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# Laser-based sensing of cocaine in perchlorethylene at 5.7 µm

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## Introduction

There is an increasing interest for portable sensors capable of detecting drugs such as cocaine, heroin and methamphetamine. Such sensors could be useful for traffic police and ambulances. Many drugs can be detected in saliva, although concentrations can be extremely low [1]. Furthermore, there can be dozens of interfering compounds present, not the least of which is water. The sensor should therefore be **robust, transportable, easy to operate, non-invasive, selective, sensitive** and **provide quantitative measurements**.

Our project focuses on the detection of **cocaine extracted from saliva.** The required **limit of detection** for a test that measures cocaine in saliva lies between **10 and 20 ng/mL**, depending on the country.

By measuring the transmission of infrared light through a sample, cocaine can be measured selectively. Due to the extremely strong absorption of water, an extraction technique was chosen whereby cocaine is extracted into a solvent more suitable for infrared measurements. The choice fell on **tetrachlorethylene** (perchlorethylene (PCE), $C_2Cl_4$) [2]. In the mid-infrared, many molecules (including cocaine) have **strong** and **characteristic absorption lines/bands** corresponding to rovibrational transitions. Unfortunately, this is true for most liquid solvents a well. The absorption due to the solvent adds to the absorption due to the analyte (cocaine) and can eclipse it by several orders of magnitude. For example, at a concentration of 10 ng/mL of cocaine in a (hypothetical) non-absorbing solvent, the absorption coefficient is approximately $\alpha^* = 2 \times 10^{-5}$ cm$^{-1}$, whereas for pure PCE it is $\alpha = 2$ cm$^{-1}$, five orders of magnitude higher. The absorption path length in a direct transmission measurement is limited to approximately $1/\alpha = 5$ mm, since otherwise insufficient power is transmitted. Extensive measurements were performed to find a spectral region (almost) free of interference from other compounds which might be extracted together with cocaine [2]. Eventually, the cocaine **absorption peak near 1757 cm$^{-1}$ (5.7 µm)** was chosen (Fig. 1).

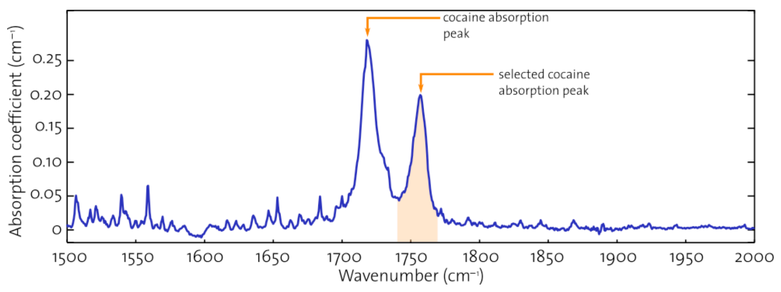



**Fig. 1 —** Absorption spectrum of cocaine (100 µg/mL) in PCE measured with a 1-mm absorption path length. The PCE spectrum has been subtracted. The stronger left absorption peaks interferes with caffeine.

## Experimental

The experimental setup is drawn schematically in Fig. 2. A continuous-wave **quantum cascade laser** with a few mW of output power provides infrared light near **1750 cm$^{-1}$ (5.7 µm)**. The strongly divergent beam is collimated by a short-focal $CaF_2$ lens prior to being split by a 50/50 $CaF_2$ beam splitter. The reflected beam passes through a cell containing liquid samples. Both the transmitted and reflected beams are focused with two $f$ = 100 mm convex $CaF_2$ lenses onto two preamplified thermoelectrically-cooled HgCdZnTe detectors. The voltages produced by the two detectors are digitized by a 14-bit analog-to-digital converter (ADC) at a sampling rate of 50 MHz, divided and yield the **signal ratio *R*,** which is proportional to the transmittance of the sample, given by **Beer-Lambert's law**:

$$\mathcal{T} = 10^{-\alpha \ell} \propto R \qquad (1)$$

where α is the **absorption coefficient** and $\ell$ is the **absorption path length**. The path length of the reflected and transmitted beams are equal, so that changes in water vapor concentration in the air affect both signals in the same way. Moreover, the entire setup is housed under a Plexiglas box which is continuously purged by dry air.

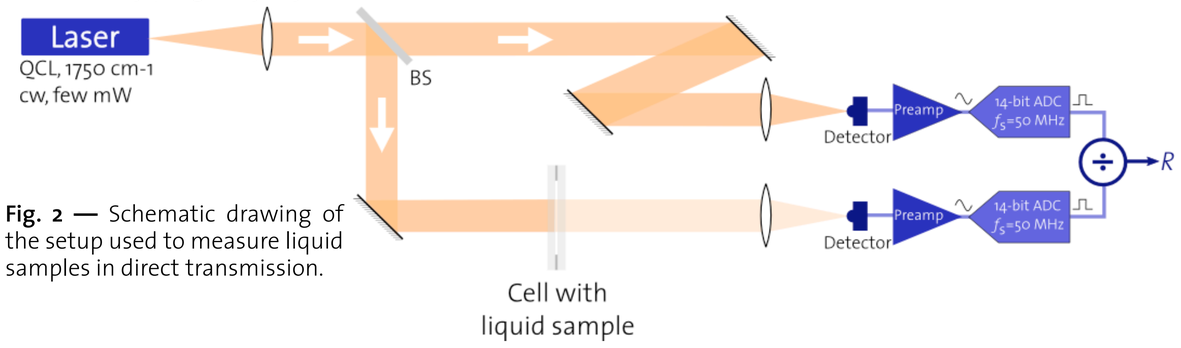



**Fig. 2 —** Schematic drawing of the setup used to measure liquid samples in direct transmission.

The liquid cell consists of two windows (of NaCl and $CaF_2$), a Teflon spacer (thickness = 1 mm) pressed between them and a metallic frame (Perkin-Elmer) to hold everything together (Fig. 3a). A second cell, consisting of two round $CaF_2$ windows, a central Teflon part and a frame made of Teflon and aluminum rings was used for measurements with longer absorption path length (5 mm, Fig. 3b).

To measure the transmission of a sample, two measurements are taken on (or as close as possible to) the cocaine absorption peak (Fig. 1). In the first one, the cell is filled with the solvent only and provides the signal ratio $R_s$ (with absorption coefficient $\alpha_s$). In the second one, the cell is filled with the solvent plus the analyte and provides the signal ratio $R_{s+a}$ (with absorption coefficient $\alpha_s+\alpha_a$). Since the signal ratios are proportional to the transmission of the measured sample, the **transmission of the analyte** can be computed with

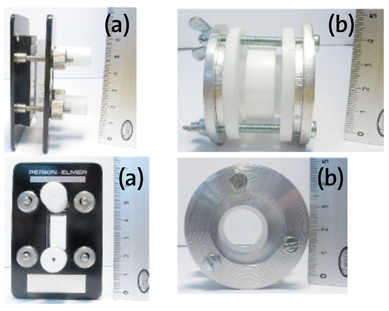



**Fig. 3 —** Photographs of the two cells used to measure the liquid samples. **(a)** 1-mm absorption path length (from Perkin-Elmer). **(b)** 5-mm path length (home-built).

$$\mathcal{T}_a = \frac{\mathcal{T}_{s+a}}{\mathcal{T}_s} = \frac{R_{s+a}}{R_s} \qquad (2)$$

The **absorption of the analyte** is defined as

$$\mathcal{A} \equiv 1 - \mathcal{T}_a \qquad (3)$$

Since the two **measurements $R_s$ and $R_{s+a}$ cannot be taken simultaneously**, any changes ("drifts") which occur in the time it takes to acquire the two values will introduce an error. If one takes a series of measurements $R_1$, $R_2$, $R_3$, $R_4$... all of the same sample, the expected value of the ratios $R_1/R_2$, $R_2/R_3$, $R_3/R_4$... is one, the expected value of the absorption (Eq. 3) is zero and the **root-mean-square of the absorption** is

$$\sigma_{\mathcal{A}} \equiv \sqrt{\langle \mathcal{A}^2 \rangle} = \sqrt{\frac{1}{N}\sum_{k=1}^{N-1}\left(1 - \frac{R_k}{R_{k+1}}\right)^2} \qquad (4)$$

## Results and Discussion

The **sensitivity** of the system is given by the **limit of detection (LOD)**, that is the smallest concentration of cocaine that can be measured reliably. It is limited by the uncertainty of the absorption (Eq. 4), which in turn is limited by the amount of **noise** in the measurements of the ratios $R_s$ and $R_{s+a}$ and by **drifts** occurring between the two measurements.

Table 1 lists the absorption coefficient and absorption of PCE and PCE plus 10 ng/mL cocaine. According to Tab. 1, the root-mean-square value of the measured absorption must be much smaller than $2.3 \times 10^{-5}$ if an absorption path length of 5 mm is chosen.

| | α (cm-1) | $\mathcal{A}$ (1 mm) | $\mathcal{A}$ (5 mm) |
|---|---|---|---|
| **PCE** | 2 | 37% | 90% |
| **+ 10 ng/mL** | + $2 \times 10^{-5}$ | **+ $4.6 \times 10^{-6}$** | **+ $2.3 \times 10^{-5}$** |

**Tab. 1 —** Absorption coefficient and absorption (for 1-mm and 5-mm absorption path lengths) of PCE and of PCE plus 10 ng/mL cocaine.

The best value for the LOD can be estimated from a continuous measurement of the signal ratio $R$ under constant conditions. Such a measurement is shown in Fig. 4a. The whole measurement sequence can be divided into contiguous groups of duration $\tau$ and the values of $R$ can be averaged within each group. The term **$(1-R_k/R_{k+1})$** in Eq. 4 is then simply the **absorption difference** between the two consecutive measurements $k$ and $k$+1, which in this case is expected to be zero. The **root-mean-square value of the absorption** (Eq. 4), plotted in Fig. 4b for different averaging times $\tau$, is an **estimator for the uncertainty of the measured absorption**. Additionally, one should allow for a "dead" time between successive averages, to take into account that the second measurement can only be started after the previous sample has been removed and the cell has been dried and refilled. The lowest value of **$9.5 \times 10^{-5}$** is reached for an averaging time of 27 seconds. If the limit of detection is set at 3 times this value, according to Tab. 1 we obtain a LOD of 120 ng/mL. Longer averaging times unnecessarily increase the measurement duration and deteriorate the sensitivity of the system.

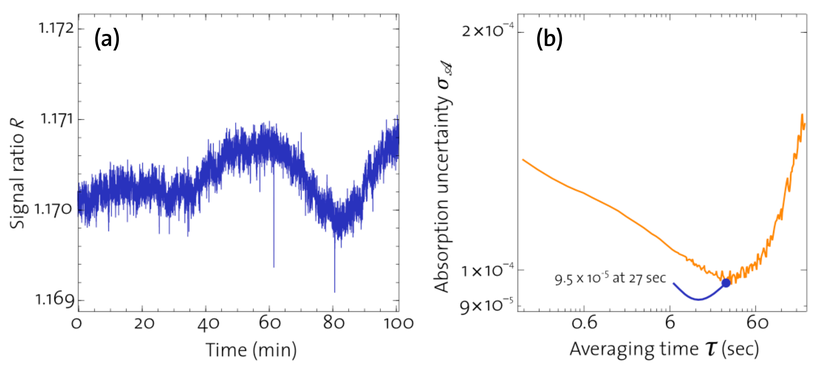



**Fig. 4 — (a)** Signal ratio $R$ measured under constant condition over 100 minutes. **(b)** Computed root-mean-square absorption as a function of averaging time.

**Additional errors** introduced by the process of **emptying, purging, drying and refilling the cell** between measurements are systematically excluded in the previous measurement. To take them into account, the cell was filled with PCE and the signal ratio $R$ was measured and averaged for 30 seconds. Then, the measurement was stopped and the PCE was pumped out of the cell. The cell was purged with air until dry, refilled with fresh PCE and the next measurement started. The result is shown in Fig. 5. The absorption difference for the 7 pairs of consecutive measurements can be computed as above. The **root-mean-square values of the absorption, absorption coefficient, equivalent cocaine concentration and limit of detection** are given in Tab. 2. The LOD is worse than previously estimated by a factor of five. This could be due to small changes in the distance between the cell windows, temperature changes, or impurities in the solution. It should be noted that the measurements in Fig. 5 were not performed on the cocaine absorption peak (Fig. 1), but slightly below 1757 cm$^{-1}$ (at 1750 cm$^{-1}$), where the absorption is half the peak value. A factor of two could therefore be gained in terms of LOD by measuring exactly on the absorption peak.

| $\sigma_{\mathcal{A}}$ | $\sigma_\alpha$ | $\sigma_c$ | LOD = $3\sigma_c$ |
|---|---|---|---|
| $4.6 \times 10^{-4}$ | $4.0 \times 10^{-4}$ cm$^{-1}$ | 200 ng/mL | **600 ng/mL** |

**Tab. 2 —** Root-mean-square values of the absorption, absorption coefficient, equivalent cocaine concentration and limit of detection (LOD) for the measurement in Fig. 5.

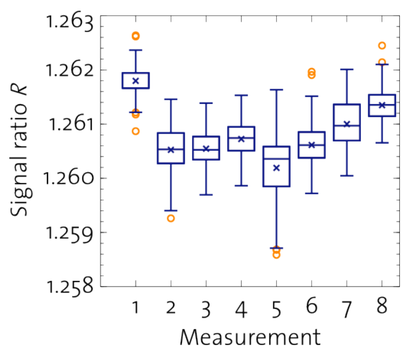
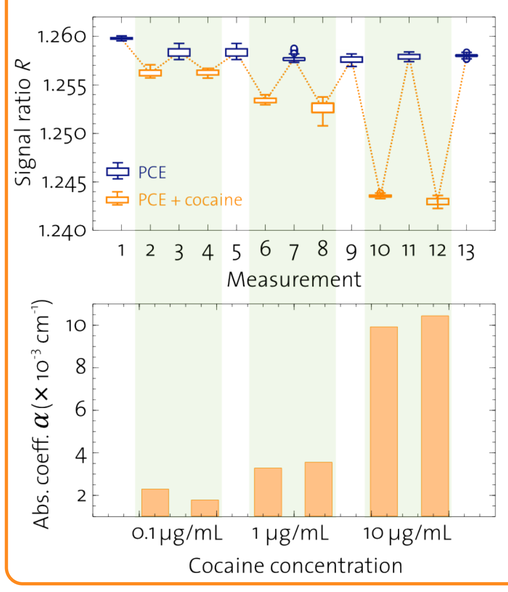



**Fig. 5 —** Averaged signal ratio $R$ for 8 consecutive measurements of PCE.




Finally, three **PCE solutions containing three different concentrations of cocaine (0.1, 1.0, 10 µg/mL)** were measured twice each (Fig. 6) at 1750 cm$^{-1}$. The fact that the absorption coefficient does not depend linearly on the concentration (Fig. 6b) indicates that the **absorption is not due exclusively to cocaine**. Moreover, the measurement at a concentration of 0.1 µg/mL (Fig. 6a) would indicate a LOD below 100 ng/mL, in contradiction with previous measurements (Fig. 5 and Tab. 2). It seems likely that the samples containing cocaine were contaminated (perhaps with water). In any case, the two pairs of measurements with concentrations of 0.1 and 1 µg/mL (difference = 0.9 µg/mL) can clearly be distinguished, in agreement with the LOD computed earlier (Tab. 2).

**Fig. 6 —** Transmission measurements of three solutions of PCE with 0.1, 1 and 10 µg/mL cocaine. **(a)** Signal ratio $R$ of alternated measurements of PCE and PCE plus cocaine. **(b)** Computed absorption coefficient for the measurements in (a).

## Conclusions

A **setup for measurements of liquid samples containing cocaine** has been demonstrated. It uses a **quantum cascade laser at 1750 cm$^{-1}$**, a cell for liquid samples (1 and 5 mm absorption path length) and two detectors. The **limit of detection of cocaine in perchlorethylene** measured at 1750 cm$^{-1}$ was computed to be **600 ng/mL** (300 ng/mL if measured on the absorption peak, SNR = 3). Actual measurements with cocaine/PCE solutions confirm this limit.

[1] W. Schramm, R.H. Smith, P.A. Craig, and D.A. Kidwell, *Journal of Analytical Toxicology* **16**, 1-9 (1992)
[2] K.M.-C. Hans, S. Müller and M.W. Sigrist, *Drug Testing and Analysis*, doi: 10.1002/dta.346, in print (2012)