APPLICATION OF REAL-TIME BREATH MONITORING TO GENERATE METABOLOMIC DATA

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ABSTRACT

Breath gas analysis is a method for non-invasive monitoring of metabolomic processes. With modern mass-spectrometric methods it is possible to take samples so rapidly that the sampling is effectively real-time, and follow individual breath cycles.

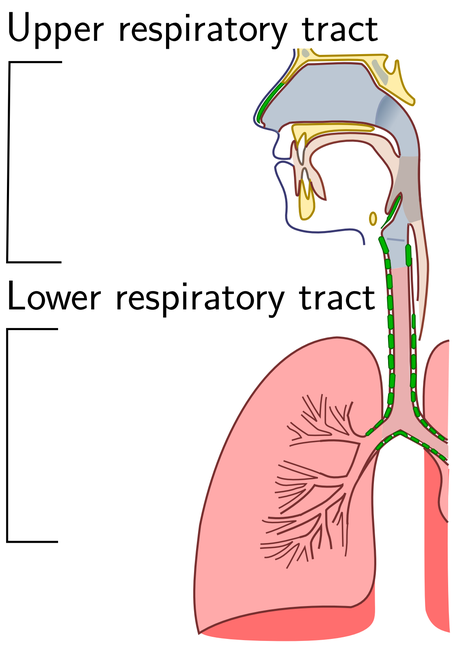
For diagnosis the concentration of metabolites in the body is relevant. Which requires two adjustments: i) for the transfer from blood to air (addressed in King et al. (2011)), ii) correction for inhaled concentration.

We address ii). Typical approaches were to ignore ambient air or subtract room air concentrations. Most metabolites relevant for breath research are simple molecules. Often present in inhaled air – sometimes in concentrations similar or even higher than exhaled. The aim of this study is to construct a method of correction for breath samples.

MODEL

In Ager et al. (2018) we propose a model that takes into account the effect of the upper respiratory tract on exhaled air concentration. Figure 1 shows the physiological relevant components. We were able to show the model under stationary conditions simplifies to already reported behaviour (Wigaeus, Holm, and Åstrand, 1981; Španěl, Dryahina, and Smith, 2013).

FIGURE 1



Credit: *cancer.gov*

We use a model comprising of three compartments: One for the body, one for the lung and one for the upper respiratory tract.

In the lung compartment efficient transfer of metabolites from blood to air takes place. The upper respiratory tract is not as well perfused but its mucus is in contact with inhaled and exhaled air.

For compounds that are highly soluble in the mucus layer significant amounts are absorbed in this mucus and further into the blood stream. This difference is the rationale for adding a further compartment.

CASE STUDY ACETONE

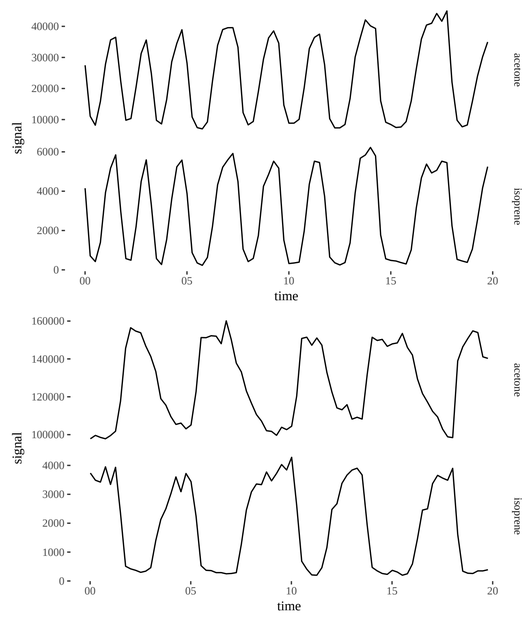
Three volunteers inhaled prepared concentrations of acetone in 6 sessions. Acetone is a well known metabolite, its production as well as metabolisation are well understood. It's also highly soluble in water as well as in fat. A future application of monitoring acetone in breath could be monitoring fat metabolism in real time.

FIGURE 2

Volunteers were wearing a mask with a heated transfer line connected to a Ionicon PTR-TOF 8000 which sampled at a rate of 5 samples per second (typical breath cycle 4 s).

The procedure lasts 45 min. During the sampling also an 10 min ergometer exercise was performed to measure production of isoprene (not shown).

FIGURE 3



We used the time profile of isoprene to track breathing patterns.

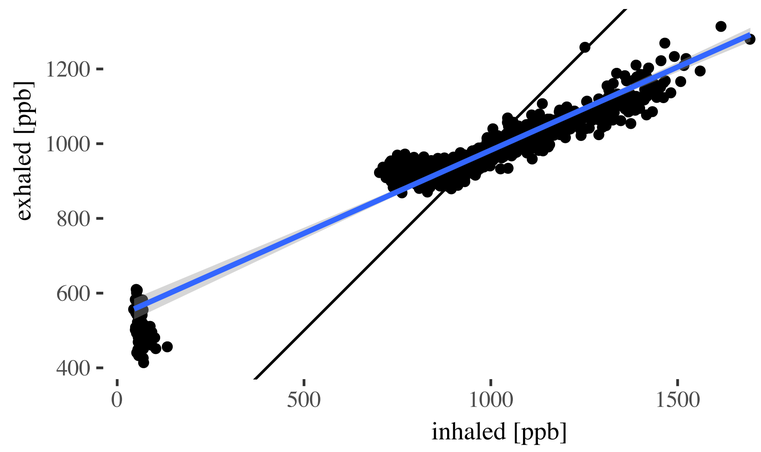
The upper figure shows a typical time profile of breath when inhaling plain room air. The time profiles acetone and isoprene behave similar shapes with local extrema at the same time.

The lower figure shows the case of elevated acetone concentration in inhaled air (2 ppm_V). Both concentration profiles show mirrored behaviour. In this case just tracking local peaks as breath would lead to erroneous data.

INTERPRETATION

Although we would not assume stationary at such small time-scales observations are not significant different to this hypothesis. Which would mean the steady state being a sufficiently good approximation.

FIGURE 4



Plot of exhaled concentration vs. inhaled concentration in ppb_V. The blue line is the estimate of the steady state model, the black line indicates where inhaled and exhaled concentrations are equal.

CONCLUSIONS

- The steady state solution (Ager et al., 2018) is accurate up to current precision (LOD ~ 1 ppm_V).
- Results agree between volunteers as well as (Wigaeus, Holm, and Åstrand, 1981; Španěl, Dryahina, and Smith, 2013).
- Exhaled breath concentration adapts quickly to inhaled concentration (2-3 breath cycles).
- The model from Ager et al. (2018) might be applied to predict corrections for compounds where the coefficients can not be directly obtained.

REFERENCES

Ager, Clemens et al. (Feb. 2018). "Modeling-based determination of physiological parameters of systemic VOCs by breath gas analysis, part 2". In: *Journal of Breath Research*. DOI: 10.1088/1752-7163/aab2b6.

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