MIRTHE and Exhaled Human Breath Analysis for Clinical, Environmental and Homeland Security Applications

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Introduction

- Motivation: Mid-IR QCL sensor for trace gas detection in exhaled breath

Exhaled breath is an instantaneous mixture of molecules from the following sources:
- molecules originating from inspiratory air
- molecules originating from dermal absorption
- molecules directly or indirectly derived from ingested food and beverages
- molecules produced by normal physiologies and can originate from tissues and cells throughout body

Breath composition will change as a function of breathing cycle

Breath molecules originate from cells throughout oral/nasal cavities, pulmonary system and cells and tissues throughout the organism

Breath composition will change with breathing physiology (hyper- or hyperventilation)

Do unique breath biomarkers exist?

- Unique biomarkers can only originate from the ingestion, inhalation, or absorption of foreign substances, or can only originate from the presence of bacteria, viruses, yeasts, molds, or fungi

- Normal and abnormal tissues will produce the same molecules abnormal physiologies will only change concentrations.

- Cellular biochemistry can only be induced, or suppressed by abnormal physiology

Some disease states can appear to be producing unique molecules; however, these results are a reflection of the detection limit of the analytical method

FDA approved breath tests

- Breath nitric oxide test to monitor therapy for asthma
- Breath carbon dioxide for capnography
- Breath hydrogen test for deammoniation deficiency
- Breath carbon monoxide test for neonate jaundice and typhoid sepsis
- Breath CO test for diagnosis of HIV infection
- Breath hydrogen for heart burn for heart burn reflux
- Breath ethanol screening for blood alcohol

Typical concentrations of endogenous molecules found in breath

- % nitrogen, oxygen, carbon dioxide, water
- ppm acetone, carbon monoxide, methane, hydrogen
- ppb formaldehyde, acetaldehyde, isoprene, pentane, ethane, ethylene, nitric oxide, methanol, ethanol, carbon monoxide, methane sulfide, methanol sulfide, ammonia, methylamine

Exhaled human breath could contain as many as 400 different molecules

Reproducible single breathing sampling

Controlled sampling based upon flow (pressure), and carbon dioxide

Biochemical basis of major endogenous breath molecules

- H₂: carbohydrate metabolism
- C₂H₅OH: gut bacteria
- H₂CO₃: lipid peroxidation metabolism
- CO: heme catalytetor (HDC)
- NO: nitric oxide synthase
- C₂H₂: lipid peroxidation
- C₄H₂: lipids, protein peroxidation
- C₆H₉N₂: carbon monoxide deamination
- NH₃: protein metabolism
- CH₄: carbohydrate metabolism
- CH₄O: ethanol metabolism
- CH₃CHO: carbohydrate biosynthesis
- CH₃H₂: fruit metabolism
- CH₃OHH: protein metabolism
- CH₃CHO: lipid peroxidation
- CH₃CN: protein metabolism
- CH₃H: methamine metabolism
- CH₃CN: methylene metabolism
- CO₂: gut bacteria
- CO₂: protein metabolism

Endogenous breath molecules and mid IR detection

| CH₃OD | 0.85–0.95 µm | C₂H₂ | 0.6–0.7 µm |
| CH₃OH | 1.13 µm | CH₃H₂ | 0.6–0.7 µm |
| CH₃SH | 0.7–0.85 µm | CH₃OH | 0.8–0.92 µm |
| CH₃NH₃ | 1.22 µm | CO | 0.4–0.5 µm |
| CH₃NH₂ | 1.08 µm | NO | 0.5–0.6 µm |
| CH₃NH₂ | 3.75–3.78 µm | CH₃CHO | 0.6–0.7 µm |
| CS₂ | 2.2–2.5 µm | CO₂ | 7.3–7.5 µm |
| CO₂ | 4.6–4.8 µm | CH₃COO | 19.3–20.3 µm |
| CH₃COO | 2.45–3.39 µm | CH₃CN | 3.3–3.5 µm |

Breath analysis and the human environment

- Exogenous compounds demonstrate uptake and bioavailability
- Timing of blood biomarker concentrations demonstrate metabolic pathways (classical PK and PBPK)
- Timing of blood biomarker concentrations demonstrate recent exposure profiles

Summary of studies to date

- Breath has been successfully used to estimate exposure to gasoline, jet fuel, inhalation anesthetics, and halothane in the general population and in occupational exposed workers.

Breath analysis and homeland security

- Breath analysis is non-invasive
- Breath can be collected multiple times without risk to the subject
- Children give breath samples willingly
- Breath can be collected from the neonate to the elderly (a mouse to an elephant)
- Breath can easily be collected in field, clinic, in-patient, OR and ICU
- The future of breath analysis for all applications is handheld devices that can respond to breath molecules faster than breathing frequency and that can provide results within 5 minutes
- Laser spectroscopy with a mid-infrared, room temperature, continuous wave, high performance QCL is a promising analytical approach for real time quantification of breath biomarkers

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