DFB-QCL based optical breath sensor for sensitive and real time ammonia detection

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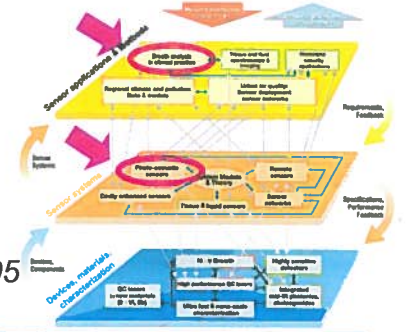


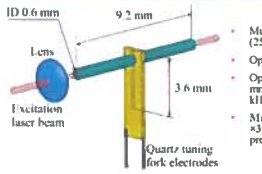
Outline

- Motivation: Real-time NH_3 breath sensor for non-invasive verification of medical condition
- Laser source: CW RT operated distributed feedback (DFB) QCL
- Detection technique: Quartz Enhanced Photoacoustic Spectroscopy (QEPAS)

Exhaled breath is a mixture of molecules, some of which are present at very low concentrations, that have both:
- endogenous origin (normal and abnormal physiological processes)
- exogenous origin (e.g. inspiratory air, ingested food and beverages)

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

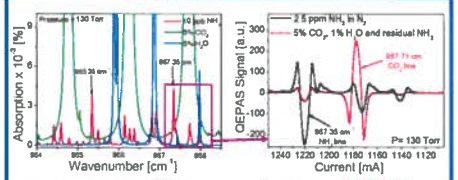
Quartz Enhanced Photoacoustic Spectroscopy



Micro-resonator (mR) tubes

- Must be close to QTF but not touch QTF (25-50 μm gaps).
- Optimum inner diameter 0.6 mm.
- Optimum micro-resonator tubes are 4.4 mm long (~λ/4=l<λ/2 for sound at 32.8 kHz).
- Maximum SNR of QTF with mR tubes: ×30 (depending on gas composition and pressure).

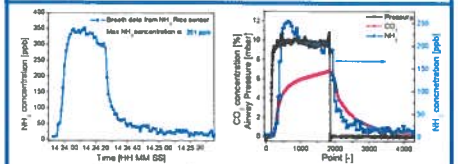
NH_3 line selection for a 10.34 μm CW RT DFB-QCL



Simulated HITRAN spectra @ 130 Torr indicating two NH_3 absorption lines of interest

No overlap between 967.35 cm^{-1} NH_3 line and neighboring CO_2 absorption line was observed.

Real-time exhaled human NH_3 Breath Measurements



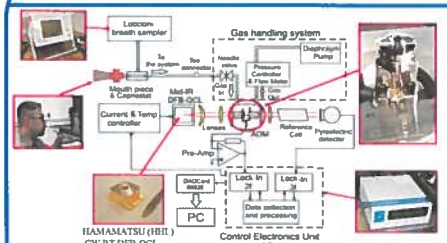
An example of typical breath ammonia profile

Airway pressure (black), CO_2 (red), and NH_3 (blue) profiles of a single breath exhalation lasting 40sec.

Important Biomedical Species

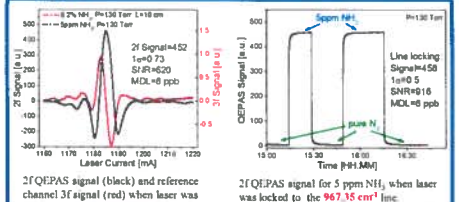
Molecule	Formula	Biological/Pathology Indication	Center wavelength [μm]
Pentane	C_5H_{12}	Inflammatory diseases, transplant rejection	6.8
Ethane	C_2H_6	Lipid peroxidation and oxidation stress, lung cancer (low ppbv range)	8.8
Carbon Dioxide Isotope ratio	$^{13}CO_2/^{12}CO_2$	Helicobacter pylori infection (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	6.6
Ammonia	NH_3	Liver and renal 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	10.5
Acetone	C_3H_6O	Ketosis, diabetes mellitus	7.3

QEPAS based NH_3 Gas Sensor Architecture



Advantages of using CW DFB-QCL in the sensor architecture:
- Small laser package -> system compactness,
- Room temperature operation, no water cooling needed,
- Performing WM spectroscopy at optimum modulation depth,
- More stable operation compared to EC-QCL.

NH_3 spectra obtained with a 10.34 μm DFB-QCL

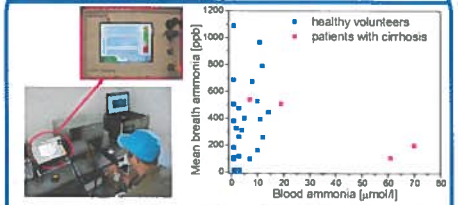


2f QEPAS signal (black) and reference channel 3f signal (red) when laser was tuned across 967.35 cm^{-1} line

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

Minimum detectable NH_3 concentration was: ~ 6 ppbv (1σ; 1 s time resolution)

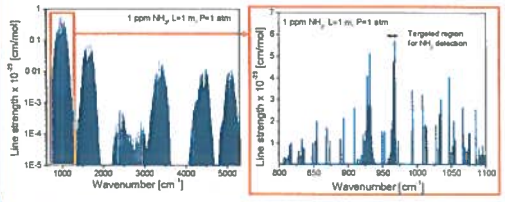
Clinical Tests of NH_3 sensor in Bethlehem, PA



NH_3 sensor test at medical breath research center in Bethlehem, PA associated with St Luke's Hospital

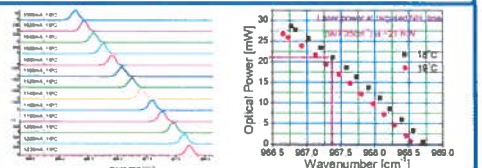
Preliminary results represent NH_3 measurements of 24 healthy volunteers (blue) provided breath (x3) and blood (x1) samples. So far only 2 patients (each provided 2 samples) with cirrhosis participated (red).

Simulated Mid-IR NH_3 Absorption Spectra



The line strength of the NH_3 absorption lines in the mid-infrared region (~1000 cm^{-1}) is 200 times higher than in the near-infrared region (~6600 cm^{-1}).

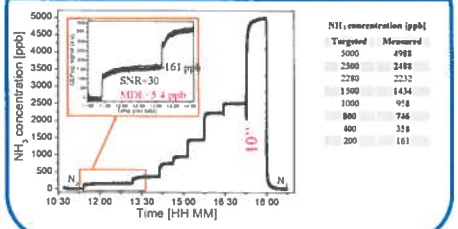
Performance of HAMAMATSU 10.34 μm CW DFB-QCL



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

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

Dilution of a 5ppm NH_3 Reference Concentration



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

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 was injected with urea and the NH_3 is labeled with ^{15}N).
- Minimum detectable concentration of NH_3 with DFB-QCL based sensor observed to date is **~ 6 ppbv (1σ; 1 s time resolution)**.
- Fast sensor response time was obtained by shortening the length of the gas flow tubes and by keeping metal components of the sensor at +38 °C to minimize ammonia adsorption effects.
- CO_2 concentration measurements are performed independently by using a commercial breath analyzer with a built-in capnograph.
- 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.
- Current tasks include miniaturization of existing NH_3 sensor platform into a compact, robust instrumentation package and improving spectraphone technology.

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