Real Time Ammonia Gas Sensor for Exhaled Human Breath Diagnostic Based on Quantum Cascade Laser

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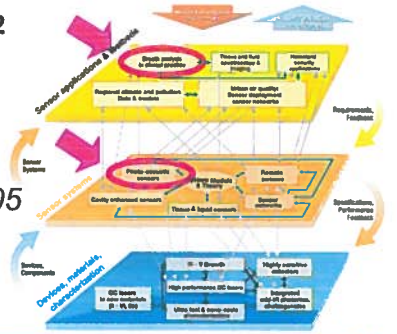


Outline

- Motivation: Mid-IR QCL sensor for trace gas detection in exhaled breath
- Laser sources: External Cavity (EC) and CW Distributed feedback (DFB) QCLs
- Detection technique: Quartz Enhanced Photoacoustic Spectroscopy (QEPAS)

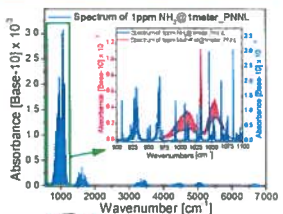
Exhaled breath is a mixture of molecules, some of which are present in our body at very low concentrations, that have both:
- endogenous origin (normal and abnormal physiological processes)
- exogenous origin (e.g. inspiratory air, ingested food and beverages...)

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

Important Biomedical Target Gases

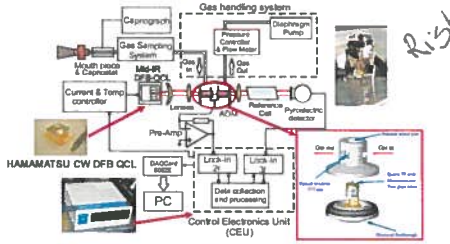
Molecule	Formula	Biological/Pathology Indication	Center wavelength [μm]
Pentane	C_5H_{12}	Inflammatory diseases, transplant rejection	6.8
Ethane	C_2H_6	Lipid peroxidation and oxidation stress, lung cancer (low ppbv range)	6.8
Carbon Dioxide Isotope ratio	$^{13}CO_2/^{12}CO_2$	Helicobacter pylori infection (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 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 (5-100 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

Simulated Mid-IR NH_3 Absorption Spectra



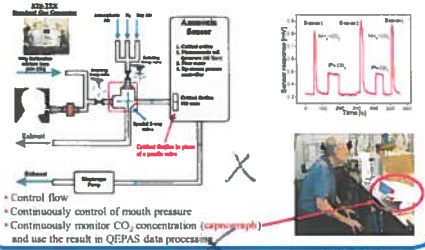
Line strength in the Mid-IR region (~1000 cm^{-1}) is 200 times higher than in the near IR region (~6400 cm^{-1}).

QEPAS based NH_3 Gas Sensor Architecture



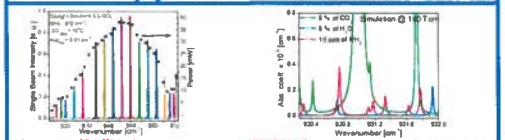
Advantages of using CW DFB-QCL in the sensor architecture:
- Small laser package -> system compactness,
- DFB-QCL RT operation & free-of using water cooling system,
- Performing WM spectroscopy at optimum modulation depth,
- Baseline reduction with 2f WM

Components of a real-time breath monitor



- Control flow
- Continuously control of mouth pressure
- Continuously monitor CO_2 concentration (capnograph) and use the result in QEPAS data processing

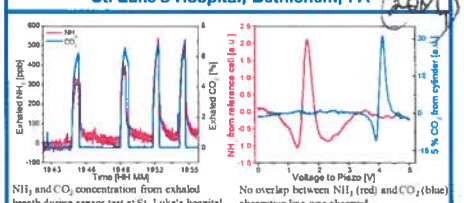
NH_3 line selection with previously used 10.6 μm CW Daylight Solutions EC-QCL source



P_{EC-QCL} up to 38 mW (cw)
Tunability 58 cm^{-1} -> (10.29μm – 10.94μm)

The 930.76 cm^{-1} NH_3 line was selected in terms of laser power, absorption coefficient and interfering species.

Real-time breath sampling data based on EC-QCL – St. Luke's Hospital, Bethlehem, PA

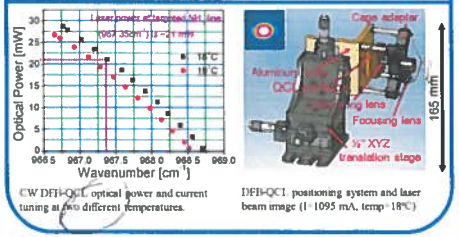


NH_3 and CO_2 concentration from exhaled breath during sensor test at St. Luke's hospital.

No overlap between NH_3 (red) and CO_2 (blue) absorption line was observed.

Minimum detectable concentration of NH_3 was: ~ 30 ppbv (3σ, 1 s DAQ time)

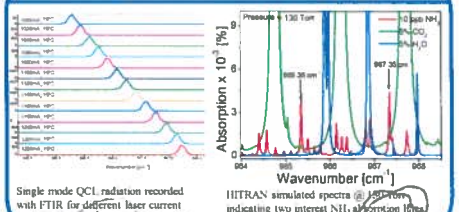
Performance of HAMAMATSU 10.34 μm CW DFB-QCL



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

DFB-QCL positioning system and laser beam image (I=1095 mA, temp=18°C)

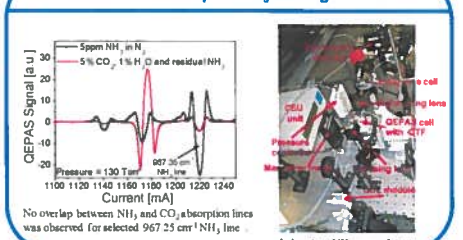
Line selection for HAMAMATSU CW DFB QCL



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

HITRAN simulated spectra @ 100 Torr indicating two interest NH_3 absorption lines

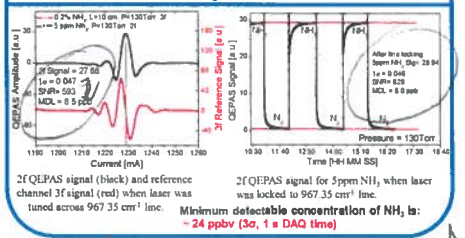
Lab tests for developed NH_3 trace gas sensor



No overlap between NH_3 and CO_2 absorption lines was observed for selected 967.25 cm^{-1} NH_3 line

Laboratory NH_3 sensor layout

Results for a 10.34 μm CW 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 5ppm NH_3 when laser was locked to 967.35 cm^{-1} line.

Minimum detectable concentration of NH_3 is: ~ 24 ppbv (3σ, 1 s DAQ time)

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.
- With EC-QCL based sensor platform the minimum detectable concentration of NH_3 in human breath was demonstrated at ~ 30 ppbv (3σ, 1 s DAQ time).
- Fast time response of ≤ 1 s was obtained by keeping sensor enclosure at 45°C (i.e. minimize ammonia adsorption effects).
- By using a commercial capnograph the CO_2 concentration measurements are perform independently.
- With DFB-QCL based sensor platform the minimum detectable concentration of NH_3 was observed at ~ 24 ppbv (3σ, 1 s DAQ time)
- Current tasks include enclosing existing NH_3 sensor platform into a compact and robust system and improving sensor response time by heating up sensing chamber.
- Laser spectroscopy in combination with a mid-infrared, continuous wave, high performance QCL is a promising analytical approach for real time breath analysis and the quantification of breath metabolites.

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