPC fabricated on a silicon substrate. The heater was fabricated by depositing a layer of Al alloy onto the surface of an etched channel. A polymeric adsorbent layer was coated inside the channel after the heater was coated with spin-on glass, which served as an adhesion layer. However, the heating rate of this μPC device was only ~20°C/s due to the large thermal mass.

Figure 1.10. Cross-section view of a “micro-hot-plate” style μPC.
To increase the sample collection area inside the chip while keeping the thermal mass as low as possible, perpendicular-flow designs have been implemented.\textsuperscript{95-96} In these designs, a Si wafer is etched through to produce suspended microheaters, which are then coated with thin-layer adsorbents. Sample flow is perpendicular to the chip surface, allowing more analytes to be trapped by the polymeric adsorbent layer. During the desorption step, the microheaters could reach 200 °C in less than 100 ms. Based on the suspended polymer-heater structure, a “smart” \( \mu \)PC device was developed in 2008, which could roughly quantify the amount of adsorbed analyte.\textsuperscript{97} In this case, the heater itself served as a pivot-plate resonator, which had a resonant frequency that was inversely proportional to the square root of its mass. When an adequate amount of sample was collected, the \( \mu \)PC circuit would automatically turn on the heater for sample desorption.

Instead of the micro-hot-plate structure design, Tian et al.\textsuperscript{98} created a suspended microheater structure with carbon-based adsorbents (shown in Figure 1.11) to achieve high sample capacity for VOCs. Deep reactive-ion etching (DRIE) was employed to etch through the Si substrate and form parallel Si beams, which served as heaters. Adsorbent particles were packed into channels between the beams and uniformly heated during the sample desorption step. The microheater was sealed by bonding the top and bottom sides with pre-etched Pyrex wafers. The air gaps between the sealing wafer and the particle/heaters created some thermal isolation to reduce the total thermal mass. A maximum heating rate of 15 °C/s was achieved with 2.25-W power, indicating a trade-off between sample capacity and power consumption. A three-stage \( \mu \)PC, consisting of a series of three channels packed with different adsorbents, was later developed and utilized in a “first generation” hybrid \( \mu \)GC system.\textsuperscript{99-100} Detection limits in the range of 5–130 ppb were achieved for an 11-component VOC mixture. Ruiz et al.\textsuperscript{101-102} reported
a similar design in which parallel silicon bars were surrounded by a dielectric membrane and sealed with two glass plates. Instead of using the silicon bars as the heating elements, a layer of boron-doped polysilicon was patterned on top of the structure as the heater, improving the overall thermal isolation of the device.

**Figure 1.11.** A µPC with suspended Si heaters.

Because carbon-based adsorbents have large surface areas, researchers have utilized simpler µPC structures while maintaining a high sample capacity. Gràcia et al.\textsuperscript{103} demonstrated a µPC with a particle-packed 10-cm spiral channel. The heater was patterned on the Pyrex glass lid of the chip. Camara et al.\textsuperscript{91} created microchannels with a porous Si surface layer by HF/EtOH electrochemical etching. The porous Si layer could accommodate a large amount of carbon nanoparticles. Although these types of devices would inevitably have lower heating rates (5–10 °C/s) and higher power consumption compared with µPCs with suspended microheaters, the microfabrication process is simpler and more straightforward.
1.7.2 Microcolumns

The majority of microcolumns have been fabricated on Si substrates. Wet etching techniques were initially employed, creating channels with a trapezoidal or tapered cross-section. Sealing of the channel was typically done by bonding the Si wafer with a Pyrex glass wafer at moderately high temperature (150–400 °C) with electric voltage applied between the two substrates. Terry et al. used a traditional dynamic coating method to lay down the stationary phase on the column walls, while Kolesar et al. employed chemical vapor deposition (CVD) to deposit a layer of copper phthalocyanine onto the wafer surface before sealing the channel. The performance of these columns were far worse than regular capillary columns.

In 2004, Lambertus et al. fabricated a microcolumn on a 3.2 cm × 3.2 cm chip with a square-spiral pattern and a rectangular cross-section (150 µm × 240 µm) using DRIE. This 3-m column, dynamically coated with dimethyl polysiloxane, produced up to 8200 plates. This performance greatly surpassed previous microcolumns, making this column feasible for on-site detection of VOCs. Following work by the same research group reduced the thermal mass of the column using back etching and wafer thinning, and improved the column efficiency to more than 4000 plates/m using static coating. To mitigate peak tailing of organophosphonate and organosulfur compounds resulting from surface adsorption on the microcolumn walls, Radadia et al. developed a deactivation method using pinacolyl methylphosphonic acid, which reacts with alkali ions and other active sites to eliminate analyte adsorption. To further increase the total number of plates of microcolumns, Nishino et al. fabricated long spiral channels, up to 17.0 m in length, on a 3-in Si wafer. A microcolumn with dimensions of 200 µm × 100 µm × 8.56 m
generated 35,000 plates, compared to an 8.56-m 150-µm i.d. capillary column which generated ~38,000 plates. To expand the usable temperature range of microcolumns, Gaddes et al.\textsuperscript{111} designed a fluidic interconnect by combining column nuts and vespel/graphite ferrules with a stainless-steel manifold, which created a gas-tight seal with a working temperature up to 450 °C. The performance gap between microcolumns and capillary columns are continually being narrowed by significant research effort.

Although siloxane-based stationary phases have been predominantly used for microcolumns, other types of stationary phases have also been explored. Zampolli et al.\textsuperscript{112} packed carbon-based particles into spiral shaped channels with cross-sectional areas up to 0.8 mm\textsuperscript{2}. The columns were then coupled to a metal oxide gas sensor for quantification of benzene, toluene and xylene (BTX) in air. A detection limit well below 5 ppb was achieved. Nakai et al.\textsuperscript{113} reported the use of parylene as a stationary phase in μGC. Thin films of parylene were deposited on a glass wafer and an etched Si wafer using CVD, and the two wafers were then thermally bonded together. A uniform layer of parylene stationary phase was observed using a scanning electron microscope (SEM). Stadermann et al.\textsuperscript{114-115} demonstrated the use of carbon nanotubes as stationary phase for ultrafast μGC separation. Catalyst metals (Al/Pt/Fe) were deposited on microchannels with an electron-beam evaporator, and carbon nanotubes were grown on the metal layer using CVD. Separation of C\textsubscript{6}−C\textsubscript{11} was achieved under 3 s. Zareian-Jahromi et al.\textsuperscript{116} fabricated a microcolumn with gold as stationary phase template. The gold layer, with thickness of 100–2000 nm, was electroplated onto the channel walls before sealing the channel. Octadecylthiol was introduced into the channel to react with the gold to form a single layer of functional groups through self-assembly. A plate number of 20,000/m for a 25-µm-wide microchannel was reported. Vial et al.\textsuperscript{117-118} employed sputtering as a method to produce a
stationary phase. Both sputtered silica and graphite stationary phases showed enhanced separation for light alkanes (C$_1$–C$_5$), which are usually insufficiently retained when using a dimethyl polysiloxane phase. Sputtered alumina was also reported recently.$^{119}$

Microcolumns have also been fabricated on non-Si substrates. Noh et al.$^{120}$ fabricated a parylene microcolumn using an etched Si wafer as a template. Parylene/Pt/Parylene films were deposited on both Si microchannel and Pyrex glass plates. The two plates were then thermally bonded and soaked in KOH to obtain a free-standing parylene column. Due to its low thermal mass, heating and cooling was significantly faster for this column compared with a Si/glass column. Bhushan et al.$^{121-122}$ demonstrated the use of LiGA (lithography, electroplating, and molding) to produce nickel-based microcolumns. Figure 1.12 summarizes the fabrication process of the nickel column. Thick polymethylmethacrylate (PMMA) photoresist was patterned, which served as a template for subsequent electroplating. A high-aspect-ratio cross-section, up to 50 $\mu$m × 600 $\mu$m, was realized. An all-glass microcolumn was reported by Lewis et al.$^{123}$ With a well-controlled HF etching process, semi-circular channel cross-sections were created on borosilicate glass wafers. A column was sealed by aligning two etched wafers and allowing them to bond at room temperature via van der Waals forces. Dziurdzia et al.$^{124}$ described a $\mu$GC system fabricated on a low-temperature co-fired ceramic (LTCC) platform. A photo-imageable thick-film process, involving multiple screen-printing, exposure, development and firing steps, was employed to create a 4.8 m × 250 $\mu$m × 80 $\mu$m column with flame ionization detector (FID) on a 65 mm × 50 mm alumina plate. Darko et al.$^{125}$ developed a more straightforward method to fabricate LTCC-based microcolumns. A channel pattern was first cut using a UV laser in an unfired ceramic tape, which was then sandwiched between two capping ceramic tapes, laminated
on a press, and cofired to form a sealed column. Malainou et al.\textsuperscript{126} fabricated polymer-based microcolumns using soft lithography and molding.

Advancements in MEMS technologies allow many features, which were considered difficult to realize in conventional GC, to be fabricated on microcolumns. Potkay et al.\textsuperscript{127} fabricated a microcolumn suspended in a micro vacuum chamber. By minimizing the thermal mass and heat convection, a 1-m column only required 11 mW to raise its temperature by 100 °C. Kim et al.\textsuperscript{128-129} designed a microfabricated thermal modulator for GC × GC based on a similar design but without a vacuum chamber. Figure 1.13 shows the fabrication process for this low-thermal-mass modulator. Very high heating rates (up to 2400 °C/s) and cooling rates (up to 37
Figure 1.13. Fabrication process for a micro thermal modulator. (A) Boron doping, (B) oxide patterning, (C) channel etching, (D) deep boron doping, (E) Pyrex glass bonding, (F) resistor patterning, (G) Si DRIE, and (H) ethylenediamine pyrocatechol (EDP) etching.

−168 °C/s) were achieved. Microfabricated multicapillary columns, reported by Zareian-Jahromi et al.\textsuperscript{130} and Li et al.\textsuperscript{131} increased the sample capacity while showing no significant eddy diffusion as often encountered in conventional multicapillary columns. In both studies, the high precision of photolithography and DRIE helped to create a bundle of channels with little discrepancy in dimensions. The multicapillary microcolumn design was also adopted in GC × GC separations, in which three identical channels with different stationary phases were employed in the second dimension.\textsuperscript{132} Semi-packed columns, first reported by Ali et al.\textsuperscript{133} and later by other research groups,\textsuperscript{134-137} utilized a micro-pillar array structure to reduce the resistance to mass transfer while producing lower back pressure than conventional packed columns. These
columns have produced more than 10,000 plates/m. The separation power of microcolumns may surpass conventional columns if they can be fabricated in larger lengths.

1.7.3 Heating techniques for microcolumns

Early μGC systems\textsuperscript{90,105} were designed for on-site chemical sensing applications. However, they did not incorporate any specific column heater in the design, but focused on the fabrication process and detector response. The lack of column temperature control limited the types of samples that these devices could address. Although the air bath oven was often employed for evaluation of microcolumn performance,\textsuperscript{106,121,138} the use of oven heating goes contrary to the purpose of using a μGC system, i.e., low power consumption and small size. Resistive heating is obviously the best choice for μGC. Heating elements could be either external heaters (Figure 1.14A) or microfabricated metal heaters incorporated directly on the planar GC chip (Figure 1.14B).

Peltier (thermoelectric) coolers are widely used for cold trapping and column cooling in GC. They can also function as heaters. Strictly speaking, a Peltier heater is not a resistive heater, because heat is transferred from the cold side to the hot side rather than generated from electrical energy. Nonetheless, the Peltier device is similar to a resistive heater in geometry and operating conditions. Robinson et al.\textsuperscript{139} designed a μGC system using either one Peltier device to heat one side of the column, or two to heat both sides. The column can be set at a sub-ambient temperature when the Peltier device is in the cooling mode, and then ramped to a higher temperature by reversing the polarity and gradually increasing the current. This is an advantage compared to conventional GC instruments, which normally require liquid CO\textsubscript{2} or N\textsubscript{2} for
programming from sub-ambient temperatures. Hastings et al.\textsuperscript{140} demonstrated a microfabricated GC column that was sandwiched between two parallel channels (Figure 1.14C). Thermoelectric materials were inserted into the channels to form two Peltier strips. Heating and cooling could be switched by changing the direction of the electric current. Because the Peltier devices were miniaturized and integrated into the chip, the size and thermal mass of the system were reduced. As a result, the transition between heating and cooling modes was faster than for regular thermoelectric units.

![Image of microfabricated GC column](image)

**Figure 1.14.** Resistive heating of \(\mu\)GC. (A) GC chip heated with thin film heater and/or Peltier device, (B) on-chip fabricated metal heater, and (C) heating and cooling with Peltier strips.

Although Peltier devices can be employed both as heaters and coolers, their heating efficiencies are considerably lower than electric heaters. Additionally, the maximum temperature
difference between the hot and cold sides is also limited to approximately 100 °C for most commercial Peltier elements.\textsuperscript{141-142} A resistive heater offers wider operating temperature range with lower power consumption. In the microfabricated planar glass GC system designed by Lewis et al.,\textsuperscript{123} a polyimide thin-film heater was employed as the primary heating element, and a Peltier cooler was used as an auxiliary heater during temperature programming. The small thickness (200–500 µm) and low thermal mass of the polyimide heater ensured adequate heating and cooling rates with power consumption less than 25 W. The maximum operating temperature of this system was 200 °C. All-polyimide heaters\textsuperscript{143} could alternatively be used to ramp the column up to 260 °C, which is high enough for many GC analyses. Higher temperatures are achievable with ceramic heaters, mica heaters, or even metal strip heaters. Thermal mass would be a major concern for these other high temperature heaters.

Patterned resistive metal layers can be deposited on the surfaces of column substrates to form robust micro heaters with good thermal conduction, wide temperature range and extremely low thermal mass. For silicon-based columns, a thin layer of Ti can be patterned on the wafer surface as an adhesion layer. Then another layer of Pt can be directly deposited on the Ti as the resistive heating layer.\textsuperscript{114-115} Deposition of a Cr/Au film as a resistive heater was reported as well.\textsuperscript{144} This type of heater can also be fabricated on Pyrex glass,\textsuperscript{116} which can be anodically bonded to silicon to form sealed channels. Intimate contact between the heater and the column allows extremely high heating rates (>2000 °C/s), which are more than enough for temperature programming, and adequate for thermal modulation in GC × GC.\textsuperscript{128} Depending on the thickness and size of the chip, a heating power consumption as low as 1 W/m is common. With the help of wafer thinning and back etching, the column mass can be further reduced to allow extremely fast temperature programming rates (>5000 °C/min) with only a 55 mW/m power pulse.\textsuperscript{127} Because
Pt is often used in RTDs, the thin metal film can also function as heater and temperature sensor simultaneously,\textsuperscript{128,145} which is advantageous for system integration compared to external heaters. The temperature is determined by measuring the resistance of the heater and calculating the value from a predetermined resistance-temperature calibration curve.

1.7.4 Microsensors

The TCD has been employed for GC analysis since 1954.\textsuperscript{146} It is a universal, non-selective detector, because almost every chemical has a lower thermal conductivity than that of hydrogen or helium carrier gas and, thus, can be detected. The TCD is also a non-destructive detector, and requires no auxiliary gas. Disadvantages of the TCD in the past have included lower sensitivity and lower linear dynamic range than other detectors.\textsuperscript{147} However, recent advances in microfabrication technologies have allowed the development of MEMS-style TCDs with sub-\(\mu\text{L}\) cell volumes and improved sensitivity. The first micro-TCD (\(\mu\text{TCD}\)) was reported along with the first \(\mu\text{GC}\) in 1979.\textsuperscript{90} A Pyrex glass layer was sputtered on a silicon wafer, and a nickel film was patterned on the glass as the resistive filament. The wafer was then back-etched and clamped to the outlet of a micro GC column. Despite the lack of reference cell and Wheatstone configuration, this TCD achieved a detection limit of \(~10\) ppm, which is comparable to traditional TCDs. Wu et al.\textsuperscript{148} fabricated a \(\mu\text{TCD}\) by patterning a nickel film on different membrane materials, including polyimide, Pyrex glass and Si\(_3\)N\(_4\). The membrane was then bonded to an open channel or sandwiched between two identical flow channels. The authors found that all three membrane materials were feasible for device fabrication, and there was no significant sensitivity difference between the single-channel structure and the sandwich structure.
Cruz et al.\textsuperscript{149} designed a μTCD with Cr/Pt heaters patterned on suspended Si$_3$N$_4$ membrane bridges. Because the membrane was oriented toward the flow direction, the gas flow impinged on the membrane instead of passing over it, and heat transfer between the gas and heater was greatly improved. This detector yielded a detection limit of 1 ppm, which is better than many commercial TCDs. Rastrello et al.\textsuperscript{150} described acquisition electronics for μTCD control with a wide gain range and a sensitivity of 15 μVs/ng. In their design, heaters were fully suspended in the flow channel, which was sealed with a Pyrex glass cover. As μTCDs have become increasingly more sensitive and reliable, commercial micro GC systems have begun to integrate on-chip μTCDs, which are capable of on-site VOC analysis.\textsuperscript{151} These detectors can achieve a detection limit of 1 ppm and a linear dynamic range of 10$^6$.

The FID has been employed for GC analysis since the late 1950s.\textsuperscript{152-154} It detects hydrocarbons and other organic compounds with a minimum detectable level of 1.5 pg carbon/s, which is at least 100-times more sensitive than the TCD.\textsuperscript{23} Because the FID requires a fuel gas and oxygen to operate, its use in μGC devices is significantly limited. Zimmermann et al.\textsuperscript{155} reported the first micro-FID (μFID) in 2000. As shown in Figure 1.15, a Pyrex-Si-Pyrex sandwich structure contained an oxyhydrogen flow channel and a sample flow channel, which were connected by a micro nozzle at the end. Small nozzle diameters (<100 μm) created a high oxyhydrogen velocity at the burner head, which prevented back firing of the flame. A detection limit of ~100 ppb for pentane was achieved with an improved design.\textsuperscript{156} A planar μFID was developed by the same group with a minimum detectable level of 450 pg carbon/s for methane.\textsuperscript{157-158} Interestingly, the sensitivity of this detector was higher for methane than pentane, while the sensitivity of the conventional FID increases with increasing molecule size. Kim et
al.\textsuperscript{159} utilized a similar quartz-Si-quartz structure in their \textmu FID design and reported a sensitivity of 0.02 C/mol for methane.

![Design of a \textmu FID.](image)

\textbf{Figure 1.15.} Design of a \textmu FID.

Metal oxide (MOX) based semiconductor sensors have been widely used for gas sensing. The basic sensing mechanism is based on the reaction between the surface adsorbed oxygen species and the target gas, which induces a resistance change of the metal oxide film.\textsuperscript{160} This type of sensor has good sensitivity to ppb-level reducing gases. However, an oxygen environment and elevated temperature (200–400 °C) is required. Another downside of MOX sensors is their slow response and recovery time (on the order of seconds).\textsuperscript{161} Afridi et al.\textsuperscript{162} described a micro-hot-plate-style MOX sensor system, in which a suspended polysilicon heater structure was fabricated first, followed by deposition of the Au electrodes and SnO$_2$/TiO$_2$ sensing films. This sensor had a thermal efficiency of 10 °C/mW, and was successfully used to detect
ppm-level H₂, CO, and methanol. Elmi et al.\textsuperscript{163} designed a SnO₂-based sensor with a detection limit of 5 ppb for benzene. Coupling of MOX sensors to µGC has been reported, showing very wide chromatographic peaks due to slow detector response.\textsuperscript{112,164}

Other types of detectors have been investigated for the µGC platform. Chemiresistors have served as µGC detectors in VOC identification and quantitation.\textsuperscript{165-168} The sensing material was gold-thiolate monolayer-protected nanoclusters coated on microelectrodes. The swelling of the thiolate monolayers, after adsorption of VOC vapors, changes the interparticle distance as well as dielectric constant of the film matrix, producing a measurable change in electric resistance of the sensor.\textsuperscript{169} An array of resistors can be easily fabricated to provide limited pattern recognition for unknown compounds. Disadvantages of chemiresistors include poor linearity and slow response. A Fabry-Pérot interferometer can be also used as GC detector.\textsuperscript{170-171} The sensor was fabricated by depositing a layer of gas-sensitive polymer (e.g., PDMS) on a reflective surface (e.g., silver or silicon) inside the sample flow channel. Analyte absorption changed the thickness and/or refractive index of the polymer, thus creating a shift in the interference spectrum of the Fabry-Pérot cavity. Good limits of detection (5–50 pg) were achieved for VOCs. This detector can be integrated into µGC systems if combined with miniaturized optical components, including laser, spectrometer/photodetector and beam splitter/collimator. Plasma-based detectors have been implemented in planar forms, using either optical emission\textsuperscript{172-173} or current change\textsuperscript{174-175} as the detection mechanism. These detectors were simple to construct and integrate with µGC, and typically had pg-level detection limits. Although a high-voltage DC power supply was required for plasma generation, the power consumption could be reduced by optimizing the size and orientation of the microplasma.
The focus of current research effort in the area of μGC can be summarized as:

(1) Individual μGC components are being integrated into micro total analysis systems (μTAS) with low power consumption and compact size to address on-site sampling, unknown identification and quantitation problems in the real world.

(2) A variety of different GC detectors, including both universal types (e.g., TCD) and selective types (e.g., chemiresistors), are being miniaturized to allow characterization of complex samples.

(3) Novel column structures (e.g., pillar arrays and multicapillaries) are being implemented to increase the theoretical plate number per meter and, thus, compensate for the limited column length on a chip.

(4) GC × GC is being investigated as a powerful method, which greatly expands the total peak capacity on short columns for VOC mixture analysis.

Despite the rapid progress in μGC instrumentation in the last twenty years, technical challenges still hinder the application and commercialization of μGC devices. Reasons for this include:

(1) Due to the limited column length, the total theoretical plate number of microcolumns, typically ranging from 5000 to 30,000, is still much lower than conventional fused-silica columns (e.g., 150,000 plates for a 30 m × 0.25 mm column). Therefore, analytes that are readily separated using a benchtop GC may coelute with a μGC, making method transfer between the two platforms problematic. Also, GC × GC has not yet been fully
appreciated for μGC, because the peak capacity of the first dimension for μGC (typically 20–100) is much lower than for conventional GC (typically 500–1000).

(2) Defects of microcolumns (e.g., dead volume and stationary phase pooling) create band broadening and distortion of peak symmetry and, thus, compromise both resolution and quantitation.

(3) Ionization-based detectors (e.g., FID and photoionization) have worse sensitivity and detection limits when miniaturized. Absorption/adsorption-based detectors (e.g., MOX sensors) generally have slow response times and are sometimes not fast enough to sense narrow (e.g., 50–500-ms-wide) peaks. Reliable detector performance, with the exception of the TCD, is yet to be achieved.

One can expect that performance issues of current μGC systems will be resolved in the near future by combining the right tools and materials to conquer technical difficulties step-by-step.

1.9 DISSERTATION OVERVIEW

This chapter provided an overview of the resistive heating methods in GC and recent research progress in μGC. The first part of this chapter critically discussed various configurations, pros and cons of different types of resistive heating techniques. The second part briefly reviewed the history of μGC by describing the evolution of major μGC components. Chapter 2 describes a novel resistive heating technique for metal GC columns. This method allows fast temperature programming rates at low power, provides reproducible retention times, and minimizes efficiency loss. Chapter 3 demonstrates the use of thermal gradient gas
chromatography (TGGC) in μGC. Peak symmetry, analysis time and peak capacity were improved by establishing a sharp temperature gradient along the microcolumn and sweeping the gradient. Chapter 4 demonstrates the use of dynamic gradient heating on μGC and its effect. Chapter 5 summarizes the results achieved in this dissertation research, and gives recommendations for future development of these techniques.

1.10 REFERENCES


NEW RESISTIVELY HEATED COLUMN TECHNOLOGY FOR FAST GAS CHROMATOGRAPHY

2.1 INTRODUCTION

The analysis time in capillary GC can be reduced by changing various parameters, such as column inner diameter, column length, carrier gas flow rate, and heating rate. Among the various fast GC approaches that have been reviewed,1-6 fast temperature programming was identified as the easiest and most effective approach. The high heating rates used for fast temperature programming require low total system thermal mass and good heat conduction from the heater to the GC column. Unfortunately, conventional benchtop gas chromatographs cannot meet these requirements due to their bulky air bath oven, which limits their maximum heating rate to around 100 °C/min. To address this problem, resistive heating techniques have been widely employed in the development of fast GC. The basic principle is the same for all of these methods: by applying a voltage to the heating element, heat is generated and instantaneously conducted to the GC column.

Resistive heating was first reported in GC in the 1950s, in which a resistive metal wire was wrapped around a packed column for heating.7 During the 1960s and 1970s, the increasing use of capillary columns and successful design of the air bath oven delayed the application of resistive heating, because at that time it was difficult to provide good electrical insulation between the heating element and the column.8 In 1989, Yost and Hail9 developed a system in which an aluminum-clad fused-silica column was coiled around a Teflon spool and resistively heated. Temperature sensing was achieved by measuring the resistance of the Al coating. This
system allowed a heating rate as high as 2400 °C/min, and the power consumption was only 35 W. However, any uneven section of the metallic coating created an unwanted temperature gradient, which affected the separation.\textsuperscript{10}

Ehrmann et al.\textsuperscript{11} provided two different improved designs for resistive heating: a coaxial heater in which a metal tube was used to heat the column (which was threaded inside) and a collinear heater in which a resistive heating wire was coiled with the column in parallel. In their work, the fused-silica column was vulnerable to abrasion by the heater ends, which tended to shorten the lifetime of the coaxial heater. Thermedics introduced a resistive heating system, the EZ Flash, in 1998.\textsuperscript{10} In this coaxial design, the fused silica capillary was inserted into a metal jacket for resistive heating. This was the first commercially available resistive heating system for GC. The device could readily achieve heating rates as high as 1200 °C/min and cooling rates around 300 °C/min.\textsuperscript{12-14} RVM Scientific followed the collinear approach and developed a low-thermal-mass (LTM) GC column assembly using a nickel wire with ceramic fiber insulation as the heating element and a platinum wire as the temperature sensor.\textsuperscript{15} Although this column assembly showed relatively good performance, the fabrication process was complex. More recently, Xu et al.\textsuperscript{16} demonstrated direct resistive heating, in which a metal column was directly heated using a pulse-width current. Despite the low thermal mass, the average power consumption of the column was ~20 W/m, limiting its use for portable instrumentation.

VICI developed resistively-heated fused-silica columns using nickel cladding or wire as the heating element.\textsuperscript{17} The Ni cladding/wire was also employed as a temperature sensing element based on a temperature-resistance calibration curve. While the Ni-clad column gave higher efficiency compared to the Ni wire-heated column, the construction of the Ni cladding required an additional electroplating process. One of the latest efforts for resistive heating of GC columns
was reported by Fialkov et al.\textsuperscript{18} In their design, a short column was inserted into a resistively heated metal tube that was located outside the GC oven. Several critical reviews on different resistive heating techniques for GC columns have been published.\textsuperscript{19-21}

This chapter describes a novel resistively heated column technology. The metal capillary column was wound into a toroid together with self-insulated resistive wires. The construction of the column bundle was simple and straightforward compared to the coaxial and collinear designs described above. Free from additional electrical insulation materials, this method provided good heat conduction and extremely low thermal mass. The temperature ramping rates and the reproducibility of retention times were satisfactory. The low power consumption and small size of this column bundle makes it promising for applications with portable GC instruments.

2.2 EXPERIMENTAL

2.2.1 Reagents and standards

Carbon disulfide, n-octane and n-decane were purchased from Spectrum Chemical (New Brunswick, NJ, USA); methanol, hexanes and n-heptane were purchased from Mallinckrodt Baker (Phillipsburg, NJ, USA); n-undecane, n-tetradecane, n-hexadecane, n-heptadecane, n-nonadecane and n-eicosane were purchased from Sigma-Aldrich (St. Louis, MO, USA); n-tridecane was purchased from Wiley Organics (Coshocton, OH, USA); GC-FID standard (part No. 18710-60170) was purchased from Hewlett-Packard (Avondale, PA, USA); D3710 test mixture (catalog No. 4-8884) was purchased from Supelco (Bellefonte, PA, USA); and 8260B calibration mix #1 (catalog No. 30152) was purchased from Restek (Bellefonte, PA, USA).
Four different samples were prepared: sample #1 was a mixture of C\textsubscript{14}, C\textsubscript{15} and C\textsubscript{16} in hexanes (~100 ppm each); sample #2 was a diluted D3710 mixture in CS\textsubscript{2} containing 19 components (~100−400 ppm each); sample #3 was a mixture of C\textsubscript{7}, C\textsubscript{8}, C\textsubscript{10}, C\textsubscript{11}, C\textsubscript{13}, C\textsubscript{14}, C\textsubscript{16}, C\textsubscript{17}, C\textsubscript{19} and C\textsubscript{20} in CS\textsubscript{2} (~300 ppm each); and sample #4 was a diluted 8260B mixture in methanol containing 75 components (~200 ppm each).

2.2.2 Preparation of column assemblies

A 5 m × 0.1 mm i.d. × 0.4 μm MXT-5 (5% diphenyl/95% dimethyl-polysiloxane) stainless steel column from Restek (Bellefonte, PA, USA) was coiled into a 55-mm diameter torus. The column torus was tightly wound with a 32 AWG Nichrome 80 resistive heating wire with double glass/silicone electrical insulation from Pelican Wire (Naples, FL, USA). The wire had a resistance of 10 Ω. Figure 2.1 shows how the wire was wound. The column bundle was then wrapped with fiberglass and aluminum foil to reduce heat loss and improve the temperature homogeneity. A 0.005” type K thermocouple from Omega (Stamford, CT, USA) was embedded in the column coil for temperature sensing. The column bundle had two leads. The lead connected to the GC injector was 17 cm in length and the lead connected to the detector was 23 cm in length. Both leads were inserted into nickel tubing, which was wrapped with resistive heating wires to eliminate cold spots. The temperature of the column leads was measured using thermocouples. Another assembly with a 1.3 m × 0.1 mm i.d. × 0.4 μm MXT-5 column was constructed in a similar way, but with a coil diameter of 20 mm. The 1.3-m short column was only used for testing temperature ramping capabilities and efficiency loss.
2.2.3 Instrumentation and GC conditions

An Agilent 6890A GC system (Santa Clara, CA, USA) with a split/splitless injector and a flame ionization detector was used for all chromatographic tests. Helium was used as the carrier gas at a constant flow rate of 0.2 mL/min for all separations. Manual injections were performed using 10-µL syringes from Hamilton (Reno, NV, USA). All injections were done using the split mode, and the split flow rate ranged between 100 and 200 mL/min. The injection volume was 1 µL for all runs. The injector and detector were kept at 250 ºC and 270ºC, respectively. The Agilent Chemstation was used to acquire all chromatograms.

Figure 2.1. Diagram of the resistively heated column assembly.
2.2.4 Temperature control set-up

The column heating wire was connected to an amplifier with a 24-V DC power supply. The heating wires for the two transfer lines (column leads) were connected to two 120-V AC variable autotransformers. The power applied on transfer line heaters was adjusted by controlling the pulse widths of two solid state relays. A small air fan with 12-V DC input was used for cooling the column. A home-built LabView program was used for temperature monitoring, fan switch and voltage control. A data acquisition board sampled the column temperature at 20-Hz rate and used a proportional-integral-derivative (PID) algorithm to provide feedback control of heating.

2.3 RESULTS AND DISCUSSION

2.3.1 Advantages of the newly designed column bundle

The low thermal conductivity of fused silica limits the configuration of resistive heaters, which are often in a coating or tubular format to maintain temperature homogeneity. Because the length of the heater must equal the length of the column, it is difficult to produce heaters with uniform thickness for long columns. In contrast, metal columns dissipate heat faster and allow the heating element to be utilized in non-coaxial geometries (e.g., collinear wire or hotplate). In this work, the heating wire and the column were tightly coiled into a torus shape, reducing the cross-sectional area of the bundle and facilitating radial heat conduction. The construction process was simple and straightforward. Figure 2.2 shows the size difference between a
commercial metal column bundle and the newly designed column bundle, both in 5-m lengths. With a lower thermal mass and a compact geometry, the new column assembly features lower power consumption and more uniform temperature distribution. Because the performance of portable instruments is often limited by battery capacity, resistive heating devices with low thermal mass have greater potential for field detection. While there are fewer stationary phases on metal columns compared to fused-silica columns, technologies of surface modification and deactivation are continually evolving and should bring more column chemistries to metal columns.

Figure 2.2. Size comparison between a commercial column bundle (left) and a home-made column bundle (right). Both columns were 5 m in length. The insulated heating wire and fiberglass material are inside the aluminum foil and, therefore, cannot be seen in the photo.
2.3.2 Column efficiency loss

Column efficiency is normally evaluated by injecting n-alkanes under isothermal conditions and calculating the effective plate number using \[ N_{\text{eff}} = 5.545 \times \left[ \frac{(t_R-t_m)}{w_h} \right]^2, \] where \( t_R \) is the retention time, \( t_m \) is the holdup time and \( w_h \) is the peak width at half maximum. An airbath oven uniformly raises the temperature of a column by strong air convection within the entire oven cavity. However, most resistive heating methods are subject to temperature variation due to slight irregularities in thickness/diameter of the heating elements and/or mass distribution of the insulating materials. Therefore, the effective plate number is usually reduced when a column is resistively heated. The effective plate numbers for isothermal oven heating and resistive heating are listed in Table 2.1. The reduction in plate number was 4.8% for a 1.3-m column and 2.8% for a 5-m column, which indicates a slight variation in the temperature profile along the column when resistive heating was used. There are several factors that might account for the lower plate numbers: (1) there is a radial temperature gradient, spanning from the heating wire to the outer column loops, and then to the inner loops; (2) manual construction of the column bundle could produce hot/cold spots where the heating wire was not equally spaced or the fiberglass was slightly overlapped; and (3) cold spots may exist where the column leads exit the bundle. Nevertheless, an efficiency loss less than 5% is negligible in most GC analyses, especially when compared to the column-to-column efficiency variation in commercial columns, which can often reach \( \pm 10\% \). If the same method is used with a long GC column (e.g., 30 m), a larger bundle diameter is preferred so that the cross-sectional area of the torus is small enough for fast heat transfer.
Table 2.1. Calculated column efficiency loss.\textsuperscript{a}

<table>
<thead>
<tr>
<th>Column length (m)</th>
<th>Heating method</th>
<th>$t_m$ (min)</th>
<th>$t_R$ (min)</th>
<th>$w_h$ (min)</th>
<th>$N_{eff}$</th>
<th>Efficiency loss</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.3</td>
<td>Oven</td>
<td>0.049</td>
<td>1.007</td>
<td>0.031</td>
<td>5296</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Resistive</td>
<td>0.049</td>
<td>1.014</td>
<td>0.032</td>
<td>5043</td>
<td>4.8%</td>
</tr>
<tr>
<td>5.0</td>
<td>Oven</td>
<td>0.237</td>
<td>3.360</td>
<td>0.050</td>
<td>21632</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Resistive</td>
<td>0.241</td>
<td>3.381</td>
<td>0.051</td>
<td>21019</td>
<td>2.8%</td>
</tr>
</tbody>
</table>

\textsuperscript{a}Conditions: 120 °C for the 1.3-m column and 150 °C for the 5-m column; 1-µL sample #1 (mixture of C\textsubscript{14}, C\textsubscript{15} and C\textsubscript{16}) injected with split ratio of 500:1 for all runs; C\textsubscript{14} was used for plate number calculations for the 1.3-m column and C\textsubscript{15} for the 5-m column.

Figure 2.3 shows chromatograms of a hydrocarbon mixture for oven and resistive heating conditions. All corresponding peaks have approximately the same retention times and peak symmetries. The peak widths are slightly larger for oven heating due to a variation in split ratio (500:1 for oven heating and 700:1 for resistive heating). The results indicate that resistive heating provides a generally uniform isothermal profile along the column.

2.3.3 Retention time reproducibility

To reliably identify the peaks in a chromatogram, good retention time reproducibility is crucial. Although resistively heated columns have often been evaluated using relative standard deviation (RSD) of retention times, it is difficult to accurately use RSD values for peak identification. Figure 2.4 demonstrates the poor relationship between RSD of retention times and
peak overlap. A more meaningful criterion for evaluating retention time reproducibility is the ratio of the run-to-run retention time standard deviation to the base peak width ($SD/w_b$).\textsuperscript{10} When chromatograms from multiple runs are overlaid, the lower the $SD/w_b$ value, the closer the peaks from the same analyte converge. Generally, there is no ambiguity in peak identification if the $SD/w_b$ value is less than 10%.

**Figure 2.3.** Isothermal chromatograms from oven heating and resistive heating for a 5-m column. Conditions: 1-μL sample #2 (D3710 mixture) injected at 150 °C for both runs.
In this work, the retention time repeatability of a 5-m column bundle was examined for both oven heating and resistive heating. Table 2.2 lists the SD/\( w_b \) values for 19 analytes with oven and resistive heating, and Figure 2.5 shows a chromatogram obtained using temperature programming by resistive heating. Five runs were performed for each condition. Under isothermal conditions, the SD/\( w_b \) value ranged between 2.5% and 7.4% for oven heating, and between 3.5% and 12.8% for resistive heating. These results indicate that the temperature fluctuation inside the oven is less than inside the wire bundle. Because the oven door was open during resistive heating runs, it is most likely that random air currents in the laboratory disturbed the temperature on the bundle and caused changes in retention times. Under temperature-programming conditions, the SD/\( w_b \) value ranged between 1.7% and 4.5% for oven heating, which was lower than for isothermal conditions. This can be explained by errors in manual injection timing, which were corrected by the 1-min initial temperature for temperature-programming conditions. For resistive heating, the SD/\( w_b \) value was below 10% for the first 14 peaks, but ranged between 12.8% and 16.4% for the last five peaks. The large retention time SD indicates that resistive heating was significantly affected by the ambient air when the column...
Table 2.2. Ratio of retention time standard deviation to base peak width for isothermal and temperature-programming conditions.a

<table>
<thead>
<tr>
<th>Peak</th>
<th>Isothermal SD/wb (%)</th>
<th>Temperature-programming SD/wb (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Oven heating</td>
<td>Resistive heating</td>
</tr>
<tr>
<td>1</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>5</td>
<td>-</td>
<td>-</td>
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<tr>
<td>6</td>
<td>-</td>
<td>-</td>
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<tr>
<td>7</td>
<td>-</td>
<td>-</td>
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<tr>
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<td>9</td>
<td>-</td>
<td>-</td>
</tr>
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<td>10</td>
<td>-</td>
<td>-</td>
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<tr>
<td>12</td>
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<td>-</td>
</tr>
<tr>
<td>13</td>
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<td>-</td>
</tr>
<tr>
<td>14</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>15</td>
<td>7.4</td>
<td>3.5</td>
</tr>
<tr>
<td>16</td>
<td>5.9</td>
<td>10.4</td>
</tr>
<tr>
<td>17</td>
<td>4.2</td>
<td>12.8</td>
</tr>
<tr>
<td>18</td>
<td>5.1</td>
<td>12.0</td>
</tr>
<tr>
<td>19</td>
<td>2.5</td>
<td>9.1</td>
</tr>
</tbody>
</table>

*aConditions: 150 °C for isothermal conditions; 40 °C for 1 min and programmed to 220 °C at 40 °C/min for temperature-programming conditions; column length 5 m; 1-μL sample #2 injected for all runs; see Figure 2.5 for peak identifications.
Temperature was higher than 150 °C (i.e., when n-butyl benzene started to elute). Temperature ramping likely caused inconsistent local air convection around the bundle and affected the heat loss rate for each run. Nevertheless, analyte identification was not significantly hindered for resistive heating, because peaks from one analyte still overlapped with each other with a $SD/W_b$ value less than 20%.

**Figure 2.5.** Temperature-programming separation of sample #2 using resistive heating.

Conditions: column held at 40 °C for 1 min and ramped to 220 °C at 40 °C/min; column length 5 m. Peak identifications: (1) n-propane, (2) 2-methylpropane, (3) n-butane, (4) 2-methylbutane, (5) n-pentane, (6) 2-methylpentane, (7) n-hexane, (8) 2,4-dimethylpentane, (9) n-heptane, (10) toluene, (11) n-octane, (12) p-xylene, (13) n-propylbenzene, (14) n-decane, (15) n-butylbenzene, (16) n-dodecane, (17) n-tridecane, (18) n-tetradecane, and (19) n-pentadecane.
2.3.4 Separation number loss

Separation number (Trennzahl) is defined as \( SN = \frac{(t_{R2} - t_{R1})}{(wh_1 + wh_2)} - 1 \), where \( t_{R1} \) and \( t_{R2} \) are the retention times of two consecutive peaks, and \( wh_1 \) and \( wh_2 \) are the peak widths at half heights of the two peaks.\(^{22}\) Unlike plate number, separation number can be applied to temperature-programming conditions to demonstrate the separation performance of a column. To evaluate the separation number loss resulting from resistive heating, sample #3 containing 10 n-alkanes was injected into a 5-m column, and the \( SN \) between each alkane pair was calculated as listed in Table 2.3. The temperature ramping rate was set at 30 °C/min, which was the upper limit for oven heating. The overall loss in \( SN \) was 2.4%, which is negligible for most GC analyses. In addition to temperature non-uniformity, another factor contributing to loss in \( SN \) is transfer line heating. In isothermal runs, the two transfer lines were set at the column temperature and did not create efficiency loss. In temperature-programming runs, however, the transfer lines were kept at 300 °C and, thus, were not utilized for analyte separation. This configuration can be improved by adding a programming function to the transfer line heating, or by moving the detector module and eliminating the transfer lines.

Although the overall percentage change in \( SN \) for the n-alkane sample was small, an 18.8% reduction was observed for the last pair of alkanes. Figure 2.6 shows the peak widths of C\(_{13}\)–C\(_{20}\) in a separation with resistive heating. It was found that the peak widths of C\(_{19}\) and C\(_{20}\), which eluted at temperatures above 200 °C, were significantly larger than other peaks. This peak broadening was caused by cold spots in a column section housed in the detector fitting. During heating, this column section was heated by hot air as well as by conduction from the detector heater. In resistive heating, however, the ambient air cooled this region and created band
Table 2.3. Separation numbers for oven heating and resistive heating under temperature-programming conditions.\textsuperscript{a}

<table>
<thead>
<tr>
<th>Analyte pair</th>
<th>$SN$ for oven heating</th>
<th>$SN$ for resistive heating</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>$C_7$−$C_8$</td>
<td>18.6</td>
<td>18.6</td>
<td>0.0%</td>
</tr>
<tr>
<td>$C_8$−$C_{10}$</td>
<td>36.9</td>
<td>36.6</td>
<td>−0.8%</td>
</tr>
<tr>
<td>$C_{10}$−$C_{11}$</td>
<td>16.4</td>
<td>16.1</td>
<td>−1.8%</td>
</tr>
<tr>
<td>$C_{11}$−$C_{13}$</td>
<td>30.4</td>
<td>30.6</td>
<td>+0.7%</td>
</tr>
<tr>
<td>$C_{13}$−$C_{14}$</td>
<td>13.2</td>
<td>12.8</td>
<td>−3.0%</td>
</tr>
<tr>
<td>$C_{14}$−$C_{16}$</td>
<td>25.1</td>
<td>24.5</td>
<td>−2.4%</td>
</tr>
<tr>
<td>$C_{16}$−$C_{17}$</td>
<td>10.7</td>
<td>10.2</td>
<td>−4.7%</td>
</tr>
<tr>
<td>$C_{17}$−$C_{19}$</td>
<td>19.9</td>
<td>19.1</td>
<td>−4.0%</td>
</tr>
<tr>
<td>$C_{19}$−$C_{20}$</td>
<td>8.5</td>
<td>6.9</td>
<td>−18.8%</td>
</tr>
<tr>
<td>Total</td>
<td>179.7</td>
<td>175.4</td>
<td>−2.4%</td>
</tr>
</tbody>
</table>

\textsuperscript{a}Conditions: 40 °C for 1 min and programmed to 270 °C at 30 °C/min.

Figure 2.6. Band broadening in a separation with resistive heating.
broadening for analytes that elute at higher temperatures. Raising the temperature of the transfer line to 350 °C produced slightly narrower peaks; however, the resolution between C_{18} and C_{19} was still lower than with oven heating. In order to resolve this issue, the detector fittings must be thermally isolated and heated with a separate heater inside the GC oven. Elimination of cold spots from the GC system are crucial for GC analysis of chemicals with low volatility.

### 2.3.5 Fast GC analysis

Generally, if a separation produced from oven heating at the maximum heating rate contains over-separated analytes, resistive heating can always be implemented for the same separation to increase the analytical throughput. While the GC oven used in this work could only sustain a maximum heating rate of 30 °C/min, the resistively heated column bundle could be ramped at much higher heating rates. Figure 2.7 shows a fast separation of sample #3 on a 5-m column. The 10 n-alkanes were separated within 2.1 min. In comparison, it took at least 6.7 min for the GC oven to finish the same separation. As shown in Table 2.4, if injection, cooling and equilibration times are taken into account, the throughput with resistive heating is 3.4 times higher than with oven heating.

EPA Method 8260 is used to identify and quantitate a variety of VOCs in solid waste matrices. Portable GC/MS systems are desirable for this application, since sample transportation and storage can be eliminated, which lowers the risk of sample loss, contamination and degradation. The resistively heated column assembly, which is designed for use with both benchtop and portable systems, was evaluated for separation of sample #4 (8260B mix) containing 75 components. Figure 2.8 is a chromatogram of the separation with a 5-m column.
The separation was finished within 6 min, and approximately 70 resolved or partially resolved peaks were observed. This result indicate good separation performance of the resistively heated column. A longer column (e.g., 10 m × 0.1 mm) can be employed to achieve better resolution of incompletely resolved analyte pairs.

Figure 2.7. Fast separation of an n-alkane mixture with resistive heating. Conditions: 40 °C for 0.7 min and programmed to 300 °C at 180 °C/min.

Table 2.4. Comparison between oven heating and resistive heating for separations of sample #3.

<table>
<thead>
<tr>
<th>Method</th>
<th>Injection time</th>
<th>Separation time</th>
<th>Cooling time</th>
<th>Equilibration time</th>
<th>Throughput (samples/h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oven heating</td>
<td>0.5</td>
<td>6.7</td>
<td>8.3</td>
<td>2.0</td>
<td>3.4</td>
</tr>
<tr>
<td>Resistive heating</td>
<td>0.5</td>
<td>2.1</td>
<td>0.9</td>
<td>0.5</td>
<td>15.0</td>
</tr>
</tbody>
</table>
Figure 2.8. Separation of sample #4 with a 5-m column bundle. Conditions: 35 °C for 2 min and programmed to 200 °C at 40 °C/min.

2.3.6 Heating/cooling speed and power consumption

Figure 2.9 demonstrates the heating and cooling capabilities of resistively heated columns. The 1.3-m column can be ramped at a maximum rate of 2000 °C/min from 25 °C to 350 °C, and cooled back down to 25 °C in 1 min. The 5-m column can be ramped at a maximum rate of 500 °C/min, and cooled from 350 °C to 25 °C in ~1.5 min. These results demonstrate that for columns with 0.1 mm i.d., a short length (1–3 m) can be used with an ultra-fast temperature program (e.g., 1000 °C/min) to separate simple mixtures within 30 s, while longer lengths (5–10
m) are desirable for separation of moderately complex mixtures by programming at 50–300 °C/min. It is worth noting that the PID parameters were selected to counteract any external disturbance (e.g., voltage fluctuation and ambient air flow), and tended to create slight distortion in temperature linearity, especially when the column temperature was above 300 °C. The precision of the temperature control may be increased by experimenting with different voltage programs and selecting one that can create a strictly linear temperature profile. This method, however, is less accurate when ambient temperature changes occur during a separation.

Figure 2.9. Column temperature profiles during resistive heating and air fan cooling.

Compared with airbath ovens, which require 1–3 kW for temperature programming, a resistively heated column only uses tens of watts. Figure 2.10 compares the power consumption of a 5-m column at different programming rates. A wattage of 45 was sufficient for the
maximum heating rate (500 °C/min). Power usage was significantly lower if the column was heated at rates below 250 °C/min. From a practical point of view, a 30-W power supply would be adequate for column heating in portable GC systems. The isothermal power consumption, which equals the heat loss rate, was approximately 2 W at 50 °C and 18 W at 350 °C. In comparison, a 0.2-m transfer line heater, not wrapped with any insulation, required 10 W at 300 °C. This difference in heat loss indicates good thermal insulation effect with fiberglass and aluminum foil in the column assembly. The air fan used in this work only needed a 7-W input.

![Figure 2.10](image)

**Figure 2.10.** Power consumption of a 5-m resistively heated column under isothermal and temperature-programming conditions.

### 2.4 CONCLUSIONS

With advantages of simple construction, low power consumption, small size and high heating and cooling rates, the resistively heated metal column assembly described here
demonstrated fast separation and reasonable reproducibility, which are essential for field portability. Compared with oven heating, resistive heating increases the analytical throughput by 3–4 fold and reduces the power requirement by 95–99%. The trade-offs are negligible losses in plate number and separation number, and a slightly lower retention time repeatability, which is still acceptable for peak identification. Cold spots in the column connections significantly affect separation at high temperatures, and should be eliminated by modifying the connection between the column and the injector/detector.

2.5 REFERENCES

3 AXIAL THERMAL GRADIENTS IN MICROCHIP GAS CHROMATOGRAPHY*

3.1 INTRODUCTION

Although conventional benchtop GC systems are efficient and reliable for routine analysis in the laboratory, their bulky sizes, low heating/cooling rates and high power consumption restrict their use for field analysis. As a result, samples collected for environmental monitoring and biomedical diagnostics are subject to loss, contamination and degradation during transport to the laboratory and storage before analysis.\(^1\) Also, applications that require fast response (e.g., toxic/explosive compound detection) must be performed in the field. To fill the need for small, low-power instruments that can provide rapid analysis of VOCs and SVOCs, researchers have been developing μGC devices based on MEMS.\(^2\)\(^-\)\(^6\) By assembling micropreconcentrator/injector, microcolumn and microsensor components into compact, low-cost, battery-operated packages, μGC systems have demonstrated promise for field applications including ambient air monitoring, hazardous materials detection, industrial exposure measurement, food quality analysis, and point-of-care diagnostics.

Despite the potential of μGC systems, their separation performance lags significantly behind conventional GC. Efficiencies of microcolumns range typically from 2500 to 5500 plates per meter,\(^7\)\(^-\)\(^10\) while commercial narrow-bore fused-silica open tubular columns can achieve over 10,000 plates per meter.\(^11\) The lower efficiency of microcolumns is mostly caused by stationary phase non-uniformity (pooling). Giddings\(^12\) investigated the relationship between surface

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structure and column performance as early as 1962. Non-uniformities in stationary phase coating due to pooling lead to inefficient columns. It was found that when coating a capillary column, a slight variation in cross-section curvature could result in significant liquid accumulation. Therefore, a uniform circular inner surface is required for producing a uniform stationary phase coating. Conventional fused-silica capillaries are manufactured by melting a raw synthetic silica tube in a high-temperature furnace and drawing it down to capillary tubing of precise dimensions. The nearly perfect round cross-section and low surface roughness allow uniform stationary phase coating with accurately determined thickness. Unfortunately, the ideal column profile is rarely achieved in microfabricated columns. Thicker and less uniform films formed at the corners of rectangular/trapezoidal cross-sections increase the plate heights for \( \mu \)GC separations. While researchers have made progress in fabricating circular cross-sectional columns and micropillar array columns to yield higher numbers of theoretical plates per meter, the fabrication processes are more complex and difficult.

Because a variety of materials and processes are involved for microcolumn fabrication, surface active sites (i.e., reactive functional groups and trace impurities that are introduced into the column during fabrication) are typically more problematic for microcolumns compared to conventional fused-silica columns. For example, the Pyrex glass used for wafer bonding contains \( \text{B}_2\text{O}_3, \text{Na}_2\text{O}, \text{Al}_2\text{O}_3, \text{Fe}_2\text{O}_3, \text{CaO}, \text{MgO} \) and \( \text{Cl} \) in addition to its main \( \text{SiO}_2 \) composition. These oxides remain on the column surface after fabrication, and obviously interact with certain analytes, which affects their separation. Ceramic-based columns create similar problems from their mixed oxide composition. When using metal columns, analytes are exposed to the metal surface, which is more reactive than silica. Polymer-based microcolumns often have chemical impurities (e.g., initiators and additives) in the polymer composition; the molding
process can also add impurities from surface contact between different substrate/template
materials. Another source of active sites is the adhesives used for capillary connection, which
can potentially adsorb certain compounds as well as outgas various contaminants. Although little
has been reported in the literature concerning the surface characterization of microchip columns,
the negative effects of active sites are evidenced by the poor peak symmetry observed in many
μGC chromatograms. Interactions between analytes and surface active sites are most common
for compounds containing hydroxyl, amine, carboxyl, and sulfur- and phosphorus-containing
functionalities.22 Significant tailing poses problems for identification and quantitation. Complete
elimination of active sites (i.e., deactivation) is more difficult and sometimes technically
impossible for μGC columns due to the complex surface chemistry on the column walls. In some
cases, multi-step deactivation procedures and prolonged pre-conditioning have shown
success;9,23 however, the long preparation times and extra costs are undesirable.

Dead volume concerns are also magnified when using μGC columns. If capillary tubing
is used for connections between the injector, column and detector, even a slight mismatch
between the tubing and the channel introduces dead volume. Dead volumes at connections
interfere with static coating7,24 as well as create extra band broadening and peak tailing in
separations.20,25 Integration of a microfabricated injector, column and detector on a single wafer
can eliminate the use of connecting tubing and fittings, and, thus, reduce the dead volume. In this
case, the whole μGC system would have to be replaced, even if only one component failed, since
disassembling is not possible with such integrated systems.

In addition to column defects that deteriorate chromatographic efficiency and peak
symmetry, the sample injection process also affects the performance of μGC. In field analysis,
analytes of interest are often present in water/air/soil at low levels26 and, therefore, large
injection volumes are desired to lower the detection limits. Regardless of injection type (i.e., liquid injection, headspace injection or thermal desorption), a few seconds to several minutes may be needed for the carrier gas to carry most of the sample into the column. Large injection bandwidths require focusing at the front of the column, usually at low temperature, in order to preserve column efficiency and obtain adequate resolution. During the low-temperature part of the temperature program, analytes are trapped in the stationary phase at the beginning of the column and little separation occurs. μGC devices are usually faster than benchtop GC because of the use of resistive heating, low thermal mass, and short column length. Therefore, sample focusing becomes a large percentage of the analysis time and restricts analysis throughput.

Regardless of the different sources and effects of the above mentioned defects/factors, they all result in unwanted band broadening. Theoretically, a negative temperature gradient along the column should mitigate band broadening by focusing the sample bands and separating them from each other at the same time. When a sample band migrates through a negative temperature gradient, the back of the band always resides at a higher temperature and travels faster than the front of the band. Separation occurs simultaneously, as less volatile analytes are slowed down at higher temperatures than volatile ones. This technique is known as TGGC, pioneered by Zhukhovitskii et al. and studied by a number of research groups in the last few decades. While the work on TGGC by Phillips et al. led to the introduction of GC × GC, TGGC itself has rarely been implemented in practice. The recent work by Contreras et al. explored some unique features of TGGC and pointed out the possibility of improving μGC separation performance by utilizing static and moving thermal gradients.

This chapter describes the first use of TGGC on a microfabricated column format. Separations under TGGC and TPGC conditions were compared to demonstrate the focusing
effect of the thermal gradient and improvements in analysis time, peak symmetry, resolution, and peak capacity.

3.2 EXPERIMENTAL

3.2.1 Reagents and standards

Pentane was purchased from EMD Millipore (Billerica, MA, USA); hexanes were purchased from Mallinckrodt Baker (Phillipsburg, NJ, USA); carbon disulfide was purchased from Fisher Scientific (Fair Lawn, NJ, USA); dicumyl peroxide, n-decane, n-undecane, n-dodecane, n-pentadecane, n-nonylamine, n-decylamine, 2-octanol and tributylphosphate were purchased from Sigma-Aldrich (St. Louis, MO, USA); and 2,4,6-trichlorophenol was purchased from Acros Organics (Morris Plains, NJ, USA). Silicone SE-54 (catalog No. 21106) and D3710 test mixture (catalog No. 4-8884) were purchased from Supelco (Bellefonte, PA, USA). The D3710 mixture contained 19 components: n-propane, 2-methylpropane, n-butane, 2-methylbutane, n-pentane, 2-methylpentane, n-hexane, 2,4-dimethylpentane, n-heptane, toluene, n-octane, p-xylene, n-propylbenzene, n-decane, n-butylbenzene, n-dodecane, n-tridecane, n-tetradecane, and n-pentadecane.

3.2.2 Column fabrication

Through-holes, 400 μm in diameter, were laser-drilled on a 1000-μm thick 4-in. silicon wafer to form the column inlet and outlet. After drilling, the wafer was re-polished using a
chemical-mechanical polisher to restore its smooth, particle-free surface. Anisotropic KOH wet etch was used to create two 1.4-m-long and one 2.7-m-long serpentine channels on a single wafer. Briefly, the wafer was: (1) heated in a furnace to form a thick layer of thermal oxide on the surface, (2) patterned with AZ P4620 photoresist and AZ 400K developer (AZ Electronic Materials, Branchburg, NJ), (3) etched in HF to remove the exposed oxide layer, (4) cleaned in Nano-Strip (Cyantek, Fremont, CA, USA) to remove residual photoresist, and (5) etched in KOH to form the channel. Figure 3.1A shows the trapezoidal cross section of the wet-etched channel, and Figure 3.1B displays the serpentine pattern and critical dimensions.

During KOH etching, the surface oxide layer was slowly thinned and became less uniform, especially around the channel. To ensure a uniform layer thickness for the subsequent wafer bonding process, surface oxide was removed by HF after KOH etching. To seal the channel, the etched wafer was bonded to another silicon wafer through fusion bonding. In the absence of commercial wafer bonders, an alternative method was employed to ensure a hermetic seal of the channel. Briefly, the two wafers were: (1) heated in a furnace to yield a thin layer of thermal oxide; (2) thoroughly cleaned and rinsed with acetone, isopropanol and deionized water; and (3) brought into contact with each other and slowly heated in a furnace. The furnace temperature started from 140 °C, ramped to 1100 °C at 2 °C/min, held at 1100 °C for 3 h, and cooled to 500 °C at −2 °C/min. Oxygen flow was directed into the furnace during the whole process. Scanning acoustic microscopy (SAM) was employed to examine the quality of the wafer bonding. The use of SAM to inspect sealed GC columns was first described by Bhushan et al. in 2004.37 Figure 3.2A shows an SAM image of a bonded 2.7-m column. No bonding defects were observed along the channel, indicating a good seal of the column. Figure 3.2B is a close-up look at a number of the 180° serpentine turns. The original pattern on the photo mask consisted of
square-shaped outer and inner turns. The inner turns on the wafer became rounded due to the anisotropic KOH etching of \(<100>\) Si. The dimensions of the microchips were 25 mm by 62 mm for the 1.4-m column and 25 mm by 100 mm for the 2.7-m column after dicing. Only the 1.4-m columns have been tested so far for chromatographic performance.

Figure 3.1. (A) Cross-sectional dimensions of the microfabricated columns and (B) critical dimensions of the serpentine pattern.
3.2.3 Column coating

Fused silica capillaries (100-μm i.d. × 310-μm o.d.) were glued with Hysol 1C epoxy (Henkel, Rocky Hill, CT, USA) into the inlet and outlet ports of the column as transfer lines. Initial attempts for coating the column using the static method were performed by filling the column with coating solution using pressurized helium, sealing one end of the transfer line with a
septum, and evaporating the solvent under vacuum. The evaporation step failed in early attempts due to cavitation of the coating solution at the joint of the transfer line and the column. When the coating solution was pressurized, the solubility of helium in the pentane solution increased, which formed bubbles when the diameter of the flow path changed abruptly (from transfer line to micro-channel). To avoid cavitation, the solution was degassed under low vacuum, loaded into a gastight syringe, and filled into the column using a syringe pump. No cavitation was observed and evaporation under vacuum was finished within one hour. The stationary phase solution was prepared by mixing 0.2 g of silicone SE-54 (5% diphenyl-94% dimethyl-1% vinyl siloxane), 0.002 g of dicumyl peroxide and 3.8 g of pentane. The column was static-coated and heated to 200 °C at 2 °C/min and held at 200 °C for 15 h to carry out the crosslinking reaction. The calculated film thickness of the stationary phase was ~1 μm.

### 3.2.4 Instrumental set-up

An Agilent model 6890A gas chromatograph equipped with split/splitless injector and flame ionization detector (Agilent Technologies, Santa Clara, CA, USA) was used for sample injection and data acquisition. The injector and detector were kept at 250 °C and 260 °C, respectively. The column transfer lines were connected to the injector and detector and heated to 200 °C using insulated heating wire (Pelican Wire, Naples, FL, USA). The column head pressure was maintained at 20 psi (~0.5 mL/min helium flow). For isothermal and temperature-programmed heating, a 1-in. by 4-in. silicone rubber heater (Omega Engineering, Stamford, CT, USA) was placed under the bottom of the microchip to uniformly heat the entire column. For thermal gradient heating, two cartridge heaters (Tempco, Wood Dale, IL, USA) were clamped to
the inlet end of the microchip. A negative temperature gradient was formed on the column when
the inlet end was heated and the outlet end was cooled with air flow simultaneously. The
temperatures of the column, transfer lines and heaters were measured using thermocouple
probes. An infrared camera (FLIR, Wilsonville, OR, USA) with 320 × 240 imaging resolution
was used for capturing temperature profiles along the entire column. A home-made LabVIEW
program was used for temperature monitoring and heating /cooling control.

3.3 RESULTS AND DISCUSSION

3.3.1 Temperature profile along the column

Although many recent μGC devices used silicon wafers as etching substrates and Pyrex
wafers as sealing material,10,16,38-39 the large difference in thermal conductivity between these
two materials (150 W·m⁻¹·K⁻¹ for silicon and 1 W·m⁻¹·K⁻¹ for Pyrex glass) would create different
temperature profiles on the opposite sides of the channel and interfere with any TGGC
separations. As a result, an all-silicon design was selected for column fabrication. There were
three steps involved in gradient heating during a separation. First, the column was at room
temperature (~25 °C) during injections. Then, the inlet end of the column was rapidly heated to
180 °C while the outlet end was cooled by air flow; analytes were separated and focused in this
step. After the inlet end reached 180 °C, the cooling air was turned off and the outlet end was
raised by heat conduction to ~140 °C; analytes were eluted during this step. The column was
never heated to above 180 °C due to the temperature limit of the epoxy that secured the transfer
lines. Figure 3.3 shows temperature profiles for a 1.4-m column during the three heating steps.
Figure 3.3. Temperature profiles for a 1.4-m column during thermal gradient heating. (A) Isothermal step, (B) gradient step, and (C) sweeping step.
Because the serpentine pattern contained many parallel segments, the temperature profile consisted of isothermal steps at decreasing temperatures. Theoretically, the step-wise gradient should maintain its focusing effect, because any analyte traveling through the isothermal steps would always experience a negative gradient at each 180° turn, reinforcing the focusing; the following experimental results verified this.

3.3.2 Column efficiency

Due to its simplicity, the dynamic coating method (i.e., coating the column by pushing a plug of concentrated stationary phase solution through the column at a specific velocity) was first evaluated for column coating. The resulting column efficiencies were always \( \sim 2500 \) plates/m, indicating significant non-uniformity in film thickness along the channel. The static coating method increased the efficiency to \( \sim 6300 \) plates/m after the cavitation problem was resolved. Figure 3.4 shows a van Deemter plot for a 1.4-m column. Plate height values were calculated for split injections of n-tridecane with column head pressures ranging from 7.5 psi to 30.0 psi. A high optimum velocity value resulted from the small column cross section. The steep slope of the curve at high velocity indicates a large increase in resistance to mass transfer, which was due to the relatively thick film (\( \sim 1 \) μm).

Figure 3.5 shows an isothermal separation and a temperature-programmed separation of the D3710 hydrocarbon mixture on the 1.4-m column. In the isothermal separation, 8 peaks were resolved from a total of 19 components, and the peak capacity was 57 between p-xylene (peak 12) and n-pentadecane (peak 19) within a time window of 3.3 min. In the temperature-programmed separation, 16 peaks were well resolved from each other. The other three
compounds were engulfed by the huge solvent peaks (hexanes), and are not clearly visible in the chromatogram. The peak capacity was 125 between n-propane (peak 1) and n-pentadecane (peak 19) within a time window of 5.3 min. All resolved peaks showed good peak symmetry, indicating no significant dead volume or poor coating inside the flow path. The column efficiency and peak capacity data for the two chromatograms are listed in Tables 3.1 and 3.2. These results are comparable to the performance of previously reported μGC columns which were static-coated.6,8,38

3.3.3 Focusing of wide injection bands

To characterize the focusing of a wide injection band, a 1.4-m column was operated in both TGGC and TPGC modes. Two split injections were made sequentially for each run. The
Figure 3.5. Separations of a hydrocarbon mixture (250 ppm each in hexanes) under (A) isothermal (120 °C) and (B) temperature-programmed (held at 40 °C for 1 min and ramped to 180 °C at 40 °C/min) conditions. Injection volume was 1 μL at 500:1 split ratio. Peak identifications: (1) n-propane, (2) 2-methylpropane, (3) n-butane, (4) 2-methylbutane, (5) n-pentane, (6) 2-methylpentane, (7) n-hexane, (8) 2,4-dimethylpentane, (9) n-heptane, (10) toluene, (11) n-octane, (12) p-xylene, (13) n-propylbenzene, (14) n-decane, (15) n-butylbenzene, (16) n-dodecane, (17) n-tridecane, (18) n-tetradecane, and (19) n-pentadecane.
Table 3.1. Retention times, peak widths, plate numbers and cumulative peak capacities for the isothermal separation shown in Figure 3.5.

<table>
<thead>
<tr>
<th>Peak</th>
<th>Retention time (min)</th>
<th>Peak width at half height (min)</th>
<th>Plate number</th>
<th>Cumulative peak capacity</th>
</tr>
</thead>
<tbody>
<tr>
<td>p-Xylene</td>
<td>0.178</td>
<td>0.008</td>
<td>2745</td>
<td>0</td>
</tr>
<tr>
<td>n-Propylbenzene</td>
<td>0.241</td>
<td>0.009</td>
<td>3976</td>
<td>3.4</td>
</tr>
<tr>
<td>n-Decane</td>
<td>0.271</td>
<td>0.010</td>
<td>4072</td>
<td>5.2</td>
</tr>
<tr>
<td>n-Butylbenzene</td>
<td>0.367</td>
<td>0.012</td>
<td>5186</td>
<td>10.4</td>
</tr>
<tr>
<td>n-Dodecane</td>
<td>0.692</td>
<td>0.020</td>
<td>6638</td>
<td>22.3</td>
</tr>
<tr>
<td>n-Tridecane</td>
<td>1.169</td>
<td>0.032</td>
<td>7400</td>
<td>33.1</td>
</tr>
<tr>
<td>n-Tetradecane</td>
<td>2.014</td>
<td>0.050</td>
<td>8997</td>
<td>45.2</td>
</tr>
<tr>
<td>n-Pentadecane</td>
<td>3.506</td>
<td>0.090</td>
<td>8415</td>
<td>57.8</td>
</tr>
</tbody>
</table>

The first injection was used to represent the beginning of a wide injection band, and the second one represented the end of the band. The time interval between the two injections marked the width of the sample band. The heating rate was adjusted so that the retention times obtained from the TGGC mode matched those from the TPGC mode. Figure 3.6A demonstrates the focusing of the wide injection band under TGGC conditions. The first injection was made when the gradient started to form on the column, while the second injection was made 15 s later when the front of the column was at approximately 125 °C. The injection band was gradually focused along the column length instead of being focused at the front of the column, as typically occurs in TPGC. The three analytes (n-decane, n-undecane and n-dodecane) were separated and focused into only...
Table 3.2. Retention times, peak widths and cumulative peak capacities for the temperature-programmed separation shown in Figure 3.5.

<table>
<thead>
<tr>
<th>Peak</th>
<th>Retention time (min)</th>
<th>Peak width at half height (min)</th>
<th>Cumulative peak capacity</th>
</tr>
</thead>
<tbody>
<tr>
<td>n-Propane</td>
<td>0.092</td>
<td>0.003</td>
<td>0</td>
</tr>
<tr>
<td>2-Methylpropane</td>
<td>0.100</td>
<td>0.003</td>
<td>0.6</td>
</tr>
<tr>
<td>n-Butane</td>
<td>0.107</td>
<td>0.004</td>
<td>1.7</td>
</tr>
<tr>
<td>2-Methylbutane</td>
<td>0.132</td>
<td>0.006</td>
<td>4.7</td>
</tr>
<tr>
<td>n-Pentane</td>
<td>0.145</td>
<td>0.006</td>
<td>6.0</td>
</tr>
<tr>
<td>n-Heptane</td>
<td>0.481</td>
<td>0.017</td>
<td>23.2</td>
</tr>
<tr>
<td>Toluene</td>
<td>0.819</td>
<td>0.026</td>
<td>32.4</td>
</tr>
<tr>
<td>n-Octane</td>
<td>1.080</td>
<td>0.029</td>
<td>38.0</td>
</tr>
<tr>
<td>p-Xylene</td>
<td>1.707</td>
<td>0.035</td>
<td>49.5</td>
</tr>
<tr>
<td>n-Propylbenzene</td>
<td>2.485</td>
<td>0.032</td>
<td>63.2</td>
</tr>
<tr>
<td>n-Decane</td>
<td>2.861</td>
<td>0.027</td>
<td>70.7</td>
</tr>
<tr>
<td>n-Butylbenzene</td>
<td>3.198</td>
<td>0.027</td>
<td>78.1</td>
</tr>
<tr>
<td>n-Dodecane</td>
<td>3.975</td>
<td>0.025</td>
<td>95.6</td>
</tr>
<tr>
<td>n-Tridecane</td>
<td>4.442</td>
<td>0.026</td>
<td>106.4</td>
</tr>
<tr>
<td>n-Tetradecane</td>
<td>4.880</td>
<td>0.027</td>
<td>116.1</td>
</tr>
<tr>
<td>n-Pentadecane</td>
<td>5.360</td>
<td>0.034</td>
<td>125.4</td>
</tr>
</tbody>
</table>

three bands. Figure 3.6B is a temperature-programmed separation of the same sample. The first injection was made when the column started to ramp at 120 °C/min, and the second injection was
made 15 s later when the entire column was at approximately 55 °C. In the absence of a thermal gradient, the n-decane and n-undecane peaks showed splitting and broader widths, indicating insufficient injection band focusing before separation occurred. Figures 3.6C and 3.6D are temperature-programmed separations under the same conditions as 3.6B except that the temperature ramp started 5 s and 20 s after the first injection, respectively. A 5-s room temperature delay was sufficiently long to focus the n-undecane peak; however, another 15 s were required to focus the n-decane peak. For TPGC, 1.55 min were required to focus a 15-s injection band and preserve the column efficiency, while the total focusing separation time was 1.20 min for TGGC. In this case ~20% of the analysis time was saved by utilizing the focusing effect of the thermal gradient. It should be mentioned that to focus more volatile analytes, the end of the column would have to be kept at lower temperature during gradient formation. Replacing silicon with materials that have lower thermal conductivity (e.g., glass or ceramic) as column substrate may allow steeper gradients and, thus, better focusing of VOCs without extra cooling.

3.3.4 Reduction of peak tailing

A mixture containing 2-octanol, n-nonylamine, n-decylamine, 2,4,6-trichlorophenol, n-pentadecane and tributylphosphate was injected into the column to test whether or not a thermal gradient could reduce peak tailing by its focusing effect. Table 3.3 lists the tailing factors of the analytes under TPGC and TGGC conditions. Because the temperature gradient flattened in an "exponential-decay" rate, it was impossible to align the retention times of all corresponding peaks in the TPGC and TGGC chromatograms, even with column pressure modulation. If higher
Figure 3.6. Separations of n-decane, n-undecane and n-dodecane after double 1-μL injections, 15 s apart, at 500:1 split ratio. (A) TGGC separation with 400 °C/min heating rate at the front of the column, (B) TPGC separation with the column being heated right after the first injection at 120 °C/min, (C) TPGC separation with the column being heated 5 s after the first injection, and (D) TPGC separation with the column being heated 5 s after the second injection.
flow rates were used in the TPGC run to match the retention times of some peaks, the resolution would deteriorate for the TPGC run and the comparison would be unfair. Therefore, instead of trying to align all of the peaks using pressure programming, a fixed column pressure (20 psi) was used, and the heating rates were selected so that analytes eluted within the same separation time window. The tailing factor was calculated according to \( T_t = (a+b)/2a \) where \( a \) and \( b \) are the front and back half-widths at 5% of the peak height, respectively. It was observed that peak tailing was always less under TGGC conditions. For analytes with a tailing factor below 2.0, the reduction was between 5-18%. For 2,4,6-trichlorophenol, which tailed much more than the other compounds, the reduction was more than 40%. Although n-pentadecane is a non-polar compound and should not interact with surface active sites on the column, it did show some tailing under TPGC conditions, which might be a result of dead volume between the transfer lines and the column. This tailing was also partially corrected by the thermal gradient.

Figures 3.7A and 3.7B show separation of this mixture under “TPGC 1” and “TGGC 1” conditions noted in Table 3.3, respectively. The large tailing of 2,4,6-trichlorophenol (peak 4) in the TPGC separation was significantly reduced in TGGC, and the S/N was also increased by more than three-fold. The reduction in peak tailing also affected the resolution between analytes (Table 3.4). Under TGGC conditions, the resolution of the last three analyte pairs was significantly improved, while the resolution of the first two pairs was slightly decreased or increased. The differences in resolution changes can be explained by the temperature dependency of the partition coefficients for different analytes. On the one hand, intermolecular interactions between alcohols/amines and the diphenyl/dimethyl siloxane phase are relatively weak. Therefore, partition coefficients of these analytes have low temperature dependency, which reduces the focusing effect of a temperature gradient. As a result, the separation of 2-
octanol, n-nonylamine and n-decylamine was not improved. On the other hand, the phenyl and methyl groups interact strongly with 2,4,6-trichlorophenol, n-pentadecane and tributylphosphate and, thus, lead to a high temperature dependency of partition coefficients for the three analytes and enhanced focusing in TGGC. These results suggest that by incorporating thermal gradient heating and matching the target analytes with a proper stationary phase (i.e., amplifying the intermolecular interactions), peak symmetry, S/N and resolution can be improved on μGC devices, which in turn would greatly benefit trace analysis and identification of unknowns.

Table 3.3. Comparison of tailing factors between TPGC and TGGC separations of a mixture containing polar and non-polar analytes.

<table>
<thead>
<tr>
<th>Chemical</th>
<th>TPGC 1&lt;sup&gt;a&lt;/sup&gt;</th>
<th>TGGC 1&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Tailing reduction</th>
<th>TPGC 2&lt;sup&gt;a&lt;/sup&gt;</th>
<th>TGGC 2&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Tailing reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-Octanol</td>
<td>1.29</td>
<td>1.22</td>
<td>5.4%</td>
<td>1.29</td>
<td>1.14</td>
<td>11.6%</td>
</tr>
<tr>
<td>n-Nonylamine</td>
<td>1.85</td>
<td>1.55</td>
<td>16.2%</td>
<td>1.67</td>
<td>1.40</td>
<td>16.2%</td>
</tr>
<tr>
<td>n-Decylamine</td>
<td>1.78</td>
<td>1.47</td>
<td>17.4%</td>
<td>1.58</td>
<td>1.41</td>
<td>10.8%</td>
</tr>
<tr>
<td>2,4,6-Trichlorophenol</td>
<td>3.36</td>
<td>1.55</td>
<td>53.9%</td>
<td>2.74</td>
<td>1.63</td>
<td>40.5%</td>
</tr>
<tr>
<td>n-Pentadecane</td>
<td>1.29</td>
<td>1.17</td>
<td>9.3%</td>
<td>1.29</td>
<td>1.12</td>
<td>13.2%</td>
</tr>
<tr>
<td>Tributylphosphate</td>
<td>1.42</td>
<td>1.18</td>
<td>17.0%</td>
<td>1.56</td>
<td>1.28</td>
<td>17.9%</td>
</tr>
</tbody>
</table>

<sup>a</sup>Heating rate was 160 °C/min for TPGC 1 and 110 °C/min for TPGC 2.

<sup>b</sup>Heating rate was 600 °C/min for TGGC 1 and 300 °C/min for TGGC 2, measured at the front of the column.
Figure 3.7. Separations of a mixture containing polar analytes (250 ppm each in methanol) with 1-μL injection at 500:1 split ratio. (A) TPGC separation at 160 °C/min and (B) TGGC separation at 600 °C/min. Peak identifications: (1) 2-octanol, (2) n-nonylamine, (3) n-decylamine, (4) 2,4,6-trichlorophenol, (5) n-pentadecane, and (6) tributylphosphate.

3.3.5 Effect on peak fronting (overloading)

Liquid samples containing high concentration of alkanes were injected into the μGC column to create overloading and peak fronting. Table 3.5 lists peak asymmetry factors for the
Table 3.4. Comparison of resolution calculated from separations under TPGC and TGGC conditions shown in Figure 3.7.

<table>
<thead>
<tr>
<th>Analyte pair</th>
<th>TPGC resolution</th>
<th>TGGC resolution</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-Octanol/n-nonylamine</td>
<td>8.7</td>
<td>8.0</td>
<td>−8.0%</td>
</tr>
<tr>
<td>n-Nonylamine/n-decylamine</td>
<td>4.9</td>
<td>5.0</td>
<td>+2.0%</td>
</tr>
<tr>
<td>n-Decylamine/2,4,6-trichlorophenol</td>
<td>3.4</td>
<td>5.0</td>
<td>+47.1%</td>
</tr>
<tr>
<td>2,4,6-Trichlorophenol/n-pentadecane</td>
<td>4.3</td>
<td>7.0</td>
<td>+62.8%</td>
</tr>
<tr>
<td>n-Pentadecane/tributylphosphate</td>
<td>7.8</td>
<td>10.2</td>
<td>+30.8%</td>
</tr>
</tbody>
</table>

three alkanes under TPGC and TGGC conditions. Although TGGC demonstrated a noticeable focusing effect on analytes with severe tailing, it only slightly improved the peak symmetry when the column was severely overloaded (>100 ng analyte). No resolution increase was observed except for the 750-ng injections. These results can be explained by reduced retention of analytes in a saturated stationary phase, since there is no longer any available space in the polymer. As a result, the focusing effect is limited to non-saturated regions, and thus only works for a small portion of the fronting peak.

3.3.6 Improvement in peak capacity

Evaluations of peak capacity under TPGC and TGGC conditions were performed by injecting 0.5 μL of D3710 solution into the column with a 500:1 split ratio. The high split ratio produced a narrow initial sample band (200–300 ms in temporal width) and eliminated any injection effects on the separation. Because all analytes in the sample were non-polar, band
Table 3.5. Peak asymmetry factors from separations with overloaded sample components.

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Injection amount$^a$ (ng)</th>
<th>Peak asymmetry factor for TPGC$^b$</th>
<th>Peak asymmetry factor for TGGC$^b$</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>n-Decane</td>
<td>750</td>
<td>3.83</td>
<td>2.74</td>
<td>−28.5%</td>
</tr>
<tr>
<td></td>
<td>300</td>
<td>2.18</td>
<td>1.92</td>
<td>−11.9%</td>
</tr>
<tr>
<td></td>
<td>150</td>
<td>1.60</td>
<td>1.40</td>
<td>−12.5%</td>
</tr>
<tr>
<td></td>
<td>75</td>
<td>1.21</td>
<td>1.12</td>
<td>−7.4%</td>
</tr>
<tr>
<td></td>
<td>30</td>
<td>1.02</td>
<td>1.00</td>
<td>−2.0%</td>
</tr>
<tr>
<td>n-Undecane</td>
<td>750</td>
<td>4.25</td>
<td>3.24</td>
<td>−23.8%</td>
</tr>
<tr>
<td></td>
<td>300</td>
<td>2.42</td>
<td>2.17</td>
<td>−10.3%</td>
</tr>
<tr>
<td></td>
<td>150</td>
<td>1.80</td>
<td>1.53</td>
<td>−15.0%</td>
</tr>
<tr>
<td></td>
<td>75</td>
<td>1.29</td>
<td>1.21</td>
<td>−6.2%</td>
</tr>
<tr>
<td></td>
<td>30</td>
<td>1.02</td>
<td>1.01</td>
<td>−1.0%</td>
</tr>
<tr>
<td>n-Dodecane</td>
<td>750</td>
<td>4.79</td>
<td>3.71</td>
<td>−22.5%</td>
</tr>
<tr>
<td></td>
<td>300</td>
<td>2.72</td>
<td>2.44</td>
<td>−10.3%</td>
</tr>
<tr>
<td></td>
<td>150</td>
<td>1.90</td>
<td>1.66</td>
<td>−12.6%</td>
</tr>
<tr>
<td></td>
<td>75</td>
<td>1.37</td>
<td>1.32</td>
<td>−3.6%</td>
</tr>
<tr>
<td></td>
<td>30</td>
<td>1.03</td>
<td>1.08</td>
<td>+4.9%</td>
</tr>
</tbody>
</table>

$^a$Splitless injection.

$^b$Heating rates were 140 °C/min for TPGC and 450 °C/min for TGGC at the front of the column.

Broadening mostly resulted from non-uniformities in stationary phase film thickness and transfer line dead volumes. Table 3.6 compares peak capacity values calculated from three sets of TPGC and TGGC separations. Under equivalent conditions, the thermal gradient improved the peak capacity by 8–10%. This improvement might be limited by the gradient profile generated by the single heater design. On the one hand, when the thermal gradient formed, the temperature was above 80 °C along the first half of the column length and dropped below 80 °C along the
following half, which means that volatile analytes were most likely becoming focused and separated on the last 50–100 cm of the column. In other words, the front portion of the column was “wasted” for early eluting compounds. On the other hand, when the thermal gradient was swept, the gradient slope became much shallower and reduced the focusing effect on later eluting analytes as they were traveling towards the end of the column. One may solve this problem by using an ideal gradient profile with a steep slope on the first 20–30 cm of the column, which would correct band broadening from injection and dead volume, and a less steep one along the remaining length, which would still provide sufficient focusing for the analytes. Such a profile requires materials with a thermal conductivity lower than Si, more durable high-temperature adhesives for transfer line connection, and multiple heaters on the column, which were not explored in this work.

Table 3.6. Peak capacities calculated from TPGC and TGGC separations of a hydrocarbon mixture.

<table>
<thead>
<tr>
<th>Separation time window (min)</th>
<th>TPGC peak capacity</th>
<th>TGGC peak capacity</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.5</td>
<td>72.9</td>
<td>78.7</td>
<td>+8.0%</td>
</tr>
<tr>
<td>2.1</td>
<td>69.5</td>
<td>76.8</td>
<td>+10.5%</td>
</tr>
<tr>
<td>1.8</td>
<td>67.2</td>
<td>73.7</td>
<td>+9.6%</td>
</tr>
</tbody>
</table>

3.3.7 Column performance evaluation

The silicone heater used for the TPGC runs had a 40-W output, and the maximum heating rate was 300 °C/min. The two cartridge heaters used for the TGGC runs had a combined wattage of 120 W, and could heat the front of the column at >600 °C/min. Figure 3.8 shows a curve of
temperature vs. time for the silicone heater and the cartridge heaters at high heating rates. Since high power consumption is not desirable for portable instruments, this can be significantly reduced by replacing the external heaters with patterned metal heaters. The mass of the column can also be further reduced by using a thinner (e.g., 300-μm) wafer for bonding. A 20-W power output should be sufficient for TGGC runs with reduced wafer/heater thickness.

Figure 3.8. Column temperature curves for the silicone heater and cartridge heaters. Power input: 96 V AC.

Compared to commercial non-polar fused-silica capillary columns, which are typically stable up to 350 °C, the working temperature of the microcolumns in this work was limited by the epoxy used for securing the transfer lines. A higher baseline was observed when the column temperature was higher than 200 °C, which indicates off-gassing and degradation of the epoxy. It
is also likely that analyte-epoxy interactions created peak tailing and band broadening. While other types of high-temperature epoxies were able to withstand 250 °C, cracking occurred after repetitive heating and cooling. Nevertheless, the columns were stable below 200 °C. Approximately 200–300 injections were performed on a single microcolumn, and no significant change in separation was observed.

Under high split flow, solvent injections and vapor injections produced very similar results. In either TPGC or TGGC, the solvent was separated from the analytes in the first few seconds, as long as there was no highly-volatile analyte. Although vapor injections eliminated the huge solvent peak, the vapor levels for each component in the sample vial slowly changed with time and led to variation in the injection amount. Therefore, solvent injections were performed for all runs to generate reproducible chromatographic peaks. TGGC should be particularly useful for splitless thermal-desorption injections, which are often used in µGC.

The trapezoidal cross-section led to pooling of the stationary phase and reduction of the column efficiency. The two sharper corners at the top are expected to create more pooling than the two bottom corners. A rectangular cross-section may give higher efficiency, because the pooling would be evenly distributed in the four corners. It would be beneficial to use SEM to characterize the pooling in columns with rectangular and trapezoidal cross-sections under different coating conditions, and relate the image data with chromatographic results. It is worth noting that with conventional coating techniques, the pooling problem will always exist for microcolumns, unless the cross-sectional profile is circular. Alternative thin-film deposition methods (e.g., chemical vapor deposition\textsuperscript{40} and self-assembled monolayer\textsuperscript{41}) have the potential to mitigate the pooling problem for a non-circular channel.
3.4 CONCLUSIONS

The results of this study suggest that TGGC can enhance the separation performance of μGC columns and provide better resolution and quantitation for μGC applications. Compared to TPGC, TGGC can focus wide injection bands without adding extra time to the analysis. Peak tailing resulting from interaction between polar analytes and surface active sites were also reduced by the focusing effect. Under TGGC conditions, increases in resolution and peak capacity were observed for separations of analytes that have strong intermolecular interactions with the stationary phase.

3.5 REFERENCES

4 DYNAMIC MICROCHIP THERMAL GRADIENT GAS CHROMATOGRAPHY

4.1 INTRODUCTION

In the early days of GC, separations were performed at constant column temperature, which is known as isothermal GC (ITGC). Although it was simple to maintain isothermal conditions along the column, separation of mixtures containing analytes with a wide range of volatilities was problematic: low temperatures are required to prevent coelution of volatile analytes, while higher temperatures are necessary to shorten the elution time of less volatile analytes. The so-called “general elution problem” in GC was solved by gradually heating the column at controlled rates, known as temperature-programmed GC (TPGC). The development of TPGC was driven by the advancement of heating technologies including air convection heating and resistive heating. Today, TPGC is the major operating mode for most GC analyses.

Although reported as early as 1951 and named chromathermography,1 the third type of GC operation, TGGC, is much less known. The concept of TGGC is that column temperature can be varied along the column length as well as in time.2 Figure 4.1 demonstrates that the temperature is fixed in ITGC, programmed along a time axis in TPGC, and manipulated along both time axis and column length axis in TGGC. One would expect that TGGC should provide extra flexibility for any GC separation. Indeed, for the last sixty years, researchers have been experimenting with different heating techniques, including moving oven,1 heating tape,3 heat exchanger,4-8 conductive paint,9 resistive heating coil,10 disk heater,11 and heating wire,12 to characterize the separation features of TGGC. The major separation behavior of a negative (lower column temperature towards the detector end) thermal gradient is its focusing effect on a
migrating solute band. As shown in Figure 4.2, the reduction in peak width results from the temperature dependency of partition coefficient of an analyte between the mobile and stationary phases. Although gradient focusing has been characterized and utilized in several other separation techniques analogous to TGGC, most instrumentation designs are limited in controlling temperature profiles along the column due to the lack of heating control for individual sections. As a result, the potential of TGGC has not been fully realized.

**Figure 4.1.** Examples 3-D temperature profiles for ITGC, TPGC and TGGC.

In 2013, Contreras et al. reported a dynamic TGGC instrument with 40 individually controlled low-thermal-mass resistive heaters that could be programmed to generate moving
axial temperature gradients with custom profiles. This work demonstrated some unique aspects of dynamic TGGC, including applicability to continuous sampling, independent control of peak width, and efficient management of the separation space using nonlinear gradients. Although the results indicated unmatched separation flexibility of dynamic TGGC when compared with TPGC, a fundamental limitation of TGGC still remains: given a fixed separation time and column length, the resolution of a closely eluting analyte pair cannot be improved by gradient focusing over TPGC under ideal conditions. Calculations by Blumberg suggested that while an axial gradient focuses a solute band, it also shortens the distance between adjacent peaks in the same linear gradient, which counteracts the peak width reduction and leads to no increase in resolution. Therefore, the development of new dynamic TGGC techniques for open-tubular columns has reached a conundrum: on the one hand, resolution or speed of analysis from current commercial GC systems generally cannot be significantly improved by TGGC and, on the other hand, realization of flexible separation control, as suggested by Contreras et al., requires individual heaters along the column and, thus, much more complexity if a long column is desired.

Figure 4.2. Mechanism of gradient focusing in TGGC.
Fortunately, microchip GC columns based on a variety of materials, including silicon,\textsuperscript{17-18} glass,\textsuperscript{19} polymers,\textsuperscript{20} metal\textsuperscript{21} and ceramic,\textsuperscript{22-23} have been fabricated and characterized for a variety of GC applications. Since creating a thermal gradient on a planar substrate is simpler than on an elongated thin tube, dynamic TGGC is much more appealing for planar columns. Moreover, defects (e.g., stationary phase pooling and active sites) present in planar columns create band broadening and peak asymmetry, which are difficult or even impossible to eliminate. Gradient focusing is ideal for mitigating these problems and bridging the performance gap between planar columns and open-tubular columns. Incorporation of dynamic TGGC into planar columns would be beneficial for both high-resolution separations on benchtop systems as well as fast on-site chemical analysis performed by \(\mu\)GC devices.

This chapter demonstrates the use of dynamic TGGC on a silicon-based microcolumn. Different from the method described in Chapter 3, in which a steep, static gradient was followed by bringing the column temperature up to a constant value, a shallow temperature gradient was created and maintained during temperature programming and separation. The effect of the gradient profile is critically discussed.

4.2 THEORETICAL CONSIDERATIONS

4.2.1 Effect of injection bandwidth

The theoretical plate number of a column, \(N\), is defined by:

\[
N = 16 \times \left( \frac{t_R}{W_b} \right)^2
\]  

(4.1)
where $t_R$ is the retention time and $w_b$ is the peak width of a retained analyte at its base under isothermal conditions.\textsuperscript{24} Although the initial peak width of a solute band is treated as zero in most theoretical GC work, the injection width of commercial GC systems using the split injection mode is usually in the range of 0.1–1 s, which contributes to $w_b$ and reduces the plate number. Specially designed valve injections can produce an initial bandwidth as short as tens of ms by sacrificing a major portion of the injected sample.\textsuperscript{25} For splitless and thermal-desorption injections, the injection width can range from a few seconds to several minutes. Wide injection bands are usually corrected by starting the temperature program at a sufficiently low temperature until the entire sample band enters the column. During this step, no separation occurs as all analytes are retained in the front portion of the column. The experimental results from Contreras et al.\textsuperscript{8,13} and in Chapter 3 have shown that TGGC can shorten the analysis time by simultaneously focusing and separating analyte bands. When a wide sample band enters a column with a negative temperature gradient, the solutes decelerate at different rates according to the rates of increase in their retention factors and, thus, can be separated from each other. The focusing effect continues through the whole separation as long as the solute band is migrating along the gradient. The temperature span of the gradient must be sufficiently large so that the end of a long injection band can catch up with the front.

Although the spread of a peak is usually reported as temporal bandwidth, on-column bandwidth correlates with the profile of the gradient and is more useful in TGGC. The initial on-column bandwidth of a solute, $l_0$, is defined as:

$$l_0 = v_0 w_{inj}$$ \hspace{1cm} (4.2)

where $v_0$ is the migrating speed of the solute band at the initial column temperature and $w_{inj}$ is the temporal injection bandwidth. The migrating speed can be calculated by:
$$v_0 = \frac{u_0}{(k_0 + 1)}$$

(4.3)

where $k_0$ is the retention factor of the solute at the initial column temperature and $u_0$ is the carrier gas velocity at the beginning of the column. The temporal injection bandwidth can be estimated by injecting an unretained analyte (e.g., methane) into the column and measuring its elution peak width. This estimation assumes that the injected volume is the same for the solute and the unretained compound, and only applies to vapor injection. For liquid injection in the split mode, the injection bandwidth is roughly the time it takes to sweep the entire liner volume with carrier gas:

$$w_{inj} = \frac{V_l}{F_t}$$

(4.4)

where $V_l$ is the volume of the injector liner and $F_t$ is the total flow rate of the carrier gas. This formula assumes that sample evaporates instantaneously after injection, which may not be true for chemicals with low volatilities. A more applicable method is to inject the sample under both the intended and ideal injection conditions (i.e., low injection amount with high split flow) at a constant column temperature. Because the elution bandwidth is the sum of band broadening from injection, longitudinal diffusion and resistance to mass transfer, the injection bandwidth can be estimated by:

$$w_{inj} = (w_2 - w_1)$$

(4.5)

where $w_1$ and $w_2$ are the elution bandwidths under ideal and intended conditions, respectively. These formulas show that the on-column injection bandwidth is largely determined by the temporal injection width and the retention factor of the solute at the initial column temperature. When an analyte is highly retained at the beginning of the separation, the effect of temporal injection bandwidth becomes negligible, which is generally the case in TPGC separations. In
contrast, the on-column bandwidth of a solute is relatively large at the beginning of a negative gradient and reduces as the solute travels through the column. When a long injection is expected, a gradient profile that quickly reaches a sufficiently low temperature (e.g., a nonlinear negative gradient with a monotonically decreasing slope) can reduce the on-column bandwidth within a short column length and, thus, is preferred for dynamic TGGC separation.

4.2.2 Effect of gradient slope

In the work by Contreras et al., a thermal gradient with certain profile propagates along the column at a constant speed. A solute band reaches an equilibrium state, at which the speed of the solute equals the gradient speed, after a certain amount of time. The temperature dependency of the retention factor, $k$, can be expressed as:

$$\ln k = \frac{a}{T_c} + b$$

(4.6)

where $T_c$ is the column temperature and $a$ and $b$ are constants associated with the property of the solute. The speed of the solute, $v_s$, can be expressed as:

$$v_s = \frac{u}{k + 1}$$

(4.7)

where $u$ is the local carrier gas linear velocity of the mobile phase. When at equilibrium:

$$v_s = \frac{u}{k + 1} = v_G$$

(4.8)

where $v_G$ is the gradient speed. Thus, the temperature of equilibrium (i.e., the elution temperature of the solute), $T_{eq}$, can be expressed as:

$$T_{eq} = \frac{a}{\ln\left(\frac{u}{v_G} - 1\right) - b}$$

(4.9)
Obviously, $T_{eq}$ can be changed by adjusting the speed of the gradient as well as the mobile phase velocity. When a mixture is separated, each analyte is focused at its own $T_{eq}$, which corresponds to a position on the gradient. Although a steep gradient can generate narrow peaks, the corresponding $T_{eq}$ positions of each analyte are also closer on the column, leading to a decrease in peak spacing. The tradeoff between peak width and peak spacing must be carefully considered when applying TGGC to a planar microchip. An optimum slope value, which produces the highest resolution for the target analytes, may be determined from experiments.

Generally, after the equilibrium state is reached, the resolution of the focused analytes does not increase with the column length. To efficiently utilize dynamic TGGC on a long column and produce a high peak capacity, the equilibrium state should not be reached until the analyte travels to the end of the column. This requirement can be achieved by establishing a decreasing negative gradient along the column and raising the temperature while maintaining the gradient profile (Figure 4.3A). Different from a gradient that moves forward (Figure 4.3B), the slope of a moving-up gradient is fixed for a given position in the column. In this case, an equilibrium state is never reached, because the axial speed of the gradient is not constant at different positions in the column. Therefore, the resolution of a solute pair continues to increase as the solutes travel through the column, while a non-zero gradient slope still maintains some of the focusing effect to reduce band broadening due to column defects. The gradient profile in Figure 4.3A is also easier to create on a planar platform, since a single heater located at one end of the column can be used to generate the profile with heat conduction, and a large heater can be used to cover the entire column area and raise the gradient uniformly. A disadvantage of this method is that an analyte does not have a defined elution temperature, and the programming of the separation space is less explicit.
Figure 4.3. Dynamic thermal gradients that move (A) upward and (B) forward. Note the slope change for position x in (B).

4.2.3 Column design

Planar columns with either a serpentine pattern or a single spiral pattern are suitable for dynamic TGGC, as a monotonic gradient is always required. Other patterns that are often
employed in planar columns (e.g., square spiral) are usually not compatible with a monotonic profile. When a gradient is formed from a point source or line source heater, the heat flux density, \( \tilde{q} \), is determined by Fourier’s Law as:

\[
\tilde{q} = -k \nabla T
\]  

(4.10)

where \( k \) is the material’s thermal conductivity and \( \nabla T \) is the temperature gradient. If only one direction is considered, Fourier’s Law can be simplified as:

\[
q_x = -k \frac{dT}{dx}
\]  

(4.11)

where \( q_x \) is the heat flux density along the x-axis. Integrating Equation (4.11) over the total surface yields:

\[
\frac{\partial Q}{\partial t} = -k \oint \tilde{v}T \, d\tilde{A}
\]  

(4.12)

where \( \partial Q/\partial t \) is the rate of heat flow and \( d\tilde{A} \) is an oriented surface area element. In the case of a planar column, the heat flow rate through the cross section can be calculated by:

\[
\frac{\Delta Q}{\Delta t} = -kA \frac{\Delta T}{\Delta x}
\]  

(4.13)

where \( A \) is the cross-sectional area of the planar substrate, \( \Delta T \) is the temperature difference between the column ends, and \( \Delta x \) is the distance between the ends. As seen in Equation (4.13), the temperature differential on the planar column is governed by the thermal conductivity, the cross-sectional area, and the heat flow rate. The thermal conductivity can be adjusted by changing the column substrate or by adding additional material (e.g., metal plate and thermal paste) to the column surface. The cross-sectional area can be changed by selecting the thickness and width of the planar substrate. The heat flow rate can be manipulated by adjusting the heating power as well as by controlling the heat loss (e.g., adding insulation material or convection cooling). With the above measures, the desired temperature profile can be created.
4.3 EXPERIMENTAL

4.3.1 Reagents and chromatography conditions

Hexanes and n-pentane were purchased from Mallinckrodt Baker (Phillipsburg, NJ, USA); n-octane, n-nonane, n-decane and n-dodecane were purchased from Spectrum Chemical (New Brunswick, NJ, USA); dicumyl peroxide was purchased from Sigma-Aldrich (St. Louis, MO, USA); and Silicone SE-54 (catalog No. 21106) and D3710 test mixture (catalog No. 48884) were purchased from Supelco (Bellefonte, PA, USA).

An Agilent 6890A GC system (Santa Clara, CA, USA) with a split/splitless injector and a flame ionization detector was used for all chromatographic tests. Helium was used as the carrier gas at a constant column head pressure of 16 psi for all separations. The fabrication of the planar column was described in Chapter 3. A 1.4-m column was used for this experiment. The column was connected to two fused-silica capillaries with a high-temperature epoxy from Aremco (Valley Cottage, NY, USA) and dynamically coated by filling the column with a concentrated stationary phase solution (~10% w/w) and quickly pushing the solution out using helium gas at a pressure of 350 psi. All injections were made using the split mode with a split flow of 100 mL/min. For plate number measurement, a 100-μL volume of headspace vapor of the alkanes was injected into the column. For peak capacity measurement, 1-μL diluted D3710 mixture (~250 ppm in hexanes) was injected into the column. The injector and detector were kept at 250 °C and 270 °C, respectively. The Agilent Chemstation was used to acquire all chromatograms.
4.3.2 Dynamic gradient set-up

As shown in Figure 4.4A, one side of the planar column was coated with a carbon paste purchased from Ted Pella (Redding, CA, USA). The coating was done by diluting the carbon paste in water and drying the suspension on the silicon surface. The carbon coating was divided into two sections: a small section as the primary heater for creating a concave up gradient, and a larger second section as the secondary heater for heating the entire column. The paste was bonded to copper electrodes, which were connected to DC power supplies. During a separation, the power applied to the primary heater was fixed, while the power applied to the secondary heater was gradually increased to raise the entire gradient. The temperature profile across the substrate during a TGGC separation is shown in Figure 4.4B. The magnitude of the gradient was approximately constant throughout the ramping. For isothermal and temperature-programmed runs, the column was heated using a polyimide heater that covered the entire substrate.

Figure 4.4. Generation of dynamic thermal gradient on a serpentine column. (A) Layout of the carbon heaters, and (B) gradient profiles measured across the silicon substrate.
4.4 RESULTS AND DISCUSSION

4.4.1 Column performance

Dynamic coating was employed for the following experiments. The coating thickness was estimated to be ~0.3 µm. The efficiency of the 1.4-m column was ~3400 plates/m, which was 45% lower than expected for a static-coated column. Nonetheless, this plate number was comparable to other dynamically coated microcolumns reported in the literature.\textsuperscript{18,26} The peak width and retention time data from an isothermal run are listed in Table 4.1. Figure 4.5 is a TPGC separation of the D3710 mixture. Good peak symmetry and resolution were observed for the 11 peaks obtained. Eight compounds were not seen due to their low retention on the thin stationary phase coating and elution in the huge solvent peak. The column was able to withstand 250 °C without leaking or degradation. A baseline increase was noticed when the column temperature was above 200 °C, which was likely due to off-gassing of the epoxy.

<table>
<thead>
<tr>
<th>Analyte</th>
<th>t\textsubscript{R} (min)</th>
<th>w\textsubscript{h} (min)</th>
<th>Plates/m</th>
</tr>
</thead>
<tbody>
<tr>
<td>C\textsubscript{8}</td>
<td>0.339</td>
<td>0.015</td>
<td>2023</td>
</tr>
<tr>
<td>C\textsubscript{9}</td>
<td>0.64</td>
<td>0.025</td>
<td>2596</td>
</tr>
<tr>
<td>C\textsubscript{10}</td>
<td>1.319</td>
<td>0.045</td>
<td>3403</td>
</tr>
</tbody>
</table>

\textsuperscript{a}Conditions: column was maintained at 60 °C and transfer lines were maintained at 200 °C to avoid inflation of plate numbers.
Figure 4.5. Separation of a hydrocarbon mixture under TPGC conditions. Conditions: column length 1.4 m, programmed from 40 °C to 200 °C at 30 °C/min, 1 µL of D3710 mixture injected, split flow 100 mL/min. Peak identifications: (1) n-heptane, (2) toluene, (3) n-octane, (4) p-xylene, (5) propylbenzene, (6) n-decane, (7) butylbenzene, (8) n-dodecane, (9) n-tridecane, (10) n-tetradecane, and (11) n-pentadecane.

4.4.2 Dynamic TGGC separations

To evaluate the behavior of dynamic thermal gradients on separations, the column was heated at different rates while the negative decreasing gradient profile and the temperature difference between the column ends was maintained throughout the analysis. Figure 4.6 demonstrates the change in analysis time and resolution with heating rate. Generally, the temporal peak width and resolution decreased with an increase in heating rate, while the elution temperature increased with heating rate. The elution temperature for n-pentadecane (last peak in the chromatograms), measured at the end of the column, was 196 °C, 183 °C, and 175 °C for
Figure 4.6. Dynamic TGGC separations with a constant gradient profile (temperature span of 30 °C across 1.4-m length) and different ramping rates (240 °C/min, 120 °C/min and 60 °C/min). See Figure 4.5 for peak identifications.

heating rates of 240 °C/min, 120 °C/min, and 60 °C/min, respectively. The resolution between toluene and n-octane was 1.3, 1.7 and 2.1 as heating rate decreased, indicating a quadratic
tradeoff between resolution and analysis time. This separation behavior, which is similar to that commonly observed in TPGC, can be explained by the shallow profile of the gradient along the major length of the column. Despite the apparent difference in temporal peak widths, which are related to the elution temperature and the carrier gas velocity, the on-column bandwidths, which are affected by the gradient slope, were approximately unchanged for the same analyte in these chromatograms.

To examine if the dynamic gradient could increase the resolution obtained from a non-ideal column, the separation numbers (SN) of TPGC and TGGC runs under equivalent conditions (i.e., same separation window) were compared. The chromatograms are shown in Figure 4.7. It was found that while all the resolved analytes have similar retention times, peaks produced from dynamic gradient heating are slightly narrower than those from TPGC, which resulted in a 3.7% increase in the cumulative separation number. When comparing the resolution change pair by pair, the first three analytes (C7, toluene and C8) were less resolved, while the other eight analytes were more resolved in TGGC, which was likely due to the higher initial temperature of the gradient (30 °C higher than TPGC). The insignificant improvement may be attributed to the magnitude of the gradient, which was only 30 °C along the 1.4-m column (~0.2 °C/cm). This shallow slope may not provide adequate focusing to reduce the peak broadening from dead volumes and pooling of the stationary phase. In this experiment, the temperature difference across the gradient was limited by the length (6.5 cm) and thickness (2 mm) of the Si substrate. To create gradients with steeper slopes, thinner wafers (e.g., 500 μm) are needed. Another factor limiting the focusing effect is the width of the carbon heaters, which was the same as the width of the serpentine segments. Because the edge of the column received less heat than the center, the temperature was raised by ~0.5−1 °C when a solute band moved
from the edge to the center in an individual column segment. This created a locally positive gradient, as shown in Figure 4.8, on every parallel segment. In contrast to a negative gradient, a positive gradient increases the on-column peak width as well as amplifies band broadening from the column defects. This “edge effect” can be corrected by increasing the distance between the column bends and the edge, adding thermal breaks (i.e., cut-through trenches) between the primary heater and the serpentine column, and replacing the secondary heater with a thin-layer ceramic/mica heater.

Figure 4.7. Comparison of peak capacities produced from TGGC and TPGC conditions. Conditions: column heated from 55 °C to 200 °C at 130 °C/min in TPGC and from 70 °C/40°C to 230 °C/200 °C at 130 °C/min in TGGC.
4.5 CONCLUSIONS

Initial on-column bandwidth, temperature profile and moving direction of a thermal gradient were shown to affect peak resolution. Dynamic thermal gradients were created on a serpentine column using a simple set-up. A shallow, negative decreasing temperature profile demonstrated separation behavior similar to those in TPGC. The peak capacity was slightly improved by the focusing effect of the dynamic gradient. Further optimization of the temperature profile, including elimination of the edge effect and increasing the slope, is necessary to achieve better separation performance.
4.6 REFERENCES

5 CONCLUSIONS AND FUTURE WORK

5.1 CONCLUSIONS

5.1.1 Resistively heated GC columns

A new resistive heating method based on metal columns and insulated heating wire was developed and tested. To construct the column assembly, a 100-μm i.d. stainless steel column was coiled to a torus and wound with thin electrically insulated Nichrome wires before being thermally insulated with fiberglass and aluminum foil. The construction process was simple and straightforward. Separations with oven heating and resistive heating were compared; the results demonstrated negligible losses in column efficiency and separation number for isothermal and temperature-programmed runs, respectively. Retention time reproducibility with resistive heating was slightly worse than with oven heating due to temperature non-uniformities in the column assembly, but still acceptable for peak identification purpose. Because of the low thermal mass, a 5-m column bundle could be heated at 500 °C/min, which was at least 10 times faster than with oven heating, and cooled from 350 °C to 25 °C in 1.5 min, while only consuming 1–5% of the power that a conventional oven would use. Because of its fast cycle time, the throughput of routine GC analysis can be increased by several fold when compared with oven heating. Overall, this method has great potential to replace conventional airbath ovens in GC instruments. It is clearly more suitable for portable GC and GC/MS systems, which usually have size and power limitations.
5.1.2 Thermal gradients in μGC

Microcolumns formed in a serpentine design were fabricated on Si wafers by using laser drilling, wet chemical etching and Si-Si fusion bonding. Columns were successfully coated with a siloxane-based stationary phase by either static or dynamic methods. A static thermal gradient was generated in a microcolumn by heating one end with resistive heaters and cooling the other end with air flow. The gradient was then swept by pausing the cooling air. With static gradient heating, a wide injection was focused into narrow sample bands without an initial low initial temperature step, which is required in TPGC for injection focusing. As a result, the analysis time was shortened by ~20%. The focusing effect of the static gradient also enhanced the S/N, reduced peak tailing for polar analytes, and increased the resolution for analytes that interact strongly with the stationary phase. Under equivalent separation conditions, peak capacity was also improved with a static gradient. A dynamic gradient with a shallow slope was generated by heating one end of the column and raising the gradient with a secondary heater. The dynamic gradient slightly improved the separation number when compared with TPGC.

These results suggest that TGGC is an appealing technique for microchip GC. On the one hand, band broadening and peak shape distortion from various defects in the microcolumn can be reduced or eliminated by incorporation of gradient heating. On the other hand, a thermal gradient can be readily created on a planar column without the use of multiple heating sections and independent controllers. The slope and speed of the gradient have critical effects on the separation performance and, thus, should be adjusted according to the properties of the sample (e.g., volatility and polarity). Further optimization in column fabrication and heating set-up is needed for bridging the performance gap between μGC and conventional GC.
5.2 RECOMMENDATIONS FOR FUTURE WORK

5.2.1 Resistively heated column assembly

The resistively heated column assembly described in Chapter 2 can be easily integrated into a portable GC or GC/MS system. The transfer lines can be eliminated in a portable system if the two interfaces are properly positioned with respect to the column bundle. Although only a 100-μm i.d. stainless-steel column was tested, columns with larger diameters (e.g., 180 μm and 250 μm) are expected to be compatible with this method. It will be useful to test the power consumption and efficiency loss of these columns, which may vary slightly from the 100-μm i.d. column due to differences in mass and wall thickness. Column heating can be further improved by using pulse-width modulation (PWM) instead of a DC voltage amplifier to control the input heating power. Heating power input from PWM prevents the formation of local hot spots where the heating wire may be more densely coiled. The thermocouple used for temperature sensing can be replaced by a miniaturized RTD to provide higher accuracy and lower drift for long-term use. An alternative option would be using insulated pure nickel wire as heating source and RTD simultaneously. Eliminating the separate sensors would create a more uniform temperature distribution on the column and, thus, preserve more theoretical plates and peak capacity.

5.2.2 High-temperature transfer line connections

The Hysol 1C epoxy used for gluing capillaries to the microcolumn has a maximum working temperature of 200 °C and, thus, limits the thermal gradient profile along the chip. The
Aremco epoxy can withstand temperatures up to 250 °C, but often cracks after repeated thermal cycles. In fact, most microcolumns reported in the literature were operated below 250 °C, above which many commercial epoxies degrade. Gaddes et al.\textsuperscript{1} expanded the working temperature range of their microcolumns up to 450 °C by using a metal manifold to support traditional column nuts and ferrules. However, this method cannot be employed in micro-TGGC (μTGGC) due to the excessive thermal mass of the external fittings. To fully appreciate the separation power of TGGC on microcolumns, an adhesive with good adhesion to silicon/silica materials, high working temperatures (>300 °C), low curing temperatures (<350 °C) and proper mechanical properties (high viscosity and low shrinkage/expansion) is required.

A possible solution would be to use SiO\textsubscript{2}-based inorganic adhesives, which have maximum working temperatures above 1000 °C, on a Pyrex glass-silicon microcolumn with inlet/outlet holes through the Pyrex glass (Figure 5.1A). The glass top plate should be thin enough to avoid interference with the gradient profile. Another option is to use small metal fittings that are bonded to the silicon wafer for capillary connections (Figure 5.1B). Depending on the contact area of the fittings, the temperature profile could be slightly affected. It is also important to eliminate any dead volume at the connection to allow good static coating. This could be achieved by adjusting the diameter of the laser-drilled holes to match the capillary.

![Figure 5.1](image_url)

**Figure 5.1.** Connecting transfer lines using (A) inorganic adhesive and (B) metal fitting.
5.2.3 Dynamic TGGC with a steep slope

Chapter 4 showed that a shallow gradient profile could not provide sufficient focusing to significantly improve the resolution. Therefore, a large temperature difference across the chip is required to achieve better separation. If a 4-in, 525-µm-thick standard Si wafer is etched and bonded to a thinner wafer (300–400 µm in thickness), the total thickness would be less than 50% of the current column and, thus, should be able to generate a gradient with larger temperature difference. In this case, deeply etched channel outlets would be necessary for secured transfer line connection from the edge. The carbon paste heaters could be replaced by patterned metal heaters, which have lower thermal mass and more uniform layer thickness. The cold end of the column could be attached to a Peltier device, which would further enlarge the gradient slope. The heating and cooling power could be adjusted synchronously so that the desired gradient profile is maintained throughout a separation. Thermal modeling and imaging would be useful for determining the proper column width and eliminating the edge effect from the heater.

5.2.4 Dynamic TGGC in a spiral column

Thermal gradient profiles in a serpentine column, as described in Chapters 2 and 3, consist of a number of isothermal steps. When a solute band travels within an isothermal step along the gradient, it is not subject to any focusing effect until it reaches the next column turn. Thus, the resolution enhancement from the gradient may not be fully achieved. A better approach may be to construct a µTGGC with a smooth temperature profile, and compare the separation performance with previous results. A microcolumn constructed on a round wafer, starting from
the center and spiraling out to the edge, can be employed for this purpose. Preliminary work indicated the shapes of temperature profiles across the diameter of several circular substrates when the center was heated. As shown in Figure 5.2, a silicon wafer gave a shallow thermal gradient due to its high thermal conductivity, while a quartz wafer produced a much steeper slope. By combining the quartz wafer with a steel plate, a moderate gradient slope was created so that the temperature did not drop too fast within the first 10 mm from the center. Figure 5.3A shows a spiral pattern that can be used for generating a smooth gradient profile. The pattern was defined by a modified Archimedean spiral equation \( r = a + b\theta \). Figure 5.3B plots the calculated temperature profiles along 3-m-long spiral columns made from the three substrates in Figure 5.2. A ring heater clamped to the spiral column could raise the gradient to elute the analytes.

### 5.2.5 Mathematical model for TGGC in planar columns

The work by Tolley et al.\(^2\) established a mathematical model that predicts the effect of a moving thermal gradient on solute bandwidth in an open-tubular column. This model can be further expanded to apply to planar columns where column defects are more prevalent. Experimental results from the previous proposed work could be used to validate the model, which in turn could help to optimize the gradient heating.

### 5.2.6 Characterization of the stationary phase coating in microchannels

Scanning electron microscopy (SEM) has been used to characterize stationary phase layers made of polymer,\(^3\) nanoparticles,\(^4\) and carbon nanotubes\(^5\). However, little information is
Figure 5.2. Thermal images of (A) 4-in, 1.5-mm-thick bonded Si wafer pair, (B) 4-in, 0.5-mm-thick quartz wafer, and (C) 4-in, 0.5-mm-thick quartz wafer on 4-in, 0.7-mm-thick steel plate when heated from the center. The temperature along the center line was plotted for each thermal image.
available about SEM characterization of conventional siloxane coatings on microcolumns. Therefore, using SEM to image siloxane-based column coatings would help to reveal the effect of column cross-sectional geometry on variation in thickness of the stationary phase. Separation performance from columns with different cross-sections (e.g., semi-circular, rectangular and trapezoidal) could be compared and related to the SEM data.

5.2.7 TGGC in a semi-packed microcolumn

Due to size limitations, μGC columns are usually 0.5−5 m in length, and generally do not produce more than 50,000 plates. Theoretically, packed columns can generate much higher plate numbers per meter. Table 5.1 lists the maximum theoretical plate numbers per meter for open-tubular and packed columns. If the particle diameter is small enough, a packed column is more
efficient than an open-tubular column and should be preferred for μGC systems. However, pneumatic resistance of a packed bed is much higher than an open tube, thus, making packed columns not practical for instruments with regular injectors. Recently, researchers have been developing semi-packed microcolumns for on-site GC applications.\textsuperscript{6-9} These columns are essentially open channels containing micro pillar arrays (Figure 5.4). Because of their lower porosities compared to packed beds, semi-packed columns can achieve high plate numbers with relatively low back pressures. On the other hand, the pillar structure significantly increases pooling of the stationary phase. As a result, conventional coating procedures are not fully compatible with semi-packed columns. One would expect that thermal gradient focusing could be applied here to mitigate the effects of pooling and eddy diffusion at the column turns. Therefore, testing of semi-packed columns in TGGC is recommended.

Table 5.1. Maximum efficiencies of open-tubular and packed columns.

<table>
<thead>
<tr>
<th>Open-tubular column i.d. (μm)</th>
<th>Theoretical plates per meter\textsuperscript{a}</th>
<th>Packed column particle diameter (μm)</th>
<th>Theoretical plates per meter\textsuperscript{a}</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.10</td>
<td>12,500</td>
<td>1.0</td>
<td>500,000</td>
</tr>
<tr>
<td>0.18</td>
<td>6,944</td>
<td>2.5</td>
<td>200,000</td>
</tr>
<tr>
<td>0.20</td>
<td>6,250</td>
<td>5.0</td>
<td>100,000</td>
</tr>
<tr>
<td>0.25</td>
<td>5,000</td>
<td>10</td>
<td>50,000</td>
</tr>
<tr>
<td>0.32</td>
<td>3,906</td>
<td>20</td>
<td>25,000</td>
</tr>
<tr>
<td>0.45</td>
<td>2,778</td>
<td>50</td>
<td>10,000</td>
</tr>
<tr>
<td>0.53</td>
<td>2,358</td>
<td>100</td>
<td>5,000</td>
</tr>
</tbody>
</table>

\textsuperscript{a}Plate numbers were calculated using an optimum reduced plate height of 0.8 for open-tubular columns and 2.0 for packed columns, as suggested by Cramers et al.\textsuperscript{10}
Figure 5.4. Top-view of a semi-packed microcolumn.

5.3 REFERENCES

APPENDIX A: MICRO-GC COLUMN FABRICATION PROCEDURES

A.1 WAFER PREPARATION

Prime-grade silicon wafers with <100> orientation, 1000-µm thickness and single-side polished surface are required for the following fabrication procedures. Before any pre-treatment, 6 through-holes (400 µm in diameter) are laser-drilled on wafers that will be used for channel etching. Figure A.1 marks the position of the 6 through-holes. After drilling, wafers are polished with a chemical-mechanical polisher to restore the original prime-grade surface finish. Wafers used for channel sealing are not drilled.

Figure A.1. Coordinates of the drilled holes on a wafer used for etching. Units are in cm.
A.2 THERMAL OXIDATION

Drilled wafers are rinsed and cleaned with isopropanol and deionized water, and dried with nitrogen. The wafers are then placed inside a diffusion furnace (Bruce Technologies, Billerica, MA, USA) to grow an oxide layer with a thickness of 700–800 nm, which protects the unexposed silicon substrate during KOH etching. A wafer boat with wide slots is required for this process, because slots of a standard wafer boat are too narrow to accommodate the wafers after thermal expansion. A 9-step temperature/gas flow program is employed for the oxide growth. Table A.1 summarizes the parameters of the program.

A.3 PHOTORESIST PATTERNING

A drilled wafer is cleaned with deionized water and placed inside a convection oven at 150 °C for 3 h. The dehydration step removes water on the wafer surface to promote adhesion of photoresist. The wafer is then cooled with nitrogen and spin-coated with AZ P4620 photoresist (AZ Electronic Materials, Branchburg, NJ) at 1500 rpm for 1 min. An acceleration of 1540 rpm/s is used. The wafer is immediately transferred to a convection oven at 80 °C for 20 min. The oven soft-bake removes solvent in the photoresist film while preventing dust from contaminating the surface. The wafer is cooled in air for 30 min to prevent bubble formation and loaded onto a mask aligner for UV exposure. Table A.2 lists the parameters for the alignment and exposure. The wafer is then developed with AZ 400K developing solution (1:4 in water) for 1 min with agitation, rinsed with deionized water, and transferred again to the convection oven at 150 °C for 90 min. The post exposure bake stabilizes the photoresist film for subsequent etching.
Table A.1. Temperature and gas flow program for the thermal oxidation process.

<table>
<thead>
<tr>
<th>Step</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
</tr>
</thead>
<tbody>
<tr>
<td>Function</td>
<td>Loading</td>
<td>Equilibration</td>
<td>Ramping</td>
<td>Equilibration</td>
<td>Dry oxidation</td>
<td>Wet oxidation</td>
<td>Cooling</td>
<td>Equilibration</td>
<td>Unloading</td>
</tr>
<tr>
<td>Temperature (°C)</td>
<td>850</td>
<td>850</td>
<td>853–1100</td>
<td>1100</td>
<td>1100</td>
<td>1100</td>
<td>1100–850</td>
<td>850</td>
<td>850</td>
</tr>
<tr>
<td>N₂ flow rate (L/min)</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>-</td>
<td>-</td>
<td>5</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Dry O₂ flow rate (L/min)</td>
<td>-</td>
<td>0.2</td>
<td>-</td>
<td>-</td>
<td>0.6</td>
<td>-</td>
<td>0.2</td>
<td>0.2</td>
<td>-</td>
</tr>
<tr>
<td>Wet O₂ flow rate (L/min)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>2</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Duration (min)</td>
<td>4</td>
<td>5</td>
<td>40</td>
<td>20</td>
<td>5</td>
<td>180&lt;sup&gt;b&lt;/sup&gt;</td>
<td>60</td>
<td>15</td>
<td>4</td>
</tr>
</tbody>
</table>

<sup>a</sup>Wet oxygen is formed by flowing dry oxygen through water at 90 °C.

<sup>b</sup>Wet oxide step is 60 min if thermal oxidation is used for wafer bonding.
Table A.2. Mask aligner parameters.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Max exposures</td>
<td>500</td>
</tr>
<tr>
<td>Exposure time</td>
<td>30.0 s</td>
</tr>
<tr>
<td>Alignment gap</td>
<td>500 µm</td>
</tr>
<tr>
<td>Resist</td>
<td>Positive</td>
</tr>
<tr>
<td>Mode</td>
<td>Manual align</td>
</tr>
<tr>
<td>WEC</td>
<td>Soft contact</td>
</tr>
<tr>
<td>Alignment check</td>
<td>Off</td>
</tr>
</tbody>
</table>

A.4 CHANNEL ETCHING

After post-bake, the patterned wafer is cooled with nitrogen and soaked in buffered HF for 7–8 min to remove exposed oxide. The patterned photoresist film is cleaned with Nano-Strip (Cyantek, Fremont, CA, USA) at 90 °C for 1 h. The wafer is then rinsed with deionized water and dried with nitrogen before etching in KOH solution (45% w/w in water) at 80 °C for approximately 60 min or until the channel depth reaches 60 µm. After etching, the remaining non-uniform oxide layer is removed by placing the wafer again in buffered HF for 10 min.

A.5 WAFER BONDING

The etched wafer and a fresh wafer are cleaned with deionized water and thermally oxidized again in the diffusion furnace using parameters listed in Table A.2. An oxide layer with a
thickness of 300−400 nm is formed in this step. Then, the two wafers are thoroughly cleaned with acetone, isopropanol and deionized water using foam swabs. Polished sides of the two wafers are brought together for initial bonding with van der Waals force. Bonded wafers are placed on a quartz dish and bonded in the diffusion furnace. Table A.3 lists the parameters for wafer bonding. After cooling, the bonded wafers are covered with tape, which keeps particles from entering the through-holes, and diced into three 1-inch-wide chips with a disc saw.

Table A.3. Parameters for wafer bonding in a diffusion furnace.

<table>
<thead>
<tr>
<th>Step</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Function</td>
<td>Loading</td>
<td>Ramping</td>
<td>Bonding</td>
<td>Cooling</td>
<td>Unloading</td>
</tr>
<tr>
<td>Temperature (°C)</td>
<td>140</td>
<td>140−1100</td>
<td>1100</td>
<td>1100−500</td>
<td>500</td>
</tr>
<tr>
<td>Dry O₂ flow rate (L/min)</td>
<td>0.6</td>
<td>0.6</td>
<td>0.6</td>
<td>0.6</td>
<td>0.6</td>
</tr>
<tr>
<td>Duration (min)</td>
<td>4</td>
<td>480</td>
<td>180</td>
<td>300</td>
<td>4</td>
</tr>
</tbody>
</table>

A.6 CAUTIONS

The processed wafer must be examined during every step. The thickness of thermal oxide layer can be measured with a film measurement system; a uniform layer is desired. The patterned photoresist should be defect-free. The depth of the channel can be measured with a profilometer and should be large enough for chromatographic tests. The surface must be contaminant-free to achieve good bonding. Bonding strength can be tested using a razor-blade; bonding defects can be examined using an infrared camera or a scanning acoustic microscope.
APPENDIX B: CARRIER GAS VELOCITIES IN TGGC

B.1 MATHEMATICAL EXPRESSIONS

The carrier gas velocity in an open-tubular column is governed by Darcy’s Law as:

\[ u = \frac{-L \partial p}{\Omega \partial x} \]  \hspace{1cm} (B. 1)

where \( u \) is the local carrier gas velocity, \( L \) is the length of the column, \( \partial p/\partial x \) is the pressure gradient and \( \Omega \) is the pneumatic resistance of the column, which is defined by:

\[ \Omega = \frac{32L\eta}{d_c^2} \]  \hspace{1cm} (B. 2)

where \( \eta \) is the viscosity of the carrier gas and \( d_c \) is the inner diameter of the column. Combining Equations (B.1) and (B.2) gives:

\[ u = \frac{-d_c^2 \partial p}{32\eta \partial x} \]  \hspace{1cm} (B. 3)

Now consider the ideal gas law:

\[ pV = nRT \]  \hspace{1cm} (B. 4)

and the definition of the gas velocity:

\[ u = \frac{dV}{Adt} \]  \hspace{1cm} (B. 5)

where \( V \) is the volume of the gas, \( n \) is the molar amount of the gas, \( R \) is the ideal gas constant, \( T \) is the temperature and \( A \) is the cross-sectional area of the column. For an infinitesimal amount of gas in the column, Equation (B.4) becomes:

\[ pdV = puAdt = RTdn \]  \hspace{1cm} (B. 6)

which can be rearranged to:
\[
\frac{pu}{T} = \frac{Rdn}{A\; dt} = \frac{RF_m}{AM}
\]  
(B.7)

where \( M \) is the molar mass of the gas and \( F_m \) is the mass flow rate of the gas. If the gas flow through the column is mass-conserving and the column i.d. is constant along the whole length, \( RF_m/AM \) is also constant, which indicates that \( pu/T \) is constant along the column. For isothermal and temperature-programming conditions, \( T \) is constant along the column at a given time. Therefore, \( pu \) is also constant. This product can be denoted as:

\[
J = pu
\]  
(B.8)

where \( J \) is the energy flux in the column. Equation (B.3) can be rewritten as:

\[
Jdx = -\frac{d_c^2 p}{32\eta} dp
\]  
(B.9)

Because \( J \) and \( \eta \) are independent of the position, integration of Equation (B.9) from \( x = 0 \) and \( p = p_i \) along the column to an arbitrary position \( x \) and the corresponding pressure \( p_x \) yields:

\[
J = \frac{d_c^2}{64\eta x} (p_i^2 - p_x^2)
\]  
(B.10)

where \( p_i \) is the pressure at the column inlet. At \( x = L \) and \( p = p_o \), Equation (B.10) becomes:

\[
J = \frac{d_c^2}{64\eta L} (p_i^2 - p_o^2)
\]  
(B.11)

where \( p_o \) is the pressure at the column outlet. By combining Equations (B.10) and (B.11), the local pressure and velocity of the carrier gas can be calculated from:

\[
p_x = \sqrt{p_i^2 - \frac{x}{L} (p_i^2 - p_o^2)}
\]  
(B.12)

and

\[
u_x = \frac{(p_i^2 - p_o^2)d_c^2}{64\eta Lp_x}
\]  
(B.13)
For thermal gradient conditions, however, the temperature along the column is not constant at any
given time. As a result, the local pressure and velocity of the carrier gas in TGGC are affected by
the entire gradient profile. In this case, Equation (B.3) can be rewritten as:

$$\frac{pu}{T} = -\frac{d^2p}{32\eta T} \frac{dp}{dx}$$

(B.14)

By denoting terms that are independent of the position as:

$$\gamma = \frac{32}{d^2} \frac{pu}{T}$$

(B.15)

Equation (B.14) can be rearranged to:

$$-pdp = \gamma \eta T dx$$

(B.16)

Note that $\eta$ is dependent on $T$ and the relationship can be expressed as:

$$\eta = \eta_0 \left(\frac{T}{T_0}\right)^c$$

(B.17)

where $T_0$ is the reference temperature (273.15 K), $\eta_0$ is the reference viscosity of the carrier gas at
$T_0$ and $c$ is a constant for the carrier gas (0.646 for helium, 0.680 for hydrogen and 0.725 for
nitrogen). Combining Equations (B.16) and (B.17) yields:

$$-pdp = \gamma_0 \frac{\eta_0}{T_0} T^{c+1} dx$$

(B.18)

Integration of Equation (B.18) from $x = 0$ to an arbitrary position $x$ yields:

$$p_x = \sqrt{p_i^2 - \frac{2\gamma \eta_0 T} {T_0^c} \int_0^x T^{c+1} dx}$$

(B.19)

Integration of Equation (B.18) from $x = 0$ to $x = L$ yields:

$$\gamma = \frac{(p_i^2 - p_o^2)T_0^c} {2\eta_0 \int_0^L T^{c+1} dx}$$

(B.20)

The local velocity of the carrier gas can be calculated by rearranging Equation (B.15) to:
\[ u_x = \frac{\gamma d_c^2 T_x}{32 p_x} \quad \text{(B.21)} \]

Equations (B.19), (B.20) and (B.21) can be used to calculate the pressure and velocity of the carrier gas at any given point along the column in TGGC, as long as the temperature-distance function is known.

**B.2 EXAMPLE CALCULATIONS**

If a 3 m × 0.1 mm i.d. open-tubular column is operated at 150 °C using helium as the carrier gas with an inlet pressure of 30 psi and an outlet pressure of 1 atm, the carrier gas velocities at the inlet, the outlet and the half length of the column can be calculated using Equations (B.12) and (B.13):

\[ x = 1.5 \text{ m} \]
\[ L = 3 \text{ m} \]
\[ d_c = 1 \times 10^{-4} \text{ m} \]
\[ \eta = 2.476 \times 10^{-5} \text{ Pa} \cdot \text{s} \]
\[ p_i = 308167.71 \text{ Pa} \]
\[ p_o = 101325 \text{ Pa} \]
\[ p_x = 229384 \text{ Pa} \]
\[ u_i = 57.8 \text{ cm/s} \]
\[ u_o = 175.8 \text{ cm/s} \]
\[ u_x = 77.7 \text{ cm/s} \]

If a linear thermal gradient, starting from 250 °C and ending at 50 °C, is applied to the same column, the temperature-distance function can be expressed as:
\[ T = 523.15 - \frac{200x}{3} \]

The carrier gas velocities at the inlet, the outlet and the half length of the column can be calculated using Equations (B.19), (B.20) and (B.21):

\[ x = 1.5 \text{ m} \]
\[ L = 3 \text{ m} \]
\[ d_c = 1 \times 10^{-4} \text{ m} \]
\[ \gamma = 1.3341 \times 10^{12} \text{ Pa} \cdot \text{s}^{-1} \cdot \text{m}^{-1} \cdot \text{K}^{-1} \]
\[ p_i = 308167.71 \text{ Pa} \]
\[ p_o = 101325 \text{ Pa} \]
\[ p_x = 210881 \text{ Pa} \]
\[ u_i = 70.8 \text{ cm/s} \]
\[ u_o = 133.0 \text{ cm/s} \]
\[ u_x = 83.7 \text{ cm/s} \]

The results indicate that the temperature gradient significantly affects the local pressure and velocity of the carrier gas, even though the average column temperature is the same for the two conditions.