Infrared Laser Spectroscopy For Sensing Applications

Markus W. Sigrist

ETH Zürich, Switzerland

sigristm@phys.ethz.ch

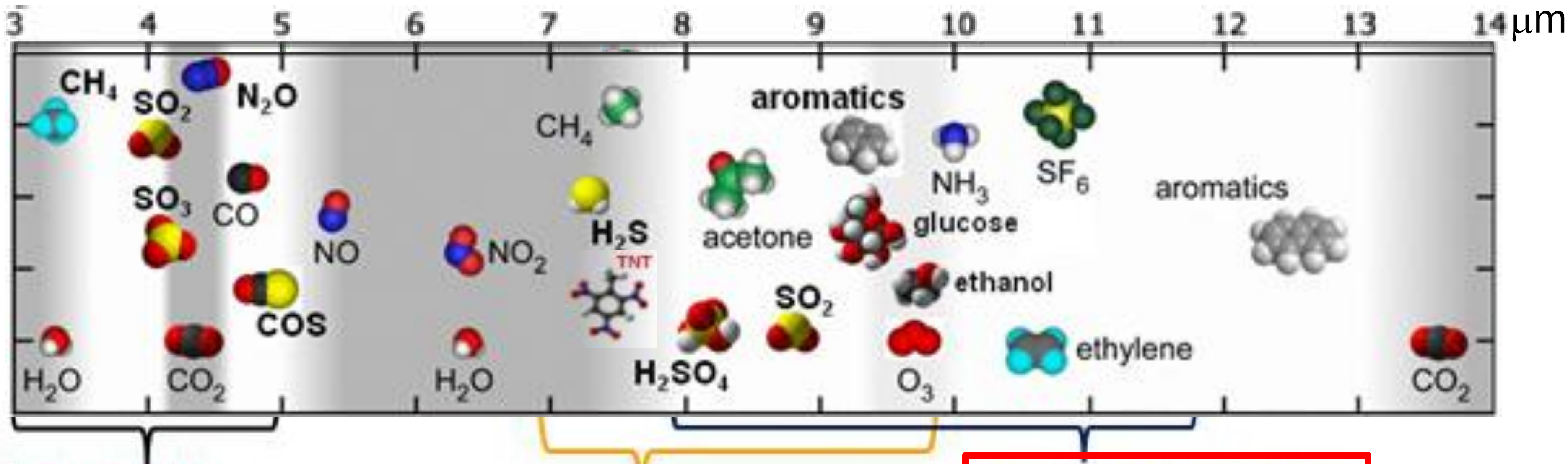
Outline

- Infrared laser spectroscopic sensing:
  Introduction, key issues, sources, detection schemes
- Mobile CO_2-laser PA system for urban pollution monitoring
- QCL-QEPAS detection of short-lived species (HONO)
- First lead salt VECSEL studies on C_1-C_4 alkanes
- DFG-system for analysis of surgical smoke
- QCL-PA system for non-invasive glucose monitoring
- Conclusions and outlook

Key issues in spectroscopic sensing

Requirements	Approach
High sensitivity	Strong fundamental absorption lines: mid-IR for low concentrations, near-IR for higher concentrations feasible, ev. Raman for homonuclear molecules and high concentrations Sensitive detection scheme
Multi – component and analytical capability	Broad, continuous tuning range
High selectivity / specificity	Narrow laser linewidth, if selectivity is not an issue broadband sources, e.g. LEDs
In – situ monitoring	Room temperature operation Compact, robust set – up Easy or no sample preparation

Molecular absorption in the mid-IR



Environmental Monitoring

- 3-5 µm
- Atmospheric monitoring and networks
- Ambient air quality
- Stack emissions

Defense and Security

- 7-10 µm
- Threat detection (chemical, explosive)

Industrial Process Monitoring

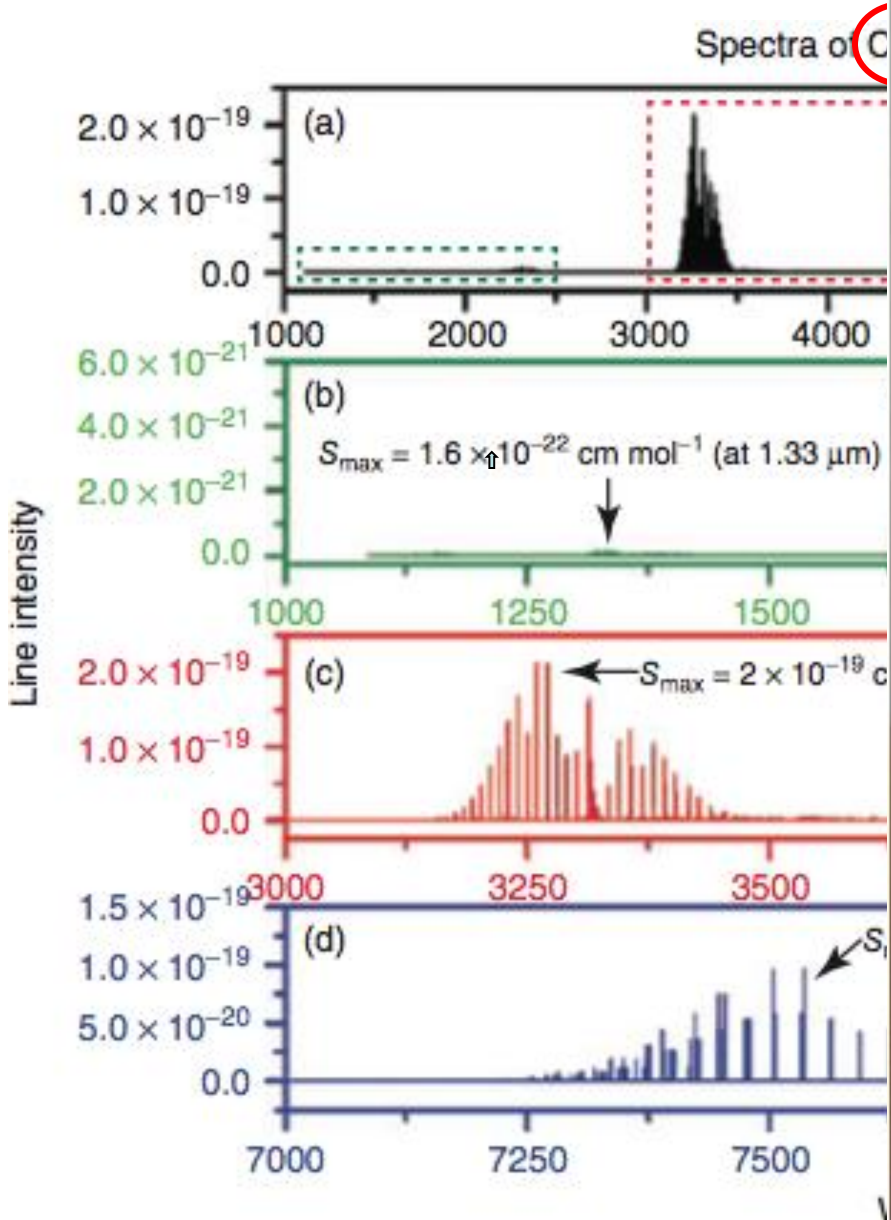
- 7-10 µm
- Leak detection

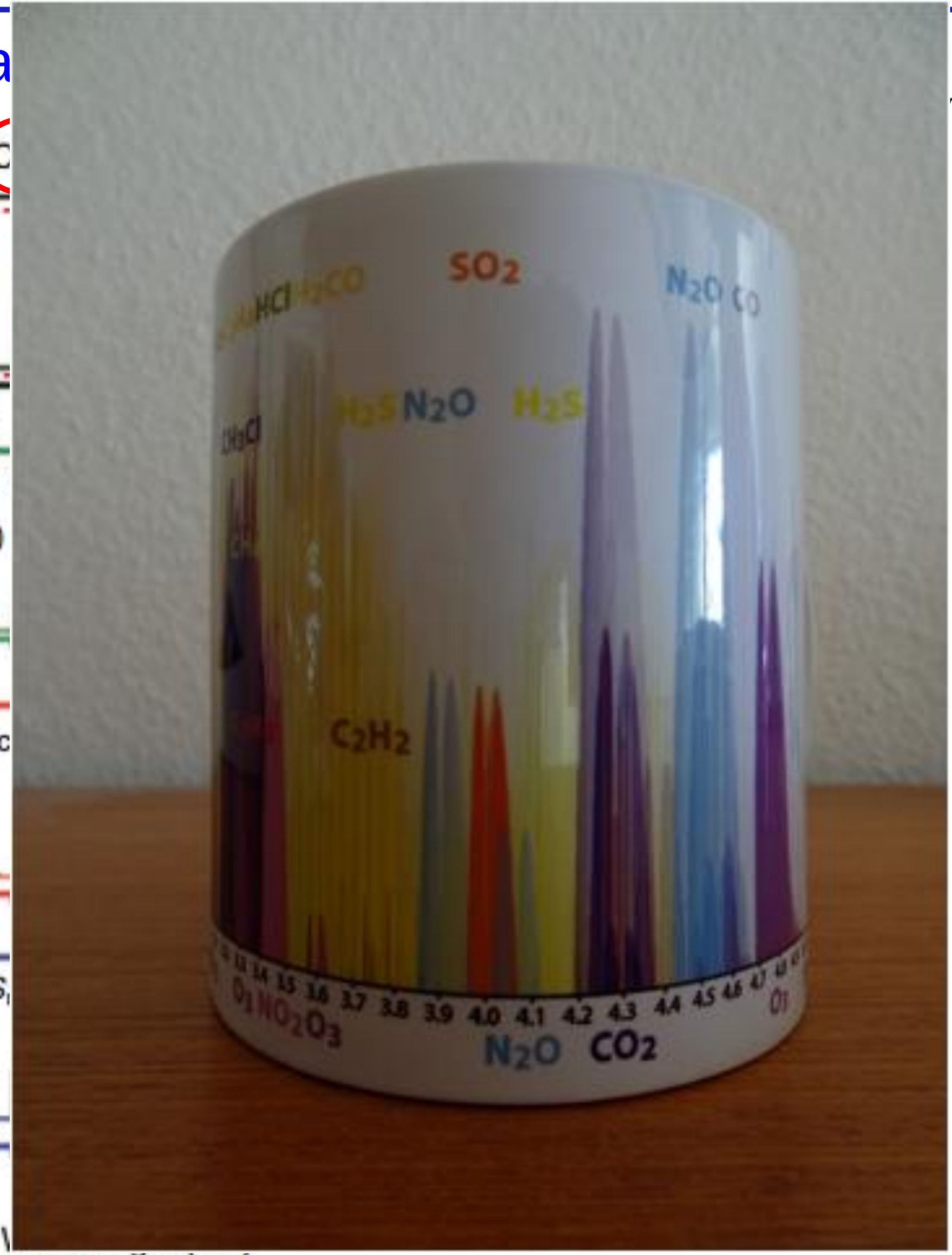
Medical Diagnostics

- 8-12 µm
- Med Imaging
  - Tissue Diagnostic
  - Cancer Screening
- Breath analysis
- Non-invasive glucose monitoring
- Cellular Diagnostics

IR-Spectroscopy: Nea

n.,





(Broadly) tunable narrow-band mid-IR lasers

Laser	Wavelength [μm]	Tuning Characteristics	Power	Operation
CO_2	9 – 11	Only line tunable	Watts	RT operation
Sb-based ICL	3 – 6	Typ. 10 nm	Few mW	RT operation
QCL	<4 – 12, THz	cm^{-1} to > 100 cm^{-1} per device	mW to W	LN_2/TE cooling, also RT
Lead-salt VECSEL	3 – 30	> 150 cm^{-1} (piezoel.)	< mW	Pulsed only TE cooling
DFG/OPO[a]	3 – 16	~ μm for specific setup (MHF)	μW to mW Watts	RT operation

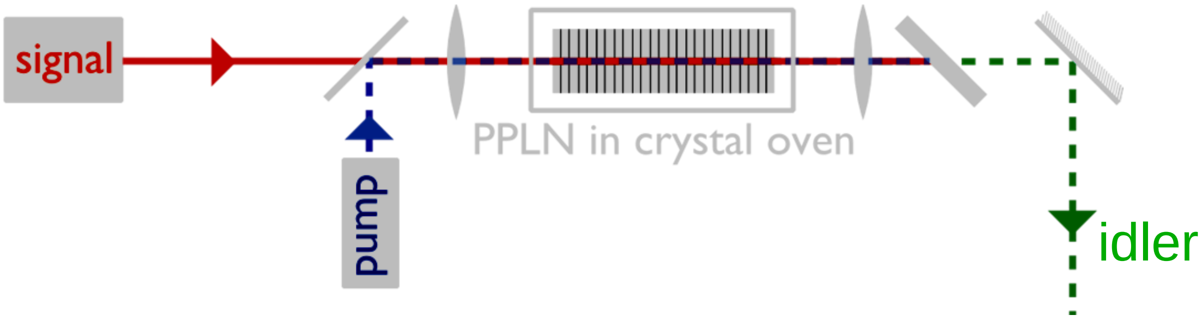
Semiconductor Lasers

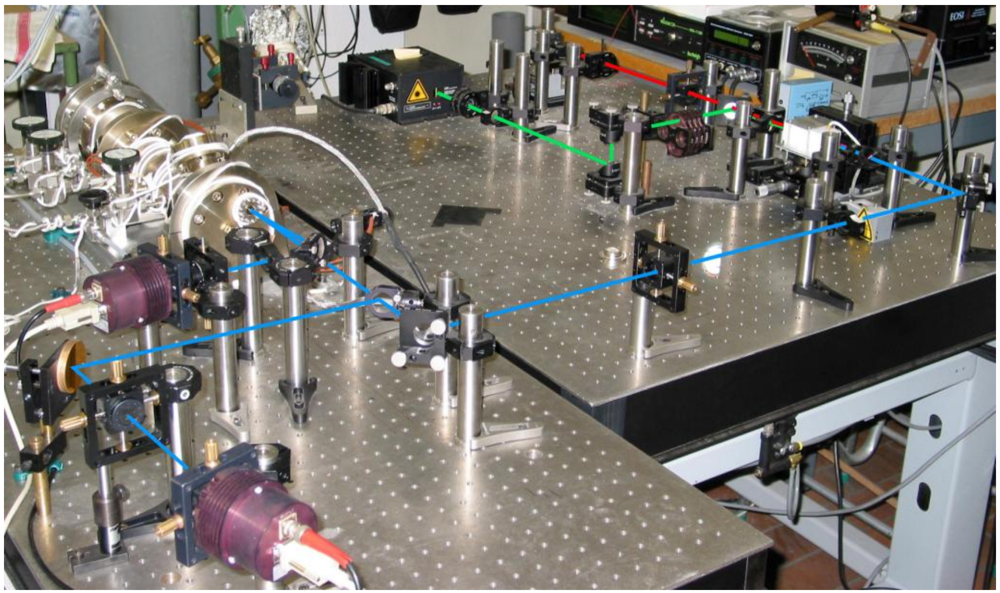
[a] DFG: difference frequency generation / OPO: optical parametric oscillator

Examples: PPLN (periodically poled lithium niobate, eventually with waveguide), OP-GaAs, $AgGaSe_2$, $LiInS_2$, $LiInSe_2$, etc.

Tunable narrowband mid-infrared lasers

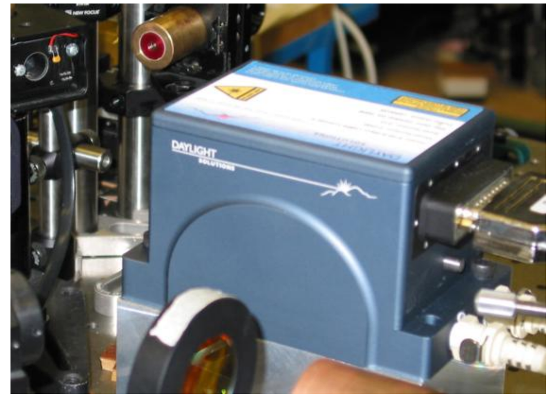
Difference frequency generation





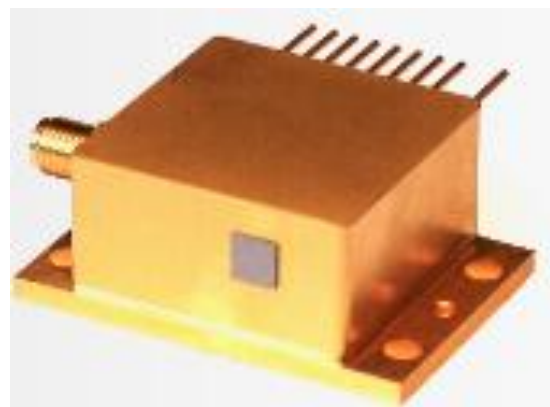
RT, 3-17 μm, broad tuning

Quantum cascade laser



TE, 4-12 μm, “broad” tuning, compact

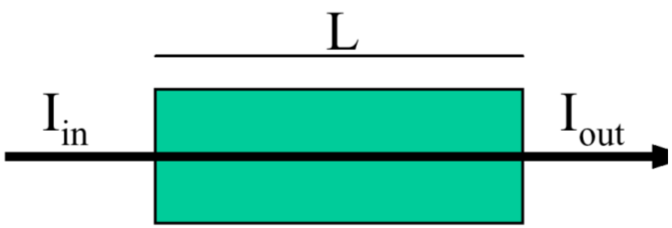
Diode-pumped VECSEL



TE, ≈ 3.4 μm, >150 cm^{-1} tuning, compact

Absorption measurement: Detection schemes

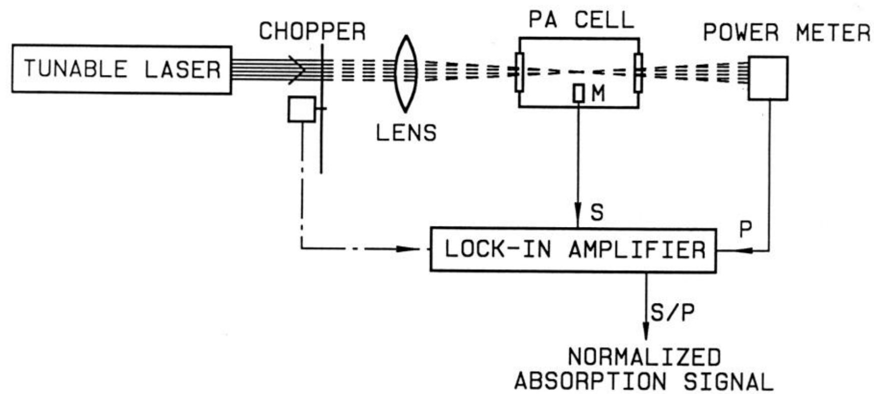
Transmission



$$I_{out} = I_{in} \cdot \exp\{-\overbrace{N\,\sigma(\lambda)}^{\alpha(\lambda)} L\}$$

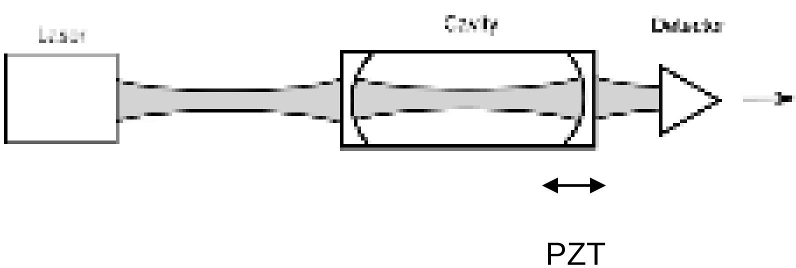
Beer-Lambert absorption law

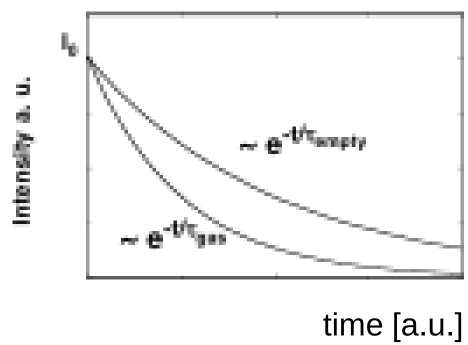
Photoacoustic



$$S(\lambda) = C\,P(\lambda)\,N_{tot}\,c_{gas}$$

Cavity Ring-down

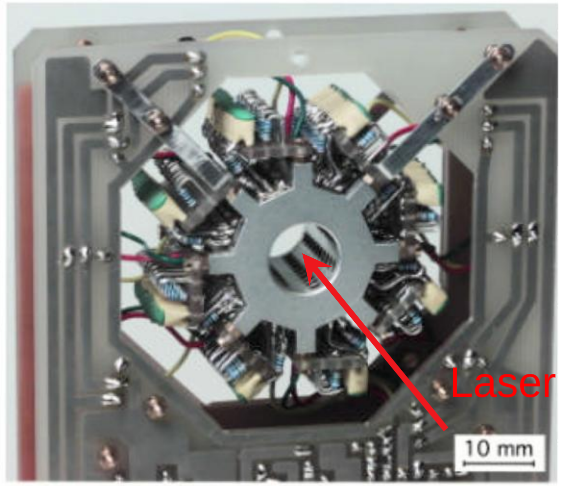




$$\alpha_{gas} = \frac{1}{c}\left(\frac{1}{\tau_{gas}} - \frac{1}{\tau_{empty}}\right)$$

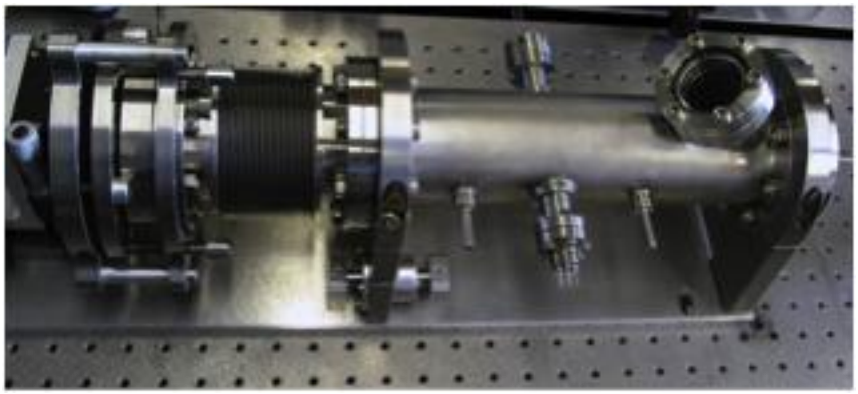
Various cell designs

V=38 ml (3.5 m pathlength cell,
EMPA / IRsweep, Switzerland)

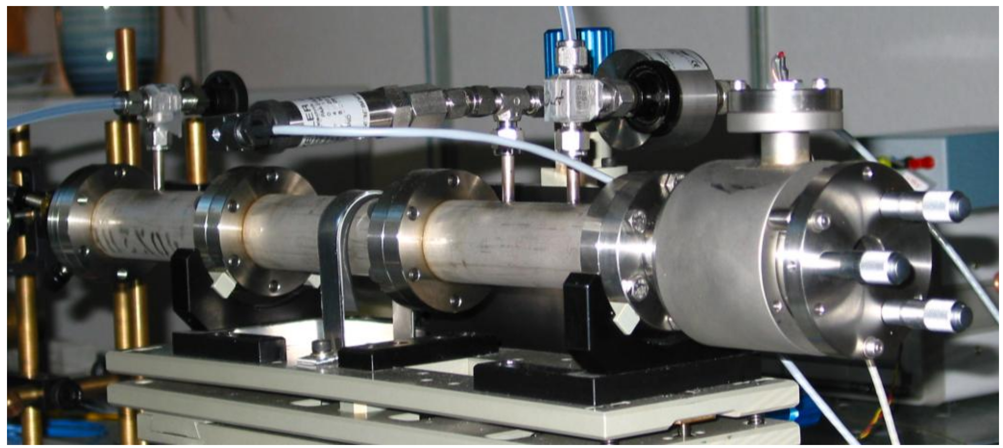


80-microphone photo-acoustic cell (A. Bohren)

QEPAS
Lei Dong et al.
Shanxi U., China



High-temperature multi-pass cell
pathlength: 9 - 35 m (R. Bartlome)

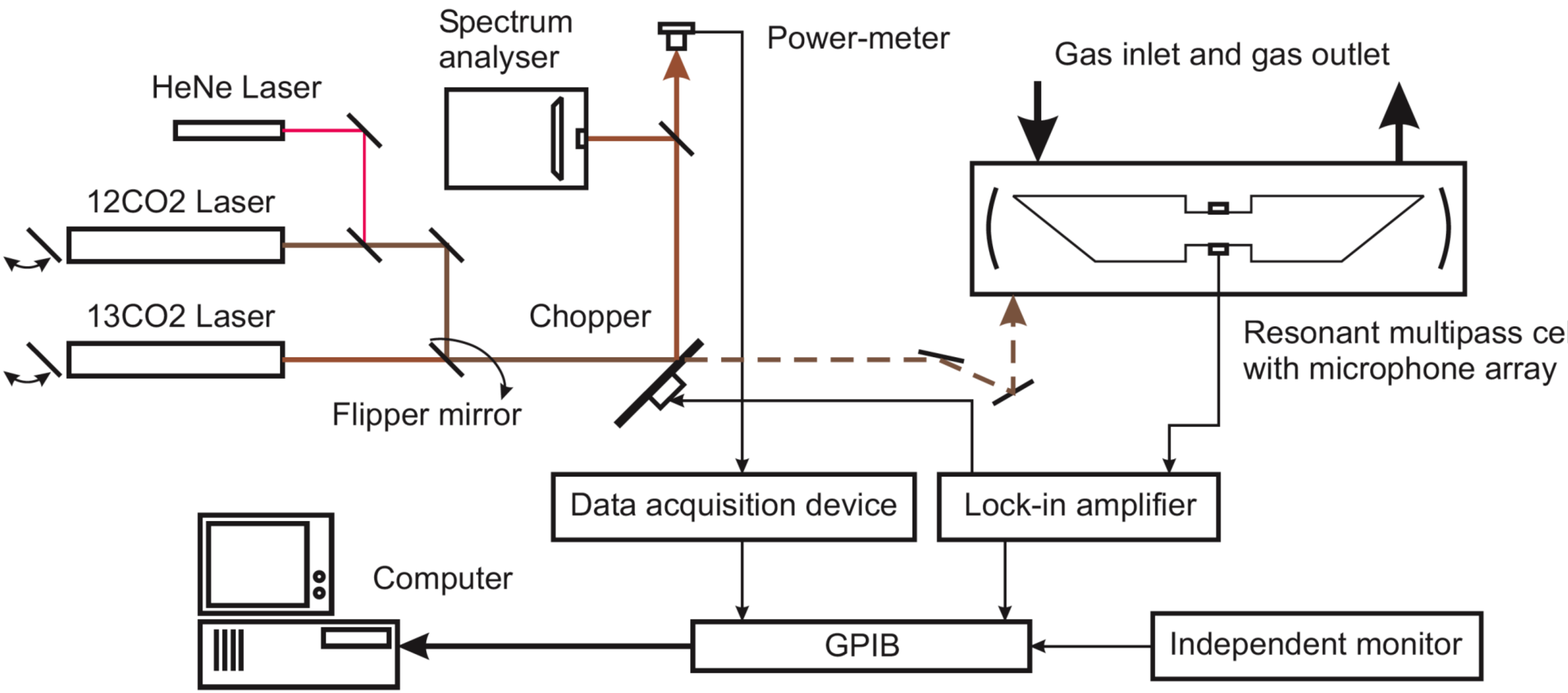


Cavity-ringdown cell für NIR (D.Vogler)

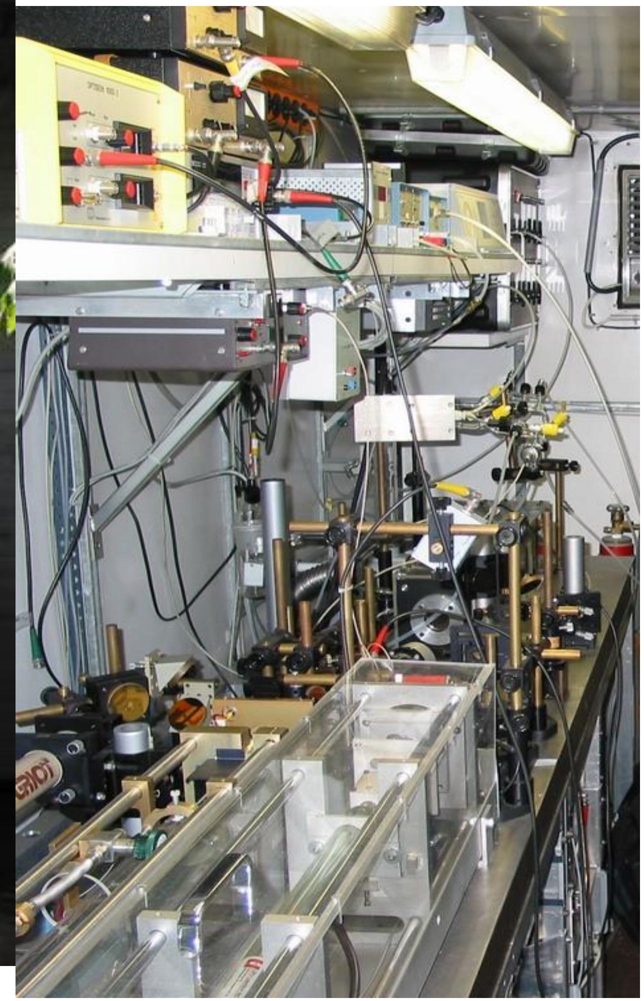
Outline

- Infrared laser spectroscopic sensing:
  Introduction, key issues, sources, detection schemes
- Mobile CO_2-laser PA system for urban pollution monitoring
- QCL-QEPAS detection of short-lived species (HONO)
- First lead salt VECSEL studies on C_1-C_4 alkanes
- DFG-system for analysis of surgical smoke
- QCL-PA system for non-invasive glucose monitoring
- Conclusions and outlook

Mobile CO_2-laser PA setup



Mobile Laser-PA system at exit of freeway tunnel



A. Thöny, M. Nägele, D. Marinov

Gas concentrations at tunnel during one week

Detection limits
Ammonia and ethene: sub-ppb
CO_2: ppm

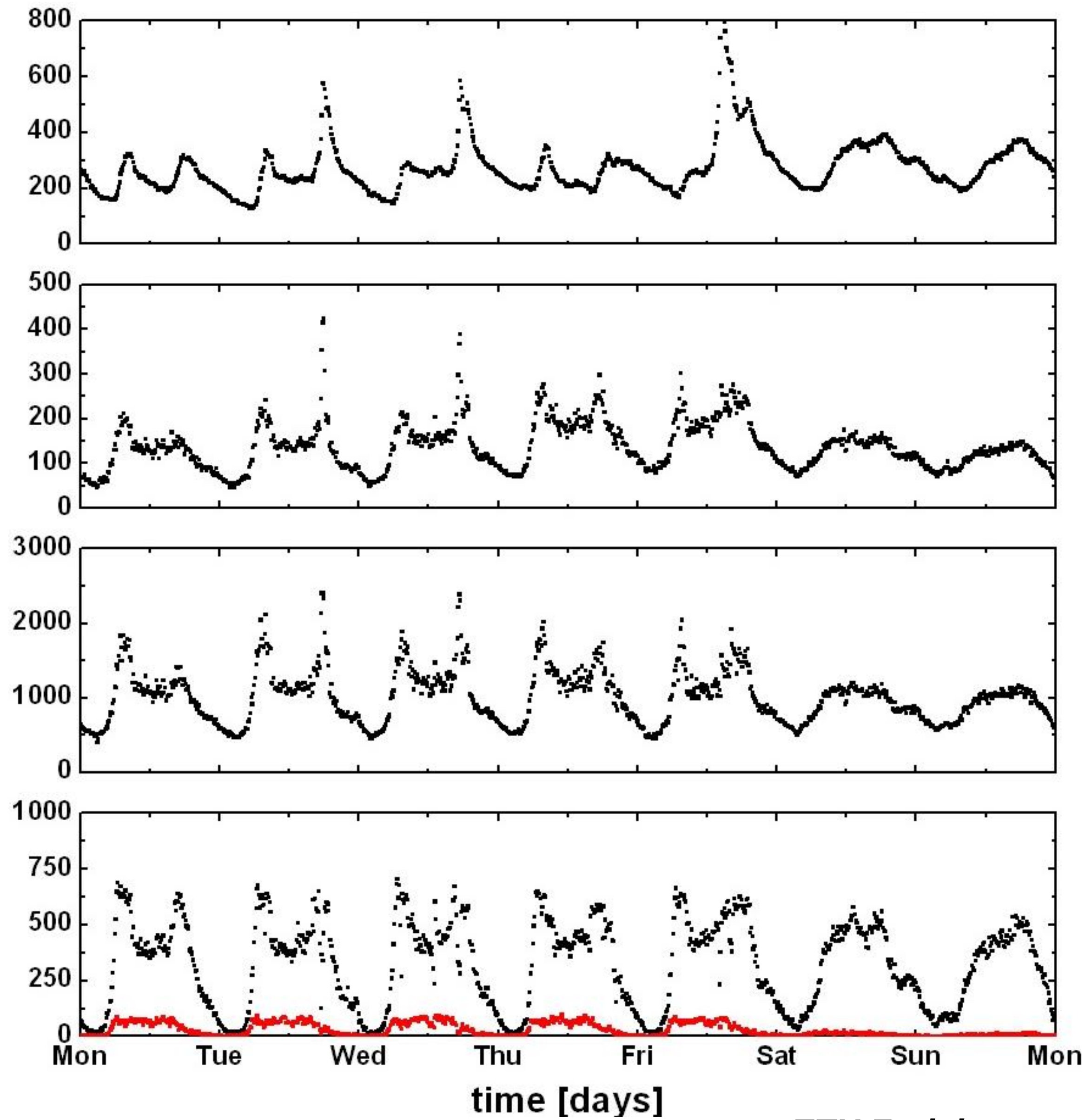
D. Marinov, M. Sigrist
Photochem. & Photobiol.
Sciences **2**, 774 (2003)

ammonia [ppb]

ethene [ppb]

CO_2 [ppm]

traffic density
and heavy trucks
[per 10 min]



Outline

- Infrared laser spectroscopic sensing:
  Introduction, key issues, sources, detection schemes
- Mobile CO_2-laser PA system for urban pollution monitoring
- QCL-QEPAS detection of short-lived species (HONO)
- First lead salt VECSEL studies on C_1-C_4 alkanes
- DFG-system for analysis of surgical smoke
- QCL-PA system for non-invasive glucose monitoring
- Conclusions and outlook

Nitrous acid (HONO)

- Important source of OH radicals in earth atmosphere

→ Key role in atmospheric oxidation capacity which affects regional air quality and global climate change

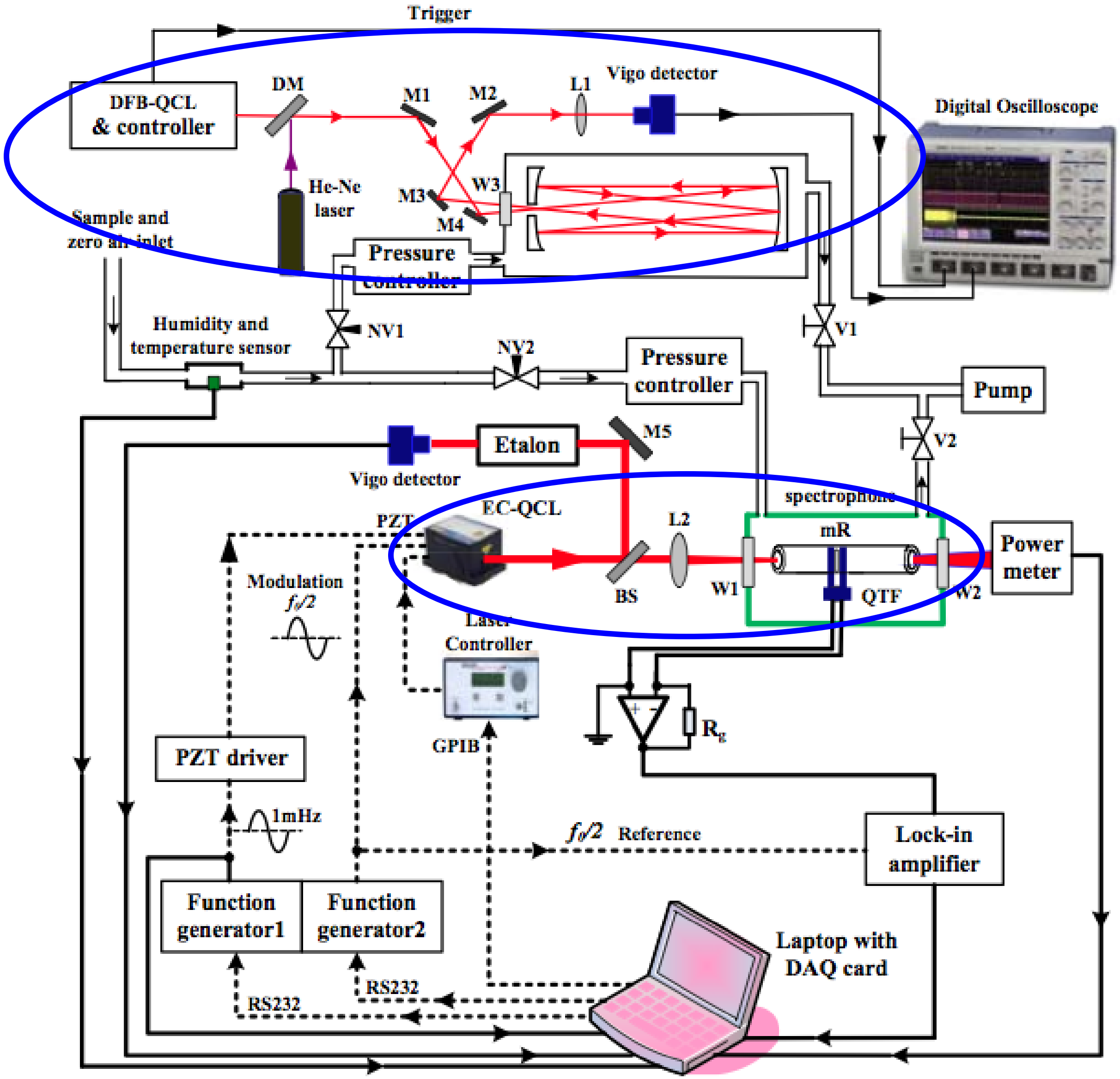
- HONO sources and sinks not well understood due to challenging measurement:

  - Atmospheric concentration only few ppb, >10 ppb indoor

  - Atmospheric lifetime: 10 - 20 minutes

→ Sensitive and fast measurement technique is essential

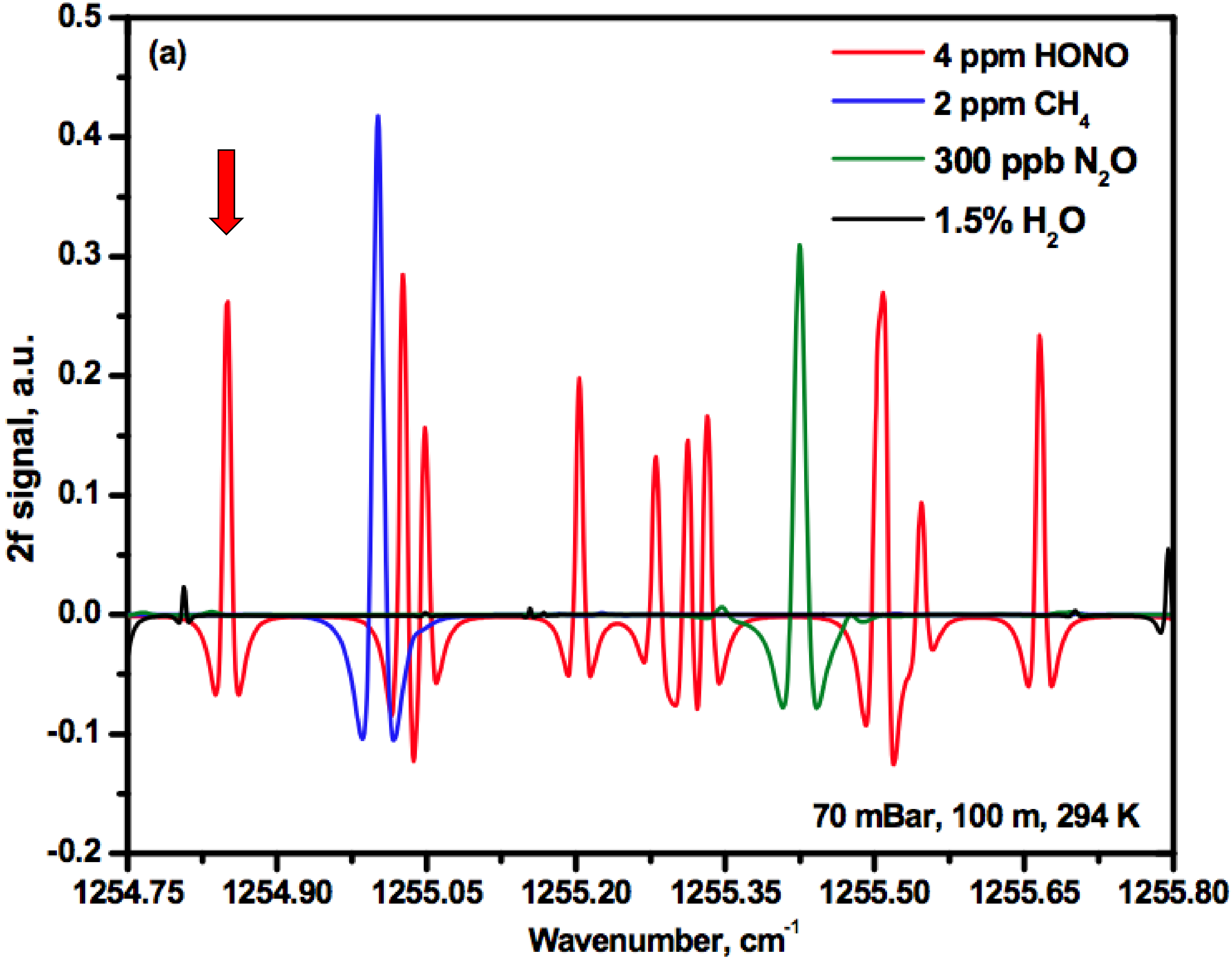
Short-lived species detection (HONO) with EC-QCL-QEPAS



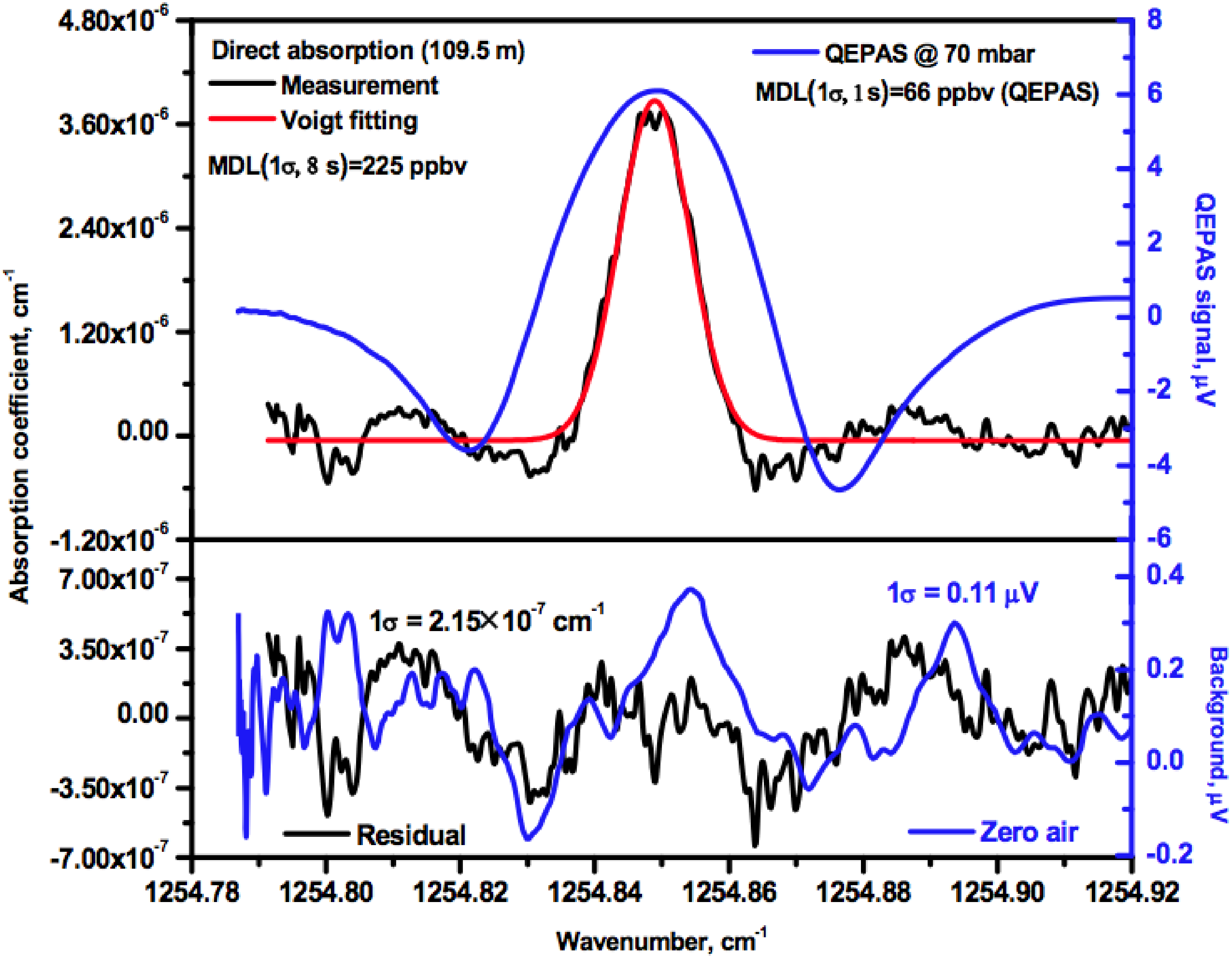
EC-QCL (ca.1255 cm^{-1})
50 mW
QEPAS with mR
compact 40 mm^3 cell

Calibration with 110 m cell and DFB QCL
Air sampling resid. time:
10 ms vs 7 min.

H. Yi, W. Chen et al.:
Appl. Phys. Lett. **106**, 101109 (2015)



Simulation of *2f* signals of HONO, CH_4 and N_2O spectra



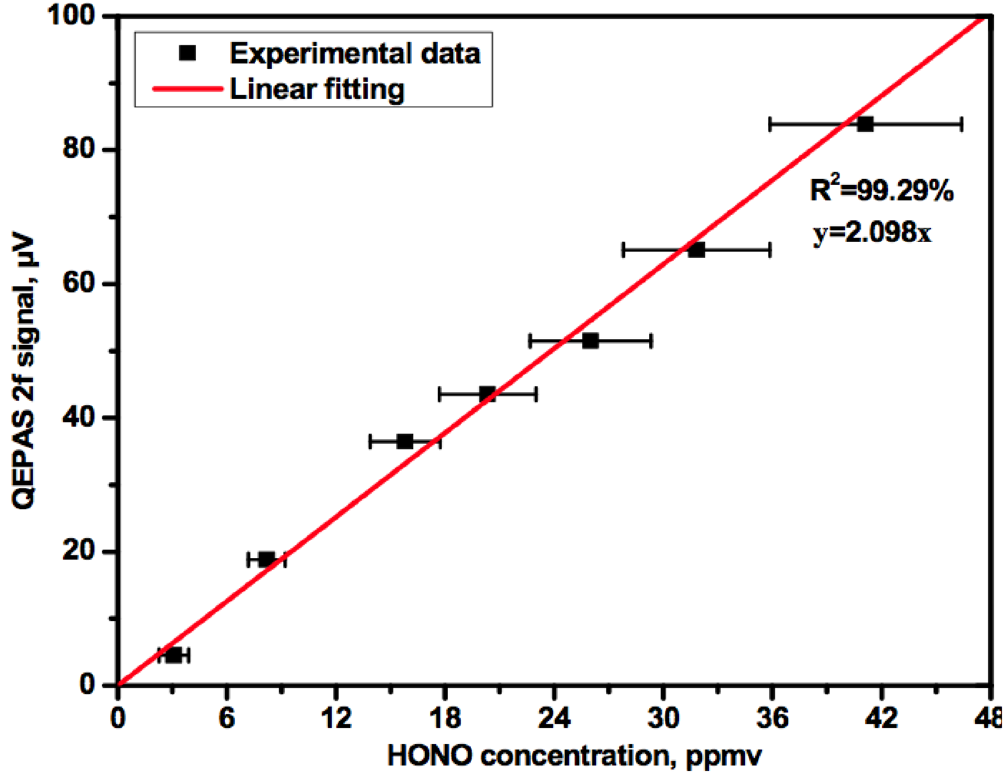
3.21 ppm HONO Direct Absorption

Voigt fit

QCL-QEPAS

Fit-Residual

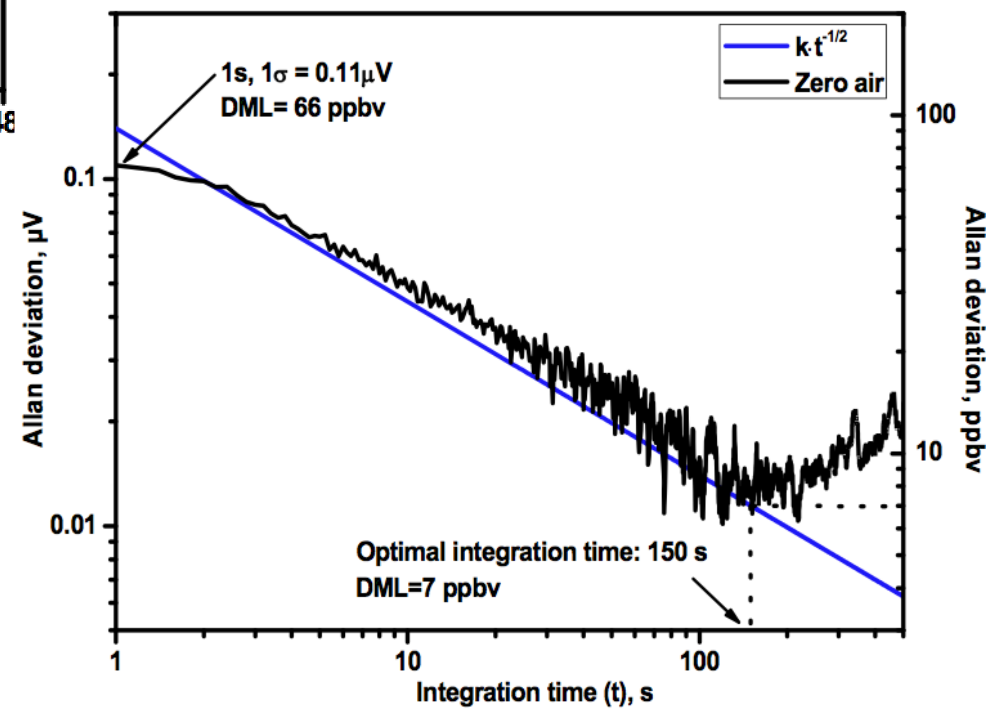
QEPAS Backgr. (zero air)



Good linearity of *2f* QEPAS signals with titrated HONO concentrations

Allan variance plot

Detection Limit 66 ppb (1 sec) , 7 ppb (150 sec)



With **1W QCL**: Extrapol.det. limit 3.3 ppb (1s), 330 ppt (150 s)

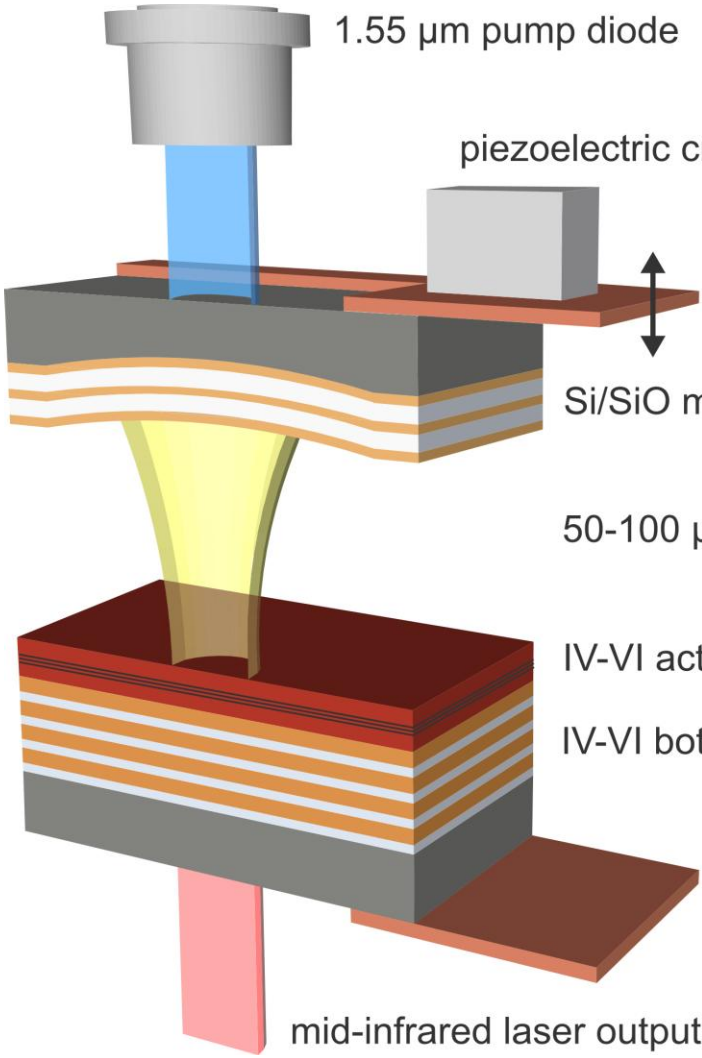
Outline

- Infrared laser spectroscopic sensing:
  Introduction, key issues, sources, detection schemes
- Mobile CO_2-laser PA system for urban pollution monitoring
- QCL-QEPAS detection of short-lived species (HONO)
- First lead salt VECSEL studies on C_1-C_4 alkanes
- DFG-system for analysis of surgical smoke
- QCL-PA system for non-invasive glucose monitoring
- Conclusions and outlook

Sensing of alkanes (methane, ethane, propane, butane)

- Natural gas / biogas composition analysis
- Energy content measurement
- Fuel blending and control
- Optimization of power generation
  (fuel cells, gas turbines)
- Monitoring of hydrocarbon leaks
  at pipelines and refineries

Diode-pumped lead salt VECSELs
(**V**ertical **E**xtended **C**avity **S**urface **E**mitting **L**asers)



$\lambda \approx 3.4\ \mu m$

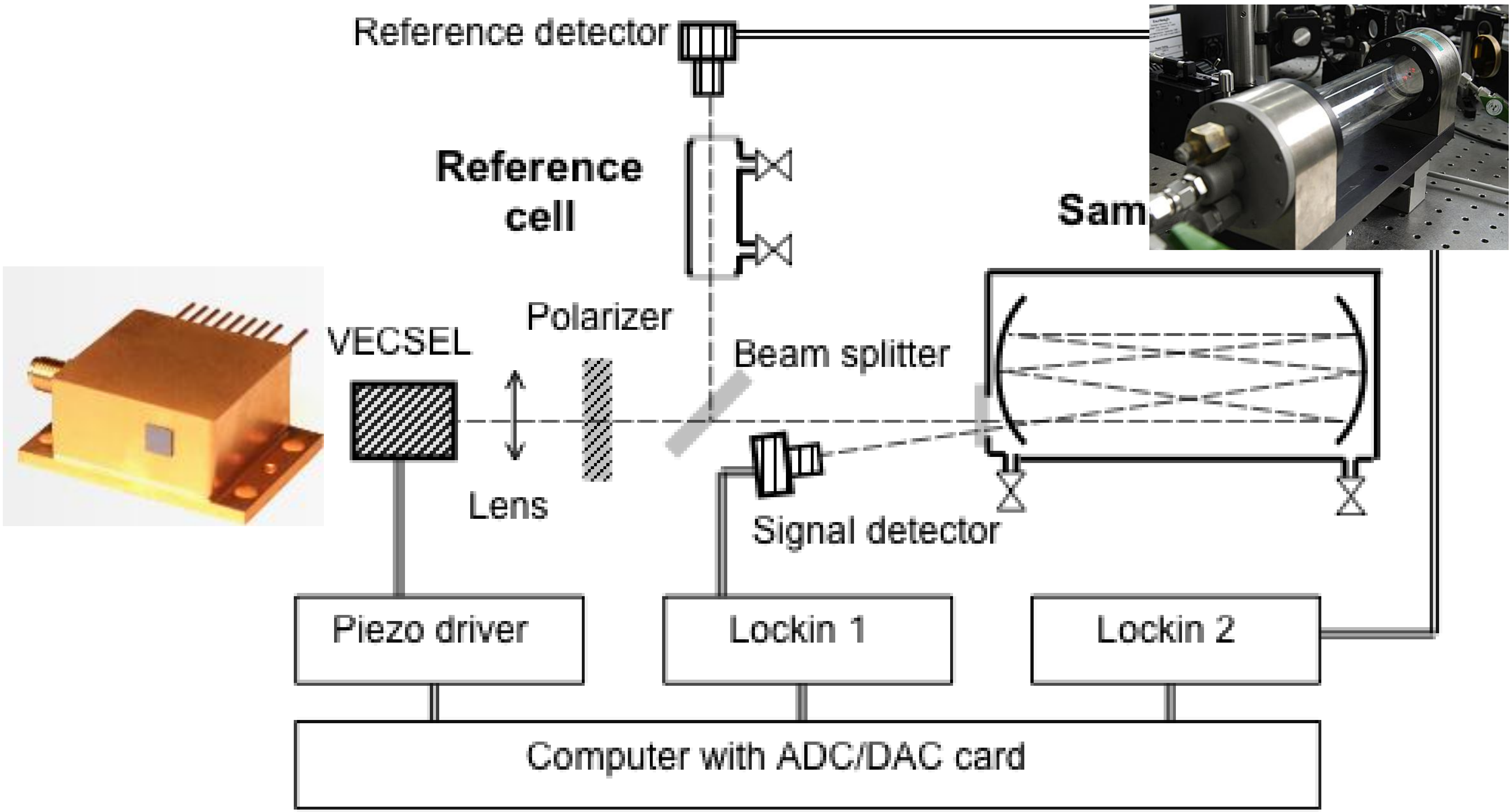
Tuning range: > 150 cm^{-1}

Pulse power: 10 mW_p

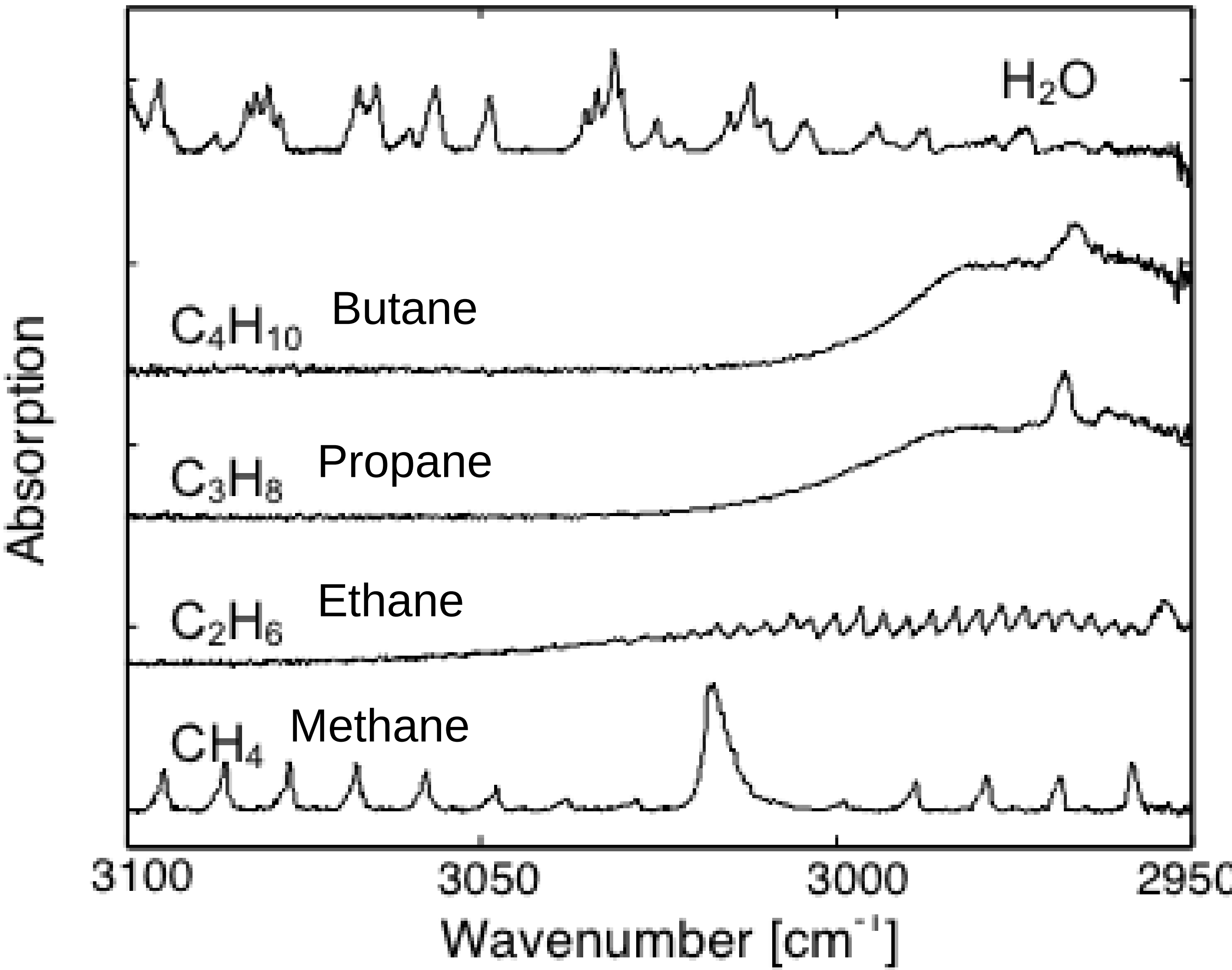
Duty cycle: 0.5%

CAMLIN TECHNOLOGIES

Experimental setup with VECSEL, sample and reference cell



Measured reference spectra of C_1 – C_4 alkanes



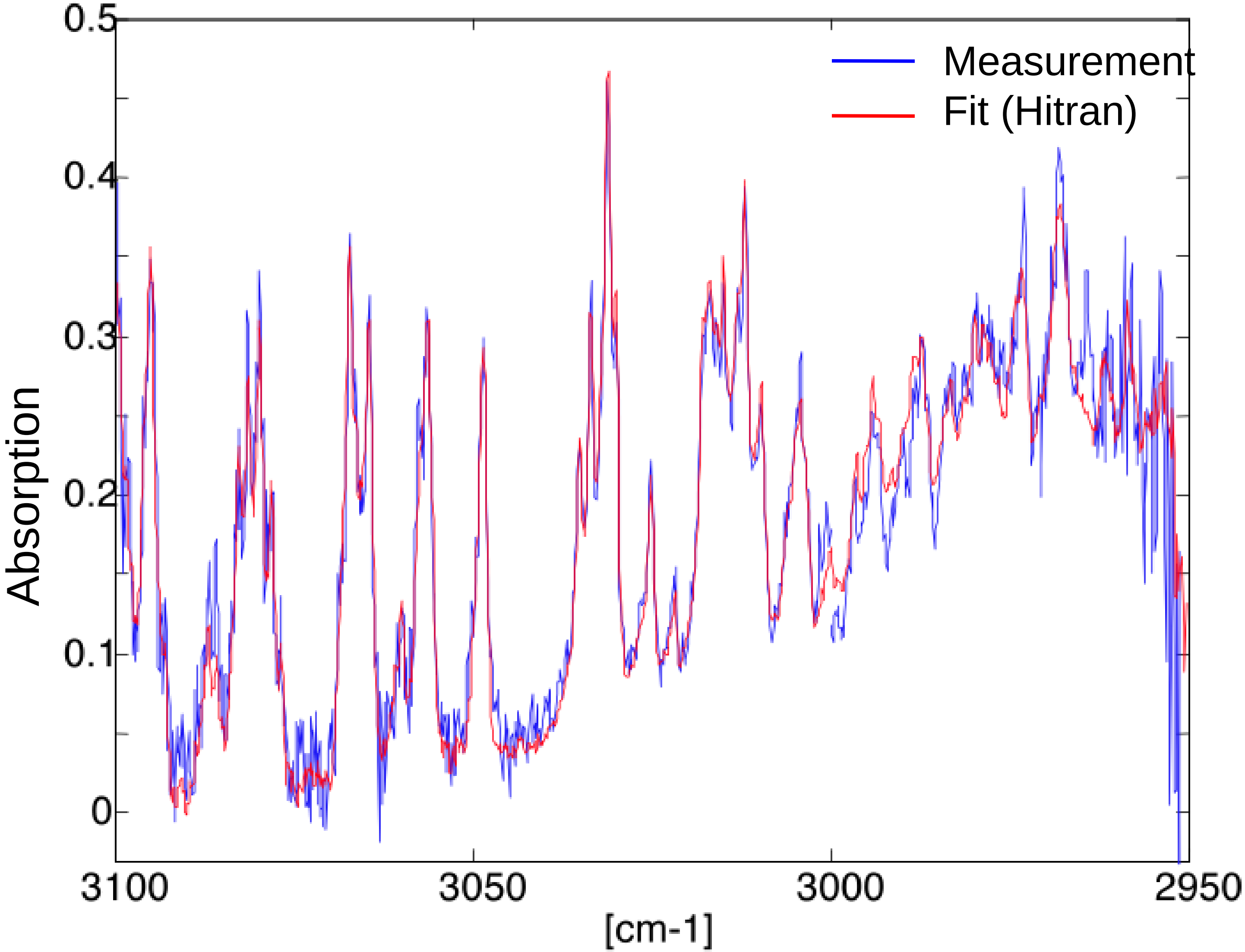
Individual gases buffered in N_2 at atm. pressure

averaged over 100 scans

Total acquisition Time: 200 s

Tuning by PZT voltage

Spectrum of mixture of C_1-C_3 alkanes and H_2O vapor



23 ppm methane
24 ppm ethane
20 ppm propane
1.7 %vv H_2O vapor
Buffer gas: N_2
atm. pressure

Measurement time
10 x 2 sec

Detection limit:
0.6 ppm

J. Rey et al.: *Appl. Phys. B* **117**, 935-030 (2014)

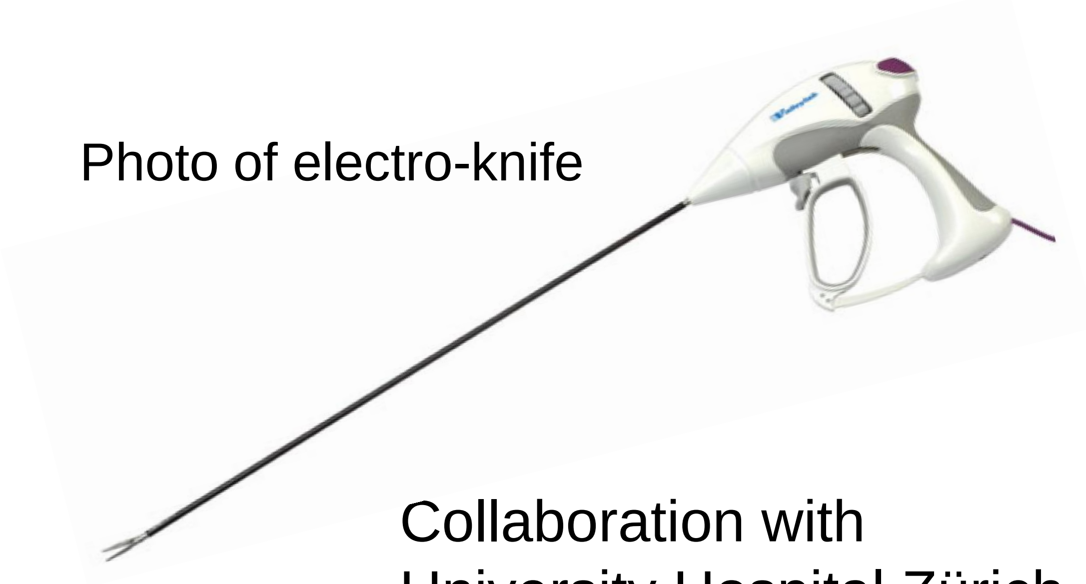
Outline

- Infrared laser spectroscopic sensing:
  Introduction, key issues, sources, detection schemes
- Mobile CO_2-laser PA system for urban pollution monitoring
- QCL-QEPAS detection of short-lived species (HONO)
- First lead salt VECSEL studies on C_1-C_4 alkanes
- DFG-system for analysis of surgical smoke
- QCL-PA system for non-invasive glucose monitoring
- Conclusions and outlook

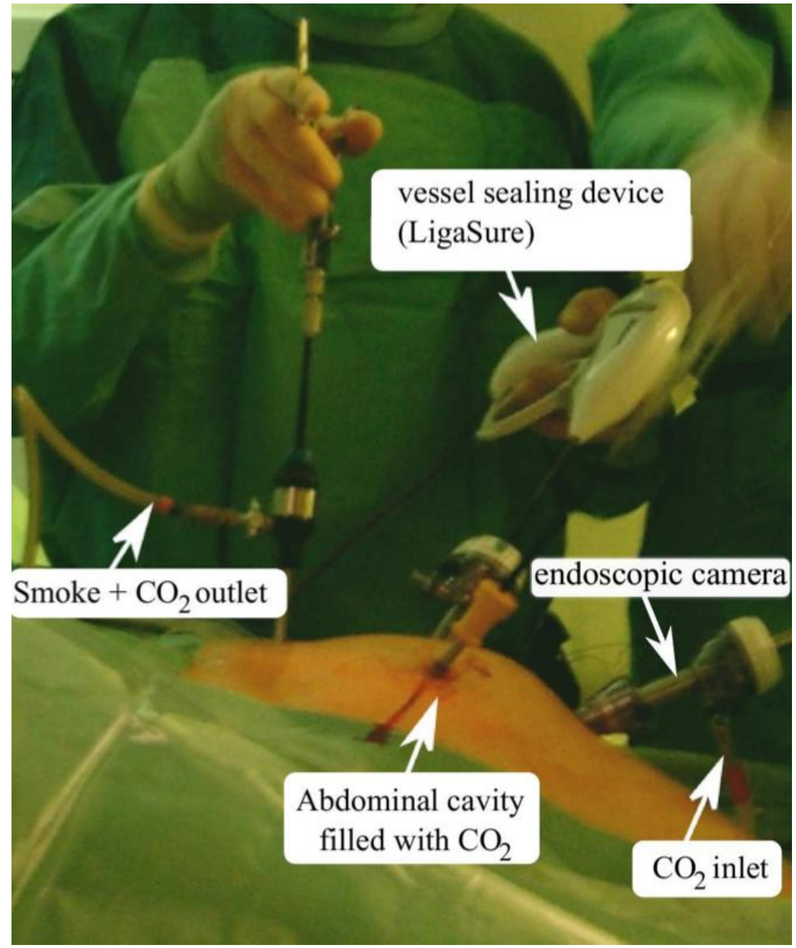
Surgical smoke: *in vivo* studies

Smoke produced during minimal-invasive surgery with electro-knives or lasers. Smoke samples are taken at the hospital, collected in Tedlar bags, followed by laser and FTIR spectroscopic analysis in our lab

Photo of electro-knife

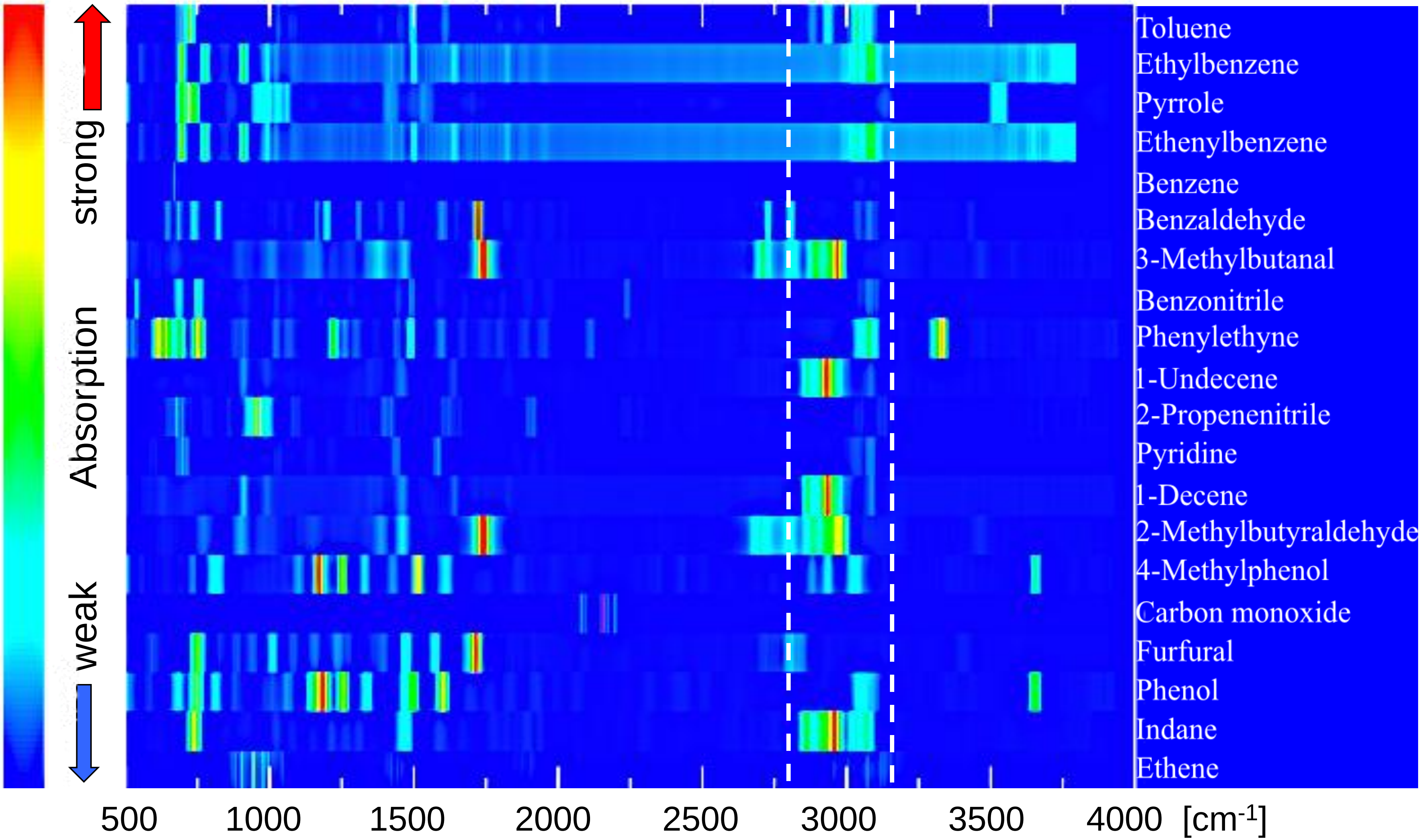


Collaboration with
University Hospital Zürich
(Dr. Dieter Hahnloser)



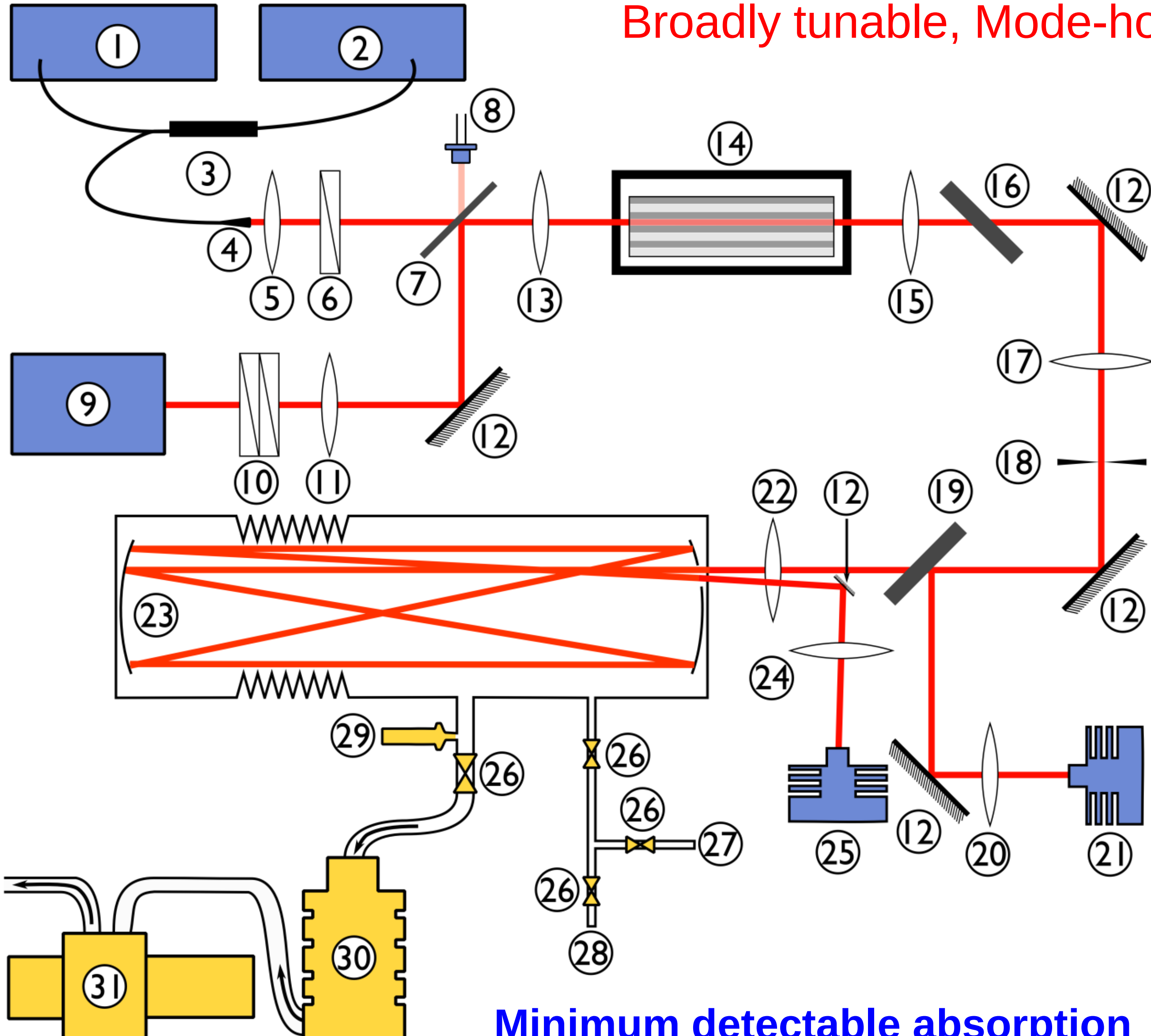
M. Gianella et al.: *Appl Phys. B* **109**, 485 (2012)
M. Gianella et al.: *Innov. Surgery* (20 June 2013)

Absorption ranges of species found in surgical smoke



DFG spectrometer

Broadly tunable, Mode-hop free, Room temperature



1 ECDL, 1520-1600nm
5 mW CW

2 Wavemeter for ECDL

9 Nd:YAG, 1064.5 nm,
5 kHz, 6 ns, 300 mW av

14 PPLN, 5 cm, 8 periods

23 Heatable multipass cell
up to 35 m

21/25 Detectors (VIGO)

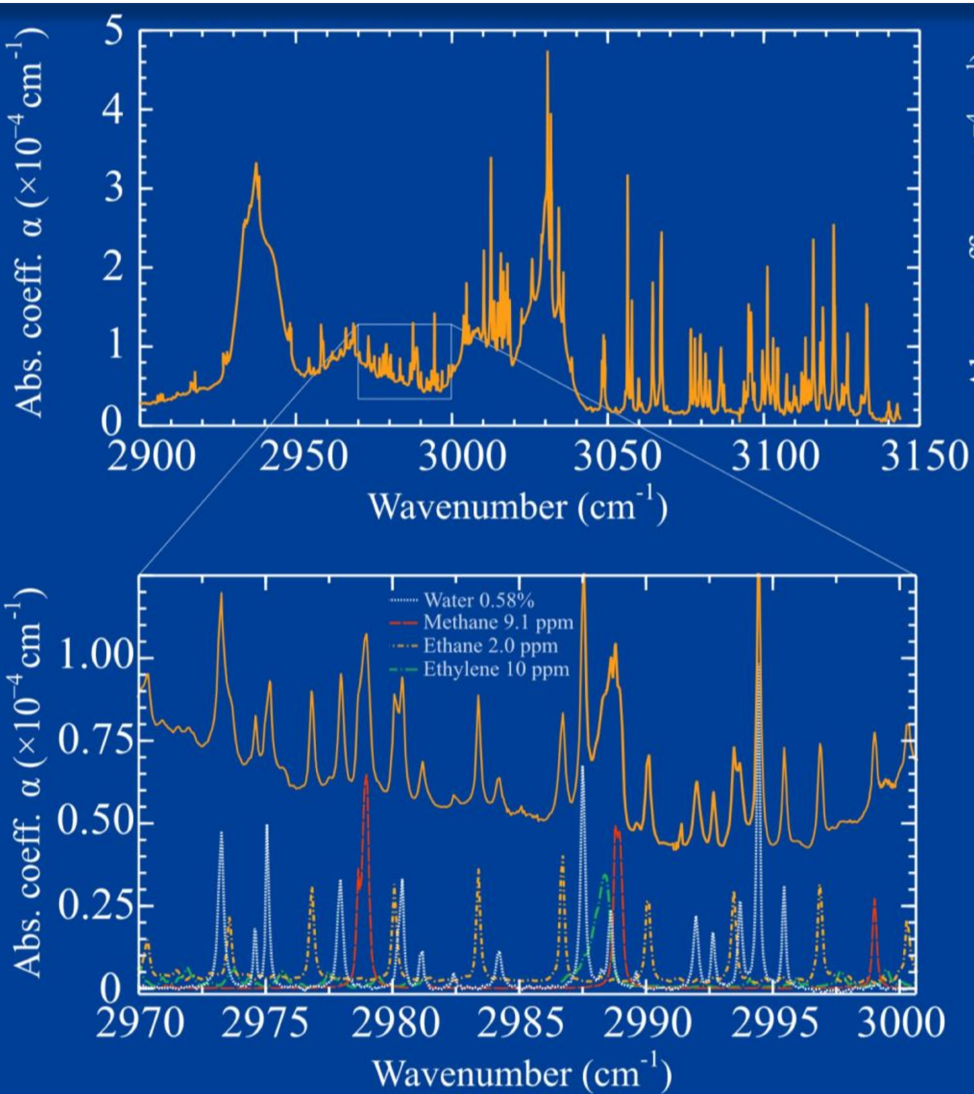
Idler: 150 μW av.
2817 - 2920 cm^{-1} (29.5 μm)
2900 - 3144 cm^{-1} (29.9 μm)
Step size 0.002 cm^{-1}

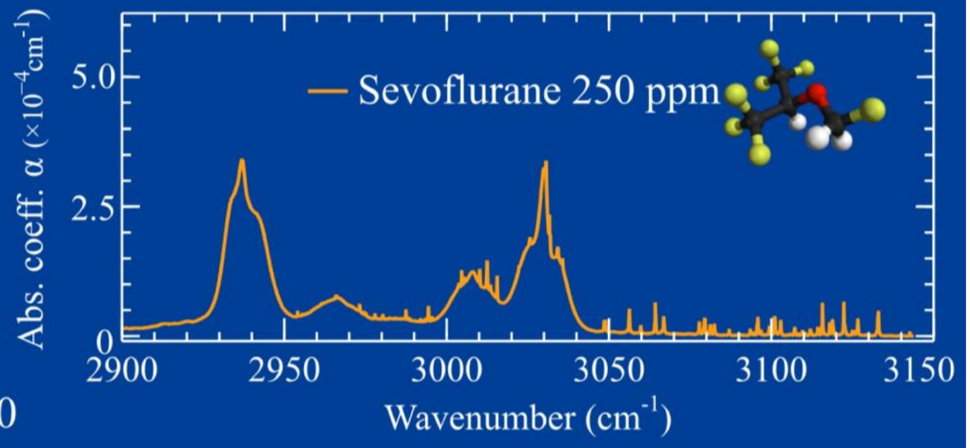
Minimum detectable absorption coefficient: 5×10^{-7} cm^{-1} $Hz^{-1/2}$

(few ppm for many compounds of interest)

Spectral analysis of surgical smoke

M. Gianella et al.: Appl. Spectr. **63**, 338-343 (2009)





Substance	Conc.	REL*
Methane	< 0.1 – 34 ppm	10000 ppm
Ethane	< 0.1 – 2.0 ppm	10000 ppm
Ethylene	< 5 – 10 ppm	10000 ppm
Water	0.27 – 1.1%	—
Sevoflurane	**< 20 – 450 ppm**	**2 ppm**

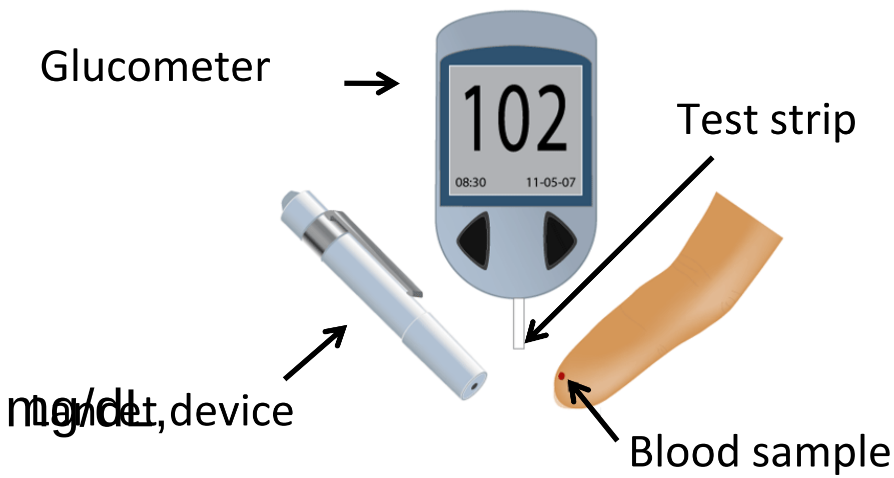
* Recommended exposure limits

Outline

- Infrared laser spectroscopic sensing:
  Introduction, key issues, sources, detection schemes
- Mobile CO_2-laser PA system for urban pollution monitoring
- QCL-QEPAS detection of short-lived species (HONO)
- First lead salt VECSEL studies on C_1-C_4 alkanes
- DFG-system for analysis of surgical smoke
- QCL-PA system for non-invasive glucose monitoring
- Conclusions and outlook

Diabetes as a human metabolic disease

- Patients need to measure the blood sugar level several times a day
- Glucose level of a healthy human: 65 - 120 mg/dl (3.6 - 6.7 mmol/L)
- Common blood sugar measurements are invasive



DIN EN ISO 15197 standard for blood glucose measurement devices: 95 % of all measurements must fall within ± 15 mg/dL for glucose concentrations < 75 mg/dL, within ± 20 % for glucose concentrations > 75 mg/dL

- **Goal**: Development of a ***non-invasive*** glucose sensor based on mid-IR laser, photoacoustic detection and glucose monitoring in interstitial fluid through skin

Interstitial fluid glucose sensing

MIR light: Strong glucose absorption, less interference than in NIR

=> Optical penetration < 100 µm

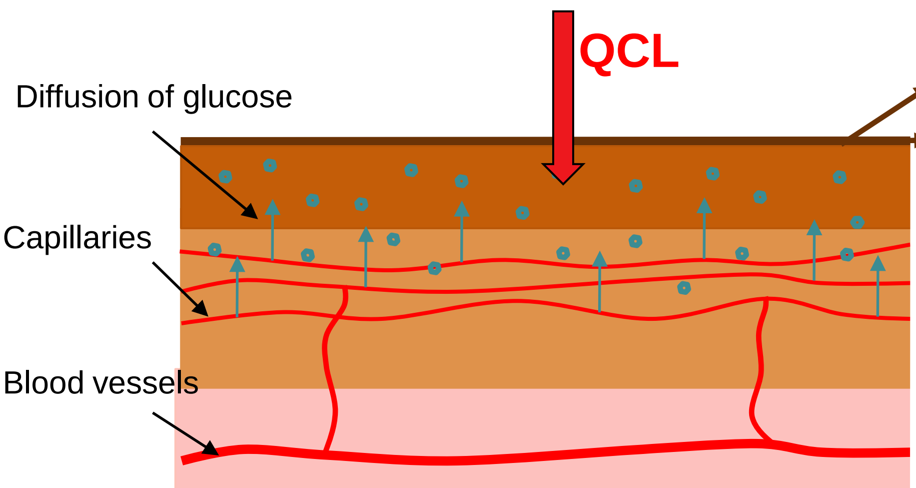
=> blood vessels are not reached

Epidermis: **=>** Glucose diffusion into epidermal interstitial fluid

=> Correlation with blood glucose

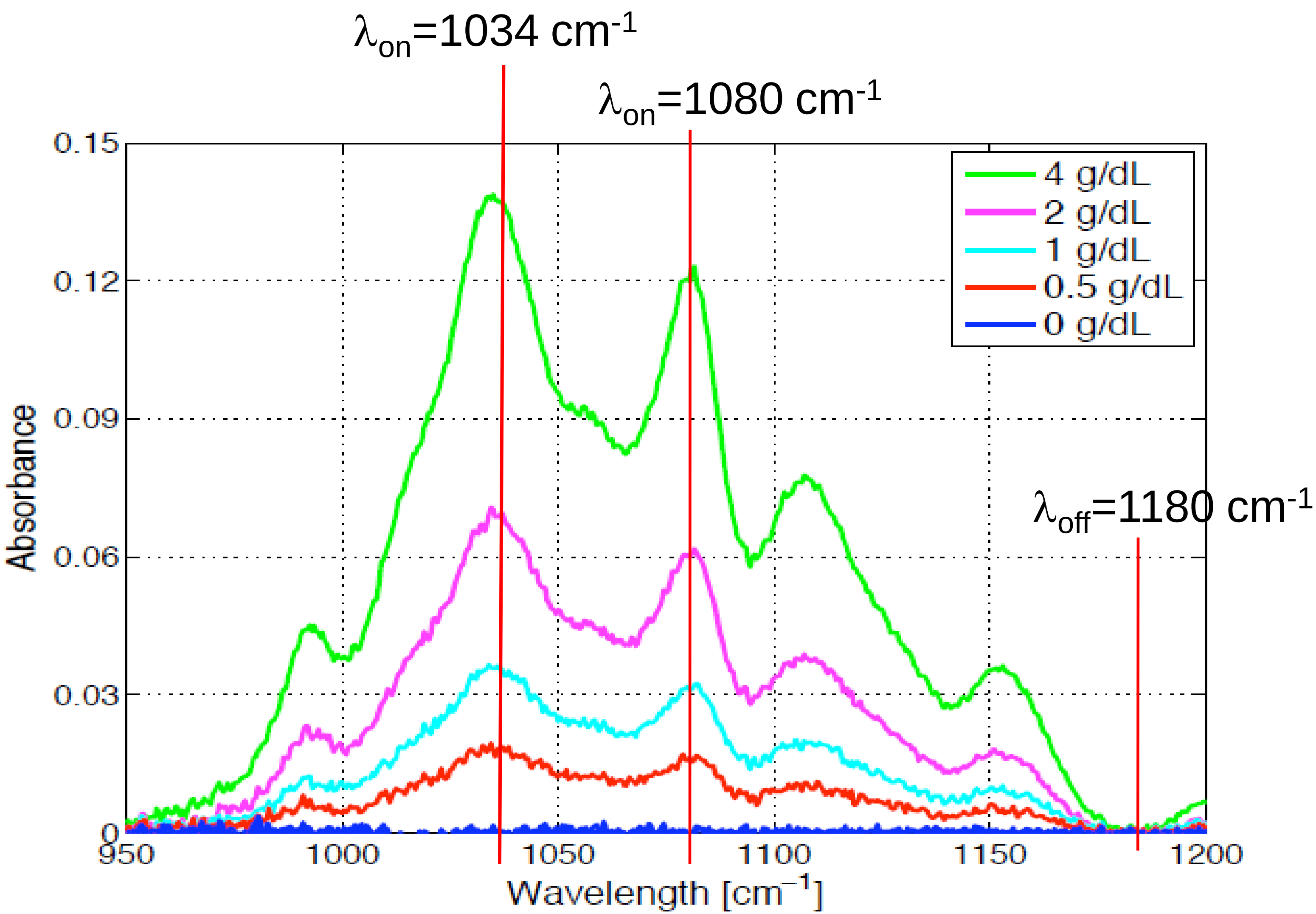
=> No glucose in the stratum corneum

QCL and PA technique } sensitive technique with potential for miniaturisation

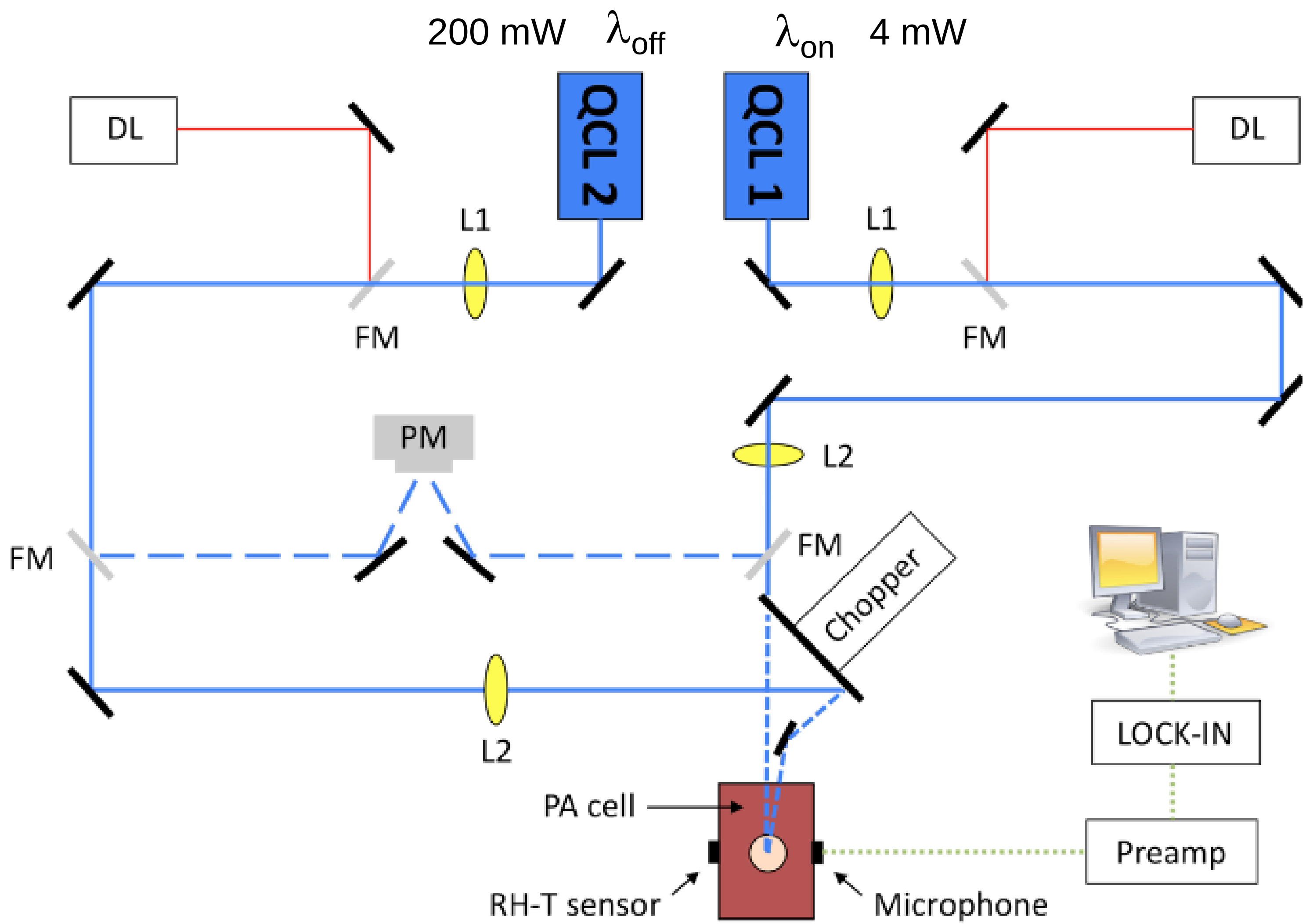


Thickness [mm]	Skin layer	Water [%]	Glucose
0.01 – 0.02	**Stratum corneum**	≈ 10	no
0.1 – 0.3	**Epidermis**	≈ 60	Interstitial fluid
1 – 2	**Dermis**	≈ 60	Blood /interstitial fluid
2 – 4	**Subcutaneous tissue**	≈ 60	Interstitial fluid

FTIR – ATR IR spectra of glucose solutions

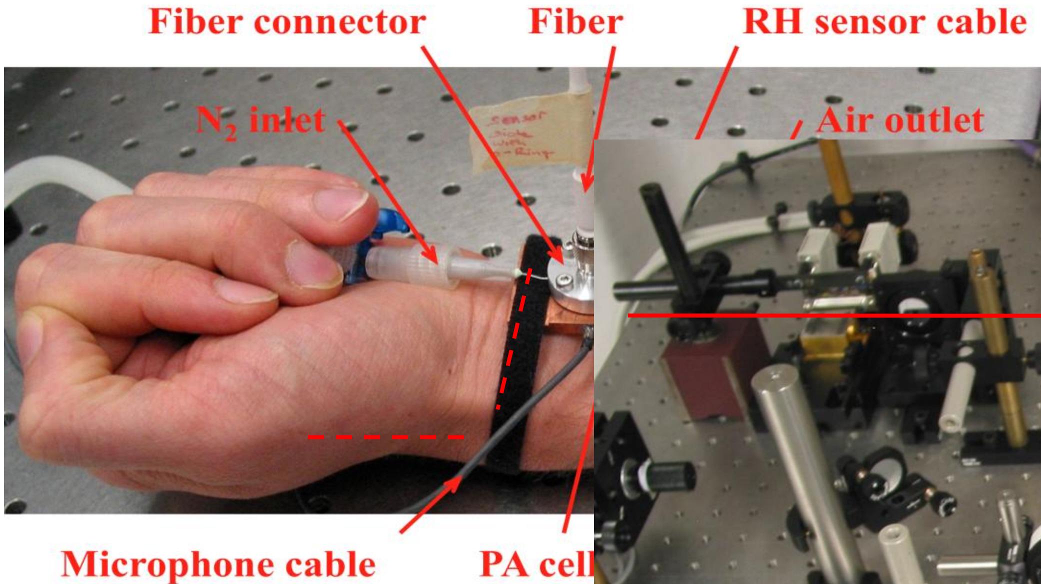


Two-QCL setup with sequential irradiation by QCL1 and QCL2

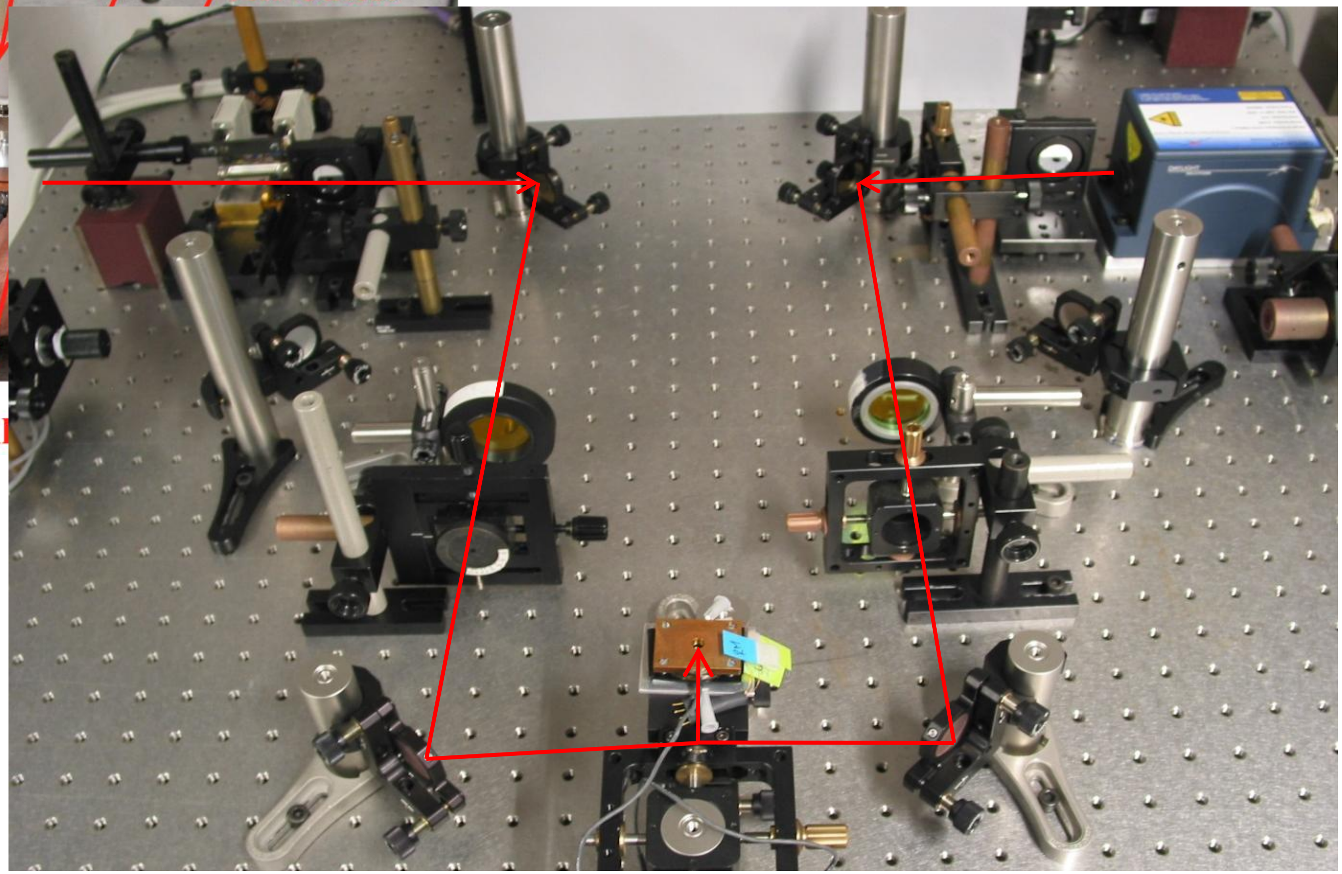


Kottmann et al.: *Sensors* **16**, 1663 (2016)

Experimental arrangements



First one-QCL setup

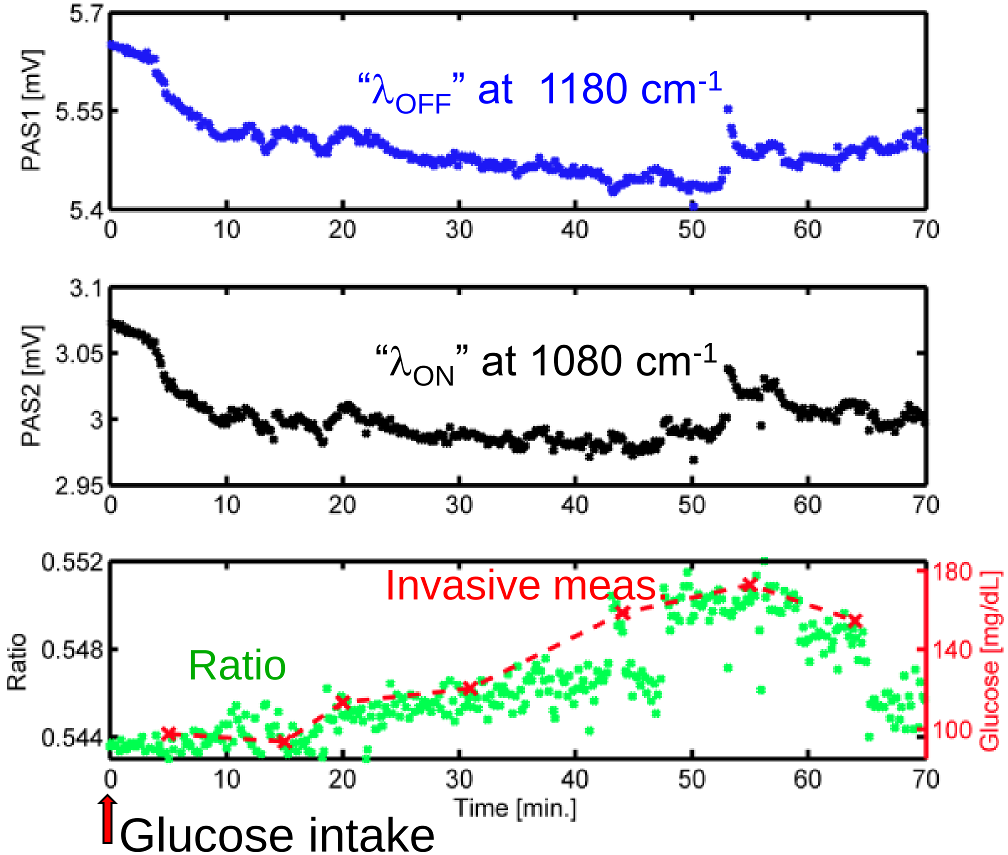


Two-QCL setup with sequential irradiation by QCL1 at λ_{on} and QCL2 at λ_{off}

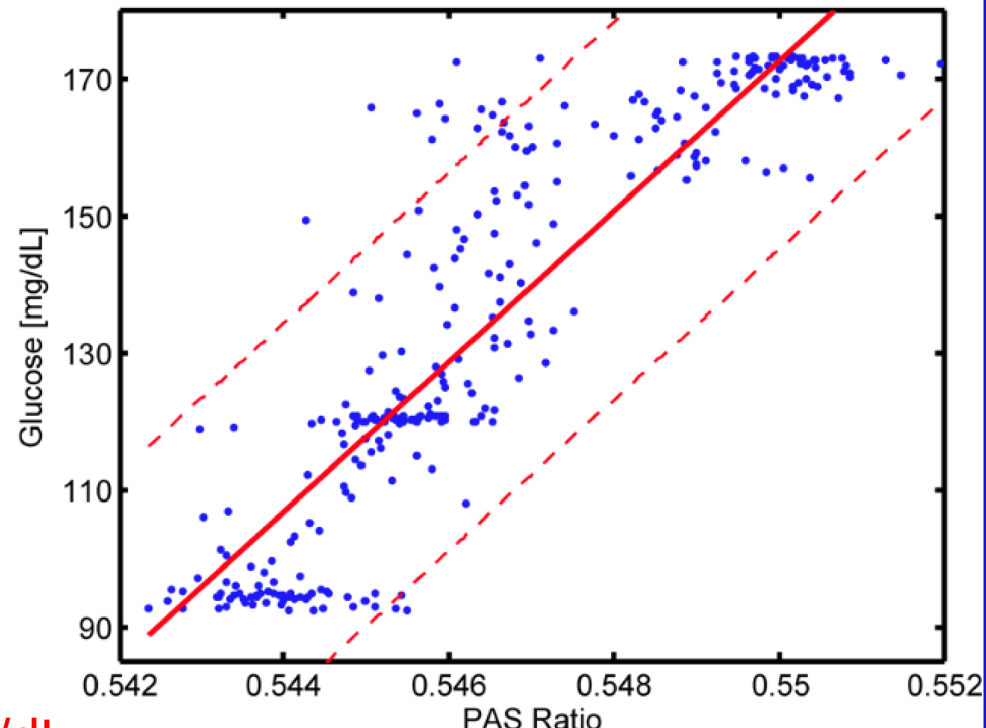
Kottmann et al.: *Sensors* **16**, 1663 (2016)

Oral glucose tolerance test with 2-QCL-setup

Continuous PAS data vs invasive measurements



Correlation between invasive measurements and PAS data



— Linear fit (r^2=0.8), --- confidence bounds
at 90 % confidence level: error: ± 30 mg/dL
just with 2 fixed λ's, no spectral fitting

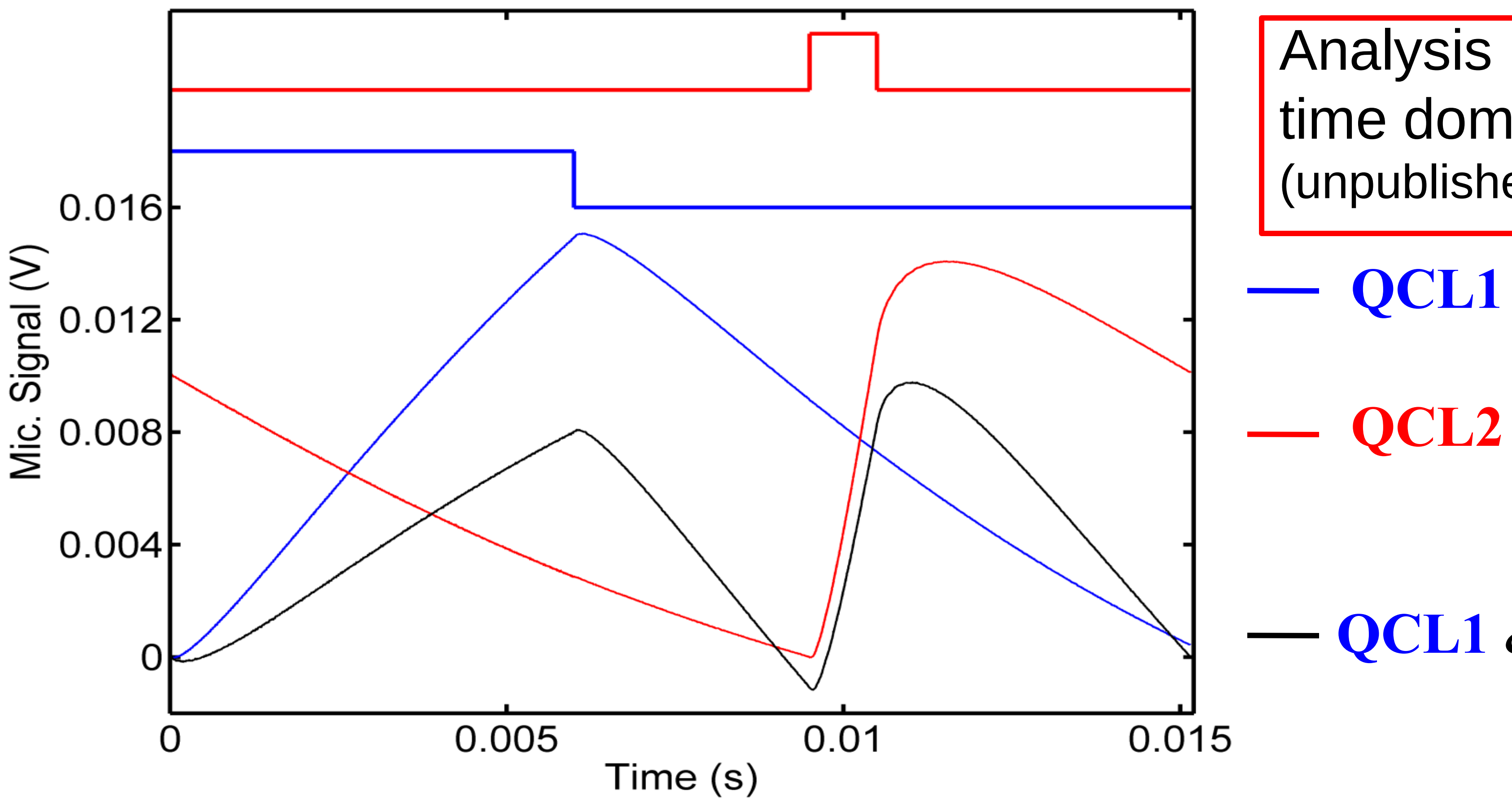
Kottmann et al.: *Sensors* **16**, 1663 (2016)

Current modulation of 2-QCL setup

In-vivo skin sample (Finger) / Total acquisition time = 50 s

QCL1: λ_{on} = 1034 cm^{-1} / Pulse length: 6ms / Rep. Rate: 66Hz

QCL2: λ_{off} = 1195 cm^{-1} / Pulse length: 1ms

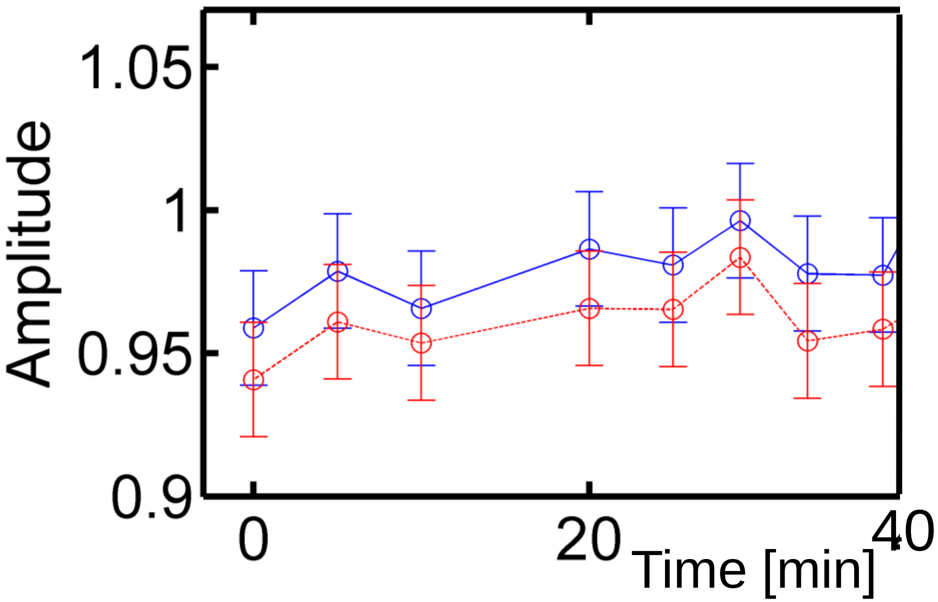


Analysis in time domain (unpublished results)

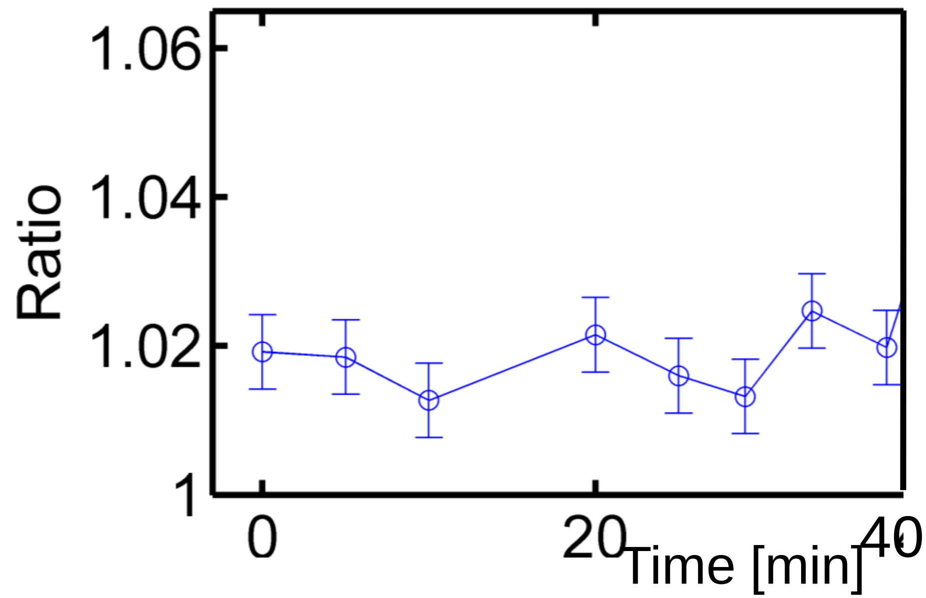
2-QCL measurement: *In vivo* test (Palm of hand)

QCL1: λ_{on}= 1034 cm^{-1}/ Pulse length = 5ms / Rep.Rate = 66Hz / 0.5mW

QCL2: λ_{off} = 1195 cm^{-1} / Pulse length = 1ms / 0.5mW



Reduced noise on amplitude = 1.5%



Reduced noise on ratio = 0.5%

Repeatability: 18-36 mg/dL

Next steps: Oral glucose tolerance tests / palm and finger tip

Conclusions

- Mid-IR Laser spectroscopy
  Strong molecular absorptions
  Broadly tunable laser sources: DFG, OPO, QCLs, VECSELs
- Mobile CO_2 laser PA system: 3 trace gases simultaneously
- QCL-QEPAS: HONO detection at ppb level
- Simultaneous C_1-C_4 alkane (ppm) detection with lead-salt VECSEL
- Surgical smoke: Multi-component *quantitative* ***analysis*** with DFG
- Non-invasive glucose monitoring in interstitial fluid via skin:
  2 QCLs with current modulation, repeatability: 18-36 mg/dL (2019)
  next: OGTT at different locations (hand palm, finger tips, ...),
  ev. more fixed wavelengths,....

Outlook

- New laser developments

  QCL arrays, ICLs, frequency combs, supercontinuum sources

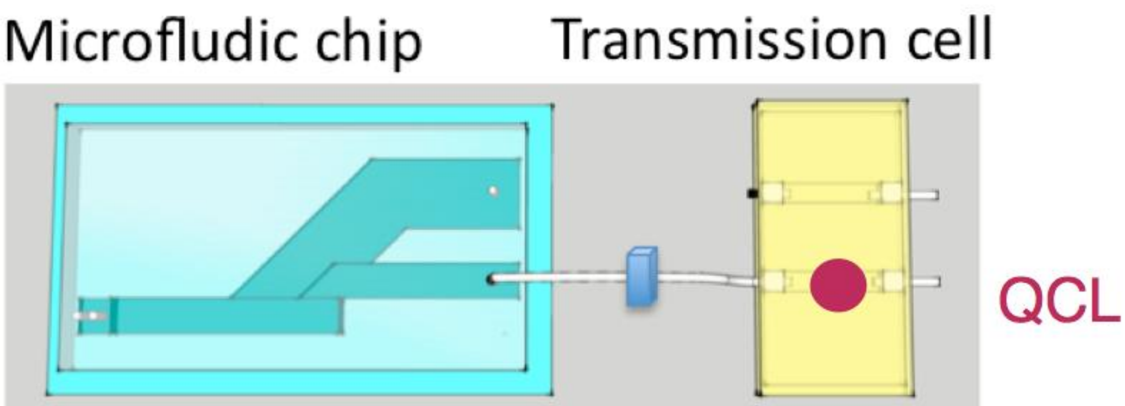
- Detection schemes

  PAS, QEPAS, Multipass Absorption, Photothermal radiometry, Backscattered radiation, ...

→ **NO “one-fits-all” solution**

- New application areas with smaller, cheaper, integrated devices:

  lab-on-a-chip, clinical, POC, & forensic applications



Quantitative detection of cocaine in human saliva

Acknowledgement


Dilyan Marinov


Michele Gianella


Jonas Kottmann


Julien Rey

zh aw


Weidong Chen

ULCO UNIVERSITÉ DU LITTORAL CÔTE D'OPALE

D. Hahnloser: University Hospital Zürich

Matthias Fill & Ferdinand Felder

CAMLIN TECHNOLOGIES

Schweizerische Eidgenossenschaft
Confédération suisse
Confederazione Svizzera
Confederaziun svizra

Swiss Confederation

Innosuisse – Swiss Innovation Agency

FNSNF
SWISS NATIONAL SCIENCE FOUNDATION

ETH zürich

GLUCOMETRIX


Thank you for your attention