

## Characterization of Puff-by-Puff Resolved Cigarette Mainstream Smoke by Single Photon Ionization–Time-of-Flight Mass Spectrometry and Principal Component Analysis

THOMAS ADAM,<sup>\*,†,‡</sup> RICHARD R. BAKER,<sup>§,||</sup> AND RALF ZIMMERMANN<sup>†,‡,⊥</sup>

Analytical Chemistry, Institute of Physics, University of Augsburg, 86159 Augsburg, Germany, Institute of Ecological Chemistry, GSF–National Research Center for Environment and Health, 85764 Neuherberg, Germany, British American Tobacco, Research and Development Centre, Southampton SO15 8TL, United Kingdom, and BIfA–Bavarian Institute of Applied Environmental Research and Technology GmbH, Environmental Chemistry, 86167 Augsburg, Germany

Soft single photon ionization–time-of-flight mass spectrometry (SPI–TOFMS) and principal component analysis (PCA) were applied for the characterization and discrimination of the chemical patterns of all individual cigarette puffs from the 2R4F University of Kentucky research reference cigarette. The SPI–TOFMS was connected to a smoking machine, and 10 cigarettes were smoked under defined smoking conditions. A total of 41 detected mass signals could be clearly assigned to smoke constituents (e.g., unsaturated hydrocarbons, aromatic species, sulfurous compounds, and nitrogen-containing substances). For further analysis, the on-line recorded mass signals were added up for each cigarette puff resulting in a single summed mass spectrum for each puff. The so-achieved puff-by-puff resolved yields were additionally normalized by the corresponding total ion signal, which eliminated the influences of varying amounts of burnt tobacco. These values were incorporated into a PCA to find differences and similarities in the chemical patterns of the individual cigarette puffs. In addition, absolute (without normalization) and normalized puff resolved yields were used to clarify occurring trends. Thereby, it was shown that the chemical pattern of the first cigarette puff was very unique, whereby extraordinary high yields of unsaturated hydrocarbons are mainly responsible for this. Depending on the smoking procedure, the chemical pattern of the second puff can also be separated from the first and the third puff. In this case, nitrogen-containing substances play an important role. Puffs three to eight show only small but observable differences. These changes are greater influenced by oxygen-containing and sulfurous smoke constituents. The findings reveal that the overall chemical patterns of machine-smoked cigarette puffs vary quite a lot during the smoking process. This lets us assume that the burden of hazardous compounds for the human smoker also differs from puff to puff.

**KEYWORDS:** Single photon ionization; cigarette smoke; tobacco; principal component analysis

### INTRODUCTION

Cigarette smoke is a highly dynamic and very complex matrix consisting of more than 4800 constituents. Some substances are highly reactive, leading to a continuously changing mixture (1). The smoke is composed of a particulate phase and a gas phase, whereas many substances are partitioned between these two phases. Therein, the gas phase is comprised of approximately 400–500 individual compounds, and most of these are at trace

levels (1, 2). Cigarette smoke analysis is mostly done by using conventional off-line techniques (3). These methods can alter the smoke composition during sampling and analytical processing such as trapping, separation, and derivatization (4, 5). Furthermore, the results usually account for total yields in smoke from whole cigarettes. Therefore, fluctuations and variations in concentration during the smoking process are not resolved. However, this information is essential to understand the complex and often interrelated formation and decay mechanisms of many smoke constituents (6).

First investigations on the analysis within single cigarette puffs were carried out by Vilcins (7) and Ceschini and Lafaye (8). Over the years, several techniques have been applied for single puff or puff-by-puff characterization such as Fourier transform infrared spectroscopy (FTIR) (9, 10) and quantum

\* Corresponding author. Fax: +49 89 3187 3510. E-mail: thomas.adam@gsf.de.

<sup>†</sup> University of Augsburg.

<sup>‡</sup> Institute of Ecological Chemistry.

<sup>§</sup> British American Tobacco.

<sup>||</sup> Present address: The Langdales, Lime Walk, Dibden Purlieu, Southampton SO45 4RA, UK.

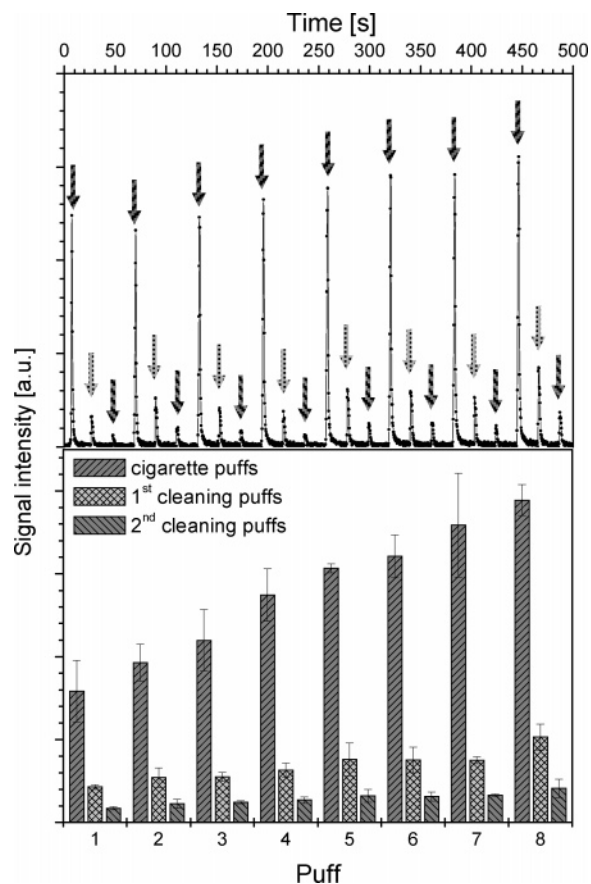
<sup>⊥</sup> Bavarian Institute of Applied Environmental Research and Technology.

cascade infrared laser spectroscopy (6, 11, 12) by Parrish and co-workers as well as quad quantum cascade laser spectrometry by Baren et al. (5). Plunkett et al. used a dual infrared tunable diode laser system (13, 14), whereas GC–MS was applied by Thomas and Koller (15), Li et al. (16), and Wagner et al. (17). In addition, Crooks and Lynn developed a technique for determining intrapuff nicotine yields (18).

Limiting factors for most of these approaches are either the low time resolution or the fact that only a few substances can be measured at the same time. Moreover, to obtain analytical information on smoke components relevant for human smokers, it is important to investigate relatively fresh smoke (ca. 1–2 s old), rather than smoke that has aged over a few minutes (19). Consequently, an analytical technique is required that can provide comprehensive real-time measurements of a wide range of smoke constituents. This technique should interfere as little as possible with the combustion and pyrolysis processes occurring in the cigarette.

Single photon ionization–time-of-flight mass spectrometry (SPI–TOFMS) has proven to be well-suited for time resolved analysis of gaseous and semivolatile compounds of the cigarette smoking process (20). Therein, vacuum ultraviolet (VUV) light laser pulses having a wavelength of 118 nm (10.49 eV) were used for the soft photoionization process of the organic molecules in the smoke. The advantage as compared to conventional ionization techniques such as electron impact (EI) is the fact that hardly any fragmentation occurs due to the little excess energy, which is transferred onto the generated ions. This enables the analysis and interpretation of complex samples containing large numbers of compounds such as cigarette smoke. The generated molecular ions are extracted into the flight tube of a reflectron time-of-flight mass spectrometer, which allows recording of complete mass spectra with a very high time resolution. Recently, the method was used to investigate the influence of different cigarette lighting devices on the chemical composition of the smoke (21). Moreover, quantification of several toxic and carcinogenic substances in mainstream smoke on a puff resolved basis was reported (22, 23). Mainstream smoke is the smoke that emerges from the mouth end of the cigarette during a puff and is inhaled by the smoker (1). Therein, it was demonstrated that many compounds feature a continuous increase from the first to the last puff. This behavior is due to a gradual reduction in tobacco length as the cigarette is consumed, which results in a decrease in filtration by the tobacco rod for species in the particulate phase of smoke and a decrease in air dilution and outward gaseous diffusion (24, 25). Condensation and evaporation reactions on the tobacco for compounds in the gas phase may also be significant (24, 25). In contrast, some substances show a completely different behavior by having the highest amounts in the first puff. This is likely to be related to the different combustion and pyrolysis conditions when the cigarette is lit. From the second puff onward, an increase in yield could be observed again as described earlier. However, it is possible that the overall chemical pattern of smoke constituents changes during the whole cigarette smoking process due to interrelated formation and decay mechanisms. These changes may be difficult to observe by the naked eye, and as a consequence, chemometric methods must be applied for their investigation.

In the framework of this work, we first report on the application of SPI–TOFMS and principal component analysis (PCA) for the investigation and characterization of all puffs of the cigarette smoking process. The aim is to characterize and compare the individual puffs by revealing similarities and



**Figure 1.** Conversion of time resolved into puff resolved data and illustration of smoking and cleaning puffs.

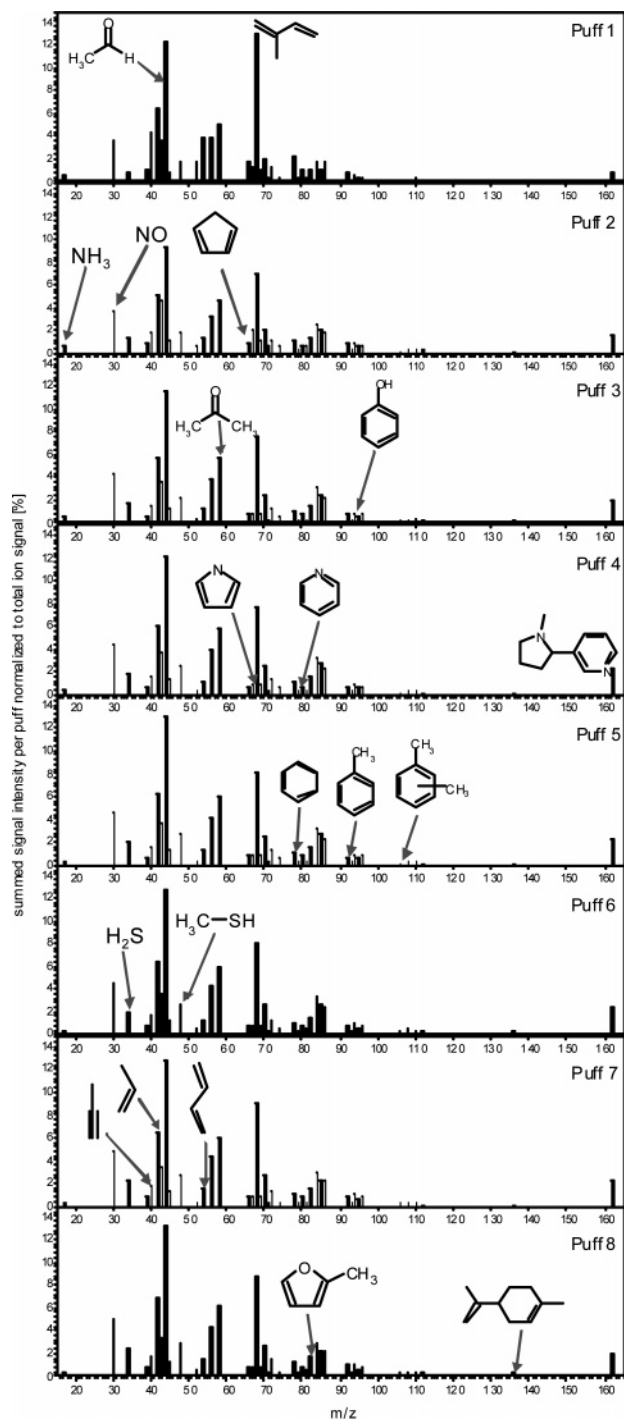
changes of the overall chemical pattern. These results may help to unravel the highly complex formation and decay mechanisms taking place when a cigarette is smoked.

## MATERIALS AND METHODS

**Chemicals and Materials.** Standard gases of benzene (10.0 ppm), toluene (9.3 ppm), and xylene (9.1 ppm) for the mass calibration of the time-of-flight mass spectrometer were purchased from Linde (Unterschleissheim, Germany). Xenon (purity 4.0) for VUV generation was supplied from Air Liquide (Munich, Germany). A deactivated fused silica capillary (i.d. 0.32 mm) was obtained from Restek (Bad Homburg, Germany). The cigarette investigated was the 2R4F Kentucky reference cigarette, which is available from the University of Kentucky, Kentucky Tobacco Research and Development Center (Louisville, KY).

**Smoking Procedure.** The cigarettes were stored for several days under controlled conditions of 60% relative air humidity and 22 °C according to the International Organization for Standardization (ISO) conditions (26). The smoking procedure was carried out by application of a custom-made smoking machine based on a Borgwaldt (Hamburg, Germany) single-port smoking machine. Modifications were necessary to reduce contamination and memory effects of the commercial smoking machine and are described in detail in ref 20. Cigarettes were lit with a Borgwaldt electric lighter and smoked under ISO conditions (35 mL puff volume, 2 s puff duration, one puff every 60 s) (26). Between the cigarette puffs, two cleaning puffs without cigarette were taken because even the modified smoking machine retained some smoke. This ensures that all remaining smoke was removed before the next smoking puff took place. When machine-smoked under ISO conditions, the 2R4F usually yielded between eight and nine puffs depending on the lighting behavior and burning characteristics. Therefore, only puffs one to eight were considered for the statistical evaluation. In total, 10 replicates were measured.

**SPI–TOFMS Analysis.** The smoking machine and the SPI–TOFMS instrument were connected by a heated sampling line



**Figure 2.** Puff resolved sum spectra of the 2R4F research cigarette normalized to total signal intensity.

(220 °C), within which ran a deactivated fused silica capillary (length ca. 1.5 m). In so doing, a small portion of smoke of about 8 mL/min was extracted and transferred into the ionization chamber of the mass spectrometer (residence time in sampling line < 1 s). The principle and setup of the home-built SPI-TOFMS is described in detail in refs 21, 27, and 28. The TOF mass spectra were recorded via two transient recorder PC cards (Aquiris, Switzerland, 250 MHz, 8 bit, 1 GS/s, 128 kb). In so doing, the two cards were operated at different gain settings. Thus, the recorded signal intensities were divided into two measurement ranges. All signal intensities were recorded by the first card, and additionally, very low signals up to a defined threshold were also recorded by the second card. This enables simultaneous recording of very low and high signal intensities with greater accuracy. In the framework of this study, the mass range was set to 5–170 *m/z*, and

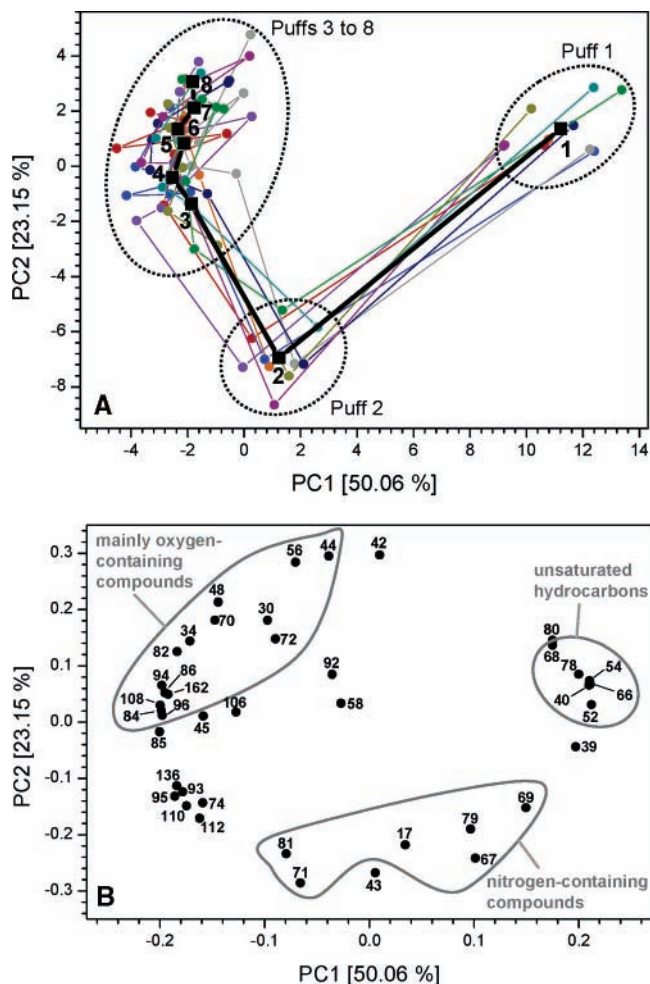
**Table 1.** Assignment of 41 Masses to Corresponding Cigarette Smoke Compounds (22)

<i>m/z</i>	compounds
17	NH <sub>3</sub>
30	NO
34	H <sub>2</sub> S
39	unidentified combustion fragment
40	propyne
42	propene
43	carbohydrate fragment: C <sub>3</sub> H <sub>7</sub> <sup>+</sup> , C <sub>2</sub> H <sub>3</sub> O <sup>+</sup>
44	acetaldehyde
45	dimethylamine, ethylamine
48	methanethiol
52	1-buten-3-yne,
54	1,3-butadiene, 1-butyne
56	2-propenal, butene, 2-methylpropene
58	acetone, propanal
66	cyclopentadiene
67	pyrrole
68	furan, isoprene, 1,3-pentadiene, cyclopentene
69	pyrroline
70	2-butenal, methyl vinyl ketone, methylbutene, pentene, butenone, 2-methyl-2-propenal
71	pyrrolidine
72	2-methylpropenal, 2-butanone, butanal
74	water-eliminated glycerol, tetrahydrofuran
78	benzene
79	pyridine
80	pyrazine
81	methylpyrrole
82	methylfuran, methylcyclopentene, cyclohexene, 2-cyclopenten-1-one
84	nicotine fragment, cyclopentanone, dimethylbutene, hexene, 3-methyl-3-buten-2-one
85	methylpyrrolidine, piperidine
86	methylbutanal, 3-methyl-2-butanone, pentanone, 2,3-butanedione
92	toluene
93	aniline, methylpyridine
94	phenol, 2-vinylfuran
95	pyridinol, ethylpyrrol, dimethylpyrrol
96	dimethylfuran, furfural
106	xylene, ethylbenzene, benzaldehyde
108	anisole, dimethylpyridine, methylphenol
110	dihydroxybenzene, 2-acetylfuran, methylfurfural
112	acetylcyclopentane, 2-hydroxy-3-methyl-2-cyclopenten-1-one
136	limonene, methoxybenzaldehyde, 2-ethyl-5-methylphenol
162	nicotine, anabasine

spectra were recorded with a laser repetition rate of 10 Hz. For the purposes of this study, three successive single laser shot mass spectra were averaged, resulting in a time resolution of 3.3 Hz. Data acquisition was done by a LabView-based (National Instruments, Austin, TX) custom written software package.

**Data Processing.** The data processing to obtain puff-by-puff resolved smoking profiles from the on-line recorded mass spectra is extensively described in ref 22 and visualized in **Figure 1**. Therein, the on-line recorded mass signals were added up for each individual cigarette puff resulting in a single summed mass spectrum for each puff. In the framework of this study, two approaches of data evaluation were carried out. First, the signals of the two cleaning puffs were added to the corresponding smoking puff since the levels of components in both the smoking puffs and the cleaning puffs are relevant to the human smoker. Second, the cleaning puffs were neglected, and only the smoking puffs without cleaning puffs were considered. Mean and standard deviation of the 10 replicates were calculated, and 41 mass signals, which could be clearly detected in the mass spectra, were selected for further analysis. The signal intensities per puff of both approaches (with and without cleaning puffs) were normalized to the corresponding total ion signal of the puff. This eliminates the influences of absolute mass signal values and enables the investigation of varying chemical patterns. Prior to the principal component analysis, autoscaling of the data set was carried out. Autoscaling is often useful when

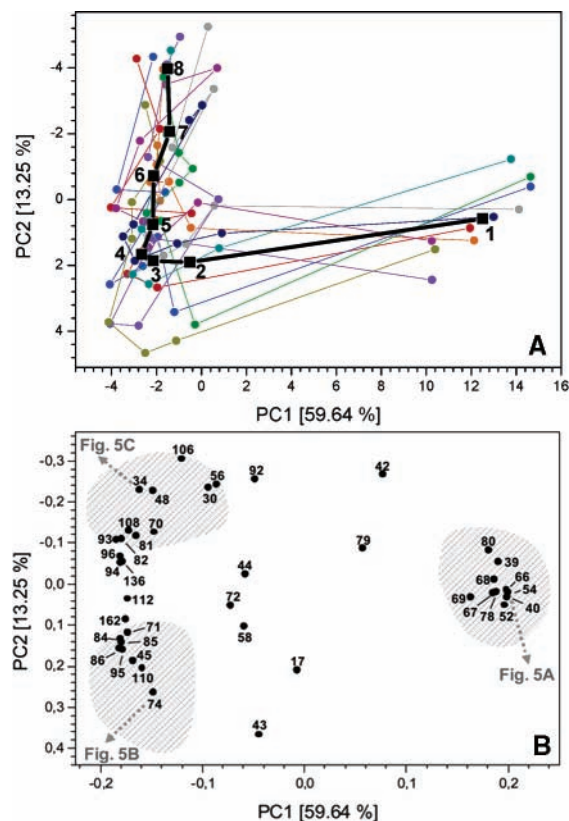




**Figure 3.** (A) Score-plot of the first and second principal components of the mean and 10 individual puff resolved cigarette smoke measurements (smoking puffs and cleaning puffs) (B) Loading-plot of the first and second principal components of the 10 puff resolved cigarette smoke measurements (smoking puffs and cleaning puffs).

variables span different ranges to make the variables of equal importance. This was done by mean centering the data (i.e., subtracting the mean and subsequent variance scaling, i.e., division by the standard deviation to make the data independent of scaling). The resultant puff resolved data sets of the 10 individual measurements were used to perform a PCA.

**Principal Component Analysis.** PCA basically seeks to reduce the dimensionality of a dataset consisting of a large number of interrelated variables, while retaining as much of the present variation as possible. This is achieved by transformation to a new set of variables, the so-called principal components (PCs), which are uncorrelated and ordered so that the first few components contain most of the variations of the entire original data set. The PCA is based on the covariance matrix of the entire data set. The eigenvectors of the covariance matrix are the loading vectors, which project the original data to the new space spanned by the principal components. The respective eigenvalues represent the fraction of the variance explained by the principal component. In many cases, a projection of the original data spanned by the first two PCs is sufficient. The outcome of PCA is usually depicted by two two-dimensional plots, the score-plot and the loading-plot. The loading-plot illustrates the influence of the original variables, here the mass signals, on the respective principal components. The score-plot shows the projected data, here the measurements, in the lower dimensional subspace defined by the PCs.



**Figure 4.** (A) Score-plot of the first and second principal components of the mean and 10 individual puff resolved cigarette smoke measurements (smoking puffs only). (B) Loading-plot of the first and second principal components of the 10 puff resolved cigarette smoke measurements (smoking puffs only).

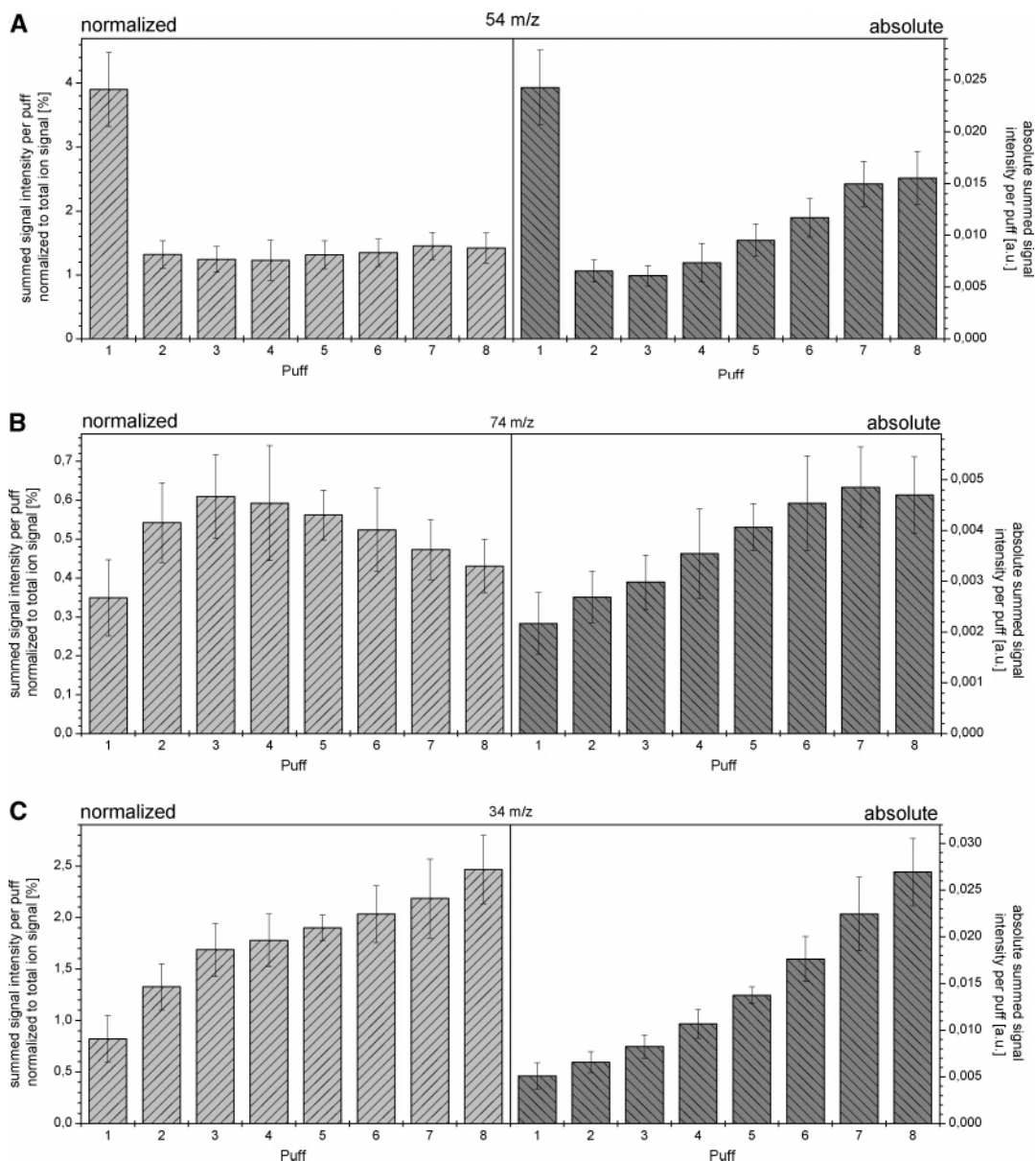
## RESULTS AND DISCUSSION

The averaged sum spectra of the first to the eighth puff of the 10 measurements (smoking puffs and cleaning puffs) are illustrated in **Figure 2**.

The signals are normalized to total ion signal and plotted with the same y-axis scaling to enable a direct comparison of the overall patterns. Some peaks are assigned to important cigarette smoke constituents such as ammonia (17 *m/z*), nitric oxide (30 *m/z*), hydrogen sulfide (34 *m/z*), acetaldehyde (44 *m/z*), butadiene (54 *m/z*), isoprene (68 *m/z*), benzene (78 *m/z*), pyridine (79 *m/z*), phenol (94 *m/z*), and nicotine (162 *m/z*). A list of all 41 masses considered together with the assignment to smoke compounds (22) can be found in **Table 1**.

In general, it can be seen in **Figure 2** that changes of the patterns occur but are difficult to interpret. Unsaturated hydrocarbons such as propyne (40 *m/z*), 1-buten-3-yne (52 *m/z*), butadiene (54 *m/z*), and isoprene (68 *m/z*) feature higher normalized yields in the first puff than in the second puff. The value of acetaldehyde (44 *m/z*) is lower in the second puff than in the others. Furthermore, the relative signal intensities of 34 *m/z* (hydrogen sulfide), 48 *m/z* (methanethiol), and 162 *m/z* (nicotine) rise with puff number. However, statistical methods are required to reveal more hidden variations. **Figure 3A** shows the score-plot of the first and second principal component of the PCA of the 10 individual measured cigarettes when the cleaning puffs were added to the smoking puffs.

It can be seen that the first puff is clearly separated on the first principal component (variance 50.06%), confirming the very unique chemical composition mentioned earlier. In addition, the



**Figure 5.** (A) Puff-by-puff resolved illustration of the first group of clustered compounds in the loading plot by means of 54  $m/z$  (butadiene). (B) Puff-by-puff resolved illustration of the second group of clustered compounds in the loading plot by means of 74  $m/z$  (3-hydroxy propanal). (C) Puff-by-puff resolved illustration of the third group of clustered compounds in the loading plot by means of 34  $m/z$  (hydrogen sulfide).

second puff is also separated but on the second principal component (variance 23.15%). This means that the chemical pattern of the second puff is not just different from the first puff but also from the following puffs three to eight. In contrast, the data points of these six puffs (three to eight) seem to form an undefined cluster. However, when incorporating the calculated mean (black dots and line) of the individual score values, even puffs three to eight show a trend and are separated on the second principal component. The black numbers refer to the puff numbers of the averaged score values. Plotting the first versus the third principal component confirms the described trends but does not give any additional information, subsequently, it is not shown here. According to these findings, all cigarette puffs have an individual chemical pattern. The first and second puff are very unique, whereas the variations within puffs three to eight are small. The corresponding loading-plot visualizes the influence of the 41 masses on the respective principal components illustrated in **Figure 3B**.

The loading-plot shows that the first puff is highly influenced by the masses 39  $m/z$ , 40  $m/z$ , 52  $m/z$ , 54  $m/z$ , 66  $m/z$ , 68  $m/z$ , 78  $m/z$ , and 80  $m/z$ . Almost all of these are unsaturated hydrocarbons, 80  $m/z$  (pyrazine) is a nitrogen-containing aromatic compound. As mentioned earlier, lighting the cigarette and heating the tobacco from ambient temperature to more than 900 °C (29) seems to enhance the formation of unsaturated species. Contamination by the lighting device can be excluded since an electric lighter was used. In contrast, the second cigarette puff was more influenced by nitrogen-containing species such as 17  $m/z$  (ammonia), 67  $m/z$  (pyrrole), 69  $m/z$  (pyrroline), 71  $m/z$  (pyrrolidine), 79  $m/z$  (pyridine), and 81  $m/z$  (methyl pyrrole). In addition, the clustered species in the bottom left corner have an effect on the separation of the second puff on the second principal component, two of them (93  $m/z$  and 95  $m/z$ ) also being nitrogen-containing smoke constituents. From the third puff onward, oxygen-containing compounds such as 30  $m/z$  (nitrogen oxide), 44  $m/z$  (acetaldehyde), 56  $m/z$  (mainly

acrolein), 70 *m/z* (mainly crotonaldehyde), and 94 *m/z* (phenol) play a greater role, but sulfurous species (34 *m/z* and 48 *m/z*) and nicotine peaks (162 *m/z* and 84 *m/z*) can also be found.

The score- and loading-plots of the PCA when the cleaning puffs are not added to the smoking puffs (Figure 4A,B) look very similar regarding the clear separation of the first puff on the first principal component (variance 59.64%).

However, two nitrogen-containing unsaturated species, 67 *m/z* (pyrrole) and 69 *m/z* (pyrroline), enlarge the cluster of compounds that is responsible for the separation. Thus, the group of smoke constituents that separated the second puff from the first and third puff when the cleaning puffs were considered (Figure 3A,B) have almost vanished. Only 43 *m/z* (carbohydrate pyrolysis fragment) and 17 *m/z* (ammonia) remain. A separation to the following puffs is visible but with approximately the same magnitude as for puffs three to eight (variance of the second principal component 13.25%). Thus, when the cleaning puffs are not added to the smoking puffs, the clear separation of the second puff is no longer observed in the score plot. Looking at the puff resolved data of the cleaning puffs revealed (not shown here) that these masses, which separated the second puff from the other puffs in Figure 3A,B, feature rather high signal intensities in the first cleaning puff of the second smoking puff. In all other cleaning puffs, the signal intensities are not exceptionally high. The reasons for this are unclear. However, it has to be stressed that the modified smoking machine has a much lower dead volume than most commercial smoking machines. For commercial machines, these effects might be even stronger.

In the following discussion, the puff-by-puff behavior of the clustered masses is considered by focusing on three different areas of the loading plot of Figure 4B (greyish areas). In so doing, the averaged normalized and averaged absolute puff yields of one selected compound each including standard deviations are illustrated in Figures 5A–C. It should be borne in mind that the PCA was carried out by the individual measurements. The standard deviations of all 10 measurements were influenced by the fact that the same puff number of different measurements can originate by a slightly different length of the cigarette rod depending on lighting behavior and burning characteristics of the cigarettes. This is confirmed by the fact that the 2R4F cigarette generally results in eight or nine puffs when smoked under ISO conditions. This variation of the cigarette rod will influence the chemical smoke composition and thus increases the corresponding standard deviation, although all individual measurements exhibit almost exclusively the same trends.

Figure 5A represents the unsaturated hydrocarbons located on the right-hand side of the loading-plots using 54 *m/z* (butadiene) as an example. This group of compounds is mainly responsible for the separation of the first puff on the first principal component. The normalized illustration on the left clearly shows that the signal intensity of the first puff is much higher than for the following puffs. Puffs two to eight feature about the same normalized yields. The absolute values on the right also exhibit the very unique behavior of the first puff. The yields of the following puffs are much lower but steadily increase from the second puff onward. The fact that the normalized yields of the second to the eighth puff do not change reveals that the influence of these species on the chemical pattern of all accessible compounds is always similar except for the first puff. Subsequently, the rising yields of the absolute values mainly originate by physical reasons (i.e., the decreasing ventilation of the decreasing cigarette rod and condensation/

desorption effects, which were mentioned earlier). A chemical influence of these compounds on the changing smoke pattern from the second puff onward is not observable.

The second class, shown in Figure 5B using 74 *m/z* (probably 3-hydroxy propanal) as an example, has a different behavior. Although the absolute values exhibit a rather steady increase in puff yields, the normalized signal intensities feature an increase in intensity from the first to the third puff followed by a decrease to the last puff. Therefore, this puff behavior is rather different as compared to the former one. The influence of these compounds on the chemical pattern seems to change during the smoking process with respect to the other accessible species.

In turn, Figure 5C illustrates another puff behavior demonstrated by 34 *m/z* (hydrogen sulfide). This class of substances shows a more or less steady increase in normalized as well as absolute signal intensities from the first to the eighth puff. Subsequently, these compounds gain importance with respect to the overall chemical pattern of observed species and influence the later puffs more than the earlier ones.

It can be said that the chemical pattern of the observed smoke constituents changes significantly during the cigarette smoking process from puff to puff. Almost every puff features a characteristic chemical composition. In this way, the varying influence of certain compound classes can be clearly seen. In this context, the composition of the first puff is unique. This is most likely related to the different combustion conditions when the cigarette is lit. The separation of the second puff is also very clear but only if the cleaning puffs are included. For puffs three to eight, a change in the chemical pattern is observable but to a much lower extent. Interrelated reactions between involved species are a possible reason for all these changes. Transferring these findings onto the human smoker, it is likely that the burden of hazardous compounds inhaled by the smoker also differs from puff to puff. Therefore, measurements with test smokers are planned to investigate the real impact of each cigarette puff on the human smoker.

## LITERATURE CITED

- (1) Baker, R. R. *Smoke Chemistry*. In *Tobacco: Production, Chemistry, and Technology*; Davis, L. D., Nielsen, M. T., Eds.; Blackwell Science: Oxford, 1999; pp 398–439.
- (2) Gaworski, C. L.; Dozier, M. M.; Eldridge, S. R.; Morrissey, R.; Rajendran, N.; Gerhart, J. M. Cigarette smoke vapor-phase effects on the rat upper respiratory tract. *Inhal. Toxicol.* **1998**, *10*, 857–873.
- (3) Green, C. R.; Rodgman, A. The Tobacco Chemists' Research Conference: a half century forum for advances in analytical methodology of tobacco and its products. *Recent Adv. Tob. Sci.* **1996**, *22*, 131–304.
- (4) Holtzclaw, J.; Rose, S.; Wyatt, J.; Rounbehler, D.; Fine, D. Simultaneous determination of hydrazine, methylhydrazine, and 1,1-dimethylhydrazine in air by derivatization/gas chromatography. *Anal. Chem.* **1984**, *56*, 2952–2956.
- (5) Baren, R. E.; Parrish, M. E.; Shafer, K. H.; Harward, C. N.; Shi, Q.; Nelson, D. D.; McManus, J. B.; Zahniser, M. S. Quad quantum cascade laser spectrometer with dual gas cells for the simultaneous analysis of mainstream and sidestream cigarette smoke. *Spectrochim. Acta, Part A* **2004**, *60*, 3437–3447.
- (6) Shi, Q.; Nelson, D. D.; McManus, J. B.; Zahniser, M. S.; Parrish, M. E.; Baren, R. E.; Shafer, K. H.; Harward, C. N. Quantum cascade infrared laser spectroscopy for real-time cigarette smoke analysis. *Anal. Chem.* **2003**, *75*, 5180–5190.
- (7) Vilcins, G. Determination of ethylene and isoprene in the gas phase of cigarette smoke by infrared spectroscopy. *Beitr. Tabakforsch. Int.* **1975**, *8*, 181–185.



- (8) Ceschini, P.; Lafaye, A. Evolution of the gas-vapor phase and the total particulate matter of cigarette smoke in a single puff. *Beitr. Tabakforsch. Int.* **1976**, *8*, 378–381.
- (9) Parrish, M. E.; Lyons-Hart, J. L.; Shafer, K. H. Puff-by-puff and intrapuff analysis of cigarette smoke using infrared spectroscopy. *Vib. Spectrosc.* **2001**, *27*, 29–42.
- (10) Li, S.; Banyasz, J. L.; Parrish, M. E.; Lyons-Hart, J.; Shafer, K. H. Formaldehyde in the gas phase of mainstream cigarette smoke. *J. Anal. Appl. Pyrolysis* **2002**, *65*, 137–145.
- (11) Parrish, M. E.; Harward, C. N.; Vilcins, G. Simultaneous monitoring of filter ventilation and a gaseous component in whole cigarette smoke using tunable diode laser infrared spectroscopy. *Beitr. Tabakforsch. Int.* **1986**, *13*, 169–181.
- (12) Parrish, M. E.; Harward, C. N. Measurement of formaldehyde in a single puff of cigarette smoke using tunable diode laser infrared spectroscopy. *Appl. Spectrosc.* **2000**, *54*, 1665–1677.
- (13) Plunkett, S.; Parrish, M. E.; Shafer, K. H.; Nelson, D.; Shorter, J.; Zahniser, M. Time resolved analysis of cigarette combustion gases using a dual infrared tunable diode laser system. *Vib. Spectrosc.* **2001**, *27*, 53–63.
- (14) Plunkett, S.; Parrish, M. E.; Shafer, K. H.; Shorter, J. H.; Nelson, D. D.; Zahniser, M. S. Hydrazine detection limits in the cigarette smoke matrix using infrared tunable diode laser absorption spectroscopy. *Spectrochim. Acta, Part A* **2002**, *58*, 2505–2517.
- (15) Thomas, C. E.; Koller, K. B. Puff-by-puff mainstream smoke analysis by multiplex gas chromatography–mass spectrometry. *Beitr. Tabakforsch. Int.* **2001**, *19*, 345–351.
- (16) Li, S.; Olegario, R. M.; Banyasz, J. L.; Shafer, K. H. Gas chromatography–mass spectrometry analysis of polycyclic aromatic hydrocarbons in a single puff of cigarette smoke. *J. Anal. Appl. Pyrolysis* **2003**, *66*, 156–163.
- (17) Wagner, K. A.; Higby, R.; Stutt, K. Puff-by-puff analysis of selected mainstream smoke constituents in the Kentucky reference 2R4F cigarette. *Beitr. Tabakforsch. Int.* **2005**, *21*, 273–279.
- (18) Crooks, E. L.; Lynn, D. The measurement of intrapuff nicotine yield. *Beitr. Tabakforsch. Int.* **1992**, *15*, 75–86.
- (19) Baker, R. R.; Proctor, C. J. *2001—A smoke odyssey*; Conference Proceedings of the 2001 Coresta Meeting: Xian, China, 2001.
- (20) Mitschke, S.; Adam, T.; Streibel, T.; Baker, R. R.; Zimmermann, R. Application of time-of-flight mass spectrometry with laser-based photo-ionization methods for time resolved on-line analysis of mainstream cigarette smoke. *Anal. Chem.* **2005**, *77*, 2288–2296.
- (21) Adam, T.; Baker, R. R.; Zimmermann, R. Investigation, by single photon ionization (SPI)—time-of-flight mass spectrometry (TOFMS), of the effect of different cigarette-lighting devices on the chemical composition of the first cigarette puff. *Anal. Bioanal. Chem.* **2007**, *387*, 575–584.
- (22) Adam, T.; Mitschke, S.; Streibel, T.; Baker, R. R.; Zimmermann, R. Quantitative puff-by-puff resolved characterization of selected toxic compounds in cigarette mainstream smoke. *Chem. Res. Toxicol.* **2006**, *19*, 511–520.
- (23) Adam, T.; Mitschke, S.; Streibel, T.; Baker, R. R.; Zimmermann, R. Puff-by-puff resolved characterisation of cigarette mainstream smoke by single photon ionization (SPI)—time-of-flight mass spectrometry (TOFMS): Comparison of the 2R4F research cigarette and pure Burley, Virginia, Oriental, and Maryland tobacco cigarettes. *Anal. Chim. Acta* **2006**, *572*, 219–229.
- (24) Baker, R. R.; Crellin, R. A. The diffusion of carbon monoxide out of cigarettes. *Beitr. Tabakforsch. Int.* **1977**, *9*, 131–140.
- (25) Baker, R. R.; Robinson, D. P. Tobacco combustion—the last 10 years. *Recent Adv. Tob. Sci.* **1990**, *16*, 3–101.
- (26) Baker, R. R. The development and significance of standards for smoking-machine methodology. *Beitr. Tabakforsch. Int.* **2002**, *20*, 23–41.
- (27) Mühlberger, F.; Hafner, K.; Kaesdorf, S.; Ferge, T.; Zimmermann, R. Comprehensive on-line characterization of complex gas mixtures by quasi-simultaneous resonance enhanced multiphoton ionization, vacuum-UV single photon ionization, and electron impact ionization in a time-of-flight mass spectrometer: Setup and instrument characterization. *Anal. Chem.* **2004**, *76*, 6753–6764.
- (28) Cao, L.; Mühlberger, F.; Adam, T.; Streibel, T.; Wang, H. Z.; Kettrup, A.; Zimmermann, R. Resonance-enhanced multiphoton ionization and VUV-single photon ionization as soft and selective laser ionization methods for on-line time-of-flight mass spectrometry: investigation of the pyrolysis of typical organic contaminants in the steel recycling process. *Anal. Chem.* **2003**, *75*, 5639–5645.
- (29) Baker, R. R. Temperature variation within a cigarette combustion coal during the smoking cycle. *High Temp. Sci.* **1975**, *7*, 236–247.

---

Received for review August 16, 2006. Revised manuscript received January 17, 2007. Accepted January 20, 2007.

JF062360X