Laser-based photoacoustic sensing of glucose in aqueous samples

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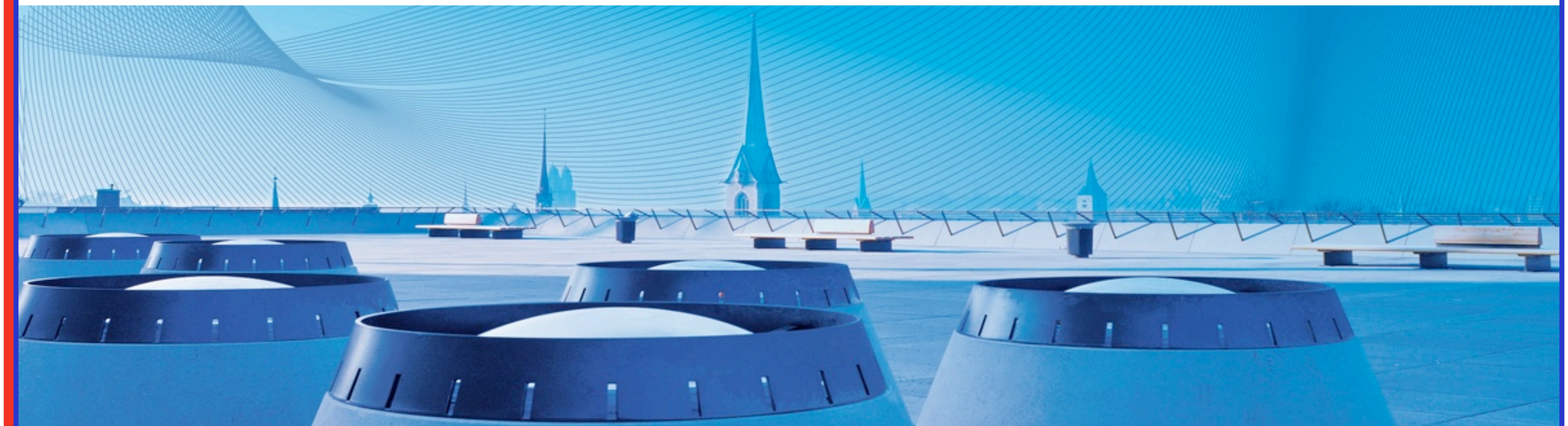
ETH Zürich
3rd of November 2010 Bern

Outline

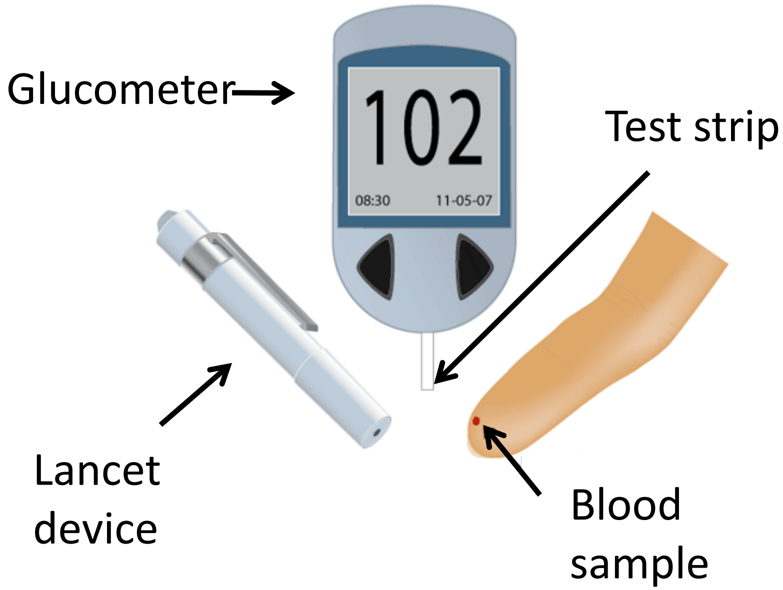
- Motivation
- Experimental Technique and Setup
- Results
- Conclusion and Outlook



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:

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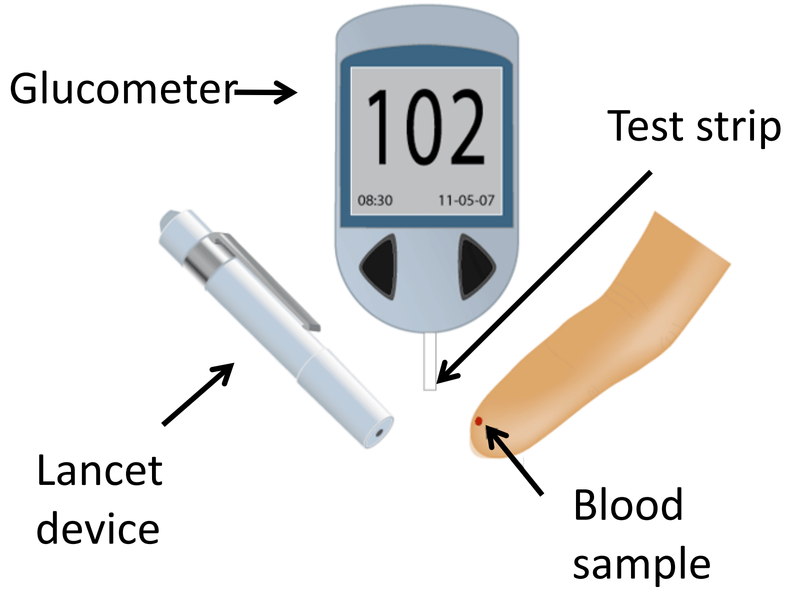
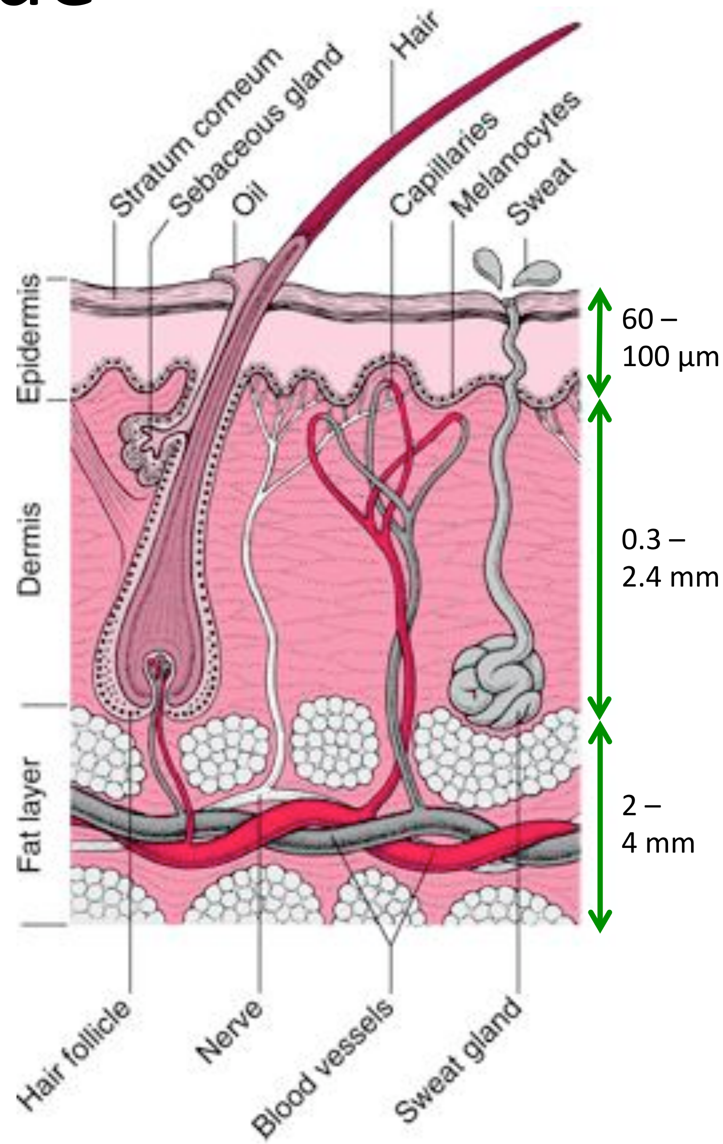
Goal: Development of a **non-invasive** glucose sensor based on

- MIR spectral region
- Photoacoustic (PA) detection
- Interstitial fluid glucose



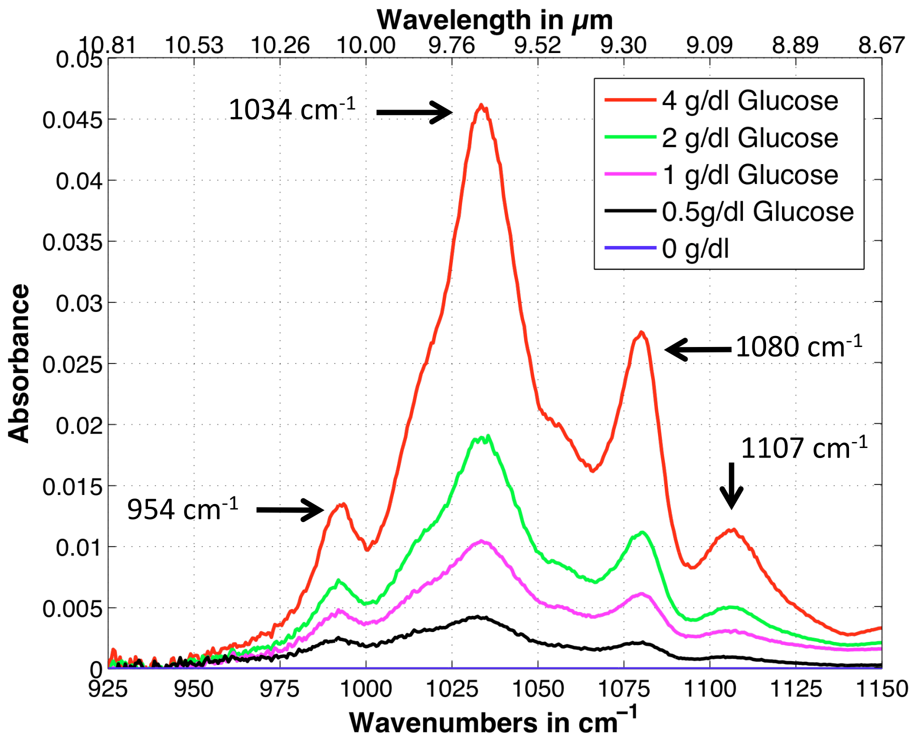
Human tissue

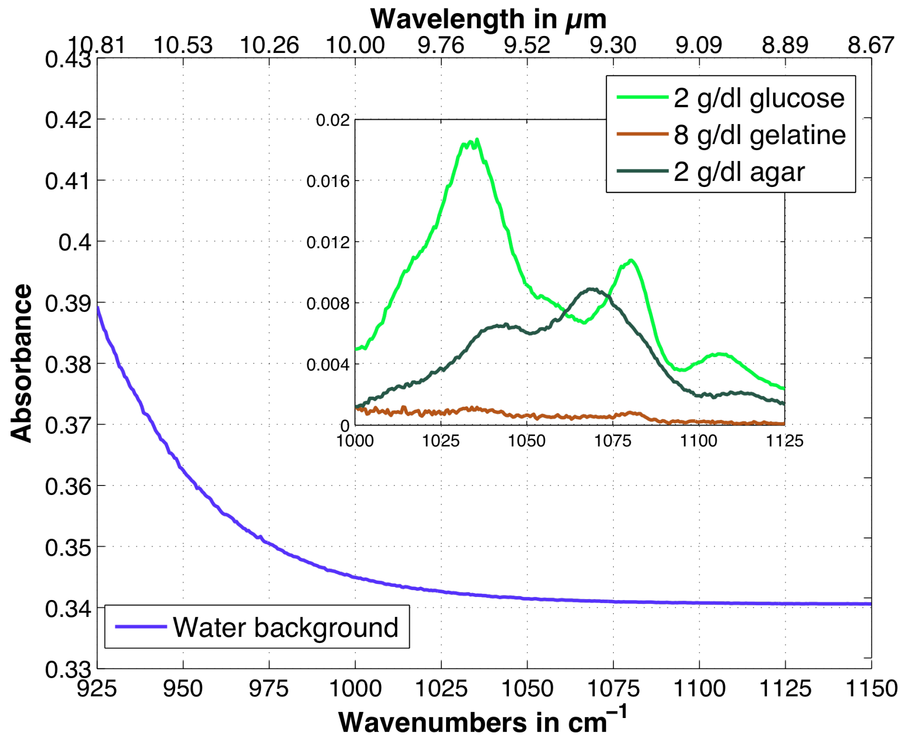
- The stratum corneum is between 10-20 µm thick with 10% water content
- Epidermis is usually between 60-100 µm thick, has a 60% water content and is not supplied with blood
- In the MIR only up to approx. 100 µm optical penetration depth
- Measurements of glucose concentration in the interstitial fluid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



Glucose and phantom tissue

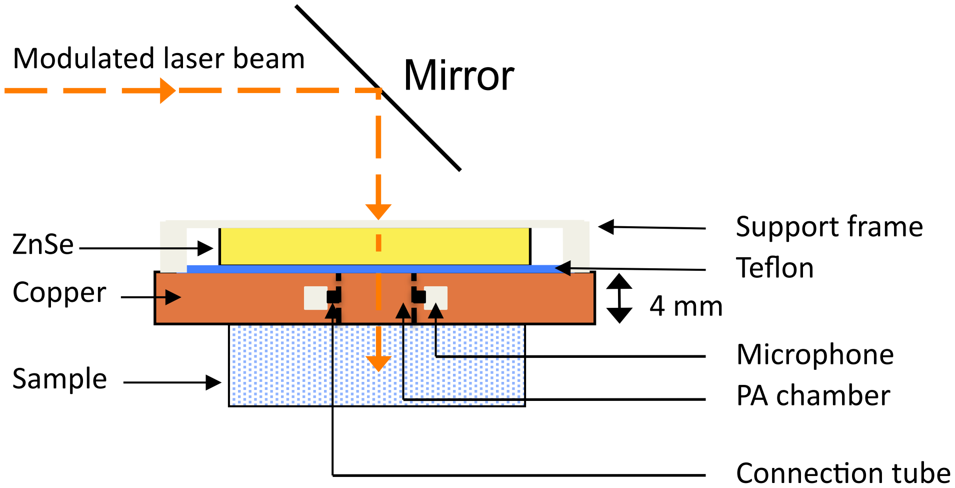
- Water, gelatine and agar as a first step towards mimicking tissue
- Characteristic glucose absorption peaks at 1034 and 1081 cm^{-1}
- Strong absorption of water in the MIR





Photoacoustic effect and cell design

- Volume 80 mm^3



Gas piston model:
Optically and thermally thick case

$$\mu_s < \mu_\alpha < \ell$$

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

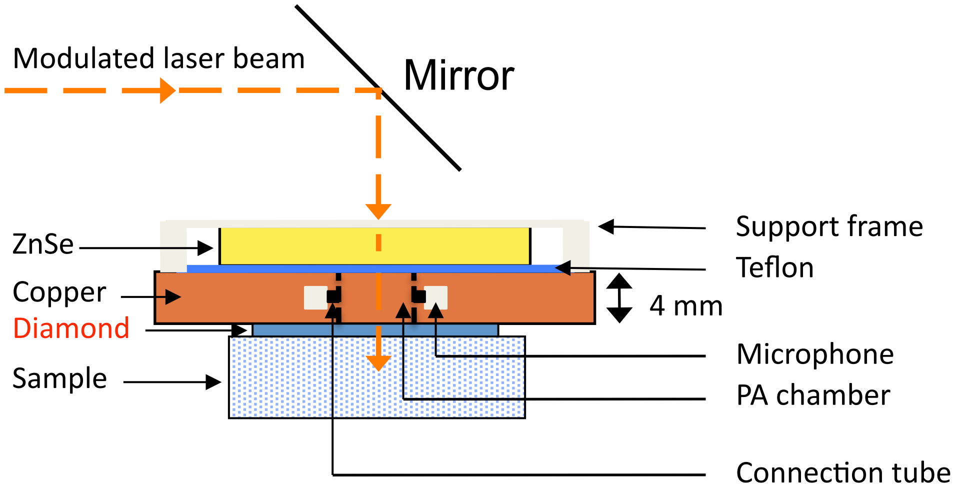
$$\mu_s = \left(\frac{D_s}{\pi f}\right)^{\frac{1}{2}} \text{ with } D_s = \text{ thermal diffusivity}$$

$$\mu_a = \frac{1}{\alpha} \text{ with } \alpha = \text{ absorption coefficient}$$

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

Photoacoustic effect and cell design

- Volume 80 mm^3
- Diamond window 163 µm



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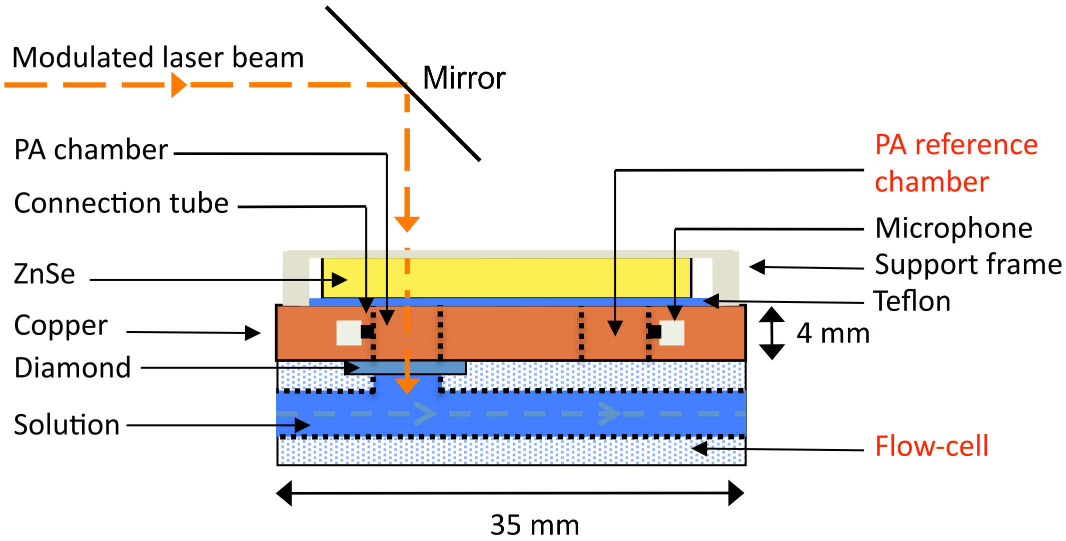
Photoacoustic effect and cell design

- Volume 80 mm³
- Diamond window 163 µm
- Flow cell
- Reference chamber



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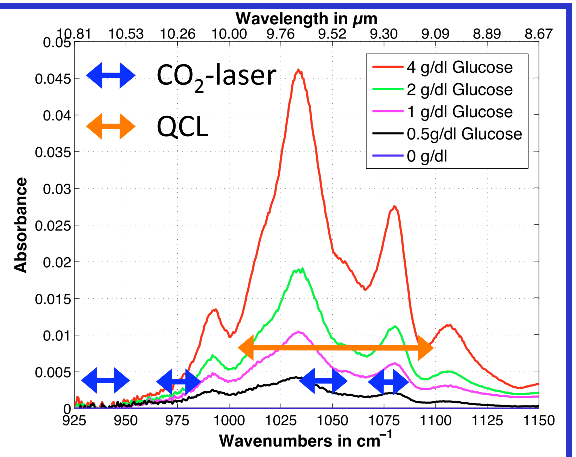
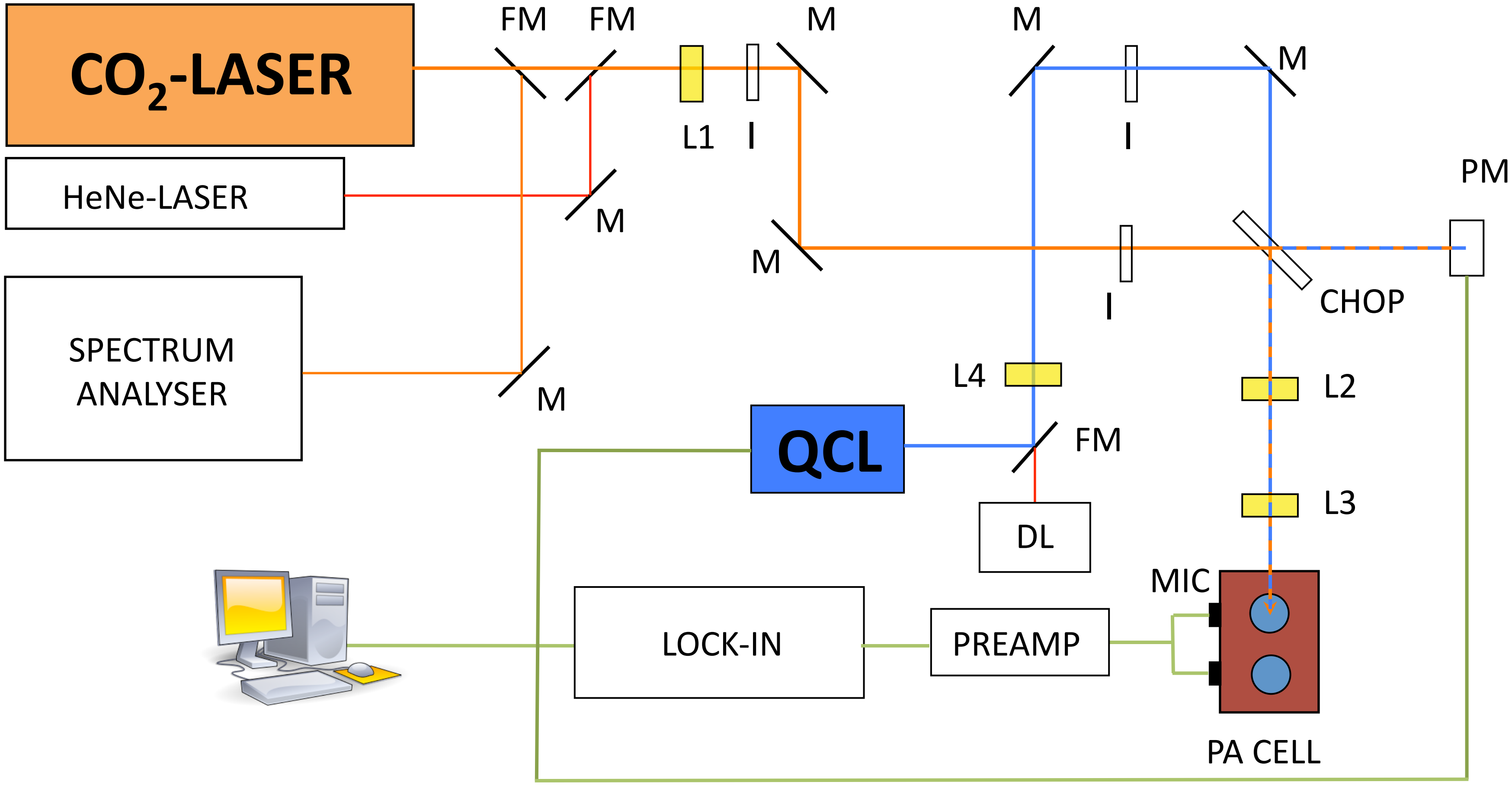
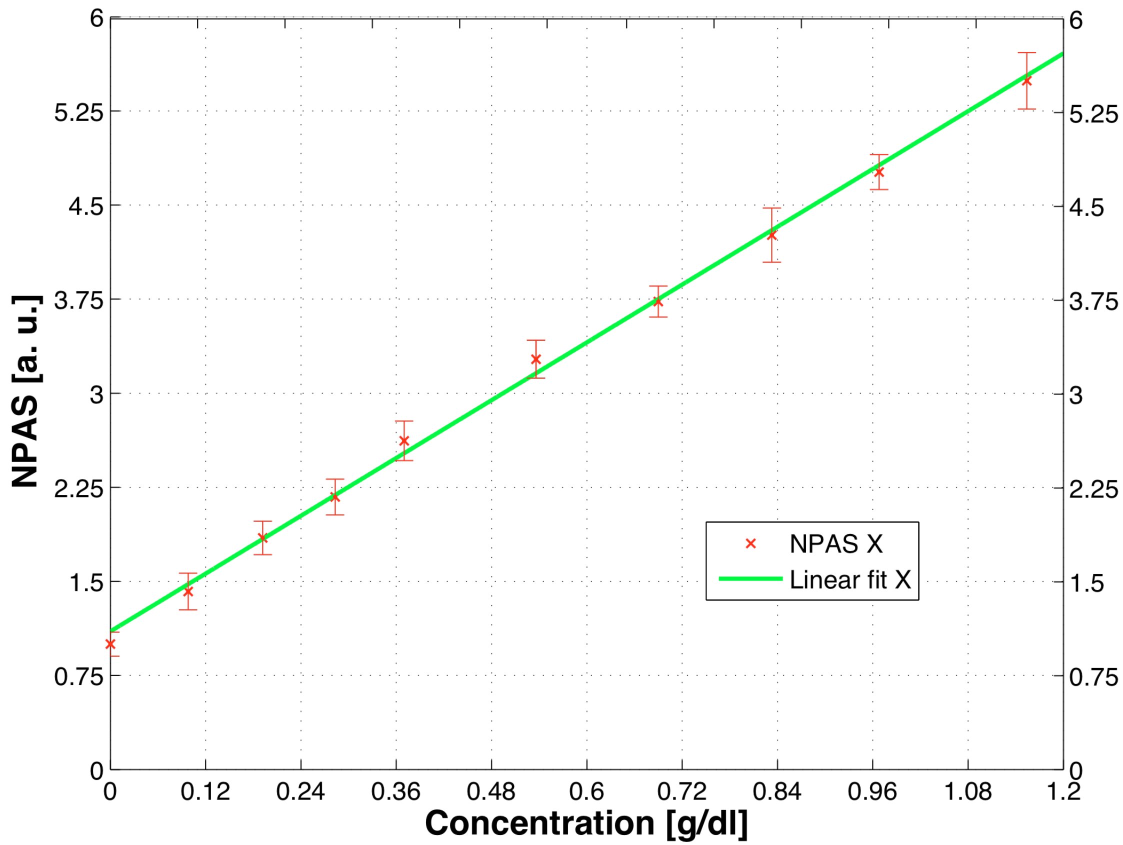
Experimental setup





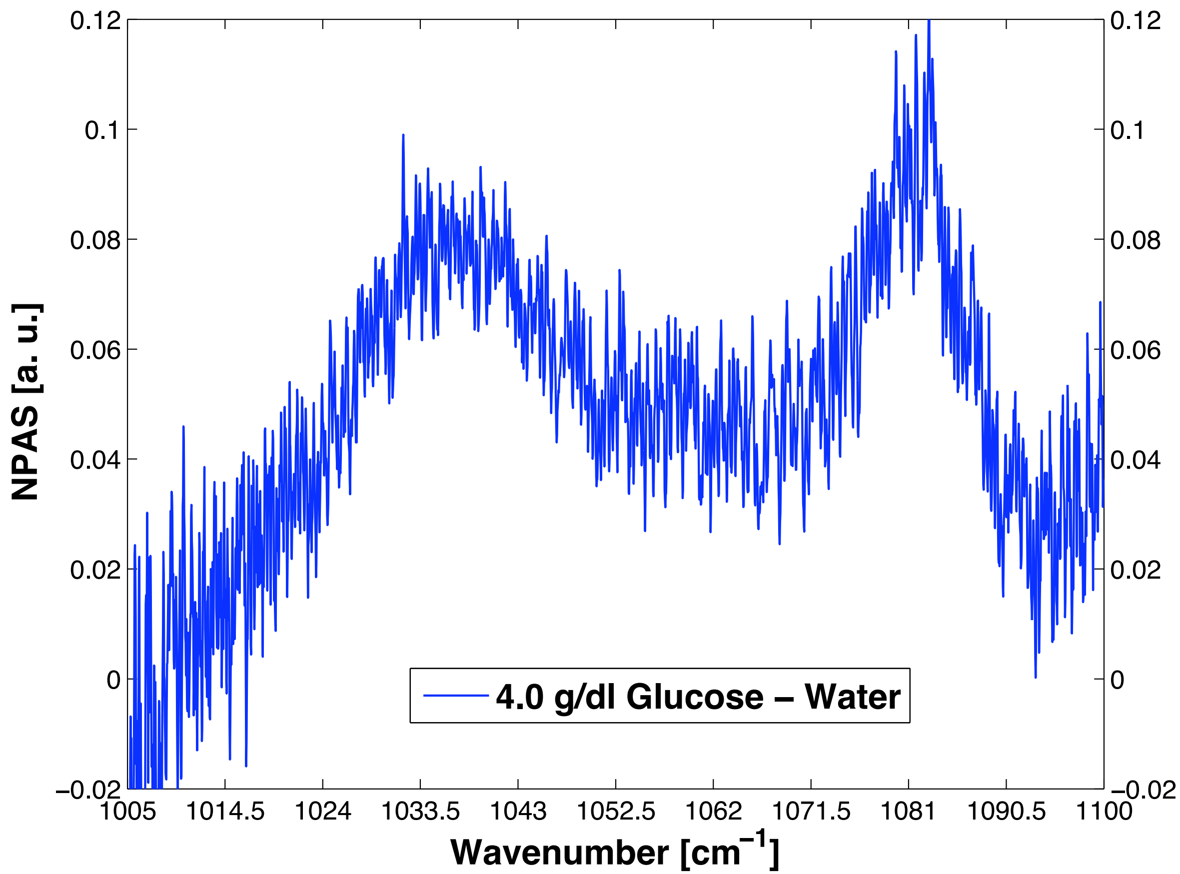
Glucose depending NPAS measured with the flow cell



- 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

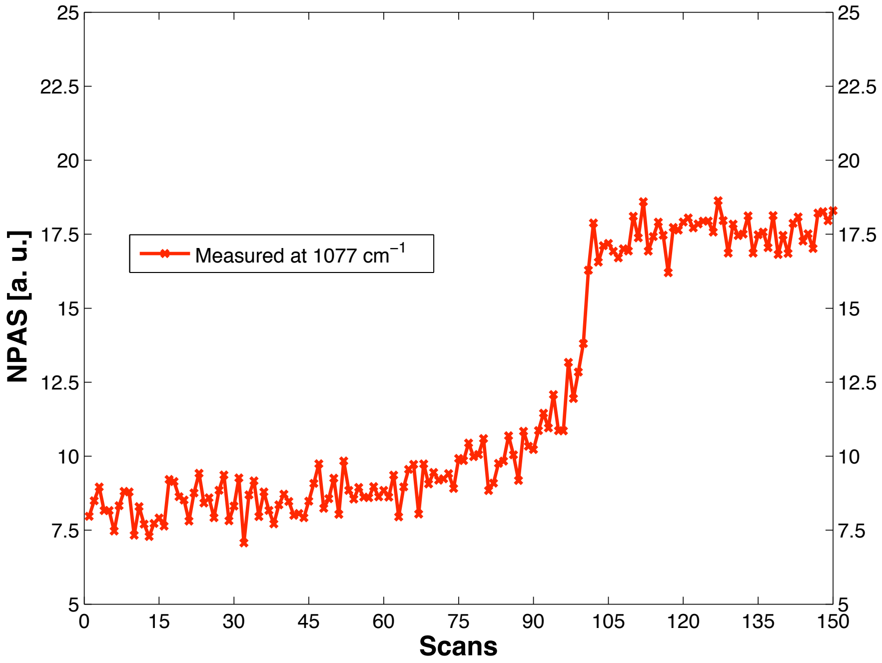
PA spectrum of glucose 1005-1100 cm^{-1}



- A single spectrum can be recorded within 5.5 s
- An averaging of the single measurement is necessary

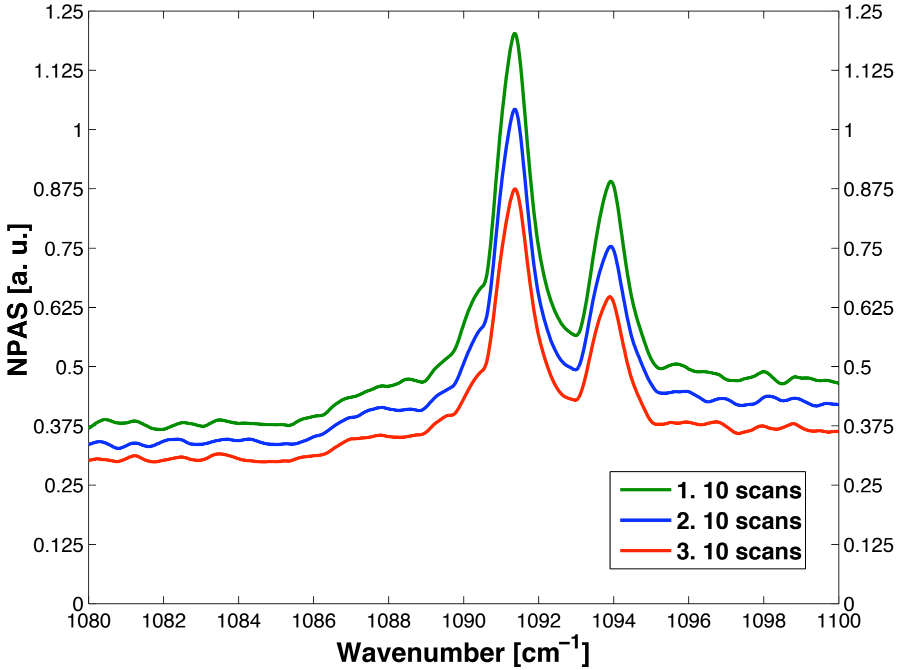
Monitoring time dependent processes with the QCL

Evaporating drop of glucose solution (1077 cm^{-1})



- The evaporation of the water leads to an increase in glucose concentration

PA spectrum of acetone vapour 1080-1100 cm^{-1}



- 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}

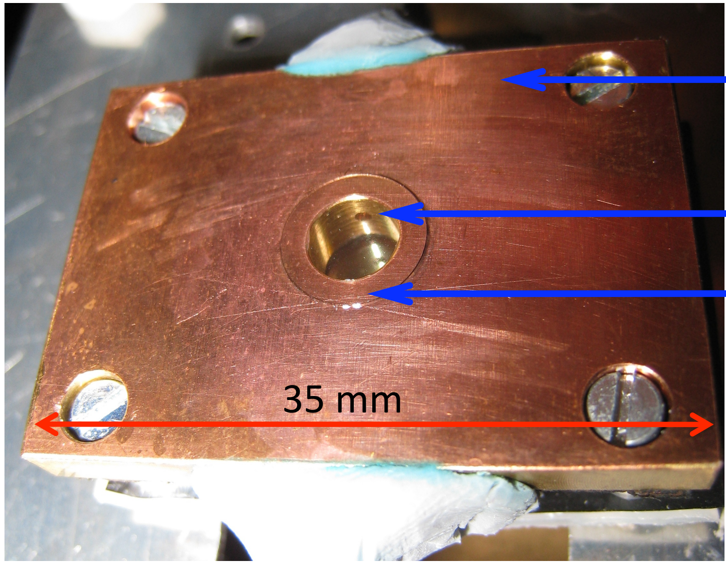
- Measurement in more complex tissue phantoms closer mimicking human tissue
- Measurement through non-glucose containing layer
- Including the measurement of different parameters (i.e. temperature, humidity and blood pulsation)
- *In-vivo* measurements with the PA sensor

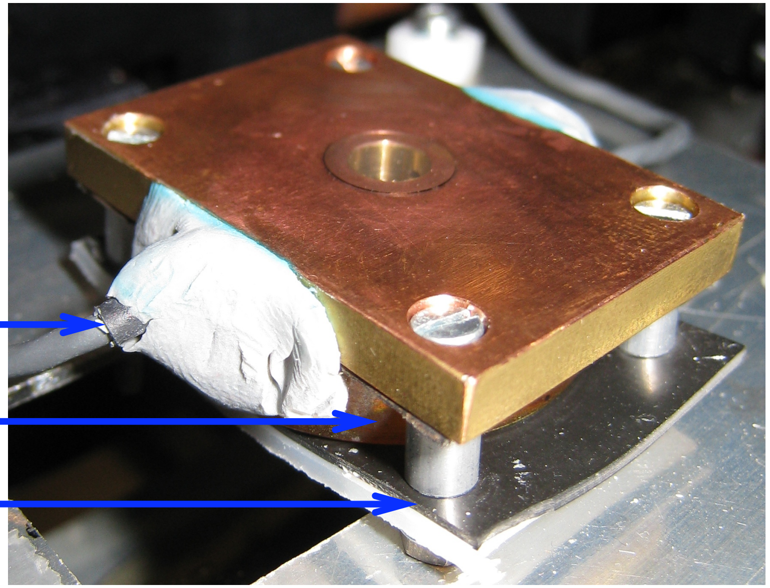
Prof. Markus W. Sigrist

Dr. Julien M. Rey

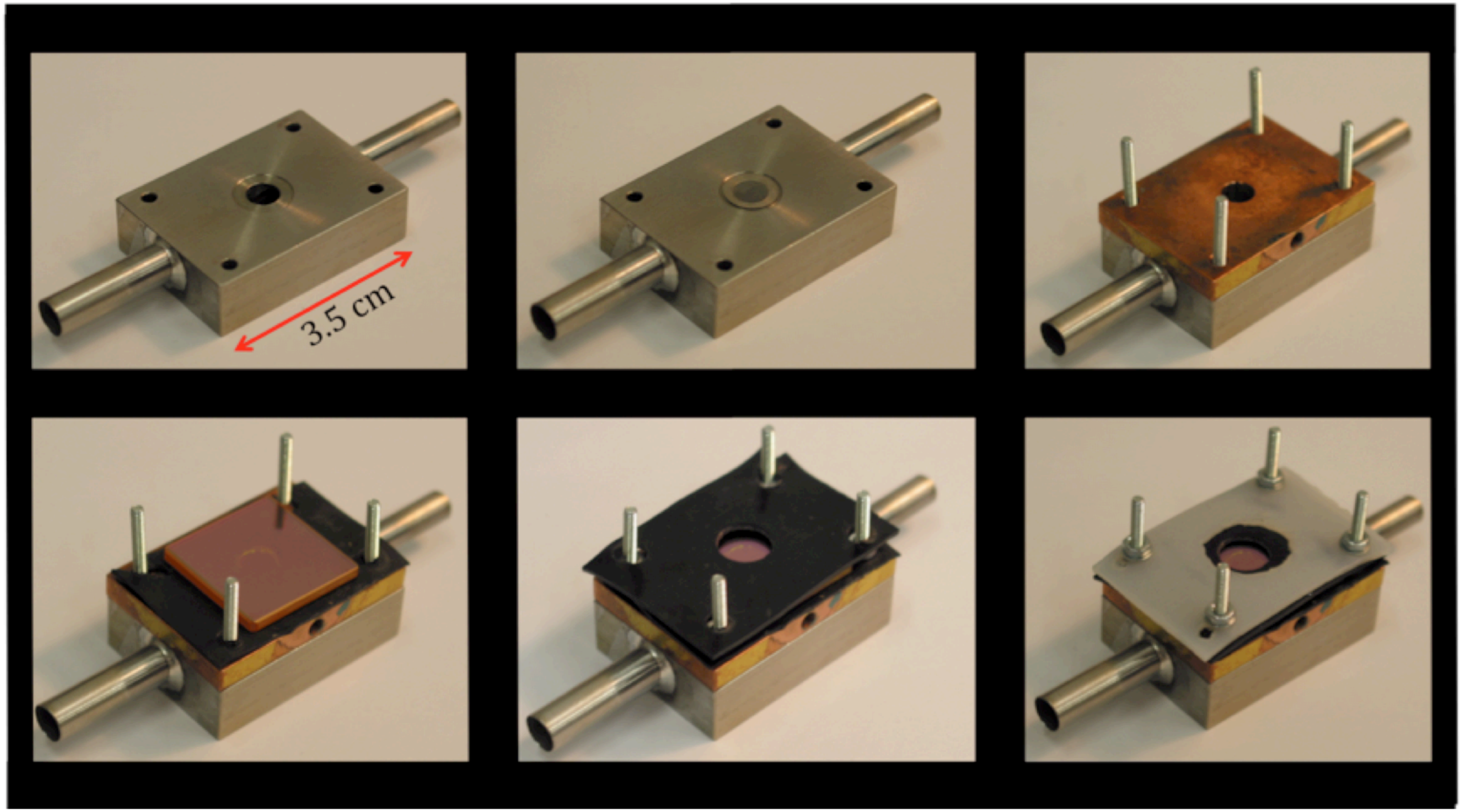
Sponsoring: ETH Zürich GlucoMetrix

Photoacoustic cell





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)

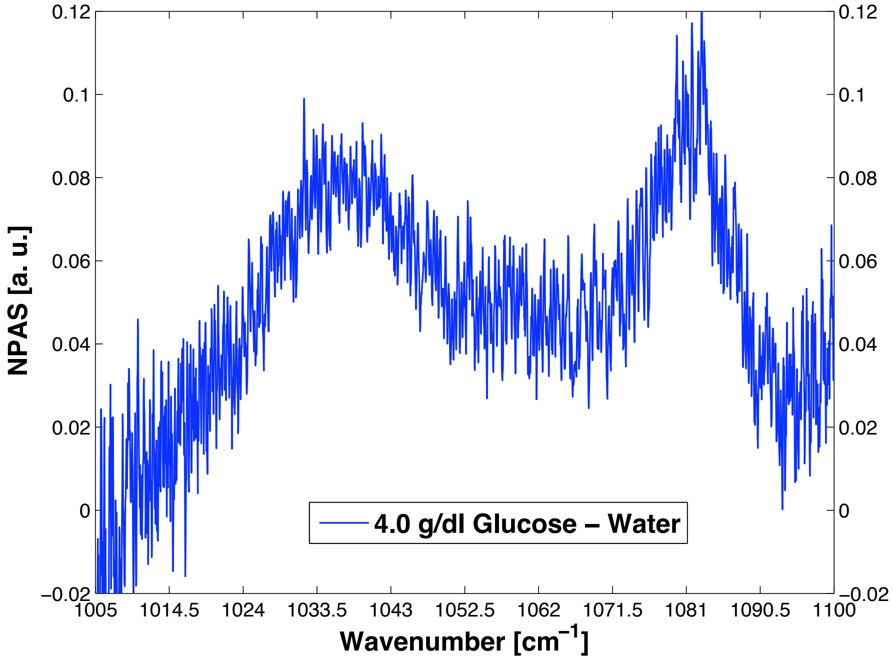
Review:

C. E. F. do Amaral and B. Wolf,

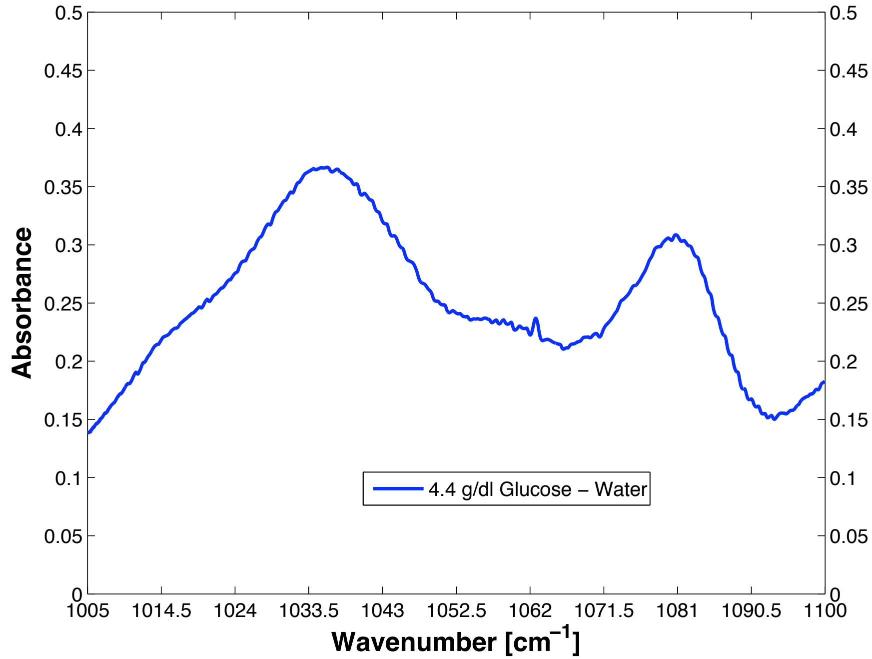
Medical Engineering & Physics 30(5), 541–549 (2008).

Fast recording of a spectrum with the QCL

PA spectrum of glucose 1005-1100 cm^{-1}



ATR spectrum of glucose 1005-1100 cm^{-1}



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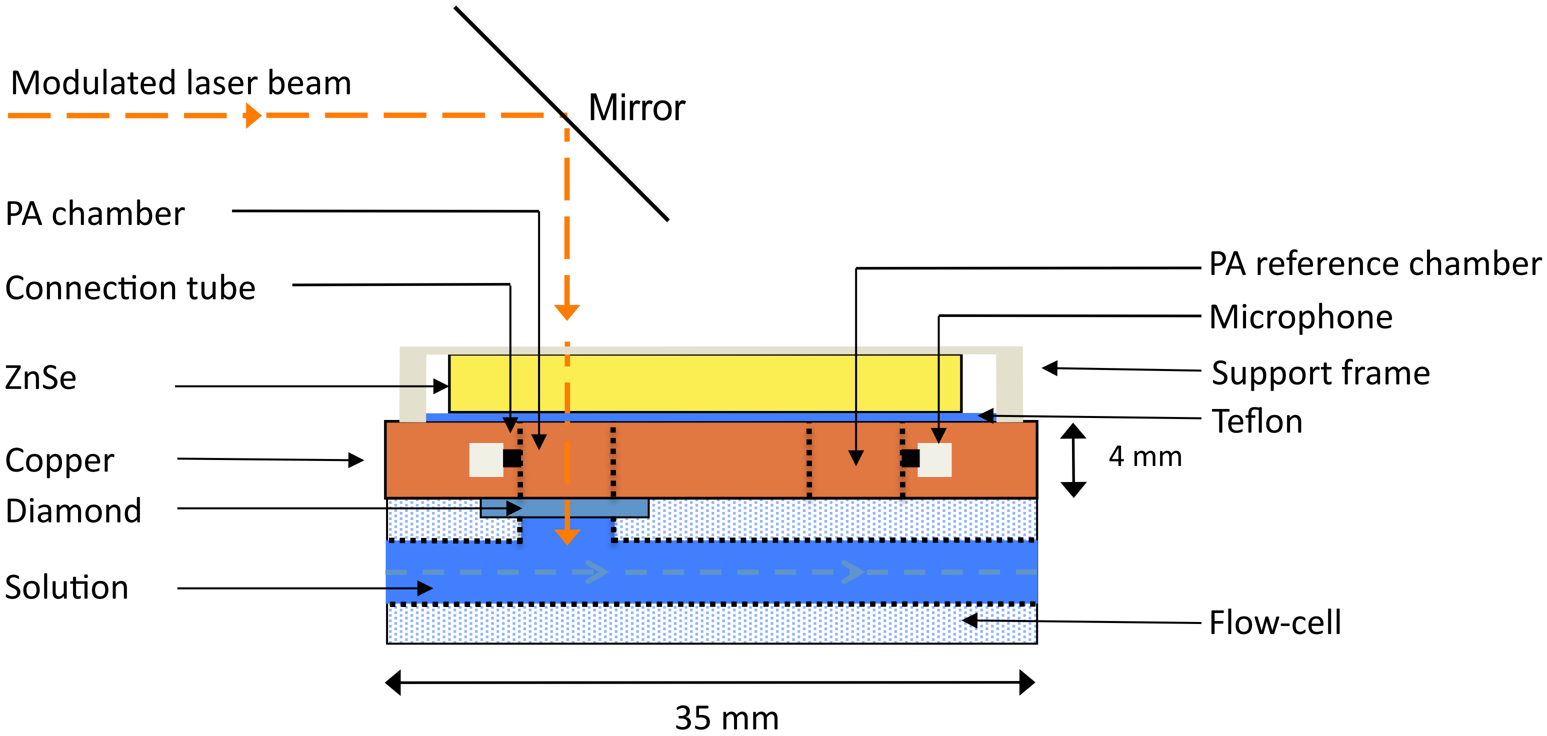
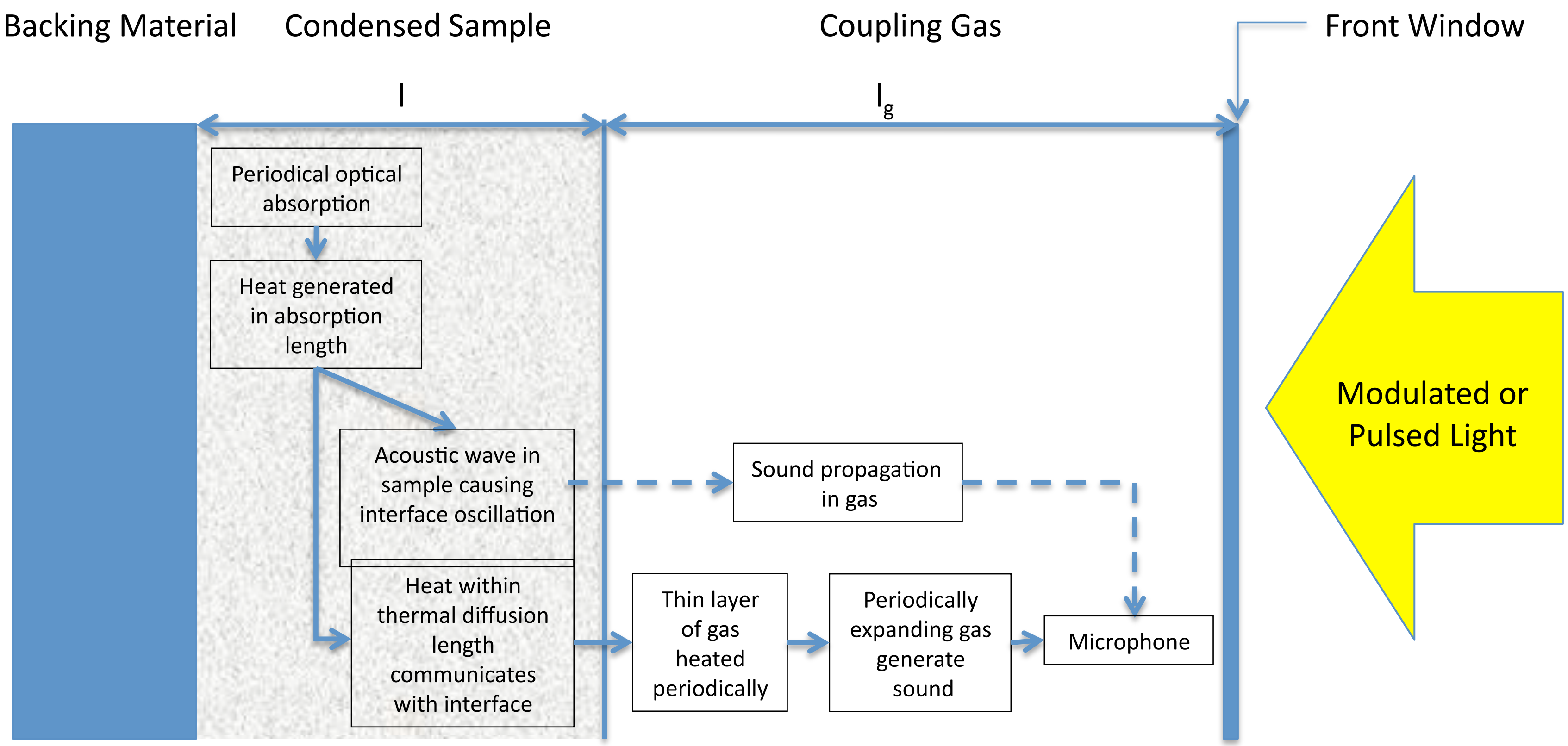
Photoacoustic cell

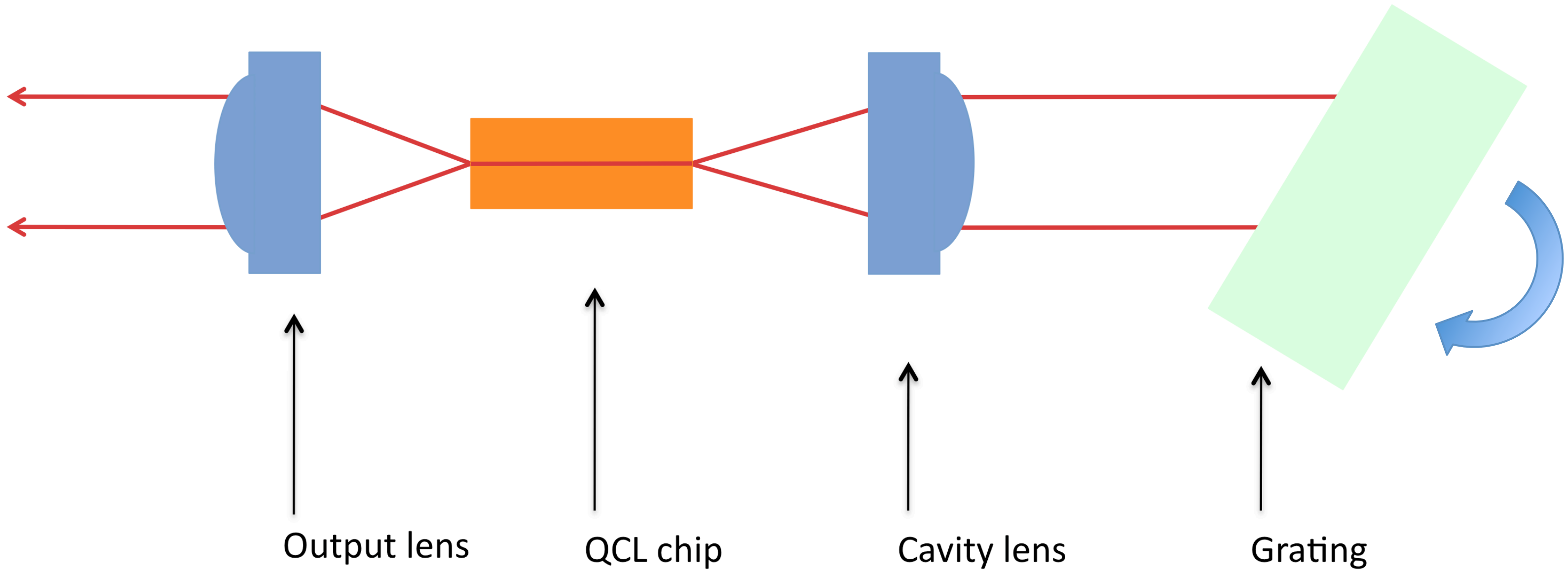


- The glucose concentration can be continuously varied
- Stable measurement conditions
- PA reference chamber for suppression of vibrations and environmental influences
- Pumping can simulate pulsation

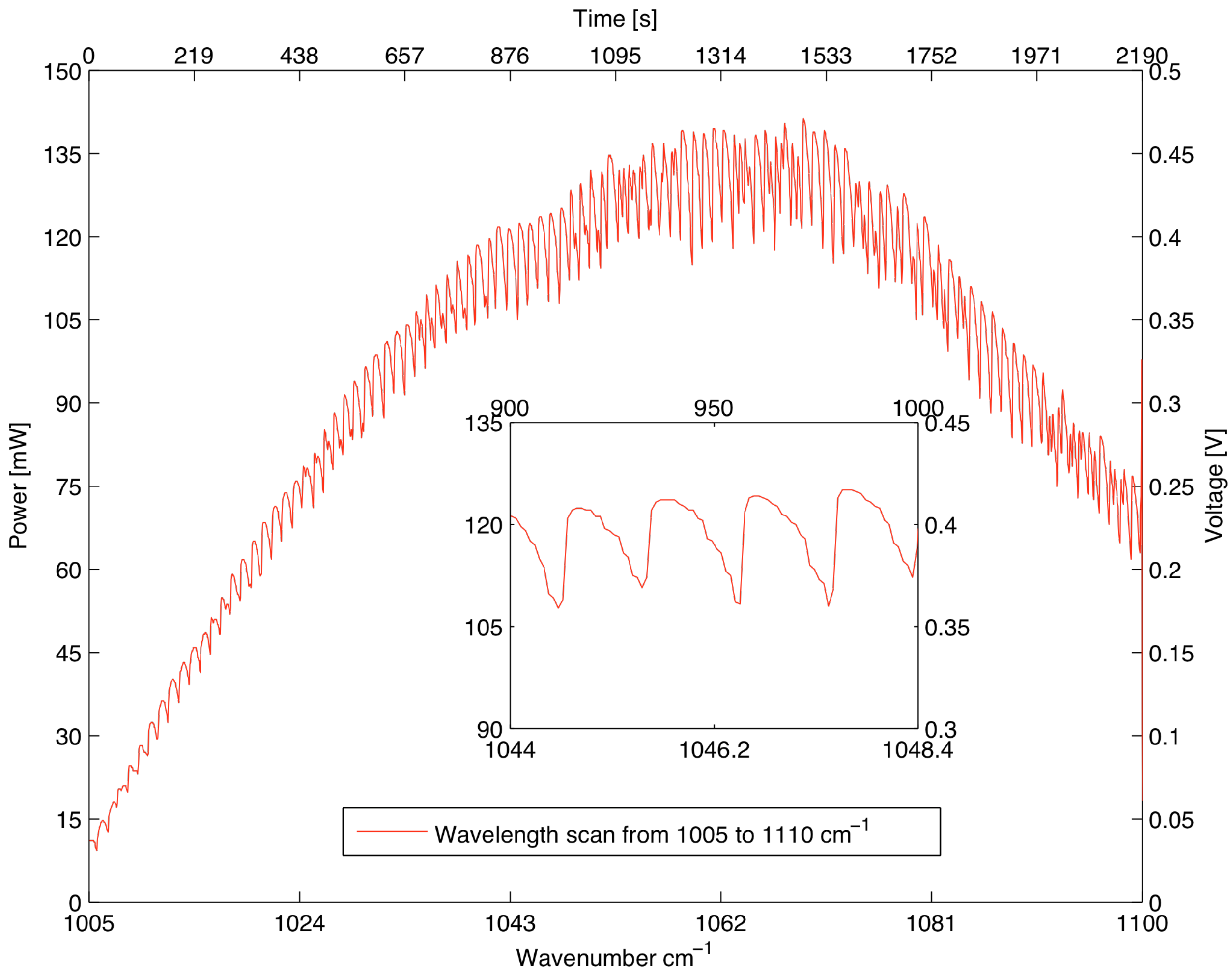
Gas coupling method



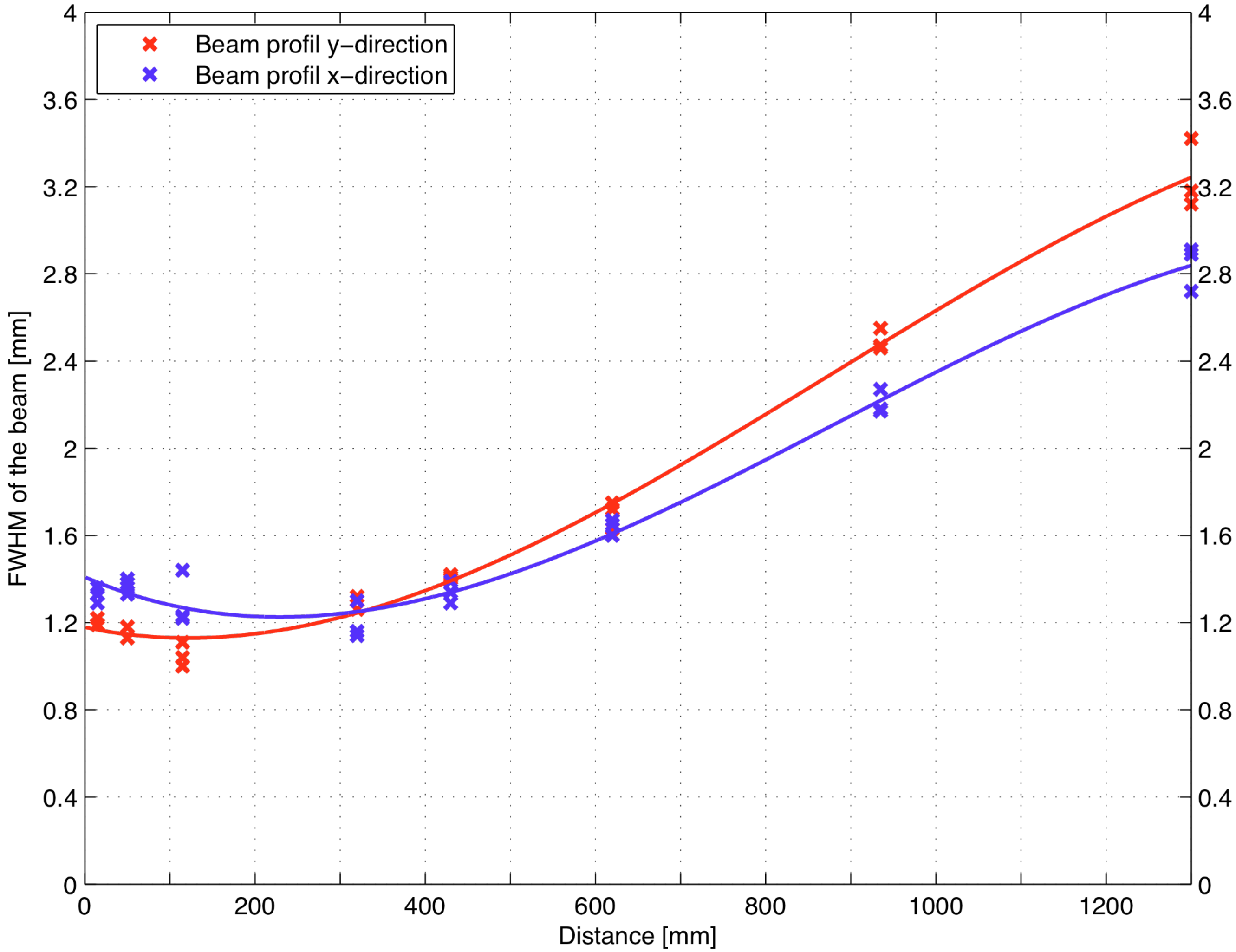
QCL cavity design



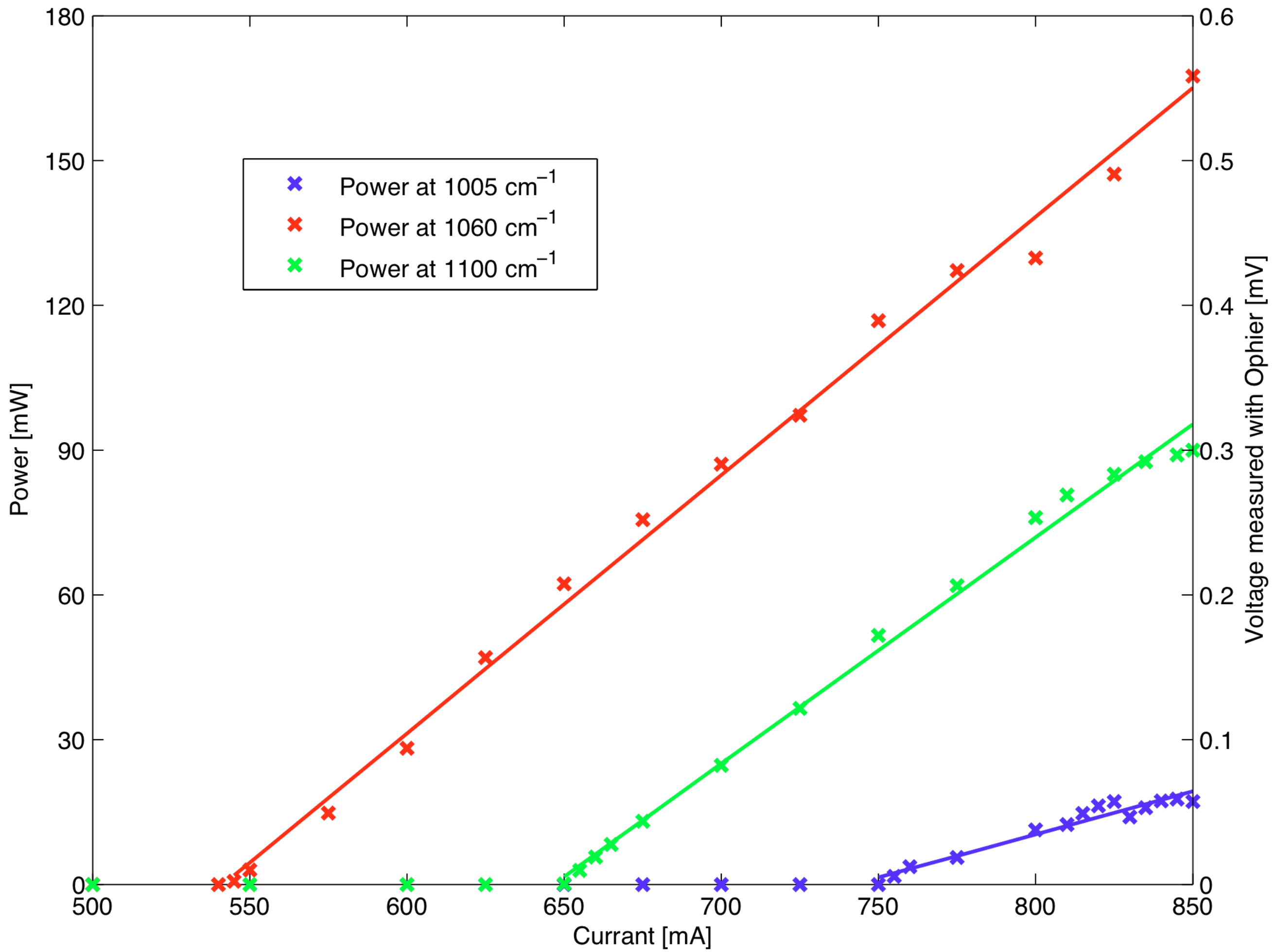
Power spectrum of the QCL at 800 mA



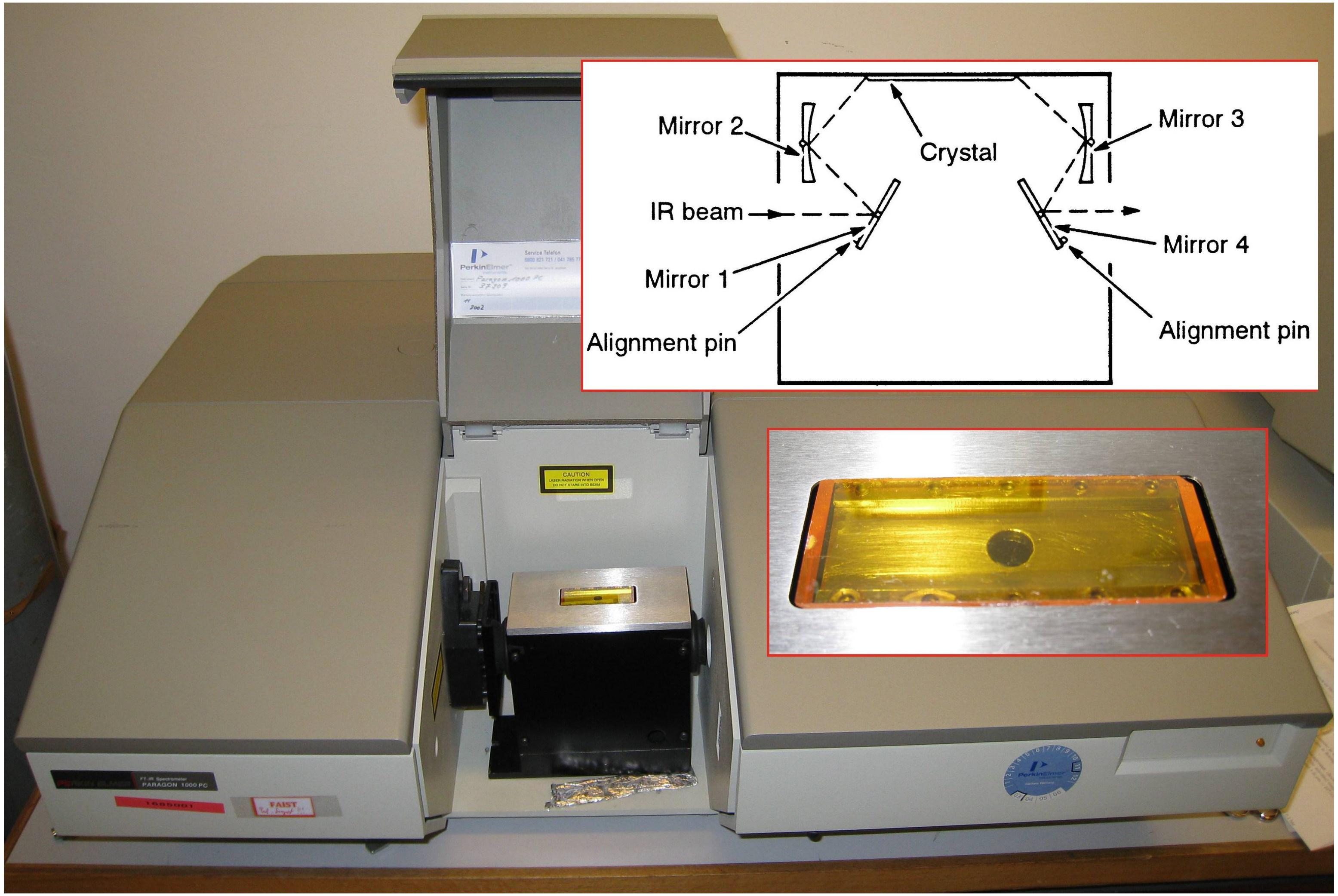
FWHM of the QCL beam versus distance from the Laser



Output power versus laser currant



FTIR spectrometer with ATR accessory



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