Anal. Chem. **2005,** *77,* 2078−2084

Stop-Flow Programmable Selectivity with a Dual-Column Ensemble of Microfabricated Etched Silicon Columns and Air as Carrier Gas

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A series-coupled ensemble of microfabricated GC columns made by dry reactive ion etching of silicon substrates is evaluated for use with pneumatic selectivity enhancement techniques for targeted pairs of volatile organic compounds. Each column is 3.0 m long with a 150 μm wide by 240 μm deep cross section. Dynamic coating was used to prepare a nonpolar column with a dimethyl polysiloxane stationary phase and a moderately polar column with a trifluoropropylmethyl polysiloxane stationary phase. Each column generates 5000−6000 theoretical plates. The columns are operated in series with the nonpolar column connected to a split inlet, the polar column connected to a flame ionization detector, and a valve connected between the column junction point and the inlet to the first column. When the valve is closed, the effluent from the first column passes directly into the second column. When the valve is open, both ends of the first column are at the inlet pressure, and flow stops in this column while increased flow is obtained in the second column. For analyte pairs that are separated by the first column but coelute from the column ensemble, the valve is opened for a few seconds after the first component of the pair has passed into the second column but the second component is still in the first column. The result is enhanced separation of the pair in the ensemble chromatogram. Relatively thick cross-linked stationary-phase films are used to increase retention for volatile compounds. The combination of air carrier gas and stationary-phase film thickness in the range 1−2 μm requires the use of relatively low average carrier gas velocities (typically less than 10 cm/s) for adequate resolving power of the column ensemble. Selectivity enhancement under isothermal conditions for a 14-component mixture of volatile organic compounds is demonstrated where neither of the columns alone nor the column ensemble without selectivity enhancement could obtain a complete separation.

The development of microfabricated components and complete systems for gas chromatography is underway in several laboratories.[1−6] These developments are driven by the need for more comprehensive and lower cost on-site environmental monitoring,[7−9] high-speed monitoring of hazardous substances including chemical warfare agents[3,10,11] and high-speed, high-sample-throughput process monitoring in the chemical industry.[1,2,6] Preliminary studies of components for autonomous instruments using ambient air[12−17] as carrier gas and microwave (wireless) communications have been reported.[18,19]

Several microfabricated column designs have been described. Most are fabricated using dry reactive ion etching in silicon substrates[3,5,17,20−23] with glass covers anodically bonded to the silicon surface to seal the channel. Columns developed at Sandia National Laboratory for a commercially available handheld chemi-

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10.1021/ac040174p CCC: $30.25
Published on Web 03/08/2005

cal warfare agent detector are 1 m long and use a 40−80 μm wide by 250 μm deep channel coated with proprietary stationary phases developed in-house.[3,25] A commercial instrument, with a column cross-sectional area equivalent to a 60-μm-i.d. round cross-section column, with etched silicon channels coated using a dimethyl polysiloxane-like stationary phase formed by plasma discharge has been described.[28] These columns use a unique channel configuration where the channel makes a large number of s-shaped turns creating a wavelike pattern, claimed to enhance performance.

Recently, 3 m long, 150 μm wide by 240 μm deep channels etched in silicon substrates have been described.[17,20−23] These columns are intended for use in a completely microfabricated GC instrument using a sorption-based concentrator and an array of chemiresistor sensors for ambient air monitoring.[17,24−26] The instrument under development is designed to target 30 or more analytes per analysis and will use air as the carrier gas. The channels were dynamically coated[17] with a nonpolar dimethyl polysiloxane or a moderately polar trifluoropropylmethyl polysiloxane stationary phase (Restek Corp., Bellefonte, PA). These stationary phases were used because of their stability in air at temperatures as high as 200 °C.[13,29] The nonpolar column generated 5000−5500 theoretical plates, while the polar column generated 5800−6300 theoretical plates when operated with air carrier gas at the flow rate giving the minimum plate height.

Because of their shorter lengths and poorer stationary-phase coating efficiencies, these microfabricated columns generally have fewer theoretical plates and thus smaller peak capacity than conventional fused-silica capillary columns. However, having available both polar and nonpolar microfabricated columns provides a means for obtaining enhanced selectivity using a tunable/programmable dual column ensemble of a nonpolar and a polar column. This allows for more efficient use of the available peak capacity and, in many cases, can improve separation quality

Several operating modes of series-coupled (tandem) ensembles of fused-silica capillary columns using adjustable carrier gas pressure at the column junction point[13,16,30−32] or independent column temperature control[33] have been described. A very useful implementation of pressure-controlled programmable selectivity uses a valve connecting the column junction point to a source of carrier gas at the GC inlet pressure to enhance the separation of targeted component pairs that are separated by the first column in the ensemble but coelute from the column ensemble by virtue of the different selectivities of the two columns. The valve is opened for a few seconds when one of the components of a targeted analyte pair has migrated across the column junction and is in the second column while the other component is still in the first column. This introduces a time interval between the peaks for the two analytes in the ensemble chromatogram while not significantly changing the elution pattern of other peaks in the ensemble chromatogram. This technique has been used with fused-silica capillary columns to achieve enhanced separations of pesticides,[30] essential oil components,[30−32] and air-borne organic vapors.[15,16]

This report describes experiments using a series-coupled ensemble of a 3-m-long nonpolar and a 3-m-long polar microfabricated column operated isothermally at room temperature with air as carrier gas. A requirement for the use of stop-flow programmable selectivity for targeting specific peak pairs for enhanced separation is that a complete separation of the targeted component pairs be achieved by the first column so that the stop-flow interval can be initiated after the first solute band of the pair has completely crossed the column junction while the other band is entirely in the first column. This is particularly challenging with microfabricated columns because of their relatively low resolving power.

The selectivities and efficiencies of the individual columns and of the series-coupled ensemble are presented. Previous studies using stop-flow selectivity enhancement methods with fused-silica columns have used two detectors, one to monitor a fraction of the effluent from the first column and the other to monitor the column ensemble. A simple procedure is described here using a single detector for the evaluation of component pairs that can be targeted for enhanced separation and for the determination of the appropriate time after sample injection for the stop-flow valve to be opened. The use of multiple stop-flow pulses for targeting several component pairs that coelute in the ensemble chromatogram is demonstrated.

EXPERIMENTAL SECTION

Apparatus. Figure 1a shows the experimental system used for implementing stop-flow programmable selectivity with microfabricated columns. The flame ionization detector (FID) and the split inlet from a Varian 3500 GC (Varian, Walnut Creek, CA) were used without modification. The two microfabricated columns, C_1 and C_2, were mounted on a platform outside the Varian GC. A low-dead-volume pneumatically actuated valve V_1 (stop-flow valve) (P/N 1236091, SGE International Pty. Ltd., Ringwood, Australia)

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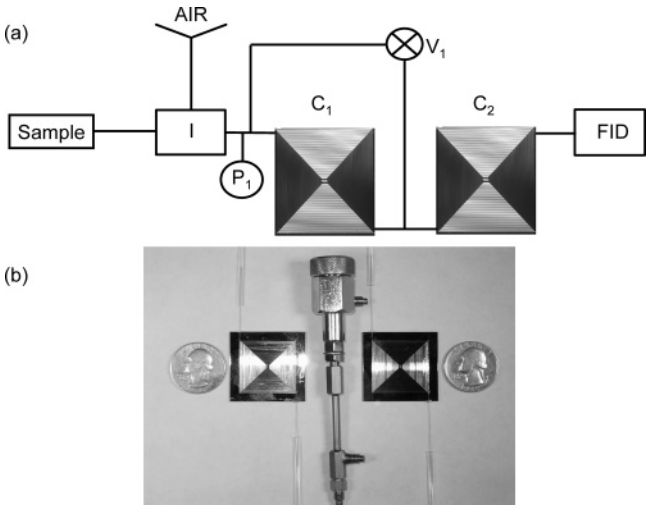

Figure 1. Apparatus for stop-flow selectivity enhancement with microfabricated columns (a) and digital photograph of the columns and stop-flow valve (b). C_1, nonpolar column; C_2, polar column; V_1, stop-flow valve; I, split inlet; FID, flame ionization detector; P_1, pressure gauge.

was connected from the column junction point to the inlet of the first column. The valve is operated by a 50−55 psig compressed air source connected through an electronically actuated solenoid valve (model 74313-0115, Schrader Bellows, Pittsburgh, PA). Connections were made by use of low-dead-volume Y connectors (MXT "Y" Connectors for 0.28-mm-i.d. tubing, Restek Corp., Bellafonte, PA). Figure 1b shows a digital photograph of the two columns and the valve.

Column Design. The columns have been described in detail.[17,20−23] Each column is etched using a modified Bosch process[20−23] on a 3.2 cm × 3.2 cm silicon chip. Four columns are etched simultaneously on a standard 4-in. silicon wafer. The channels are sealed by anodically bonding a Pyrex 7740 glass cover plate to the silicon wafer and the wafer diced to obtain the four columns. The 150 μm wide by 240 μm deep rectangular cross section channel is 3.0 m long and etched as a double square spiral with a turnaround connecting the two parts of the channel at the center of the chip. After dicing, 30-cm-long, 100-μm-i.d., 245-μm-o.d. deactivated fused-silica connecting lines (BGB Analytik, Anwil, Switzerland) were epoxyed (Hysol Epoxy Patch, Dexter Corp., Seabrook, NH) into 300 μm wide by 300 μm deep ports that were etched at opposite corners of the chips. The epoxy was cured at 140 °C for 2 h.

The columns were coated at Restek Corp. using a dynamic coating procedure with a film of nonpolar dimethyl polysiloxane (Rtx-1) or moderately polar trifluoropropylmethyl polysiloxane (Rtx-200). Both stationary phases contained a proprietary, thermally activated cross-linking agent. After coating and drying overnight, the head pressure was set to 10 psig, and the temperature was increased at 10 °C/min to 250 °C. The chips were maintained at 250 °C with helium flow for 4 h and then cooled to ambient. Stationary-phase film thickness is estimated at 1−2 μm for both columns.

Materials and Procedures. Compressed air after passing through traps for water vapor and hydrocarbons was used as carrier gas. Compounds used in the test mixture are listed in Table 1. All compounds are reagent grade or better. All chromatograms

Table 1. Compounds and Retention-factor Values for the 14-component Test Mixture

components	retention factors: dimethyl polysiloxane	retention factors: trifluoropropylmethyl polysiloxane
(1) methanol	0.20	0.26
(2) ethanal	0.15	0.48
(3) pentane	0.61	0.29
(4) isoprene	0.63	0.45
(5) propanal	0.47	1.28
(6) cyclopentane	1.18	0.58
(7) acetone	0.47	1.83
(8) 1-hexene	1.53	0.82
(9) isopropyl ether	2.04	1.13
(10) butanal	1.30	3.19
(11) benzene	2.81	2.48
(12) ethyl acetate	1.81	3.46
(13) cyclohexene	3.50	1.79
(14) heptane	4.69	1.90

were obtained isothermally at ambient temperature (22−23 °C). Injections were typically 0.5 μL of individual components or mixtures with a split ratio of 300:1. No solvent was used. For column efficiency studies, the columns were placed in the Varian oven operated at 70°C, and 2-μL samples of *n*-nonane headspace vapor injected with a split ratio of 300:1.

Average carrier gas velocity values were computed from holdup time measurements using methane injection. The holdup times for the individual columns when used in the column ensemble were measured using a series of methane injections, where the time after injection for the opening of the stop-flow valve was varied. The valve was opened for a few seconds and then closed. If the methane band is in the first column when the valve is opened, the ensemble retention time increases by an amount equal to the time the valve is open. If the band is in the second column, the ensemble retention time decreases. If the valve is opened during the passage of the band from the first to the second column, a double peak is observed in the ensemble chromatogram. The first-column holdup time is taken as the valve opening time after injection required to produce two peaks with equal areas. The Varian FID was interfaced to a PC by means of a 16-bit A/D board (PCI-DAS 1602/16, Computer Boards, Inc., Marshield, MA). The board was controlled by LabTech Notebook software (Laboratory Technologies Inc., Wilmington, VA). Chromatograms were processed by GRAMS/32 software (Galactic Industries, Salem, NH).

RESULTS AND DISCUSSION

The microfabricated columns used here employ relatively thick stationary-phase films in order to increase retention for volatile organic compounds. This coupled with the use of air as carrier gas results in relatively low optimum flow rates (flow rate producing the smallest height equivalent to a theoretical plate). Golay plots (height equivalent to a theoretical plate versus average carrier gas velocity) were constructed for the nonpolar column, the polar column, and the column ensemble using *n*-nonane at a column temperature of 70 °C. Retention factors for *n*-nonane for the two columns are 4.2 and 1.7, respectively. The ensemble retention factor is 3.1. The corresponding average carrier gas velocities were found to be 8.8 and 7.8 cm/s, respectively, for the

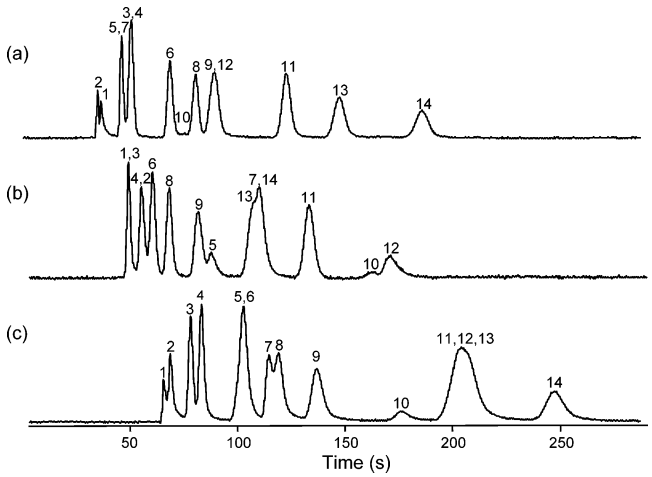

Figure 2. Chromatograms of the 14-component test mixture using air as carrier gas: (a) nonpolar column; (b) polar column; (c) column ensemble. Peak numbers correspond to compound numbers in Table 1. Chromatograms a and b were obtained at the corresponding optimum carrier gas velocities, and (c) was obtained at about twice the optimal carrier gas velocity for the column ensemble.

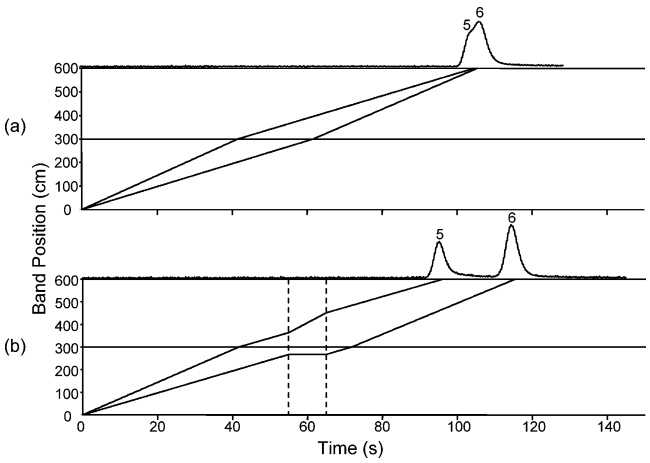

Figure 3. Band position versus time and the corresponding chromatograms of components 5 and 6 without a stop-flow pulse (a) and with a 10-s-long stop-flow pulse initiated 55 s after injection (b).

individual columns, and 6.3 cm/s for the ensemble. The number of plates produced by the columns under these conditions are 5400 and 6000, respectively, for the individual columns and 9500 for the ensemble.

Figure 2 shows chromatograms for the 14-component test mixture using the nonpolar column (a), the polar column (b), and the column ensemble (c) with the corresponding optimal average carrier gas velocities for the individual columns and about twice the optimal velocity (~13.4 cm/s) for the column ensemble. This higher velocity is used to reduce analysis time. At this carrier gas velocity, the number of plates generated by the ensemble (*n*-nonane, 70 °C) is reduced to ~7700. Relatively symmetric peaks with minimal artifacts are observed. The analysis is complete in less than 200 s for the individual columns and in ~250 s for the column ensemble. In no case is a complete separation obtained. For the nonpolar column, compound pairs 3/4, 5/7, 8/10, and 9/12 all coelute. For the polar column, compound groups 1/3, 2/4, and 7/13/14 all coelute. The column ensemble fares no better with groups 5/6, 7/8, and 11/12/13 showing inadequate separation. The resolution of component pair 1/2 on the column ensemble is less than 1.0 and is comparable to the nonpolar column alone, but with a reversal of elution order.

Stop-Flow Operation. Note that the component groups 5/6, 7/8, and 11/12/13, which all coelute in the ensemble chromatogram, are all completely separated by the nonpolar column and thus enhanced separation of these components in the ensemble chromatogram should be possible by the use of stop-flow operation of the first (nonpolar) column. This is illustrated for components 5 and 6 in Figure 3 for the case with no stop-flow pulse (a) and for the case of a 10-s-long pulse (valve open time) beginning at 55 s after injection (b). When the pneumatic valve is open, the head pressure of the first column is applied at the junction point, while maintaining the pressure at the inlet to the first column. This nearly stops flow on the first column while increasing the pressure drop along the second column and, thus, the volumetric flow rate through the column. The band trajectory plots (solute band position along the column axis versus time) were constructed from retention factor data for the two columns (see Table 1) and measured values for the holdup times for the two columns when used in the series-coupled ensemble. Injection occurs at the lower left corner of the plots, and the horizontal line at a band position of 300 cm corresponds to the junction point of the column ensemble. Elution occurs at 600 cm corresponding to the total length of the column ensemble.

These band trajectory plots are only approximate since they neglect gas compression effects. Some curvature of the straight-line segments occurs when gas compression effects are considered. First-column retention times are accurate to within ±1 s and are very useful in determining when a stop-flow pulse should be applied in order to enhance the separation of a targeted peak pair. The band trajectory plots for both compounds show distinct slope change across the column junction due to the different retention factors for the two compounds in the two columns. In the nonpolar column, component 5 has a smaller retention factor than component 6; while the situation is reversed for the polar column. The result is that the two compounds are well separated by the first column, but coelute from the column ensemble (chromatogram a).

If the stop-flow valve is opened for 10 s beginning 55 s after injection, compound 5 has crossed the ensemble junction point and is entirely in the second column, while compound 6 is still entirely in the first column. The flow stops in the first column as indicated by the horizontal region of the band trajectory plot for compound 6 in Figure 3b (enclosed by dashed lines). During the stop-flow pulse, the flow in column two increases as indicated by the increased slope of the band trajectory plot for compound 5. After the valve is closed, the flow rates in the two columns return to their initial values. The result is the complete separation of the targeted component pair in the ensemble chromatogram.

Previous studies with stop-flow selectivity enhancement used an independent source of carrier gas at the GC inlet pressure to ensure that the flow completely stopped in the first column when the valve was open.[30] This minimizes the risk of the second component of the targeted pair reaching the column junction point and partially migrating into the second column before the end of the stop-flow pulse. The stop-flow system described here uses a single carrier gas supply, and when the valve is open, the pressure

Table 2. Statistical Data from Plots of Retention Time Change versus Stop-Flow Pulse Duration

components	slope	R^2
(1) methane	0.9762	0.9998
(2) ethanal	0.9799	0.9997
(3) pentane	0.9763	0.9997
(4) dichloromethane	0.9777	0.9997
(5) acetone	0.9713	0.9996

drop from the tubing connecting the head of the first column to the column junction point results in a small residual flow in the first column.

To evaluate the residual band migration rates in the first column during a stop-flow pulse, the change in ensemble retention times versus the stop-flow pulse duration was measured for methane, ethyl alcohol, *n*-pentane, dichloromethane, and acetone. The pulse was initiated 20 s after injection, and all five compounds were in the first column. Ten different values of pulse duration from 1.0 to 30 s were used, with the expectation that the change in retention time for components that are on the first column during the pulse will be nearly equivalent to the length of the stop-flow pulse. Table 2 lists statistical data for linear regression fits that illustrate the variations in the changes in retention times as a function of pulse duration for several components. The linear fit is very good with correlation coefficients all in the range 0.9996 to 0.9998. Previous work with stop-flow selectivity enhancement used conventional, wall-coated fused-silica columns, which obtained substantially greater resolving power and used average carrier gas velocities typically 10-fold greater than the values used here with microfabricated silicon−glass columns. This requires longer stop-flow pulses with the microfabricated columns to achieve equivalent resolution enhancements for targeted peak pairs. If flow completely stops in the first column during the pulse, the slopes of plots of retention time change versus pulse duration should be 1.0. The slope data in Table 2 indicate that, during the stop-flow pulse, the band velocities are reduced to 2−3% of the values with the stop-flow valve closed.

Figure 4 shows the effects of stop-flow pulse initiation time (column A) and pulse duration (column B) on the separation of propanal and cyclopentane. Chromatogram a in column A shows the coelution of peaks 5 and 6 for the case where the stop-flow valve is closed during the entire separation. Chromatogram b was obtained using a 10-s-long stop-flow pulse initiated 35 s after injection. Both solute bands are in the first column during the pulse, and the retention time of both peaks is increased by ∼10 s with no significant change in the separation. For chromatogram c, a 10-s-wide pulse was initiated 55 s after injection. This is the case shown in Figure 3b, where the stop-flow pulse is initiated after band 5 has crossed the junction but band 6 is entirely in the first column. The results are a 10-s increase in the retention time for peak 6, and a smaller decrease in the retention time for peak 5 and the complete separation of the two peaks.

For chromatogram d, a 10-s pulse was initiated 65 s after injection. At this time, band 5 was entirely in the second column but the tailing portion of band 6 was still in the first column. This results in a double peak for component 6 with the bulk of the peak coeluting with peak 5. The smaller portion of peak 6 remains in the first column during the stop-flow pulse, and the retention time is shifted ∼10 s latter than in chromatogram a with no stop-flow pulse. For chromatogram e, the pulse was initiated 70 s after injection when both bands are completely in the second column. The two peaks coelute, but their retention times are shifted to smaller values relative to the no-pulse case.

For chromatograms f−j, the stop-flow valve was opened 55 s after injection, with pulse durations of 1.0, 3.0, 5.0, 7.5, and 10 s, respectively. As the pulse width is increased, the retention time of peak 6 steadily increases, and that of peak 5 steadily decreases. Complete separation is achieved for pulse durations of 5 s or more.

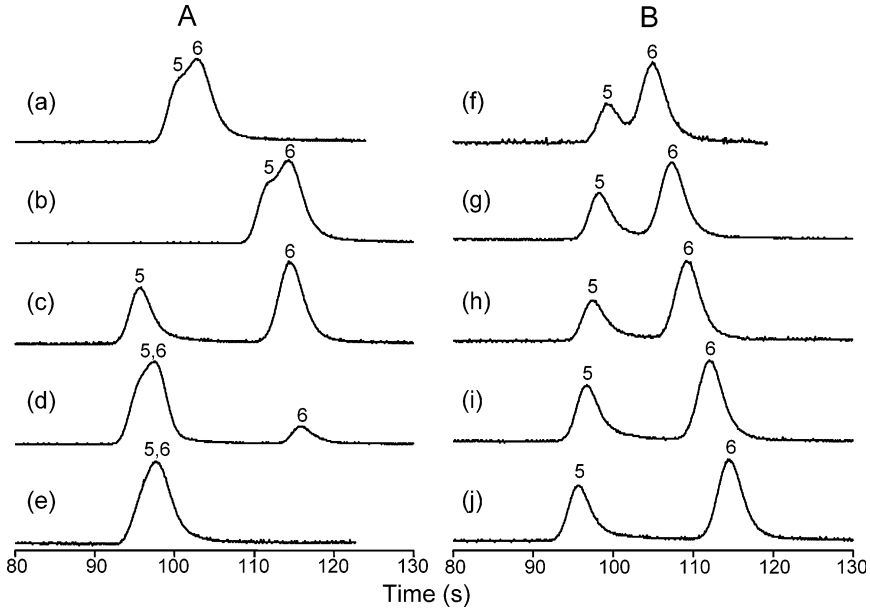

Figure 4. Effects on retention times and peak separation of stop-flow pulse initiation time (column A) and pulse width (column B) for component pair 5/6: (a) no stop-flow pulse; (b) pulse initiated when both bands are in C_1; (c) pulse initiated when band 5 is in C_2 and band 6 is in C_1; (d) pulse initiated when band 5 and part of band 6 are in C_2; (e) pulse initiated when both bands are in C_2; (f) 1-s pulse; (g) 2-s pulse; (h) 4-s pulse; (i) 7.5-s pulse; (j) 10-s pulse after component 5 crosses the junction point and component 6 remains in the first column.

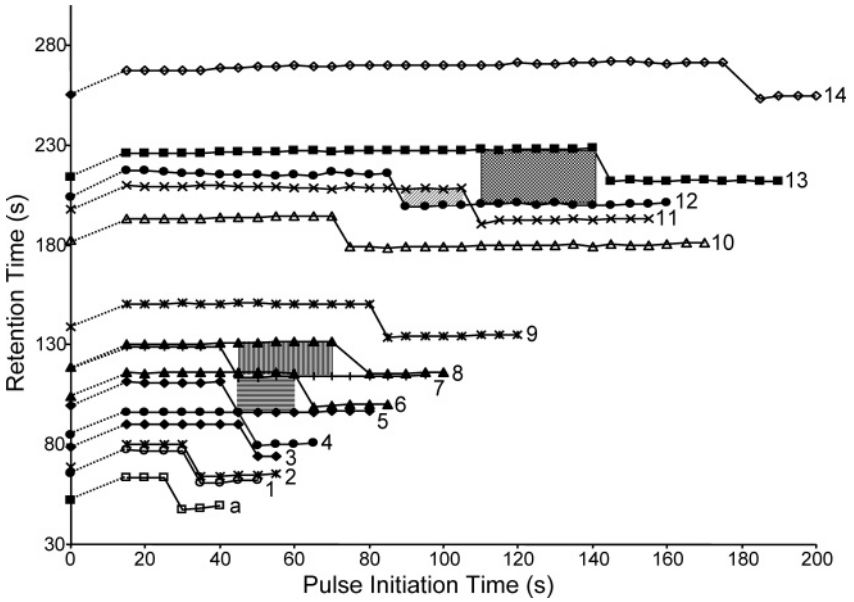

Figure 5. Retention time versus pulse initiation time for 10-s-long stop-flow pulses. Plot numbers correspond to compound numbers in Table 1. Plot a is for methane. Data points along the vertical axis are for the case with no stop-flow pulse. Shaded areas correspond to time windows when a stop-flow pulse would be effective in enhancing the separation of the corresponding coelutions in Figure 2.

Multiple Stop-Flow Pulses. As shown in Figure 2, the 14-component test mixture produces several coelutions with the individual columns and with the column ensemble. While multiple stop-flow pulses should be effective, since for each of these ensemble coelutions, the components are completely separated on the first column, the appropriate selection of the initiation time and duration of each pulse is a critical issue. Previous stop-flow work with laboratory instruments[30−32] used two detectors, one monitoring a few percent of the effluent from the first column and the other monitoring the ensemble effluent. The microfabricated GC that will incorporate stop-flow selectivity enhancement will only have ensemble detection.

Figure 5 illustrates a graphical procedure for determining the initiation times for multiple stop-flow pulses using only ensemble detection. The procedure requires no prior knowledge of component retention factors. For targeted analysis when the individual components are available, a plot of ensemble retention time versus pulse initiation time is constructed for each component. If the mixture is unknown, or standards not available, a similar plot is obtained for every peak apex in the ensemble chromatogram. The data in Figure 5 are for a pulse width of 10 s. The pulse initiation time was varied in 5-s intervals. Numbers by the plots correspond to the compound numbers in Table 1. The plot for an unretained peak (methane) is also shown (plot a). Data points on the vertical axis show the retention time without the stop-flow pulse. Since the analysis is complete in less than 5 min, methods development can be relatively rapid.

Every plot shows an abrupt decrease in retention time of ~10 s at the pulse initiation time corresponding to the solute band eluting from the first column and entering the second column. To the left of this retention time change, the stop-flow pulse occurs while the band is in the first column, and the retention time is increased by the pulse duration (10 s) relative to the case with no stop-flow pulse. To the right of the abrupt retention time change, the pulse occurs when the band is in the second column, and there is a very gradual increase in ensemble retention time with increasing pulse initiation time.

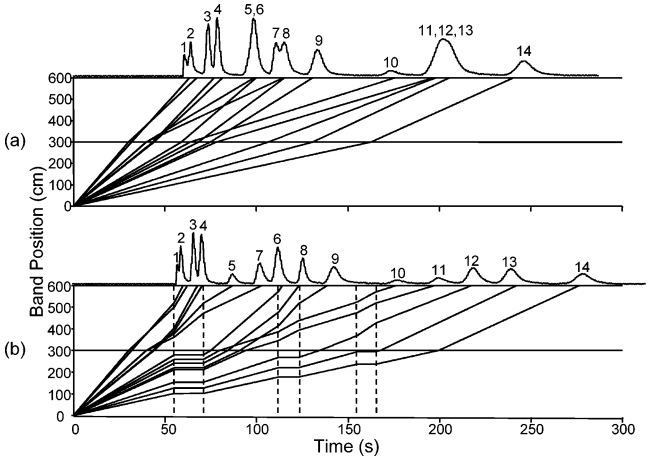

Figure 6. Band position versus time and the corresponding chromatograms of the 14-component test mixture with no stop-flow pulses (a) and three pulses time as indicated by the vertical broken lines (b). See text for details. Peak numbers correspond to compound numbers in Table 1.

The shaded areas in Figure 5 correspond to the coelutions observed in the ensemble chromatogram (Figure 2c). The coelutions are easily recognized by the similar ensemble retention times for component pairs 5/6, 7/8, and the three components 11/12/13. The left and right boundaries of each shaded area indicate the pulse initiation times corresponding to the times for the two bands, respectively, to cross the junction. A stop-flow pulse during this interval should enhance the separation of the corresponding components.

Figure 6 shows chromatograms and band trajectory plots for the 14-component mixture with no stop-flow pulse (a) and with three pulses used to enhance the separation of the coeluting groups (b). The first pulse, used for component pairs 5/6 and

7/8, is 15 s long and is initiated 50 s after injection. Components 5 and 7 are in the second column during the pulse, and their ensemble retention times are shifted to shorter values. Components 6 and 8 are in the first column during the pulse, and their ensemble retention times are increased by 15 s relative to the no-pulse case. Initial studies with a 10-s wide pulse showed that the peak for component 6 was shifted into peak 7 and they coeluted in the ensemble chromatogram. By increasing the pulse width to 15 s, peak 6 was shifted sufficiently to elute from the column ensemble between peaks 7 and 8.

The next pulse, used to enhance the separation of component 11 from 12 and 13 is initiated 112 s after injection. A 10-s-wide pulse was found to be adequate. The data in Figure 5 suggest that the time window for the initiation of this pulse is 90−105 s after injection. However, this window is shifted to latter times by 15 s, since the first stop-flow pulse resulted in all component bands in the first column during the pulse crossing the column junction 15 s later than indicated in Figure 5. Finally, a third pulse, 10 s in width and initiated 155 s after injection, was used to enhance the separation of components 12 and 13. Note that the initiation time for this third pulse is delayed by 25 s relative to the value suggested by Figure 5 due to the fact that bands for both components 12 and 13 were in the first column during the first two stop-flow pulses (25 s total time), and thus they reach the column junction 25 s later than predicted by Figure 5. Note, that the use of three appropriately timed stop-flow pulses greatly enhances the separation quality while adding only 35 s to the total analysis time.

CONCLUSIONS

The data presented in this report are the first to use pneumatic selectivity enhancement techniques to improve separation quality with an ensemble of microfabricated columns. The key is the availability of both polar and nonpolar microfabricated columns with adequate separation power. While these columns have less resolving power than conventional fused-silica columns due to shorter lengths and poorer efficiencies, the nonpolar column used here generates ~5400 theoretical plates, which has been shown to obtain adequate first-column separation to facilitate stop-flow selectivity enhancement. A performance goal for the microfabricated instrument under development is the separation of 30−50 target compounds in less than 10 min.

The system described here differs from laboratory stop-flow systems where a separate pressure-controlled carrier gas supply can be used at the column junction point and a separate junction point detector can be used to monitor the first-column effluent for the direct determination of appropriate stop-flow initiation times for targeting specific groups of components for enhanced separation. The microfabricated instrument will require a direct connection from the column ensemble junction point to the upstream end of the first column through a low-pressure-drop connection. This approach was shown to work well with migration rates in the first column during a stop-flow pulse of only 2−3% of the values when the stop-flow valve is closed. This is necessary to minimize partial migration of solute bands across the column junction during the pulse.

A relatively straightforward procedure has been developed for determining stop-flow pulse initiation times with only an ensemble detector. The method was applied to the case of targeted analysis where retention standards are available for all mixture components. This procedure can also be used for unknown mixtures where undetected ensemble coelutions occur but the components are adequately separated by the first column. For an undetected ensemble coelution, the single peak will split into its components as the pulse initiation time is varied.

An important limitation of the system described here is the stop-flow valve. While smaller and lower power valves are available, no normally closed microfabricated valve is available that will meet the power budget specification for the instrument. A low-power silicon MEMS valve is under development for this project. Another important limitation is that only ambient-temperature operation is possible. The column ensemble can be heated and temperature programmed in a variety of ways, but columns with microfabricated heaters will be needed to achieve instrument size and power specifications. Silicon MEMS columns of the type used in this study but with microfabricated heaters and temperature sensors on the column chip have been successfully tested.

ACKNOWLEDGMENT

Funding for this work was provided by the University of Michigan Center for Wireless Integrated Microsystems (WIMS) through the Engineering Research Centers Program of the National Science Foundation under Award ERC-9986866. Additional support provided by Grant R01-OH03692 from the National Institute for Occupational Safety and Health of Centers for Disease Control and Prevention (NIOSH-CDCP).

Received for review November 1, 2004. Accepted January 16, 2005.

AC040174P