# An Optical Breath Sensor Based on a Distributed Feedback Quantum Cascade Laser for Real Time Ammonia Detection

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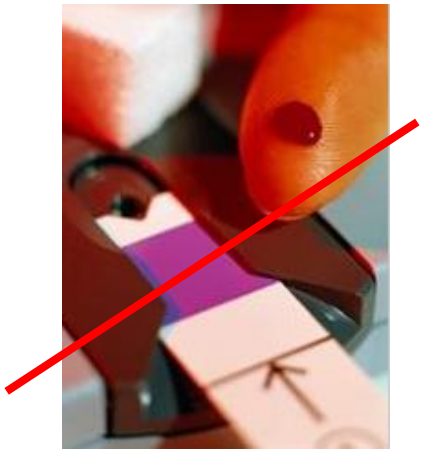
## OUTLINE:

- Motivation: Mid-IR QCL sensor for trace gas detection in exhaled breath
- Quartz Enhanced Photoacoustic Spectroscopy (QEPAS) method
- $NH_3$ sensor architecture
- Performance of the CW Distributed feedback (DFB) QCL
- Performance of the $NH_3$ sensor and results of real-time human breath data
- Summary

# Motivation

**Mid-IR quantum cascade laser based sensor for:**

- Non-invasive verification of patient medical condition



**Sensor requirements:**

- High sensitivity and selectivity
- Simple in use and robust
- Breath results available in real time
- Breath samples collected multiple times

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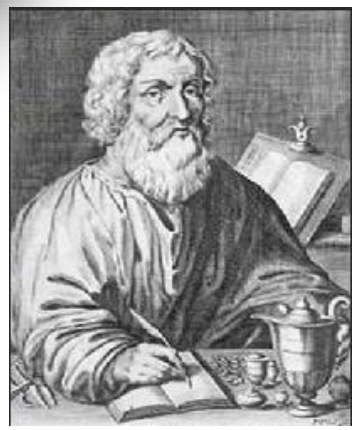
# Breath – a marker for diseases



- Exhaled human breath have both:
  - endogenous origin
  - exogenous origin
- The source of endogenous molecules are normal and abnormal physiological processes.
- The sources of exogenous molecules are:
  - inspiratory air,
  - ingested food and beverages,
  - any exogenous molecule that has entered the body by other routes (e.g. dermal absorption) [1]

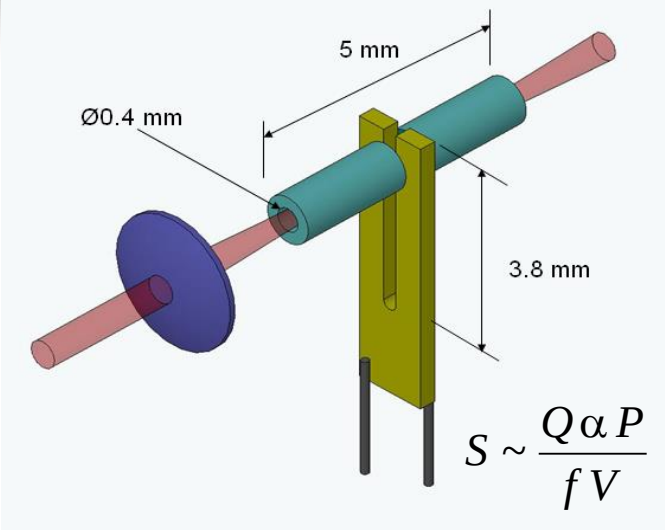
**Exhaled human breath contains ~ 400 different molecules, which can serve as biomarkers for the identification and monitoring of various types of human diseases or wellness states.**

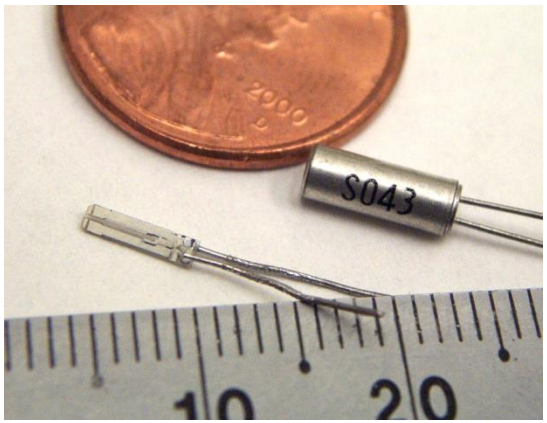
1. T.H. Risby, S. F. Solga, "Current status of clinical breath analysis", Appl. Phys. B 85, 421–426 (2006)

# Important biomedical molecules

| Molecule | Formula | Biological/Pathology Indication | Center wavelength [μm] |
|---|---|---|---|
| Pentane | $C_5H_{12}$ | Inflammatory diseases, transplant rejection | 6.8 |
| Ethane | $C_2H_6$ | Lipid peroxidation and oxidation stress, lung cancer (low ppbv range) | 6.8 |
| Carbon Dioxide isotope ratio | $^{13}CO_2/^{12}CO_2$ | Helicobacter pylori infection (peptic ulcers, gastric cancer) | 4.4 |
| Carbonyl Sulfide | COS | Liver disease, acute rejection in lung transplant recipients (10-500 ppbv) | 4.8 |
| Carbon Disulfide | $CS_2$ | Disulfiram treatment for alcoholism | 6.5 |
| Ammonia | $NH_3$ | Liver and kidney diseases, exercise physiology | 10.3 |
| Formaldehyde | $CH_2O$ | Cancerous tumors (400-1500 ppbv) | 5.7 |
| Nitric Oxide | NO | Nitric oxide synthase activity, inflammatory and immune responses (e.g. asthma) and vascular smooth muscle response (6-100 ppb) | 5.3 |
| Hydrogen Peroxide | $H_2O_2$ | Airway inflammation, oxidative stress (1-5 ppbv) | 7.9 |
| Carbon Monoxide | CO | Smoking response, lipid peroxidation, CO poisoning, vascular smooth muscle response | 4.7 |
| Ethylene | $C_2H_4$ | Oxidative stress, cancer | 10.6 |
| Acetone | $C_3H_6O$ | Ketosis, diabetes mellitus | 7.3 |

# Quartz enhanced photoacoustic spectroscopy




- Miniature size, <3 mm$^3$ detection volume
- Dimensions in mm: length = 3.8, gap size = 0.3, thickness = 0.3, width = 0.58
- Piezo-active material
- Signal currents ≈ pA
- Intrinsically high *Q* factor, ~10,000 at ambient pressure; *Q*vacuum ~ 125,000
- Optimum micro-resonator tubes are 4.4 mm long (~λ/4<l<λ/2 for sound at 32.8 kHz) and 0.6 mm in diameter
- Maximum SNR of QTF with mR tubes**:** **×30** (depending on gas composition and pressure)

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# *QEPAS based $NH_3$ Gas Sensor Architecture*

Loccioni breath analyzer

Needle valve

Gas handling system

Diaphragm Pump

Shut off valve

To the system

Needle valve

Pressure Controller & Flow Meter

Mouth piece & Capnostat

Gas In

Gas Out

Mid-IR DFB-QCL

Current & Temp controller

Lenses

ADM

Reference Cell

Pyroelectric detector

Function Generator

Pre-Amp

DAQCard 6062E

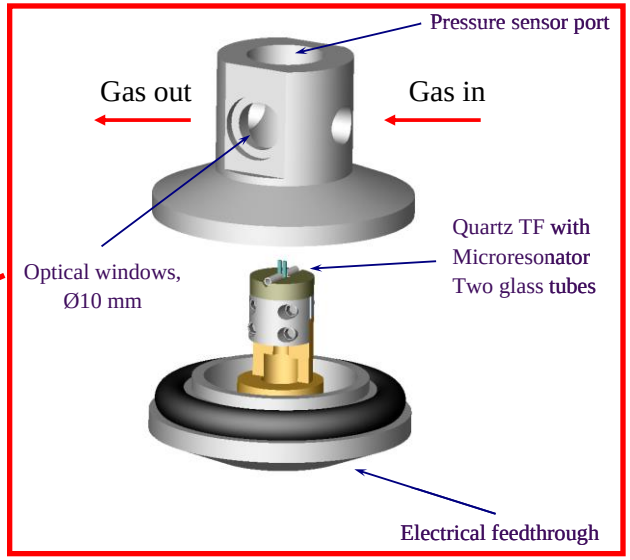
Lock-In 2f

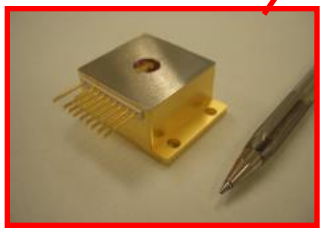
Lock-In 3f

Data collection and processing

PC

Control Electronics Unit (CEU)



High Head Load (HHL) package of DFB-QCL

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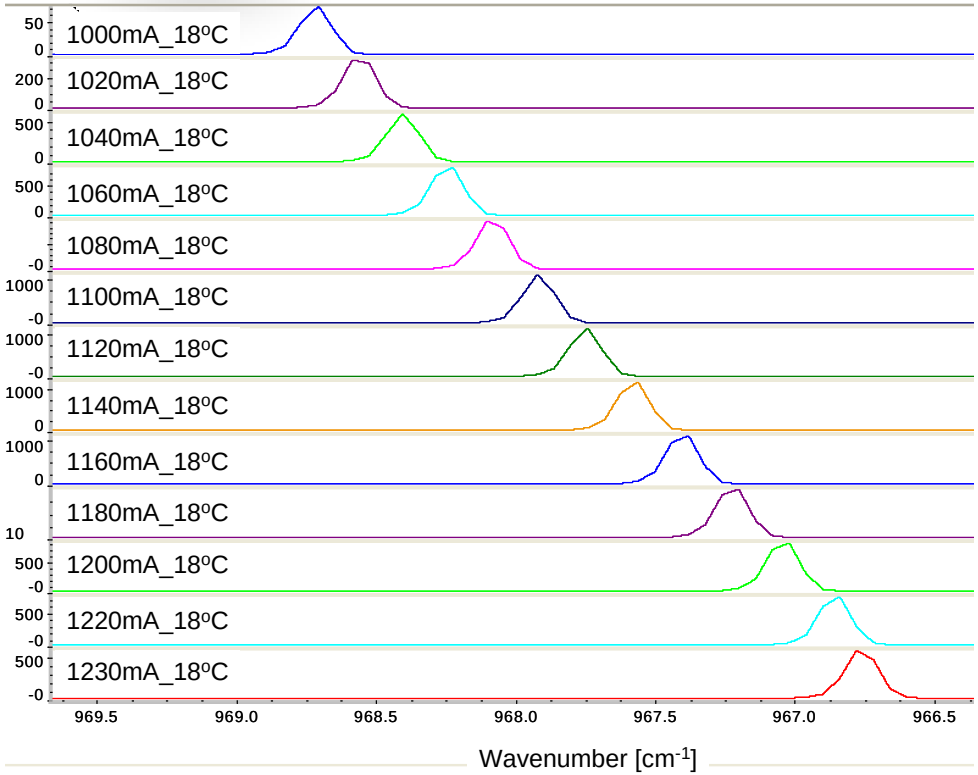
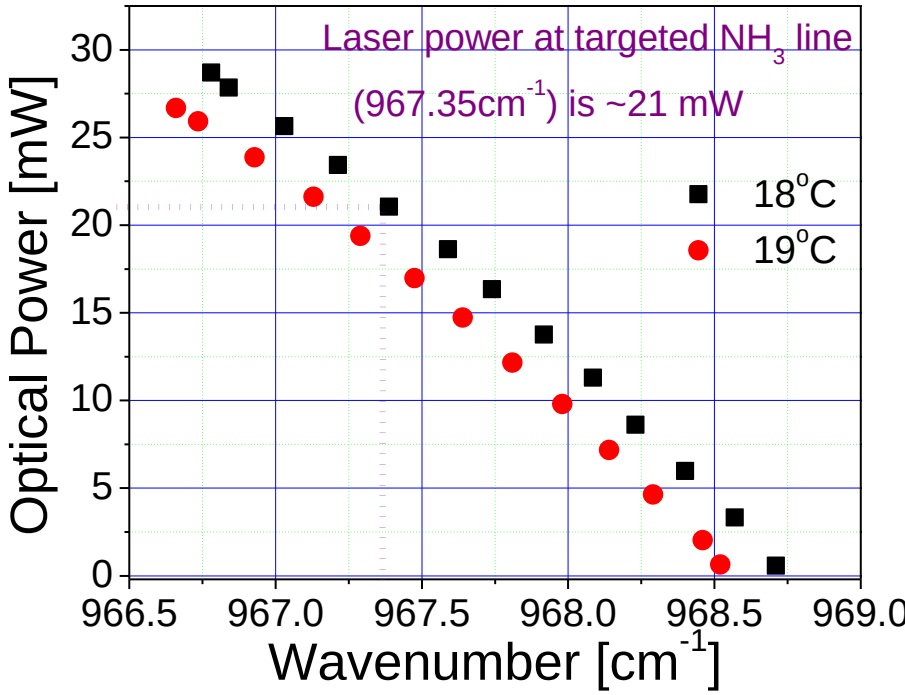
# Performance of the HAMAMATSU 10.34 μm CW DFB QCL




Single mode QCL radiation recorded with FTIR for different laser current values at a laser temperature of 18°C.




CW DFB-QCL optical power and current tuning at two different quasi-RT temperatures.

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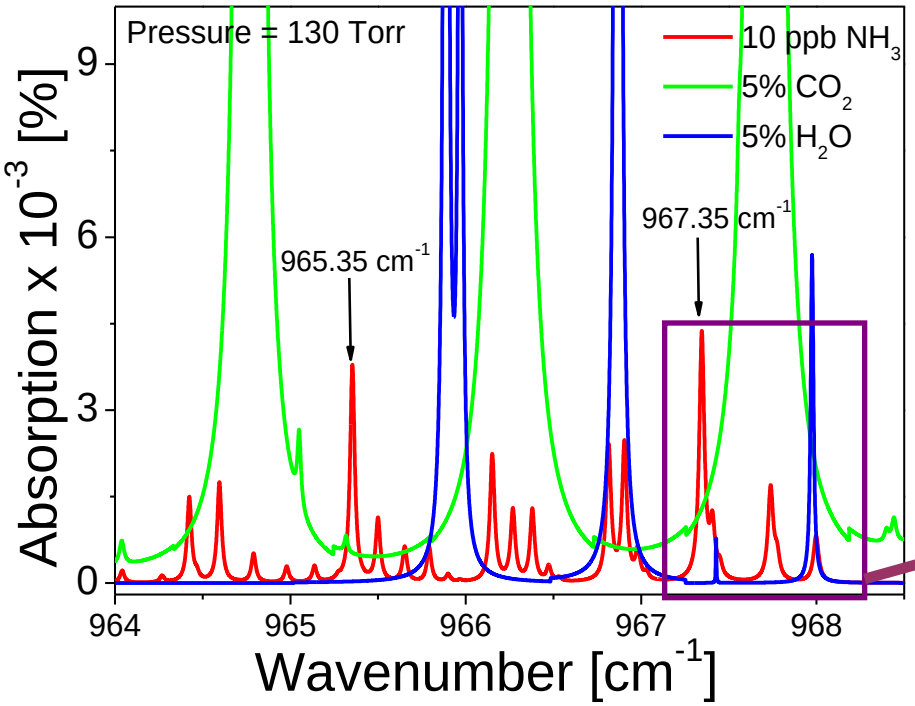
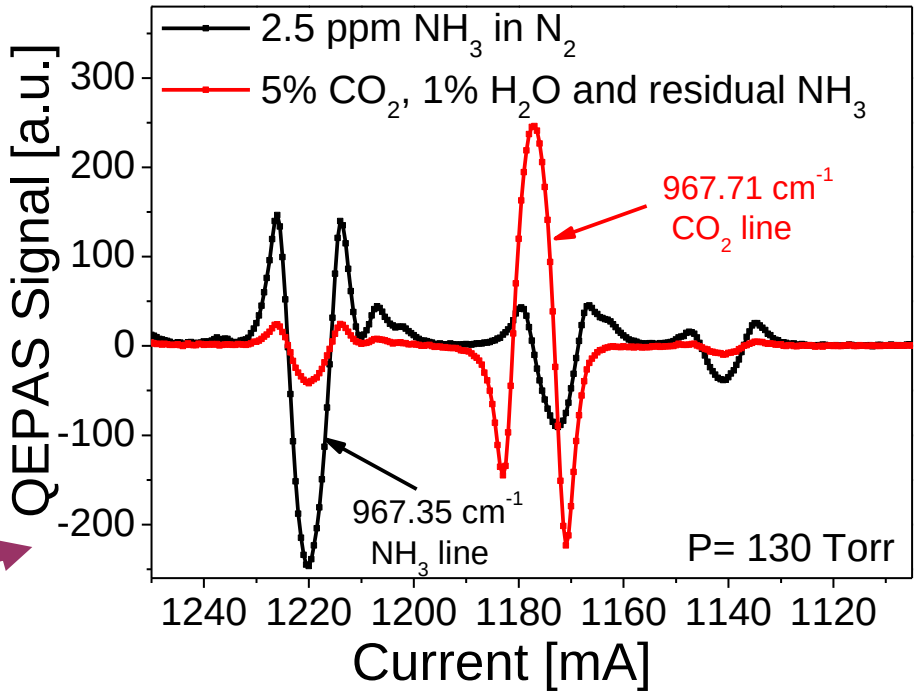
# $NH_3$ line selection for HAMAMATSU 10.34 μm CW DFB QCL

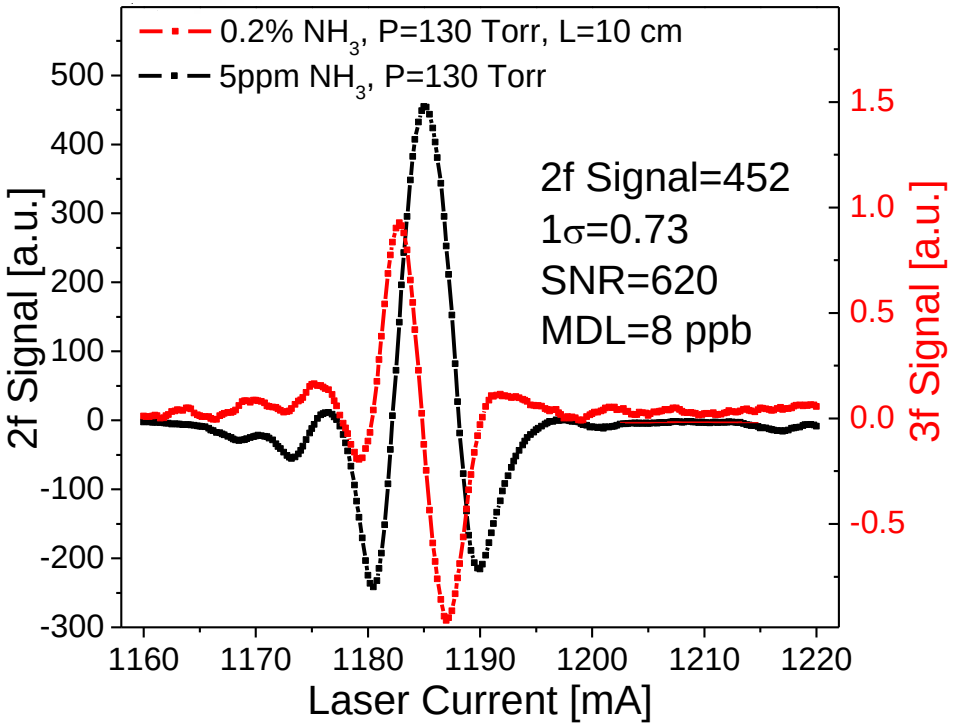


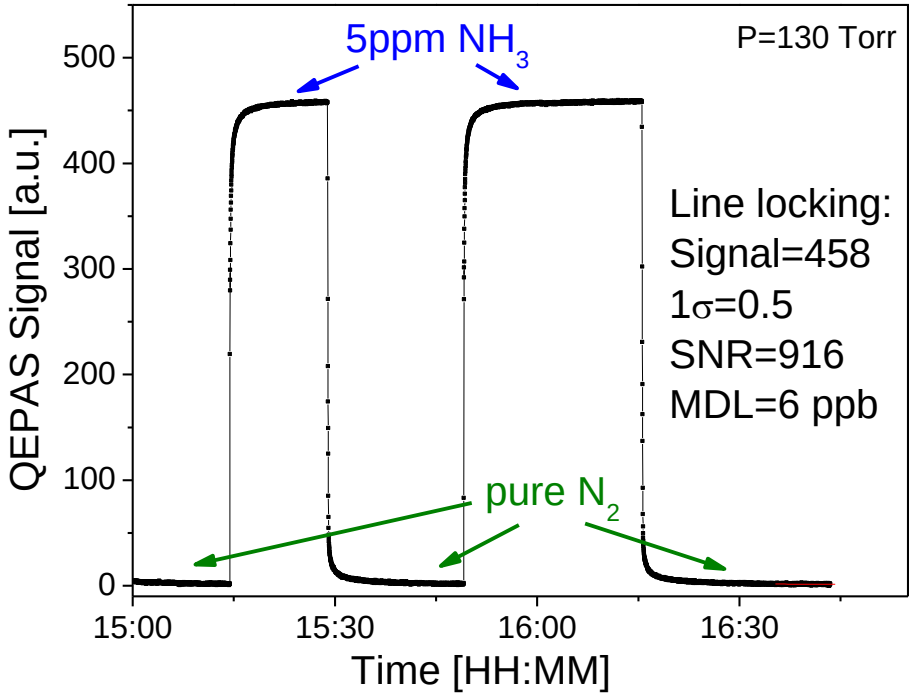

HITRAN simulated spectra @ 130 Torr indicating two potential $NH_3$ absorption lines of interest

No overlap between $NH_3$ and $CO_2$ absorption lines was observed for the selected **967.35 $cm^{-1}$** $NH_3$ line.

# Results obtained with a DFB-QCL based $NH_3$ gas sensor




2f QEPAS signal (black) and reference channel 3f signal (red) when laser was tuned across **967.35 cm$^{-1}$** line.




2f QEPAS signal for 5 ppm $NH_3$ when laser was locked to the **967.35 cm$^{-1}$** line.

**Minimum detectable limiting (MDL) concentration of $NH_3$ is:**
**~ 6 ppbv (1σ; 1 s time resolution)**

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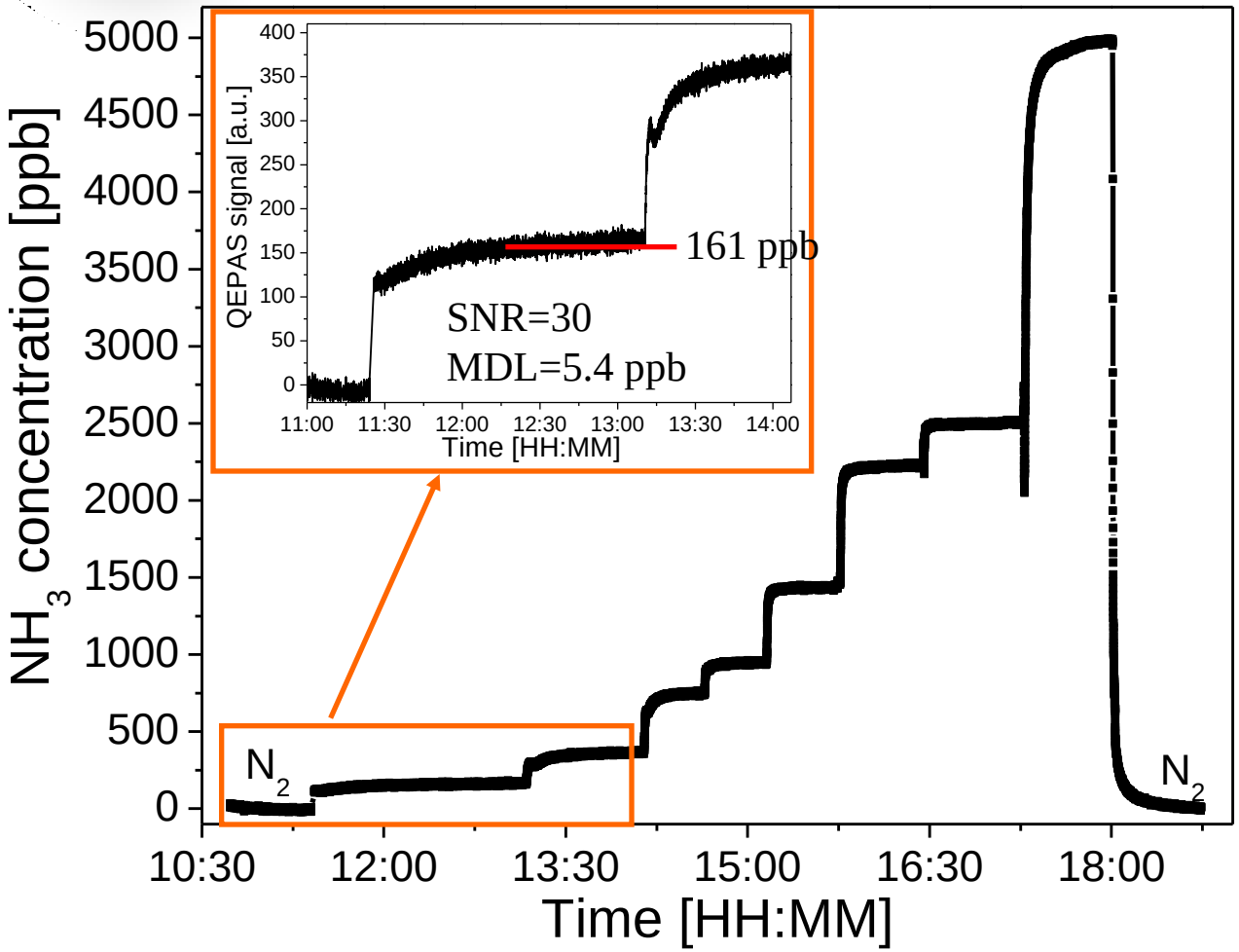
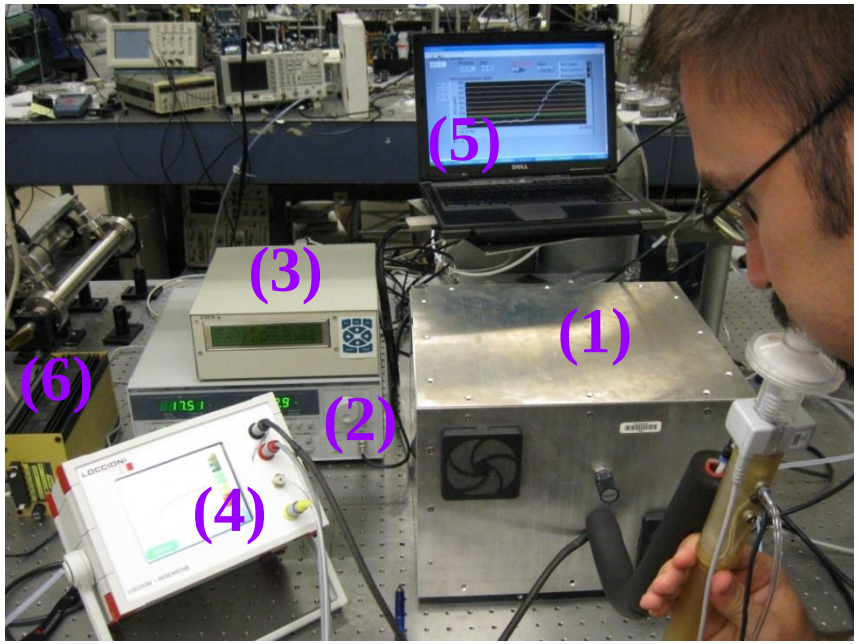
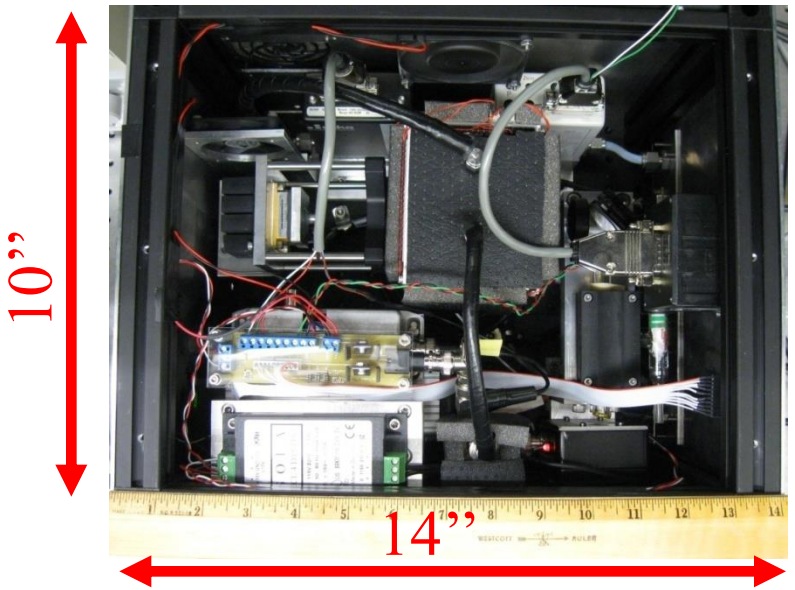
# Dilution calibration of the 5ppm $NH_3$ concentration




| $NH_3$ concentration [ppb] | |
|---|---|
| **Targeted** | **Measured** |
| 5000 | 4988 |
| 2500 | 2488 |
| 2280 | 2232 |
| 1500 | 1434 |
| 1000 | 958 |
| 800 | 746 |
| 400 | 358 |
| 200 | 161 |

# $NH_3$ breath sensor

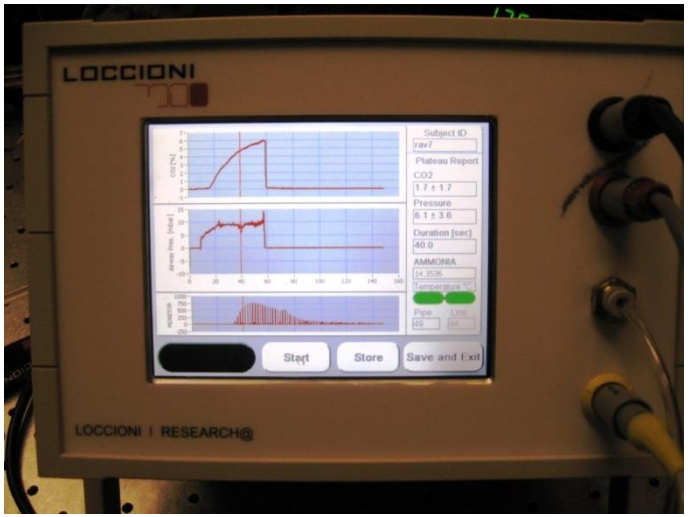



$NH_3$ sensor layout closed in a 14” x 10” x 12” box.

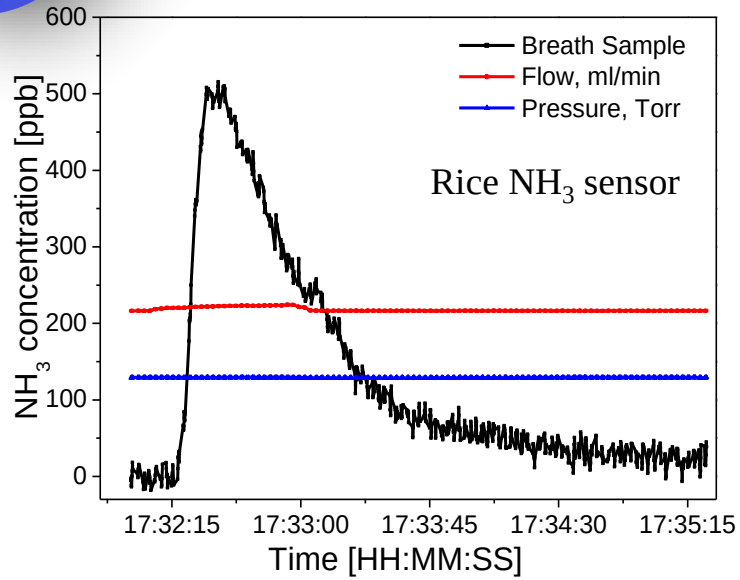
**$NH_3$ sensor system uses:**

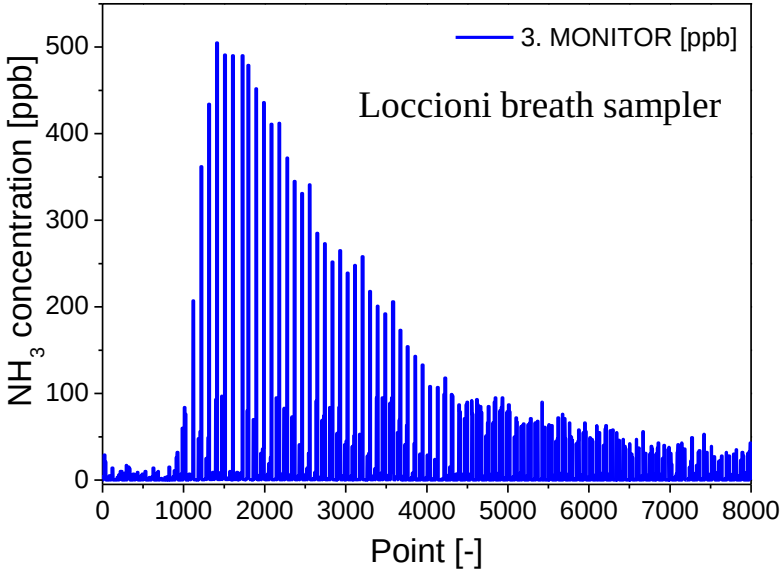
- $NH_3$ sensor box (1)
- ILX laser diode controller (2)
- Control electronics unit (3)
- Loccioni breath analyzer (4)
- Laptop (5)
- Power supply (6) and pump

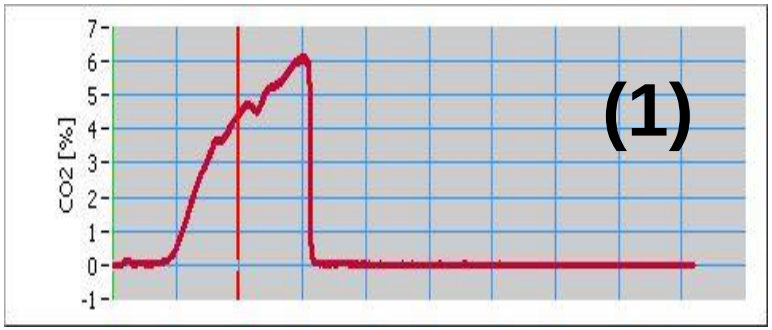


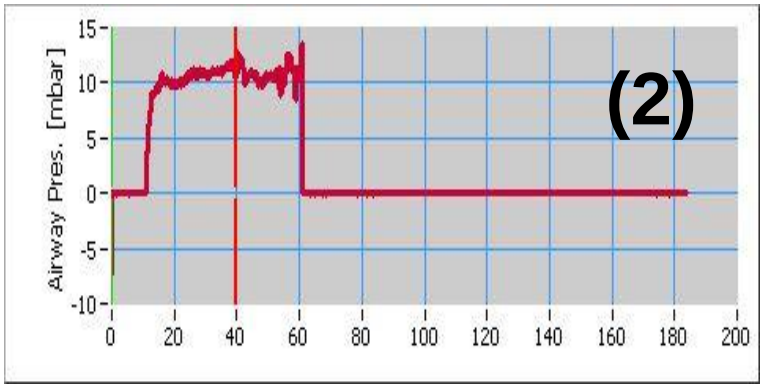

Breath analyzer from Loccioni

# Real-time human breath data of $NH_3$




For each patient, a separate folder is created on the Loccioni memory stick.
Each folder contains:
-excel worksheet with 3 columns data: CO2 [%], Airway pressure [mbar] and Ammonia [ppb]
-CO2 [%] plot (1)
-Airway pressure [mbar] plot (2)
The Ammonia [ppb] data is not saved as a plot.

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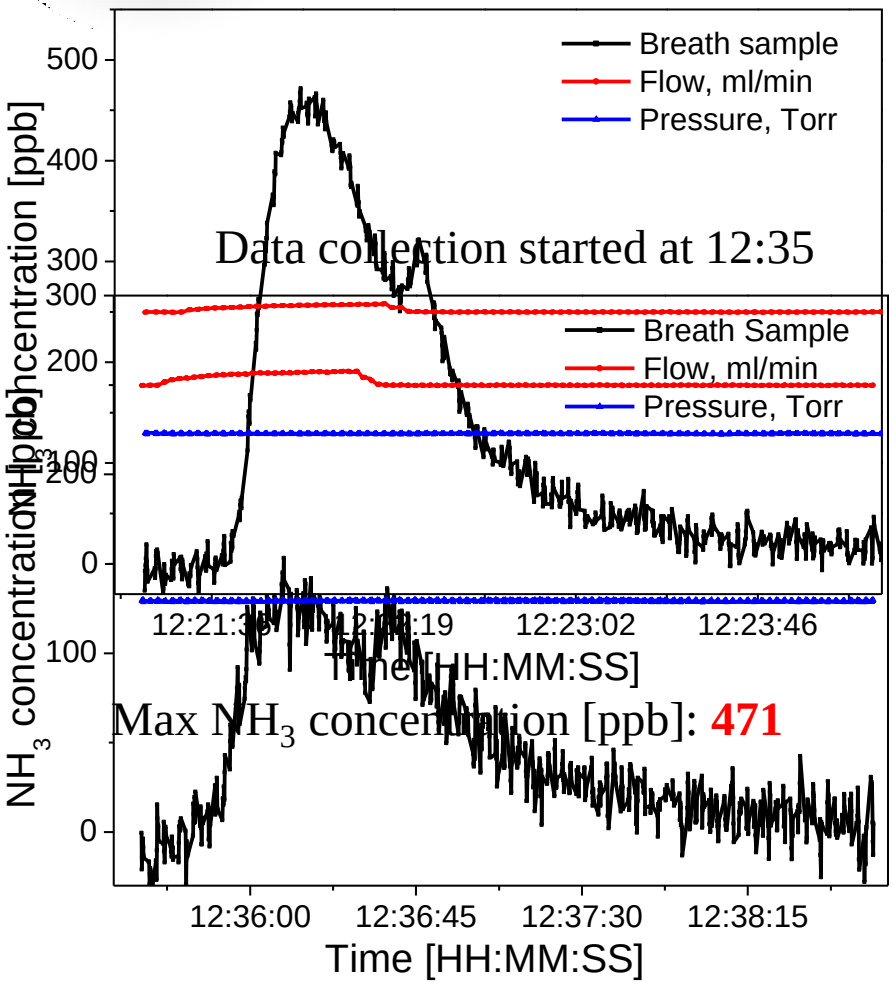
# Real data for human breath sample after mouth wash

Data collection started at 12:21



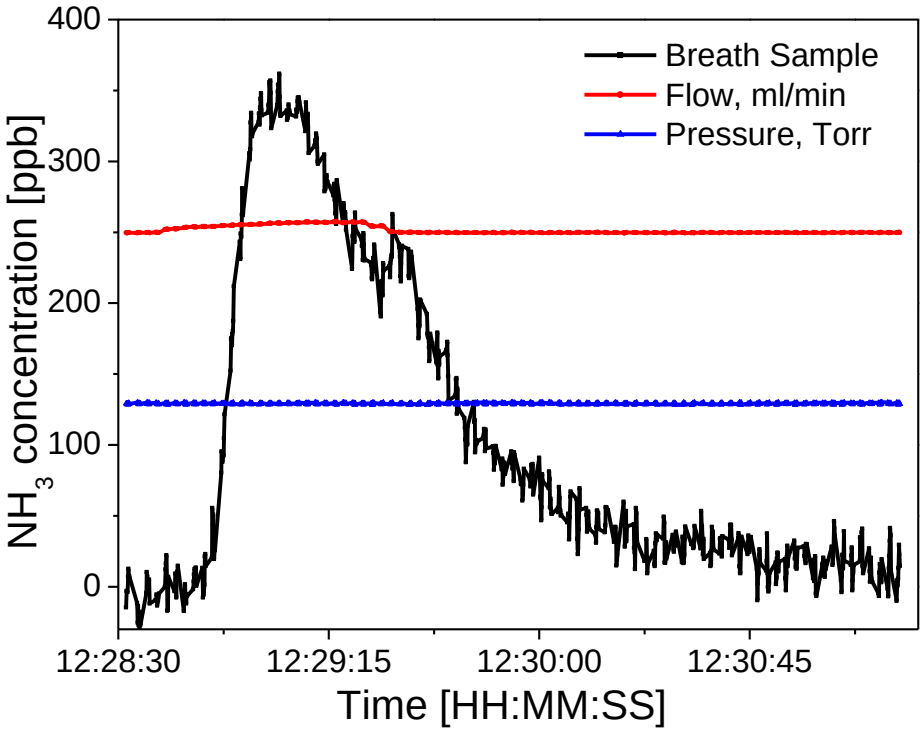

Max $NH_3$ concentration [ppb]: **153**

Data collection started at 12:35




Max $NH_3$ concentration [ppb]: **471**

Data collection started at 12:28




Max $NH_3$ concentration [ppb]: **361**

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# Summary

- Monitoring of ammonia concentration in exhaled breath using laser spectroscopy techniques provides a **fast, non-invasive** diagnostic method for patients with liver and kidney disorders, and helicobacter pylori infections (if patient has injected urea and the $NH_3$ is labeled with $^{15}N$).
- Minimum detectable concentration of $NH_3$ with DFB-QCL based sensor was observed at **~ 6 ppbv (1σ; 1 s time resolution)**.
- Fast time response was obtained by keeping sensor enclosure at 38°C to minimize ammonia adsorption effects.
- By using a commercial breath analyzer with built-in capnograph device the $CO_2$ concentration measurements are performed independently.
- Laser spectroscopy with a mid-infrared, room temperature, continuous wave, high performance DFB QCL is a promising analytical approach for real time breath analysis and the quantification of breath metabolites.

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# *Future goal - Ideal breath analyzer*

- **Hand–held device**
- **Fast – real–time results**
- **Accurate – Self calibrating**
- **Sensitive – sub ppb detection**
- **Inexpensive**

Dr. Beverly Crusher uses a medical tricorder in 2369.

**THANK YOU!!!**