Prototyping a Microfluidic Sensor for Real-Time Detection of Airborne Formaldehyde

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Abstract—Formaldehyde is a carcinogenic volatile organic compound that is largely used in the fabrication process of a variety of household products, being sometimes released indoor in concentrations that are beyond the limits recommended by the World Health Organization. The current commercially available formaldehyde sensors are far from simultaneously being ultra-portable, highly sensitive (< 1 ppb), real-time, and especially cost-efficient. This work aims to study the feasibility to miniaturize the formaldehyde sensing system down to a palm hand device, based on the microfluidic Hantzsch reaction method and fluorescence detection. A Gas-Liquid Micro-Reactor based on integration of a hydrophobic membrane inside a polymer flat chip is proposed and its formaldehyde trapping yield is planned to be further tested. By combining contact sensing with time-resolved CMOS sensors, the dimensions of the fluorescence detection component could go down to 10 mm × 20 mm × 30 mm by using commercial-available components and therefore, enabling continuous and fast-response measurements using small volumes and low concentration samples.

Index Terms—Contact sensing, micro-fabrication, on-chip membrane-based gas-liquid contacting, time-resolved CMOS sensing.

I. INTRODUCTION

The indoor environment is a major source of concern since the concentrations of pollutants might reach up to five times concentrations values than outdoors [1]. People usually spend more than 90% of their time indoors, and many causalities and diseases are linked to the presence of specific chemical compounds in the air, such as volatile organic compounds (VOCs). VOCs have a boiling point lower than room temperature, a characteristic that makes them have a high partial pressure and being released gradually in the surrounding air. One of the VOCs that raises increased concern is formaldehyde, a compound that is carcinogenic and mutagenic [2]. It is largely used in the fabrication of building materials, household products, and resins for wood products. There are research projects looking for a formaldehyde none harmful alternative in the form of bio-based platform chemical 5-HMF (5-Hydroxymethylfurfural) [3], but meanwhile, the formaldehyde industrial consumption is continuously growing. The World Health Organization recommends today a value of 30 µg/m³ as acceptable concentration of formaldehyde indoor and from 2023 onwards, 10 µg/m³ will be accepted [1].

The sensors existing today on the market are far from being ultra-portable and low-cost. One miniaturized sensor answering these goals and providing real-time information about the low-limits formaldehyde concentration, could be used for more reliable measurements that could give a better insight about the formaldehyde releasing behavior in specific environments, and, finally, a better understanding of the formaldehyde impact on people’s health.

This project aims to explore the miniaturization possibilities towards the lab-on-a-chip integration of the Hantzsch reaction coupled to fluorescence optical detection microfluidic method, used for the real-time detection of the low-limits formaldehyde (Fig. 1).

![Fig. 1. Formaldehyde detection methodology.](image)

The Hantzsch reaction is a derivatization process of the formaldehyde molecules into 3,5-diacyl-1,4-dihydrolutidine (DDL), a fluorescent chemical compound. The fluoral-P or acetylacetone based solutions are used as reagents for the derivatization process, once the formaldehyde molecules are trapped into the solution. This technique is a very sensitive and a relatively simple tool to
detect formaldehyde.

By better understanding the fluidics in micro and nano channels, enhanced mass-transfer could be achieved and, therefore, miniaturized and highly autonomous gas-liquid micro-reactors might be developed. The gas-liquid micro-reactors are devices that are designed to contact two micro streams of fluids, in order to trap specific molecules from a phase to another. The efficiency of the process is governed by a multitude of parameters, such as the hydrodynamics, the contacting method, the fluid-solid interactions, and the volume-to-surface area coefficient. A chemical reaction usually enhances the process since it helps diminishing the polarization effects at the gas-liquid interface.

Fluorescence represents the property of a molecule to emit light at a specific wavelength and specific intensity, once it is excited by a light pulse. By measuring the fluorescence intensity emitted by the molecules located inside a known interrogation volume, at a specific period of time, the concentration of those molecules could be quantified. Among all optical methods, fluorescence sensing is the most common analytical and diagnostic method in biological, chemical and medical applications [4]-[6], and it is widespread due to its capability to attain ultra-low detection limits, being considered the most sensitive and robust methodology [7], [8].

A first prototype concept is here proposed, aiming to embed all the required functions of the process in a modular palm-hand device. For a better understanding and control of the parameters involved, formaldehyde derivatization are assigned to a sub-device, named Gas-Liquid Micro-Reactor, and the fluorescence detection system to another sub-system, named optical detector.

A micro-machined polymer chip, embedding a flat hydrophobic membrane, stands for continually contacting the two streams using an overlapping network of meandering channels. The interest here is to study the feasibility of enabling enhanced formaldehyde trapping inside relatively cheap on-chip membrane-based polymer chips.

The optical detection sub-system targets the development of a miniaturized device for the fluorescence intensity quantification based on the contact sensing and the time-resolved CMOS fluorescence sensing in low interrogation volumes (600 nL - 5 μL).

II. DETECTION METHODOLOGY

Prior to the Hantzsch reaction, the formaldehyde molecules are continuously trapped from the atmospheric air flow by contacting the air stream and the reagent stream into a microfluidic network of overlapping micro-channels. Once the formaldehyde derivatization process is finished, after a molecule residence time of about three minutes at 65°C, the liquid carrying the DDL molecules is streamed towards the interrogation chamber (Fig. 1), where a beam of 412 nm wavelength light excites the molecules and makes them fluoresce at a 510 nm wavelength. The fluorescence read-out intensity signal gives the concentration of DDL that is correlated with the trapping efficiency of the gas-liquid micro-reactor and indicates the formaldehyde concentration in the environment.

The concentration of formaldehyde can be determined by controlling and measuring the volume of the air that is contacted with the liquid reagent, knowing the diffusion efficiency of the system, and the rate of replacement of the liquid from the interrogation volume in the optical detector.

The gas-liquid contacting method influences the trapping efficiency or the mass transfer yield. Gas-Liquid contacting could be realized using a solid, molecule permeable medium, such as a polymer membrane, or by a direct gas-liquid interaction in the same micro-channel. Each choice comes with advantages and disadvantages. While the gas-liquid contactors based on membranes provide a system where the hydrodynamic conditions could be easily and precisely controlled, the physical medium represented by the membrane increases the mass transfer resistance and decreases the diffusion. By introducing in the same micro-channel a gas and a liquid stream, different flow patterns (e.g. slug flow, annular flow, churn flow or bubbly flow) are realized, depending on the hydrodynamic conditions that are accomplished. These methods are usually characterized by a better diffusion at the gas-liquid interface, but they strongly depend on the stability of the hydrodynamic conditions which are difficult to be controlled at micro-scale, especially for annular flow. An annular flow provides very good characteristics for this particular application since it contacts a large volume of gas with a low volume of liquid without using a membrane [1].

Formaldehyde trapping from a microfluidic gas stream into the reagent stream is mathematically described using advection-diffusion equation that is assumed to govern the flow of the solute in the channels, separated by the porous membrane (Fig. 2). In equilibrium at temperature T,

\[ n_L = H(T) n_G \]  

(1)

\[ n_L \] and \[ n_G \] are the equilibrium number densities of the solute in the liquid and the gas phase, respectively, if the solution is in the ideal regime. If not, equation (1) has to be replaced by a more complicated relationship. However, any change in equation (1) does not affect the model described below. Let \[ n_L \] and \[ n_G \] denote arbitrary values of densities in the liquid and the gas when the system is not in equilibrium. In these conditions, the liquid phase injects \( J^* \) molecules per unit time and unit area into the gas. According to the Henry law,

\[ J^* = \sigma \frac{n_L}{H(T)} \sqrt{\frac{RT}{2\pi}} \]  

(2)
\[ \sigma \] stands for a sort of evaporation/condensation coefficient. On the other hand, the flux of the gas phase molecules condensing (trapped) onto the liquid phase is

\[ J = \sigma n_l \sqrt{\frac{RT}{2\pi}} \]  

(3)

Hence, the total net solute molecules flux across the interface is:

\[ J = \sigma n_l \sqrt{\frac{RT}{2\pi}} \left( \frac{n_l}{H(T)} - n_c \right) \]  

(4)

\( J = 0 \), when \( n_l \) and \( n_c \) obey the Henry Law. It is assumed that advection is negligible within nano-pores and the diffusion is the main mechanism. Also, the diffusion will be considered quasi-steady inside a pore:

\[ n_c(x) = n_c^{(0)} + \frac{n_c^{(1)} - n_c^{(0)}}{L} x \]  

(5)

Since \( J = -D \frac{\partial n_c}{\partial x} \) (6), it results:

\[ \frac{n_c^{(1)} - n_c^{(0)}}{L} = -\frac{1}{D} \sigma \sqrt{\frac{RT}{2\pi H(T)}} \left( n_l - n_c^{(0)} \right) \]  

(7)

\[ n_c^{(0)} = \frac{n_c^{(1)} + \sigma \sqrt{\frac{RT L}{2\pi D H(T)}} n_l}{1 + \sigma \sqrt{\frac{RT L}{2\pi D}}} \]  

(8)

It should be noted that equation (8) allows computing \( J \) knowing the solute densities, \( n_c(L) \) and \( n_c(0) \) in the gas channel and the liquid channel. It is worth noting that \( D \) in the above equations has to be considered an effective diffusion coefficient because the diffusion of the solute through the carrier gas may not be the only mechanism and the rarefaction effects affect the diffusion process in the carrier gas. It will be assumed that the advection-diffusion equation governs the flow of the solute in the channels, separated by the porous membrane. The liquid channel is now considered and the following assumption is made, where \( \alpha r n_L \) is a sink term due to the chemical reaction:

\[ \frac{\partial n_c}{\partial t} + V_x \frac{\partial n_c}{\partial x} = D_L \nabla^2 n_c - \alpha r n_L \]  

(9)

The average of \( n_c \) over a channel section is considered.

\[ \Phi_c(x,t) = \frac{1}{S} \int dy dz n_c, S = Ly \times Lz \]  

(10)

Substituting in equation (9) and integrating, it yields:

\[ \frac{\partial \Phi_c}{\partial t} + \nabla_x \cdot \Phi_c = D_L \nabla_x^2 \Phi_c - \alpha r \Phi_c + \frac{1}{L_y} \int A_f \]  

(11)

\( \bar{V} \) is the average flow velocity across the channel section and \( A_f \) is the fraction of permeable membrane area. Applying the same assumptions for the gas layer, it results a similar equation.

\[ \frac{\partial \Phi_g}{\partial t} + \nabla_x \cdot \Phi_g = D_g \nabla_x^2 \Phi_g - \alpha r \Phi_g + \frac{1}{L_y} \int A_f \]  

The above-described model can be used for the characterization of the trapping efficiency of the gas-liquid contactor and, furthermore, to conduct a parameterization study once the effective diffusion coefficient is measured from experimental assays, in order to determine optimal dimensional characteristics for achieving the desired limit of detection.

III. GAS-LIQUID MICRO-REACTOR

This part of the work aims to study the feasibility of developing cheap, efficient, and disposable gas-liquid contacting chips from polymer materials, such as poly methyl methacrylate (PMMA). The gas-liquid contacting chip is integrated in between two upper and lower holders (Fig. 3). The holders are micro-machined in polyether ether ketone (PEEK) which is used due to its low thermal conductivity 0.25 W/mK. They host fluidic leakage-free connections for gas (Swagelok, SS-100-1-1, 1/16) and liquid (N-333, Idex-HS) streams, the flat copper foils thermally controlled by cartridge heaters (Watlow, CIA-9602, 30 W power, 24V voltage), in order to heat up the fluid streams inside the chip to 65°C, and O-rings (Parker, 6-1735 E540-80, 0.7 × 0.5 mm) – one for each fluidic inlet/outlet – that assure the leakage-free condition when the chip is clamped in between the holders.

Double-sided commercial-available hydrophobic ePTFE membranes (Aspire® QP955 and Aspire® QL217) were considered for being on-chip integrated and further tested (Fig. 4). They have a reference pore diameter of 200 nm and the contact angle is 120° [9]. The polymer chip hosts a network of two overlapping meandering micro-channels, one channel being assigned to the liquid stream and the other one to the gas stream. They are milled with good precision on two 1 mm thick PMMA sheets (Fig. 5). A vacuum chamber was used to maintain the horizontality of the PMMA sheets, in order to avoid its wavy form and assure a constant depth of the channel over the length. The two meter overlapping channels have: (a) 400 μm × 200 μm cross section dimension for the gas carrying channel and (b)
100 µm × 200 µm for the liquid carrying channel, respectively. A hot embossing procedure was used to bond the two PMMA sheets (Fig. 5 (c)) embedding the hydrophobic membrane that was precisely cut by a CO₂ laser (Fig. 5 (a)) to fit the pocket on the PMMA gas sheet. Two interior strips were provided on the PMMA gas sheet, in order to prevail swelling behavior.

Experiments were conducted to test the leakage of the system for a flow rate of 20 µL/min. After six minutes of continuous liquid pumping, leakage could be observed around the connectors, the pumping being stopped. When the chip was verified it could be observed that the PMMA bonding did not last as well, water filling in the micro-channels for only one third out of the total two meter length. In conclusion, for the next chip contactor prototype the micro-channel length will be reduced according to the experimental observations. This is a compromise that surely will be diminishing the uptake concentration of formaldehyde molecules per unit time from the gas phase to the liquid phase, since the contacting area will be reduced.

Fig. 4. Scanning Electron Microscopy analysis of the double-sided membrane. (a) Pore distribution on the Teflon side. (b) Cross-section thickness distribution with 40 µm Teflon and 150 µm backer material (polypropylene for Aspire QP955 and polyester for Aspire QL217).

This aspect shifts the focus on the optofluidic system that has to compensate through a very low limit of detection capability. If the limit of detection to be achieved by the optofluidic system is lower enough, reducing the length of the micro-channel might be an advantage in the end, the final aim being detection of formaldehyde concentrations at 1 ppb.

Fig. 5. Fabrication steps of the gas-liquid chip contactor. (a) CO₂ membrane cut. (b) Meandering channels micro-milling process. (c) PMMA sheets bonding using hot embossing method.

After re-fabrication of the chip contactor, a further experimental work is currently envisaged for the determination of the formaldehyde diffusion coefficient in different flow conditions. This coefficient could be used to conduct an optimization study, in order to identify the optimal dimensions and working parameters. The description and the results of these steps will be further published in a separate paper.

IV. OPTOFIUIDIC DETECTION SYSTEM

The optical detection sub-system combines the contact sensing and the time-resolved CMOS fluorescence sensing in low interrogation volumes (600 nL - 5 µL), in order to develop a robust, low-power, and sensitive micro-detector. Fluorescence is the property of a molecule to absorb light at a specific wavelength and emit it at a longer wavelength, a phenomenon known as the Stoke shift (Fig. 6). Consequently, its quantification involves a light emission source and a light detector. The amount of fluid involved in the microfluidic systems is by definition reduced and hence the emitted fluorescence signal is weak. The lifetime of the DDL molecule in methanol solution was determined in [10] to be \( \tau_f = 20.9 \text{ ns} \). The quantum yield of the DDL molecule in aqueous solution is \( \phi(20^\circ C) = 0.005 [10] \). The three orders of magnitude difference between excitation light intensity and emitted fluorescence intensity makes the implementation of a complex optical path usually necessary, involving a system of lenses to focus the fluorescence onto a photon detector.

Fig. 6. General fluorescence detection scheme (orthogonal).

In contact sensing, the samples are placed in close proximity of the sensor surface without intermediate optics. Due to the short distance between the sensor and the sample, the optical loss can be small. The CMOS technology enables on-chip detection and signal processing, significantly reducing size and power consumption. CMOS time-resolved contact sensing microsystems are emerging today as sound technologies for application specific, low-cost and time-resolved detection devices. Time-gating the excitation time and the reading-out time, by carefully considering the rise
and falling time of the LED or the laser diode, the fluorescence signal and the noise could be discriminated in time. Falling time of the laser diode is a crucial parameter. It is important that the emission time of the molecule to be larger than the falling time, in order to be able to implement the time-resolved methodology. A smart integration of the concepts above-mentioned should provide a promising and cheap miniaturized sensing prototype [4].

For this first sub-device (Fig. 7), commercial-available laser-diode (typ. 415 nm) (Roithner Lasertechnik GmbH, RLT415-200PMG, typ. 200 mW (max. 1 W)) and CMOS image sensors (Anitoa® USL24) are used. Anitoa® USL24 CMOS image sensor was specifically developed for spectroscopic measurements and possesses a signal-to-noise ratio larger than 13 dB at its 3.0 x 10⁶ lux detection threshold. The upper and the lower holders are 3D printed and the fluidic interrogation cell is fabricated in quartz and SU-8, the fabrication process being described in [11]. The linearity of the CMOS image sensor over the integration time (y = 247.82x – 348.26, R² = 0.9848) and over the light intensity (y = 16.209x + 106.38, R² = 0.9968) were determined experimentally for a 520 nm wavelength light beam.

The description of the experimental results will be further published in a separate paper.

V. CONCLUSION

Successful development of a micro-total-analysis system for the continuous detection of the low-limits gaseous formaldehyde is highly desired since this carcinogenic substance largely used in the fabrication of household products is continually released indoors. This project aims to study the possible paths towards on-chip real-time detection of low-limits indoor formaldehyde concentrations, a laboratory prototype being today developed based on the Hantzsch reaction coupled to the optical fluorescence detection method. The gas-liquid micro-reactor relies on a disposable PMMA gas-liquid contacting chip that uses as separation medium a hydrophobic polymer membrane. The fluorescence optical detection system combines the contact sensing of a disposable quartz/SU-8 interrogation fluidic cell with the CMOS time-resolved spectroscopy. After the successful fabrication of the sub-systems, further results are expected in order to experimentally prove the concept.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

D.M. conducted the research and wrote the paper; L.B. and S.C. helped with the fabrication process of the fluidic cells. S.L.C. provided the chemicals and expertise required for the experimental work. J.B. provided fabrication and design feedback regarding the conception of the gas-liquid contactor. L.B., S.C., S.L.C., J.G.K. and J.B. have participated to the supervision of the work; all authors had approved the final version.

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He has co-authored more than 75 scientific publications in peer-reviewed journals, over 140 presentations at national and international conferences, and several international patents. He has also received several national awards related to his technological innovations in the field of analysis of air pollutants, allowing the creation of a company. He has been the principal investigator of nearly 30 national or European projects, including 14 as coordinator.

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