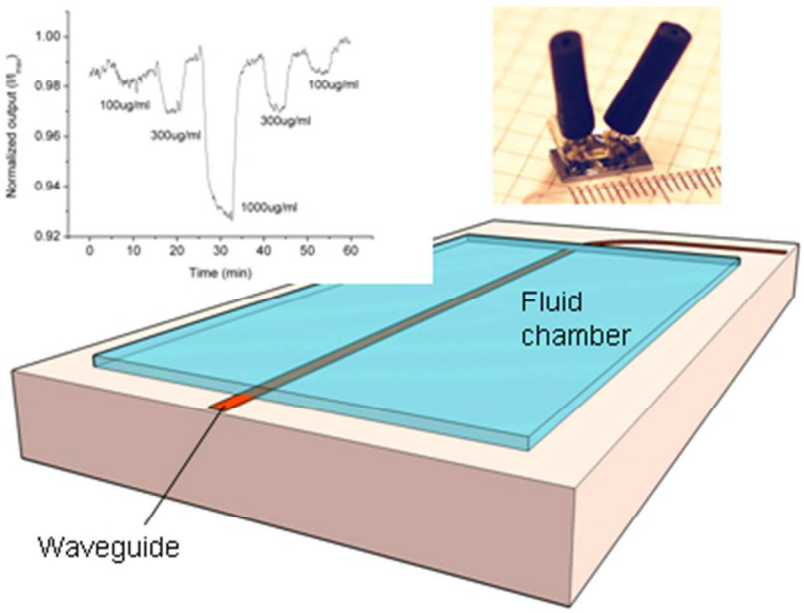
Normalized output (I/I$_{max}$)
1.00
0.98
0.96
0.94
0.92
0
10
20
30
40
50
60
Time (min)
100ug/ml
300ug/ml
1000ug/ml
100ug/ml
300ug/ml
Fluid
chamber
Waveguide

Cocaine Detection by a Mid-Infrared Waveguide Integrated with a Microfluidic Chip

Yu-Chi Chang,*[a] Philip Wägli,[b] Vincent Paeder,[a] Alexandra Homsy,[b] Lubos Hvozdara,[a] Peter van der Wal,[b] Joab Di Francesco,[a] Nico F. de Rooij,[b] and Hans Peter Herzig[a]

Received (in XXX, XXX) Xth XXXXXXXXX 20XX, Accepted Xth XXXXXXXXX 20XX
DOI: 10.1039/b000000x

A germanium (Ge) strip waveguide on a silicon (Si) substrate is integrated with a microfluidic chip to detect cocaine in tetrachloroethylene (PCE) solutions. In the evanescent field of the waveguide, cocaine absorbs the light near 5.8 µm, which is emitted from a quantum cascade laser. This device is ideal for (bio-)chemical sensing applications.

Chemical detection and identification based on Mid-Infrared (mid-IR) spectroscopy has been widely used for samples in gases, liquids, or solids. In the condensed phase, attenuated total reflection Fourier transform infrared spectroscopy (ATR-FTIR) can conveniently probe the analyte in the evanescent field, but it was often limited to laboratories due to its large footprint.[1,2] During the last few decades, the progress of mid-IR spectroscopy with mid-IR fiber probes[3] or planar waveguides largely reduces the device size and the sample volume. These waveguides are based on silver halides, chalcogenide glasses, GaAs, or hollow waveguides.[4-8] In addition, mid-IR quantum cascade lasers (QCLs) provide light sources with high power, high tunability, and compact sizes, which can further reduce the size of sensor systems.[9]

Microfluidic systems have been used in combination with IR-detection. The most commonly used techniques are chromatography[10-13] and electrophoresis[10,14,15] on a separate microfluidic chip for sample preparation and preconcentration prior the conventional IR-detection. Also a microfluidic device integrated with a planar chalcogenide glass waveguide on a silicon substrate was presented for detection of N-methylaniline at the wavelength of 1.55 µm[6]. Beside, commercial products combining QCLs and flow cells for the detection of oil in water are available[16].

Here, we demonstrate a chemical sensor utilizing a mid-IR single-mode strip waveguide in liquid environments. It is integrated with a microfluidic chip[17] and evaluated with a QCL at the wavelength of 5.8 µm. This is the first integration of a Ge strip waveguide with a microfluidic chip and evaluated in the wavelength of mid-IR. The laser wavelength is chosen to be at one of the absorption peaks of cocaine[18], which is our exemplary analyte to prove this technology.

The sensing scheme is illustrated in Fig.1a, where the light is injected into the waveguide. The analyte in the evanescent field has absorption peaks overlapping with the laser wavelength. The information of analyte concentration can be determined by measuring the output light from the waveguide.

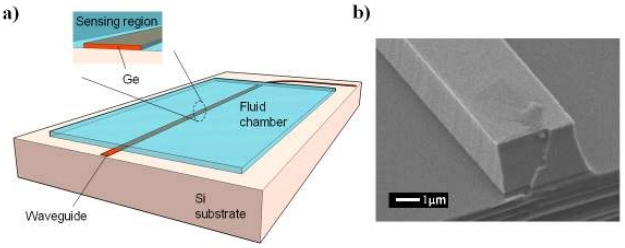

Fig. 1 a) Scheme of the waveguide spectroscopy sensor in liquids: A microfluidic chamber can be bonded on the substrate. The analyte absorbs light in the evanescent field. b) Image of the cross-section of Ge waveguide on Si taken with a scanning electron microscope (Ref.20)

The mid-IR waveguide is made from a mono-crystalline Ge layer on a Si substrate with standard photolithography and reactive ion etching by CF4. Intrisic Ge and Si have low absorption in a wide range of mid-IR. This material combination is biocompatible[19] and Si-process compatible, and can be further integrated with current Si technology. Figure 1b shows the cross-section of the strip waveguide. It is single mode for transverse magnetic polarization at the wavelength of 5.8 µm, while the thickness is 2 µm and the width is 2.9 µm[20]. Compared to a slab waveguide, a single mode strip waveguide has higher fraction of energy in the evanescent field and hence increases the sensitivity[21].

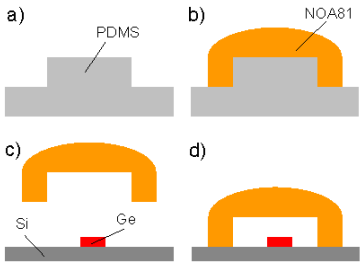

Fig. 2 Device fabrication: a) PDMS master for rapid prototyping, b) NOA81 casted on PDMS, c) Ge optical waveguide on Si substrate and unmolded microfluidic system on top, d) final device; microfluidic system bonded on Si substrate forming the chamber for liquid detection

The material for the microfluidic system is a UV-curable adhesive NOA81 (Norland Products Inc., Cranbury, NI, USA). Compared to PDMS (polydimethylsiloxane), the most widely

used polymetric material for microfluidic devices, this low-cost commercially available adhesive has better chemical resistance, is impermeable to air and water vapor, and is less prone to swelling upon contact with infrared-transparent organic solvents[17,22]. Moreover, it shows low adsorption of cocaine in aqueous or organic solvents, and proteins (interleukins) from blood[23,24]. Cured NOA81 has higher stiffness (~1GPa) than PDMS[25]. This allows building wide microfluidic channels which do not collapse under negative pressure which is used to suck the liquids through the microfluidic chip.

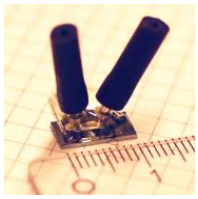

Fig. 3 Image of the Ge waveguide bonded to the microfluidic channel: The microfluidic channel is 1mm wide, 7mm long, and 50μm deep.

We made the microfluidic system by means of rapid prototyping using NOA81 and by following the fabrication process presented in ref. 16. As shown in fig.2, the adhesive was cured on a PDMS master. It is then bonded to the silicon substrate of the Ge waveguide by using oxygen plasma. The adhesive was cured further under the UV-lamp after the bonding. The device showed best adhesion after a high temperature treatment at 130 °C for 1 hour. As shown in fig.3, the microfluidic design consists of a simple straight channel (1 mm wide, 7 mm long and 50 μm deep) with an inlet and an outlet. After usage, the low-cost, disposable, polymeric microfluidic system can be detached from the substrate by soaking it in acetone and the waveguide can be recycled.

Cocaine detection is a pilot demonstration for this device. The wavelength of the QCL is 5.8 μm, which overlaps with the specific absorption peak of cocaine. We dissolved cocaine (purity>98%, Lipomed AG Switzerland, purchased with permission of the cantonal drug administration of Neuchatel) into PCE, which has high transmission in a large mid-IR band.

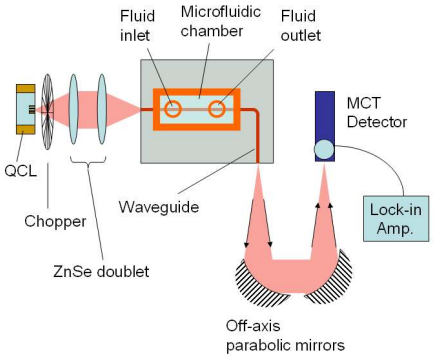

Fig. 4 Measurement setup: The waveguide is coupled with the QCL by a ZnSe doublet and to a MCT detector by two parabolic mirrors. Light-liquid interaction happens in the microfluidic chamber in which cocaine solutions with different concentrations keep a constant flow.

The measurement setup consists of an optical system measuring the waveguide output, and a syringe pump system for liquid sample handling. In fig. 4, the light emitted from the QCL was coupled into the strip waveguide with a 1/f ZnSe doublet. After interaction with the sample in the liquid chamber, the light went through a waveguide bend and redirected to a MCT (mercury cadmium telluride) detector by two parabolic mirrors. The use of a bended waveguide avoided the stray light on the emission axis of the QCL and increased the signal to noise ratio.

A syringe pump connected to the outlet of the microfluidic system sucked the liquid through the device. The multiselection valve at the inlet allowed to switch between reservoirs of pure PCE solvent and reservoirs with different concentrations of cocaine dissolved in PCE.

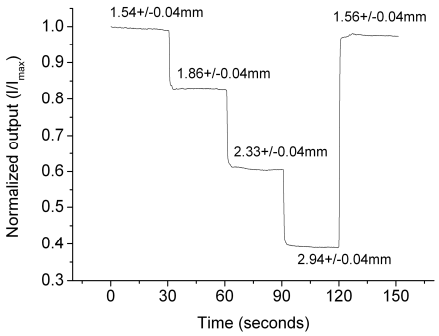

Fig. 5 Water drop test without a microfluidic chip: The water drop covered different lengths of the waveguide when we changed the drop-size in real time. The waveguide transmission showed a fast response.

Before the measurement of cocaine, the device was tested using a waveguide without a microfluidic chip. We put a water drop on the substrate and controlled its size dynamically with a pipette. Since water has strong absorption near this wavelength, when the water drop covered the waveguide by different lengths, the light transmission of the waveguide changed simultaneously. Figure 5 shows the real time measurement with 5 different water-covered lengths. The response time is about 0.5 seconds.

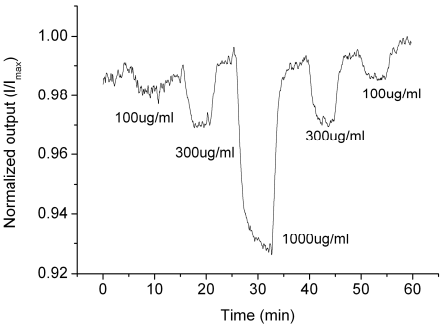

Fig. 6 Waveguide output with different cocaine concentrations: In the dynamic measurement, the smallest detected concentration is 100 μg/ml.

For cocaine measurement, we used a waveguide integrated with a microfluidic chip. The result is shown in fig. 6, in which the waveguide output light intensity was measured when we switched different concentrations of cocaine in real time. The flow rate is 50 μl/min. Between each concentration, we added 5-7 minutes of pure PCE solvent. The device responded well to each switch of concentration. The

transmission drop was linearly proportional to the cocaine concentration, while the lowest detected concentration was 100 µg/ml. The detection limit can be further improved by reducing the system noise and using a longer waveguide. The shift of the average output-power is due to the fluctuation of alignment between the laser and the waveguide.

The slow response to the switch of concentrations was due to the length of the tubing between the device and the fluidic valve. This is tested by using a long (~20cm) tube and a short (~6cm) one for measuring the switch from pure PCE to the cocaine concentration of 100 µg/ml. Figure 7 shows the response time with the two tubes, and the shorter tube responses about two times faster than the longer one. The response time is the duration between 10% and 90% of the difference of the two mean values of the two concentrations.

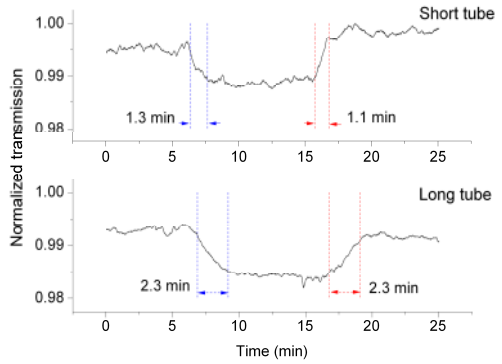

Fig. 7 Response time: It is related to the tubing length between the fluidic valve and the device. Between pure PCE and 100 µg/ml cocaine in PCE solution, the shorter tube showed a faster response time

Cocaine detection in human saliva is a potential application and also a goal of this study. In parallel to the presented device, we are developing an integrable microfluidic system for efficient liquid-liquid extraction of the analyte cocaine from saliva to PCE[18,26]. This sample pretreatment allows analyte preconcentration and avoids issues of light absorption in the water. As the peak value of cocaine concentration in saliva can be as high as 500µg/ml[18], the current detection limit of this device can be improved to a practical level. The signal to noise ratio of this device is now mainly limited by the alignment fluctuation of the laser. An integrated splitter and a reference waveguide can eliminate this noise and an improvement of a magnitude can be expected. Stabilized temperature and mechanical vibration can also reduce the noise. Further improvement includes the use of a long waveguide, which can be supported by the high output power of the QCL and the low loss Ge waveguides[20]. The coupling efficiency of the laser is currently around 9% and can be improved by 5-10 fold with butt coupling method.

This device demonstrated the integration of a mid-IR Ge waveguide with a microfluidic system. Cocaine detection is a pilot example of this technology. The detection limit of this device still needs optimization when it is compared with other optical methods which have detection limits in the range from several ng/ml to several µg/ml[18], but this device has the advantage to obtain the spectral information if a tunable QCL is used. The compact size of the QCL and the waveguides allows the design of portable systems. In addition, this real time experiment shows the capability of this device for in-line measurement and studying dynamic phenomena in liquids. The integrated microfluidics enables further developments of on-chip sample handling and treatment before or after the optical sensing.

This project is scientifically evaluated by SNSF, financed by the Swiss Confederation and funded by Nano-Tera.

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[a]*Ecole Polytechnique Fédérale de Lausanne (EPFL), Institute of Microengineering, Optics & Photonics Technology laboratory, Rue A.-L. Breguet 2, Neuchâtel, Switzerland; E-mail: yu-chi.chang@epfl.ch*
[b]*Ecole Polytechnique Fédérale de Lausanne (EPFL), Institute of Microengineering, The Sensors, Actuators and Microsystems Laboratory (SAMLAB), Rue Jaquet-Droz 1, 2000 Neuchâtel, Switzerland*

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