On-Line Aerosol Characterization within Exposure Systems Using Soft Ionization Time of Flight Mass Spectroscopy

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Introduction

The comprehensive understanding of the biological responses to *in vitro* aerosol exposures requires knowledge of the chemical composition of the test aerosol. The term test aerosol thereby refers to what gets into direct contact with the biological test system. Since between generation and interaction with a biological test system, an aerosol may be changed due to interactions with the used aerosol exposure system and due to ageing, it is not necessarily the same as the aerosol originally generated. Aerosol characterization in close proximity to the biological test system is therefore required.

The challenge thereby is to not disturb the exposure or the biological test system, whilst still reaching a high analytical sensitivity, selectivity and accuracy.
We developed a procedure for using a Single Photon Ionization Time of Flight (SPI TOF) Mass Spectrometer (Photonion GmbH, Schwerin, Germany) for the on-line chemical characterization of diluted tobacco product derived aerosols within the Vitrocell 24/48 aerosol exposure system. A physical system setup and procedures for aerosol sampling and the quantification of eight targeted smoke constituents were established and tested.

Equipment, Materials and Methods

The Vitrocell 24/48 aerosol exposure system (Figure 1): The test aerosol (in this work smoke generated from 3R4F reference cigarettes (University of Kentucky) according to the Health Canada smoking regime (Health Canada Test Method T-115;1999) or aerosols generated by electronic cigarettes) passes through a dilution system. It is serially diluted and sampled into exposure trumpets projecting into the exposure chambers. In each dilution row, one sampling line allows on-line quantification of aerosol mass deposition by Quartz Crystal Microbalances (QCM). The volume flow rate through the exposure trumpets and the QCM channels are kept at 2 mL/minute. The dilution airflow rates applied in the present work are indicated in Figure 1.

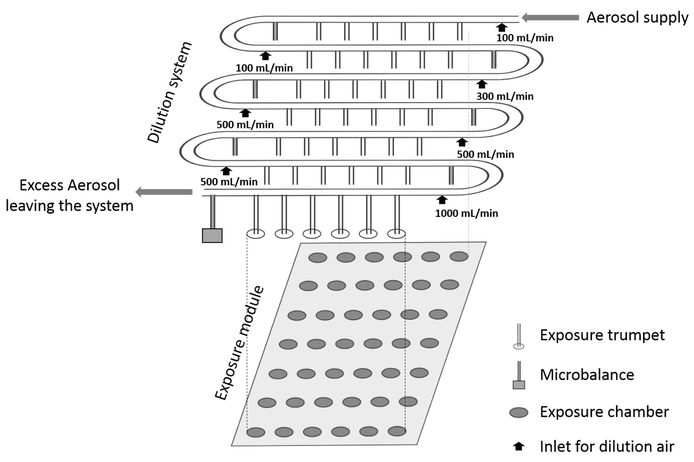

Figure 1: Schematic representation of the Vitrocell 24/48 aerosol exposure system. Only seven of the eight available exposure rows are shown, row eight is usually used for negative controls (exposure to clean air) and is not connected to the aerosol supply.

The Photonion SPI TOF-MS (Figure 2): The heated sampling capillary takes samples of 3 – 5 mL/minute. The samples are ionized by VUV light of ~120-160 nm (ionization energy of ~10.3 eV) and enter the TOF by linear extraction. Mass spectra are reported at a frequency of 1 Hz, the covered mass range is 10-2000 m/z.
Absolute quantification is based on compound specific cross sections (ionizabilities) relative to toluene, determined using 100 ppm reference gases.
Photo-ionization results in only limited fragmentation of analytes. Known aerosol constituents can therefore be identified based on their molecular mass (⟶ risk of biased quantification in presence of isobaric molecules).

Sampling within the Vitrocell 24/48 aerosol exposure system (Figure 3): The sampling capillary (heated to 280°C) was directly inserted into the tube connecting the dilution system to the QCM modules. Special holders for the transfer line were developed for this purpose. The length of the uncovered (not heated) capillary segement could be kept below 5 mm, thereby avoiding aerosol condensation and clogging.

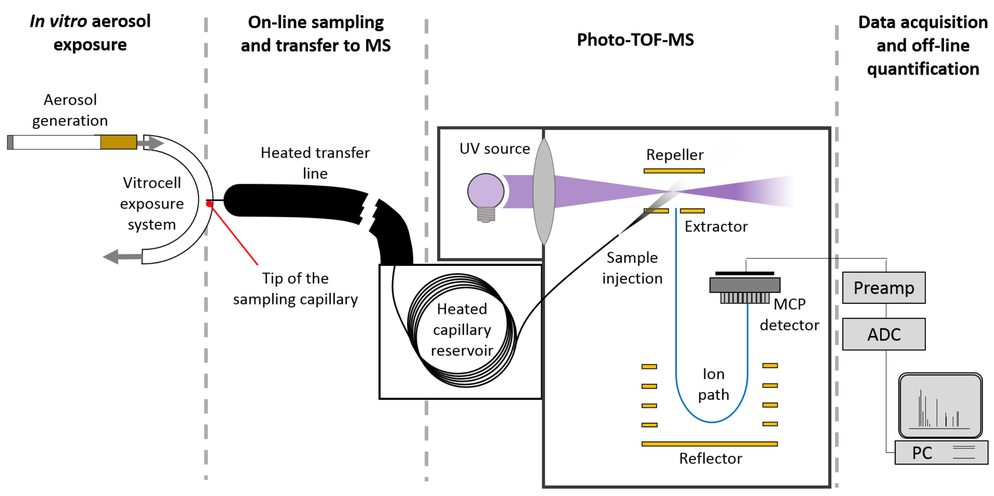

Figure 2: Schematic representation of the Photonion Photo-TOF MS and its connection to the Vitrocell 24/48 aerosol exposure system.

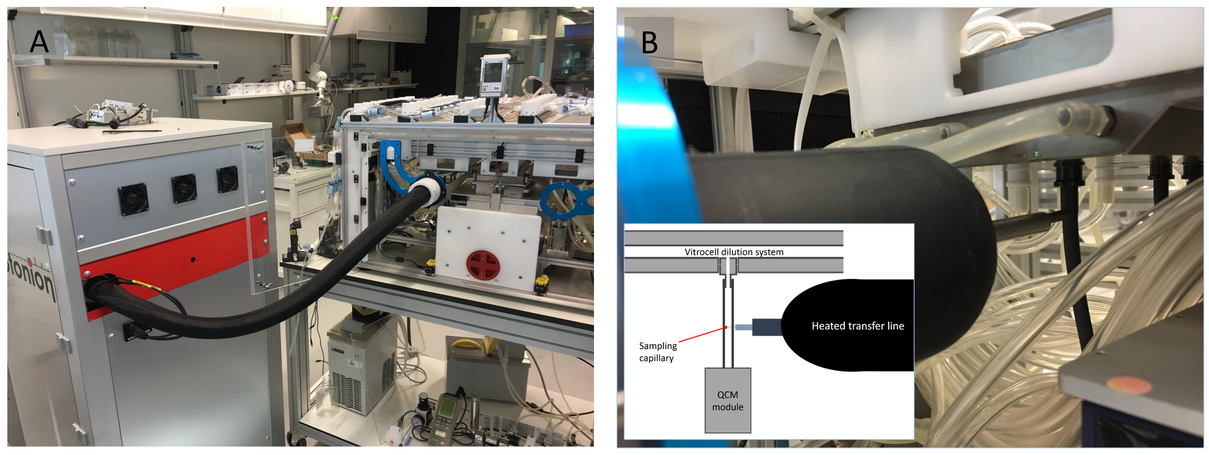

Figure 3A: The heated transfer line connecting the Photonion Photo TOF-MS (left in the picture) to to the Vitrocell 24/48 aerosol exposure system (right in the picture). The holder designed to fix the heating line at the Vitrocell system is visible (blue). It fixes the heated transfer line in a position that allows stably introducing the sampling capillary into the tubings that connect the dilution system to QCM modules. **Figure 3B** shows the position at which sampling occurred. The tube wall was pierced by the sampling capillary, which was inserted into the tube so samples were taken approximately in the center of the tube.

Results and Conclusions

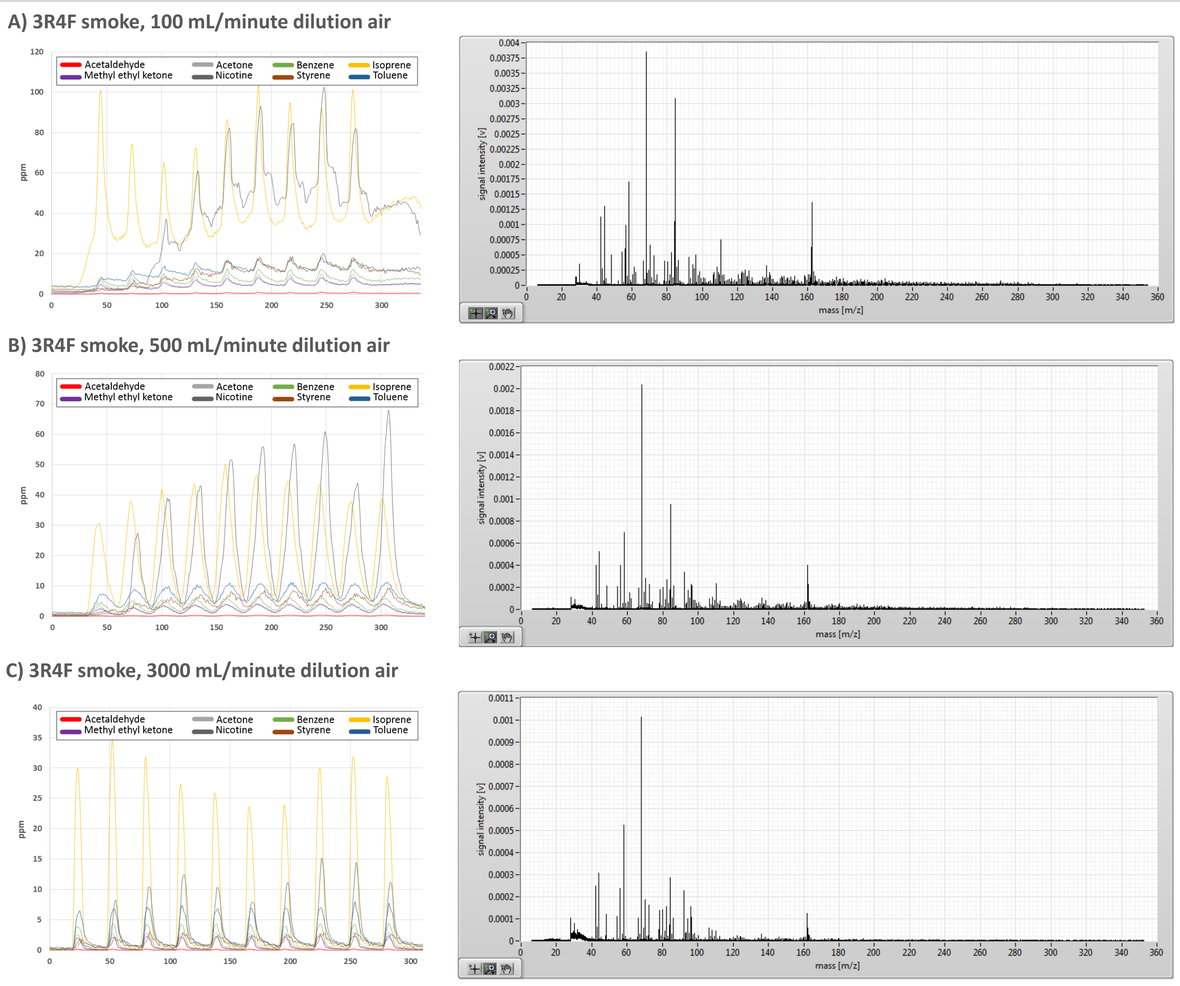

Figure 4: Time profile of the sampling showing ppm of eight targeted 3R4F smoke constituents at a resolution of 1 Hz (left side) and mass spectra (right side) measured at dilution air flow rates of **A)** 100 mL/minute, **B)** 500 mL/minute and **C)** 3000 mL/minute. The mass spectra in each case show one single spectrum, taken at the peak of the fifth puff.

Table 1: Masses of the targeted 3R4F smoke constituents reaching the exposure chambers[a]. Only values for highly diluted smoke are listed, the calculated dilution ratios and the observed decreases in concentration are listed for each dilution step. The table further shows a comparison to expected yields per cigarette and the according delivery efficiencies. The molecular masses are listed for assisting peak identification in Figure 4.

3R4F Smoke constituent	Total mass sampled into exposure chamber[a] (µg/3R4F cig)							Predicted yield/cig[b] at 3000 mL/minute (µg/3R4F cig)	Delivery efficiency at 3000 mL/min	Molecular mass (g/mol)
	at 1000 mL/ minute 29% smoke	x 0.74	at 1500 mL/ minute 22% smoke	x 0.79	at 2000 mL/ minute 17% smoke	x 0.71	at 3000 mL/ minute 12% smoke			
Acetaldehyde	4.98	x 0.72	3.57	x 0.70	2.49	x 0.71	1.77	0.73	2.43	44
Acetone	1.17	x 0.70	0.83	x 0.71	0.58	x 0.72	0.42	0.33	1.26	58
Benzene	0.12	x 0.73	0.09	x 0.72	0.06	x 0.73	0.04	0.06	0.77	78
Isoprene	0.97	x 0.69	0.67	x 0.72	0.48	x 0.71	0.34	0.61	0.56	68
Methyl ethyl ketone	0.39	x 0.72	0.28	x 0.71	0.20	x 0.73	0.15	0.09	1.56	72
Nicotine	0.45	x 0.72	0.33	x 0.64	0.21	x 0.80	0.17	1.15	0.15	162
Styrene	0.02	x 0.69	0.01	x 0.76	0.01	x 0.77	0.01	0.01	0.87	104
Toluene	0.23	x 0.71	0.16	x 0.77	0.13	x 0.75	0.09	0.10	0.99	92

a) The sampling line of the QCM chambers is considered equivalent to the exposure trumpets
b) Based on Eldridge et al. Regulatory Toxicology and Pharmacology 71 (2015): 409 - 527 and orrected for the sampling volume flow rate (2 mL/minute)

- **A setup for sampling and analyzing complex aerosols on-line during exposures was established**
- **Quantitative data for eight targeted aerosol constituents were obtained**
  - Aerosol dilution is reflected by the measured concentrations
  - Calculated delivery efficiencies are not commonly equal to 1, which can be attributed to:
    i) Presence of isobaric molecules (⟶ delivery efficiency > 1)
    ii) Losses in the Vitrocell system due to condensation (⟶ delivery efficiency < 1)
    iii) Selective sampling into sampling capillary
- **The puffing profile could be resolved at low aerosol concentrations**
  - Puff-wise chemical aerosol analysis is possible
  - With increasing aerosol concentration the resolution decreases drastically (puff-to-puff carry over)
- **No compouds of molecular masses higher than 200 Da were detected in significant amounts**
  - These compounds are potentially lost in the Vitrocell system due to condensation
- **Future steps:**
  - Verification of complete aerosol sampling at capillary tip
  - Increasing the set of targeted compounds
  - Increasing specificity, *e.g.* by identification of mass fingerprints for compounds for which fragmentation occurs

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Competing Financial Interest
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