
Modeling the dynamic of breath methane concentration profiles during exercise on an ergometer

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ABSTRACT:

We develop a simple model based on mass balance equations which describes the dynamic of breath methane concentration profiles during exercise on an ergometer. With the help of this model it is possible to calculate the endogenous production of methane in the large intestine by measuring breath gas concentration of methane.

1 INTRODUCTION

Methane plays an important role in atmospheric chemistry, and it is the second principal anthropogenic greenhouse gas after carbon dioxide. Its average atmospheric concentration is currently about 1.8 ppm. It is produced primarily by methanogens under anaerobic conditions in wetlands, farmlands, landfills, the gastrointestinal tract of mammals, and by non-microbial emissions from fossil fuel use and biomass burning.

Various studies demonstrated that blood-borne methane in humans is mainly originating from anaerobic fermentation in the large intestine. Methane can then traverse the intestinal mucosa and be absorbed into the systemic circulation. Since methane has a low solubility it is rapidly excreted by the lungs. If the methane concentration of exhaled breath exceeds the ambient air level by 1 ppm, the subject is considered to be a methane producer. Approximately 30-50% of adults were found to be methane producers. Considering methane production, gender, age, and ethnic differences were usually observed, additionally a significant day-to-day variation was reported. However, the factors influencing the number of methanogens and the amount of produced methane are still unexplored.

The methane breath test is increasingly used in the diagnostics of certain gastrointestinal conditions. In clinical practice, a combined hydrogen and methane breath test has been shown to be superior for the diagnosis of carbohydrate malabsorption syndromes and small intestinal bacterial overgrowth. Additionally, numerous studies have found correlations between breath methane levels and diseases such as irritable bowel syndrome, large bowel cancer, and constipation. However, the results are controversial and the significance of endogenous bacterial methane generation is still not known with certainty.

In our recent paper [1] the dynamics of endogenous methane release through the respiratory system has been investigated by measuring breath methane concentration profiles during exercise on an ergometer. In this article we develop a simple model which explains the observed breath methane concentration profiles and allows to calculate the production of methane in the large intestine from measured breath gas concentrations.

2 MODELING METHANE DISTRIBUTION IN THE BODY

Methane is produced by enteric bacteria in the large intestine of humans (part of the intestinal flora) and distributed by the venous blood leaving the intestine into the rest of the body. From

the lung it is released into breath. The basic equation which describes the connection between breath and venous blood concentration of methane reads (Farhi equation)

$$C_A = \frac{C_{\bar{v}}}{\frac{\dot{V}_A}{\dot{Q}_c} + \lambda_{b:air}}, \quad (1)$$

where C_A and C_v denote the methane concentration in the alveolar air (inhaled concentration C_I already subtracted) and in mixed venous blood, respectively. \dot{V}_A is the alveolar ventilation, \dot{Q}_c is the cardiac output, and $\lambda_{b:air}$ refers to the blood-air partition coefficient which is 0.03 for methane. Consequently it is negligible from the Farhi equation

$$C_A = \frac{\dot{Q}_c}{\dot{V}_A} C_{\bar{v}}. \quad (2)$$

Equation (2) shows that the exhaled methane concentration strongly depends on the ventilation-perfusion ratio $r = \dot{V}_A / \dot{Q}_c$. This can be verified by changing the breathing pattern (e.g., hyperventilation) at rest as demonstrated in figure 4a-b in [1].

The ventilation-perfusion ratio r at rest is approximately one and doubles for a moderate exercise with 75 Watts since the cardiac output increases approximately two fold while the ventilation increases four fold. Hence one would expect from Equation (2) that the alveolar concentration of methane should decrease by a factor of two when exercising.

However, measurements [1] of breath methane concentrations show instead a drop by a factor of 3 to 4 when exercising with 75 Watts as demonstrated in figure 2 in [1].

This is intuitively clear. The intestinal bacteria are the only source of methane. About 15% of the blood flow at rest of 5 l/min go through the intestine (=0.75 l/min). When exercising the absolute blood flow through the intestine stays constant but the relative blood flow decreases since most of the blood flow powers the working muscles. Hence the relative contribution of the venous blood from the intestine with its high methane concentration to the mixed venous blood decreases.

To model the dynamic of breath methane concentrations in exhaled breath when exercising we therefore use a three compartment model based on mass balance equations.

The structure of this model consists of a lung compartment, a gut compartment, and a richly perfused compartment which comprises the rest of the body. It is shown in Figure 1.

The system of mass balance differential equations for this model reads

$$\begin{aligned} \tilde{V}_A \frac{dC_A}{dt} &= \dot{V}_A (C_I - C_A) + \dot{Q}_c (C_{\bar{v}} - C_a), \\ \tilde{V}_{gut} \frac{dC_{gut}}{dt} &= q_{gut} \dot{Q}_c (C_a - \lambda_{b:gut} C_{gut}) + \mu k_{pr}^{gut}, \\ \tilde{V}_{rpt} \frac{dC_{rpt}}{dt} &= (1 - q_{gut}) \dot{Q}_c (C_a - \lambda_{b:rpt} C_{rpt}). \end{aligned} \quad (3)$$

Here \tilde{V}_x denotes the effective volume of the corresponding compartment X , C_I the inhaled concentration, $\lambda_{b:x}$ the partition coefficient between blood and compartment X , C_x the concentration

in compartment X , q_{gut} the relative blood flow into the gut compartment, and k_{pr} the production in the gut compartment. The factor μ reflects the fact that 80% of methane is lost by flatus. We assume that the alveolar concentration C_A and the arterial concentration C_a are in equilibrium according to Henry's law $C_a = \lambda_{\text{b:air}} C_A$.

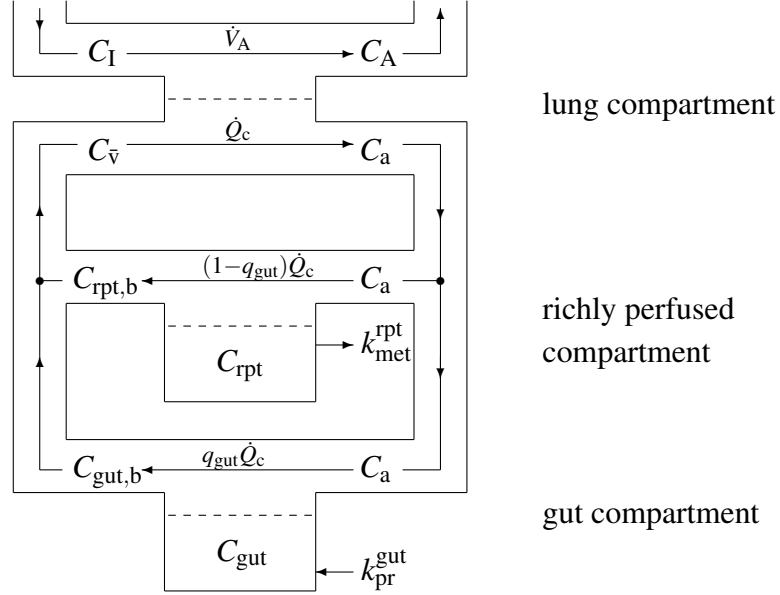


Figure 1. Three compartment model for methane: lung compartment with gas exchange, gut compartment with production of methane by enteric bacteria, and richly perfused tissue compartment containing the rest of the body including muscles (no production).

When in a steady state the system of differential equations (3) reduces to a linear algebraic system. This system can be solved with respect to C_{rpt} , C_{gut} , and k_{pr}

$$\begin{aligned}
 C_{\text{rpt}}(C_I) &= \frac{\lambda_{\text{b:air}}}{\lambda_{\text{b:rpt}}} C_A(C_I), \\
 C_{\text{gut}}(C_I) &= \frac{\lambda_{\text{b:air}}}{\lambda_{\text{b:gut}}} \left(C_A(C_I) + \frac{r}{q_{\text{gut}} \lambda_{\text{b:air}}} (C_A(C_I) - C_I) \right), \\
 k_{\text{pr}}^{\text{gut}} &= \frac{1}{\mu} \dot{V}_A (C_A(C_I) - C_I).
 \end{aligned}$$

(4)

Discussion of the results:

- (i) The methane concentration in the richly perfused tissue compartment C_{rpt} is proportional to the alveolar concentration C_A . However, C_{rpt} is much smaller than C_A since $\lambda_{\text{b:air}}$ ($= 0.03$) is very small.
- (ii) The alveolar concentration C_A is proportional to C_{gut} . The proportionality is given by the relative blood flow times the partition coefficient $\lambda_{\text{b:gut}}$ divided by the ventilation perfusion coefficient r .

- (iii) Since we also expect the production rate k_{pr} to be constant on a “medium time scale” (during an ergometer session) we get $C_A(0) = (C_A(C_i) - C_i)$ is proportional to $1/V_A$. Thus we have $C_A(0) = \mu k_{pr}/V_A$.
- (iv) This yields for the production rate: $k_{pr} = C_A(0) V_A / \mu$.

2.1.1 Simulation of an ergometer session.

For the simulation of the breath methane concentration during an ergometer session (see Figure 2) we use step functions for \dot{Q}_c , V_A , and q_{gut} with following values

\dot{Q}_c : 5 l/min (rest) 10 l/min (75 Watts)
 \dot{V}_A : 6 l/min (rest) and 24 l/min (75 Watts)
 q_{gut} : 0.15 (rest) and 0.075 (75 Watts)

and the following model parameters:

$C_i = 1.8$ ppm, $V_{mol} = 27$ l, $\tilde{V}_A = 3$ l, $\tilde{V}_{rpt} = 4$ l, $\tilde{V}_{gut} = 1$ l, $\lambda_{b:a} = 0.03$, $\lambda_{b:rpt} = 0.5$, $\lambda_{b:gut} = 0.5$, $\mu = 0.2$.

Then $C_A(0) = 4$ ppm yields $C_{rpt} = 0.348$ ppm, $C_{gut} = 64.35$ ppm, and $k_{prod} = 4.27$ mg/h.

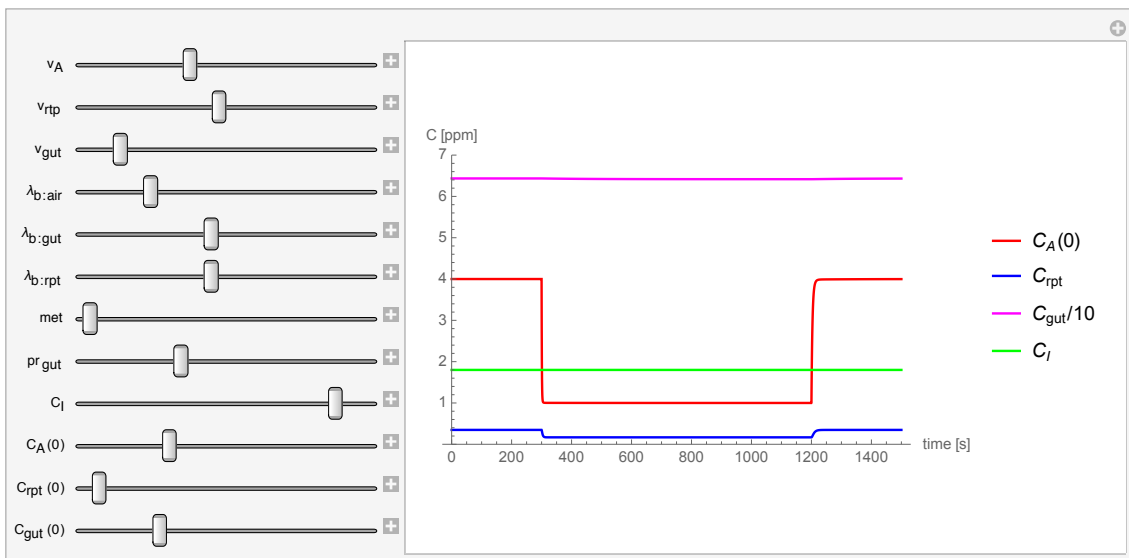


Figure 2. Simulation of an ergometer challenge with the 3-compartment model: (i) rest for 5 min – (ii) 75 Watts for 15 min – (iii) rest for 5 min; $C_A(0) = 5.82$ ppm (red), $C_{rpt} = 0.348$ ppm (blue), $C_{gut} = 64.35$ ppm (magenta), $C_i = 1.8$ ppm (green).

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