Breath Gas Analysis Pipeline

For dynamic concentration profiles

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Introduction

Institute for Breath Research

Figure 1: Photo of group with current leader Christopher Mayhew.

Breath Gas Analysis

- novel application for gas analysis
- my topics
    - consider dynamic data
    - modelling breath concentration profiles
- relevance
    - interpretation of breath concentration profiles
    - extraction of metabolomic data
    - potential diagnostic tool

Concepts

- utilise fast and efficient gas exchange in lung
- focus on trace metabolites
- measurement methods in ensemble
- features

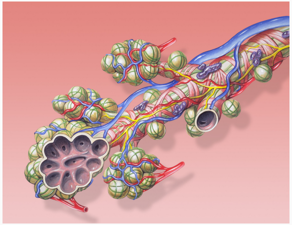


Figure 2: Sketch of alveoli (By Patrick J. Lynch[CC BY 2.5]) Only membranes separate blood from air.

Concepts

- utilise fast and efficient gas exchange in lung
- focus on trace metabolites
- measurement methods in ensemble
- features

"A metabolite is the intermediate end product of metabolism." (Definition)

- molecular weight in the range 20 amu to 150 amu
- typical concentration range 1 ppt (parts-per-trillion) to 10 ppm (parts-per-million)

note: oxygen and carbon dioxide fall out of this range

Concepts

- utilise fast and efficient gas exchange in lung
- focus on trace metabolites
- measurement methods in ensemble
- features

different characteristics

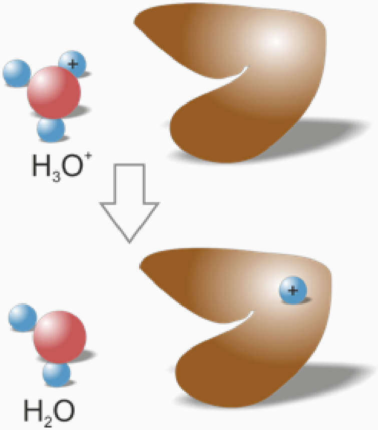
- proton transfer - time of flight - mass spectrometer (PTR-TOF-MS) has high time and mass resolution
- gas chromatography - mass spectrometer (GC-MS) for unambiguous identification
- ion mobility spectrometer (IMS) and semiconductor based devices for mobile measurements

Concepts

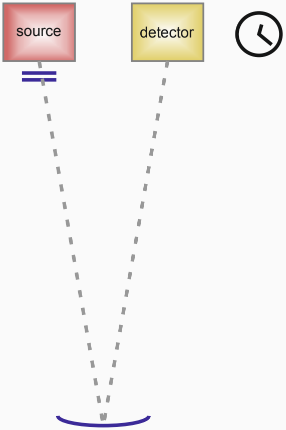
- utilise fast and efficient gas exchange in lung
- focus on trace metabolites
- measurement methods in ensemble
- features

- information comparable to blood test
- non-invasive, ”user friendly” sampling
- rapid real-time possible
- ”unlimited” sample (breath is ”waste product” continuously produced)

Principle PTR-TOF



(a) Soft ionisation through proton transfer reaction (PTR).

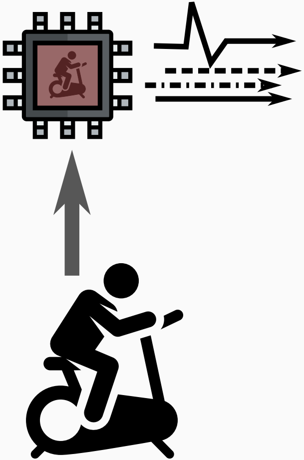


(b) Schema of time of flight mass spectrometry (TOF-MS).

Figure 2: Principal of operation of PTR-TOF device.

My Research Topics

Modelling

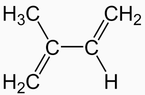


- physiological representation (necessary)
- access parameter through fit
- interpretation of measurement in terms of representation
- plans for online tracking

Experiments

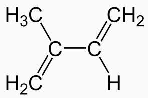
Isoprene

- Is one of the most common observed metabolite.
- high variability in human breath
- Production unclear



- After methane the most common VOC.
- Produced in great concentration by plants.

Isoprene



- Is one of the most common observed metabolite.
- high variability in human breath
- Production unclear

- Breath concentrations over wide range typically 10 ppb to 100 ppb.
- Breath concentrations can rise 5 times in concentration for short times.
- Often suggested as biomarker in breath.

Isoprene

- Is one of the most common observed metabolite.
- high variability in human breath
- Production unclear

Production mechanism is known in plants and single cell organism. This mechanism is not present in animals. Relation to cholesterol hypothesised.

Isoprene Ergometer Experiment

Figure 3: Photo of the setup. Volunteer lies on ergometer. PTR-TOF behind wall. Typical protocol: baseline - exercise - rest (each about 10 min).

Typical Isoprene Exercise Data

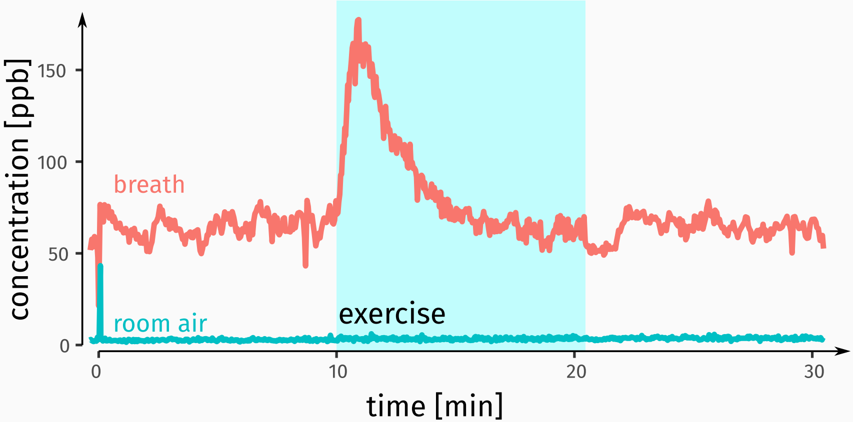


Figure 4: Observation of an experiment. There is a typical spike at begin of exercise.

Isoprene Model

- Simple model
- Localisation Production
- Localisation Metabolisation

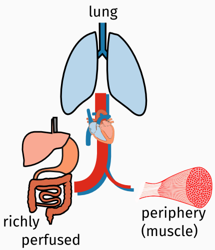


Figure 5: At least two body compartments and one lung compartment required to explain signal as observed. The flow between compartments is shifted during exercise.

Isoprene Model

- Simple model
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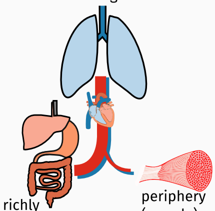


Figure 5: At least two body compartments and one lung compartment required to explain signal as observed. The flow between compartments is shifted during exercise.

Hypothesis test: significant production in periphery compartment.

Isoprene Model

- Simple model
- Localisation Production
- Localisation Metabolisation

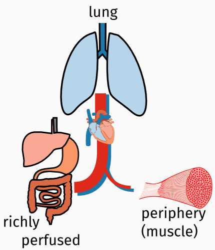
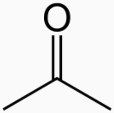


Figure 5: At least two body compartments and one lung compartment required to explain signal as observed. The flow between compartments is shifted during exercise.

No compartment significant metabolisation.

Acetone Inhalation Experiment

- Simplest ketone
- production well understood
- medical interest
- inhalation experiment



- Common VOC
- Often present as contaminant
- Soluble in water and fat

Acetone Inhalation Experiment

- Simplest ketone
- production well understood
- medical interest
- inhalation experiment

During ketosis - energy from ketone bodies (instead of glycolysis).

Acetone Inhalation Experiment

- Simplest ketone
- production well understood
- medical interest
- inhalation experiment

- related to fat metabolism
- interest ketogenic diet
- indicator for ketoascidosis in diabetes melitus

Acetone Inhalation Experiment

- Simplest ketone
- production well understood
- medical interest
- inhalation experiment

- setup as before
- self experiment
- release of acetone & deuterated acetone during experiment

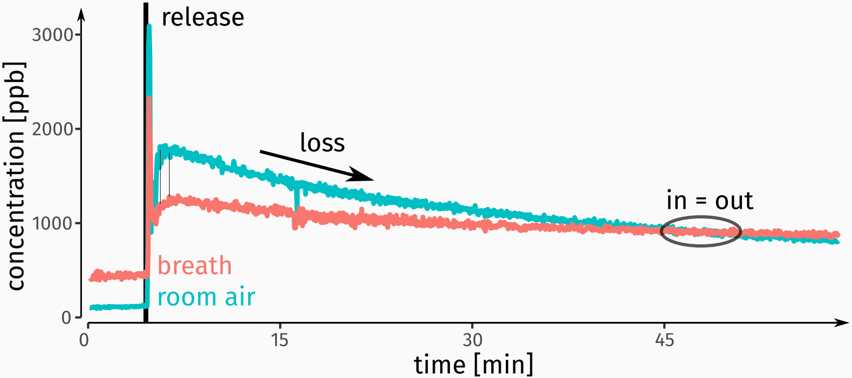


Figure 7: Profile of acetone in breath and room air. After 5 min acetone is released into room air. Room air concentration is then higher than exhaled. Breath signal about 2 to 3 breath strokes delayed.

Acetone Model

- Include effect of upper air way
- Model consists of two respiratory compartments and one body compartment.

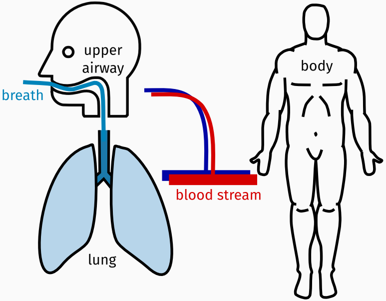


Figure 8: Model for acetone. Toward upper airways transport is in air as well as blood.

Take away

Developments for breath gas analysis

- capture time resolved breath concentration profiles
- estimate inaccessible parameter
- localise processes
- correct inhaled concentrations

References

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Thank you