Lab on a Chip

COMMUNICATION

Cocaine detection by a mid-infrared waveguide integrated with a microfluidic chip

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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 has largely reduced 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 chromato-graphy[10–13] and electrophoresis[10,14,15] on a separate microfluidic chip for sample preparation and preconcentration prior to the conventional IR-detection. A microfluidic device integrated with a planar chalcogenide glass waveguide on a silicon substrate was presented for the detection of *N*-methylaniline at a wavelength of 1.55 μm.[6] Commercial products combining QCLs and flow cells for the detection of oil in water are also 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 a wavelength of 5.8 μm. This is the first integration of a Ge strip waveguide with a microfluidic chip and evaluated at a mid-IR wavelength. The laser wavelength is chosen to be at one of the

absorption peaks of cocaine,[18] which is our example analyte to demonstrate 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 analyte concentration can be determined by measuring the output light from the waveguide.

The mid-IR waveguide is made from a mono-crystalline Ge layer on a Si substrate with standard photolithography and reactive ion etching by CF_4. Undoped Ge and Si have low absorption over a wide range of mid-IR wavelengths. This material combination is biocompatible[19] and compatible with Si-processing, and can be further integrated with current Si technology. Fig. 1b shows the cross-section of the strip waveguide. It is single mode for transverse magnetic polarization at a 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 a higher fraction of energy in the evanescent field, and hence increases the sensitivity.[21]

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 polymeric material for microfluidic devices, this low-cost, commer-cially available adhesive has better chemical resistance, is imperme-able 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 in proteins (interleukins from blood).[23,24] Cured
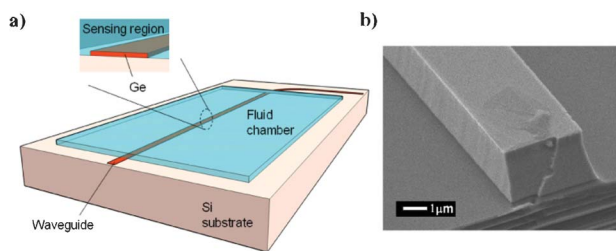

Fig. 1 a) Scheme of the waveguide spectroscopy sensor in liquids: a microfluidic chamber can be bonded onto the substrate. The analyte absorbs light in the evanescent field. b) Image of the cross-section of the Ge waveguide on Si taken with a scanning electron microscope (ref. 20).

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NOA81 has a higher stiffness (∼1 GPa) than PDMS.[25] This allows the building of wide microfluidic channels which do not collapse under the negative pressure used to suck the liquids through the microfluidic chip.

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 was then bonded to the silicon substrate of the Ge waveguide using oxygen plasma. The adhesive was cured further under the UV-lamp after bonding. The device showed the best adhesion after a high temperature treatment at 130 °C for 1 h. 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 use, 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 Neuchâtel) in PCE, which has high transmission in a large mid-IR band.

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 with the strip waveguide by a $1/f$ ZnSe doublet. After interaction with the sample in the liquid chamber, the light went through a waveguide bend and was redirected to an MCT (mercury cadmium telluride) detector by two parabolic mirrors. The use of a bent waveguide avoided 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 multi-selection valve at the inlet enabled switching between reservoirs of pure PCE solvent and reservoirs with different concentrations of cocaine dissolved in PCE.

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. Fig. 5 shows the real time measurement with 5 different water-covered lengths. The response time is about 0.5 s.
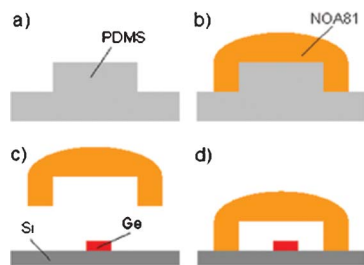

Fig. 3 Image of the Ge waveguide bonded to the microfluidic channel: the microfluidic channel is 1 mm wide, 7 mm long, and 50 μm deep.

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 was 50 μl min^{-1}. Between each concentration, we added pure PCE solvent at the same flow rate for 5–7 min. 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^{-1}. 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 (∼20 cm) and a short (∼6 cm) tube for measuring the switch from pure PCE to a cocaine concentration of 100 μg ml^{-1}. Fig. 7 shows the response times with the two tubes, and the shorter tube responds about twice as fast as the longer one. The response time is the time taken for the transmission value to change between 10% and 90% of the difference between the mean transmission values of pure PCE and 100 μg ml^{-1} cocaine (as shown in Fig. 7).

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]

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.

Fig. 2 Device fabrication: a) PDMS master for rapid prototyping, b) NOA81 cast on PDMS, c) Ge optical waveguide on Si substrate and unmolded microfluidic system on top, d) final device: microfluidic system bonded onto Si substrate forming the chamber for liquid detection.
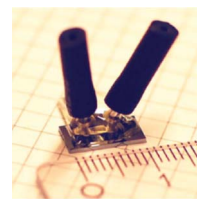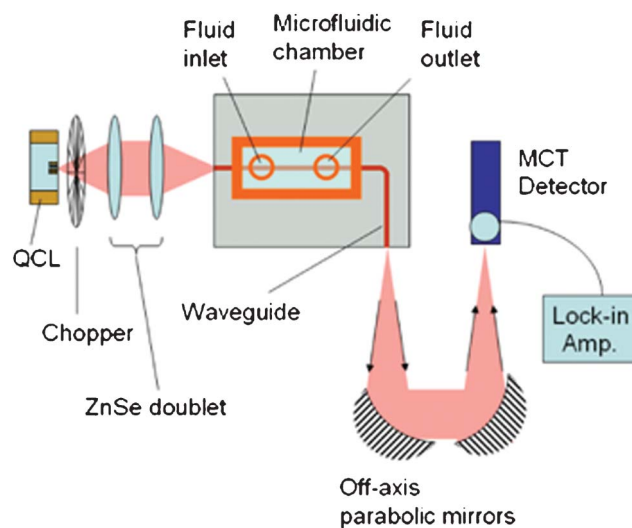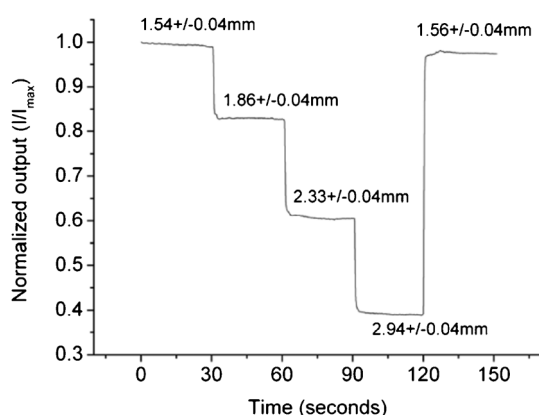
Fig. 5 Water drop test without a microfluidic chip: the water drop covered different lengths of the waveguide when we changed the drop-size in real time. The waveguide transmission showed a fast response.

This sample pretreatment allows analyte preconcentration and avoids the problem of light absorption in the water. As the peak value of cocaine concentration in saliva can be as high as 500 μg ml^{-1},[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 a large improvement 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 of Ge waveguides.[20] The coupling efficiency of the laser is currently around 9%, and can be improved 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 of several ng ml^{-1} to several μg ml^{-1},[18] but this device has the advantage of the ability to obtain 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
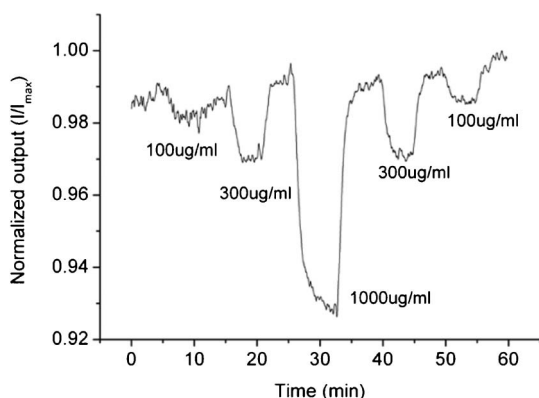

Fig. 6 Waveguide output with different cocaine concentrations: in the dynamic measurement, the smallest detected concentration was 100 μg ml^{-1}.

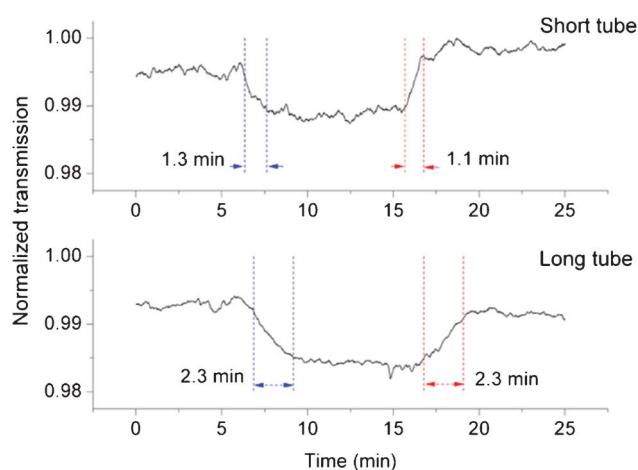**Fig. 7** Response time: it is related to the tubing length between the fluidic valve and the device. Between pure PCE and 100 μg ml^{-1} cocaine in PCE solution, the shorter tube showed a faster response time.

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.

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