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## A REVIEW OF THE ADAPTION OF THE RESPIRATORY SYSTEM

Mandour<sup>✱</sup>, R. El-Awady<sup>✱✱</sup> and H. Meleis<sup>✱✱✱</sup>

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### ABSTRACT:

The main objective of this paper is to consider the analysis of the block diagram representation of the respiratory system. It considers a review of the adaptive structure of the lung and the pulmonary ventilation. The discussion reviews the nature of the adaptive mechanism of the system when the environmental pressure increases or decreases around the normal pressure. Several models of the adaptive structure have been discussed to show the engineering sense of the adaptive respiratory system.

Part (I):

### INTRODUCTION

The most important function of the lung and of pulmonary ventilation is to supply tissue cells with enough  $O_2$  and to remove excess  $CO_2$ . To accomplish this, pulmonary ventilation must increase the partial pressure of  $O_2$  in the alveoli well above that in the venous blood flowing through the alveolar capillaries. This loads the blood flowing to tissue cells with  $O_2$ . It must also lower the partial pressure of  $CO_2$  in the alveoli below that in venous blood. This unloads excess  $CO_2$  from the blood destined for tissue cells. Gases move between alveoli and their capillary blood and between tissues and their capillary blood because of a difference in their partial pressure. In the lungs, the gases are  $O_2$ ,  $CO_2$ ,  $N_2$  and  $H_2O$

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(as water vapour); at 37°C. Their partial pressures are 104, 40, 569 and 47 mm Hg. respectively [1]. These are average values for healthy resting man at sea level; values of  $PO_2$ ,  $PCO_2$  and  $PN_2$  fluctuate from breath to breath and during a single breath. Total ventilation is the volume of air entering or leaving the nose and mouth during each breath (tidal volume) [1]. Alveolar ventilation is the volume of fresh air entering the alveoli each breath. Alveolar ventilation is always less than total ventilation. The discrepancy between alveolar and total ventilation depends on the anatomic dead space, tidal volume and frequency of breathing.

There is a high partial pressure of  $N_2$  in blood and in tissues because man breathes 79%  $N_2$  and is surrounded by 79%  $N_2$ . Since  $N_2$  is not used in metabolic processes, it acts as an inert gas and simply dissolves in blood and body tissues. Henry's law states that such gases dissolve in liquids in direct proportion to their partial pressure.

If man ascends to a high altitude, the  $PN_2$  decreases in inspired air and alveolar gas, but is still high in tissues and blood. Dissolved  $N_2$  must then diffuse from tissues to blood and from blood to alveolar gas until tissue and blood and air tension of  $N_2$  are again equal. If the ascent and resulting decrease in ambient  $PN_2$  occur slowly, nitrogen gradually leaves the tissues and blood by diffusion and no symptoms occur. If however, the ascent is abrupt, the dissolved  $N_2$  in tissues and blood comes out of solution too rapidly to be carried away by diffusion, and gas bubbles form (just as when water that has been equilibrated with air is exposed to a vacuum). If  $O_2$  bubbles form, these can be used locally in tissue metabolism,  $CO_2$  is not involved, since there is very little  $CO_2$  in ambient air. Thus the problem is largely one of  $N_2$  bubbles, which can be removed only by diffusion.

When man breathes air at 3 atmospheres, his alveolar  $P_{N_2}$  rises about 3 fold. This causes 3 times as much  $N_2$  to dissolve in pulmonary capillary blood, and the blood distributes this to body tissues. But blood volume is only 8% of the body volume, and considerable time is needed for blood to carry enough  $N_2$  to tissues to saturate them at new  $P_{N_2}$ . Some tissues that have a rapid blood flow and dissolve little  $N_2$  come to the new  $P_{N_2}$  quickly other tissues, such as fat cells full of fat droplets, have less blood flow per gram of tissue but dissolve 5 times as much  $N_2$  per gram; these come to the new  $P_{N_2}$  much more slowly. If man goes to 3 atmosphere pressure for brief periods, he adds little  $N_2$  to his tissues and will not suffer if he ascends rapidly. If he stays long enough for his tissues to load up more  $N_2$ , he must come up (decompress) slowly. A diver can escape the bends and chokes by breathing  $O_2$  for several hours before diving; this eliminates dissolved  $N_2$  from the tissues. If after  $N_2$  elimination, he dives, breathing air at high pressure, he will accumulate  $N_2$  but the total body  $N_2$  will be much less because his tissues started near zero level of  $N_2$ .

#### Part (II):

#### THE ADAPTIVE STRUCTURE OF THE RESPIRATORY SYSTEM.

The respiratory center in the brain is responsible for the adaptation or regulation of breathing due to any changes of respiratory parameters. The informations go to brain by neural pathways. Regulation depends on:

- ) Local gas pressures and PH in blood and in brain tissue (cerebrospinal fluid), allowing for direct "chemical" control.
- ) Neural information "feed-back" from chemosensitive nervous structure in the carotid body and aortic arch, which allows for "neurochemical" control.

- 3) Afferent neural informations from stretch receptors in the tissues of the lung, airways, and chest wall, allowing for "neuromechanical" control, (Fig. 1).

A schematic representation of the human respiratory system is shown in (Fig. 2). [11]. Respiration is dependent upon neural impulses which originate in the lower brain (medulla) and are transmitted to the chest cavity (thorax) and diaphragm to govern both the rate and depth of breathing. Control of both rate and depth of breathing is governed primarily by neural signals initiated at central and peripheral sites in the body and transmitted to respiratory center, (Fig. 1). Because of the importance of the chemoreceptors in the automatic feedback control of respiration, it is customary to distinguish between chemical control and nonchemical control and to refer to the latter as neural. As indicates in (Fig. 1), the neural control can be reflex in nature, as are the signals arising from stretch receptors in the lungs, etc., or it can be at the conscious level, associated with vocalization, emotion, or exercise anticipation.

Chemoreceptors involved in respiration are located centrally at or near the respiratory center and peripherally in the carotid body, the aortic body, and with less importance, in other locations. The central chemoreceptors are responsive primarily to carbon dioxide and hydrogen ion concentration. Their location in the medulla, perfused with blood and bathed in cerebrospinal fluid, suggests that these chemoreceptors are responsive to chemical changes in both cerebral blood and cerebrospinal fluid. The carotid chemoreceptor is located in the neck near the bifurcation of the common carotid artery. The aortic chemoreceptors are situated in the arch of the aorta, the main blood vessel leaving the heart. Information about the oxygen concentration of the blood comes primarily from these peripheral chemoreceptors, although they are also sensitive, to a lesser extent, to carbon dioxide and hydrogen ion concentration.

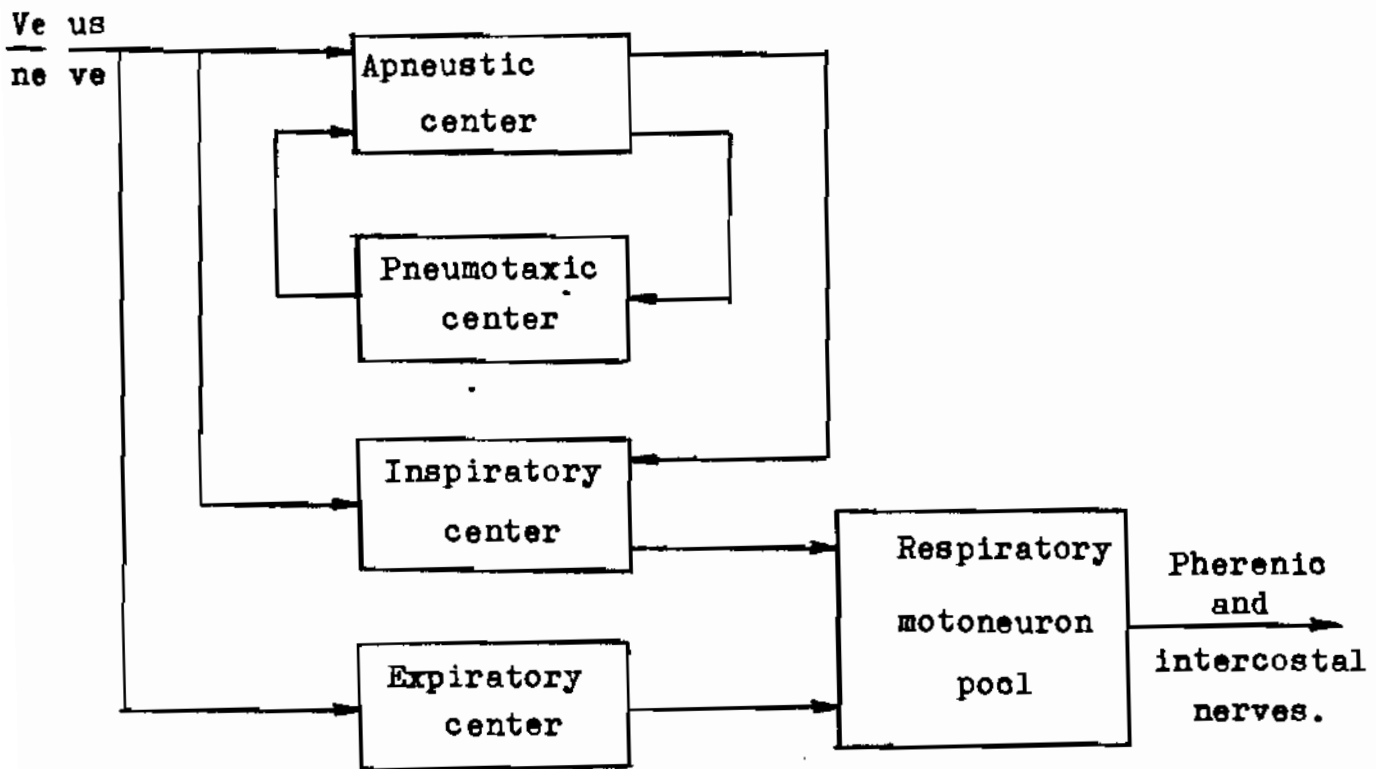


Fig. (1): Signal flow of respiratory center.

Part (III):

PREVIOUS TESTS ON RESPIRATORY CONTROL SYSTEM.

A number of tests, both chemical and experimental, have been devised to elicit information about the human respiratory system. The discussion here will emphasize only those which relate to the control aspects of respiration.

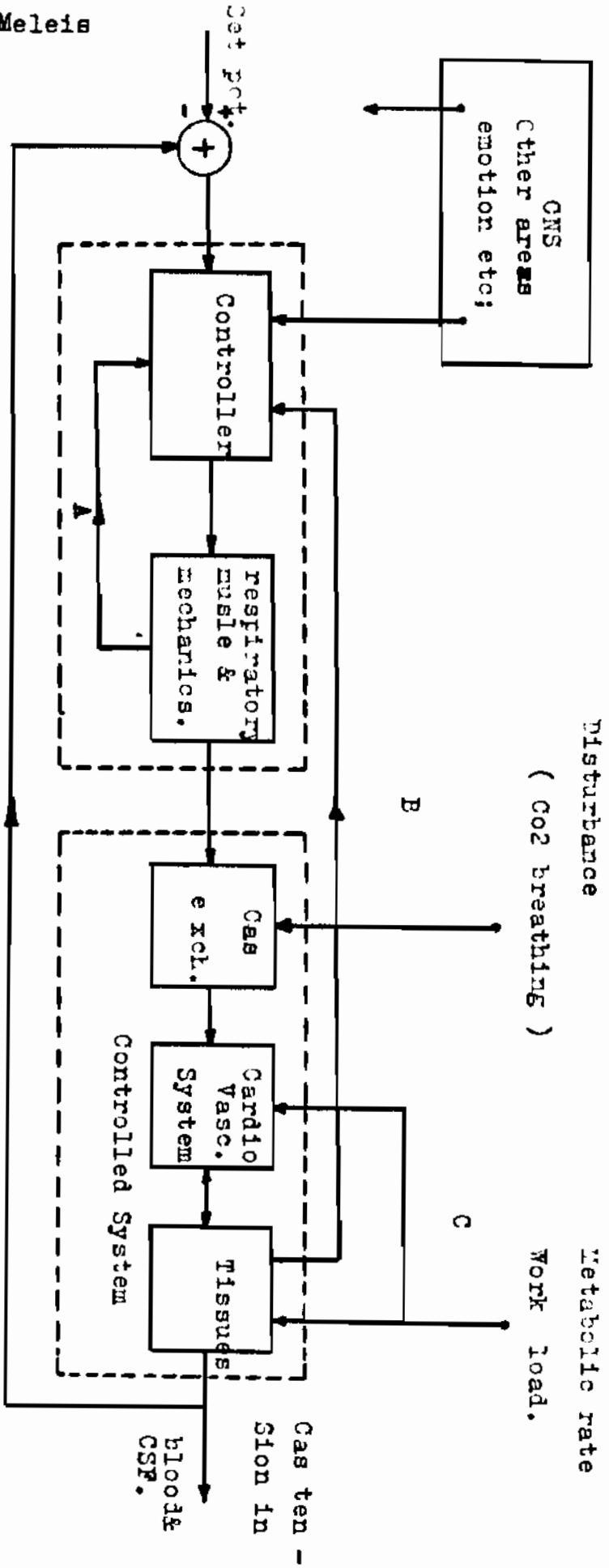


Fig. 2 : Functional Block Diagram of Respiratory Control System .

- A = local control loop is involved in control of respiratory rhythm and depth.
- B = Represents afferent neural pathways from muscles that probably are involved in causing exercise hyperpnea.
- C = Indicated how the respiratory system is coupled with circulation.

In a classical work on the regulation of respiration Douglas and Haldane [12] conducted a series of tests designed to investigate the cause of periodic breathing. This term refers not to the regular inhalation and expiration of air which normal man experiences, but to a periodicity in the total effect - ventilation as measured in liters per minute. Ventilation is normally relatively constant at about six to eight liters per minute. However, there are subjects in which ventilation, at rest, is periodic. Ventilation builds up from zero to perhaps 16 liters per minute and back to zero in cyclic fashion with a period of 30-90 seconds. For 10-30 seconds of this period apnea exists, i.e., there is no breathing. Douglas and Haldane showed that transient periodic breathing could be induced in a normal individual by a period of two minutes of hyperventilation (deep breathing). This resulted typically in an apneic period of about two minutes, followed by several cycles of periodic breathing. In this investigation, Douglas and Haldane reported a number of variations on the basic experiment, including shortening the period of forced breathing, breathing pure oxygen during the last two or three breaths of hyperventilation, and breathing an oxygen-poor mixture for the last two or three breaths of hyperventilation. They also showed that periodic respiration could be induced by having the subject breathe through a tin of soda-lime (which removes  $\text{CO}_2$  from the air passing through it), the distal end of which is connected to a long tube. Effectively, the subject rebreathes his own expired air after it has been deprived of  $\text{CO}_2$ . Variations on this experiment include changing the length of the tube and removing the  $\text{CO}_2$  filter.

The effect of inhaling carbon dioxide on the respiratory patterns of patients exhibiting periodic breathing has been investigated by Lange [13]. An interesting animal experiment showing the effect of cerebrospinal fluid composition on respiration was reported by Mitchell [14], who were able to change



suddenly the carbon dioxide concentration in the d cerebrospinal fluid of the cat and observe the consequent effects on respiration.

One of interesting investigations for studying the dynamics of exercise was reported by Mandour and El-Awady [15]. It was generally accepted that the control of respiration during exercise is dependent on chemical factors. A respiratory adaption curve due to change in value of exercises was deduced, this value was measured by the amount of lactic acid in the body; (Fig. 3).

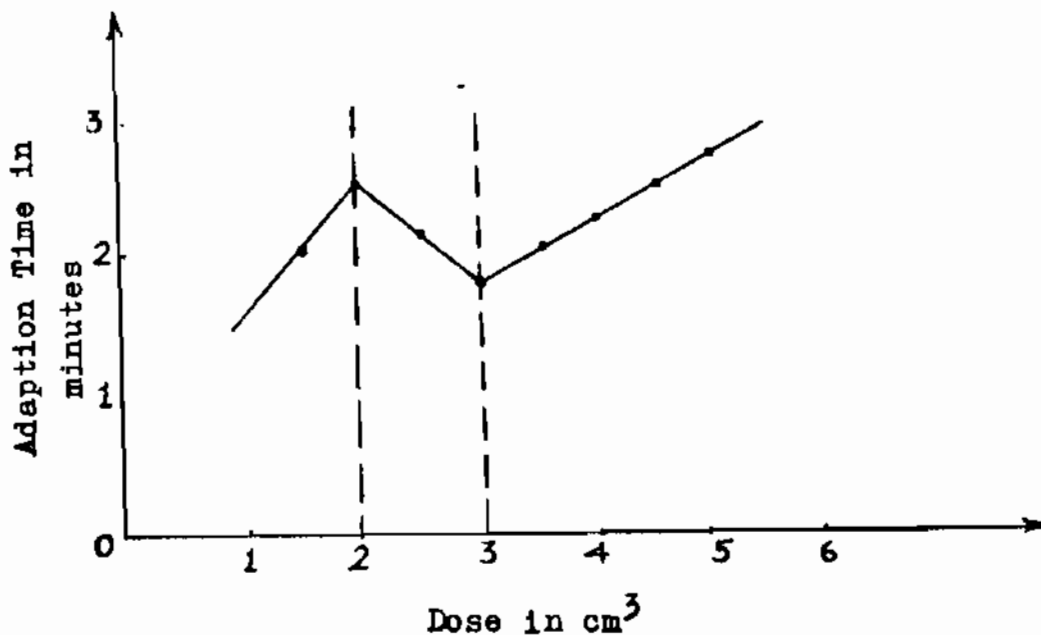


Fig. (3): Respiratory Adaption Time due to Dynamics of Exercise.

Part (IV):

#### MATHEMATICAL MODELING OF THE RESPIRATORY CONTROL SYSTEM.

Grodins and his associates, in the classical work published in 1954, [16], were the first to apply the techniques of mathematical modeling to the respiratory control system. A block diagram illustrating their concept is shown in (Fig. 4). In this

model, as in most that have followed, individual events during the respiratory cycle or cardiac cycle are not represented.

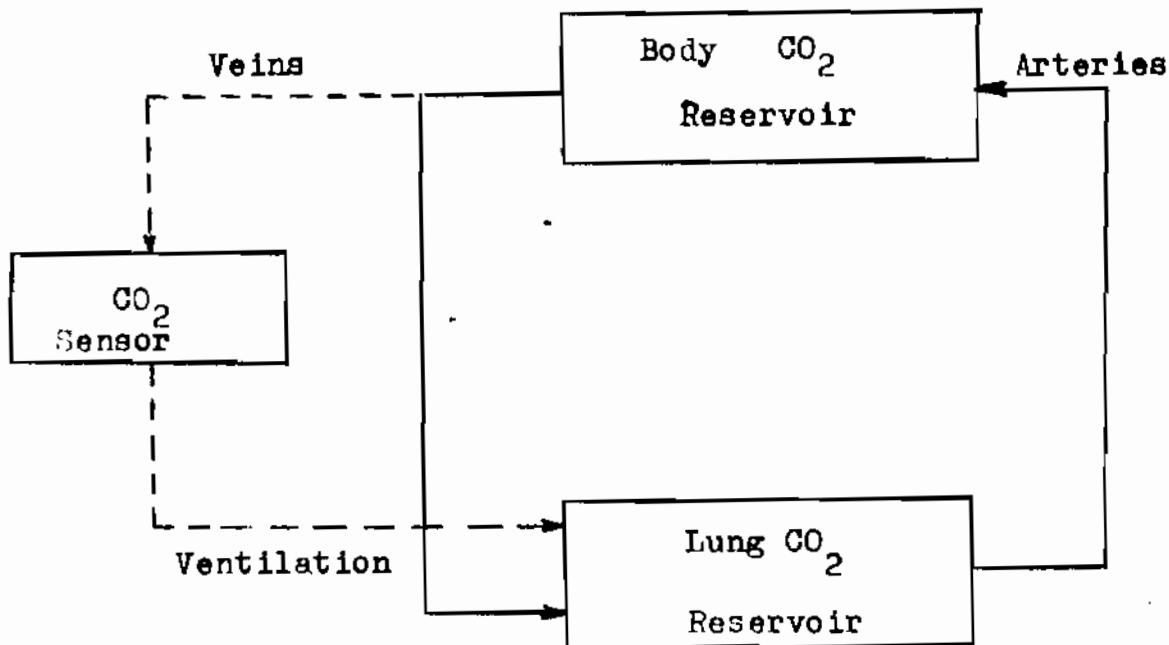


Fig. (4): Block Diagram of Grodins Model of the Respiratory Control System. 1954.

The lungs are viewed as a rigid box through which air circulates at the ventilation rate and exchanges gases with blood flowing at a fixed rate. In Grodins' model, the ventilation rate is assumed to be linearly dependent on the partial pressure of carbon dioxide in the venous blood. The linear, steady-state relationship between alveolar ventilation and the  $P_{aO_2}$  partial pressure of arterial blood had been established earlier by Gray [17]. He had also shown the linear relationship between the concentration of hydrogen ions and  $CO_2$  partial pressure of normal blood. Therefore, the effects of PH and

CO<sub>2</sub> changes are combined in the model. In Grodins' model, the effect of O<sub>2</sub> partial pressure on the control of ventilation is neglected. Gray had shown this to be approximately valid for O<sub>2</sub> partial pressures of 75 percent normal and above. Two single time constant reservoirs for carbon dioxide are included in the model.: The lung reservoir and the body tissue reservoir.

In an effort to gain better understanding of periodic breathing, Horgan and Lange [18] presented a model in 1962 in which ventilation was assumed to be dependent on arterial blood, as shown in (Fig. 5). Transport delay and mixing were introduced between lung and arterial chemoreceptors to simulate the flow of blood through the lung and left heart. This delay time was closely related to the period of Cheyne-Stokes respiration as had been observed in patients by Lange and Hecht [19]. In a 1963 publication of Horgan and Lange, [20]. The chemoreceptor characteristic was restored to Gray's form and a second oxygen control loop was added (Fig. 6).

In 1964, Horgan and Lange [21] presented a model of the respiratory control system which included the effects of CO<sub>2</sub> in the cerebrospinal fluid and brain tissue. A more detailed account was published in 1965 [22]. This refinement developed as a result of attempts to simulate CO<sub>2</sub> inhalation with an earlier model [20]. Such simulation was successful only if one of the model time constants associated with mixing in the left heart was arbitrarily increased from 10 to 20 seconds. Unfortunately, induced periodic breathing could not be simulated with this change. Fortunately, the experimental work of Mitchell [14]. Made it possible to induce the effect of cerebrospinal fluid, which was associated with a time constant of 20 seconds, and thus develop a simulation which could mimic both the high frequency phenomena associated with Cheyne-Stokes respiration and the low-frequency phenomena associated with CO<sub>2</sub>

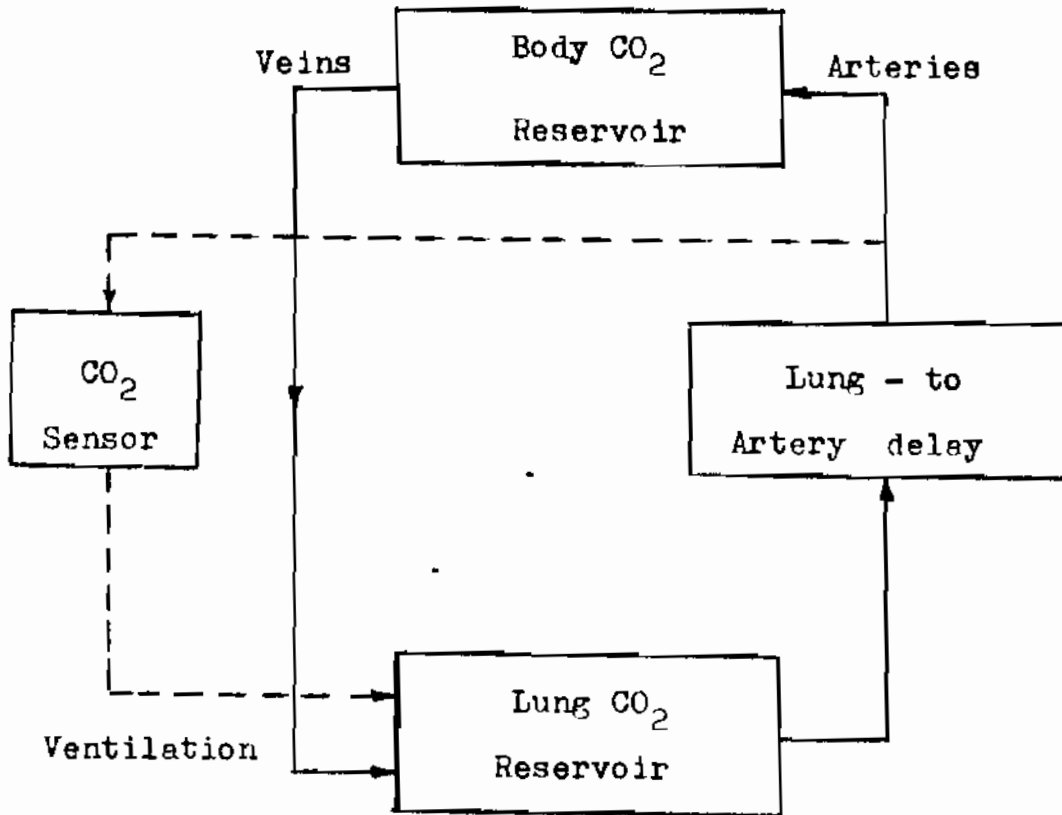


Fig. (5): Block Diagram of Horgan and Lange Respiratory System. 1962.

inhalation. (Fig. 7) shows the block diagram of this model.

In 1965, Milhorn and Guyton published an analogue computer analysis of Cheyne-Stoke breathing [23]. The model, an extension of Grodins' earlier model, includes the addition of circulation times and ventilatory dead space. Like Grodins, they assumed that the chemoreceptor was responsive to tissue CO<sub>2</sub> concentration rather than to the CO<sub>2</sub> in the arterial blood. Thus, while the model could successfully simulate the relatively slow phenomena observed in CO<sub>2</sub> inhalation, it could demonstrate Cheyne-Stokes respiration only when one or more parameters

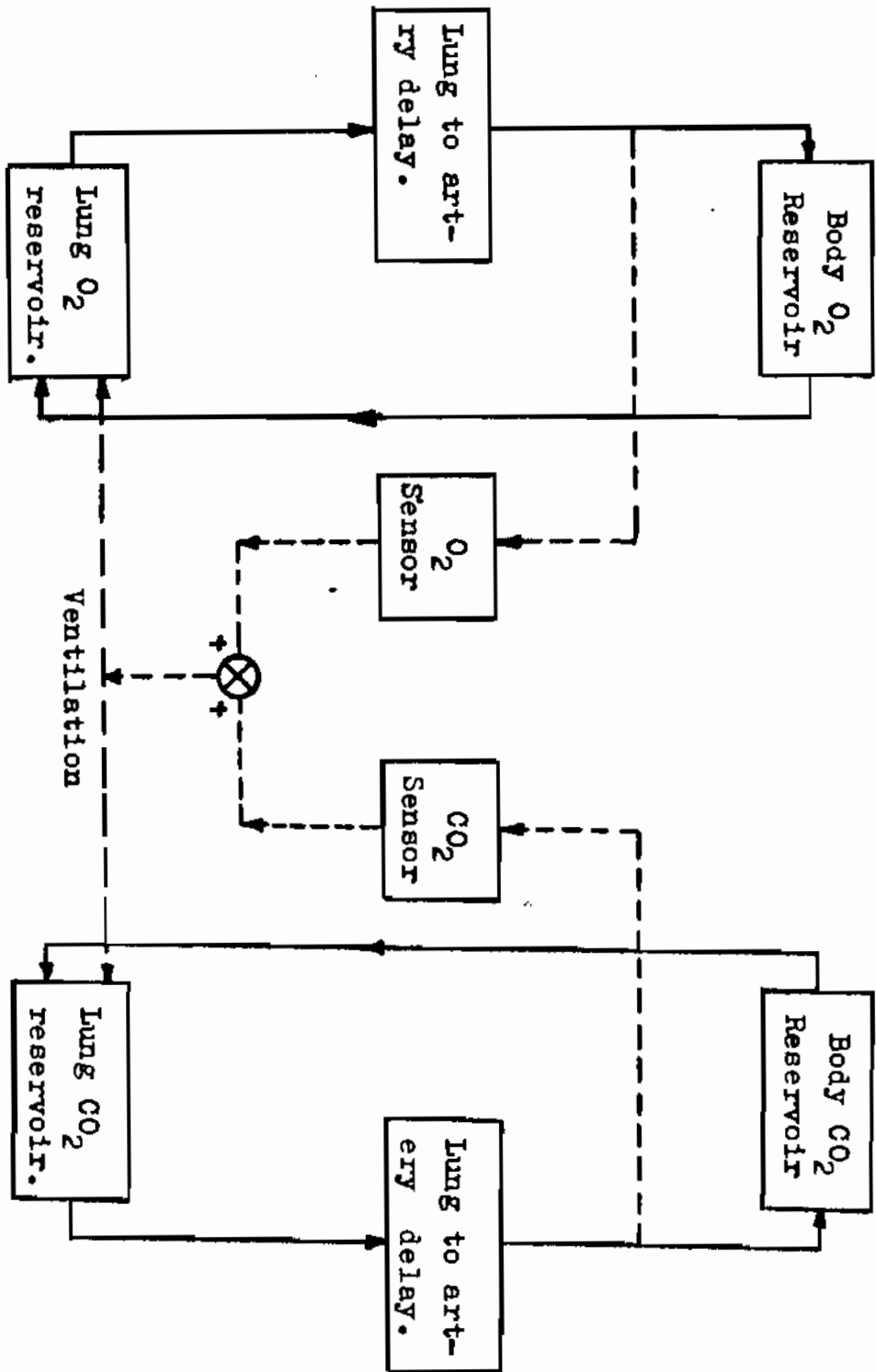


Fig. (6): Block Diagram of Horgan and Lunge form of Respiratory System. 1963.

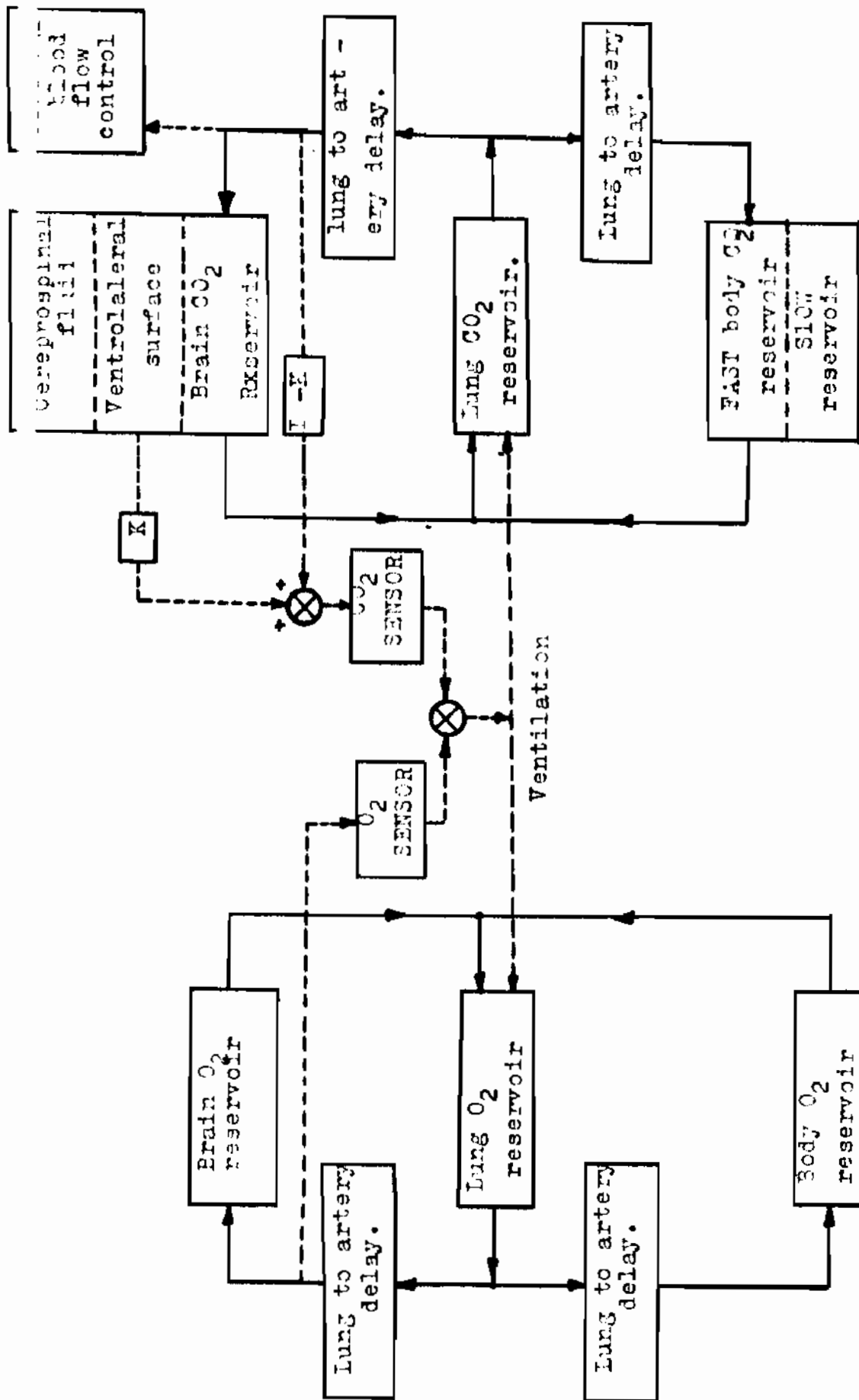


Fig. 7 : Block Diagram of Respiratory System by Holman 1964.

were adjusted to unusually high or low values. For example, if controller gain is normal, circulation delay time in the model had to be increased to three and one-half minutes, corresponding to a period of seven minutes, to produce sustained periodicity.

A more detailed model was also published by Milborn in 1965 [24]. It is essentially a three-reservoir model which includes a lung reservoir, a brain reservoir and a body reservoir, with circulation time delays between each (Fig. 8). The effects of both  $\text{CO}_2$  and  $\text{O}_2$  on cerebral blood flow, as well as on ventilation, are included. The  $\text{CO}_2$  chemoreceptor was now assumed to be responsive to cerebral venous blood. This introduced an additional 80 seconds first order time lag, as compared with a chemoreceptor responsive to arterial blood, making Cheyne-Stokes simulation difficult.

In 1966, Longobarda [17]. Published the model of the human respiratory system shown in (Fig. 9). It is similar to the model published earlier by Milborn and Guyton [24], with two important differences: (1) The chemoreceptor is assumed to be responsive to arterial blood rather than cerebral venous blood. (2) The response to  $\text{CO}_2$  and  $\text{O}_2$  is taken to be multiplicative rather than additive as in all previously published models. Evidence for this multiplicative relationship has been presented by Nielsen and Smith [26] and others.

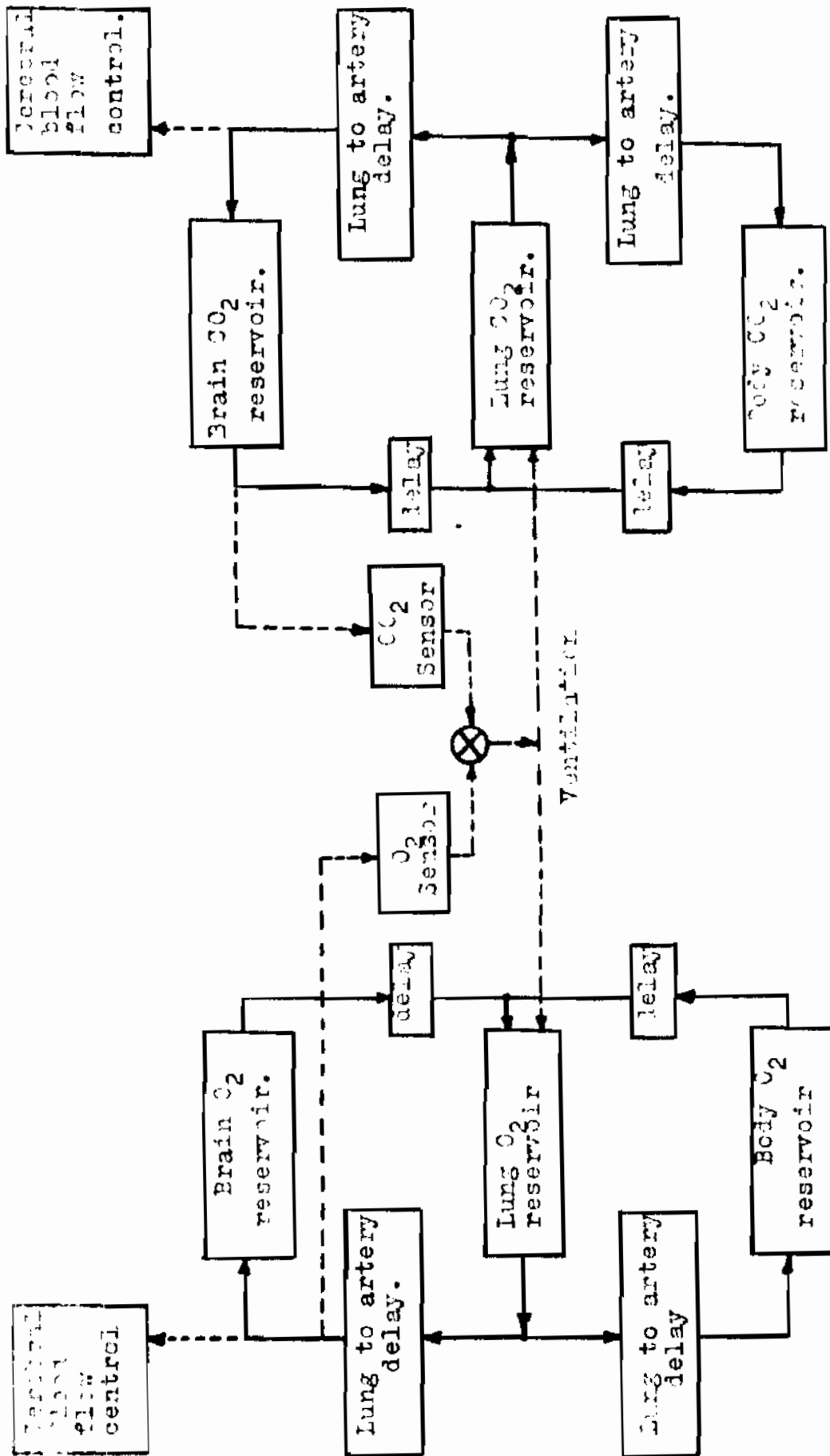


Fig. 3 : Blood Diagram of the C.S.ulatory Control

By LITKOFF 1965.



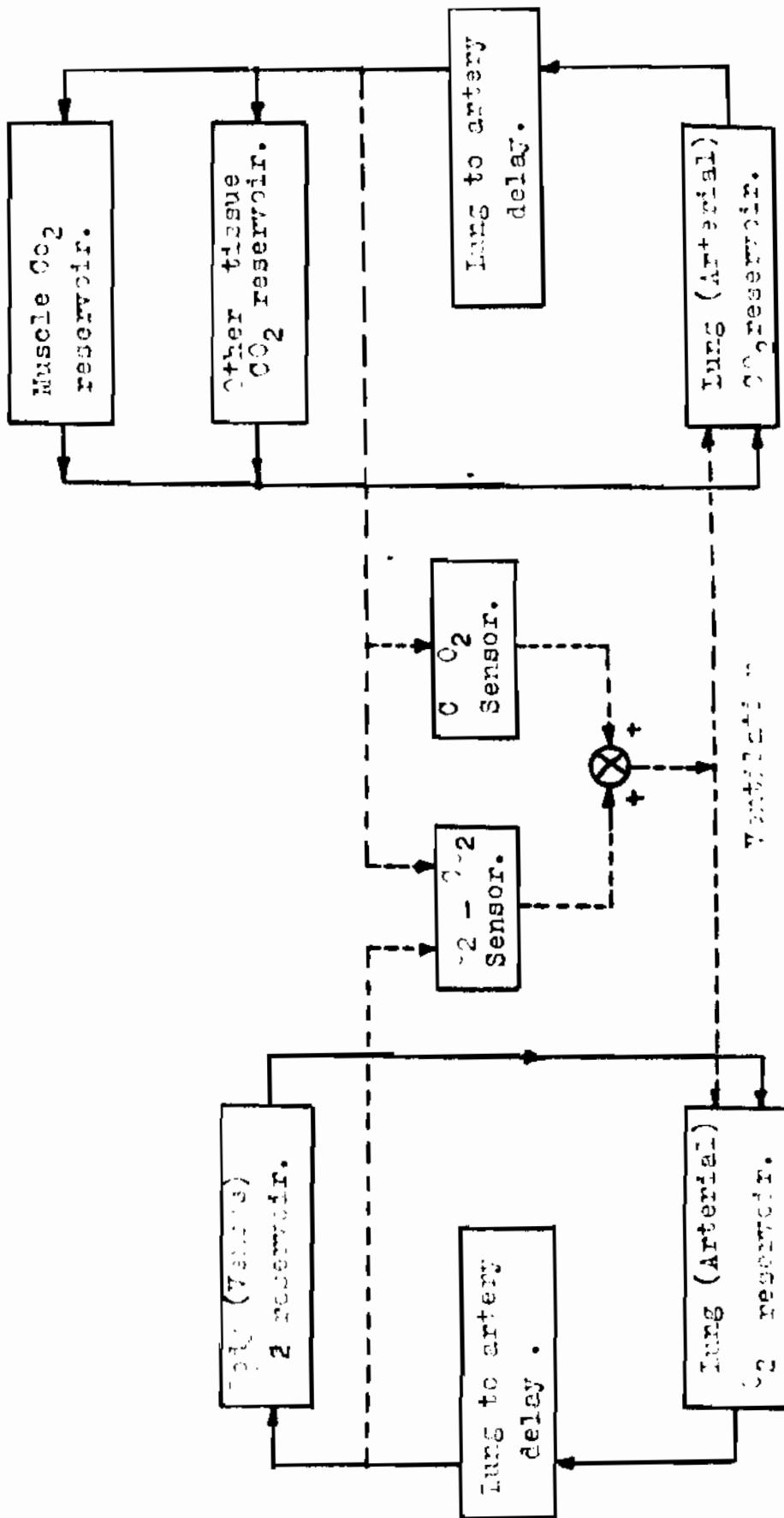


Fig. 9 : Block Diagram of the Respiratory System Model  
by Longobardi 1966.

REFERENCES

- [ 1 ] Julius H, Comroe "Physiology of Respiration" Year Book Medical Publishers INC. 1974.
- [ 2 ] M.Talaat "Physiology in Medical Practice". The Anglo-Egyptian Book-shop, 1965.
- [ 3 ] Samson Wright, "Applied Physiology" Oxford Medical Publication, 1968.
- [ 4 ] Lloyed. B.B. The Chemical Stimulus to Breathing Brit Med. Bull 1963.
- [ 5 ] Lanphier, E.H.: Medical Progress; Diving Medicine, N. Engl. J. Med. 256 : 120 1957.
- [ 6 ] Lanfant, C. and Sullivan, K: Adaptation to High altitude, N. Engl. J. Med. 284 : 1298, 1971.
- [ 7 ] Porter, R, and Knight, J. (eds.): High Altitude Physiology: Cardic and Respiratory effects (London : Churchill Livingstone, 1971).
- [ 8 ] Physiology Symposium: Respiratory Physiology in manned Spacecraft, Fed. Proc. 22 : 1022, 1963.
- [ 9 ] Bullard, R.W.: Physiological Problems of Space Travel, Annu. Rev. Physiology 1972.
- [ 10 ] Chiodi, H.: Respiratory adaptations to Chronic high altitude Hypoxia, J. Appl, Physiology 1957.
- [ 11 ] James "Chemical Control in the Respiratory System" IEEE Transactions on Bio-medical Eng., April, 1968.
- [ 12 ] C.G. Douglas and I.S. Haldane "The Causes of Periodic or Cheyne-Stokes Breathing" J. Physiology (London), Vol. 38, pp. 401-419 1909.

- [13] R.L. Lange, J.T. Botticelli "Observation and Simulation of The Circulation acid-base balance and response to CO<sub>2</sub> in Cheyne-Stokes respiration", 1968.
- [14] R.A. Mitchell, H.H. Loeschcke "Respiratory Responses Mediated Through Superficial Chemosensitive Areas on The Medulla" J. Appl. Physiology, Vol. 18, p 523, 1963.
- [15] Dr. Ibrahim Mandour, Dr. R. El-Awady, "Analysis of Adaptation time in Biological Systems". The first biomedical Engineering Conference, March 1976, Cairo.
- [16] E.S. Grodins, J.S. Gray "Respiratory Responses to CO<sub>2</sub> inhalation. At Theoretical Study of non Linear Biological regulator" J. Appl. Physiology, Vol. 7 pp. 283-308, 1954.
- [17] J.S. Gray, Pulmonary Ventilation and its Physiological Regulation. Springfield, Ill: Thomas, 1950.
- [18] J.D. Horgan and R.L. Lange "Analog Computer Studies of Periodic Breathing" IRE Trans. Bio-Medical Electronics, Vol. BME-9 pp. 221-228, October 1962.
- [19] R.L. Lange and H.H. Hecht "The Mechanism of Cheyne Stokes Respiration", J. Clin. Invest., Vol. 41. pp. 42-52, 1962.
- [20] J.D. Horgan and R.L. Lange "Digital Computer Simulation of the Human Respiratory System" IEEE International Conv. Rec., pt. 9, pp. 149-157, 1963.
- [21] J.D. Horgan and R.L.: Lange "A model of the Respiratory Control System Which Includes the Effect of Cerebrospinal Fluid and Brain Tissue" Proc. Ann. Conf. Engrg. in Med. and Biol. Vol. 6, p. 10, 1964.

- [ 22 ] J.D. Horgan and R.L. Lange "Digital Computer Simulation of respiratory response to Cerebrospinal fluid  $PCO_2$ , in the Cat" *Biophys. J.* Vol. 6, pp. 935-945, 1965.
- [ 23 ] H.T. Molborn, Jr. and A.C. Gayton "An Analog Computer Analysis of Cheyne-Stokes breathing" *J. Appl. Physiology*, Vol. 20, pp. 328-333, 1965.
- [ 24 ] H.T. Molborn, Jr., K. Benton, R. Ross, and A.C. Cuyton "A Mathematical Model of the Human Respiratory Control System" *Bio-Phys. J.*, Vol. 5, pp. 27-46, 1965.
- [ 25 ] G.S. Longobardo, W.S. Cherniak, and A.P. Fishman "Cheyne Stokes Breathing Produced by a Model of the Human Respiratory System" *J. Appl. Physiol.*, Vol. 21 pp. 1839-1846, 1966.
- [ 6 ] M. Nielsen and H. Smith "Studies on the Regulation of Respiration in Actute Hypoxia" *Acta Physiol. Scand.*, Vol. 24, pp. 293-313, 1951.
- [ 7 ] Grodins, F.S., J. Buell and A. J. Bart. "Mathematical Analysis and Digital Simulation of the respiratory Control System" *J. Appl. Physiology* 22: 260-276, 1967.
- [ . ] Samuel Armstrong, "Systems Physiology" John Wiley, 1973.
- [ : ] Lloyed, B.B. The chemical Stimulus to Breathing *Brit Med. Bull* 1963.