# Modeling of Production and Elimination of Hydrogen and Methane in the Human Body

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***Abstract* — The study presents a three-compartment mathematical model of hydrogen and methane production and elimination in the large intestine. The intestinal compartment takes into account the metabolic processes of carbohydrate-utilizing bacteria (hydrogen producers), acetogenic bacteria, and methane producers. The model also includes a highly perfused compartment and a lung compartment through which hydrogen and methane pass into the alveolar space. The model allows for the estimation of the number of microorganisms producing hydrogen and methane in the small intestine based on their concentrations. The aim of the research is to develop a mathematical model that links the concentration of gases in exhaled air with the bacteria that produce them. The model should correspond to the practical measurements. The dynamic model obtained in the study is consistent with the literature sources. The numerical calculations of hydrogen and methane concentrations in exhaled air correspond to practical measurements. Unlike the already known works, this model takes into account the processes of gas synthesis in the intestine in more detail and allows identifying the connection between the concentration of gases in exhaled air and the state of the microbiota synthesizing it.**

## I. Introduction

Studying the microbial community in the intestine is crucial for understanding the role of these microorganisms in human health [1, 2, 3]. However, traditional methods for analyzing the composition of intestinal bacteria can be expensive and time-consuming. An approach is proposed that allows for non-invasive measurement of the gut microbiota composition using samples of exhaled air. By analyzing the concentration of certain gases, including hydrogen and methane, produced by intestinal bacteria, valuable information can be obtained and the number of microorganisms present in the intestine can be estimated [4], as there is a correlation between the concentration of exhaled gases and the fermentative activity and bacterial count in the large intestine [5, 6]. This study proposes a model that links the amount of carbohydrates consumed, the quantitative ratio of corresponding microorganisms, and the concentration of hydrogen and methane in exhaled air.

The human large intestine is a biomechanical environment with low redox potential and a constant temperature of 37 °C [7]. The large intestine consists of three anatomical regions: the ascending (proximal) colon, the transverse colon, and the descending (distal) colon. The large intestine receives nutrient substrates from the small intestine.

Carbohydrates make up about 85% of all substances fermented in the large intestine. The main ones are resistant starch (RS) (not digested by pancreatic enzymes) and non-starch polysaccharides (NSP) [8].

The intestine is covered with an epithelium that secretes mucus. The mucus secretions form a matrix of polymers that allow microorganisms to attach to the intestinal walls, providing resistance to shear forces. The human intestine can be seen as a bioreactor [9]. To create the most comprehensive mathematical model of the intestine, it is necessary to consider the intestine in three aspects: a chemical reactor, a hydraulic model, and a substance transport model [10, 11].

The intestine can be divided into two regions: the lumen and the mucosa. The mucosa provides a medium for the growth and metabolism of various microorganisms. In this model, the lumen and the mucosa are represented as a single compartment washed by a continuous flow of substances. It is assumed that the contents of the compartment are fully mixed, and dead zones are absent [11]. This assumption is partially justified by the presence of peristalsis and gas production. Due to the lack of reliable data and the potential complexity of the model, the hydraulic regime throughout the entire intestine is assumed to be the same. Since microorganisms individually cannot overcome hydraulic forces and washout, they are unable to attach for long periods in the human intestine. Instead, they form aggregates consisting of food particles, epithelial cells, and secretions. The model takes into account the adsorption of acetate, water in the lumen, and the transport of fluids and gases, as well as the resistance to shear for the microbiota [12]. The hydraulic and transport aspects of the model are presented in Fig. 1.

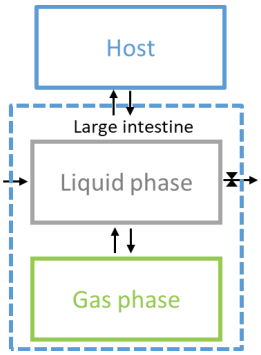


Fig. 1. Block diagram of the hydraulic model of the large intestine, consisting of two compartments [12].

The microbiota of the large intestine represents a branched network of carbohydrate processing [13]. The schematic representation of the network is shown in Figure 2.

The state of the microbiota is closely related to the environment in which it resides. Bacteria in the model are classified into functional groups according to their role in the metabolic chain [14]. Accordingly, there is a specific functional group of bacteria for each substrate involved in its production [15]. By classifying microorganisms into functional groups, conclusions made on a specific individual can be extrapolated to the entire population. Research shows that different compositions of microbial communities have similar functional characteristics [16]. The model assumes that metabolic pathways in the large intestine are limited, and this limitation is due to the redundant species of bacteria belonging to a specific functional group [17, 18]. Numerous studies have shown that despite the diversity of microorganisms among individuals, metabolic pathways, and consequently functional groups, remain the same from organism to organism [19]. This allows for mathematical modeling.

## II. Mathematical model

The compartment of the intestine in the model is described by a state vector:

$$\zeta = (s^T, z, x^T, C^T) \quad (1)$$

where $s = (s_{su}, s_{H_2}, s_{CH_4}, s_{CO_2}, s_{H_2O},)^T$ is the vector of concentrations of dissolved components in the liquid phase (glucose (sugar), hydrogen, methane, carbon dioxide, and water). $z$ is the concentration of complex polysaccharides. . $x = (x_{su}, x_{H_2a}, x_{H_2m})^T$. is the vector of populations of microbiological functional groups corresponding to the substrates they utilize (glucose for hydrogen producers, and hydrogen for methanogenesis and acetogenesis). $C = (C_{H_2}, C_{CH_4}, C_{CO_2})^T$ is the vector of concentrations of components in the gas phase. Let's assume that the volume of

each phase in the compartment does not change. The volume of free-floating liquid and gas in the intestinal lumen is denoted as $V_l$ and $V_g$. $v_m$ and $v_g$ are the volumes of the liquid and gas phases of the mucous membrane. The mass balance equation is written in the following form [12]:

$$\dot{s}_i^l = \frac{q_{in}}{V_l} s_{i,in}^l - \frac{q_n}{V_l} - \gamma_i^l s_i^l + \sum_{j=1}^{5} Y_{i,j}^l \rho_j(\xi^l) - Q_i^l - \mu \frac{k_{pr,i}^{gut}}{v_g} \quad (2)$$

where $\dot{s}_i^l$ is the time derivative of the i-th soluble component in the lumen of the intestine. $\xi^l$ is assumed to be the vector of component concentrations in the liquid phase. $q$ is the rate of flow of free liquid phase through the intestinal lumen. $Q$ is the diffusion across the liquid-gas interface. $\gamma$ is the transport coefficient. For glucose, transport is carried out by diffusion.

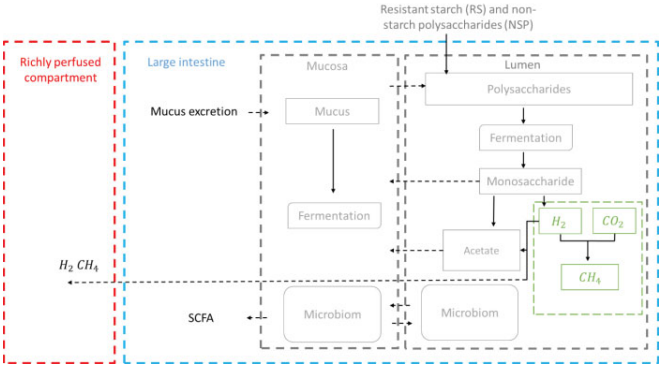


Fig. 2. A flowchart of carbohydrate fermentation and absorption in the large intestine between the host organism and the intestinal lumen. Dotted lines symbolize transport, solid lines symbolize metabolic transformations [12].

Let's assume that soluble components from the upper sections do not enter the large intestine $s_{i,in}^l = 0$. The coefficient $\mu$, production $k_{pr,i}^{gut}$, and volume $v_g$ will be described later.

The kinetic rate of substrate transformation processes (hydrolysis, utilization, and decomposition of glucose and hydrogen by microorganisms in methanogenesis) is represented by the term $\rho_j(\xi^l)$ and is described by the Monod/Contois equation. Tables I-II [35].

It is considered that acetogenesis and methanogenesis are competing processes, the predominance of which depends on the pH level of the environment [20,21]. The model assumes that the pH level is constant throughout the intestine. Let's assume that half of the consumed hydrogen is used by acetogenic bacteria, and the other half is consumed by methanogens.

The rate of biomass decomposition in the model is described by first-order kinetic equations. The biochemical processes of growth synthesis and decomposition, as well as stoichiometric coefficients, are presented in Tables I and II. This form of writing the system of differential equations is known as the Peterson matrix [22].

The values of constants $Y_{i,j}$ from source [12] were revised as a result of computational experiments. The yield coefficient $Y_{i,j}$ is a measure of the amount of product formed per unit of substrate consumed in a biochemical reaction. The element i,j of the Y matrix represents the yield coefficient of the i-th component in the j-th process. $\xi$ is the vector of concentrations in the liquid phase. In the lumen compartment, z represents the concentration of polysaccharides that enter the intestine from the outside and those formed inside the organism by the mucin of the mucous membrane. On the mucous membrane, represents the mucin produced by the host organism [12].

All carbohydrates entering the large intestine in the model are represented as a single polysaccharide $z^l$ and are described by equation (3) [12]:

TABLE I. MATRIX OF BIOCHEMICAL REACTIONS FOR SOLUBLE COMPONENTS [12]

| i components→ | 1 | 2 | 3 | 4 | 5 | 6 | Kinetic rate j process |
|---|---|---|---|---|---|---|---|
| j process ↓ | $s_{su}$ | $s_{ac}$ | $s_{H_2}$ | $s_{CH_4}$ | $s_{CO_2}$ | $s_{H_2O}$ | |
| Hydrolysis polysaccharide | $Y_{su,z}$ | | | | | | $\rho_1(\xi^l)$ |
| Glucose utilization | -1 | $Y_{ac,su}$ | $Y_{H_2,su}$ | | $Y_{CO_2,su}$ | $Y_{H_2O,su}$ | $\rho_2(\xi^l)$ |
| Carbon dioxide utilization: Methanogenesis | | | | $Y_{CO_2,H_2m}$ | | | $\rho_3(\xi^l)$ |
| Hydrogen utilization: Homoacetogenesis | | $Y_{ac,H_2O}$ | -1 | | $Y_{CO_2,H_2a}$ | $Y_{ac,H_2a}$ | $\rho_4(\xi^l)$ |
| Hydrogen utilization: Methanogenesis | | | -1 | $Y_{CH_4,H_2m}$ | $Y_{CO_2,H_2}$ | $Y_{ac,H_2m}$ | $\rho_5(\xi^l)$ |

TABLE II. MATRIX OF BIOCHEMICAL REACTIONS FOR PARTICLES [12]

| i components→ | 7 | 8 | 9 | 10 | Kinetic rate j process |
|---|---|---|---|---|---|
| j process ↓ | $z$ | $x_{su}$ | $x_{H_2a}$ | $x_{H_2m}$ | |
| Hydrolysis | -1 | | | | $\rho_1(\xi) = k_{hyd,z}\frac{zx_{su}}{K_{x,z}x_{su}+z}$ |
| Glucose utilization | | $Y_{su}$ | | | $\rho_2(\xi) = k_{m,z}\frac{s_{su}x_{su}}{K_{s,su}+s_{su}}$ |
| Carbon dioxide utilization: Methanogenesis | | | | $-Y_{CO_2,H_2m}$ | $\rho_3(\xi) = k_{m,CO_2}\frac{s_{CO_2}x_{H_2m}}{K_{s,CO_2}+s_{CO_2}}$ |
| Hydrogen utilization: Homoacetogenesis | | | $Y_{H_2a}$ | | $\rho_4(\xi) = k_{m,H_2a}\frac{s_{H_2}x_{H_2a}}{K_{s,H_2}+s_{H_2}}$ |
| Hydrogen utilization: Methanogenesis | | | | $Y_{H_2m}$ | $\rho_5(\xi) = k_{m,H_2m}\frac{s_{H_2}x_{H_2m}}{K_{s,H_2}+s_{H_2}}$ |
| Decay of $x_{su}$ | | --1 | | | $\rho_6(\xi) = k_d x_{su}$ |
| Decay of $x_{H_2a}$ | | | --1 | | $\rho_7(\xi) = k_d x_{H_2a}$ |
| Decay of $x_{H_2m}$ | | | | -1 | $\rho_8(\xi) = k_d x_{H_2m}$ |

$$\dot{z}^l = \frac{q_{in}}{V_l}z_{in}^l - \frac{q_n}{V_l}z^l - \rho_1(\xi^l) \quad (3)$$

The growth rate of the i-th microbiological functional group:

$$\dot{x}_i^l = \frac{q_{in}}{V_l}x_{i,in}^l - \frac{1}{\tau_i + \frac{V_l}{q_n}}x_i^l + b_i\frac{v_m}{V_l}x_i^l - a_i x_i^l - \frac{q_n}{V_l}x_i^l + \sum_{j=2}^{8}Y_{i,j}^l\rho_j(\xi^l) \quad (4)$$

The coefficients $a_i$ and $b_i$ model the phenomena of attachment and detachment of microorganisms from the intestinal mucosa. $x_i^l$ - the aggregates of microbiological groups also take into account the residence time $\tau_i$ [12]. Let's assume that bacteria from the upper sections do not enter the large intestine $x_{i,in}^l$ = 0. The kinetic parameters of the model, including the reaction yield constants $Y_{i,j}$, growth rates $k_{i,j}$ and Michaelis constant $K_{i,j}$, are described in Table V.

The dimensions of all concentrations in the equations are in moles, except for the concentration of polysaccharides in grams/liter. To calculate the biomass concentration, it is proposed to use the empirical molar mass of 113 grams/mol [23].

The filling rate $q_n$, assuming $V_l$=const, is calculated according to the equation [12]:

$$q_n = q_{in} - \sum_{i=1,2,6}\gamma_i^l s_i^l V_l\frac{w_i}{r_i} - \sum_{i=8}^{10}a_i x_i^l V_l\frac{w_i}{r_i} \quad (5)$$

where $r_i$ is the density and $w_i$ is the molecular weight of the i-th component. Equation (5) imposes constraints on the transport coefficients to ensure a positive flow direction $q_n$. Let's assume that the density and molecular weight are the same for all components, $w_i = w, r_i = r$. The values of the constants are given in Table III.

The mass balance equation for components in the gas phase [12]:

$$\dot{C}_i^l = \frac{q_{g,in}}{V_g}(C_{i,in}^l - C_i^l) - \frac{q_{g,\lg t} - q_n}{V_g} C_i^l + Q_i^l \frac{V_l}{V_g} \quad (6)$$

The transport speed of liquid-gas transport is recorded as [12]:

$$Q_i^l = k_L a(s_i^l - K_{H,i} RTC_i^l \quad (7)$$

where $k_L a$ is the transport coefficient across the liquid-gas boundary multiplied by the phase area, $K_{H,i}$ is the Henry constant (Henry's law - Dalton's law, according to which the solubility (concentration) of a gas in a given liquid is directly proportional to the pressure of that gas above the solution), $R$ is the gas constant, $T$ is the absolute temperature [24]. The constants for the gas phase equations are presented in Table IV.

The gas flow at the outlet is given by:

$$q_{g,out} = q_{g,in} - q_{g,\lg t} \quad (8)$$

where $q_{g,\lg t}$ is the gas flow through the liquid-gas phase, calculated according to [12]:

$$q_{g,\lg t} = \frac{RT}{P_{atm} - p_{H_2O}} V_l (Q_{H_2} + Q_{CH_4} + Q_{CO_2}) \quad (9)$$

where $P_{atm}$ is the atmospheric pressure, $p_{H_2O}$ is the vapor pressure of water, at 37 °C $p_{H_2O}$ =0.08274 bar. Let's assume that the flow of the i-th gases from the upper compartments is zero $q_{q,in} = 0$.

The content of the lumen of the large intestine and the liquid phase is periodically emptied. The emptying in Figure 1 symbolizes a control valve that remains closed until the liquid in the lumen reaches a threshold value. Therefore, the liquid phase in the lumen is modeled as a semi-periodic reactor. The total volume of the intestinal lumen V is constant, but the volume of the liquid and gas phases constantly changes, maintaining the relationship $V = V_l + V_g$. The rate of volume change is recorded as [12]:

$$\dot{V}^l = -\dot{V}_g = q_n \quad (10)$$

Unlike [12, 25], the proposed model does not separately consider the compartments of the intestinal lumen and mucous membrane, as it is necessary to account for mass transfer between the colon and the rest of the body, while considering mass transfer between the mucosa and lumen would unnecessarily complicate the model.

Additionally, the absence of a mucous membrane compartment in the model is compensated by the introduction of coefficients a_i and b_i, which simulate the phenomena of detachment and attachment of microorganisms, preventing complete washout. Furthermore, unlike [12], the proposed model does not account for the difference between the transverse proximal and distal parts of the colon. As demonstrated by modeling [12], the difference in the concentration of emitted gases between these compartments can be neglected. A drawback of the works [26, 27] is the absence of metabolic components in the models.

A part of the hydrogen and methane produced in the intestine is absorbed into the blood, spreads throughout the body, and is exhaled through the lungs. Let's supplement the existing equations with equations for the elimination of intestinal gases through the respiratory system.

The amount of methane/hydrogen exhaled into the lungs through the blood over time t is expressed as [28]:

$$\dot{Q}_C(t)(C_{i,\bar{V}}(t) - C_{i,a}(t)) \quad (11)$$

where $\dot{Q}_C$ is the cardiac output, $C_{i,\bar{V}}$ is the average concentration of the i-th gas in the vein, $C_{i,a}$ is the average concentration of the i-th gas in the artery [28].

On the other hand, the concentration in exhaled/inhaled air is calculated as [28]:

$$\dot{V}_A(t)(C_{i,I} - C_{i,A}(t)) \quad (12)$$

where $V_A$ is the alveolar ventilation, $C_{i,I}$ is the concentration of hydrogen/methane in the inhaled air, $C_{i,A}$ is the concentration of the gas in the alveoli. For methane, the concentration $C_{CH_4,I}$ in room air is approximately 1.8 ppm [29], and for hydrogen, $C_{H_2,I}$ is approximately 0.6 ppm [15].

By combining these two equations, we obtain the following equations for the mass balance of gases in the lungs [28]:

$$\dot{C}_{i,A} = \frac{\dot{V}_A}{\tilde{V}_A}(C_{i,I} - C_{i,A}) + \frac{\dot{Q}_C}{\tilde{V}_A}(C_{i,\bar{V}} - C_{i,a}) \quad (13)$$

In equilibrium, equation (14) is written as $0 = \dot{V}_A(C_{i,I} - C_{i,A}(C_{i,I})) + \dot{Q}_C(C_{i,\bar{V}}(C_{i,I}) - C_{i,a})$ and according to Henry's law - Dalton's law (at constant temperature, the solubility of a gas in a given liquid is directly proportional to the pressure of that gas above the solution)

$$C_{i,a} = \lambda_{b:air} C_{i,A} \quad (14)$$

We obtain that,

$$C_{i,A}(C_{i,I}) = \frac{C_{i,I}}{\frac{\lambda_{b:air,i}}{r} + 1} + \frac{C_{i,\bar{V}}(C_{i,I})}{\lambda_{b:air,i} + r_{V/P}} \quad (15)$$

where $r_{V/P} = \frac{\dot{V}_A}{\dot{Q}_C}$ is the ventilation-perfusion ratio. In respiratory physiology, the ventilation/perfusion ratio is the ratio used to

assess the efficiency and adequacy of the match between two variables: $V$ - ventilation - air reaching the alveoli, $Q$ - perfusion - blood entering the alveoli through capillaries. $\lambda_{b:air,i}$ is the blood-to-air distribution constant.

At rest, the large intestine receives approximately 15% of the total blood flow, around 5 L/min, and the perfusion rate reaches 0.75 L/min in absolute value $q_{gut}$ in Table III. These values satisfy the metabolic needs of the intestine.

The gas elimination model from the large intestine consists of a lung compartment, a large intestine compartment, and a highly perfused compartment that models the remaining part of the organ chain involved in the removal of hydrogen and methane from the body (Figure 3).

Then, the mass balance equation for the large intestine is [28]:

$$\dot{C}_{i,gut} = \frac{q_{gut}\dot{Q}_C}{v_g}(C_{i,a} - \lambda_{b:gut}C_{i,gut}) + \mu\frac{k_{pr,i}^{gut}}{v_g} \qquad (16)$$

where $v_g$ is the effective volume of the intestine equal to the volume of the gas phase in the mucosal membrane. The coefficient $\mu \approx 0,2$ is based on the assumption that 80% of intestinal gases are released through flatus without entering the bloodstream [30]. In this model, $k_{pr,H_2}^{gut}$, $k_{pr,CH_4}^{gut}$ are calculated as the average value of the corresponding gas released in the intestine compartment per day.

Similarly, for the highly perfused compartment symbolizing the rest of the body (including muscles) [28]:

$$\dot{C}_{rpt} = \frac{1-q_{gut}}{\tilde{V}_{rpt}}\dot{Q}_C(C_{i,a} - \lambda_{b:rpt}C_{i,rpt}) - \frac{\lambda_{b:rpt}k_{i,met}^{rpt}}{\tilde{V}_{rpt}}C_{i,rpt} \qquad (17)$$

where $\tilde{V}_{rpt}$ is the effective volume of the considered compartment, $k_{i,met}^{rpt}$ is the flow caused by the metabolism of the i-th gas within the highly perfused compartment. It is assumed that gas production does not occur within this compartment. According to [27], in the first approximation, the terms with the multiplier $k_{i,met}^{rpt}$ can be neglected.

The mixed gas concentration in the veins can be found from the weighted sum of concentrations in the two compartments [28]:

$$C_{\bar{V}} = (1-q_{gut})\lambda_{b:rpt}C_{rpt} + q_{gut}\lambda_{b:gut}C_{gut} \qquad (18)$$

The overall mass balance equation from equations (13), (16), (17) is written as a system of first-order ordinary differential equations [28]:

$$\dot{c}(t) = A_i(t)c_i(t) + b_i(t) \qquad (19)$$

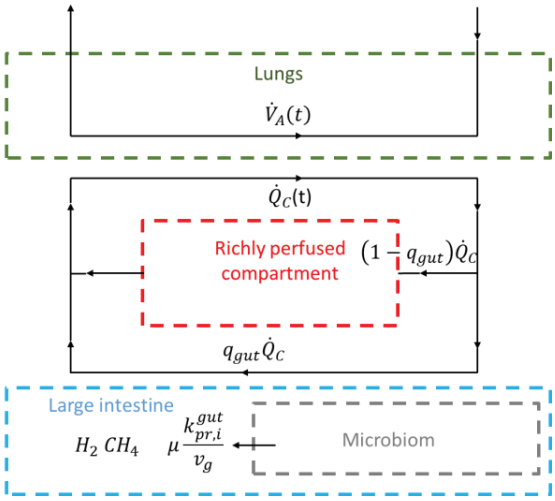


Fig. 3. Three-compartment model of gas elimination from the large intestine [28]

where the vector of unknown concentrations [28]:

$$c_i(t) = (C_{i,A}(t), C_{i,rpt}(t), C_{i,gut}(t))^T \qquad (20)$$

Unlike the study [28], the proposed model significantly refines the processes of gas production $k_{pr,i}^{gut}$ of the investigated gases. The model considers production as a function of the concentration of incoming polysaccharides and the concentration of corresponding producer bacteria, which meets the requirements and interests of this study.

In the study [31], the lung compartment is decomposed into alveoli and bronchi, and gas exchange between the two compartments is characterized by diffusion dependent on the parameter $\lambda_{b:air,i}$, following an exponential law, so that as the parameter approaches zero, diffusion tends to infinity. In this model, for methane, $\lambda_{b:air,i}$ is set to 1, and the difference in concentrations of exhaled gases between the bronchi and alveoli is negligibly small.

The variables and constants in equations 1-20 are described in Tables III-V.

## III. Assumptions and Limitation

Model assumptions:

- Acidity reactions necessary for expressing the pH of the environment are not included in the model.
- The pH is assumed to be the same throughout the entire intestine.
- All polysaccharides entering the large intestine are aggregated into one variable.
- The concentration of microorganisms used in the model does not take into account the physical characteristics of bacteria, which affects the quality of estimation.

- The rest of the body, except for the lungs and intestines, is approximated by a single highly perfused compartment.
- The compartment of the large intestine in the model aggregates two physiologically and functionally separate organs: the intestinal tissue and its vascularization, as well as the mucous membrane and lumen of the intestine, are represented as one compartment.
- Perfusion coefficients do not depend on time and physiological parameters.
- The model uses the Henry-Dalton law, which is valid for ideal solutions and low pressures.
- The coefficients μ and $q_0$ are constant and estimated.
- The model does not take into account the spatial distribution of gases in the compartments.

However, the mathematical model is not without limitations: in addition to the main assumptions associated with the use of laws valid under ideal conditions and other simplifications, the mathematical model has a weak predictive ability. Unlike machine learning approaches, the mathematical model is less flexible and adaptive. In cases where there are extensive nonlinear and hidden relationships between variables, mathematical modeling may encounter insurmountable limitations, making the use of machine learning more preferable. On the other hand, the mathematical model is interpretable, allowing us to understand which variables and factors influence which processes.

## IV. Results

The model presented in the study numerically relates the concentration of hydrogen and methane exhaled by a person to the concentration of bacteria producing these gases in the intestines. Since the model is dynamic, different time scales are used for the two processes, gas production and elimination. The time scale chosen for gas production processes is in days, while for elimination processes it is in minutes. The coefficients of the mathematical model were taken from sources and calibrated through computational experiments.

The two processes, gas production and elimination, are linked through the average gas concentration in the intestines. For the production process, this value is measured in moles/liter/day, while for elimination processes it is converted to moles/liter/min.

The highly perfused compartment is considered as an abstract volume of the organism without specific attachment to particular tissues, so the coefficients and are assumed to be equal to 1, which corresponds to the measured coefficients of perfusion of the gases in rabbit brain tissue [32].

For the process describing gas production in the intestines, the following parameters were taken. The inflow into the intestines is approximately 1 liter/day. The intake of dietary fibers is modeled as an average continuous value, which varies as 10, 20, 50 grams/day. Mucus production is 5 grams/day. The volume of excretion is set at 300ml, meaning that when the volume of the intestines is completely filled, which is 0.7 liters, the volume is reduced to 0.4 liters [33,34]. The change in the volume of the liquid phase of the intestines is shown in Figure 4A.

The rational approach to modeling gas elimination processes from the intestines is intuitive and consists of the following assumptions. The main source of hydrogen and methane in the body is the intestines. During rest, the intestines receive about 15% of the total blood flow, which is approximately 5 liters/minute, and the absolute perfusion is about 0.75 liters/minute, which is sufficient for normal intestinal metabolism [28]. The values of other model coefficients are given in Tables III-V. The results of the modeling are presented in Fig. 4-7.

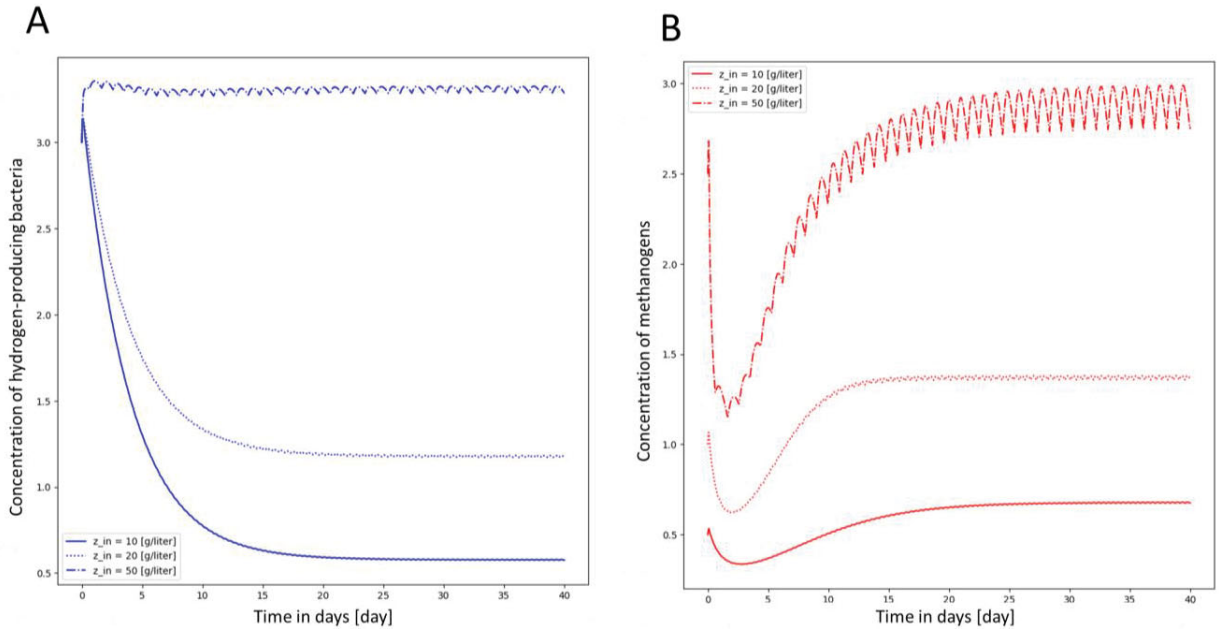


Fig. 4. - concentrations of hydrogen A and methane-producing B bacteria in the intestinal compartment at different flow rates of dietary fibers $z_{in}$

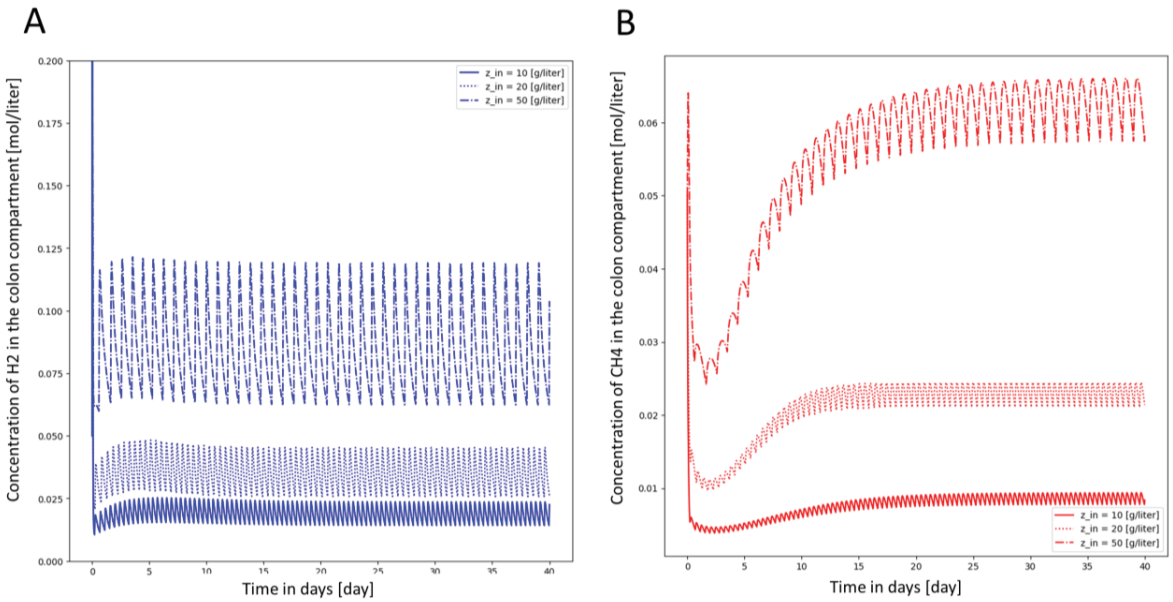


Fig. 5. A - Concentration of hydrogen in the liquid phase of the intestinal compartment at different masses of dietary fiber intake $z_{in}$ . B - Concentration of methane in the liquid phase of the intestinal compartment at different flow rates of dietary fibers $z_{in}$ .

The modeling was performed on the Google Colab platform and took about 30 minutes. Modeling periodic emptying of the intestines is a resource-intensive process that requires lengthy calculations.

For a flow rate of dietary fibers in the large intestine compartment corresponding to a value of 20 grams/day, the concentration value of hydrogen producers $x_{su}$ is 1.4 and 1.2 moles/liter (Figure 4B). In this case, an average of 0.02 moles/liter of methane and 0.037 moles/liter of hydrogen is excreted in the intestines per day, as shown in figure 4C. Some of the gases transition into the gaseous phase of the intestines, which amounts to 0.00026 moles/liter of methane and 0.0029 moles/liter of hydrogen

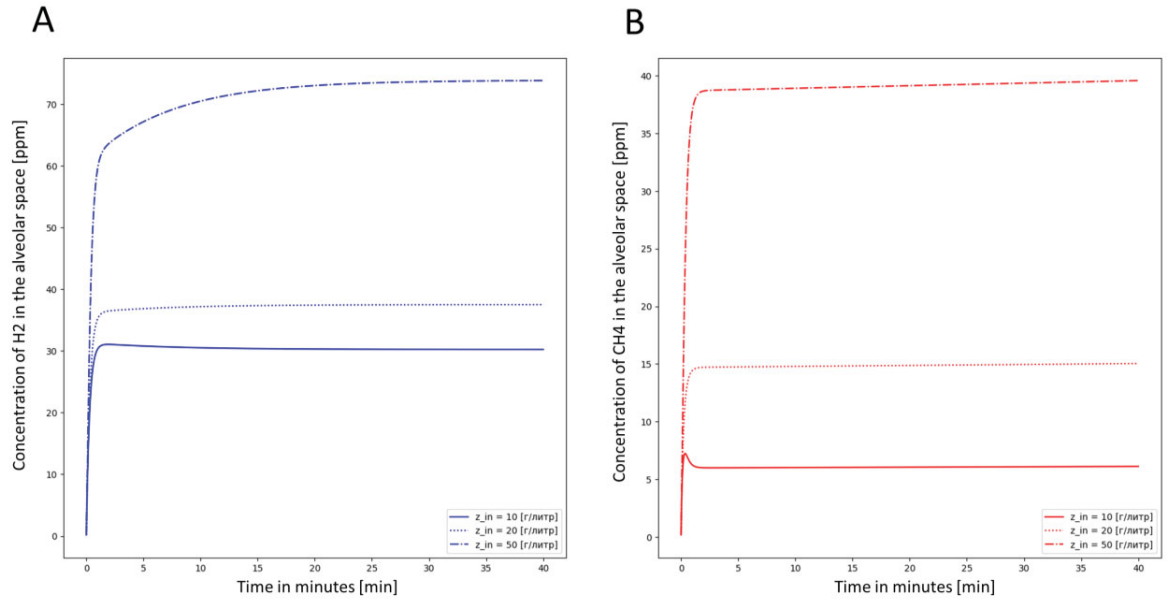


Fig. 6. A - Concentration of hydrogen in the alveolar space according to the proposed model. B - Concentration of methane in the alveolar space according to the proposed model.

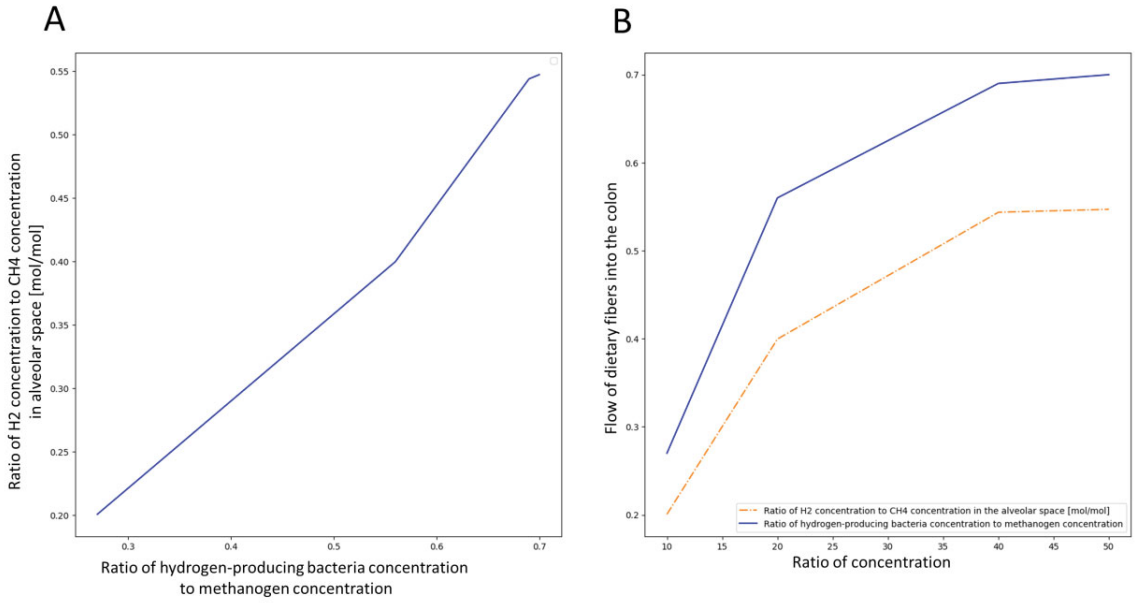


Fig. 7. A - Dependence of $\frac{C_{CH_4,A}}{C_{H_2,A}}$ on $\frac{x^l_{CH_4}}{x^l_{H_2}}$ at values of polysaccharide flow $z^l_{in}$ = (10,20,30,40,50) [g/l]. B - Dependence of $\frac{C_{CH_4,A}}{C_{H_2,A}}$ and $\frac{x^l_{CH_4}}{x^l_{H_2}}$ on polysaccharide flow $z^l_{in}$ [g/l].

Some of the gases are released into the blood, which is estimated as the production of hydrogen and methane in the intestines equal to $k^{gut}_{pr,H_2}$ = 37 and $k^{gut}_{pr,CH_4}$ = 14 micromoles/(liter min), respectively. The gases released in the intestines with this concentration enter the highly perfused compartment, where their concentration is estimated to be 2.06 and 5.11 micromoles/liter for hydrogen and methane, respectively. They are then released into the alveolar space. Thus, the modeling shows the concentration of hydrogen and methane in exhaled air at levels of 1.36 and 0.54 micromoles/liter or 36.9 and 14.8 ppm, respectively (Fig. 6A-B).

To convert the concentration from x micromoles/liter to ppm, the ratio $\frac{x}{V_m}$ [ppm] was used, where $V_m$ is calculated using the following formula [28].

$$V_m = \frac{RT}{p} = \frac{8.314(273.15+34)}{94600} = 27[liter] \quad (21)$$

Thus, the relationship between the ratio of hydrogen concentration to methane concentration in exhaled air and the ratio of hydrogen producers' concentration to methane producers' concentration in the large intestine has the following form in Figure 7A. This relationship takes a linear form, meaning that the ratio of product concentrations in exhaled air is directly proportional to the ratio of bacterial populations producing them.

According to the presented model, at sufficiently high values of polysaccharide flow $z^l_{in}$, the ratio of methane concentration to hydrogen concentration tends to average values close to 1, which means equality of target gas concentrations in exhaled air. The values of the ratios of hydrogen-producing bacteria concentration to methane-producing bacteria concentration are close to 1/2 (Fig. 7B).

## V. Conclusion

This study provides a mathematical representation of the processes of hydrogen and methane production and elimination in the human body. The model presents the assimilation of carbohydrates in the colon by hydrogen-producing bacteria, shows the dynamics of methane-producing microorganisms metabolism, and proposes mathematical relationships for estimating the concentration of hydrogen and methane in exhaled air. The model also allows for numerical estimation of the concentration of microorganisms from two functional groups, as well as their level of metabolism. Thus, the results of the modeling are consistent with the results of sources and practical data [12, 28]. Further development of the model will require additional experiments and validation.

TABLE III. MAIN PARAMETERS OF THE MODEL FOR THE PRODUCTION AND ELIMINATION OF HYDROGEN AND METHANE IN THE HUMAN BODY [12, 28]

| Parameter | Symbol | ValueUnit of measurement |
|---|---|---|
| Cardiac output | $\dot{Q}_C$ | 5.41 [L/min] |
| Alveolar ventilation | $\dot{V}_A$ | 10.69 |

| | | |
|---|---|---|
| | | [L/min] |
| Average concentration of the i-th gas in the veins | $C_{i,\bar{V}}$ | [mol/L] |
| Arterial concentration of the i-th gas | $C_{i,a}$ | [mol/L] |
| Concentration of the i-th gas in the atmosphere | $C_{i,I}$ | [ppm] |
| Alveolar concentration of the i-th gas | $\dot{C}_{i,A}$ | [ppm] |
| Concentration of the i-th gas in the highly perfused compartment | $C_{i,rpt}$ | [mol/L] |
| Concentration of the i-th gas in the intestinal compartment (Concentration on the mucous membrane) | $C_{i,gut}$ | [mol/L] |
| Effective lung volume | $\tilde{V}_A$ | 4 [liters] |
| Effective volume of the highly perfused compartment | $\tilde{V}_{rpt}$ | 15.22 [liters] |
| Effective volume of the intestine | $v_g$ | 0.129 [liters] |
| Flow caused by the production of the i-th gas inside the intestine | $k_{pr,i}^{gut}$ | [mol/min] |
| Blood-air perfusion coefficient for hydrogen | $\lambda_{b:air,H_2}$ | 0.66 [1] |
| Blood-air perfusion coefficient for methane | $\lambda_{b:air,CH_4}$ | 0.066 [1] |
| Blood-highly perfused compartment perfusion coefficient | $\lambda_{b:rpt}$ | 1 [1] |
| Blood-intestine perfusion coefficient | $\lambda_{b:gut}$ | 1 [1] |
| Proportion of blood flow to the intestine | $q_{gut}$ | 0.15 [1] |
| Proportion of gas entering the bloodstream from the intestine | $\mu$ | 0.2 [1] |
| Concentration of i-th soluble components in the liquid phase | $s_i$ | [mol/L] |
| Concentration of i-th soluble components in the gas phase | $C_i$ | [mol/L] |
| Concentration of i-th bacterial groups | $x_i$ | [mol/L] |
| Concentration of polysaccharides | \ | [grams] |
| Concentration vector in the liquid phase | $\xi$ | |
| State vector of the intestinal model | $\zeta$ | |
| Adhesion coefficient of organisms to the intestinal mucosa | $a_i$ | 0.1 [1/day] |
| Detachment coefficient of organisms from the intestinal mucosa | $b_i$ | 0.3 [1/day] |
| Bacterial decay constant | $k_d$ | 0.01 [1/day] |
| Density of the i-th component | $r$ | 1000 [grams/liter] |
| Molecular weight of the i-th component | $w$ | 113 [grams/mol] |
| Additional residence time of bacteria in the intestinal lumen | $\tau_i$ | 4 [days] |
| Kinetic rate of the j-th process | $\rho_j$ | [mol/L day] |
| Flux across the liquid-gas boundary of the i-th component | $Q_i$ | [liter/day] |
| Atmospheric pressure | $P_{atm}$ | 1.013 [bar] |
| Water vapor pressure | $p_{H_2O}$ | 0.08314 [bar] |
| Gas constant | $R$ | 0.0831 [bar / (mol/L K)] |
| Flow | $q$ | [liter/day] |
| Temperature | $T$ | 310.15 [K] |
| Volume of the liquid phase of the lumen compartment | $V_l$ | 0.7 [liter] |
| Volume of the gas phase of the lumen compartment | $V_g$ | 0.07 [liter] |
| Endogenous mucus production | $\Gamma$ | 5 [grams/day] |

TABLE IV. MODEL PARAMETERS RELATED TO TRANSPORT PROCESSES IN THE INTESTINAL COMPARTMENT [12]

| | | |
|---|---|---|
| Henry-Dalton constant for hydrogen | $K_{H,H_2}$ | $7.2 \cdot 10^{-4}$ [mol/liter]/[бар] |
| Henry-Dalton constant for carbon dioxide | $K_{H,CO_2}$ | 0.0011 [mol/liter]/[бар] |
| Henry-Dalton constant for methane | $K_{H,CH4}$ | 0.0255 [mol/liter]/[бар] |
| Liquid-gas diffusion coefficient multiplied by the phase area | $k_L a$ | 25 [1/1day] |
| Transport coefficient of the i-th component. | $\gamma_{su}$ | 6.3 [liter/day] |
| | $\gamma_{ac}$ | 18.9 [1/day] |
| | $\gamma_{H_2O}$ | 6.3 [1/day] |

TABLE V. KINETIC PARAMETERS OF THE MODEL IN THE INTESTINAL COMPARTMENT [12]

| | | |
|---|---|---|
| Rate of carbohydrate hydrolysis of the component | $k_{hyd,z}$ | $1.2 \cdot 10^3$ [grams / mol day] |
| Maximum glucose consumption by hydrogen producers | $k_{m,su}$ | 7.29 [mol /mol day] |
| Maximum hydrogen consumption by acetogens | $k_{m,H_2a}$ | 130 [mol /mol day] |
| Maximum hydrogen consumption by methanogens | $k_{m,H_2m}$ | 15,5 [mol /mol day] |
| Maximum carbon dioxide consumption by methanogens | $k_{m,CO_2}$ | 15,5 [mol /mol day] |
| Constant equal to the substrate concentration at which the bacterial growth rate is half of the maximum for carbohydrates | $K_{x,z}$ | 29.99 [(mol/liter) / (mol/ liter)] |
| Constant equal to the substrate concentration at which the growth rate is half of the maximum for glucose utilization | $K_{s,su}$ | 0.0026 [mol/liter] |
| Constant equal to the substrate concentration at which the growth rate is half of the maximum for hydrogen utilization by acetogens | $K_{s,H_2a}$ | 0.02 [mol/liter] |
| Constant equal to the substrate concentration at which the growth rate is half of the maximum for hydrogen utilization by methanogens | $K_{s,H_2m}$ | 0.17 [mol/liter] |
| Constant equal to the substrate concentration at which the bacterial growth rate is half of the maximum for carbohydrates | $K_{s,CO_2}$ | 0.17 [mol/liter] |
| Yield coefficients of the i-th component during the utilization of the j-th component in the reaction. | $Y_{su,z}$ | 0.18 [mol] $s_{su}$ / [mol] $z$ |
| | $Y_{H_2,su}$ | 9.2 [mol] $s_{H_2}$ / [mol] $s_{su}$ |
| | $Y_{ac,su}$ | 0.576[mol] $s_{ac}$ /[mol] $s_{su}$ |
| | $Y_{ac,H_2a}$ | 0.143[mol] $s_{ac}$ /[mol] $s_{H_2a}$ |
| | $Y_{ac,H_2m}$ | 0.095[mol] $s_{ac}$ /[mol] $s_{H_2m}$ |
| | $Y_{CH_4,H_2m}$ | 0.27[mol] $s_{CH_4}$ /[mol] $s_{H_2m}$ |
| | $Y_{CO_2,su}$ | 1.1[mol] $s_{CO_2}$ / [mol] $s_{su}$ |
| | $Y_{CO_2,H_2a}$ | -0.5[mol] $s_{CO_2}$ /[mol] $s_{H_2a}$ |

| | | |
|---|---|---|
| | $Y_{CO_2,H_2m}$ | -0.45 [mol] $s_{CO_2}$ /[mol] $s_{H_2m}$ |
| | $Y_{H_2O,su}$ | 1.44[mol] $s_{H_2O}$ / [mol] $s_{su}$ |
| | $Y_{H_2O,H_2a}$ | 0.629[mol] $s_{H_2O}$ /[mol] $s_{H_2a}$ |
| | $Y_{H_2O,H_2m}$ | 0.686[mol] $s_{H_2O}$ /[mol] $s_{H_2m}$ |
| Mass yield coefficient of the j-th bacterial group during the consumption of the j-th component. | $Y_{su}$ | 0.3 [mol] $x_{su}$ / [mol] $s_{su}$ |
| | $Y_{H_2a}$ | 0.043[mol] $x_{H_2a}$ /[mol] $s_{H_2a}$ |
| | $Y_{H_2m}$ | 0.124[mol] $x_{H_2m}$ /[mol] $s_{H_2m}$ |

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