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Full Length Research Paper

Study of periodic breathing and human respiratory system

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A theoretical study of respiratory stability, based on a simple CO_2 and O_2 model of the respiratory system has been investigated. A model of the human respiratory system is proposed which has a satisfactory performance under different physiological conditions. It is shown that the central component is not involved in respiratory instability phenomena such as periodic breathing whereas the peripheral component plays a major role.

Key words: Respiratory, CO_2 and O_2 model, instability.

INTRODUCTION

Mathematical modeling of the respiratory system started with the work of Gray (Gray, 1949) which was published in 1945. He formulated pulmonary ventilation in relation to hydrogen ion concentration, carbon dioxide and oxygen tensions of arterial blood in the steady-state and in doing so becomes the first person to provide a mathematical description of the chemical control of ventilation. Periodic breathing, characterized by rhythmic waxing and waning of the ventilation of the lungs, occurs in respiretory disease. The phenomenon is accompanied by cyclical changes in arterial carbon dioxide partial pressure, which rises with increased ventilation and falls with decreased ventilation. Periodic breathing has been extensively investigated along clinical, experimental and theoretical lines to obtain insight into the underlying mechanisms. The most likely hypothesis is those periodic breathing results from dynamic interactions between the controlled system (also called the plant) and the feed back control loop of the respiratory system.

The theoretical studies are based on the idea that the stability characteristic of the respiratory system determines the occurrence of periodic breathing. Milhorn (Milhorn and Guyton, 1965) calculated the critical value of each parameter at which oscillations in ventilation barely occur. Khoo et al. (1982) and Carley (1988) determined an implicit analytical criterion of stability to study the global influence of parameters.

In this chapter, periodic breathing uses a realistic physiological model of respiration to define an explicit analytical criterion for the stability of the respiratory system. A model of the CO_2 plant and O_2 plant with two state variables (lungs and tissues) based on the law of conservation of mass is developed. The model leads to a two-dimensional nonlinear differential system. Some deductions are made and results have been compared with those of Vielle (1993).

Analysis

The respiratory system can be considered to be made up of two interconnected subsystems: the plant, in which CO_2 processes takes place, and the controller, which regulates CO_2 concentrations in the body with two feed back control loops, central and peripheral.

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Symbols and units used for the model: $\dot{M}$; CO_2 metabolic production rate in tissues, $mLCO_2/S$, **S**; equivalent gas storage; **P**; CO_2 partial pressure, mmHg, **λ„**; controller curve slope, mL/mmHg, **B**; barometric pressure, mmHg, **C**; CO_2 concentration, $mLCO_2/Ml$, $\dot{Q}$; blood flow in cardiovascular loop, ml/S, **V**; volume, ml, $\dot{v}$; air flow in lungs, ml/S, **α**; CO_2 dissociation curve loop $mlco_2/mmHg$, **r**; time lag, s, **β**; CO_2 dissociation curve intercept, $mlCO_2/ml$, **μ**; controller curve intercept, ml/S, **T**; time; **A**, arterial circulation; **AL**; arterial blood leaving lungs; **AT**, arterial blood entering. Tissues, **I**; inspired air, **C**; central controller lungs, **L**; lungs **P**; peripheral controller tissues, **T**; tissues, $\mathbf{v_L}$; venous blood entering lungs and $\mathbf{v_T}$; venous blood leaving; lungs.

The plant consists of the blocks lungs, brain, cerebrospinal fluid and lumped body tissue. Also included are the central receptors of the medulla and peripheral receptors of the carotid body, a blood transport time delay being interposed on gas concentration changes between the lungs and carotid body receptors. Figure 1 shows tissues, in which CO_2 is produced; lungs, in which CO_2 is eliminated; and the cardiovascular loop, in which CO_2 is transported from lungs to tissues (arterial circulation) and from tissues to lungs (venous circulation).

Tissues and lungs are assimilated to two homogeneous compartments, each with a uniform CO_2 concentration, whereas the cardiovascular loop is viewed as a component producing a time lag in the arterial CO_2 concentration from lungs to tissues (arterial time lag) and in the venous CO_2 concentration from tissues to lungs (venous time lag). The symbols and units used for the model are defined in this work above.

Plant equations

The law of conservation of mass to CO_2 in tissue compartment (Figure 1), the rate of change in the amount of CO_2 in the tissues is expressed as:

$$\frac{d(v_T C_T(t))}{dt} = \dot{Q}C_{AT}(t) - \dot{Q}C_{vT}(t) + \dot{M} + \frac{v}{p_b - 47}\cdot\frac{dp_{ACO_2}}{dt}$$

$$+ \frac{p_{ACO_2} - p_{ICO_2}}{p_b - 47}\cdot\frac{dv}{dt} \quad (1)$$

Where; $\dot{Q}C_{AT}$ is the rate at which CO_2 is brought into the tissues by the arterial blood, $\dot{Q}C_{vT}$ the rate at which CO_2 leaves the tissues with the venous blood, $\dot{M}$ the rate at which CO_2 is produced inside the tissue, v is the volume and $(p_b - 47)$ is barometric pressure less water vapour pressure at body temperature.

Now, the rate change in the amount of CO_2 in the lungs is expressed as:

$$\frac{d(v_L C_L(t))}{dt} = \dot{Q}C_{vL}(t) - \dot{Q}C_{AL}(t) + \dot{v}C_I - \dot{v}C_L(t) + \frac{v}{p_b - 47}\cdot\frac{dp_{ACO_2}}{dt}$$

$$+ \frac{p_{ACO_2} - P_{ICO_2}}{p_b - 47}\cdot\frac{dv}{dt} \quad (2)$$

Where; $\dot{v}$ is the air flow in the lungs, C_I are constant parameters. Now, the plant equation in O_2 term can be written as:

$$(C_{aO_2} - C_{vTO_2})\dot{Q}_T + (C_{aO_2} - C_{VBO_2})\dot{Q}_B = \frac{-v}{p_b - 47}\cdot\frac{dp_{AO_2}}{dt}$$

$$+ \frac{p_{IO_2} - p_{AO_2}}{p_b - 47}\cdot\frac{dv}{dt} \quad (3)$$

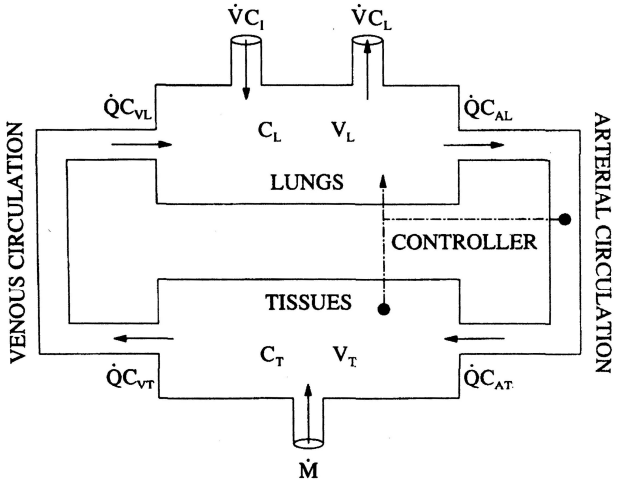

Figure 1. Respiratory system.

Equations (1) and (2) can be written in terms of related CO_2 partial pressures by assuming a single straight line:

$$C_{AL}(t) = \alpha\, p_{AL}(t) + \beta, \quad C_{AT}(t) = \alpha\, p_{AT}(t) + \beta$$

$$C_{vL}(t) = \alpha\, p_{vL}(t) + \beta, \quad C_{vT}(t) = \alpha\, p_{vT}(t) + \beta \quad (4)$$

$$C_T(t) = \alpha\, p_T(t) + \beta \quad (5)$$

Where; α, β, constant parameters, are the slope and intercept of the CO_2 dissociation curve.

The air in the lungs and the arterial blood leaving the lungs yields:

$$p_{AL}(t) = p_L(t) \quad (6)$$

The CO_2 partial pressure in the arterial blood entering the tissues is equal to the CO_2 partial pressure in arterial blood leaving the lungs that is, equation (6) becomes:

$$p_{AT}(t) = p_{AL}(t - r_A) = p_L(t - r_A) \quad (7)$$

Where; the constant parameter is r_A in the arterial circulation time lag. Similarly, for the venous blood:

$$p_{vT}(t) = p_T(t) \quad (8)$$

Assuming equilibrium between the tissues and the venous blood leaving the tissues and:

$$p_{vL}(t) = p_{vT}(t - r_v) = p_T(t - r_v) \quad (9)$$

For blood tissues:

$$C_{vTCO_2}.\dot{Q}_T = C_{aCO_2}.\dot{Q}_T + \dot{M}R_{TCO_2} - \frac{S_T.dC_{TCO_2}}{dt} \quad (10)$$

$$C_{vTCO_2} - \dot{Q}_T = C_{aO_2}.\dot{Q}_T - \dot{M}R_{TO_2} - \frac{S_T.dC_{TO_2}}{dt} \quad (11)$$

For brain tissues:

$$C_{vBCO_2}.\dot{Q}_B = C^1_{aCO_2}.\dot{Q}_B - \dot{M}R_{BCO_2} - \frac{S_B.dC_{BCO_2}}{dt} \quad (12)$$

$$C_{vBO_2}.\dot{Q}_B = C^1_{aO_2}.\dot{Q}_B - \dot{M}R_{BO_2} - \frac{S_B.dC_{BO_2}}{dt} \quad (13)$$

From equations (3) to (8) into equation (1) and (2), we get:

$$\frac{dp_T(t)}{dt} = -\frac{\dot{Q}\alpha p_T(t)}{v_T} + \frac{\dot{Q}}{v_T}p_L(t-r_A) + \frac{\dot{M}}{v_T} + \frac{v}{p_b-47}.\frac{dp_{ACO_2}}{dt}$$

$$+ \frac{p_{ACO_2} - p_{ICO_2}}{p_b-47}.\frac{dv}{dt} \quad (14)$$

$$\frac{dp_L(t)}{dt} = -\frac{\alpha\dot{Q}}{v_L}p_T(r-r_v) - \frac{\alpha\dot{Q}+vp_L(t)}{v_L} + \frac{\dot{v}p_I}{v_L} + \frac{v}{p_b-47}.\frac{dp_{ACO_2}}{dt}$$

$$+ \frac{p_{ACO_2} - p_{ICO_2}}{p_b-47}.\frac{dv}{dt} \quad (15)$$

These two equations describe the dynamics behavior of the plant with two state variables, the CO_2 partial pressure in the tissues (p_T) and in lungs (p_L).

Analysis of respiration with central regulation

To maintain the CO_2 and O_2 concentrations in physiological range the respiratory controller regulates ventilation in lungs by using information concerning the CO_2 and O_2 partial pressure monitored by chemoreceptors located in the carotid body. With the central feed back control loop, the value of the air flow in lungs is determined at each instant from the value of the CO_2 partial pressure in the tissues monitored by central chemoreceptors.

Assuming a linear relationship between O_2 and iCO_2 partial pressure:

$$\dot{v}(t) = \lambda_C p_T(t) + \mu_C \quad (16)$$

Where the constant parameters $\lambda_C(\lambda_C > 0)$ and μ_C are respectively, the slope and the intercept of the central controller curve.

Equation (16) simplified system (p) in which air flow is now considered a time-dependent variable.

Now, the differential system:

$$\frac{dp_T(t)}{dt} = -\frac{\dot{Q}}{v_T}p_T(t) + \frac{\dot{Q}}{v_T}p_L(t) + \frac{\dot{M}}{\alpha v_T} + \frac{v}{p_b-47}.\frac{dp_{ACO_2}}{dt}$$

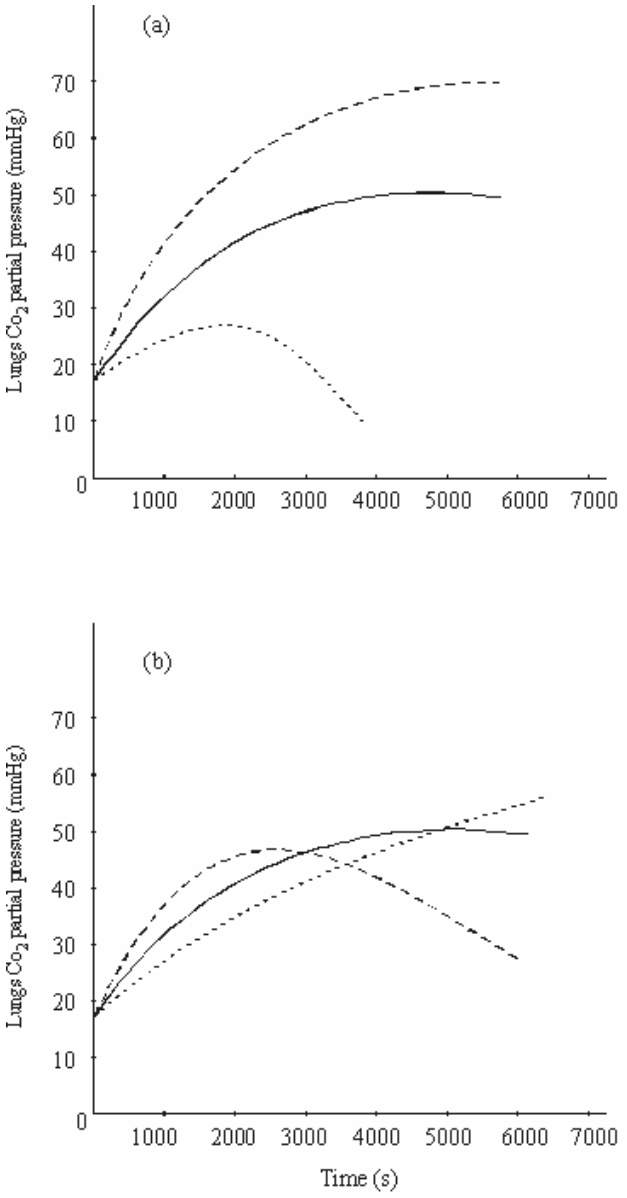

Figure 2. Influence of the respiratory parameters on the lungs component of the trajectory of the plant in a non-stationary state (initial state: Pr = 45.2 mmHg, Pl = 39.0 mmHg). A) arterial circulation time lag ($r_{A)}$, B) the venous circulation time lag ($r_{v)}$.

$$\frac{p_{ACO_2} - p_{ICO_2}}{p_b-47}.\frac{dv}{dt} \quad (17)$$

$$\frac{dp_L(t)}{dt} = -\frac{\lambda_C p_1 + \alpha\dot{Q}}{v_L}p_T(t) - \frac{\alpha\dot{Q}+\mu_C}{v_L}p_L(t) - \frac{\lambda_C}{v_L}p_T(t)p_L(t)$$

$$+ \frac{\mu_C p_I}{v_L} + \frac{v}{p_b-47}.\frac{dp_{ACO_2}}{dt} + \frac{p_{ACO_2} - p_{ICO_2}}{p_b-47}.\frac{dv}{dt} \quad (18)$$

Which describes the dynamics behaviour of the respiratory system

with central regulation.

The equilibrium points of the autonomous non linear ordinary differential system are the constant solution $(p_T(t), p_L(t)) \equiv (\overline{p}_T, \overline{p}_L)$ of the non linear system.

$$-\frac{\dot{Q}}{v_T}\overline{p}_T(t)+\frac{\dot{M}}{\alpha v_T}+\frac{v}{p_b-47}\cdot\frac{dp_{ACO_2}}{dt}+\frac{p_{ACO_2}-p_{ICO_2}}{p_b-47}\cdot\frac{dv}{dt}=0 \quad (19)$$

$$\frac{\lambda_C p_1+\alpha\dot{Q}}{v_L}\overline{p}_T-\frac{\alpha\dot{Q}+\mu_C}{v_L}\overline{p}_L-\frac{\lambda_C}{v_L}\overline{p}_T\overline{p}_L+\frac{\mu_C p_1}{v_L}+\frac{v}{p_b-47}\cdot\frac{dp_{ACO_2}}{dt}$$

$$+\frac{p_{ACO_2}-p_{ICO_2}}{p_b-47}\cdot\frac{dv}{dt} \quad (20)$$

From equations (19) and (20):

$$\overline{p}_T=\overline{p}_L\frac{\dot{M}}{\alpha\dot{Q}}+\frac{v}{p_b-47}\cdot\frac{dp_{ACO_2}}{dt}+\frac{p_{ACO_2}-p_{ICO_2}}{p_b-47}\cdot\frac{dv}{dt}$$

$$\overline{p}_L^2=\left(\frac{\dot{M}}{\alpha\dot{Q}}+\frac{\mu_C}{\lambda_C}-P_I\right)\overline{p}_L-\frac{\mu_C p_I+\dot{M}B}{\lambda_C}-\frac{\dot{M}p_I}{\alpha\dot{Q}}+\frac{v}{p_b-47}\cdot\frac{dp_{ACO_2}}{dt}$$

$$+\frac{p_{ACO_2}-p_{ICO_2}}{p_b-47}\cdot\frac{dv}{dt}=0$$

RESULTS AND DISCUSSION

In this chapter, a simple model of the CO_2 plant was derived from physiological considerations taking into account the fundamental parameters of respiration – the CO_2 metabolic production rate in tissues, the CO_2 partial pressure in the inspired air, the blood flow, the arterial and venous circulation time lags, the volume of tissues and lungs and slope of the CO_2 dissociation curve (Figure 2). The description of the plant is based on a classical two – compartment representation (the tissues and the lungs) for the storage of CO_2 and O_2. This is justified by the results of the analytical and numerical studied of the dynamic behavior of the plant. Breathing was stabilized by inspiring O_2 and Co_2 enriched gas by enlarging stores of these gases of lungs and body at the same time.

The central components of the feed back control loop of respiration are represented by the classical linear relationships between the ventilation and delayed CO_2 partial pressure in the lungs and between the ventilation and the CO_2 partial pressure in tissues. The control components analyze the respective influence on the occurrence of periodic breathing.

Conclusion

The significant role of the lungs volume in respiratory system is demonstrated in this chapter. It would be of good interest to integrate ventilatory mechanics, as previously investigated by Chauvet (1978). The present results to a more realistic representation of respiration. Finally, this analysis should be incorporated into a larger study based on a physiological representation of respiration that takes the cyclic nature of ventilation into account.

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