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
- NH₃ sensor architecture
- Performance of the CW Distributed feedback (DFB) QCL
- Performance of the NH₃ sensor and results of real-time human breath data
- Summary
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
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.

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

- Miniature size, <3 mm³ 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)
QEPAS based NH₃ Gas Sensor Architecture

High Head Load (HHL) package of 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.

Laser power at targeted NH₃ line (967.35 cm⁻¹) is ~21 mW.
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.

Minimum detectable limiting (MDL) concentration of NH$_3$ is:

~ 6 ppbv (1σ; 1 s time resolution)
Dilution calibration of the 5ppm NH₃ concentration

<table>
<thead>
<tr>
<th>NH₃ concentration [ppb]</th>
<th>Targeted</th>
<th>Measured</th>
</tr>
</thead>
<tbody>
<tr>
<td>5000</td>
<td>4988</td>
<td></td>
</tr>
<tr>
<td>2500</td>
<td>2488</td>
<td></td>
</tr>
<tr>
<td>2280</td>
<td>2232</td>
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<tr>
<td>1500</td>
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<tr>
<td>1000</td>
<td>958</td>
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<tr>
<td>800</td>
<td>746</td>
<td></td>
</tr>
<tr>
<td>400</td>
<td>358</td>
<td></td>
</tr>
<tr>
<td>200</td>
<td>161</td>
<td></td>
</tr>
</tbody>
</table>
NH₃ breath sensor

NH₃ sensor layout closed in a 14” x 10” x 12” box.

**NH₃ sensor system uses:**
- NH₃ 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
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.
Real data for human breath sample after mouth wash

Data collection started at 12:21

Max NH₃ concentration [ppb]: 471

Data collection started at 12:28

Max NH₃ concentration [ppb]: 361

Data collection started at 12:35

Max NH₃ concentration [ppb]: 153
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.
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!!!