Quantitative trace gas analysis of the anesthetic isoflurane using the FT-IR gas analyzer MATRIX II-MG5

Application Note M147

Introduction

Isoflurane (100% (RS)-1-chloro-2,2,2-trifluoroethyl difluoromethyl ether, CAS# 26675-46-7, molecular weight 184.5 g/mol, density 1.496 mg/µL at 20 °C) is an inhalation anesthetic for animals, in particular for dogs, cats and mice. Isoflurane is a liquid at room temperature (25 °C) with a vapor pressure of around 400 mbar and a boiling point of 48.5 °C. Isoflurane is vaporized in a controlled manner in an oxygen stream. With half-closed rebreathing systems, evaporator gas flows in the range of 1 L/min are applied with isoflurane volume fractions of 1.5 – 3% by volume (evaporation rate 75 – 150 µL/min).

Species	Initiation	Preservation
Cats	< 4.0%	1.5% – 3.0%
Dogs	< 5.0%	1.5% – 1.8%

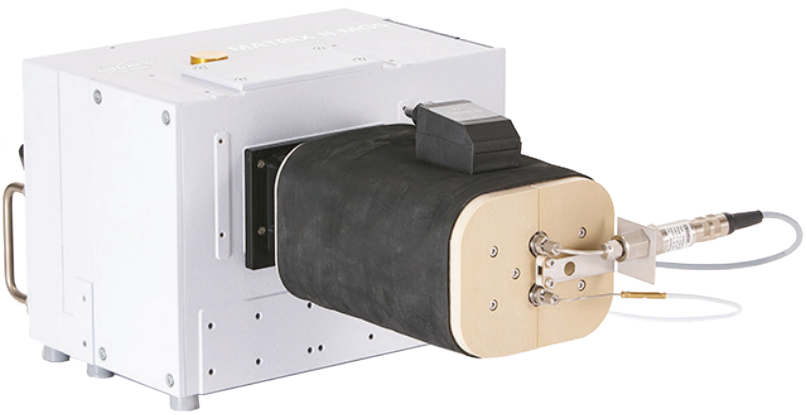
Table 1
Initiation and maintenance of anesthesia; volume fractions of isoflurane in oxygen.

Due to the high volatility of isoflurane, high levels of workplace exposure may occur during use. The recommended maximum occupational exposure for an assumed working time of 8 hours is in the range of 10 – 50 ppm. This relatively high volume fraction can easily be quantitatively tested with the sub-ppm sensitivity of the MATRIX II-MG5.

As a basis for the gas analytical determination, a reference spectrum was first recorded with the VERTEX 80 FT-IR; this barometric calibration provides accuracy better than 2 vol%.

This reference spectrum was then used to create an analysis method for the OPUS GA analysis software. For quantitative verification of the analytical method, the following measurements were carried out:

- Injection of isoflurane into a dry and humidified air stream.
- Determination of the detection limit and water vapor cross sensitivity.
- Verification of detection limits in outside air.
- Discontinuous injection of constant volumes in the dry air stream (quantification).
- Analysis of the volume fractions (ppm) and amounts of substance (µL) after release of small amounts of isoflurane in a closed room.



MATRIX II-MG5 gas analyzer with 5 m gas cell.

Experiments and Measurement Results:

Determination of the detection limit

The 5 m gas cell of the MATRIX II-MG is flowed through with a dry air flow of 10 to 20 L/min (mass flow controller up to 50 L/min). Isoflurane and downstream water are injected at two upstream injectors with the aid of gas-tight syringes and syringe pumps.

Note: When humidifying the sample gas flow, it should be noted that the water volume flow additionally dilutes the isoflurane sample. The volume fraction of the sample decreases by x% as the moistening increases the water content from 0 to x vol%, e.g. the isoflurane volume fraction falls to 99% of its value when the water volume fraction is increased from 0 – 1%. A relative humidity of 50% (at 25°C and 1013 mbar) equals 1.56 vol% = 15,600 ppm. Only deviations in the isoflurane volume fraction other than -1.6% are attributable to analytical cross-sensitivity to water.

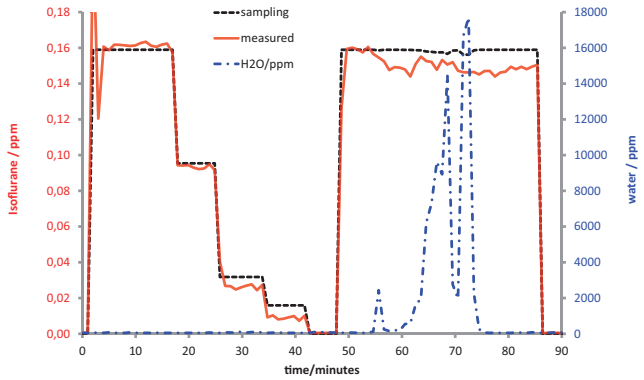


Fig. 1
FT-IR readings (OPUS GA) and setpoints (volumetric calibration) for isoflurane in outdoor air. The detection limit is in the range of 20 ppb.

Verification of detection limits in outside air

In this experiment, outside air is sucked through the gas cell via a membrane pump. The reference measurement was made for outside air and isoflurane injected in front of the gas cell with a syringe pump. With a rotameter at the outlet of the diaphragm pump, the stability of the volume flow was roughly checked. The effective volume flow was calibrated to the FT-IR analysis value (OPUS GA) of 0.59 ppm to 539 sccm. With a gradual reduction of the injection rate, a detection limit of about 20 ppb can be derived from the FT-IR analysis values.

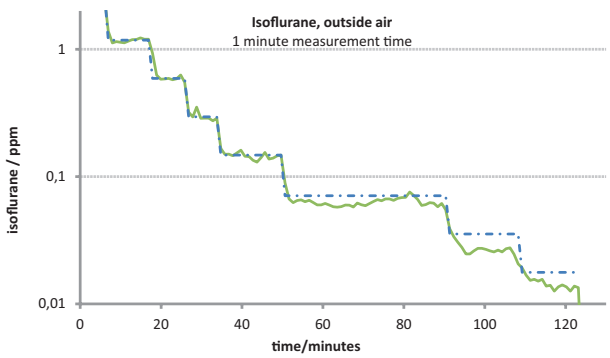


Fig. 2
F-TIR measured values and setpoints for isoflurane in outside air (measuring time 1 min).

Table 2
Mean values, standard deviation (rms) and expected values for the dilution series of isoflurane in outside air according to Fig. 2 (measuring time 1 min, spectral resolution 0.5 cm^{-1}).

Isofluorane			
measured / ppm	**rms / ppm**	**rms%**	**expected / ppm**
1.17	0.04	3.0	1.1
0.59	0.02	3.6	0.59
0.30	0.02	7.9	0.29
0.15	0.01	5.6	0.15
0.063	0.004	6.4	0.071
0.027	0.002	8.3	0.035
0.014	0.001	7.1	0.018

Determination of the amount of substance

If the carrier gas flow is sufficiently well known, the FT-IR analysis values can be integrated in time to a total amount of substance. The accuracy of the result allows a statement about the accuracy of the FT-IR analysis values. For this experiment, multiple defined volumes of 0.2, 1 and 5 µL of isoflurane were injected into a defined airflow using a syringe pump. The carrier gas flow (dry air) was monitored via a mass flow controller with a max. volume flow (final value) of 1000 sccm (MFC1) and 50000 sccm (MFC2). The accuracy of the MFC is according to the manufacturer 0.5% of the measured value and 0.2% of the final value, i.e., 0.7% for 1000 sccm (MFC1) and 1.5% for 10000 scm (MFC2). Significantly larger deviations can be attributed to the FT-IR gas analysis (OPUS GA, < 2%) or the experimental setup (for example, faulty injection, leakage currents).

The integrated FT-IR analysis values ("analyzed" see Table 3) show deviations in the range of 2 – 4% and are still within the expected confidence interval.

Table 3
Injected and analyzed amounts of isoflurane in µL (liquid phase).

Isofluorane n µL			
sampled / µL	**analyzed / µL**	**deviation / %**	**flow / sccm**
1.6	1.63	1.6	1000 MFC1
11	10.6	-3.5	10000 MFC2
50	50.8	1.6	1000 MFC1

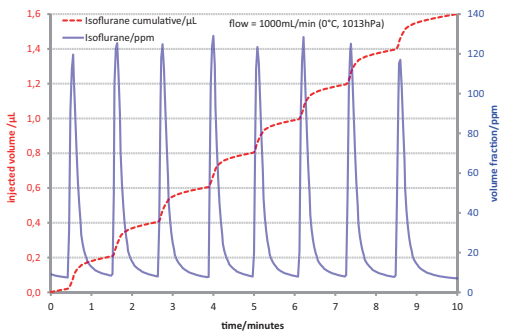


Fig. 3 (left)
Measured volume fractions of isoflurane (blue, right ordinate) and derived quantities (red, left ordinate). Injected volumes 8 × 0.2 µL = 1.6 µL @ 1000 sccm.

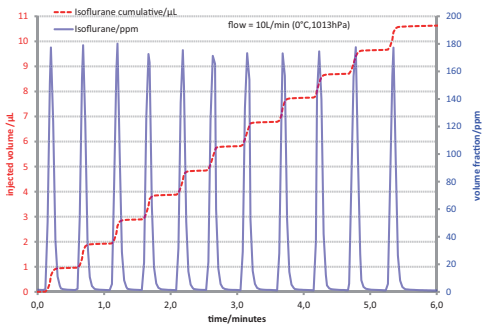


Fig. 4 (right)
Measured volume fractions of isoflurane (blue, right ordinate) and derived amounts (red, left ordinate). Injected volumes 11 × 1 µL = 11 µL @ 10,000 sccm.

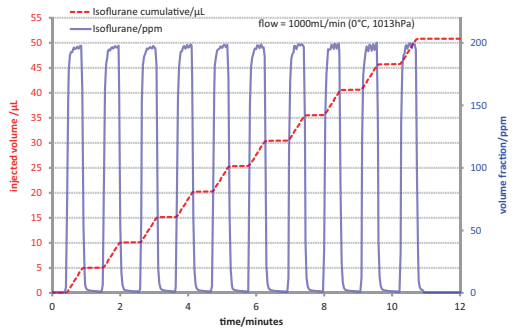


Fig. 5 (below)
Measured volume fractions of isoflurane (blue, right ordinate) and derived quantities (red, left ordinate). Injected volumes 10 x 5 µL = 50 µL @ 1000 sccm.

Analysis of the volume fractions (ppm) and amounts of substance (µL) after release of small amounts of isoflurane in a closed room

For the anesthesia devices, leakage rates of < 50 mL/min (maximum 150 mL/min) should be achieved; for 1 vol% of isoflurane this release rate corresponds to less than 150 µL of fluid within 1 h.

In a space of 5 m x 7 m x 3 m = 105 m^3, the vaporization of this amount of material would nominally produce a volume fraction of 0.28 ppm (at 25 °C and 1013 mbar). In this experiment, 50 µL and 200 µL of isoflurane were released and the time course of the volume fractions was measured (see Figure 6).

Nominally, the evaporation of 50 µL and 200 µL of isoflurane in 105 m^3 (at 25 °C and 1013 mbar) gives average volume fractions of 0.11 ppm and 0.44 ppm, 20 – 30% less than the initial peak values of 0.14 ppm and 0.6 ppm (s. Figure 6).

After the release of 50 µL and 200 µL of isoflurane, the mass flow can be integrated to 0.06 µLand 0.19 µL. From the ratio of sampled volume (270 L and 130 L) and the total volume of 100 m^3, a total amount of 22 µL and 146 µL can be calculated. This allows the magnitude of the amount of released material to be derived experimentally.

	lab volume / 100 m^3	
probed volume at end time / m^3	0.27	0.13
measured amount at end time / µL	0.058	0.19
estimated amount / µL	22	146
released isoflurane / µL	50	200

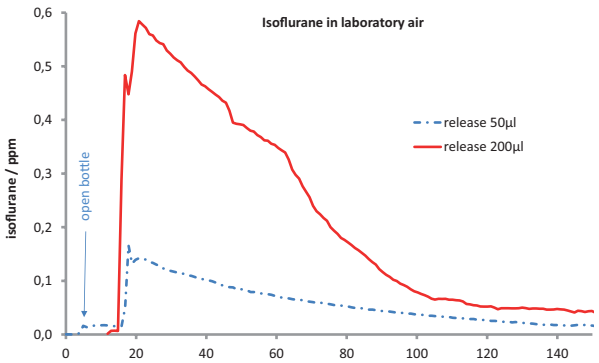


Fig. 6
Measurement of the volume fraction of isoflurane after evaporation of 50 and 200 µL in a room of about 100 m^3. The opening of the storage bottle ("open bottle") resulted in the first test (50 µL) measurable isoflurane volume fractions of 16 ppb (blue arrow).

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