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MODIFICATION OF THE QUASILINEAR CONTROL SYSTEM OF BIOMEDICINE

Abstract. The stability of the respiratory chemostat on a finite time interval was studied and the task of stabilizing the biomedical system of the respiratory chemostat for linear and quasilinear control systems was solved. The study of such regulatory processes in the body plays an important role in the development of technical life support systems, and this applies not only to the voltage regulating system of the of carbon dioxide and oxygen (the "respiratory chemostat" system), but also to a number of other vital systems. First of all, this refers to the "cardiovascular chemostat" system, which, as a biological self-regulation system, has the task of washing the tissue reservoir with fresh blood at such a rate as to maintain the voltage of carbon dioxide and oxygen in tissues at normal or near levels. This is a complex hydrodynamic system of biological self-regulation, the numerous parameters of which are under continuous influence of various kinds of control signals, which in turn depend on external conditions relative to the organism and perturbations. The regulating regime of this system is continuously subjected to sharply and suddenly changing external influences, which have an extreme character.

Keywords: respiratory chemostat, control system, biological system, finite interval, stability.

The problem of the stability of the medical and biological system is one of the main problems of system analysis, mathematical ecology and biomedicine. The task of synthesizing vector control from a given class for a managed medical-biological system and population dynamics of a community with self-limiting by mathematical models is represented in the form of quasilinear equations. The models of biomedicine are considered and the quasi-linear control system of the respiratory chemostat on a finite time interval is investigated.

Changing $F^I_{CO_2}$, we act on an isolated controlled system, it behaves like a simple linear system with constant coefficients. Concentration of $CO_2(F^I_{CO_2})$ functions as a direct driving force. When the respiratory center affects the controlled system, this effect is manifested through ventilation $\dot{V}_A$. When considering the behavior of the chemostat in the steady state, we assumed for convenience that the input signals of the control system are determined by the levels of $pCO_2,[H^+]$ and pO_2 in arterial blood [1].

Receptors are really located on the path of arterial blood, but proceed only from the fact that in each particular considered steady situation the values of these parameters are closely related to their effective values in those places where the real receptors are located.

Let us consider the time course of pulmonary ventilation and changes of pCO_2 in arterial blood with a sudden change in the concentration of carbon dioxide in the inspired air.

To simplify the analysis, we introduce a number of additional assumptions: 1) the lungs are a reservoir of constant volume vented by a continuous gas stream with a dead space equal to zero, and with a uniform composition; 2) the respiratory coefficient (RQ) at each moment of time is equal to one; 3) transport delays in the transfer of blood are negligible; 4) the respiratory center and other tissues are a homogeneous reservoir, washed by a constant flow of blood; 5) arterial blood, venous blood and "tissues"

are characterized by the same linearized absorption curve CO_2; 6) the partial pressures CO_2 in the exhaled air and in the alveolar air and the tension CO_2 in the arterial blood are always equal to each other, as well as the stresses CO_2 in the "tissues" and in the venous blood; 7) the control system is a simple inertial-free (that is, does not contain dynamic elements) proportional regulator.

To obtain equations describing the dynamic behavior of the biomedical system, we use the same general principles of equilibrium and continuity, on which Newton's Laws of motion and Kirchhoff's laws for electric circuits are based. We start with the pulmonary or alveolar reservoir and write down the "continuity equation for carbon dioxide", which states that the rate of change in concentration of CO_2 in the alveolar gas $\dot{\theta}_A$ is equal to the quotient of dividing the difference between the rates of intake and washing out of carbon dioxide by the volume of the reservoir K_A [1]:

$$\dot{\theta}_A = \frac{1}{K_A}[\dot{V}_A F^I_{CO_2} + q_3 - q_1 - q_2] \tag{1}$$

Carbon dioxide enters the lungs with inhaled gas at a rate equal to the product of pulmonary ventilation by the concentration of $F^I_{CO_2}$ in the inspired air, and with venous blood at the rate q_3, and leaves the lungs with exhaled air at the rate q_1 and with arterial blood at the rate q_2. Next, we will write down another equation of continuity for the tissue reservoir: the rate of change in the concentration of carbon dioxide in the tissues ($\dot{\theta}_A$) is equal to the sum of the rates of formation of CO_2 during the exchange (*MR*) of CO_2 with arterial blood flow (q_2) and leaching of CO_2 with venous blood (q_3) divided by the volume of the tissue reservoir K_T:

$$\dot{\theta}_A = \frac{1}{K_T}[MR + q_2 - q_3]. \tag{2}$$

Let us write down three equilibrium equations.

The first of them reflects the equality of concentrations of carbon dioxide in the alveolar and exhaled air:

$$\theta_A = \frac{q_2}{\dot{V}_A}. \tag{3}$$

The second equation describes the equilibrium of concentrations of CO_2 in the alveolar air and in the arterial blood, taking into account the linearized CO_2 absorption curve:

$$\frac{q_2}{Q} = BA_S(\theta_A) + A_i, \tag{4}$$

where Q minute volume of the heart, B - atmosphere pressure, A_S and A_i - respectively, the slope of the linear absorption curve and the ordinate of the point of its intersection with the ordinate axis.

The third equation expresses the equality of carbon dioxide concentrations in tissues and venous blood:

$$\theta_T = \frac{q_3}{Q}. \tag{5}$$

To study the behavior of an isolated controlled system, it is necessary to solve this system of equations. There are different ways for this, but in any case, we should, first of all, choose which of the five dependent variables is considered the output (or outputs) of the system and which of the nine independent variables ($\dot{V}_A, F^I_{CO_2}, MR, K_A, K_T, Q, B, A_S, A_i$) is considered to be the input (or inputs) of the system. We choose the variables θ_T and θ_A as the outputs of the system, and as the input - $F^I_{CO_2}(t)$. Thus, we assume that the variables $\dot{V}_A, MR, K_A, K_T, Q, B, A_S$ and A_i do not change with time. Combine the five obtained basic equations so as to get a differential equation with respect to one of the dependent variables, θ_T or θ_A. So, if we solve equation (3) relative to q_1, (4) - relative to q_2 and equation (5) – relative to q_3.

Substituting these values into equations (1) and (2), we obtain

$$\dot{\theta}_A = \frac{1}{K_A}[\dot{V}_A(F^I_{CO_2} - \theta_A) + Q(\theta_T - BA_S\theta_A - A_i)] \tag{6}$$

and

$$\dot{\theta}_A = \frac{1}{K_A}[MR - Q(\theta_T - BA_S\theta_A - A_i)]. \tag{7}$$

Solving equation (7) with respect to θ_A, we obtain

$$\theta_A = \frac{1}{QBA_S}(K_T\dot{\theta}_T - MR - QA_i + Q\theta_T)]. \tag{8}$$

The differentiation of (8) gives

$$\dot{\theta}_A = \frac{1}{QBA_S}(K_T\ddot{\theta}_{Ti} + Q\dot{\theta}_T)]. \tag{9}$$

Substituting (8) and (9) into (6), we obtain the required equation relative to θ_T:

$$\frac{K_AK_T}{Q\dot{V}_A}\ddot{\theta}_T + \left[\frac{K_A}{\dot{V}_A} + \frac{K_TBA_S}{\dot{V}_A} + \frac{K_T}{Q}\right]\dot{\theta}_T + \theta_T = BA_SF^I_{CO_2}(t) + \frac{BA_SMR}{\dot{V}_A} + \frac{MR}{Q} + A_i. \tag{10}$$

Having obtained the equation with respect to θ_T, we can find θ_A in several ways. From equation (8), find the expression for the concentration θ_A, substituting in (8) the expressions for θ_T and $\dot{\theta}_T$. But there is another method of determination θ_A, analogous to the method used to derive equation (10) with respect to θ_T. It consists in the fact that equation (6) is solved relatively to θ_T, the result obtained is differentiated (in this case, an expression for $\dot{\theta}_T$ is obtained) and the expressions for θ_T and $\dot{\theta}_T$ in equation (7) are substituted. The equation derived in this way has the following form [5]:

$$\frac{K_AK_T}{Q\dot{V}_A}\ddot{\theta}_A + \left[\frac{K_A}{\dot{V}_A} + \frac{K_TBA_S}{\dot{V}_A} + \frac{K_T}{Q}\right]\dot{\theta}_A + \theta_A = F^I_{CO_2}(t) + \frac{K_T}{Q}\dot{F}^I_{CO_2}(t) + \frac{MR}{\dot{V}_A}. \tag{11}$$

Equations (10) and (11) describe the behavior of an isolated controlled system under the assumption that the driving function is the concentration of carbon dioxide in the inspired air $F^I_{CO_2}(t)$. We solve these equations with respect to $\theta_T(t)$ and $\theta_A(t)$ for the case when $F^I_{CO_2}(t)$ represents a jump with amplitude $(F^I_{CO_2}(t))_1$. To solve these equations, we apply the classical method or the Laplace transform method.

The control system should be a "simple proportional regulator that does not contain dynamic elements". We suppose now that the same relation can be written in such a way that the concentration θ_T is included in it, and that it is valid for both transitional and steady-state conditions. We write down the equation of the control system in the following form:

$$\dot{V}_A = k_p[\theta_T - \theta_{Ti}] + \dot{V}_{Ar}. \tag{12}$$

In this equation θ_{Ti} - preset value, $\dot{V}_{Ar}$ - bias signal. The gain of the proportional regulator is k_p.

Equations of motion (12) can be reduced to the following form, assuming $y = \theta_T$:

$$M\frac{d^2y}{dt^2} + R\frac{dy}{dt} + Ky = F, \tag{13}$$

where

$$M = \frac{K_AK_T}{Q\dot{V}_A},\quad R = \frac{K_A}{\dot{V}_A} + \frac{BA_SK_T}{\dot{V}_A} + \frac{K_T}{Q},\quad K = 1,\quad F = BA_SF^I_{CO_2}(t) + \frac{BA_SMR}{\dot{V}_A} + \frac{MR}{Q} + A_i.$$

The angular frequency: $\varpi_n = \left(\frac{K}{M}\right)^{1/2} = \frac{1}{\sqrt{M}}$.

Attenuation factor: $b = \frac{R}{2(KM)^{1/2}} = \frac{R}{2\sqrt{M}}$.

Consequently, the equation (13) takes the form:

$$\frac{1}{\varpi_n^2}\cdot\frac{d^2y}{dt^2} + \frac{2b}{\varpi_n}\cdot\frac{dy}{dt} + y = \left[\frac{1}{K}\right]F = F\,, \tag{14}$$

or

$$\frac{d^2y}{dt^2} + 2b\cdot\varpi_n\frac{dy}{dt} + \varpi_n^2 y = \varpi_n^2 F \tag{15}$$

with boundary conditions

$$y(0) = y_0, \qquad \dot{y}(0) = y_1, \qquad y(T) = y_T, \qquad \dot{y}(T) = 0\,.$$

Using the change of variables

$$x = y - y_T$$

we have that

$$\frac{d^2x}{dt^2} + 2b\cdot\varpi_n\frac{dx}{dt} + \varpi_n^2 x = \varpi_n^2(F - y_T) = u\,,$$

where

$$x = x_1, \qquad u = \varpi_n^2(F - y_T).$$

This differential equation in the Cauchy normal form takes the form:

$$\begin{cases} \dot{x}_1 = x_2 \\ \dot{x}_2 = -\varpi_n^2 x_1 - 2b\varpi_n x_2 + u \end{cases} \tag{16}$$

with boundary conditions

$$\begin{gathered} x_1(0) = x_{10} = y_0 - y_T\,, \\ x_2(0) = x_{20} = y_1. \\ x_1(T) = 0, \\ x_2(T) = 0. \end{gathered} \tag{17}$$

In the vector-matrix form:

$$\dot{x} = Ax + Bu, \qquad x(0) = x_0, \qquad x(T) = 0\,,$$

where

$$A = \begin{pmatrix} 0 & 1 \\ -\overline{\omega}_n^2 & -2b\overline{\omega}_n \end{pmatrix}, \quad B = \begin{pmatrix} 0 \\ 1 \end{pmatrix}, \quad x = \begin{pmatrix} x_1 \\ x_2 \end{pmatrix}, \quad u - \text{scalar}.$$

Fundamental system

$$\hat{O}(t) = A\hat{O}(t), \quad \hat{O}(0) = \hat{A}$$

is represented as:

$$\begin{pmatrix} \hat{O}_{11} & \hat{O}_{12} \\ \hat{O}_{21} & \hat{O}_{22} \end{pmatrix} = \begin{pmatrix} 0 & 1 \\ -\omega_n^2 & -2b\omega_n \end{pmatrix}\begin{pmatrix} \hat{O}_{11} & \hat{O}_{12} \\ \hat{O}_{21} & \hat{O}_{22} \end{pmatrix} = \begin{pmatrix} \hat{O}_{21} & \hat{O}_{22} \\ -\omega_n^2\hat{O}_{11} - 2b\omega_n\hat{O}_{21} & -\omega_n^2\hat{O}_{12} - 2b\omega_n\hat{O}_{22} \end{pmatrix}.$$

Hence we have

$$\begin{cases} \dot{\Phi}_{11} = \Phi_{21}, \\ \dot{\Phi}_{21} = -\varpi_n^2 \Phi_{11} - 2b\varpi_n \Phi_{21}, \\ \dot{\Phi}_{12} = \Phi_{22}, \\ \dot{\Phi}_{22} = -\varpi_n^2 \Phi_{12} - 2b\varpi_n \Phi_{21} \Phi_{22}, \end{cases} \tag{18}$$

$$\hat{O}_{11}(0) = 1, \qquad \hat{O}_{21}(0) = 0, \qquad \hat{O}_{12}(0) = 0, \qquad \hat{O}_{22}(0) = 1.$$

Next we get

$$\ddot{O}_{11} + 2b\omega_n \ddot{O}_{11} + \omega_\delta^2 \hat{O}_{11} = 0, \qquad \ddot{O}_{12} + 2b\omega_n \ddot{O}_{12} + \omega_\delta^2 \hat{O}_{12} = 0. \tag{19}$$

We note that the disturbance $F_{CO_2}^I(s)$ is the direct driving force for the controlled system, and the control value $\dot{V}_A(s)$ excites the system due to parametric influence. The latter is the source of the nonlinearity of the system, as can be verified by substituting the equation (6) in (19).

We obtain the following equation of a closed system with respect to θ_T:

$$a\ddot{\theta}_T + \beta\dot{\theta}_T + \gamma\dot{\theta}_T\theta_T + \theta_T^2 + \eta\theta_T = \lambda, \tag{20}$$

where

$$\alpha \equiv \frac{K_A K_T}{k_p Q},$$

$$\beta \equiv \frac{K_A + K_T BA_S}{k_p} - \frac{K_T \theta_{Ti}}{Q} + \frac{K_T \dot{V}_{Ar}}{k_p Q}, \quad \gamma \equiv \frac{K_T}{Q},$$

$$\eta \equiv \frac{\dot{V}_{Ar}}{k_p} - \theta_{Ti} - BA_S F_{CO_2}^I - \frac{MR}{Q} - A_i,$$

$$\lambda = \frac{BA_S MR}{k_p} + \left[\frac{\dot{V}_{Ar}}{k_p} - \theta_{Ti}\right]\left[BA_S F_{CO_2}^I + \frac{MR}{Q} + A_i\right].$$

The equation (20) is a nonlinear differential equation, since it contains terms of the second degree $\dot{\theta}_T\theta_T$ and θ_T^2. Since $\dot{V}_A$ is a linear algebraic function of θ_T concentration (equation 6), then the equation of a closed system with respect to $\dot{V}_A$ in the form would be identical to equation (20). Relatively to θ_A, a complex nonlinear equation can also be obtained [2].

Let us consider the stabilization of the motions of the quadratic system (20) on a finite interval of time [4].

We denote $\bar{u} = \dot{V}_{A_r}$ – as control

$$\beta = \beta_1 + \beta_2 \bar{u},$$

$$\eta = \eta_1 \bar{u} - \eta_2, \qquad \gamma_1 = \gamma/\alpha, \qquad \lambda_1 = \lambda/\alpha, \qquad \eta_1 = 1/\alpha,$$

$$\lambda = \lambda_1 + \lambda_2 \bar{u},$$

where