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Article

On-Line Gaseous Formaldehyde Detection Based on a Closed-Microfluidic-Circuit Analysis

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Abstract: This paper describes a compact microfluidic analytical device in a closed-circuit developed for the detection of low airborne formaldehyde levels. The detection is based on the passive trapping of gaseous formaldehyde through a microporous tube into the acetylacetone solution, the derivative reaction of formaldehyde with acetylacetone to form 3,5-Diacetyl-1,4-dihydrolutidine (DDL) and the detection of DDL by fluorescence. The recirculation mode of the analytical device means that the concentration measurement is carried out by quantification of the signal increase in the liquid mixture over time, the instantaneous signal increase rate being proportional to the surrounding gaseous formaldehyde concentration. The response of this novel microdevice is found to be linear in the range 0–278 $\mu\text{g m}^{-3}$. The reagent volume needed is flexible and depends on the desired analytical resolution time and the concentration of gaseous formaldehyde in the environment. Indeed, if either the gaseous concentration of formaldehyde is high or the reagent volume is low, the fluorescence signal of this recirculating liquid solution will increase very rapidly. Consequently, the sensitivity simultaneously depends on both the reagent volume and the temporal resolution. Considering a reagent volume of 6 mL, the hourly and daily detection limits are 2 and 0.08 $\mu\text{g m}^{-3}$, respectively, while the reagent autonomy is more than 4 days the airborne formaldehyde concentration does not exceed 50 $\mu\text{g m}^{-3}$ as it is usually the case in domestic or public indoor environments.

Keywords: formaldehyde; recirculation; closed-circuit; fluorescence; microdevice; air quality

1. Introduction

While most scientific studies in the past century were focused on the quality of outdoor air, the quality of indoor air is nowadays the subject of growing interest in the scientific community, such as attests the numerous studies of the two last decades [1–5]. Indoor air contains a multitude of pollutants, but some of these pollutants attract more attention because of their occurrence, their high levels, and their harmful effects on health.

Among them, formaldehyde is considered as a major indoor air pollutant due to its many emission sources such as construction materials, furniture, glues and paints, etc. [6,7]. As a result, European and French formaldehyde concentrations in indoor air typically vary between 10 $\mu\text{g m}^{-3}$ and 100 $\mu\text{g m}^{-3}$ [6,8–10], much higher than those found in the corresponding outdoor environments, which are of the order of 1 $\mu\text{g m}^{-3}$ to 10 $\mu\text{g m}^{-3}$ in most cases [11]. Several studies have reported that formaldehyde is always present in indoor environments, such as in homes [7,12] or in schools [13,14]. Several publications have shown that formaldehyde is responsible for allergic diseases in people with asthma [15–17]. In 2004, the International Agency for Research on Cancer classified formaldehyde as a

carcinogenic molecule [18]. To reduce health problems related to formaldehyde, French regulations have set a threshold of $30 \mu\text{g m}^{-3}$ and $50 \mu\text{g m}^{-3}$ for chronic and acute exposures, respectively [19].

Formaldehyde concentrations in indoor or outdoor air are most often quantified using the reference analytical technique based on passive or active sampling by means of 2,4-Dinitrophenylhydrazine (DNPH) tubes [20,21]. This sampling can take several hours or even days before being analysed by High Performance Liquid Chromatography coupled to UV detection (HPLC/UV) [22–25] which is a time-consuming method since it requires several user's manipulations. The instruments are also expensive, bulky, and therefore sedentary, which does not allow direct on-site quantification. In addition, the results obtained via this off-line method only make it possible to obtain the average value of the concentration over the sampling duration.

Many alternatives to the reference method exist, such as Gas Chromatography coupled to Mass Spectrometer (GC-MS), infrared diode laser spectroscopy and proton transfer mass spectrometry (PTR-MS) [26–29]. These methods are based on the formaldehyde quantification directly in the gas phase. However, the poor portability and high costs of these instruments do not allow their deployment on site on a large scale. Other analytical methods rely on trapping and derivatizing gaseous formaldehyde in a solid matrix to generate a highly absorbent or fluorescent compound. Miniature analysers are then developed based on the colour change on a solid detection element [30,31]. However, these solid materials are quickly saturated over time and cannot be automatically replaced, making it impossible to monitor airborne formaldehyde independently and continuously.

Other analytical methods listed in Table 1 are based on the transfer of gaseous formaldehyde into an aqueous solution, its almost immediate reaction with a specific derivative agent and its quantification by colorimetry [32–35] or fluorescence [13,36–40]. Acetylacetone has been most often used for the quantification of formaldehyde [13,35,37–40] because it has the least interferences, but other derivative agents have also been successfully tested [30,32–34,36]. Studies carried out before 2013 used high liquid reagent flow rates, from $500 \mu\text{L min}^{-1}$ to $1300 \mu\text{L min}^{-1}$ [34,36–38,41]. The integration of microfluidics has enabled the flow rates involved to be reduced to $100 \mu\text{L min}^{-1}$ [30] or even better, i.e., down to $5\text{--}35 \mu\text{L min}^{-1}$ [13,35,39,40]. The contribution of microfluidics has also made it possible to reduce very significantly the weight of the instruments from around 20 kg to only 4–6 kg. The analytical instruments listed in Table 1 have very good sensitivity regarding the indoor air concentrations of $10\text{--}100 \mu\text{g m}^{-3}$ with their Limit Of Detection (LOD) varying between $0.09 \mu\text{g m}^{-3}$ and $2.5 \mu\text{g m}^{-3}$, and most of them are even sensitive enough to monitor outdoor air quality. Their associated temporal resolutions vary between 0.03 min [13] and 7 min [32] which appears to be sufficient in most needs. Note that all these instruments require a waste container to collect the used reagent.

Among the techniques listed in Table 1, certain technological developments have been made in our laboratory [13,35,39,40], which have led to the obtaining of a patented [13] and commercialized formaldehyde analyser ($\mu\text{-F1}$, In'Air Solutions, Strasbourg, France). This formaldehyde analyser is based on the trapping of gaseous formaldehyde into a solution, by means of the establishment of an annular flow in a fused-silica capillary, followed by its derivatization according to the Hantzsch mechanism and the quantification of the reaction product by fluorescence. This portable formaldehyde analyser (about 6 kg) is efficient and very sensitive with a detection limit of $1 \mu\text{g m}^{-3}$. It has a battery autonomy of 4 h, a response time of about ten minutes and a temporal resolution of 2 s to 120 s (0.03 min to 2 min).

Table 1. Transportable and portable devices for gaseous formaldehyde monitoring based on the gas uptake into an aqueous reagent solution, its derivatization and its on-line colorimetric or fluorescence detection.

Detection Mode	Reagent	Liquid Flow Rate ($\mu\text{L min}^{-1}$)	Trapping Mode	Weight (kg)	LOD ($\mu\text{g m}^{-3}$)	Temporal Resolution (min)	Reference
Colorimetry	Chromotropic acid	Droplet of 15 μL	Sampling chamber	N/A ^a	2.5	7	[32]
Fluorescence	Dimedone	500–1300	Two-channel flow	N/A ^a	1.1	N/A	[36]
Aerolaser AL4021	Acetylacetone	500	N/A	20 ^b	0.19	1.5	[41]
Fluorescence	Acetylacetone	500–1300	Two-channel flow	17.4 ^c	0.09	N/A	[37]
Fluorescence	Acetylacetone	1200	Diffusion scrubber	8 ^c	0.5	6–10	[38]
Spectrophotometry	MBTH hydrochloride	Stopped-flow	Gas diffusion scrubbers	8.5 ^c	0.1	5	[33]
Fluorescence	Pentanedione	100–150	Microchannel scrubber	N/A ^a	0.12	0.83 s	[30]
Colorimetry	MBTH hydrochloride	1000	Glass stripping coil	N/A ^a	0.005	15	[34]
Fluorescence	Acetylacetone	5–35	Microfluidic annular flow	5 ^c	1.8	1–2	[39]
Colorimetry	Acetylacetone	5–35	Microfluidic annular flow	5 ^c	0.7	1–2	[35]
Fluorescence	Acetylacetone	17	Microfluidic annular flow	4 ^{c,d}	≤ 1.0	0.03–2	[13]
Fluorescence	Acetylacetone	17	Passive diffusion	4 ^c	0.13–0.4	3.5	[40]
Fluorescence in recirculation mode	Acetylacetone	17	Passive diffusion	<3 ^e	2–0.08	60–1440	This work

^a N/A: data not available; ^b Weight of the formaldehyde analyser marketed by Aero-laser GMBH (AL4021, Garmisch-Partenkirchen, Germany); ^c Weight of the laboratory prototype;

^d The commercial formaldehyde analyser ($\mu\text{-F1}$, In'Air Solutions, Strasbourg, France) derived from Trocquet et al. (2019) [13] weights about 6 kg; ^e This weight is estimated for a future commercial device from the development performed in this work.

However, despite its very high analytical performances, like those of other instruments (see Table 1), [30,33,37,41], the device may appear to be oversized and thus not suitable for certain applications where a less efficient, more compact and less expensive device could be more appropriate, such as continuous monitoring of indoor environments like professional environments or even public places (schools, anatomy pathology of hospitals, etc.)

The main objective of this work was thus to develop a compact device for the continuous analysis of formaldehyde in air, based on a reliable analytical method. To meet the need for regulations in indoor environments, this device must be able to measure concentrations in the range 10–100 $\mu\text{g m}^{-3}$. In terms of sensitivity, the instrument must therefore be able to precisely quantify a concentration of 10 $\mu\text{g m}^{-3}$ with a time resolution of 30 min to 1 h, which would allow the satisfactory monitoring of most indoor environments

This work reports the instrumental development carried to obtain a functional prototype, based on an original method of airborne formaldehyde quantification. The originality relies on a closed-circuit operation, where gaseous formaldehyde uptake is achieved via a porous interface into a re-circulating aqueous solution. This study reports the implementation of this analytical method under controlled laboratory conditions for formaldehyde concentrations varying between 0 $\mu\text{g m}^{-3}$ and nearly 300 $\mu\text{g m}^{-3}$. The detection and quantification limits as well as the linearity were determined as function of certain analytical parameters such as the reagent volume used which varies between 3 mL and 24 mL. The different conditions are discussed in terms of potential applications in the field.

2. Materials and Methods

2.1. Chemicals

The Hantzsch reaction makes it possible to quantitatively transform the formaldehyde trapped in the acetylacetone solution into 3,5-Diacetyl-1,4-dihydrolutidine (DDL) [42]. The acetylacetone solution (0.01 M) consists of 15.4 g of ammonium acetate (98%, Sigma-Aldrich, St. Louis, MO, USA), 0.2 mL of acetylacetone (99%, Merck) and 0.3 mL of acetic acid (100%, Merck) in 200 mL Milli-Q water (18.2 M Ω .cm at 25 °C, Millipore, Burlington, MA, USA). This solution should then be stored at 4 °C in the refrigerator, protected from light while avoiding contact with ambient air to limit contamination of the reagent solution with ambient formaldehyde.

To conduct the tests in controlled laboratory conditions, a home-made gaseous formaldehyde generator based on permeation principle was used. Gaseous formaldehyde mixtures were generated with dilution in pure air (>99.999%, Messer, France) in the concentration range 16–278 $\mu\text{g m}^{-3}$ (13–227 ppb) with an output gas flow rate of 500–2000 NmL min⁻¹. The generated concentrations of formaldehyde were verified by experimental measurements performed in the generators outlet with the conventional reference analytical method, i.e., active adsorption on a DNPH tube followed by an HPLC/UV analysis [12,28,43,44]. The resulting formaldehyde concentration uncertainties of the gas generator were derived from the uncertainties related to the gas sampling volume and HPLC analysis, and they were estimated to be equal to 9–11%.

2.2. Setups and Experimental Conditions

2.2.1. Overall Device Configuration

The configuration of the device proposed for the detection of gaseous formaldehyde is shown in Figure 1. This instrument operates in a closed circuit, where an aqueous reagent flows at a constant flow rate, and is divided into 4 parts coupled to each other: (1) the passive trapping of formaldehyde in acetylacetone solution thanks to a microporous tube, (2) the derivatization reaction using an oven regulated at 65 °C to convert trapped formaldehyde into the fluorescent molecule 3,5-Diacetyl-1,4-dihydrolutidine (DDL), (3) the dilution of the resulting DDL into the vial containing

the total volume of the acetylacetone solution and finally, (4) the detection of DDL contained in the vial by fluorescence spectroscopy.

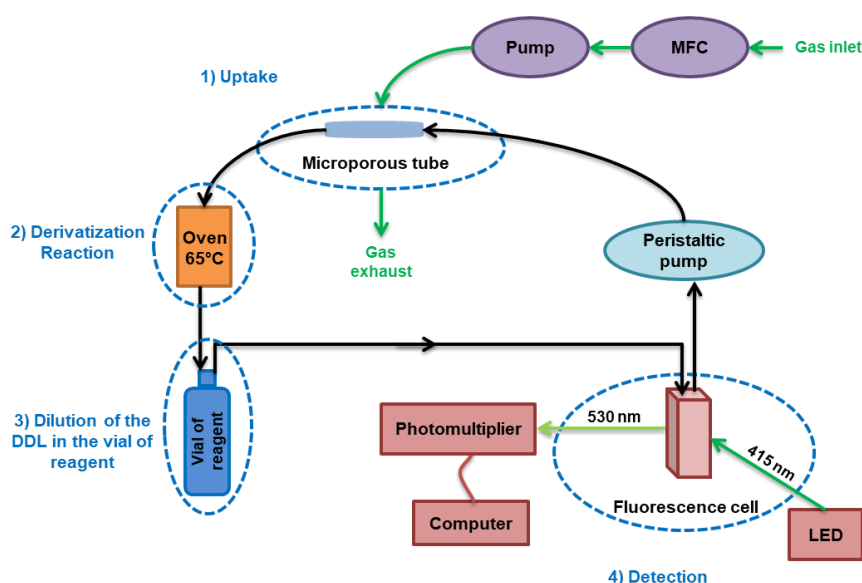


Figure 1. Schematic representation of the novel microdevice based on a liquid reagent recirculation mode used for the quantification of gaseous formaldehyde.

As shown in Figure 1, the novel formaldehyde microanalyser is mainly composed of a reagent vial, a peristaltic pump, a fluorescence cell coupled to an LED and a Photomultiplier Tube (PMT) detector, a microporous tube, 1/16 Teflon tubing of 250 μm ID and a temperature-controlled mini-oven.

In real environment conditions, the microporous tube is placed in ambient air containing formaldehyde, and the later diffuses to the porous interface and dissolves in the acetylacetone solution [45] according to its high Henry's law constant of 5000 M atm^{-1} [46]. To facilitate and accelerate the gas diffusion of formaldehyde, which can be the limiting step, one or more fans can be used to direct an air stream towards the porous membrane. Such a passive device could also be used in the laboratory if a formaldehyde generation chamber of at least several hundred litres is available to install the instrument inside.

However, for reasons of simplicity during laboratory tests and calibration, the microporous tube was here surrounded by a small sealed enclosure through which an airborne formaldehyde mixture flowed at a constant gas flow rate of 250 NmL min^{-1} .

The liquid solution flows into the closed-circuit device at a constant flow rate of 17 $\mu\text{L min}^{-1}$ thanks to a peristaltic micropump (RP-TX series RP-TX, Takasago Electronic INC, Nagoya, Japan). The microporous tube (Sumitomo) has a length of 10 cm, a porosity of 60%, an internal diameter of 0.0354 inch (0.90 mm) and an external diameter of 0.0669 inch (1.70 mm). This microporous tubing is connected to the fluid system through two 1/16-inch connectors at the inlet and outlet of the tube. Once airborne formaldehyde trapped into the acetylacetone solution, the derivatization reaction between formaldehyde and acetylacetone occurs at 65 $^{\circ}\text{C}$ and results in the production of 3,5-Diacetyl-1,4-dihydrolutidine (DDL) [13,39,40]. Then the acetylacetone solution containing the produced traces of DDL returns to the reagent vial where DDL is diluted in the total reagent volume.

The diluted liquid mixture is then injected to the fluorescence cell where DDL is quantified according to the well-documented technique already used in our previous studies [13,39,40]. The DDL is excited at 415 nm and the resulting fluorescence is collected at 530 nm on the Photomultiplier, the fluorescence signal being amplified with a fixed gain set at 50% and averaged over two seconds. The power of the LED (1 Watt) was set at about 5% of its maximal capacity to avoid any photodissociation of DDL. Due to the proposed recirculation mode, it is the vial content and therefore the total liquid

DDL concentration in the whole circuit, which is continuously quantified, the DDL concentration being proportional to that of gaseous formaldehyde trapped in liquid phase. During the measurements where the microporous tube is exposed to gaseous formaldehyde, the solution will be gradually loaded in aqueous formaldehyde and thus the DDL concentration will gradually increase. Therefore, the instantaneous signal increase rate is expected to be correlated to the surrounding gaseous formaldehyde concentration.

Compared to our previous developments [13,39,40], the novelty of this device lies in the fact of a recirculation of the reagent in a closed circuit. The positions of the reagent vial and the fluorescence cell were also inverted to measure the increase of the fluorescence signal linked to the formation of DDL in the whole solution and not the fluorescence related to the last quantity of gaseous formaldehyde trapped.

2.2.2. Prototype of the Reagent Vial

The proposed configuration implies that the reagent vial has both an inlet and an outlet enabling liquid flow through it. Two commercial vials of 6.21 mL (G004-W-D, 15 mm ID, 45 mm high) and 12.31 mL (GO74Y-23/045-SKFW16-D, 23 mm ID, 45 mm high) manufactured by InfoChroma (Goldau, Switzerland) were used in this study. Note that the exact given volumes correspond to the quantity of water introduced when they were completely full, this information being obtained by precise weighing using a balance with an accuracy of ± 0.2 mg (Toledo, AG204, Illkirch-Graffenstaden, France). The two commercial vials are made of borosilicate glass to protect the acetylacetone solution from UV light. These vials are inert and hermetic to gas thanks to a cap including a silicone/PTFE septum, avoiding any air contamination from outside. Note that at the start of the measurements, the vial is almost fully filled with the reagent solution to limit the presence of air in contact with this solution.

For user safety reasons and ease of implementation in the overall device, these vials are introduced into two different custom-made housings according to the vial size as displayed in Figure 2. Each housing comprises two integrated needles which are connected to two 1/16 Teflon tubes by means of low-cost fluidic connectors (male luer fluid connector, ChipShop, Jena, Germany), the later are inserted into the reagent acetylacetone solution by crossing the septum. In this configuration, the two parallel needles are not accessible, which provides protection when changing the reagent vial and helps to prevent user injuries. The vial housing was made by rapid prototyping thanks to a 3D printer (Extended 3, Ultimaker, Utrecht, The Netherlands) with ABS as the 3D printing material.

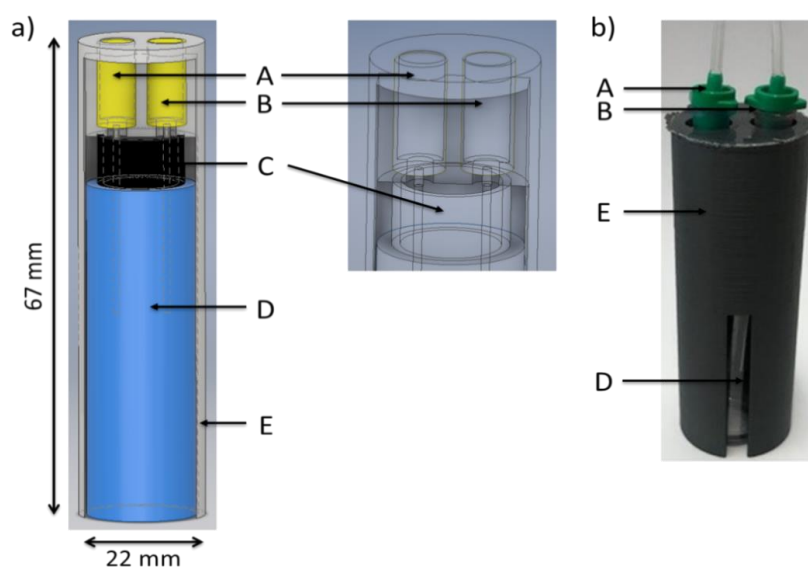


Figure 2. Setup of the 6 mL-reagent vial housing. [A] and [B] are the two needles for reagent flow inlet and outlet, [C] plug with septum for needles, [D] reagent vial and [E] the protective housing. (a) image produced in CAD; (b) picture of the prototype.

It should be noted that when the signal is saturated, the solution must be changed so that the closed-circuit is rinsed with the same acetylacetone solution prior to install the new reagent vial.

2.2.3. Integration in the Formaldehyde Microanalyser Prototype

This study was carried out using the commercialised formaldehyde analyser (μ F-1, In'Air Solutions, Strasbourg, France) shown in Figure 3a. More precisely, its detection part and the associated efficient electronics were used to monitor the fluorescence signal. However, the other constituent elements of our proposed system were placed outside the device for carrying out the experiments due to lack of authorization by the company to dismantle the whole instrument. In these conditions, the resulting internal volume of the closed circuit was measured to be 410 μ L by precisely weighing the water inside, without considering the volume of the vial. The main contributions to this overall internal fluidic volume was the microporous tube (80 μ L), the oven (72 μ L) and the fluorescence cell and its specific tubing and connectors (about 100 μ L).

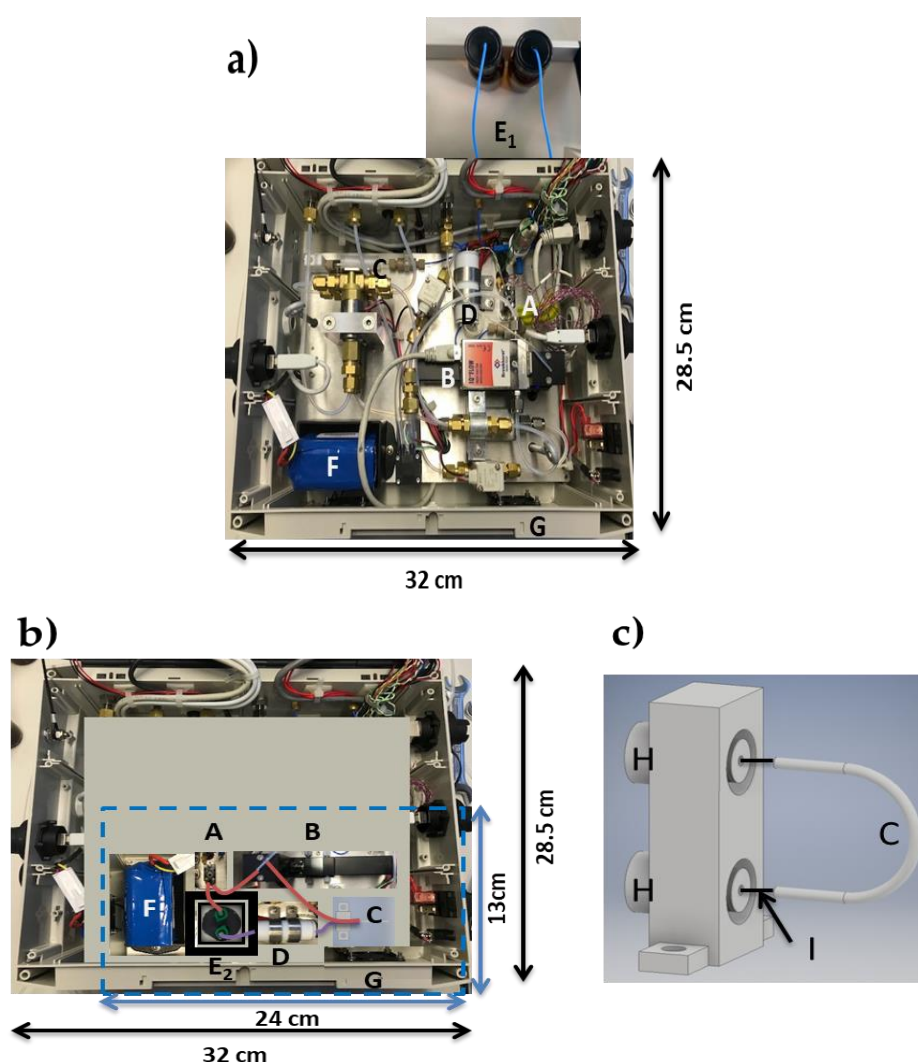


Figure 3. Evolution of the marketed formaldehyde analyser: (a) the current marketed formaldehyde analyser (μ F-1, In'Air Solutions, Strasbourg, France); (b) the formaldehyde analyser modified with the integration of the recirculation mode (this work); (c) the new trapping part (this work). The different elements are the following: the peristaltic pump (A), the Photomultiplier (B), the microporous tube (C), the oven (D), the reagent bottle already used in the current analyser (E_1) or the reagent vial proposed in this work (E_2), the battery (F), the fans (G), the fluidic connectors (H) and the steel connector tubes (I).

However, it is useful to visualize the potential gain in terms of miniaturization and the corresponding dimensions. To serve this purpose the new elements proposed by this work were arranged in the current formaldehyde analyser using Computer Aided Design (CAD). The current formaldehyde analyser is 28.5 cm wide, 32 cm long and 14 cm high, which corresponds to a total volumetric size of 12.8 L (Figure 3a). Note that in the current analyser reagent vial is placed outside the analyser box on a dedicated location. Comparison of Figure 3a,b shows that the fluidic part could thus be reduced by about 70%, the same battery being preserved. The modified trapping part integrating the microporous tube is shown in Figure 3c.

Therefore, the new recirculating microsystem potentially saves significant space and permits a consequent miniaturization of the instrument. Moreover, the internal fluidic volume could be easily reduced to 300 μL in this optimal configuration. The size of the new microdevice could be on the order of 24 cm wide, 13 cm long and 14 cm high, i.e., a volumetric size of 4.4 L, if the current electronic could be consequently reduced once some elements (mass flow controller, gas pump, two three-way valves, etc.) being removed from the original formaldehyde analyser.

3. Results

Four series of experiments were carried out, the parameters of these experiments being summarized in Table 2. The results of series of experiments 1 to 4 are detailed below and are plotted in Figures 4–7.

Table 2. Experimental values of parameters for four series of experiments performed in this work.

Parameters	Series of Experiments			
	1	2	3	4
Detection module	$\mu\text{-F1, In'Air Solutions}$	$\mu\text{-F1, In'Air Solutions}$	Laboratory Prototype	$\mu\text{-F1 In'Air Solutions}$
Liquid flow rate ($\mu\text{L min}^{-1}$)			17	
Gas flow rate (mL min^{-1})			250	
Formaldehyde concentration ($\mu\text{g m}^{-3}$)	54 or 278	16–278	35–278	278
Reagent volume (mL)	5.85	5.87	5.88 or 11.54	5.79
Microporous tube length (cm)			10.0 \pm 0.2	
PMT Gain (%)	50	50	48	50

3.1. Signal Behavior as Function of Formaldehyde Microanalyser

The recirculation mode means that the concentration measurement is carried out by quantifying the signal increase in the liquid mixture over time, the instantaneous signal increase rate being proportional to the surrounding gaseous formaldehyde concentration.

The new configuration of this formaldehyde analyser has been optimized and evaluated under controlled laboratory conditions by varying the reagent volume and the concentration of gaseous formaldehyde. It should be noted that the liquid and gaseous flow rates were optimized during a previous study [40] where the analyser was not operating in recirculation mode. For this reason, all the experiments were performed in this work with optimal gas and liquid flow rates of 250 mL min^{-1} and 17 $\mu\text{L min}^{-1}$, respectively. For a fixed usual photomultiplier gain of 50%, the time required before saturation of the detector was also investigated according to the gaseous concentration of formaldehyde and the volume of reagent used. The results are detailed and are discussed in the sections below.

Figure 4 shows the experimental signals (black line) typically obtained during the recirculation mode analysis. Before each measurement with a known concentration of gaseous formaldehyde, pure air is injected to obtain a reference signal called baseline (analytical blank). This resulting baseline is a constant and stable signal (signals A, C and E in Figure 4) in the absence of new formaldehyde molecules entering the acetylacetone solution.

Conversely, when a given concentration of gaseous formaldehyde is injected or present around the microporous tube, the signal increases linearly. Only small variations are observed, the experimental curve almost merging with the linear regressions (red and blue dashed lines in Figure 4). Thus, the slope corresponding to the signal vs. time increases when the concentration of formaldehyde increases as illustrated in Figure 4. For example, the slope is equal to $36.3 \pm 2.53 \mu\text{V s}^{-1}$ and $6.10 \pm 0.92 \mu\text{V s}^{-1}$ for formaldehyde concentrations of $277.7 \mu\text{g m}^{-3}$ and $54.0 \mu\text{g m}^{-3}$, respectively (parts B and D in Figure 4), where the quoted errors correspond to two times the standard deviation.

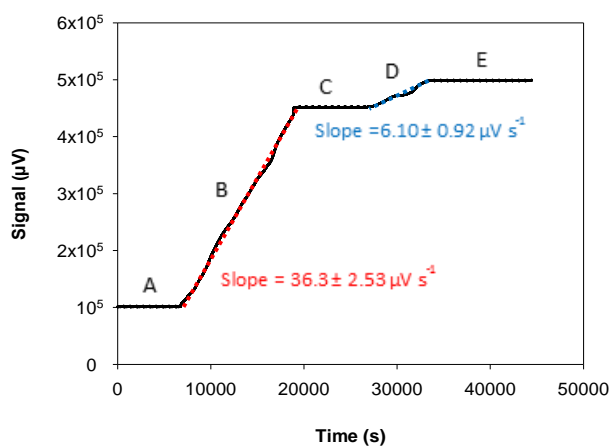


Figure 4. Example of the signal in recirculation mode with a reagent volume of 5.85 mL for two formaldehyde concentrations of $277.7 \mu\text{g m}^{-3}$ and $54.0 \mu\text{g m}^{-3}$ with gas and liquid flow rates of 250 mL min^{-1} and $17 \mu\text{L min}^{-1}$, respectively. The parts [A], [C] and [E] correspond to blanks obtained by injecting pure air around the microporous trapping tube; [B] corresponds to a formaldehyde concentration set at $278 \mu\text{g m}^{-3}$; [D] corresponds to $54 \mu\text{g m}^{-3}$ of formaldehyde. The black line corresponds to the experimental values while the dashed red and blue lines correspond to the linear regressions made in the corresponding time interval for $278 \mu\text{g m}^{-3}$ and $54 \mu\text{g m}^{-3}$, respectively. The quoted slope uncertainties correspond to two times the standard deviation.

3.2. Influence of the Gaseous Formaldehyde Concentration on the Signal Slope

The influence of the formaldehyde concentration on the slope of the plot representing the signal as a function of time was studied between $16 \mu\text{g m}^{-3}$ and $278 \mu\text{g m}^{-3}$ using the formaldehyde analyser ($\mu\text{-F1}$, In'Air Solutions, France) modified to operate in recirculation mode, as previously explained. The reagent volume was set at $5.87 \pm 0.09 \text{ mL}$ where the quoted error corresponds to the standard deviation, whereas the gas and liquid flow rates were fixed at 250 mL min^{-1} and $17 \mu\text{L min}^{-1}$, respectively. Note that exact reagent volume used was precisely determined by weighing for each experiment performed, which can induce small volume variations of less than 1.5%.

The slope of the fluorescence signal increase is plotted in Figure 5 as a function of the gaseous formaldehyde concentration in the range $16.3\text{--}277.7 \mu\text{g m}^{-3}$. The slope of the linear fit is equal to $0.137 \pm 0.010 \mu\text{V s}^{-1} \mu\text{g}^{-1} \text{ m}^3$ where the quoted errors correspond to two times the standard deviation.

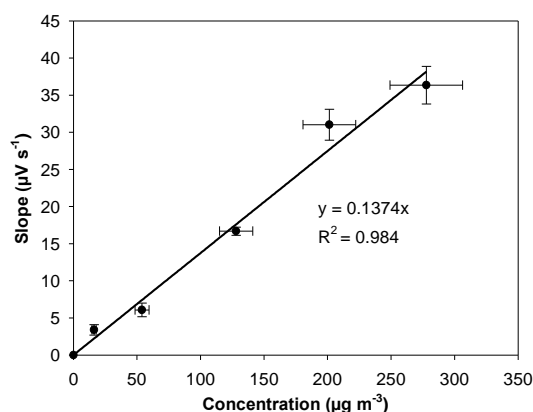


Figure 5. Calibration of the proposed prototype using the detection module of the commercialized formaldehyde analyser (μ -F1, In’Air Solutions, France) integrating the recirculation mode with an average reagent volume of 5.87 mL, formaldehyde concentrations varying between $16 \mu\text{g m}^{-3}$ and $278 \mu\text{g m}^{-3}$, gas and liquid flow rates of 250 mL min^{-1} and $17 \mu\text{L min}^{-1}$, respectively. The vertical error bars correspond to two times the standard deviation. The horizontal quoted error bars are calculated from uncertainties on the sampling volume and the subsequent HPLC analysis of DNPH tubes.

3.3. Influence of the Reagent Volume on the Signal Slope

For a given concentration of gaseous formaldehyde, the volume of reagent has a direct impact on the slope values of the curve representing the fluorescence signal as a function of time. Indeed, the higher the volume of reagent involved, the more the trapped formaldehyde and the produced DDL will be diluted resulting in lower slope values. This is illustrated in Figure 6a where two distinct calibration plots were obtained for two different volumes of reagent (6 mL and 12 mL) with the detection module of the laboratory prototype in recirculation mode with formaldehyde concentrations ranging between $35 \mu\text{g m}^{-3}$ and $278 \mu\text{g m}^{-3}$, a gas flow of 250 mL min^{-1} and a liquid flow of $17 \mu\text{L min}^{-1}$.

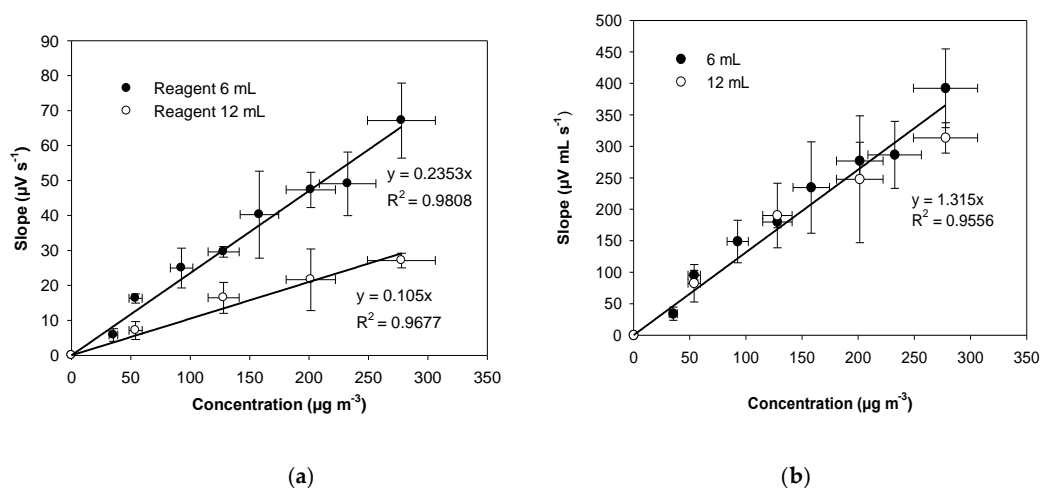


Figure 6. Calibration plots obtained with a laboratory prototype of formaldehyde microanalyser in recirculation mode for two different average volumes of reagent (5.88 ± 0.09 and 11.54 ± 0.08 mL, the quoted errors being the standard deviation), with concentrations of formaldehyde ranging between $35 \mu\text{g m}^{-3}$ and $278 \mu\text{g m}^{-3}$, a gas flow rate of 250 mL min^{-1} and a liquid flow rate of $17 \mu\text{L min}^{-1}$. The data are presented by considering either (a) two separated linear plots where the slope is in $\mu\text{V s}^{-1}$ or (b) one single linear plot where the slope is normalized according to the reagent volume used and expressed in $\mu\text{V mL s}^{-1}$. The vertical error bars correspond to two times the standard deviation. The horizontal quoted error bars are calculated from uncertainties on the sampling volume and the subsequent HPLC analysis of DNPH tubes.

For a reagent volume of approximately 6 mL, the slope of the linear calibration plot is $0.235 \pm 0.013 \mu\text{V s}^{-1} \mu\text{g}^{-1} \text{m}^3$ whereas for a volume of about 12 mL the slope is equal to $0.105 \pm 0.011 \mu\text{V s}^{-1} \mu\text{g}^{-1} \text{m}^3$, which corresponds approximately to the ratio of reagent volume. The quoted errors on these slopes correspond to two times the standard deviation derived from the linear fit. In Figure 6b, the slopes values have been normalized with respect to the exact reagent volume used and obtained by weighing for each experiment and are therefore expressed in $\mu\text{V mL s}^{-1}$. Figure 6b exhibits then the linear plot of normalized slope of fluorescence signal increase vs. the gaseous formaldehyde concentration in the range 35–278 $\mu\text{g m}^{-3}$.

3.4. Fluorescence Signal Saturation and the Resulting Autonomy

The saturation of the fluorescence signal is caused by an excessive concentration of DDL in the closed circuit, which requires the change of the acetylacetone reagent solution to continue the measurements.

The following experiment aimed at determining the saturation level of the fluorescence signal and at verifying if the signal increases linearly up to this saturation level when the microdevice is exposed to a constant formaldehyde concentration. To study this phenomenon, a high concentration of gaseous formaldehyde mixture, i.e., 278 $\mu\text{g m}^{-3}$, is injected in the vicinity of the microporous tube and analysed until the signal saturation as shown in Figure 7. This figure shows weak signal disturbances during the experiment due to possible instabilities of the gas pump and/or the gaseous formaldehyde concentration generated by the permeation tube source over very prolonged use as previously observed sometimes in our previous studies. With the electronics of the commercialised formaldehyde analyser ($\mu\text{F-1}$, In'Air Solutions, Strasbourg, France), the signal saturation is observed at a fixed value of $2.1 \times 10^6 \mu\text{V}$.

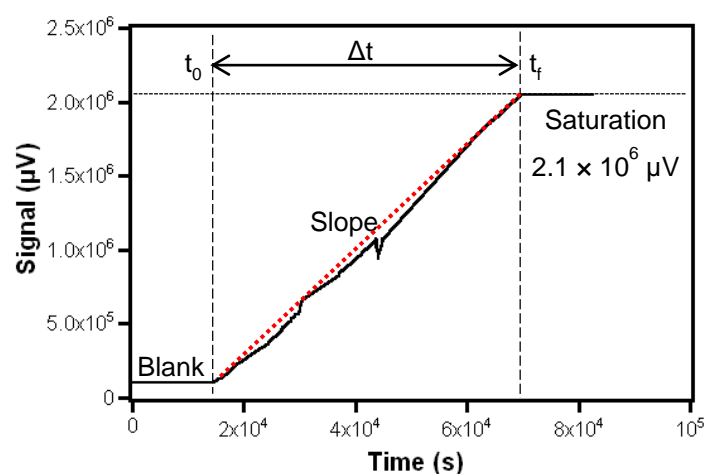


Figure 7. Experimental study of the saturation of the signal of detection. The concentration of formaldehyde used for this is 278 $\mu\text{g m}^{-3}$. The gas and liquid flow rates are 250 mL min^{-1} and 17 $\mu\text{L min}^{-1}$, respectively. The volume of reagent is 5.79 mL and the microporous tube length is 10 cm. The black and dashed red lines correspond to the experimental values and the linear regression, respectively.

Such experimental study of this signal is essential to determine the operating autonomy of this novel microdevice in terms of reagent solution. The time needed to get the fluorescence signal saturation, called saturation time Δt , is represented in Figure 7. More precisely, Δt is calculated from the final time (t_f) where the signal is saturated and the initial time (t_0) where a residual background is obtained with a fresh acetylacetone solution. This saturation time is itself influenced by the gaseous formaldehyde concentration measured and by the reagent volume used.

With a formaldehyde concentration of $278 \mu\text{g m}^{-3}$ and a reagent volume of 5.79 mL, the experimental average slope of the fluorescence signal increase is found to be $36.3 \mu\text{V s}^{-1}$. The resulting saturation time Δt derived is then $55.7 \times 10^3 \text{ s}$ (15.5 h) when the signal increases from 1.0×10^5 to 2.1×10^6 .

3.5. Analytical Performances

The noise of the fluorescence signal is obtained by measuring the height of the peak-to-peak signal during an analytical blank (parts B and D of the curve presented in Figure 4) and is typically equal to $500 \mu\text{V}$ for the commercialised formaldehyde analyser. Considering the linear calibration performed in Section 3.2 with the microdevice coupled to the detection module of the commercialised formaldehyde analyser and its associated electronics, the lowest concentration measured in this set of experiments is $16 \mu\text{g m}^{-3}$ (slope of $3.39 \mu\text{V s}^{-1}$). This makes it possible to extrapolate the sensitivity of the novel microdevice. With an average volume of 5.87 mL, the hourly detection and quantification limits are $2.0 \mu\text{g m}^{-3}$ (1.6 ppb, S/N = 3) and $6.6 \mu\text{g m}^{-3}$ (5.4 ppb, S/N = 10), respectively.

The linear calibrations obtained for volumes 6 and 12 mL (see Section 3.3) were obtained with the proposed device equipped with the same detection module but coupled to a more rudimentary electronics of a laboratory prototype. The hourly detection limits obtained by extrapolation were logically slightly higher, i.e., $2.5 \mu\text{g m}^{-3}$ (2.0 ppb, S/N = 3) and $3.2 \mu\text{g m}^{-3}$ (2.6 ppb, S/N = 3) for 6 mL and 12 mL respectively.

However, the detection limits strongly depend on the temporal resolution considered as discussed later in the manuscript.

3.6. Influence of Reagent Volume on the Temporal Resolution

Figure 8 represents the slope of the fluorescence signal increase as a function of the reagent volume used for three concentrations studied, the points in red correspond to experimental data while those in black have been calculated from the calibration performed in Section 3.2 using the detection module of $\mu\text{F-1}$ (In'Air Solutions) with an average reagent volume of 5.87 mL. Since the DDL concentration and therefore the slope are directly impacted by the dilution due to the total reagent volume used in the microdevice, the other slopes expressed in $\mu\text{V mL s}^{-1}$ were calculated for reagent volumes of 9, 12, 18 and 24 mL, respectively. Note that series of experiments obtained in Figure 6a cannot be used since they have not been performed with the same detection module.

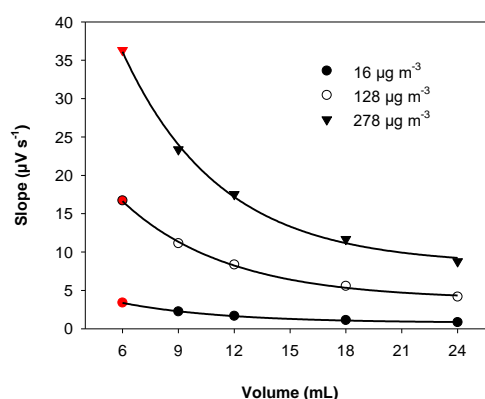


Figure 8. Fluorescence signal increase slope vs. reagent volume for three gas formaldehyde concentrations of 16, 128 and $278 \mu\text{g m}^{-3}$ and five different reagent volumes, i.e., 6, 9, 12, 18 and 24 mL. The gas and liquid flow rates are set to 250 mL min^{-1} and $17 \mu\text{L min}^{-1}$, respectively. The microporous tube length is 10 cm. Data in red correspond to experimental values while those in black have been calculated.

For a reagent volume of 5.87 mL (red points), the slope of the fluorescence signal varies from $3.4 \mu\text{V s}^{-1}$ to $36.3 \mu\text{V s}^{-1}$, i.e., from $20.1 \mu\text{V mL s}^{-1}$ to $210.4 \mu\text{V mL s}^{-1}$, between $16 \mu\text{g m}^{-3}$ and $278 \mu\text{g m}^{-3}$, respectively. For a fixed formaldehyde concentration of $278 \mu\text{g m}^{-3}$, the slope of the fluorescence signal increase varies, from $36.3 \mu\text{V s}^{-1}$ to $8.8 \mu\text{V s}^{-1}$, between 5.87 mL and 24 mL, respectively. Note that $8.8 \mu\text{V s}^{-1}$ is obviously four times lower than $36.3 \mu\text{V s}^{-1}$ according to the reagent volume ratio of 6/24.

As mentioned before, the noise of the fluorescence signal is typically equal to $500 \mu\text{V}$ (S_{Noise}) or sometimes a little bit less. A detectable increase in the fluorescence signal is therefore equal to three times this value, i.e., $1500 \mu\text{V}$. The detection time (t_{LOD}) is defined as the minimum time associated with measuring a detectable increase of $1500 \mu\text{V}$. Thus, t_{LOD} (in seconds) corresponds to the minimum detectable signal increase ($S_{\text{LOD}} = 1500 \mu\text{V}$) divided by the slope (in $\mu\text{V s}^{-1}$) for a given gaseous formaldehyde concentration and reagent volume. Similarly, t_{LOQ} refers to minimum time associated with measuring a quantifiable increase of $5000 \mu\text{V}$ (S_{LOQ}).

From the experimental slopes obtained in Section 3.3 (see Figure 5), the detection time (t_{LOD}) has been calculated as a function of the reagent volume used for the three gas formaldehyde concentrations, i.e., 16, 128 and $278 \mu\text{g m}^{-3}$, and reported in Figure 9. The points in red correspond always to experimental data where the average reagent volume is 5.87 mL, while those in black have been calculated for 3, 9, 12, 18 and 24 mL, similarly to Figure 8.

In Figure 9, considering a fixed formaldehyde concentration of $16 \mu\text{g m}^{-3}$, t_{LOD} varies from 224 s to 1791 s, i.e., from 3.7 min to 29.8 min, for a reagent volume of 3 mL and 24 mL, respectively. For a maximum reagent volume of 24 mL, t_{LOD} varies from 1791 s to 171 s, i.e., from 29.8 min to 2.85 min, for formaldehyde concentration of $16 \mu\text{g m}^{-3}$ and $278 \mu\text{g m}^{-3}$, respectively.

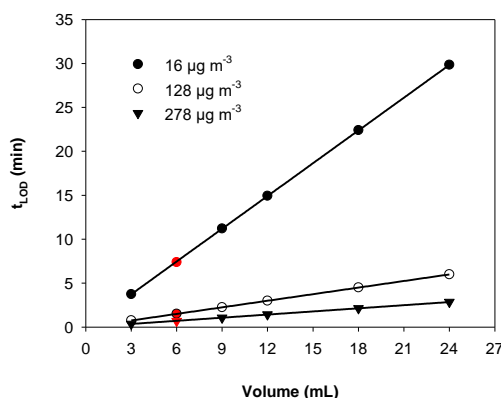


Figure 9. Detection time t_{LOD} (in second) vs. reagent volume for three gaseous formaldehyde concentrations of 16, 128 and $278 \mu\text{g m}^{-3}$ and six different reagent volumes, i.e., 3, 6, 9, 12, 18 and 24 mL. The gas and liquid flow rates are set to 250 mL min^{-1} and $17 \mu\text{L min}^{-1}$, respectively. The microporous tube length is 10 cm. Data in red correspond to experimental values while those in black have been calculated.

4. Discussion

The fluorescence signal being perfectly constant during the blanks carried out with pure air (parts B and D of Figure 4), this confirms the absence of DDL photodissociation under our experimental conditions.

In the novel microdevice developed in the present work, the unique vial of 6–12 mL replaces and combines the 100 mL-reagent bottle and the 100 mL-waste bottle, i.e., the two liquid reservoirs used in our previous investigations [13,35,39,40]. The resulting space saving reduces the instrument size thus improving the portability. In addition, in the case of an analytical system without recirculation, a DNPH tube is usually placed on the reagent bottle to purify the ambient air which enters the reagent

bottle when this later is emptied. In a recirculation analysis system, the vial is always completely full which avoids inconvenience and the need for DNPH tube purifier.

4.1. Influence of the Gaseous Formaldehyde Concentration

Figure 5 shows that the slope of fluorescence signal increase expressed in $\mu\text{V s}^{-1}$, increases perfectly linearly with the gaseous formaldehyde concentrations in the range investigated, with a slope equal to $0.137 \pm 0.010 \mu\text{V s}^{-1} \mu\text{g}^{-1} \text{m}^3$ where the quoted error correspond to two times the standard deviation. The slope of the DDL fluorescence signal increase is therefore proportional to the gas concentration of formaldehyde when the experimental conditions are optimal.

This observation tends to show that this new configuration of the formaldehyde analyser can be used to accurately quantify formaldehyde in indoor or outdoor air.

4.2. Influence of the Reagent Volume

As already mentioned in the Section 3.3, the slopes normalized according to the reagent volume used and expressed in $\mu\text{V mL s}^{-1}$, are in excellent agreement as displayed in Figure 6b, when considering the experimental error bars. The two series of data obtained respectively for 6 and 12 mL are thus advantageously complemented, showing the consistence of the results obtained here. In other words, this indicates that the DDL analysis contained in the reagent vial is representative of the gaseous formaldehyde sample regardless of the reagent volume.

In practice, for the analysis of high formaldehyde concentrations, it will be necessary to choose a high volume of reagent allowing a longer analysis time before the saturation of the detector. Conversely, when analysing low concentrations, the choice of a small volume of reagent will be preferable. Indeed, the smaller the volume, the faster the signal increase will be detectable.

This observation suggests a great flexibility of the method developed according to the encountered concentrations range, typically either 0–100 $\mu\text{g m}^{-3}$ in domestic environments or up to several hundred of $\mu\text{g m}^{-3}$ in industrial environments.

4.3. Fluorescence Signal Saturation and the Resulting Autonomy

As mentioned above, the fluorescence signal saturation of $2.1 \times 10^6 \mu\text{V}$ implies a change of the reagent which is preceded by a rapid rinsing of the entire circuit with the same acetylacetone solution so as to decrease to an initial residual fluorescence signal on the order of $1.0 \times 10^5 \mu\text{V}$ depending on the age of the reagent solution and the efficiency of the circuit rinse.

Since the measurement range of the fluorescence signal is fixed between $S_0 = 1.0 \times 10^5$ and $S_f = 2.1 \times 10^6 \mu\text{V}$, the measurement autonomy will directly depend on the average slope in fluorescence signal increase. As previously observed, this depends both on the concentration of formaldehyde used (see Figures 5 and 6) but also on the volume of reagent used (Figure 6a).

Table 3 summarizes the values of the gaseous formaldehyde concentrations measured in Section 3.2 (see Figure 5), the reagent volume used for each experiment and the experimental slope (in $\mu\text{V s}^{-1}$) obtained for each formaldehyde concentration. The values of the initial signal (S_0) and the final signal (S_f) being fixed, the time values needed to reach saturation, i.e., the device autonomy in terms of reagent, are calculated for each investigated concentration. These values of autonomy are expressed in hours and days in Table 3.

Table 3. Calculation of the device autonomy (Δt) in terms of acetylacetone solution with a reagent volume of 5.87 ± 0.09 mL for experimental gaseous formaldehyde concentration in the range $0\text{--}278 \mu\text{g m}^{-3}$.

Formaldehyde Concentration	Reagent Volume	Slope ^a	Slope \times Volume	S_0 at t_0 ^b	S_f at t_f ^c	Time Required for Saturation (Δt)	
($\mu\text{g m}^{-3}$)	(mL)	($\mu\text{V s}^{-1}$)	($\mu\text{V mL s}^{-1}$)	(μV)	(μV)	(hours)	(days)
0	0	0.0	0.0	1.0×10^5	2.1×10^6	0.0	0.0
16	5.93	3.39 ± 0.71	20.1	1.0×10^5	2.1×10^6	165.8	6.9
54	5.86	6.10 ± 0.92	35.6	1.0×10^5	2.1×10^6	92.5	3.9
128	6.00	16.7 ± 0.54	100.1	1.0×10^5	2.1×10^6	33.7	1.4
201	5.78	31.0 ± 2.07	179.3	1.0×10^5	2.1×10^6	18.1	0.8
278	5.79	36.3 ± 2.53	210.4	1.0×10^5	2.1×10^6	15.5	0.6

^a The quoted errors correspond to two folds the standard deviation obtained by the linear fit (see Figure 4); ^b S_0 is the initial at $t = 0$; ^c S_f corresponds to the saturation signal.

4.4. Analytical Performances and Comparison with Literature

The new formaldehyde microanalyser has a perfectly linear response between $0 \mu\text{g m}^{-3}$ and $278 \mu\text{g m}^{-3}$ (227 ppb), this latter value being representative of indoor industrial pollution.

The analytical sensitivities were calculated from the various calibrations carried out (Figure 5 in Section 3.2 and Figure 6 in Section 3.3). With the electronics of the analyser's detection module currently on the market, the sensitivity of the instrument is slightly better, and the hourly detection limit is $2.0 \mu\text{g m}^{-3}$ (1.6 ppb) with an average reagent volume of 5.87 mL.

Reducing the reagent volume by a factor of 5 (for example from 6 mL to 1.2 mL) could theoretically further improve this hourly sensitivity by a factor of 5 as well, i.e., $0.4 \mu\text{g m}^{-3}$. However, such drastic reagent volume reduction will be performed to the detriment of the instrument autonomy. This can therefore be undertaken for a very specific need, such as the measurement of very low gaseous formaldehyde concentrations outdoors.

4.5. Influence of Reagent Volume on the Temporal Resolution

Figure 8 shows that the fluorescence signal slope strongly depends on the concentration and the volume of reagent used for the analysis. For a given concentration, this slope decreases sharply with the increase in the reagent volume used. For a given volume of reagent, the slope increases appreciably with the increase in concentration as already observed in Figures 5 and 6.

Table 3 gathers the values of the gaseous formaldehyde concentrations measured in Figure 5, the reagent volume and the experimental slope (in $\mu\text{V s}^{-1}$) determined in Section 3.2. The noise of the fluorescence signal (S_{Noise}) is fixed to $500 \mu\text{V}$ while the detection and quantification signals are set to $1500 \mu\text{V}$ and $5000 \mu\text{V}$, respectively. The minimum times to detect or quantify each studied formaldehyde concentration, i.e., t_{LOD} and t_{LOQ} , were then calculated reported in Table 4.

With a concentration of $278 \mu\text{g m}^{-3}$, 0.69 min and 2.29 min are necessary to detect or quantify this concentration using a reagent volume of approximately 6 mL. For a significantly lower concentration of $16 \mu\text{g m}^{-3}$, it takes 7.37 min and 24.58 min to detect and quantify this concentration. Thus, with an hourly measurement which is largely sufficient for most field applications, we can hope to detect a minimal concentration of about $2 \mu\text{g m}^{-3}$ with a reagent volume of 6 mL. This hourly detection limit can be reduced to $0.4 \mu\text{g m}^{-3}$ when reducing the acetylacetone reagent volume from 6 mL to 1.2 mL. If 6 mL of reagent is kept, a daily measurement would make it possible to detect or quantify concentrations of airborne formaldehyde, equal to $0.08 \mu\text{g m}^{-3}$ and $0.27 \mu\text{g m}^{-3}$, respectively.

Table 4. Calculation of the time needed to detect and to quantify, i.e., t_{LOD} and t_{LOQ} respectively, the experimental gaseous formaldehyde concentration in the range 0–278 $\mu\text{g m}^{-3}$ with a reagent volume of 5.87 ± 0.09 mL.

Formaldehyde Concentration ($\mu\text{g m}^{-3}$)	Reagent Volume (mL)	Slope ^a ($\mu\text{V s}^{-1}$)	S_{Noise} (μV)	S_{LOD} (S/N = 3)	t_{LOD} (min)	S_{LOQ} (S/N = 10)	t_{LOQ} (min)
0	0	0.0	500	1500	0.00	5000	0.00
16	5.93	3.39 ± 0.71	500	1500	7.37	5000	24.58
54	5.86	6.10 ± 0.92	500	1500	4.11	5000	13.71
128	6.00	16.7 ± 0.54	500	1500	1.50	5000	5.00
201	5.78	31.0 ± 2.07	500	1500	0.81	5000	2.69
278	5.79	36.3	500	1500	0.69	5000	2.29

^a The quoted errors correspond to two times the standard deviation obtained by the linear fit (see Figure 4).

4.6. Comparison with Literature

The characteristics of the instruments and its associated analytical performances such as the LOD are reported in Table 1 for comparison with the other formaldehyde analysers based on trapping of formaldehyde into an aqueous solution and a derivatisation reaction before the detection of the reaction product by either colorimetry [32–35] or fluorescence [13,30,36–40].

This microdevice is the lightest since a weight of less than 3 kg could be expected for a commercial version where the fluidic part could contribute to only few hundreds of grams. It is also the only one to operate in a microfluidic closed-circuit, which avoids the use of a waste bottle can, which is also bulky especially when the flow rates used are high such as observed for many of them [34,36–38,41]. Furthermore, its practical use is greatly simplified compared to previous instruments such as for example the prototype of Sassine et al. (2013) [34] or the analyser AL4021 [41], which require several reagents, these latter must be kept in a cooler at 4 °C in the case of AL4021. Our microanalyser has a comparable sensitivity to the apparatus listed in Table 1 when considering hourly and daily LOD of 2 and 0.08 $\mu\text{g m}^{-3}$, respectively; however the other listed instruments exhibit much better time resolution varying between 0.03 min to 15 min.

In addition, the technical and analytical information related to the three instruments recently developed in our laboratory [13,40] are reported in Table 5 for comparison purpose. The three studies used the same derivative agent and the same fluorescence detection module so that they can be easily and advantageously compared. As mentioned before, the size and weight of the novel microanalyser are significantly reduced. For typical indoor formaldehyde concentration lower than 50 $\mu\text{g m}^{-3}$, the reagent autonomy will be comparable, i.e., on the order of 4 days. For this autonomy, the reagent volume will be reduced from 100 mL to only ~6 mL. The operation principle of the recirculation mode proposed in this work modifies the data treatment, the gaseous formaldehyde concentration being proportional to the signal increase slope and not to the fluorescence signal intensity.

Table 5. Comparison of characteristics of the instruments developed in our laboratory [13,40] including technical details, cost, analytical principle and performances.

Parameters	Trocquet et al. (2019) [13]	Becker et al. (2019) [40]	This Work
Technical Details and Cost			
Size (length × width × height) (cm)	32 × 28.5 × 13	32 × 28.5 × 13	24 × 13 × 13
Weight (kg)	6 ^a	4 ^b	<3 ^b
Battery autonomy (h)	4 ^c	>6 ^d	>6 ^d
Reagent volume (mL)	100	100	~6 ^e
Reagent autonomy (day)	4.1	4.1	>4 ^f
Waste bottle	yes	Yes	no
Cost (k€)	~30 ^g	<10 ^h	<10 ^h
Analytical Principle and Performances			
Derivative reagent	Acetylacetone	Acetylacetone	Acetylacetone
Trapping mode	Microfluidic annular flow	Passive diffusion	Passive diffusion
Circulation mode	Classic	Classic	Recirculation
Detection	Fluorescence	Fluorescence	Fluorescence
LOD ($\mu\text{g m}^{-3}$)	≤ 1.0	0.13–0.4 ⁱ	0.08–2 ^j
Time resolution (min)	0.03–2 ^k	3.5	60–1440 ^l
Determination of HCHO concentration	Intensity ^m	Intensity ^m	Slope ⁿ
Blank necessity	yes	Yes	no

^a Weight of the commercial product; ^b Estimated weight of the commercial product from the prototype one; ^c Experimental value; ^d Estimated value; ^e The reagent volume can be adapted to the user needs; ^f Value estimated for formaldehyde concentration lower than $54 \mu\text{g m}^{-3}$; ^g Approximate price of the commercial product; ^h Estimated price; ⁱ The detection limit varied in the range $0.13\text{--}0.4 \mu\text{g m}^{-3}$ when determined with formaldehyde concentration of $16 \mu\text{g m}^{-3}$ and $35 \mu\text{g m}^{-3}$, respectively; ^j The detection limit varies in the range $0.08\text{--}2 \mu\text{g m}^{-3}$ with a reagent volume of 6 mL for time resolution of 1 day and 1 h, respectively (This work); ^k The time resolution of 0.03–2 min corresponds to the fluorescence signal integration time; ^l The time resolution can be reduced when using a lower reagent volume; ^m The gaseous formaldehyde concentration is directly proportional to the fluorescence intensity; ⁿ The gaseous formaldehyde concentration is directly proportional to the slope of fluorescence signal increase.

The use of this new microanalyser brings also practical advantages compared to the solutions previously reported in the literature [13,30,32–41]. One of these advantages are related to its high flexibility since the reagent volume can be adapted to the user needs: a small reagent volume will be chosen for relatively clean environments or short time measurements where precision and/or fast response are required. Conversely, a large volume will be chosen for high concentrations or if autonomy is favoured to the detriment of temporal resolution. More remarkably, data analysis no longer requires experimental blanks, unlike all the methodologies presented in Tables 1 and 5. This difference implies that the user does not need to bring some pure air cylinder to perform blanks on site. Besides, in the case of trapping gaseous formaldehyde into an aqueous solution by establishing an annular flow, i.e., a diphasic flow, in a capillary, it is possible to observe unwanted air bubbles in the fluorescence detection cell when all the air is not evacuated by means of the microporous tube placed at the outlet of the capillary. In the present work, the use of passive trapping via a microporous tube overcomes this kind of problem.

However, the use of this new microanalyser also implies constraints compared to the solutions previously reported in the literature [13,30,32–41]. As mentioned before, changing the reagent involves rinsing the circuit beforehand. In practice, the most suitable solution will first be to rinse the entire circuit (without operating in recirculation) with a new reagent solution for approximately 15 min considering the internal volume of the circuit of about $250 \mu\text{L}$ and a flow rate of $17 \mu\text{L min}^{-1}$. Once done, the liquid flow will be stopped for a few moments. A new reagent vial recently unsealed and prepared either in the factory or in the laboratory, will be installed before restarting the instrument. This new reagent vial will contain the exact quantity of reagent desired by the user, e.g., 5.8 mL, like in the present work. This technical solution has the advantage of not requiring any specific equipment as a precise balance. However, an alternative solution could be the use of a previously calibrated precision pipette to fill the reagent vial after the rinsing step. This maintenance will therefore last 15–20 min with this new instrument against only a few minutes in the case of the other analysers mentioned in Table 1

where the reagent solution(s) can be quickly changed. This small disadvantage is counterbalanced by the advantage of not having a waste bottle, which must be emptied regularly and each time the reagents are changed, otherwise it could overflow near the instrument and damage it.

5. Conclusions

This work reports the development of an original device operating in a closed-circuit making it possible to trap gaseous formaldehyde into a solution through a porous interface and to quantify it by fluorescence after derivatization. This new approach has made it possible to reduce the size of the instrument by at least half, compared to the previous instrument currently on the market (μ F-1, In'Air Solutions, Strasbourg, France), which operates based on a microfluidic device where the gaseous formaldehyde is trapped by means of an annular flow. The novel formaldehyde microanalyser has therefore a better portability for on-site measurements.

The instrument is very flexible since the reagent volume can be adapted to the range of formaldehyde concentrations to be measured. A large reagent volume will be chosen for high concentrations that can be encountered in industrial environments or very polluted environments. Conversely, a small reagent volume can be chosen to monitor low airborne concentrations and/or obtain a very short measurement time step. In the latter case, it will be at the expense of the device autonomy in terms of reagent since the acetylacetone solution will be more rapidly saturated. In other words, the sensitivity of this instrument strongly depends on the reagent volume used and the integration time used to measure the slope of the fluorescence signal increase.

With an hourly measurement which is largely sufficient for standard indoor quality monitoring where the formaldehyde concentrations are in the range $0\text{--}50\ \mu\text{g m}^{-3}$, as observed in more than 97% or 98% of schools by Kirchner et al. (2018) [47] and Michelot et al. (2012) [48], the expected hourly detection limit is about $2\ \mu\text{g m}^{-3}$ when considering a reagent volume of 6 mL. In these experimental conditions and regarding our experimental results obtained for $16\ \mu\text{g m}^{-3}$ and $54\ \mu\text{g m}^{-3}$, the expected autonomy should be at least 4 days. This new microanalyser appears as a compromise between a fast, sensitive, and expensive formaldehyde analyser [13,30,33–36,39] and measurements with DNPH tubes because it provides information on the temporal evolution of the gas concentration, the measurement being able to be integrated over a very long time (24 h for example) to give an average daily value with an excellent sensitivity, i.e., a LOD equal to $0.08\ \mu\text{g m}^{-3}$.

In the future, the integration of an automatic gain applicable to the fluorescence signal would avoid saturation of the signal by reducing the gain from 50% to 45% and then to 40% for example. However, this requires that the instrument has been previously calibrated with all these gains in the range of investigated formaldehyde concentrations.

Ideally, the on-chip integration of the fluorescence cell, LED and a miniaturized detector such as micro PMT would make it possible to reduce very significantly the size of the detection module which represents currently 35–40% of the total volume of the components as displayed in Figure 3. Such improvement could also reduce the price of the detection module by approximately ten when produced in large series. So far, no study and even the very recent work of Mariuta et al. (2020) [49], using the same derivative reagent to detect formaldehyde in liquid solution, was able to reach a satisfactory sensitivity using on-chip integration. Indeed, Mariuta et al. (2020) showed that the sensitivity reached is approximately 100 times less so than that reported in this work, which is still very insufficient to allow precise and sufficiently rapid quantification of gaseous formaldehyde in the recirculation configuration.

6. Patents

Based on the technological development and the experimental results obtained in this work, the authors have submitted a patent in France: le Cavé, S.; Andrikopoulou, C.; Becker, A.; Bernhardt, P.; Trocquet, C.; Plaisance, H. Procédé et dispositifs d'analyses microfluidiques pour la quantification de polluants gazeux solubles dans l'eau, French patent n° FR1906855, submitted on 25 March 2019.

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Conflicts of Interest: The authors declare no conflict of interest.

References

1. Dehghani, M.H.; Zarei, A.; Farhang, M.; Kumar, P.; Yousefi, M.; Kim, K.-H. Levels of formaldehyde in residential indoor air of Gonabad, Iran. *Hum. Ecol. Risk Assess. Int. J.* **2020**, *26*, 483–494. [[CrossRef](#)]
2. Babeş, B.; Martonş, I.M.; Matei, A.T. Ventilation and Indoor Air Quality in Learning Environments from Cluj-Napoca (Romania). In Proceedings of the Air and Water Components of the Environment Conference, Cluj-Napoca, Romania, 22–24 March 2019; pp. 23–36. [[CrossRef](#)]
3. Saini, J.; Dutta, M.; Marques, G. A comprehensive review on indoor air quality monitoring systems for enhanced public health. *Sustain. Environ. Res.* **2020**, *30*, 1–12. [[CrossRef](#)]
4. Orola, B.A. Seasonal variations in indoor air quality parameters and occupants self-reported physical health within a warm humid climatic environment. *Sustain. Build.* **2020**, *5*, 2. [[CrossRef](#)]
5. Yuan, Y.; Alahmad, B.; Kang, C.-M.; Al-Marri, F.; Kommula, V.; Bouhamra, W.; Koutrakis, P. Dust Events and Indoor Air Quality in Residential Homes in Kuwait. *Int. J. Environ. Res. Public Health* **2020**, *17*, 2433. [[CrossRef](#)] [[PubMed](#)]
6. Wang, B.; Lee, S.C.; Ho, K.F. Characteristics of carbonyls: Concentrations and source strengths for indoor and outdoor residential microenvironments in China. *Atmos. Environ.* **2007**, *13*, 2851–2861. [[CrossRef](#)]
7. Salthammer, T. Formaldehyde sources, formaldehyde concentrations and air exchange rates in European housings. *Build. Environ.* **2019**, *150*, 219–232. [[CrossRef](#)]
8. Gilbert, N.L.; Guay, M.; Gauvin, D.; Dietz, R.N.; Chan, C.C.; Lévesque, B. Air change rate and concentration of formaldehyde in residential indoor air. *Atmos. Environ.* **2008**, *10*, 2424–2428. [[CrossRef](#)]
9. Salthammer, T.; Mentese, S.; Marutzky, R. Formaldehyde in the Indoor Environment. *Chem. Rev.* **2010**, *110*, 2536–2572. [[CrossRef](#)]
10. Wang, X.; Wang, H.; Wang, S. Ambient formaldehyde and its contributing factor to ozone and OH radical in a rural area. *Atmos. Environ.* **2010**, *44*, 2074–2078.
11. Liu, C.; Miao, X.; Li, J. Outdoor formaldehyde matters and substantially impacts indoor formaldehyde concentrations. *Build. Environ.* **2019**, *158*, 145–150. [[CrossRef](#)]
12. Marchand, C.; Bulliot, B.; Le Calvé, S.; Mirabel, P. Aldehyde measurements in indoor environments in Strasbourg (France). *Atmos. Environ.* **2006**, *40*, 1336–1345. [[CrossRef](#)]
13. Trocquet, C.; Bernhardt, P.; Guglielmino, M.; Malandain, I.; Liaud, C.; Englaro, S.; Le Calvé, S. Near Real-Time Monitoring of Formaldehyde in a Low-Energy School Building. *Atmosphere* **2019**, *10*, 763. [[CrossRef](#)]
14. Brdarić, D.; Kovač-Andrić, E.; Šapina, M.; Kramarić, K.; Lutz, N.; Perković, T.; Egorov, A. Indoor air pollution with benzene, formaldehyde, and nitrogen dioxide in schools in Osijek, Croatia. *Air Qual. Atmos. Health* **2019**, *12*, 963–968. [[CrossRef](#)]
15. Casset, A.; Marchand, C.; Purohit, A.; Calve, S.L.; Uring-Lambert, B.; Donnay, C.; Meyer, P.; Blay, F.D. Inhaled formaldehyde exposure: Effect on bronchial response to mite allergen in sensitized asthma patients. *Allergy* **2006**, *61*, 1344–1350. [[CrossRef](#)] [[PubMed](#)]
16. Yu, L.; Wang, B.; Cheng, M.; Yang, M.; Gan, S.; Fan, L.; Wang, D.; Chen, W. Association between indoor formaldehyde exposure and asthma: A systematic review and meta-analysis of observational studies. *Indoor Air* **2020**, *30*, 682–690. [[CrossRef](#)]
17. McGwin, G., Jr.; Lienert, J.; Kennedy, J.I., Jr. Formaldehyde Exposure and Asthma in Children: A Systematic Review. *Environ. Health Perspect.* **2010**, *118*, 313–317. [[CrossRef](#)]
18. IARC Overall evaluation of carcinogenicity to humans, formaldehyde. *Oncol. Times* **2004**, *26*, 72. [[CrossRef](#)]

19. ANSES—Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail. Valeurs Guides de Qualité d'Air Intérieur (VGAI) Le Formaldéhyde. Available online: <https://www.anses.fr/fr/system/files/AIR2017SA0041Ra.pdf> (accessed on 22 November 2019).
20. Williams, J.; Li, H.; Ross, A.B.; Hargreaves, S.P. Quantification of the influence of NO₂, NO and CO gases on the determination of formaldehyde and acetaldehyde using the DNPH method as applied to polluted environments. *Atmos. Environ.* **2019**, *218*, 117019. [[CrossRef](#)]
21. Herrington, J.S.; Hays, M.D. Concerns regarding 24-h sampling for formaldehyde, acetaldehyde, and acrolein using 2,4-dinitrophenylhydrazine (DNPH)-coated solid sorbents. *Atmos. Environ.* **2012**, *55*, 179–184. [[CrossRef](#)]
22. Hornshøj, B.H.; Kobbelgaard, S.; Blakemore, W.R.; Stapelfeldt, H.; Bixler, H.J.; Klinger, M. Quantification of free formaldehyde in carrageenan and processed Eucheuma seaweed using high-performance liquid chromatography. *Food Addit. Contam. Part A* **2015**, *32*, 152–160. [[CrossRef](#)]
23. de Freitas Rezende, F.B.; de Souza Santos Cheibub, A.M.; Pereira Netto, A.D.; Marques, F.F.D.C. Determination of formaldehyde in bovine milk using a high sensitivity HPLC-UV method. *Microchem. J.* **2017**, *134*, 383–389. [[CrossRef](#)]
24. Rosenberger, W.; Beckmann, B.; Wrbitzky, R. Airborne aldehydes in cabin-air of commercial aircraft: Measurement by HPLC with UV absorbance detection of 2,4-dinitrophenylhydrazones. *J. Chromatogr. B* **2016**, *1019*, 117–127. [[CrossRef](#)] [[PubMed](#)]
25. Soman, A.; Qiu, Y.; Chan Li, Q. HPLC-UV Method Development and Validation for the Determination of Low Level Formaldehyde in a Drug Substance. *J. Chromatogr. Sci.* **2008**, *46*, 461–465. [[CrossRef](#)] [[PubMed](#)]
26. Salthammer, T. Photophysical properties of 3,5-diacetyl-1,4-dihydrolutidine in solution: Application to the analysis of formaldehyde. *J. Photochem. Photobiol. A Chem.* **1993**, *74*, 195–201. [[CrossRef](#)]
27. Jobson, B.T.; McCoskey, J.K. Sample drying to improve HCHO measurements by PTR-MS instruments: Laboratory and field measurements. *Atmos. Chem. Phys.* **2010**, *10*, 1821–1835. [[CrossRef](#)]
28. Hanoune, B.; LeBris, T.; Allou, L.; Marchand, C.; Le Calvé, S. Formaldehyde measurements in libraries: Comparison between infrared diode laser spectroscopy and a DNPH-derivatization method. *Atmos. Environ.* **2006**, *40*, 5768–5775. [[CrossRef](#)]
29. Vlasenko, A.; Macdonald, A.M.; Sjøstedt, S.J.; Abbatt, J.P.D. Formaldehyde measurements by Proton transfer reaction–Mass Spectrometry (PTR-MS): Correction for humidity effects. *Atmos. Meas. Tech.* **2010**, *3*, 1055–1062. [[CrossRef](#)]
30. Toda, K.; Tokunaga, W.; Gushiken, Y.; Hirota, K.; Nose, T.; Suda, D.; Nagai, J.; Ohira, S.-I. Mobile monitoring along a street canyon and stationary forest air monitoring of formaldehyde by means of a micro-gas analysis system. *J. Environ. Monit.* **2012**, *14*, 1462–1472. [[CrossRef](#)]
31. Allouch, A.; Guglielmino, M.; Bernhardt, P.; Serra, C.A.; Le Calvé, S. Transportable, fast and high sensitive near real-time analyzers: Formaldehyde detection. *Sens. Actuators B Chem.* **2013**, *181*, 551–558. [[CrossRef](#)]
32. Pretto, A.; Milani, M.R.; Cardoso, A.A. Colorimetric determination of formaldehyde in air using a hanging drop of chromotropic acid. *J. Environ. Monit.* **2000**, *2*, 566–570. [[CrossRef](#)]
33. Toda, K.; Yoshioka, K.-I.; Mori, K.; Hirata, S. Portable system for near-real time measurement of gaseous formaldehyde by means of parallel scrubber stopped-flow absorptiometry. *Anal. Chim. Acta* **2005**, *531*, 41–49. [[CrossRef](#)]
34. Sassine, M.; Picquet-Varrault, B.; Perraudin, E.; Chiappini, L.; Doussin, J.F.; George, C. A new device for formaldehyde and total aldehydes real-time monitoring. *Environ. Sci. Pollut. Res. Int.* **2014**, *21*, 1258–1269. [[CrossRef](#)] [[PubMed](#)]
35. Guglielmino, M.; Bernhardt, P.; Trocquet, C.; Serra, C.A.; Le Calvé, S. On-line gaseous formaldehyde detection by a microfluidic analytical method based on simultaneous uptake and derivatization in a temperature controlled annular flow. *Talanta* **2017**, *172*, 102–108. [[CrossRef](#)]
36. Sakai, T.; Tanaka, S.; Teshima, N.; Yasuda, S.; Ura, N. Fluorimetric flow injection analysis of trace amount of formaldehyde in environmental atmosphere with 5,5-dimethylcyclohexane-1,3-dione. *Talanta* **2002**, *58*, 1271–1278. [[CrossRef](#)]
37. Li, J.; Dasgupta, P.K.; Luke, W. Measurement of gaseous and aqueous trace formaldehyde: Revisiting the pentanedione reaction and field applications. *Anal. Chim. Acta* **2005**, *531*, 51–68. [[CrossRef](#)]
38. Zheng, W. Développement d'un Analyseur Rapide et Transportable du Formaldéhyde dans L'air. Ph.D. Thesis, University of Strasbourg, Strasbourg, France, 2010.

39. Guglielmino, M.; Allouch, A.; Serra, C.A.; Calvé, S.L. Development of microfluidic analytical method for on-line gaseous Formaldehyde detection. *Sens. Actuators B Chem.* **2017**, *243*, 963–970. [[CrossRef](#)]
40. Becker, A.; Andrikopoulou, C.; Bernhardt, P.; Ocampo-Torres, R.; Troquet, C.; Le Calvé, S. Development and Optimization of an Airborne Formaldehyde Microfluidic Analytical Device Based on Passive Uptake through a Microporous Tube. *Micromachines* **2019**, *10*, 807. [[CrossRef](#)]
41. Hak, C.; Pundt, I.; Trick, S.; Kern, C.; Platt, U.; Dommen, J.; Ordóñez, C.; Prévôt, A.S.H.; Junkermann, W.; Astorga-Lloréns, C.; et al. Intercomparison of four different In-Situ techniques for ambient formaldehyde measurements in urban air. *Atmos. Chem. Phys.* **2005**, *5*, 2881–2900. [[CrossRef](#)]
42. Eisner, U.; Kuthan, J. Chemistry of dihydropyridines. *Chem. Rev.* **1972**, *72*, 1–42. [[CrossRef](#)]
43. Cerón, R.M.; Cerón, J.G.; Muriel, M. Diurnal and seasonal trends in carbonyl levels in a semi-urban coastal site in the Gulf of Campeche, Mexico. *Atmos. Environ.* **2007**, *41*, 63–71. [[CrossRef](#)]
44. Wangchuk, T.; He, C.; Dudzinska, M.R.; Morawska, L. Seasonal variations of outdoor air pollution and factors driving them in the school environment in rural Bhutan. *Atmos. Environ.* **2015**, *113*, 151–158. [[CrossRef](#)]
45. Le Calvé, S.; Andrikopoulou, C.; Becker, A.; Bernhardt, P.; Trocquet, C. Procédé et Dispositif d'Analyse Microfluidique Pour la Quantification de Polluants Gazeux Solubles dans L'eau. French Patent n1906855, 25 June 2019.
46. Allou, L.; Maimouni, L. Henry's law constant measurements for formaldehyde and benzaldehyde as a function of temperature and water composition. *Atmos. Environ.* **2011**, *45*, 2991–2998. [[CrossRef](#)]
47. Kirchner, S.; Dassonville, C.; Mandin, C.; Sivanantham, S.; Wei, W.; Malingre, L.; Grégoire, A.; Ramalho, O.; Ribéron, J.; Derbez, M.; et al. Qualité de l'air et Confort dans les écoles en France: Premiers Résultats de la Campagne Nationale. Available online: <https://www.cstb.fr/fr/actualites/detail/premiers-resultats-qualite-air-confort-ecoles-france-0618/> (accessed on 26 June 2018).
48. Monitoring Indoor Air Quality in French Schools and Day-Care Centres. Results from the First Phase of a Pilot Survey. Available online: https://www.researchgate.net/publication/311846852_Monitoring_indoor_air_quality_in_French_schools_and_day-care_centres_Results_from_the_first_phase_of_a_pilot_survey (accessed on 26 June 2020).
49. Mariuta, D.; Govindaraji, A.; Colin, S.; Barrot, C.; Le Calvé, S.; Korvink, J.G.; Baldas, L.; Brandner, J.J. Optofluidic Formaldehyde Sensing: Towards On-Chip Integration. *Micromachines* **2020**, *11*, 673. [[CrossRef](#)]



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