Mathematical essay

Modeling periodic function of human breathing.

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"*My only value is Breath, -*
said the Arif, firm in the faith -
Without looking back, without looking forward
I am doing one thing: breathing."
(Haft Awrang, y.1485, Nūr ad-Dīn 'Abd ar-Rahmān Jāmī)

Abstract

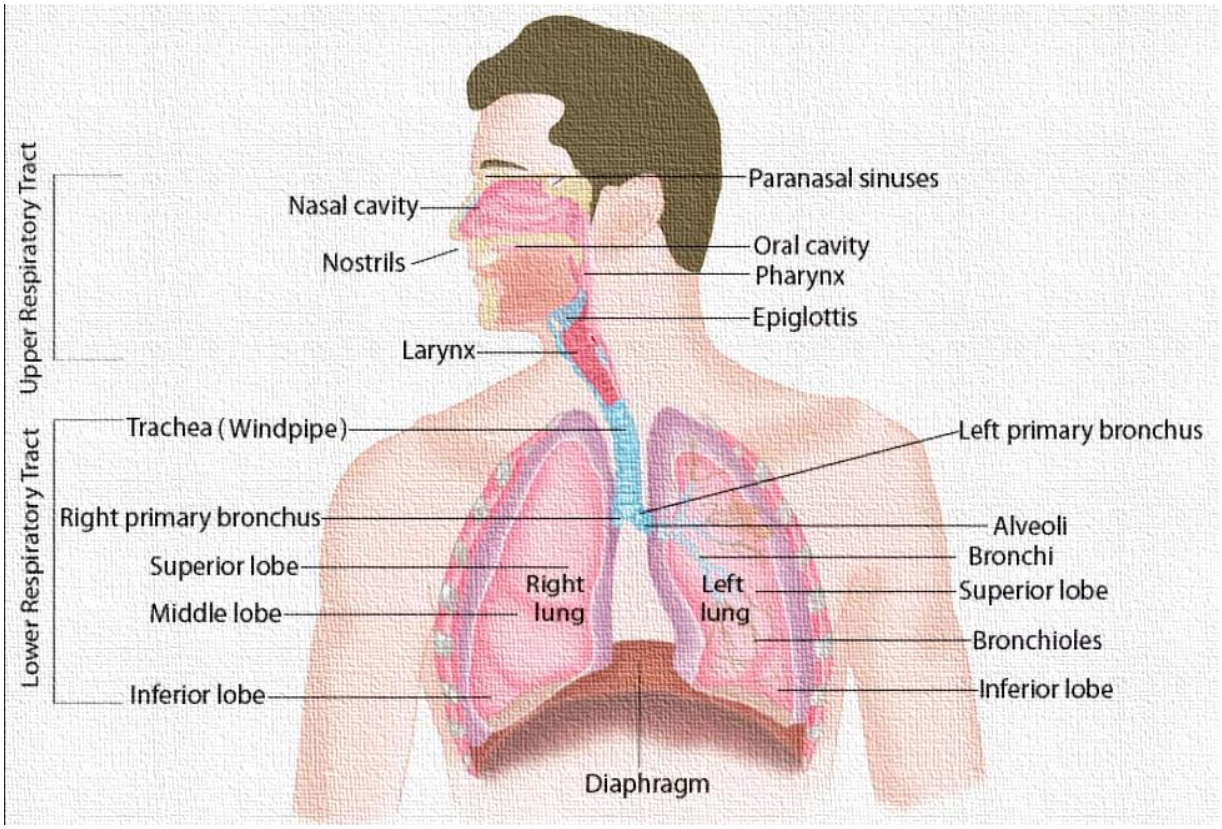
Currently, the existence of such scientific disciplines that are engaged in the fundamental and practical research of various aspects of human behavior, such as psychology, physiology and psychophysiology, as well as a number of other specialized scientific areas of knowledge, which are widely recognized in the world scientific community and actively used in the medical research, as well as in the field of performing the security of the state and business, including for the assessing of the reliability of information provided by a person. Since this scientific direction continues to actively develop, practicing medical and scientific workers, as well as polygraph specialists, should receive the highest quality, relevant and constantly updated knowledge, including about to how the peripheral nervous system and the associated respiratory system, integumentary system and the blood circulation system in the human body responds to the various cognitive and emotional stimuli perceived by it. Changes in breathing are often associated with the peculiarities of the brain's perception to events, occurred in the external environment, as well as with congenital and acquired features of the development of the human body, different past diseases, injuries and harmful effects of the environment reflected to a human being. This topic of scientific research has a huge particular interest of mine, because of the possible choice of my further profession in the field of medicine, psychology and psychophysiology.

Introduction

The respiratory system of the human body is designed to extract oxygen from the atmosphere and return carbon dioxide to the atmosphere. The respiratory system has direct contact with the external environment, and therefore is constantly under the threat of attack by airborne infectious pathogens, against which this system has numerous protective mechanisms. It is important to know

that the process of external respiration has a significant effect on the dynamics of blood pressure. In particular, during inhalation, the pressure inside the chest decreases. This leads to an increase in the lumen of the vena cava and, accordingly, a decrease in their hydrodynamic resistance, which facilitates the suction of blood to the heart and an increase in blood pressure. There is also a slight increase in heart rate during inhalation, commonly called sinus respiratory arrhythmia[1].

Formally, the ventilation process begins with the passage of air through the nostrils or mouth. After which it enters the pharynx, from there into the larynx and then into the trachea (see draft 1). The airway into the larynx and trachea is protected from food or liquid by a cartilaginous lobe called the epiglottis.



Draft 1

From the larynx, air enters the trachea. The trachea is divided into two bronchi - the right and the left, which continue to branch out like a tree, forming a huge number of bronchioles that decrease in size. This branching ends with millions of microscopic thin-walled sacs called autols and

[1] Sinus and Escape Rhythms. Ary L. Goldberger MD, FACC, Alexei Shvilkin MD, PhD, in Goldberger's Clinical Electrocardiography (Eighth Edition), 2013

surrounded by a dense network of capillaries along which red blood cells move, taking oxygen from the air contained in the autols, and transferring carbon dioxide brought from organs and tissues to them.

We must understand that the gas exchange in the lungs is the basis of all metabolic processes in the human body. The exchange of oxygen (O_2) and carbon dioxide (CO_2) in the alveoli, like many other physiological processes in the body, obey the laws of mathematics and physics, namely, the movement of gases is carried out in accordance with their gradient - from an area with a high concentration to an area with a low concentration , the breathing mechanism is described by various mathematical functions, the number of variables in which can reach up to twenty.

During the past years a series of mathematical models has been formulated in an attempt to account for periodic breathing as a manifestation of instability in the respiratory control system[2][3]. The rationale is based on the negative feedback nature of respiratory control. Disturbances in blood gas tensions from desired set points induce changes in ventilation that tend to compensate for the disturbances. Because the blood gas detector and effector organs are separated by circulatory convection delays, “corrective” adjustments in ventilation may potentially lead to either damped or sustained oscillations in the control system.

On average, while resting, an adult performs 14-18 breathing cycles (inhalation and exhalation) per minute. Inhalation begins with the contraction of the muscles in the diaphragm, which separates the abdominal and chest cavities. With the contraction of the diaphragm, its dome flattens and, as a result, an increase in the volume of the chest cavity and expansion of the lungs begin. Following the contraction of the muscles of the diaphragm, contraction of the external intercostal muscles, located between the ribs of the chest, begins. This leads to a lift and expansion of the chest and an additional increase in the volume of the chest cavity. When, in the exhalation phase, all these muscles relax, the volume of the chest cavity and, accordingly, the lungs decrease, the pressure in them increases, and the air flow from them rushes out. The ratio of the duration of

[2] Grodins F.S., J. Buell and A. Bart. A mathematical analysis and digital simulation of the respiratory control system. J. Appl. Physiol. 22: 260-276, 1967.

[3] Horgan J.D., Lange D.L. Analog computer studies of periodic breathing. IRE Trans. Biomed. Elec. 9: 221-228, 1962.

inhalation to the duration of exhalation in a person at rest is 1: 1.2. This ratio is called the Störring-Benassi[4] coefficient, which also shows that the ratio of the duration of inhalation and exhalation of a person depends on the level of a person's emotional tension, or acquired physiological characteristics. For an average adult, the amount of air exchanged in the lungs in one breathing cycle is approximately 500 ml.

The regulation of the respiratory cycle is carried out by the somatic nervous system. Respiratory control centers are mainly located in the medulla oblongata, which is part of the brainstem. The nature of the respiratory cycle could be changed as a result of changes in the chemical composition of the blood, namely, deviations from the normal concentration of oxygen, carbon dioxide, acidity, etc. Such changes occur as a result of changes in the activity of certain organs or systems of the body. The most important respiratory center that controls the state of blood chemical parameters is the so-called posterior group of respiratory neurons of the medulla oblongata. With a deviation in the indicators of blood composition, neurons of this group[5] send action potentials to the spinal cord, in the cervical region of which phrenic nerves are formed, which innervate the muscles of the diaphragm. These pathways mainly affect the inspiratory phase of the respiratory cycle.

This phenomenon is known as the Hering-Breuer reflex[6], e.g. that during exhalation, the lungs stretch, causing irritation of the mechanoreceptors in the alveoli, intercostal muscles and diaphragm. From these mechanoreceptors, nerve impulses travel along the vagus nerve[7] to the respiratory center of the medulla oblongata, where neurons are activated, initiating relaxation of the respiratory muscles, leading to exhalation. Thus, the human body has a physiological mechanism that provides a fairly stable rhythm of respiratory movements. An irregular breathing pattern can occur in individuals with organic brain diseases, as well as those under the influence of pharmacological

[4] Review of Gustav Störring's Mental Pathology and Its Relation to Normal Psychology. Boris Sidis. The Journal of Philosophy, Psychology, and Scientific Methods, 1908, 5, 382-389;
[5] https://qbi.uq.edu.au/brain/brain-anatomy/types-neurons;
[6] https://www.britannica.com/science/Hering-Breuer-reflex;
[7] https://en.wikipedia.org/wiki/Vagus_nerve/.

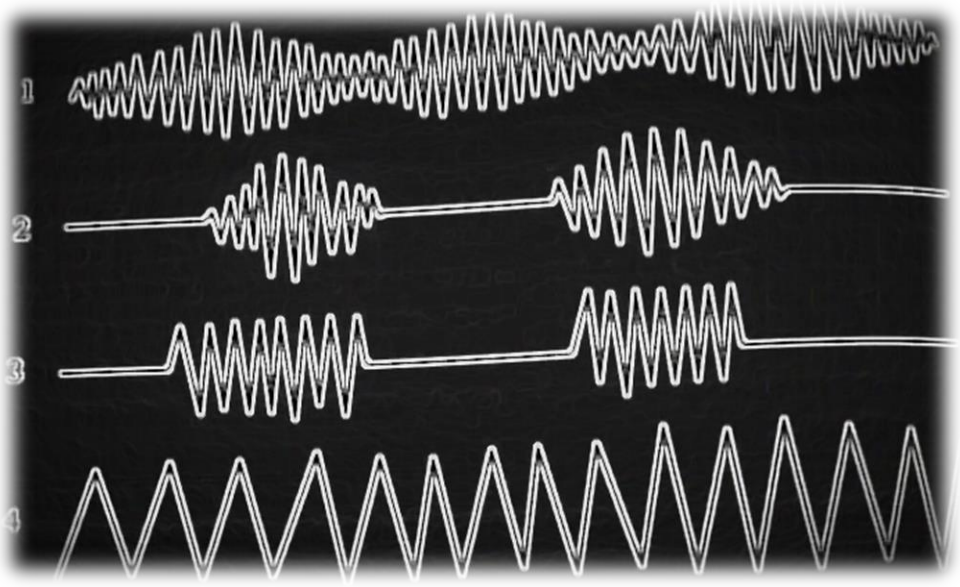
substances or illegal drugs, that depress the respiratory center. Here only will mark few pathological breath types[8] (see draft 2):

1. **Grokko's breathing** - a wave-like increase in the amplitude of breathing, followed by its decrease;

2. **Cheyne-Stokes** breathing - an increase in the amplitude of breathing with its subsequent decrease and apnea up to 25-60 seconds;

3. **Biotta breathing** - breathing movements with constant amplitude, suddenly stopping with pauses up to 30 seconds;

4. **Kussmaul's breath** - deep, rare, noisy breathing.



Draft 2

Investigation

Scope of the model.

This model is explicitly designed to investigate approximate 10-15 ventilatory oscillators referred to as periodic breathing[9]. This model is intended to describe the control system responses to transient disturbances from an equilibrium condition but not the transition from one equilibrium to another. Restricting the model to operate at selected equilibria allows us to linearize the inherently nonlinear equations describing the physiological control system. The linearized model may predict

[8] https://en.sodiummedia.com/4280182-the-most-common-pathological-types-of-respiration.
[9] onward – PB.

the conditions sufficient for oscillations and the frequency of at least the first few oscillations (18), it cannot be used to predict the precise magnitude or morphology of the respiratory parameter oscillations inherent in PB.

Variable	Description	Units
t	time	s
d	partial derivative	
Q_c	cardiac output	l/s
C_{co2}	CO_2 concentration	
$Cvco_2(t)$	mixed venous CO_2 concentration	
$Caco_2(t)$	mixed arterial CO_2 concentration	
$Faco_2(t)$	alveolar CO_2 mole fraction	BTPS (Body Temperature and Pressure, Saturated)
$Fico_2(t)$	inspired gas CO_2 mole fraction	BTPS
P_{co2}	partial pressure of CO_2	Torr (≈ 133.32 Pa)[10]
$Pvco_2(t)$	mixed venous P_{CO_2}	Torr
$Paco_2(t)$	arterial P_{CO_2}	Torr
$PAco_2(t)$	alveolar P_{CO_2}	Torr
$PIco_2(t)$	inspired gas P_{CO_2}	Torr
$P_{cr}(t)$	$P_{CO_2}(t)$ at chemoreceptor	Torr
$Pa^0co_2(t)$	equilibrium value of $Paco_2(t)$	Torr
P_B	barometric pressure	Torr
P_w	water-vapor pressure at body temperature	Torr
K_{s1}*	Slope of CO_2 dissociation curve at BTPS	$Torr^{-1}$
K_{s2}	CO_2 solubility constant	
$Vaco_2(t)$	total lung volume of CO_2	liters
mlv	effective lung volume of CO_2	liters
V_A	continuous alveolar ventilation	l/s
V_A^0	equilibrium value of V_A	l/s
T_L	lung equilibration time constant	s
f	frequency	s^{-1}
f_c	critical (crossover) frequency	s^{-1}
f_d	disturbance frequency	s^{-1}
f_0	corner frequency	s^{-1}
$A(f)$	controller transfer function	
A	magnitude of $A(f)$	$1 \cdot s^{-1} \cdot Torr^{-1}$
$B(f)$	controlled system transfer function	
$\|B(f)\|$	magnitude of $B(f)$	$Torr \cdot 1^{-1} \cdot s^{-1}$
B	equilibrium value of $\|B(f)\|$	$Torr \cdot 1^{-1} \cdot s^{-1}$
$<A(f)$	phase shift of controller	degrees
$<B(f)$	phase shift of controlled system	degrees
$<D(f)$	phase shift of circulation delay	degrees
|LG(f)|	loop gain magnitude at f	
<LG(f)	Loop phase shift at f	degrees
S	controller set point	Torr
D	pure delay	s
R	relative stability	
Δ	Change from equilibrium value	

Table 1. Definitions of abbreviations

[10] https://en.wikipedia.org/wiki/Torr

Assumptions and symbols.

The following assumptions will be introduced into the model development. 1) The respiratory controller acts instantaneously to adjust alveolar ventilation in linear proportion to deviations of P_{CO_2} from a fixed set point. 2) The sole effect of changes in arterial P_{O_2} is to alter the controller sensitivity to disturbances in P_{aco_2}. 3) detection occurs at the carotid bodies and in the brain stem, with all chemo detection units separated from the lungs by equal circulation delays. 4) Gas exchange in the lungs is a diffusion process between single well-mixed gas and blood compartments. 5) Diffusion equilibrium occurs between these two compartments. 6) No intracardiac shunting of blood occurs. 7) Mixed venous P_{CO_2}, cardiac output, circulation delay, and mean lung volume are constant. 8) A single linear CO_2 dissociation curve applies to arterial and venous blood. The symbols defined in *Table 1* will be employed.

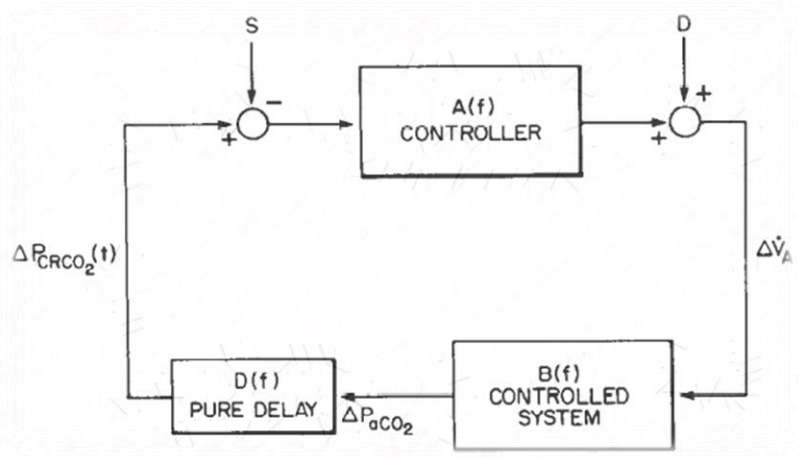
Stability of the linear control system.

Draft 3 shows a linear model of respiratory control consistent with above assumptions. The signal representing P_{aco_2} is detected and compared with a set point value S. Their difference is the "error signal" acted on by the controller, whose output represents alveolar ventilation (V_A). These operations reflect the actions of the chemo receptors, the brain stem respiratory centers, the respiratory muscles, and the mechanics of the biological system. A single controlled system element describes the gas exchange processes. The output of this element represents P_{aco_2}. A pure delay element reflects the circulation transit time.

Each of these linear model elements may be characterized by a transfer function, a complex quantity representing the gain and effective delay or phase shift between input and output. The gain (or magnitude) of the controller transfer function is $|\boldsymbol{A(f)}| = \mathbf{dV_A / d\,(Pa_{co_2} - S)}$ (1). For the controlled system it will be as follows $|\boldsymbol{B(f)}| = \mathbf{dPa_{co_2}/dV_A}$ (2). The pure delay has no effect on the single amplitude $|\boldsymbol{D(f)}| = \mathbf{1}$ (3).

In normal operations, this model achieves an equilibrium characterized by unchanging V_A and P_{aco_2}. Breath holding, apneas, and sighs are modeled as disturbances (D) that may interrupt this equilibrium. The dynamics of the response to such a disturbance are determined by the system

stability. The model of *draft 3* is a single-loop proportional control system; a derivation of the appropriate stability conditions is found in most control theory texts[11].



We shall consider the model to be stable if after any bounded disturbance, the system returns to equilibrium. If the model is unstable, any disturbance will create sustained oscillations.

Draft 3

Mathematically, stability is defined by the loop gain |LG(f)|, a dimensionless system parameter

$$\mathbf{LG(f) = \mathit{A}(f)\mathit{B}(f)\mathit{D}(f)} \qquad (4)$$

that has a magnitude and a phase shift that are function of frequency. The relations between LG(f) and absolute stability is provided by the Nyquist criterion, which states that if the magnitude of $LG(f_c)$ is greater than unity, the system is unstable. The phase shift of 180^o in $LG(f_c)$ implies that the total effective delay through all three system elements is exactly 1 cycle at frequency f_c because an additional 180^o phase shift is contributed by the sign inversion inherent in the controlled system. Unstable operation is characterized by oscillations in V_A and P_{aco_2} with a frequency of f_c and an amplitude that increases with time. In a physical or physiological control system these oscillations will eventually cease to grow as the system exceeds its linear operating range. It is in this context that the sustained oscillations of PB have been hypothesized to reflect unstable control system operation.

Furthermore, the relative stability of human respiration is the tendency for the biological system to damp oscillations and can be characterized by many empirical measures. We shall define one measure [relative stability (R)] and illustrate its application to human respiratory control.

[11] Dorf R.C. Modern Control Systems. Reading, MA: Addison-Wesley, 1974.

Model equations.

Modeling the alveoli and pulmonary capillaries as single well-mixed spaces, and with the assumption that constant temperature, pressure, and humidity are maintained in the gas compartment, the conservation of mass demands conservation of volume, yielding Fick equation[12] for CO_2: $\mathbf{dVaco_2(t)/d}t = \mathbf{Q_c}(t)\mathbf{[Cvco_2(t) - Caco_2(t)]} + \mathbf{V_A}(t)\mathbf{[Fico_2(t) - Faco_2(t)]}$ (5). Several assumptions allow simplification of Eq. 5. 1) Constant cardiac output (Q_C) and venous P_{co2} imply $\mathbf{Q_c}(t) = \mathbf{Q_c}$ (6) and $\mathbf{Pvco_2(t)} = \mathbf{Pvco_2}$ (7). 2) The linear relationship between P_{co2} and C_{co2} concentration (C_{co2}) implies $\mathbf{C_{co2}} = \mathbf{K_{s1}}\,\mathbf{P_{co2}} + \mathbf{K_{s2}}$ (8) where K_{s1} and K_{s2} are constants. 3) Diffusion equilibration between pulmonary capillary blood and alveolar gas, and no intracardiac shunting imply $\mathbf{PAco_2(t) = Paco_2(t)}$ (9). Combining Eqs. 5-8 gives $\mathbf{dVaco_2(t)/d}t = \mathbf{Q_cK_{s1}[Pvco_2 - Paco_2(t)] - V_A}(t)\mathbf{[FAco_2(t) - FIco_2(t)]}$ (10). In addition, from Dalton's Law[13]: $\mathbf{FAco_2(t) = PAco_2(t) / (P_B - P_W) = VAco_2(t) / mlv}$ (11), $\mathbf{FIco_2(t) = PIco_2(t) / (P_B - P_W)}$ (12). Combining Eqs. 9-12 $\mathbf{dPaco_2(t)/d}t = \mathbf{(P_B - P_W)\,[Q_cK_{s1}(Pvco_2 - Paco_2(t)]} - \mathbf{V_A[Paco_2(t) - PIco_2(t)]} / \mathbf{mlv}$ (13). Setting the time derivative in Eq. 13 equal to zero gives the equilibrium expression relating P_{aco_2} to V_A:

$\mathbf{Paco_2} = \mathbf{Q_c(P_B - P_W)K_{s1}Pvco_2} + \mathbf{V_APIco_2} / \mathbf{(P_B - P_W)\,K_{s1}Q_c} + \mathbf{V_A}$ (14). Equation 14 provides an equilibrium expression for the relationship between the controlled system input V_A and its output P_{aco_2}. Even when P_{ICO_2} is zero, this relationship is nonlinear.

Within the local vicinity of any initial operating point, we may satisfy our requirement for a linear transfer function by assuming $P_{ICO_2} = 0$ and approximating Eq. 14 with two terms of its Taylor series expansion[14], obtaining $\mathbf{Paco_2} = -\frac{Qc(P_B - P_W)Ks1Pvco2)}{[V_A^0 + Qc(PB - PW)Ks1]^2)} \times \mathbf{(VA - V_A^0)} + \mathbf{Pa^0co_2}$ (15), where V_A^0, $Pa^0{}_{CO_2}$ = initial equilibrium point. Thus, for incremental changes in equilibrium, the input/output relationship of the controlled system is given by $\frac{\mathbf{dP_{aco2}}}{dV_A} = -\frac{Qc(P_B - P_W)Ks1Pvco2)}{[V_A^0 + Qc(PB - PW)Ks1]^2)} = B$ (16). With the assumption of typical adult values for each parameter Pa_{co_2} fluctuations of plus or minus 5 Torr, about a values 0f 40 Torr, create a <10% error when using Eq. 16 to approximate the underlying steady-state hyperboloid relationship.

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[12] https://derangedphysiology.com/main/cicm-primary-exam/required-reading/cardiovascular-system/Chapter%20811/ficks-principle-cardiac-output-measurement;

[13] https://www.sciencedirect.com/topics/engineering/daltons-law-of-partial-pressure;

[14] https://en.wikipedia.org/wiki/Taylor_series.

For time varying, rather than steady-state departures from V_A^0, Pa^0co_2, Eq. 13 indicates that the gases stored in the controlled system act approximately as a first-order system. To obtain the equivalent time constant of this element we set $P_{Ico_2} = 0$ and solve the homogeneous form of Eq. 13 as $\frac{dP_{aco2}(t)}{dt} + \mathbf{Paco_2(t)} \frac{Q_c(P_B - P_W)K_{s1} + V_A}{mlv} = \mathbf{0}$ (17) to see that $\mathbf{T_L} = \frac{mlv}{Q_c(P_B - P_W)K_{s1} + V_A}$ (18). Identical results for dPa^0co_2/dV_A and T_L can be obtained by the Laplace transform technique if higher than firs-order are disregarded. From Eqs. 16 and 18 we may write the approximate linear controlled system transfer function $|\boldsymbol{B(f)}| = \frac{B}{[(2\pi f T_L)^2 + 1]^{0.5}}$ (19), $\boldsymbol{B(f)} = -[\pi + \tan^{-1}(2\pi f T_L)]$ **radians** (20). The -π term is contributed by the sign inversion in B (Eq. 16), whereas the inverse tangent term derives from the time constant T_L.

Relative stability.

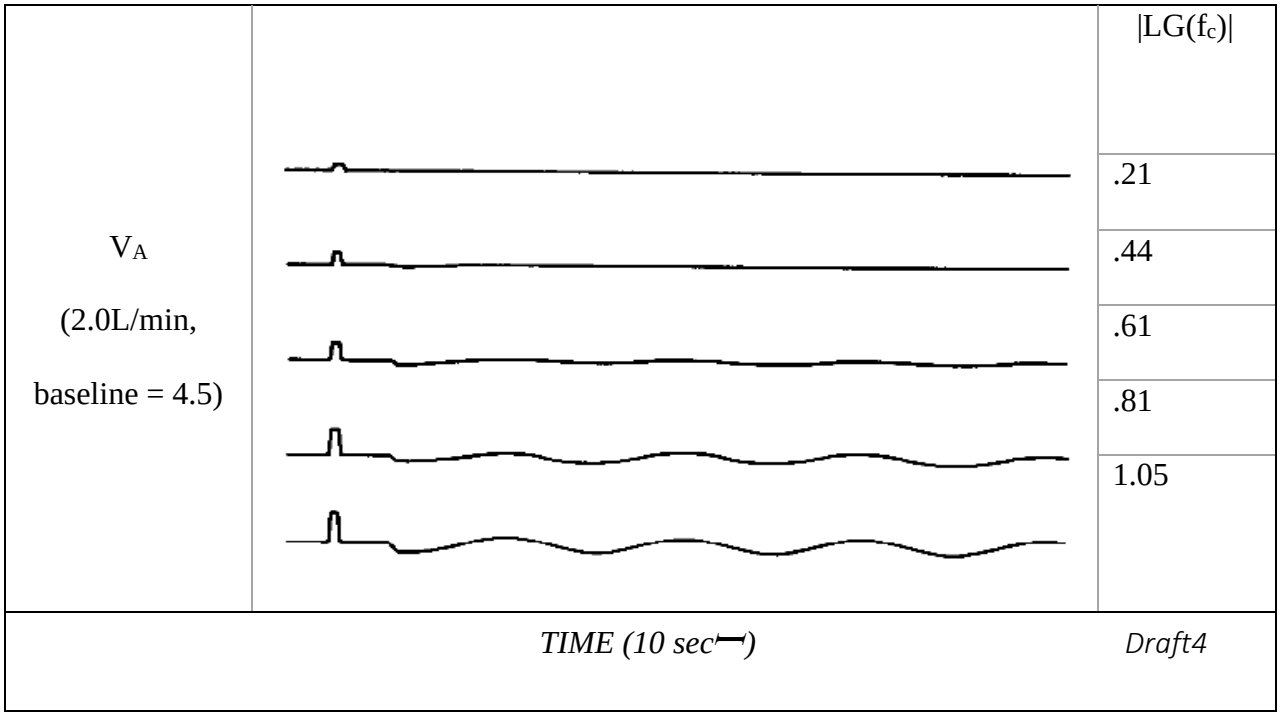
The binary concept of absolutely stable versus unstable model operation is extended by defining relative stability as a continuous measure of system behavior, one extreme of which is unstable operation. Many measures of relative stability have been deployed for physical control system analysis. Commonly, the system response to an impulsive disturbance provides a continuously measure of relative stability[15].

For linear mathematical models, a fixed quantitative relationship exists between the LG and any impulse response measures of relative stability. For this reason, $|\mathbf{LG(f_c)}|$ itself is often used as a measure of relative stability in mathematical models. The full range of relative stability in mathematical models. The full range of relative stability is defined by $\mathbf{0} < |\mathbf{LG(f_c)}| < \mathbf{1}$. $|\mathbf{LG(f_c)}| = \mathbf{0}$ implies an absence of feedback and $|\mathbf{LG(f_c)}| > \mathbf{1}$ implies unstable operations.

The minimal model relationship between $|\mathbf{LG(f_c)}|$ and relative stability is implicitly illustrated in Draft 4, which depicts the controller output V_A, as a function of time, parameterized by $|\mathbf{LG(f_c)}|$. Each waveform illustrates the equilibrium V_A, followed by the response to a 2.5-s, 1-Torr increase in $\mathbf{Paco_2}$. With increasing $|\mathbf{LG(f_c)}|$, both the amplitude and duration of poststimulus oscillation increase. For $|\mathbf{LG(f_c)}| = \mathbf{1.05}$ the model is unstable, and the oscillation amplitude increase from cycle

[15] Relative Stability Analysis of Linear Systems Based on Damped Frequency of Oscillation Sreekala K, Sivanandam S.N., Journal of Electrical and Electronics Engineering (IOSR-JEEE), 2016, 1-5.

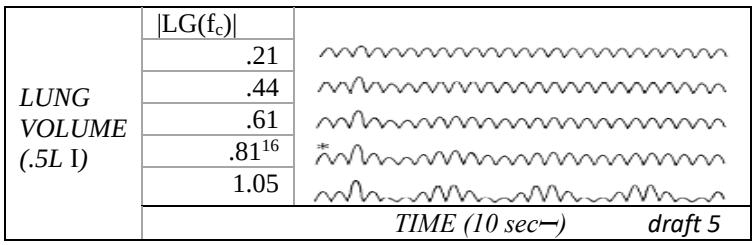
to cycle. This waveform is intended only to illustrate that the initial equilibrium for **LG = 1.05** is unstable. It is not a prediction of the precise cycle morphology, as such a prediction would violate the linearizing assumptions of the model formulation.



For the model, V_A is a continuous nonnegative quantity that is constant equilibrium. The equilibrium state of human respiration, however, is characterized by phasic fluctuations in lung volume and therefore V_A . The controller output of the model may be taken as the net alveolar ventilation that occurs with each breath in human respiration. The lack of direct correspondence between human respiration and model output poses a methodological problem for the following reason. One common technique is to convert recorded breathing patterns to a continuous V_A waveform by updating the V_A estimate once per breath (13, 16). This technique is undesirable in model validation for two significant reasons. 1) Information regarding independent oscillations in the rate and depth of breathing is declared. 2) Because the breathing rate is not fixed. Data samples are uniformly spaced in time. The first consideration may cause a bias toward erroneously accepting model predictions of experimental observations, and the second requires that different considerations be applied to the signal processing of model and experimental waveforms.

In adults, the physiological oscillations in tidal volume (V_T) typical of PB occur above a relatively constant function residual capacity. As an adequate means of representing this “one-

sided" modulation of V_T, the model waveform V(t) is $\mathbf{V(t) = V_A|\sin(0.1\pi t)|}$. The absolute value of the 0.1-Hz sine wave creates a 0.2-Hz phasic output whose amplitude is continuously modulated by the controller. The V(t) wave describes fluctuations in alveolar volume. Dead space is assumed to be constant and is not included. The generation of V(t) neither introduces a nonlinearity into the control loop nor invalidates the model expressions derived for LG(f) and f_c. Draft 5 uses V(t) to illustrate relative stability in the style of draft 4. The **$Paco_2$** disturbance occurs on the third "breath" of each waveform. Postdisturbance oscillations analogous to Draft 4 occur in tidal depth. Again, for $|LG(f_c)| = 1.05$ the waveform represents unstable behavior.

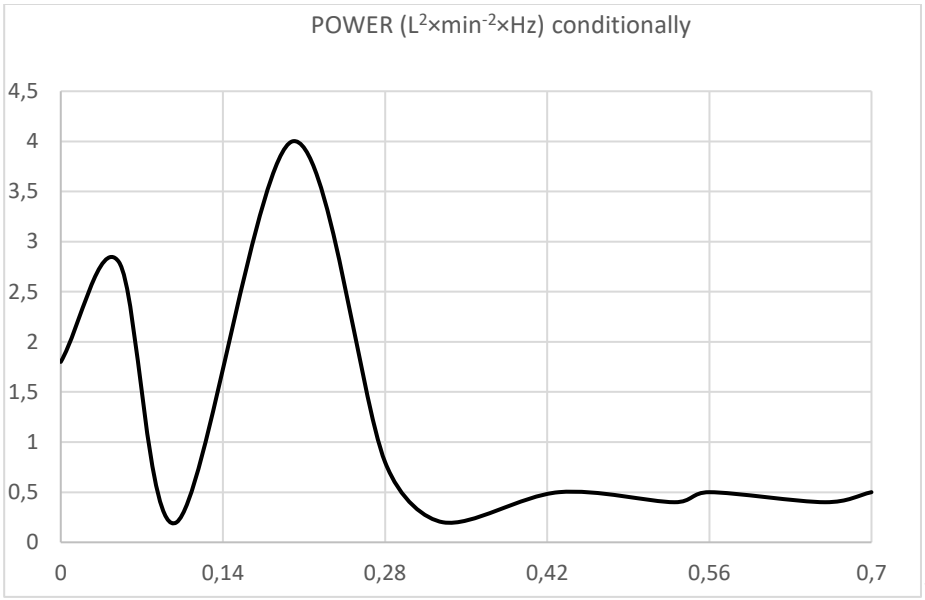


Defining the measure of relative stability.

Draft 5 and draft 4 illustrate the relationship between the system response to an impulsive disturbance and the value of $|LG(f_c)|$. Several common impulse-based measures of relative stability are peak amplitude of the first cycle, time after disturbance of the first peak, and effective damping coefficient. Because the human control system is not truly a linear second-order system, because the system contains significant random variability, we have defined a more robust measure of relative stability based on the power spectrum of the impulse response. Draft 6 depicts the power-density spectrum [S(f)] of the impulse response for $|LG(f_c)| = 0.81$. This power spectrum is dominated by two peaks. The peak centered at 0.05 Hz is inducted by the impulse disturbance and provides a measure of relative stability/ The 20-s period of the induced oscillation is typical of PB and is a function of the phase shifting element of the control system: the circulating relative stability is not designed as the optimal general approach but as an adequate technique for use with transient response that is identically applicable to both model simulations and experimental observations.

[16] Power-density spectrum shown in draft 6

Two waveforms are obtained and sampled at 0.2-s intervals. 1) The peristimulus epoch = 102.4 s of ventilation waveform obtained immediately before the onset of the disturbance. 2) The poststimulus epoch = 102.4 s of ventilation waveform obtained immediately after the onset of the disturbance (henceforth termed the stimulus).



The power-density spectrum of both the pre- and poststimulus time series [$S_0(f)$, $S_1(f)$, respectively] is computed from periodograms. As this technique is intended for physiological waveforms that contain noise, we have employed raised cosine periodogram smoothing with four effective degrees of freedom[17]. To guard against contamination of low-frequency power estimates by leakage we have removed the means and linear trends from the pre- and poststimulus epochs before computing $S_0(f)$ and $S_1(f)$[18]. As an additional safeguard against contamination by nonsinusoidal transient responses we have rejected any epoch for which the first periodogram coefficient (0.0098 Hz) was a local maximum. The relative stability was computed as $\mathbf{R} = \frac{\int_{0.01}^{0.1} S_1(f)df - \int_{0.01}^{0.1} S_0(f)df}{I\int_{f_1}^{f_u} S_0(f)df}$ where f_u and f_1 are upper and lower 10% limits for peak at breathing frequency, respectively, and I is intensity of stimulus in Torr. Thus, R is the power between 0.01 and 0.1 Hz inducted by the stimulus, normalized by the prestimulus phasic breathing power and stimulus size.

[17] Openheim A.V. and Schafer R.W. Digital Signal Processing, Englewood Cliffs, NJ: Prentice Hall, 1975
[18] Glaser E.M. and Ruchkin D.S. Principles of Neurobiological Signal Analysis. New York: Academic, 1976

Conclusion

The foregoing analysis demonstrates several points. Under "normal" conditions the model shows little tendency to oscillate in response to disturbance, but relatively slight changes in physiological or environment conditions may induce significantly more power oscillation. This phenomenon has in fact been observed in spontaneous ventilation during mild hypoxia[19]. The optimal model is the simplest model that performs as well as all more complicated models under the specified conditions. We have focused on two metrics of model performance: 1) the ability of a model to accurately predict the relative stability of any equilibrium operating point and 2) its ability to predict oscillations of the correct frequency, measures that are consistent with those employed in previous modeling work[20]. On these bases the current model compares favorably with previous more complex models while reducing the number of parameters by more than threefold.

The reduction has been achieved by placing additional constraints on the conditions to which the model may be applied. First, the model describes only the local stability about an equilibrium operating point. It cannot simulate the effects of nonlocal perturbations or transitions from one equilibrium to another. I agree with Khoo M.C. that these limitations are acceptable. If the magnitude of $\mathbf{Paco_2}$ perturbations is within ±5 Torr of the equilibrium, the model should account for the relative stability of the biological system.

The dynamic storage and exchange of gases is also modelled by a single element. Although CO_2 stores have been quantitatively modeled for lung, blood, various organs, bones, and other tissues, only the alveolar gas / pulmonary-capillary blood stores can respond significantly to ventilatory fluctuations at the frequency of PB[21]. T_L is the time constant for this compartment and its normal range is 2.5 – 10 s. The normal time constant for a single lumped body tissue compartment is > 30 min. Information transfer from the lungs to chemoreceptors is modeled as a pure delay. It is

[19] Brusil P.J., Waggener T.B., Kronauer R.E., and P. Gulesian. Methods for identifying respiratory oscillation disclose altitude effects. J. Appl. Physiol. 48: 546-556, 1980.
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known that mixing in the heart and vasculature can cause additional signal smoothing with time constants in the 1- to 2-s range[22]. By taking no account of this smoothing effect. The model underestimate fc and therefore overestimate $|LG(f_c)|$. The relative importance of such errors must be determined experimentally.

In experimental waveforms, random noise is combined with the impulse response. Spectrum analysis is often used to characterize random or stochastic systems (8). Mathematical theory requires that the probabilistic description of the system remains fixed during the observation period for valid inferences to be made. Confusion may result when analyzing deterministic impulse responses in the presence of noise. However, if these two components are additively combined, the effect of the noise is simply to introduce uncertainty into the estimation of the impulse-response spectrum. In integrating the power spectra from 0.01 to 0.1 Hz to obtain R, this uncertainty is substantially reduced.

In summary, a minimal model of PB has been described that is characterized by only five independent and readily measured physiological parameters. This model is therefore suitable for direct experimental validation. Despite its conceptual simplicity and analytical format, the relative stability of this model compares favorably with another models. The model, however, is not suitable for investigating large departures from equilibrium such as apnea durations in PB waveforms or transitions between equilibria such as post hyperventilation responses. We have defined a robust measure of relative stability that can be applied to both model simulations and physiological waveforms with use of identical signal-processing techniques. This provides a quantitative basis for characterizing the relative stability of respiration throughout the stable range.

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