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PAPER

A microfluidic lab-on-chip derivatisation technique for the measurement of gas phase formaldehyde

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A microfluidic lab-on-chip derivatisation technique has been optimized to achieve a rapid, automated and sensitive determination of ambient gaseous formaldehyde when used in combination with GC-MS. The method used a Pyrex micro-reactor comprising three inlets and one outlet, gas and fluid splitting and combining channels, mixing junctions, and a 2.0 m long, 620 μm internal diameter reaction micro-channel. The micro-reactor integrated three functions, that of: (1) mixer and reactor, (2) heater, and (3) preconcentrator. The flow rates of the gas sample and derivatisation solution and the temperature of the micro-reactor were optimized to achieve a near real-time measurement with a rapid and high efficiency derivatisation step following gas sampling. The enhanced phase contact area-to-volume ratio and the high heat transfer rate in the micro-reactor resulted in a fast and high efficiency derivatisation reaction. Calibration showed good linearity in the range of 26 to 331 ppb with correlation coefficients $R^2 = 0.988$ and 0.997 for PFPH and PFBHA derivatives. For low gas phase formaldehyde mixing ratios (<26 ppb) the derivatisation solution could be repeatedly recycled through the chip enabling pre-concentration of the derivative – hydrazone. The calibration curves for this recycling approach also showed good linearity from 4.0 to 26 ppb with method detection limits (MDLs) of 2.1 ppb and 1.1 ppb for PFPH and PFBHA derivatives. The feasibility of the technique was assessed using measurements of laboratory ambient air, with formaldehyde the predominant carbonyl compound at a 12.5 ppb level. The proof of principle experiments demonstrated the potential of the approach for on-line measurements of other carbonyls including acetaldehyde, acetone and propionaldehyde.

1. Introduction

Developing a rapid and sensitive analytical technique for formaldehyde has been a priority for researchers over several decades since formaldehyde plays a pivotal role in atmospheric chemistry and is a very common indoor air pollutant. Formaldehyde is a significant source of HO_X radicals, the key oxidant in the troposphere.[1] Several decades ago formaldehyde was classified as a carcinogen to humans by the International Agency for Research on Cancer (IARC).[2] In recent years formaldehyde concentrations in both urban ambient air and indoor air have increased due to increasing emissions from vehicular exhausts and interior decoration materials.[3,4] In indoor micro-environments and urban air, formaldehyde concentration mostly varies from 10 to 100 ppb[4–7] while in remote clean oceanic areas formaldehyde average concentrations are 0.1–1.0 ppb.[8,9] Rapid and sensitive measurements of formaldehyde in ambient and indoor environments are of great utility therefore to environmental toxicology and atmospheric chemistry.

In recent years, several *in situ* techniques have been developed for the measurement of formaldehyde. Several spectroscopic techniques have been reported including differential optical absorption spectroscopy (DOAS),[10,11] Fourier transform infrared (FTIR) absorption,[12] laser-induced fluorescence spectroscopy (LIFS),[13] tuneable diode laser absorption spectroscopy (TDLAS),[14,15] and incoherent broadband cavity enhanced absorption spectroscopy.[16] Many spectroscopic techniques have required complicated instruments or long optical paths however, which restrict their suitability and portability for routine field applications. Automated fluorometric determination of formaldehyde in air is possible through a diffusion denuder or scrubber or glass coil to strip formaldehyde from air into water.[17–19] The aqueous formaldehyde then reacted with a fluorescent probe and was simultaneously determined by a fluorometer. The fluorometric techniques in the literature are sensitive, with method detection limits (MDL) of tens of pptv, but such techniques offer limited selectivity in their response over other carbonyls. Proton-transfer reaction mass spectrometry (PTR-MS) has been successfully used for monitoring formaldehyde, although formaldehyde is more difficult to detect using PTR-MS than other

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carbonyls due to the loss of the protonated ion resulting from the reaction with water. A continuous measurement of atmospheric formaldehyde was developed based on a capillary GC with a pulsed discharge helium ionisation detector but its cryogenic preconcentration by liquid nitrogen and a water condensation trap limited its practical application.[20] Gu *et al.* used a metal–organic framework as the sorbent in combination with thermal desorption GC/MS to determine atmospheric formaldehyde directly[21] although formaldehyde is generally considered to be too small to produce unique ions in the MS detector. Recently, Hopkins *et al.* developed a dual channel GC-FID method to analyze *in situ* some carbonyls but not formaldehyde, with MDLs in the range 1–5 ppt.[22,23]

Given the increasing demand for fast and simple indoor formaldehyde monitoring methods, sensor technology has progressed greatly in recent decades. Feng *et al.* developed a colorimetric sensor for formaldehyde using ordinary pH indicators in an amine-functionalized polymer film, which discriminated formaldehyde over a wide range from 20 ppm to 250 ppb.[24] Lv *et al.* reported a microgas sensor based on a micro hotplate, which detected a gas phase concentration of 60 ppb.[25] Zhou *et al.* described a cataluminescence-based gas sensor using nano-sized $V_2Ti_4O_{13}$ as a probe for online determination of formaldehyde with an MDL of 0.06 mg m^{-3}.[26] A semiconductor gas sensor of tin oxide doped with hydroxyl-functionalized multiwall carbon nanotubes had been designed and tested by Wang *et al.*[27] However, sensors suffer from comparatively high detection limits of more than 50 ppb, which make the techniques mainly suitable for workplace environments.[4]

A common and versatile method for formaldehyde measurement uses the principle of chemical derivatisation. Such methods have acceptable sensitivity, are carbonyl specific and generally have good reproducibility. For example formaldehyde and other carbonyls may be trapped on solid absorbents coated with a suitable derivatisation agent, *e.g.* *O*-(2,3,4,5,6-pentafluorobenzyl) hydroxylamine (PFBHA),[28,29] pentafluorophenyl hydrazine (PFPH),[30–32] and 2,4-dinitrophenylhydrazine (DNPH).[33,34] These resulting chromophores can then be desorbed by an appropriate solvent and then separated and detected by GC/MS or HPLC/UV. Although derivatisation methods are state-of-the-art for the analysis of formaldehyde, the drawbacks of these methods are long sampling times, typically 0.5–2 h, and the procedure of derivatisation and solvent extraction/reduction is cumbersome and unattractive for continuous analysis. To overcome such drawbacks other related sampling techniques have been developed. PFPHA coated denuder-filter sampling techniques were developed for the simultaneous collection of gas and particle phase formaldehyde.[35,36] However, the preparation of denuder sampling devices, solvent extraction and preconcentration remain time consuming and complicated. Annular diffusion scrubbers have been used in near-real time for measurement of formaldehyde in indoor air, ambient air, and vehicular exhaust fumes, consisting of a hydrophobic porous PTFE tube within a Pyrex-glass tube and a scrubbing solution for trapping formaldehyde.[37–39] The scrubbers used in these examples were fragile and significant quantities of solvent were needed. PFBHA-derivatisation and GC/MS analysis, coupled with an impinger, a mist chamber or a denuder can also be used to identify and quantify airborne formaldehyde.[29,40] Although this technique is highly specific to individual carbonyl structures, it involved batch sampling followed by a manual procedure of derivatisation and solvent extraction, making it difficult to automate and unsuitable for routine field measurement. Solid-phase microextraction with on-fiber PFBHA derivatisation has been employed to determine formaldehyde in indoor air with a high MDL of 5 ppb.[41,42] A continuous automated analysis HPLC system was recently reported using a single silica micro-cartridge based on DNPH derivatisation.[43] Despite this diversity of approaches in the literature, there remains a pressing need for the development of a rapid and highly convenient formaldehyde detection method which has low MDLs and high specificity to this and other carbonyls. Additionally, it should be acknowledged for derivatisation methods that potential interferences with formaldehyde and other carbonyls in ambient air cannot be avoided during transportation, sampling and analyzing processes.[30,32]

Microfluidic analysis systems, also called lab-on-a-chip, have developed rapidly over the past decade in diverse fields including chemical synthesis, biological sensing, medical diagnostics, environmental analysis and energy conversion. They are attractive for many reasons; of relevance here for field measurements are their economical consumption of reagents and energy.[44–46] An advantage of undertaking reactions in microfluidic systems is that enhanced reaction efficiency may be achieved due to a high phase contact area-to-volume ratio in micro-channels.[47–49]

In this study, a rapid, simple and sensitive microfluidic approach was developed by achieving the highly efficient derivatisation reactions (Fig. 1) between formaldehyde and two common derivatisation reagents, pentafluorophenyl hydrazine (PFPH) and *O*-(2,3,4,5,6-pentafluorobenzyl) hydroxylamine (PFBHA), in a micro-reactor. The micro-reactor is a planar Pyrex glass microfluidic chip containing a long circular structure micro-channel inside, providing a capillary volume for the reaction to occur in. The microfluidics technique realised a near real-time analysis based on a rapid derivatisation reaction occurring simultaneously with air sampling at high chip temperature. Combined with the auto-sampler of a GC-MS, the microfluidics approach achieved continuous sampling and analysis with a time resolution of around 30 minutes.

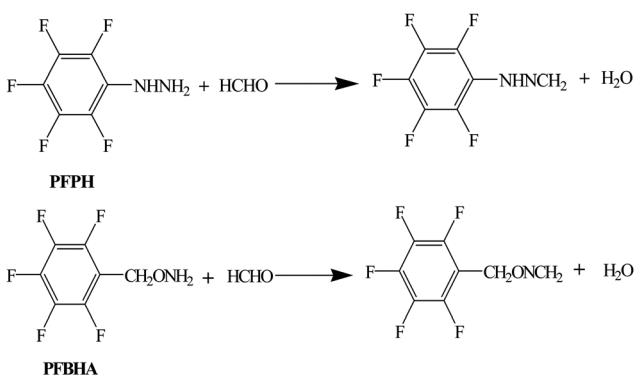

Fig. 1 Derivatisation reactions of formaldehyde with PFPH (upper panel) and PFBHA (lower panel) to form their corresponding derivatives – hydrazones.

2. Experimental

Micro-reactor layout

The glass microfluidic chip was fabricated by a specialised manufacturer of micro-scaled glass devices (Dolomite Centre, UK) using HF etching and thermal bonding processes. The basic layout of the micro-reactor is shown in Fig. 2a with a size of 90 mm × 45 mm × 4.5 mm (length × width × thickness). The microfluidic chip was installed with a chip holder and chip header to allow quick connection to 1/16″ tubing through its three inlets and one outlet (Fig. 2b). Air and the solution of the derivatisation reagent were passed into the splitting channel (hemispherical profile with 620 μm internal diameter and 2.1 cm length) and then mixed with each other through the mixing junctions. The reaction micro-channel between the mixing junctions and output (circular profile with 620 μm internal diameter and 208 cm length) provided space and time for the reaction between formaldehyde and derivatisation reagents to occur. The maximum operating temperature and pressure of the chip were 300 °C and 30 bar, respectively, but all experiments here were conducted under much less extreme conditions.

Materials and apparatus

All chemicals unless otherwise stated were purchased from Sigma-Aldrich Company (Gillingham, UK). Hexane was chosen as the solvent in part because of its favourable wetting characteristics on the glass surface and in part because its intermediate volatility allows for evaporation and liquid phase concentration of derivatives in the solution in the chip. Hexane (HPLC grade) was purchased from Fisher company (UK). Two derivatisation reagents, pentafluorophenyl hydrazine (PFPH) (97%) and *O*-(2,3,4,5,6-pentafluorobenzyl) hydroxylamine (PFBHA) (98%), were purified further through recrystallization before use in this study. A gaseous formaldehyde standard (331 ppb) was produced from a formaldehyde permeation tube (HRT-010.3024/80, Kin-tek, LaMarque, TX, USA) contained in an oven held at the temperature of 80.0 °C with a nitrogen (high purity 5.0 grade) flow of 400 mL min^{-1}. Formaldehyde standard gases at different concentrations were prepared using nitrogen dilutions. To eliminate formaldehyde and other carbonyl compounds contained in nitrogen gas, a DNPH-coated silica cartridge (Supelco, USA) was connected to the nitrogen cylinder outlet. The flow rates of nitrogen, test formaldehyde gas and lab air (pumped by a new KNF air pump (Germany)) were controlled by a mass flow controller (MKS Instrument, UK), itself calibrated by a gas flow meter (Alicat Scientific, USA). Flow of the derivatisation solution was generated and controlled by a peristaltic pump (Watson Marlow 205S, UK), varying from 20 μL min^{-1} to 120 μL min^{-1}. A magnetic stirrer hotplate (RH Basic 2 IKAMAG, UK) with a contact thermometer was used to heat the chip directly. Separation and detection of PFPH and PFBHA derivatives of formaldehyde were performed with a GC-MS system incorporating an Agilent 6890N GC (USA) and a Leco Pegasus III reflection time-of-flight MS (USA) equipped with an HP5 column (30 m × 320 μm × 0.25 μm, length × internal diameter × film thickness).

Analysis system design

The microfluidic chip integrates three key functions: (1) mixing and reaction, (2) heating, and (3) pre-concentration. Formaldehyde gas was passed into the micro-reactor through inlet 3 by the air pump and the derivatisation solution (PFPH or PFBHA) was passed into the micro-reactor simultaneously through inlet 1 and inlet 2 by the peristaltic pump (Fig. 2c). The chip was fixed securely on the surface of a hotplate head for direct heating. Formaldehyde in the gas stream reacted with the derivatisation solution with high efficiency in the micro-channel through diffusion into the derivatisation solution which formed a laminar layer on the channel walls (Fig. 3), analogous to a capillary chromatography stationary phase. A stainless metal coil (50 cm in length) was connected to the outlet of the micro-reactor, and placed in an ice–salt bath with a temperature of −1 °C. When formaldehyde concentrations were higher than around 26 ppb, the reaction solution eluting from the stainless coil was collected directly into a sample vial within the autosampler for the GC-MS (Fig. 4a). When the formaldehyde concentration was lower than

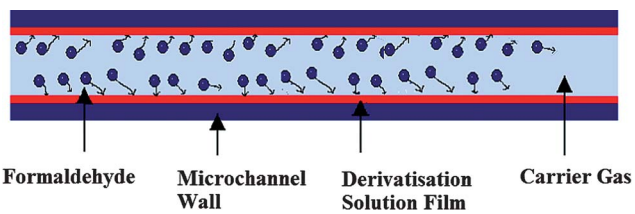

Fig. 3 The mixing profile of formaldehyde and derivatisation solution inside the micro-channel.

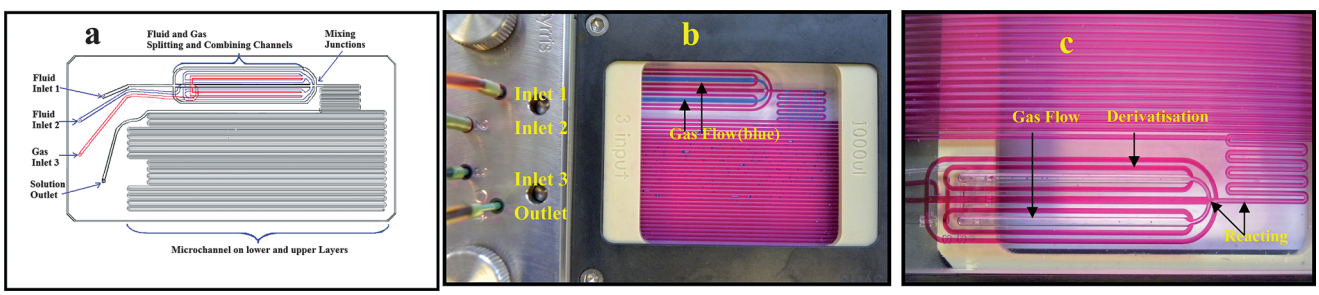

Fig. 2 Panel a: basic layout of a micro-reactor including three inputs, one output, splitting and combining channel, mixing junctions, and 208 cm reaction channel. Panel b: the detailed layout of a micro-reactor and the flow of formaldehyde (blue flow) and derivatisation solution (red flow). Panel c: mixture and reaction between formaldehyde and derivatisation solution (red flow) in a reaction micro-channel.

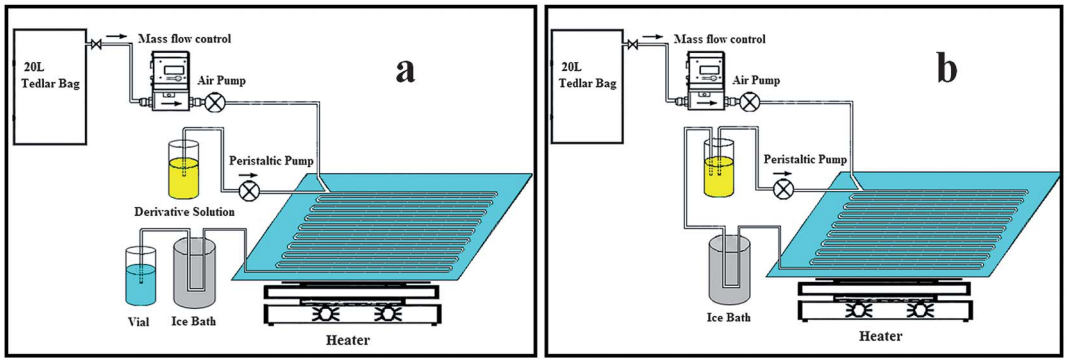

Fig. 4 Schematics of the microfluidic lab-on-chip derivatisation system. Panel a: when the formaldehyde level was greater than 26 ppb, the reaction solution was collected directly from the micro-reactor. Panel b: when the formaldehyde level was less than 26 ppb the reaction solution was recycled and preconcentrated further before analysis since the concentration is outside the range of the calibration performed in the situation of panel a.

26 ppb, the reaction solution was recycled again through the peristaltic pump and then the chip, to increase the liquid phase concentration of the derivative before detection by GC-MS (Fig. 4b).

Detection and data processing

For analysis of the resulting PFPH–HCHO derivative, the GC conditions were the following: the GC oven temperature was initially set at 70 °C and programmed to give a temperature ramp of 8 °C min^{-1} up to 150 °C and held at this for 2 min. The solvent delay was set at 5 min to avoid possible damage to the MS detector due to the high level of PFPH. For the PFBHA–HCHO derivative, the GC oven temperature was initially set at 85 °C and kept isothermal for 2 minutes, then programmed to give a temperature ramp of 9 °C min^{-1} up to 130 °C and finally held at this for 5 min. For the two derivatives, the GC injection mode was set as splitless. The GC inlet temperature was kept at 275 °C and the GC-MS transfer line temperature was 290 °C. The mass spectrometer was operated in scan mode with a mass range of 50–500 Da to identify the most abundant ions. Formaldehyde gases in different concentrations were prepared by dilution of the 331 ppb standard gas in a 20 L Tedlar bag (SKC, USA) with nitrogen of high purity grade (99.999%), which was further purified using an Aeronex® trap. In these experiments, blank samples were prepared in another Tedlar bag without formaldehyde input and measured using the same process as for the formaldehyde standard gas. The blank values were around 1.5 ppb at a flow rate of 200 mL min^{-1}. This value is relatively high but reflects the difficulty in generating formaldehyde free air in a Tedlar bag and when using the pumps and other gas handling equipment employed here. All results shown hereafter have been corrected from blank samples. The chromatograms of the most abundant ions, which are 155 and 181 for PFPH–HCHO and PFBHA–HCHO derivatives respectively, were used to quantify the concentration of derivatives in solution. The method detection limit (MDL) was calculated based on the equation of MDL = $3s/m$ (s is the standard deviation of the blank values and m is the slope of the calibration curve).

To evaluate the reaction efficiency (RE) of formaldehyde and the derivatisation solution in the micro-reactor the emerging gas flow was passed through a small downstream impinger filled with 1.0 mL of the derivatisation solution in series after passing out from the stainless coil and the vial. The reaction efficiency was calculated as RE% using $100 \times (1 - A_b/A_f)$, where A_f and A_b are the amounts of formaldehyde collected in the vial and the impinger, respectively.

3. Results

Optimization of flow rates of gas and solution

Since formaldehyde gas and derivatisation solution mix with each other and react in the channel of the micro-reactor, their individual flow rates greatly influence the mixing conditions and reaction efficiency (RE). If the flow rate of the test gas was too high, formaldehyde was not absorbed completely by the derivatisation solution, causing the RE to decrease. When the formaldehyde gas flow rate was low, the total amount of solution phase derivatives formed was also low impacting on the MDL of the method. When the solution flow was too high, the corresponding derivative concentrations were highly diluted and led to low signals in the GC-MS chromatogram. If the solution flow was too slow, the solvent in the micro-channel was at risk of complete evaporation by the sample gas flow, with no reacted solution available for collection from the micro-reactor outlet. The concentration of the derivatisation solution prepared in hexane was chosen as 5.0×10^{-4} mol L^{-1}, which is 20 times greater than the concentration of the derivatisation agent needed for a flow of 40 μL min^{-1} for derivatising the equivalent of a 331 ppb formaldehyde gas flowing at 400 mL min^{-1}.

Six flow rates of formaldehyde gas varying from 50 to 300 mL min^{-1} were evaluated for RE with the derivatisation solution flow rate set at 40 μL min^{-1} and the temperatures of the micro-reactor at 60 °C and 70 °C for PFPH and PFBHA respectively. As shown in Fig. 5a, flow rates of formaldehyde varying between 50 and 300 mL min^{-1} gave similar RE values all close to 100%. In this study the optimal flow of formaldehyde in gas was chosen as 200 mL min^{-1}. Five flow rates of the derivatisation solution varying from 20 to 120 μL min^{-1} were assessed based on their RE when the test gas formaldehyde flow was kept at 200 mL min^{-1}. When the solution flow rate was equal to or higher than 30 μL min^{-1}, the RE reached 90% (Fig. 5b). The optimal flow rates of two derivatisation solutions were chosen as 40 μL min^{-1}.

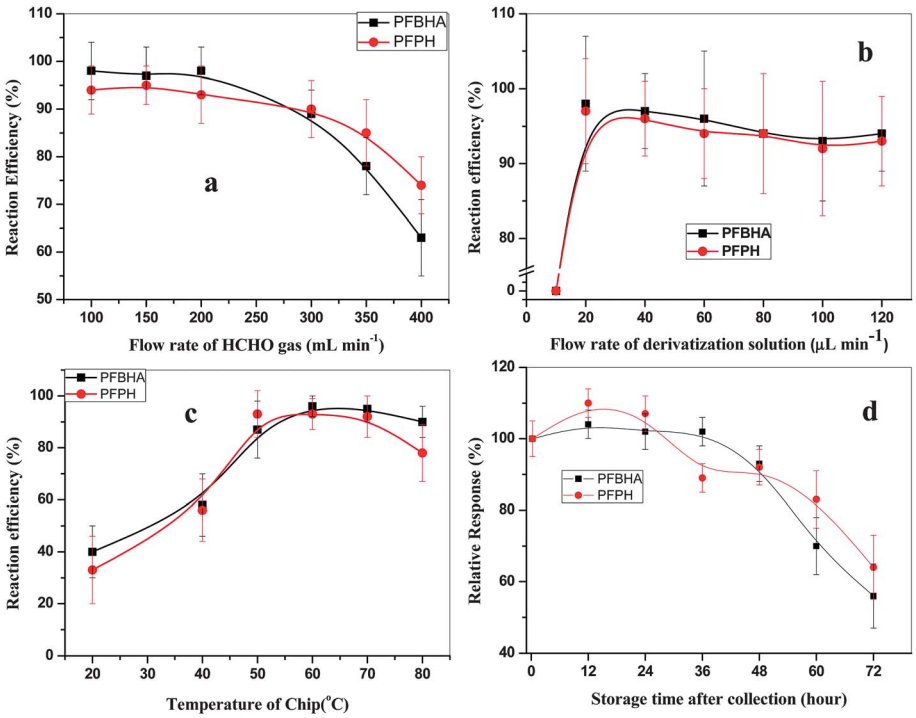

Fig. 5 Influences of flow rates of formaldehyde gas (panel a) and derivatisation solution (panel b), temperature of the micro-reactor (panel c) and storage time after collection (panel d) on reaction efficiency or intensities of the derivative solution. Error bars indicate the relative standard deviation (RSD) for five data points obtained for each measurement.

Optimization of temperature

The micro-reactor can be heated directly to an elevated temperature, unlike the more commonly used bubblers and impingers that are used often for stripping and derivatising reactions. Higher temperatures in the micro-channel can significantly enhance the RE but too high a temperature leads to rapid solvent evaporation. As Fig. 5c shows, the influence of five different temperatures of the micro-reactor on RE was evaluated. The REs of both derivatisation reactions were about 40% at normal laboratory temperature (20 °C) but were significantly promoted to 90% as the temperature increased to 60 °C. The RE of the reaction between PFPH and formaldehyde decreased when the temperature increased to 80 °C. In this study the optimal microreaction temperature was chosen as 60 °C.

Influence of reaction and storage times

The diffusion of formaldehyde into solution and the derivatisation reaction are not instantaneous and in this, as with other methods, it takes some time to reach equilibrium. In this study the peak areas of derivatives in the GC-MS chromatogram quickly reached a maximum and relatively constant level after the reaction had occurred for around ten minutes in the micro-channel (Fig. 5d). The derivatisation reaction in the micro-reactor was considered therefore sufficiently fast that it could be used for near real-time measurement of formaldehyde with the liquid samples passed for immediate GC-MS analysis. Such an approach then circumvents problems associated with slow storage reactions and long-term degradation of derivative samples in solution. In previous studies, the PFPH or PFBHA derivative yields have been reported to increase significantly after several days of storage.[21,23] Whilst we anticipate using the micro-channel method on-line, we also tested to see how storage of samples in vials changes these over time. In this experiment derivative yields were seen to increase only slightly (10% after 12 hours and 24 hours' storage), with increases much smaller in this study compared with those reported previously. After 48 hours, the derivative yields both decreased dramatically (Fig. 5d).

Calibration and application to air sample monitoring

Based on the above approaches, the optimal conditions of the micro-reactor for measurement of gas phase formaldehyde are shown in Table 1.The working calibration curves under optimal conditions show good linearity in the range of 26 to 330 ppb with correlation coefficients of $R^2 = 0.994$ and 0.993 for PFPH and PFBHA derivatives, respectively (Fig. 6a) and the chromatogram is shown in Fig. 7a. When the formaldehyde concentration was less than 26 ppb, the reacted solution collected from the outlet of the micro-reactor was recycled *via* the peristaltic pump to react further with more gaseous formaldehyde. This led to an

Table 1 Optimal conditions for PFPH and PFBHA derivatisation reactions with formaldehyde in a micro-reactor

Derivatisation Reagents	Temperature (°C)	Flow rate of HCHO (mL min^{-1})	Flow rate of solution (μL min^{-1})
PFPH	60	200	40
PFBHA	70	200	40

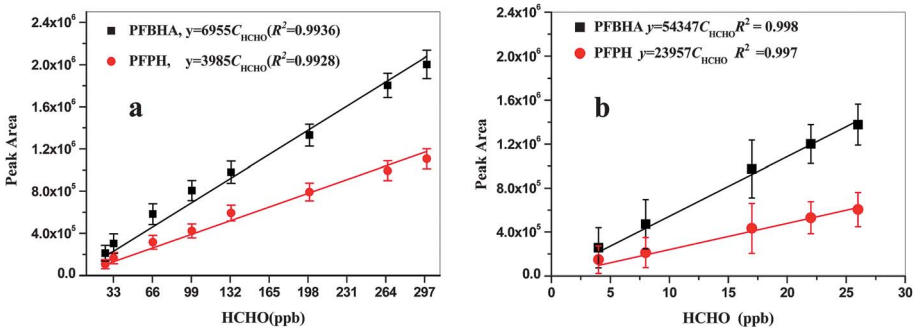

Fig. 6 Calibration curves for formaldehyde measured by the microfluidic derivatisation technique under optimal conditions described in the text. Panel a: calibration when formaldehyde concentrations were greater than 26 ppb. Panel b: calibration when formaldehyde concentrations were less than 26 ppb. Error bars indicate the RSD for five data points obtained for each measurement.

increasing concentration of the derivative in the solution with enhanced peak sizes in the GC-MS chromatogram. In this experiment 3.0 mL of the derivatisation solution reacted with formaldehyde gas in recycle mode for 30 minutes at 60 μL min^{-1}, reducing to a final 0.5 mL solution through evaporation. Using this approach a linear relationship was found between the peak area of the MS signal and formaldehyde concentration from 4.0 to 26 ppb with a correlation coefficient of $R^2 = 0.998$ and $R^2 = 0.997$ for PFPH and PFBHA derivatives (Fig. 6b). Their MDLs were calculated as 2.1 ppb and 1.1 ppb for PFPH and PFBHA derivatives under 200 mL min^{-1} air flow, with typical chromatograms shown in Fig. 7b. To test the feasibility for ambient measurements, laboratory air was sampled by this technique using 3.0 mL PFPH solution reacting with carbonyl compounds in air in recycling mode for 30 minutes, prior to GC-MS. Formaldehyde was found to be the predominant carbonyl compound at a 12.5 ppb level with acetaldehyde, acetone and propionaldehyde detected as other major carbonyls in laboratory indoor air (Fig. 7c).

4. Discussions

In a circular micro-channel, the head pressure of the channel is defined by the required flow rate of the solution, solution viscosity, internal diameter and length and it can be calculated based on the following equation.[50]

$$P = Q \times (6.79 \times 10^{-9} \times L \times \mu)/d^4$$

P: pressure (bar); Q: velocity of solution in channel (μL min^{-1}); d: pipe internal diameter (mm); L: tube length (mm); μ: solution viscosity (cP or mPa s).

In this study the flow rate of the tested gas (100–400 mL min^{-1}) was much higher than that of the derivatisation solution (40–60 μL min^{-1}) from the peristaltic pump and the pressure in the microchannel was controlled mainly by the tested gas. The air pump used in this study provided a maximum gas pressure of two Bar which generated a maximum gas flow of 600 mL min^{-1} in the micro-reactor. Since the flow rate of the tested gas was much higher than that of the derivatisation solution, a thin film of liquid was dragged along the micro-channel wall by the higher linear velocity of the gas (Fig. 3). Under such conditions formaldehyde gas was absorbed into the liquid film in a diffusive manner and then reacted with the derivatisation reagent in solution (Fig. 3). According to the experimental observations, it took about 10 minutes for the derivatising solution to pass through the whole micro-channel. A basic geometric calculation, assuming even coating, would indicate a thickness of around 100 μm of the liquid film on the micro-channel walls when 400 μL of the solution was introduced to the reactor. Under such conditions the derivatisation solution forms a film on the wall of the micro-channel and sample gases diffuse into and out of this film in a manner analogous to capillary gas chromatography.

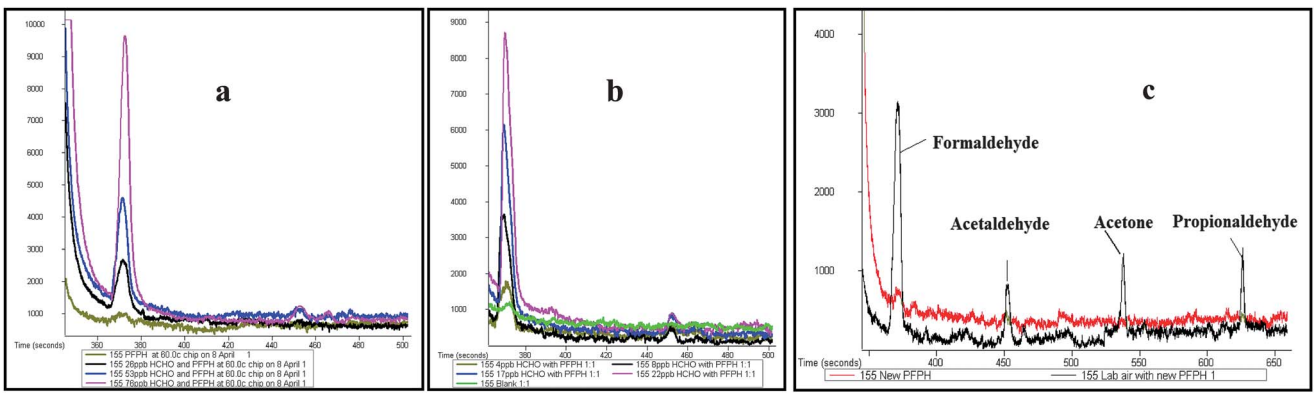

Fig. 7 Chromatograms of a formaldehyde PFPH derivative at different formaldehyde concentrations (panel a: peak height increases from 26 to 76 ppb; panel b: peak height increases from 4 to 22 ppb) and panel c: chromatogram of formaldehyde and other carbonyls detected in laboratory indoor air.

Table 2 Preconcentration effect of a micro-reactor under different conditions

Temp. (°C)	Flow rate of formaldehyde (mL min^{-1})	Volume of solution to inlet (mL)	Volume of solution from outlet (mL)	Enriching ratio
60	100	1.0	0.70	1.43
	200	1.0	0.48	2.08
	300	1.0	0.36	2.77
70	100	1.0	0.60	1.67
	200	1.0	0.45	2.22
	300	1.0	0.30	3.33
80	100	1.0	0.40	2.50
	200	1.0	0.30	3.33
	300	1.0	0.20	5.00

The high surface area to volume ratio of the micro-channel is therefore highly favourable for exposing formaldehyde to the derivatisation solution.

The planar structure and low thermal mass of the chip result in a high heat transfer rate when the chip is heated directly. In this study the derivative yields were relatively stable after only ten minutes of collection, with evidence for only limited continued slow reactions post-sampling over the next 12–24 hours. This phenomenon contrasts with reaction yields that increased significantly with post-collection storage times up to 3–5 days in previous studies.[21,23,24] A multiple-step reaction mechanism has been proposed for the reactions of formaldehyde with PFPH and PFBHA with the formation rates of the hydrazones limited by the later step in those studies.[21,23,24] In this experiment, the evidence suggests that both initial and later reaction steps were completed in the chip, enabled by the elevated reaction temperatures.

A final element worthy of discussion is the ability of the micro-reactor to act as an analyte concentrator. Solvent evaporation occurs inside the micro-channels from the film layers on the walls and is accelerated by elevated temperatures. By using a relatively low boiling point solvent such as hexane (boiling point: 69 °C) and a reaction temperature of 60 °C, a substantial fraction of the initial solvent could be evaporated by the channel exit point. For a fixed temperature, the relative flow rates of gas and liquid control the degree of evaporation. The evaporation of the solvent has the effect of gradually increasing the liquid phase concentration of derivative – hydrazones – hence the concentration effect. Table 2 shows the enriching ratios that are achieved through the evaporation effect of the solvent in the micro-channels, measured as a ratio of volumes of the solution pumped into the micro-reactor to the volumes of the solution collected from the outlet.

5. Conclusions

A rapid and sensitive microfluidic derivatisation technique has been developed and optimized to determine gaseous formaldehyde. For high formaldehyde concentrations *e.g.* above around 25 ppb, 10 minutes of the reaction time in the chip is sufficient to reach the reaction equilibrium between formaldehyde and derivatisation reagents, and to gain sufficient analyte for direct GC-MS measurement. A near real-time formaldehyde analytical system has been demonstrated by combining the reaction chip with GC autosampler and GC-MS. For formaldehyde concentrations below around 25 ppb, recycling of the derivatisation solution allows for liquid phase analytes to accumulate in solution greatly increasing method sensitivity. A thirty minute recycling time (roughly the same as the length of the time needed for the GC separation) reduces the MDL for formaldehyde to about 1 ppb. All measurements made here have been performed using a relatively poor sensitivity GC-TOF. The MDLs may be further enhanced at least 10 times by the use of selected ion monitoring for specific reaction products using GC-quadrupole MS.

Although not calibrated in this study, the on-chip derivatisation solution also reacts with other carbonyl compounds, and species such as acetone, acetaldehyde and propionaldehyde were readily detected in ambient lab air. The method offers significant opportunities to build on the specificity of carbonyl derivatising methods, but using very low reagent volumes, fast reaction times and with on-line coupling with GC-MS.

Acknowledgements

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