Laser-based photoacoustic sensing of glucose in aqueous samples

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Outline

• Motivation
• Experimental Technique and Setup
• Results
• Conclusion and Outlook
Motivation

Diabetes as a human metabolic disease:

- Patients need to measure their blood sugar level several times per day
- Preprandial glucose level of a healthy human: 65 – 120 mg/dl
- Common blood sugar measurements are invasive
Motivation

Diabetes as a human metabolic disease:
- Patients need to measure their blood sugar level several times per day
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Goal: Development of a non-invasive glucose sensor based on
- MIR spectral region
- Photoacoustic (PA) detection
- Interstitial fluid glucose
Human tissue

- The stratum corneum is between 10-20 µm thick with 10% water content
- Epidermis is usually between 60-100 µm thick, has a 60% water content and is not supplied with blood
- In the MIR only up to approx. 100 µm optical penetration depth
- Measurements of glucose concentration in the interstitial fluid (ca. 15 min time delay)
Glucose and phantom tissue

- Water, gelatine and agar as a first step towards mimicking tissue
- Characteristic glucose absorption peaks at 1034 and 1081 cm\(^{-1}\)
- Strong absorption of water in the MIR
Photoacoustic effect and cell design

- Volume 80 mm³

Gas piston model:
Optically and thermally thick case

\[ \text{PA signal} \propto \frac{I \cdot \alpha}{V \cdot f^{1.5}} \]

Tam C., Rev. Mod. Phys., 1986, 58, 381-434

\[ \mu_s < \mu_\alpha < \ell \]

\[ \mu_s = \left( \frac{D_s}{\pi f} \right)^{\frac{1}{2}} \]
with \( D_s = \) thermal diffusivity

\[ \mu_\alpha = \frac{1}{\alpha} \]
with \( \alpha = \) absorption coefficient
Photoacoustic effect and cell design

- Volume 80 mm³
- Diamond window 163 µm

Gas piston model:
Optically and thermally thick case

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**Photoacoustic effect and cell design**

- Volume 80 mm$^3$
- Diamond window 163 µm
- Flow cell
- Reference chamber

Gas piston model:
Optically and thermally thick case

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Experimental setup

**CO₂-LASER**

HeNe-LASER

SPECTRUM ANALYSER

**QCL**

**LOCK-IN**

**PREAMP**

**MIC**

**PA CELL**

**ETH Zurich**

*Laser Spectroscopy and Sensing*
Glucose depending NPAS measured with the flow cell

- NPAS at 1082 cm\(^{-1}\) (QCL) – 944 cm\(^{-1}\) (CO\(_2\)-laser) measured in PA chamber A
- NPAS reference measurement measured in chamber B (without laser)
- Shown signal A – B
- 100 mg/dl detectable
Fast recording of a spectrum with the QCL

A single spectrum can be recorded within 5.5 s
An averaging of the single measurement is necessary
Monitoring time dependent processes with the QCL

- The evaporation of the water leads to an increase in glucose concentration
- Over time the concentration of acetone in the PA chamber decreases
Conclusion & Outlook

- Implementation of MIR laser based PA sensor using a double-chamber PA cell closed with a diamond window => strong and stable signals
- Glucose concentrations within the physiological range detected in aqueous samples
- Fast tuning of the EC-QCL allows monitoring time-dependent spectral changes between 1000-1100 cm\(^{-1}\)
- Measurement in more complex tissue phantoms closer mimicking human tissue
- Measurement through non-glucose containing layer
- Including the measurement of different parameters (i.e. temperature, humidity and blood pulsation)
- In-vivo measurements with the PA sensor
Photoacoustic cell

Copper block
Gold coated cell walls and connection tube to the microphone
Diamond window

Microphone cable
ZnSe window
Support frame

35 mm
Combining the PA cell and the flow cell
Overview of *in-vivo* Glucose Measurements

- Making the blood sample-taking more convenient
- Implanted sensors
- Methods of non-invasive glucose measurements:
  - Reverse iontophoresis (GlucoWatch)
  - Optical absorption spectroscopy (NIR and MIR)

Review:
C. E. F. do Amaral and B. Wolf,
Fast recording of a spectrum with the QCL

- A single spectrum can be recorded within 5.5 s
- An averaging of the single measurement is necessary
• The glucose concentration can be continuously varied
• Stable measurement conditions
• PA reference chamber for suppression of vibrations and environmental influences
• Pumping can simulate pulsation
Gas coupling method

Back ing Material  Condensed Sample  Coupling Gas

Heat generated in absorption length

Periodical optical absorption

Acoustic wave in sample causing interface oscillation

Heat within thermal diffusion length communicates with interface

Sound propagation in gas

Thin layer of gas heated periodically

Periodically expanding gas generate sound

Microphone

Modulated or Pulsed Light

Front Window

Laser Spectroscopy and Sensing

ETH Zurich
QCL cavity design

- Output lens
- QCL chip
- Cavity lens
- Grating
Power spectrum of the QCL at 800 mA
FWHM of the QCL beam versus distance from the Laser
Output power versus laser currant

[Graph showing the relationship between output power and laser current with different wavelengths marked: Power at 1005 cm\(^{-1}\), Power at 1060 cm\(^{-1}\), Power at 1100 cm\(^{-1}\).]
FTIR spectrometer with ATR accessory
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