FLUID BIOMECHANICS AND RESPIRATION

Arthur T. Johnson
University of Maryland, USA

Keywords: Resistance, Compliance, Inertance, flows, models

Contents

Summary

Of all the bodily functions performed during exercise, respiration appears to be one of the most highly regulated and optimized. The amount of work performed by respiratory muscles to supply air for the exercising body can be considered to be a large part of the body's overhead. Respiratory work, which accounts for 1% to 2% of the total body oxygen expenditure during rest, may rise to as much as 10% or higher during exercise. This represents oxygen that is unavailable to the skeletal muscles for performing useful work. It appears reasonable, therefore, that neural mechanisms regulating respiration would aim to minimize the work of respiration. Simultaneous adjustments in airflow pattern, respiration rate, and respiratory mechanics appear to be directed toward minimizing oxygen expenditure of the respiratory overhead.

Respiratory ventilation during rest is subject to a high degree of voluntary control. In exercise, this does not appear to be true. Except for specialized sports such as swimming (where breathing must be synchronized to gulp air, not water) and weight lifting (where breath holding is practiced to increase torso rigidity), respiration during exercise appears to be very highly deterministic; conscious control is difficult and is usually not brought to bear. We thus find that models to predict respiratory responses usually match experimental findings very well. Even when external events such as stepping during running and pedaling during bicycling tend to synchronize breathing, many respiratory parameters can be predicted.

The increase in ventilation during exercise is driven by the same requirements as the cardiac response, the need to avoid an acidic shift in the pH of the blood. Aerobic metabolism produces CO_2, which can directly and indirectly affect pH. Additional metabolic acidosis accompanies lactic acid formation. Ventilation must therefore increase to eliminate metabolic CO_2 and transform lactic acid into glucose. A failure to do so results in respiratory acidosis of the blood and body fluids (Wasserman et al., 1999).

1. Introduction: Respiratory Mechanics

Respiratory mechanics, perhaps more than the mechanics of other physiological systems, is an extremely complicated topic. The respiratory system functions to bring air to the blood (Figure 1). It also functions to maintain thermal equilibrium and acid–base balance of the blood. Furthermore, flow in the respiratory system is bidirectional rather than unidirectional. Even while its primary function of air movement is occurring, there are gaseous fluid mechanics, physical diffusion, gas-to-liquid mass transport, muscular movement, and neural integration to consider. Although it can be argued that many of the same processes occur in the cardiovascular system, for instance, respiratory responses do not occur spontaneously without central nervous system control, as they can in the cardiovascular system.

Mechanical properties of the respiratory system are best understood by first reviewing respiratory anatomy. Following that, it is clearer how various mechanical models are formulated to account for structural considerations.

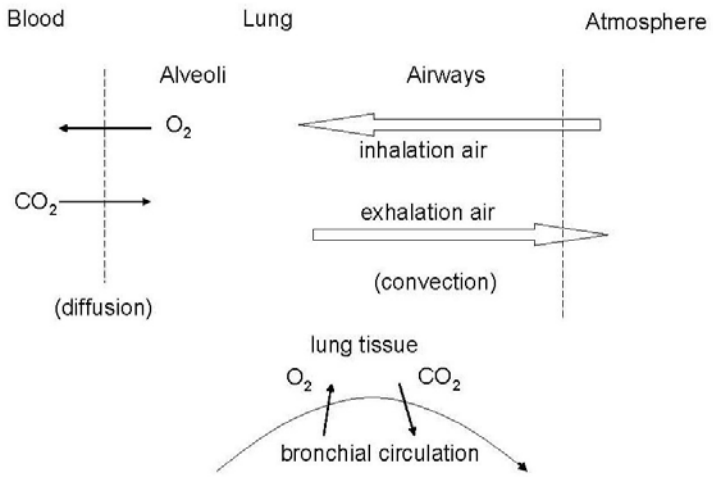

Figure 1. Gas moves by convection in the airways and by diffusion from the alveoli into blood. The bronchial circulation serves metabolic needs of lung tissue.

2. Respiratory Anatomy

The respiratory system consists of the lungs, conducting airways, pulmonary vasculature, respiratory muscles, and surrounding tissues and structures (Figure 2). Each of these is discussed to show the ways in which it influences respiratory responses.

2.1. Lungs

There are two lungs in the human chest; the right lung is composed of three incomplete divisions called lobes and the left lung has two. The right lung accounts for 55% of total gas volume and the left lung accounts for 45% (Figure 2). Lung tissue is spongy due to the very small (200 to 300×10^{-6} m diameter in normal lungs at rest) gas-filled cavities called alveoli, which are the ultimate structures for gas exchange. There are 250 million to 350 million alveoli in the adult lung, with a total alveolar surface area of 50 to 100 m^2, depending on the degree of lung inflation (Hildebrandt and Young, 1965).

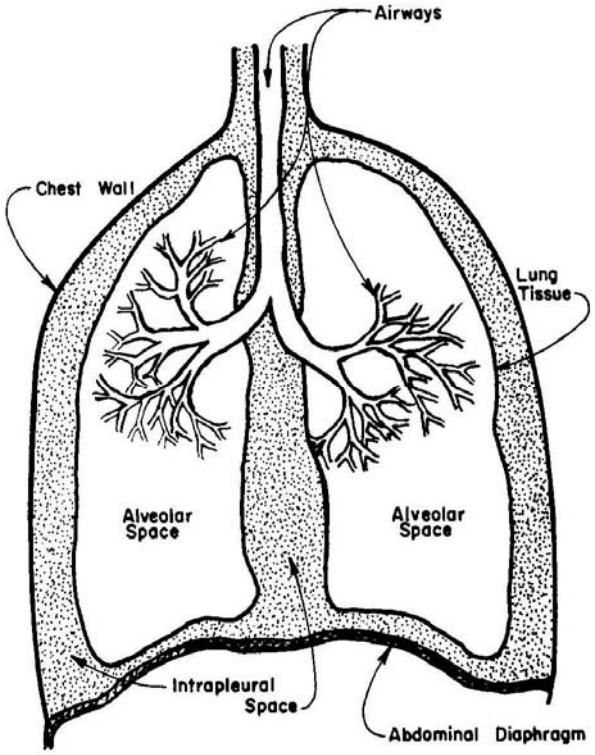

Figure 2. Schematic representation of the respiratory system.

Ochs et al. (2004) have measured the number of alveoli in the human lung as 480 million, ranging from 274 million to 790 million. Alveolar number was closely related to total lung volume because the mean volume of a single alveolus does not vary much from 4.2×10^{-12} m^3. Because alveolar size is determined mostly by diffusion of oxygen and
CO_2, need for higher levels of gas exchange is met with greater number of alveoli and larger lung sizes. There is, however, a vertical gradient in alveolar size in the lung; gravity pulls on the lung and makes lower alveoli larger (Macklem, 2004).

The lungs are both enclosed in a membrane called the pleura. This membrane is in intimate contact with lung tissue, and intrapleural pressure is often taken to be the driving pressure for lung volume changes.

2.2. Conducting Airways

Air is transported from the atmosphere to the alveoli beginning with the oral and nasal cavities, and through the pharynx (in the throat) past the glottal opening, into the trachea, or the windpipe. The larynx, or the voice box, at the entrance to the trachea, is the most distal structure of the passages solely for conduction of air. The adult trachea is a fibromuscular tube 10 to 12 cm in length and 1.4 to 2.0 cm in diameter (Sackner, 1976). At a location called the carina, the trachea terminates and divides into the left and right bronchi. Each bronchus has a discontinuous cartilaginous support in its wall (Astrand and Rodahl, 1970). Muscle fibers capable of controlling airway diameter are incorporated into the walls of the bronchi, as well as in the air passages closer to the alveoli. The general tendency of airways closer to the alveoli is to be less rigid and more

controllable by muscle fibers. Smooth muscle is present throughout the respiratory bronchioles and the alveolar ducts but is absent in the last alveolar duct, which terminates into one to several alveoli (Sackner, 1976). The alveolar walls are shared by other alveoli and are composed of highly pliable and collapsible squamous epithelium cells.

The bronchi subdivide into subbronchi, which further subdivide into bronchioles, which further subdivide, and so on, until finally reaching the alveolar level. The Weibel (1963) model is commonly accepted as one geometrical arrangement of air passages (another more complicated asymmetrical model is described in Yeates and Aspin, 1978). In the Weibel model, each airway is considered to branch into two subairways. In the adult human, there are considered to be 23 such branchings, or generations, beginning at the trachea and ending in the alveoli.

Dichotomous branching is considered to occur only through the first 16 generations, which is called the conductive zone because these airways serve to conduct air to and from the lungs. After the 16th generation, branching proceeds irregularly dichotomously or trichotomously for three generations. A limited amount of respiratory gas exchange occurs in this transition zone. In the respiration zone, generations 20 to 23, most gas exchange occurs.

Movement of gases in the respiratory airways occurs mainly by bulk flow (convection) throughout the region from the mouth and nose to the 15th generation. Beyond the 15th generation, gas diffusion is relatively more important (Pedley et al., 1977; Sackner, 1976). With the low gas velocities that occur in diffusion, dimensions of the space over which diffusion occurs (alveolar space) must be small for adequate oxygen delivery to the walls; smaller alveoli are more efficient in the transfer of gas than larger ones. Thus, animals with higher levels of oxygen consumption are found to have smaller diameter alveoli compared with animals with lower levels of oxygen consumption.

2.3. Alveoli

Alveoli are the structures through which gases diffuse to and from the body.

One would expect, then, that alveolar walls would be extremely thin for gas exchange efficiency, and that is found to be the case. Total tissue thickness between the inside of the alveolus and the pulmonary capillary blood plasma is only $\approx 0.4\times10^{-6}$ m. From the relative dimensions, it is apparent that the principal barrier to diffusion is not the alveolar membrane but the plasma and the red blood cell (Hildebrandt and Young, 1965).

Molecular diffusion within the alveolar volume is responsible for mixing of the enclosed gas. Due to the small alveolar dimensions, complete mixing probably occurs in less than 10 ms (Astrand and Rodahl, 1970), fast enough that the alveolar mixing time does not limit gaseous diffusion to or from the blood.

Of particular importance to proper alveolar operation is a thin surface coating of surfactant. Without this material, large alveoli would tend to enlarge and small alveoli would collapse. From the law of Laplace, for spherical bubbles,

$$p = 2\tau \Delta r / r \qquad (1)$$

where p is the gas pressure inside the bubble measured in cm H_2O; τ is the surface tension in cm H_2O; r is the bubble radius in cm; Δr is the wall thickness in cm.

Large spherical bubbles (r large) have small internal pressures. Smaller bubbles have larger internal pressures. Connect the two bubbles together, and the contents of the smaller bubble are driven into the larger one. If we generalize this instability to the lung, it is not hard to imagine the lung composed of one large, expanded alveolus and many small, collapsed alveoli. Surfactant, which acts like a detergent, changes the stress–strain relationship of the alveolar wall and stabilizes the lung (Notter and Finkelstein, 1984).

Lung surfactant is spread one molecule thick over the surface of lung airspaces. When these air spaces contract, as during exhalation, these molecules are forced together and some are forced off the surface. When the surface again expands during inhalation, old surfactant molecules do not spread very rapidly onto the surface. Newly secreted surfactant is required to replace gaps in the old surfactant, and it does so by rapid spreading. Previously used surfactant is expelled from the lung. When the need for new surfactant exceeds the rate of supply, as in premature infants whose lungs have not matured, the mechanisms for surfactant production, lung injury can occur (Tierney, 2003).

2.4. Pulmonary Circulation

The pulmonary circulation is relatively low in pressure (Fung and Sobin, 1977). Due to this, pulmonary blood vessels, especially capillaries and venules, are very thin walled and flexible. Unlike systemic capillaries, pulmonary capillaries increase in diameter with any increase in blood pressure or decrease in alveolar pressure. Flow, therefore, is significantly influenced by elastic deformation.

Pulmonary circulation is largely unaffected by neural and chemical control (Fung and Sobin, 1977). It responds promptly to hypoxia, however. A key anatomical consideration is that pulmonary capillaries within alveolar walls are exposed to alveolar air on both sides, because alveolar walls separate adjacent alveoli.

The pressure-reduction function performed by the systemic arterioles is not matched by the pulmonary arterioles. Therefore, pulmonary vessels, including capillaries and venules, exhibit blood pressures that vary ≈30% to 50% from systole to diastole (Fung and Sobin, 1977). There is also a high-pressure systemic blood delivery system to the bronchi that is completely independent of the pulmonary low-pressure (≈35 cm H_2O) circulation in healthy individuals (Fung and Sobin, 1977). In diseased states, however, bronchial arteries are reported to enlarge when pulmonary blood flow is reduced, and some arteriovenous shunts become prominent (Fung and Sobin, 1977).

Pulmonary arterial blood is oxygen poor and CO_2 rich. It exchanges excess CO_2 for oxygen in the pulmonary capillaries, which are in close contact with alveolar walls.

CO_2 diffusion is so rapid that CO_2 partial pressure in the blood is equilibrated to that in the alveolus by 100 msec after the blood enters the capillary and oxygen equilibrium is reached by 500 msec (Astrand and Rodahl, 1970). At rest, the transit time for blood in the pulmonary capillaries is about 1sec, but can become as small as 0.2 sec during exercise.

At rest, pulmonary venous blood returns to the heart nearly 97% saturated with oxygen. During exercise, hemoglobin saturation may be limited because blood transit time is not long enough.

2.5. Respiratory Muscles

The lungs fill because of a rhythmic expansion of the chest wall. The action is indirect in that no muscle acts directly on the lung.

The diaphragm is the muscular mass accounting for 75% of the expansion of the chest cavity (Ganong, 1963). The diaphragm is attached around the bottom of the thoracic cage, arches over the liver, and moves downward like a piston when it contracts (Ganong, 1963). The external intercostal muscles are positioned between the ribs and aid inspiration by moving the ribs up and forward. This, then, increases the volume of the thorax. Other muscles are important in the maintenance of thoracic shape during breathing.

Quiet expiration is usually considered to be passive; pressure to force air from the lungs comes from elastic expansion of the lungs and the chest wall. Actually, there is evidence (McIlroy et al., 1963; Hämäläinen and Viljanen, 1978; Loring and Mead, 1982) that even quiet expiration is not entirely passive. Sometimes, too, inspiratory muscle activity continues through the early part of expiration. During moderate to severe exercise, the abdominal and the internal intercostal muscles are very important in forcing air from the lungs much more quickly than it would be otherwise.

Inspiration requires intimate contact between lung tissues, pleural tissues (the pleura is the membrane surrounding the lungs), and chest wall and diaphragm. This contact is maintained by reduced intrathoracic pressure (which tends toward negative values during inspiration). Any accumulation of gas in the intrapleural space in the thorax, which would ruin tissue-to-tissue contact, is absorbed into the pulmonary circulation because pulmonary venous total gas pressure is normally subatmospheric (Astrand and Rodahl, 1970).

The diaphragm is the most important respiratory muscle in developing the muscle pressure required to move air into the lungs. Its shape is largely determined because it separates the air-filled, spongy, and easily deformed lung material from the largely liquid abdominal contents. Due to the difference in height of the liquid in the abdomen across the dome shape assumed by the diaphragm, there is a significant vertical hydrostatic pressure gradient in the abdomen and a consequent difference in transdiaphragmatic pressure over the surface of the diaphragm (Whitelaw et al., 1983). Diaphragm tension should be able to be determined from its shape by the law of Laplace (Equation 1).

As the lungs fill, they become stiffer. The diaphragm must be able to produce higher pressures to move air into filled lungs. Normally, this would run counter to the muscular length–tension relationship, which indicates higher muscular tensions for longer lengths. In any case, muscular efficiencies would be expected to change during the respiratory cycle, and muscle pressures exerted on the lungs would be expected to vary with position.

3. Lung Volumes and Gas Exchange

Of primary importance to lung functioning is the movement and mixing of gases within the respiratory system. Depending on the anatomical level under consideration, gas movement is determined mainly by diffusion or convection. This discussion begins with determinants of convective gaseous processes, that is, the lung volumes that change from rest to exercise.

3.1. Lung Volumes

Without the thoracic musculature and rib cage, the barely inflated lungs would occupy a much smaller space than they occupy in situ. However, the thoracic cage expands them and holds them open. Conversely, the lungs exert an influence on the thorax, holding it smaller than should be the case without the lungs. Because the lungs and the thorax are connected by tissue, the volume occupied by both together is between the extremes represented by relaxed lungs alone and thoracic cavity alone. The resting volume V_r is the volume occupied by the lungs with glottis open (the glottis is the opening between the vocal cords in the larynx), muscles relaxed, and with no elastic tendency to become larger or smaller.

Functional residual capacity (FRC) is often taken to be the same as the resting volume.

There is a small difference between resting volume and FRC because FRC is measured while the subject breathes, whereas resting volume is measured with no breathing. FRC is properly defined only at end expiration at rest and not during exercise.

Tidal volume V_T is the amount of air exhaled at each breath. Some people define tidal volume as the quantity of air inhaled during each breath. The two volumes are not the same due to the different temperatures of the inhaled and exhaled air, and, to a lesser extent, due to water vapor addition and different gas composition of exhaled air. Inhaled volume is somewhat easier to measure because higher resting flow rates are usually incurred. Tidal volume increases as the severity of exercise increases. Dividing V_T by respiratory period (the time between identical points of successive breaths), T, gives the minute volume $\dot{V}_E$, or the amount of air that would be exhaled per unit time if exhalation could be sustained. Sometimes $\dot{V}_E$, is measured as accumulated exhaled air for 1 min.

Lung volumes greater than the resting volume are achieved during inspiration. Maximum inspiration is represented by inspiratory reserve volume (IRV). IRV is the

maximum additional volume that can be accommodated by the lung at the end of inspiration.

Lung volumes less than the resting volume do not normally occur at rest but do occur during exhalation while exercising (when exhalation is active). Maximum additional expiration, as measured from lung volume at the end of expiration, is called expiratory reserve volume (ERV).

A small amount of air remains in the lung at maximum expiratory effort. This is the residual volume (RV), sometimes called the closing volume of the lung.

Vital capacity (VC) is the sum of ERV, IRV, and V_T. Total lung capacity (TLC) is the sum of VC and RV. These volumes are illustrated in Figure 3.

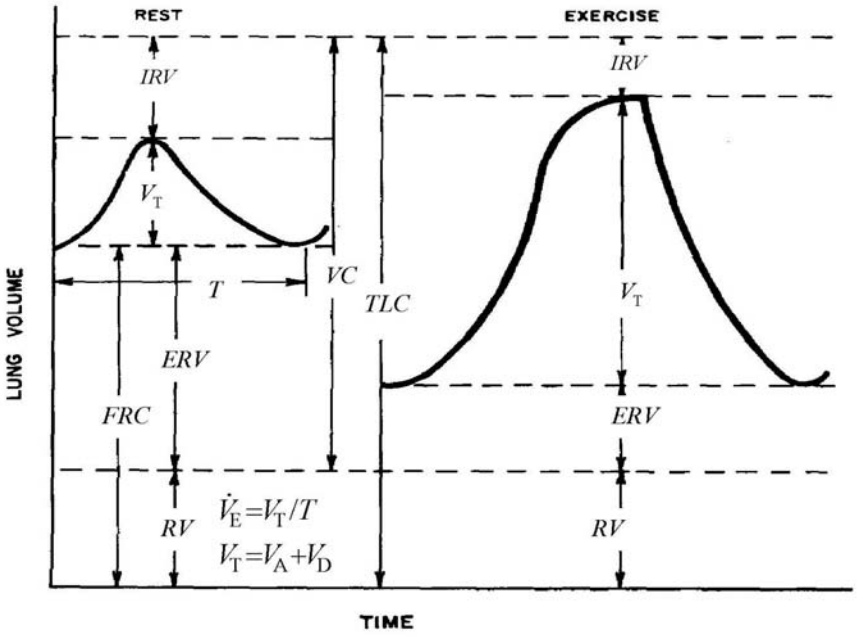

Figure 3. Representation of lung volume definitions (Johnson, 2007). Symbols are defined in the text.

Tidal volume ventilates both the active (alveolar) regions, composed of alveolar ventilation volume VA, and inactive regions of the lung, called dead volume V_D or dead space. Alveolar ventilation volume consists of air that diffuses to and from the pulmonary circulation. Respiratory dead volume is air that does not take part in gas exchange. Not all air that reaches the alveoli interacts with gases in the blood, and thus there is a portion of the total dead volume known as alveolar dead volume. The volume occupied by the respiratory system, exclusive of the alveoli, is normally called anatomic dead volume. The volume of gas not equilibrating with the blood is called physiological dead volume. Normally, anatomical and physiological dead volumes are nearly identical, but during certain diseases, when portions of the lung are unperfused by blood, they can differ significantly.

-

-

-

Bibliography

Agostoni, E., and J. Mead. (1964). Statics of the Respiratory System, in *Handbook of Physiology*, Vol. 1, Section 3. Respiration,W.O. Fenn and H. Rahn, eds, American Physiological Society,Washington, D.C., Chapter 13. pp. 387–410.].[*This reference contains basic information about respiratory mechanics.]*

Astrand, P.O., and K. Rodahl. (1970). *Textbook of Work Physiology*. McGraw-Hill, New York [*This is a classic book on work physiology, and includes more than respiratory physiology*].

Barnas, G.M., N.C. Heglund, D. Yager, K. Yoshino, S.H. Loring, and J. Mead. (1989a). Impedance of the Chest Wall during Sustained Respiratory Muscle Contraction. *J. Appl. Physiol.* 66:360–369 [*This and the other papers by Barnas are really good for frequency dependence*].

Barnas, G.M., C.F. Mackenzie, M. Skacel, S.C. Hempleman, K.M. Wicke, C.M. Skacel, and S.H. Loring. (1989b). Amplitude Dependency of Regional Chest Wall Resistance and Elastance at Normal Breathing Frequencies. *Am. Rev. Respir. Dis.* 140: 25–30. [*Tidal volume has an effect on respiratory mechanical properties.]*

Barnas, G.M., K. Yoshino, J. Fredberg, Y. Kikuchi, S.H. Loring, and J. Mead. (1990). Total and Local Impedance of the Chest Wall up to 10 Hz. *J. Appl. Physiol.* 68: 1409–1414. [*This is a work on the chest wall*].

Bartlett, R.G. (1973). Respiratory System, in *Bioastronautics Data Book*, J.F. Parker, Jr and V.R. West, eds, NASA, Washington, D.C., pp. 489–531 [*This is a good reference for many aspects of physiology*].

Blide, R.W., H.D. Kerr, and W.S. Spicer. (1964). Measurement of Upper and Lower Airway Resistance and Conductance in Man. *J. Appl. Physiol.* 19: 1059–1069. [*This work gives data partitioned by upper and lower resistances.]*

Bouhuys, A., and B. Jonson. (1967). Alveolar Pressure, Airflow Rate, and Lung Inflation in Man. *J. Appl. Physiol*. 22: 1086–1100 [*This is a classic work with lots of data*].

Cerny, F.J. (1987). Breathing Pattern during Exercise in Young Black and Caucasian Subjects. *J. Appl. Physiol.* 62: 2220–2223. [*Breathing patterns are detailed.]*

Cherniack, R.M. 1959. The Oxygen Consumption and Efficiency of the Respiratory Muscles in Health and Emphysema. *J. Clin. Invest.* 38: 494–499. [*This is a good reference for respiratory efficiencies.]*

Corsico, A., M. Milanese, S. Baraldo, G.L. Casoni, A. Papi, A.M. Riccio, I. Cerreri, M. Saetta, and V. Brusaco. (2003). Airway Hyperresponsiveness: From Molecules to Bedside. Small Airway Morphology and Lung Function in the Transition from Normality to Chronic Airway Obstruction. *J. Appl. Physiol*. 95: 441–447. [*This work compares normal and disease states.]*

de Bisschop, C., A.Pichon, H. Guénard, and A. Denjean. (2003). Accounting for Flow Dependence of Respiratory Resistance during Exercise. *Respir. Physiol. Neurobiol.* 136: 65-76. [*This reference supplements the Rohrer descriptions of airway mechanics.]*

Ferris, B.G., J. Mead, and L.H. Opie. (1964). Partitioning of Respiratory Flow Resistance in Man. *J. Appl. Physiol.* 19: 653–658 [*This is a classic work with good measurements*].

Fung, Y.C., and S.S. Sobin. (1977). Pulmonary Alveolar Blood Flow, in *Bioengineering Aspects of the Lung*, J.B. West, ed., Marcel Dekker, New York, pp. 267–359 [*This book has all the basics*].

Ganong, W.F. (1963). *Review of Medical Physiology*. Lange Medical Publications, Los Altos, CA, pp. 198–199, 482–552 [*This book is very easy to read*].

Grodins, F.S., and S.M. Yamashiro. (1978). *Respiratory Function of the Lung and Its Control.* Macmillan, New York [*Grodins and Yamashiro approach the respiratory system from a bioengineering perspective*].

Hämäläinen, R.P., and A.A. Viljanen. (1978). Modelling the Respiratory Airflow Pattern by Optimization Criteria. *Biol. Cybern.* 29: 143–149 [*Hämäläinen models the respiratory system as an optimization problem*].

Hildebrandt, J., and A.C. Young. (1965). Anatomy and Physics of Respiration, in *Physiology and Biophysics*, T.C. Ruch and H.D. Patton, eds, W.B. Saunders, Philadelphia, PA, pp. 733–760. [*This is a good general description of all aspects of respiratory physiology.]*

Jacquez, J.A. (1979). *Respiratory Physiology*. McGraw-Hill/Hemisphere, New York. [*This has a lot of good background on the respiratory system.]*

Johnson, A.T. (1984). Multidimensional Curve Fitting Program for Biological Data. *Comp. Prog. Biomed.* 18: 259–264. [*Although the emphasis of this paper is on the curve-fitting program, examples are given relevant to respiratory physiology.]*

Johnson, A.T., (2007), *Biomechanics and Exercise Physiology: Quantitative Modeling*, Taylor and Francis, Boca Raton, FL [*This book covers energetics, cardiac function, thermoregulation, and respiration, especially during exercise*].

Johnson, A.T. (1986). Conversion between Plethysmograph and Perturbational Airways Resistance Measurements. *IEEE Trans. Biomed. Eng*. 33: 803–806. [*The third Rohrer coefficient is introduced in this paper.]*

Johnson, A.T. 1991. *Biological Process Engineering*, John Wiley and Sons, New York [*This book looks at biology from a systems perspective*].

Johnson, A.T. (2012). Variation of Respiratory Resistance Suggests Optimization of Airway Caliber. *IEEE Trans. Biomed. Eng.* 59: 2355-2361 [*This paper presents data about natural variation of respiratory resistance*].

Johnson, A.T., P. Chapain, D. Slaughter, S. Gallena, and J. Vossoughi. (2013). Inspiratory and Expiratory Resistances during Exercise. *Br. J. Med. Med. Res.* 3(4): 1222-1232 [*This paper demonstrates that respiratory resistance does not change immediately after exercise ceases*].

Johnson, A.T. and J.M. Milano. (1987). Relation between Limiting Exhalation Flow Rate and Lung Volume. *IEEE Trans. Biomed. Eng.* 34: 257-258. [*The third Rohrer coefficient is introduced in this paper.]*

Johnson, A.T., W.H. Scott, E. Russek-Cohen, F.C. Koh, N.K. Silverman, and K.M. Coyne. (2005). Resistance Values Obtained with the Airflow Perturbation Device. *Int. J. Med. Implants Dev.* 1:137–151. [[*Data from over a thousand measurements are given and statistical analysis presented.]*

Jones, N.L. (1984b). Dyspnea in Exercise. *Med. Sci. Sports Exerc.* 16: 14–19. [*Breathing difficulty in exercise is explored.]*

Jones, A.S., J.M. Lancer, A.A. Moir, and J.C. Stevens. (1985). Effect of Aspirin on Nasal Resistance to Airflow. *Br. Med. J.* 290: 1171–1173. [*Certain drugs have respiratory mechanics effects.]*

Lausted, C.G., A.T. Johnson, W.H. Scott, M.M. Johnson, K.M. Cayne, and D.C. Coursey. (2006). Maximum Static Inspiratory and Expiratory Pressures with Different Lung Volumes. *Biomed.Engr. Online* 5:29 doi 10.1186/1475-925x-5-29. www.biomedical-engineering-online.com/content/pdf/1475-925x-5-29.pdf/

[*Maximum developed respiratory pressures are dependent on lung volume.]*

Lightfoot, E.N. (1974). *Transport Phenomena and Living Systems*. John Wiley & Sons, New York, p. 100 [*This book presents mathematical analyses in biology*].

Lopresti, E. R., A. T. Johnson, F. C. Koh, W. H. Scott, S. Jamshidi, and N. K. Silverman (2008). Testing Limits to Airflow Perturbation Device (APD) Measurements. *Biomed.Engr. Online* 7:28 doi 10.1186/1475-925x-7-28. www.biomedical-engineering-online.com/content/pdf/7/1/28. [*This work explores respiratory resistance measurement limitations.]*

Loring, S.H., and J. Mead. (1982). Abdominal Muscle Use during Quiet Breathing and Hyperpnea in Uninformed Subjects. *J. Appl. Physiol.* 52: 700–704. [*This is a work on the respiratory system musculature.]*

Love, R.G. (1983). Lung Function Studies before and after a Work Shift. *Br. J. Ind. Med.* 40: 153–159. [*Respiratory mechanics can vary over time.]*

Macklem, P.T. (1980. The Paradoxical Nature of Pulmonary Pressure–Flow Relationships. *Fed. Proc*. 39: 2755–2758. [*This is a work on the respiratory mechanics.]*

Macklem, P.T. 2004). A Century of the Mechanics of Breathing. *Am. J. Respir. Crit. Care Med*. 170: 10–15 [*This is a good review*]. [*This paper reviews respiratory mechanics work.]*

McParland, B.E., P.T. Macklem, and P.D. Pare´. (2003). Airway Wall Remodeling: Friend or Foe? *J. Appl. Physiol.* 95: 426–434 [*Airway remodeling is the change of anatomy that responds to stress.]*

McIlroy, M.B., D.F. Tierney, and J.A. Nadel. (1963). A New Method for Measurement of Compliance and Resistance of Lungs and Thorax. *J. Appl. Physiol.* 18: 424–427. [*This paper explores new measurement methods.]*

Mead, J. (1961). Mechanical Properties of Lungs. *Physiol. Rev.* 41: 281–330. [*This is a work on the respiratory system*]. [*Mead's work is classic.]*

Mead, J. (1978). Analysis of the Configuration of Maximum Expiratory Flow–Volume Curves. *J. Appl. Physiol.* 44: 156–165. [*Mead was one of the foremost respiratory physiology pioneers.]*

Mead, J. (1980). Expiratory Flow Limitation: A Physiologist's Point of View. *Fed. Proc*. 39: 2771–2775 [*Mead is one of the pioneers of respiratory mechanics measurement. His writing requires careful reading to understand*].

Mead, J., J.M. Turner, P.T. Macklem, and J.B. Little. (1967). Significance of the Relationship between Lung Recoil and Maximum Expiratory Flow. *J. Appl. Physiol.* 22: 95–108. [*Although difficult to read, this paper has good basic information.]*

Mines, A.H. (1981). *Respiratory Physiology.* Raven Press, New York, pp. 131–157. [*This paper gives much general information about the respiratory system.]*

Muir, D.C.F. (1966). Bulk Flow and Diffusion in the Airways of the Lung, *Br. J. Dis. Chest* 60: 169-176. [*Basic information about mass transfer is given.]*

Notter, R.H., and J.N. Finkelstein. (1984). Pulmonary Surfactant: An Interdisciplinary Approach, *J. Appl. Physiol.* 57: 1613–1624. [*Surfactant in the pulmonary system is needed to keep the airways open.]*

Ochs, M., J.R. Nyengaard, A. Jung, L. Knudsen, M. Voight, T. Wahlers, J. Richter, and H.J.G. Gundersen. (2004). The Number of Alveoli in the Human Lung. *Am. J. Respir. Crit. Care. Med.*169: 120–124. *Use for respiratory system anatomy.]*

Pedley, T.J., R.C. Schroter, and M.F. Sudlow. (1977). Gas Flow and Mixing in the Airways, in *Bioengineering Aspects of the Lung*, J.B. West, ed., Marcel Dekker, New York, pp. 163–265. [*This is a work on the respiratory system*].

Petrini, M.F. (1986). Distribution of Ventilation and Perfusion: A Teaching Model. *Comput. Biol. Med.* 16: 431–444. [*This is a work on the respiratory system*].

Rohrer, F. (1915). Flow Resistance in the Human Air Passages and the Effect of Irregular Breathing of the Bronchial System on the Respiratory Process in Various Regions of the Lungs, in *Transitions in Respiratory Physiology*, J.B. West, ed., Dowden, Hutchinson, and Rose, Stroudsburg, PA. pp. 3-66 [*This is a classic work, reprinted*].

Sackner, M.A. (1976). Pulmonary Structure and Pathology, in *Biological Foundations of Biomedical Engineering*. J. Kline, ed., Little, Brown and Company, Boston, MA, pp. 231–241. [*This is a work on the respiratory system*].

Silverman, N.K., A.T. Johnson, W.H. Scott, and F.C. Koh. (2005). Exercise-Induced Respiratory Resistance Changes as Measured with the Airflow Perturbation Device. *Physiol. Meas.* 26:29–38. [*Data is given for respiratory resistance during exercise.]*

Skelland, A.H.P. (1967). *Non-Newtonian Flow and Heat Transfer*. John Wiley & Sons, New York, p. 125. [*This is a general heat and mass transfer book for basic information.]*

Suki, B., and J.H.T. Bates. (1991). A Nonlinear Viscoelastic Model of Lung Tissue Mechanics. *J. Appl. Physiol.* 71: 826–833 [*Bates has been one of the most prolific researchers in respiratory mechanics measurement*].

Suzuki, S., H. Sasaki, K. Sekizawa, and T. Takishima. (1982). Isovolume Pressure–Flow Relationships in Intrapulmonary Bronchi of Excised Dog Lungs. *J. Appl. Physiol.* 52: 295–303. [*Gives data about respiratory mechanical properties.]*

Tatsis, G., K. Horsfield, and G. Cumming. (1984). Distribution of Dead Space Volume in the Human Lung. *Clin. Sci.* 67: 493–497. [*Data given for respiratory dead volume.]*

Tiddens, H.A.W.M., W. Hofhuis, J.M. Bogaard, W.C.J. Hop, H. de Bruin, L.N.A. Willems, and J.C. de Jongste. (1999). Compliance, Hysteresis, and Collapsibility of Human Small Airways. *Am. J. Respir. Crit. Care Med.* 160: 1110–1118. [*Respiratory airways mechanics data are given.]*

Tierney, D.F. (2003). Ventilator-Induced Lung Injury Occurs in Rats, But Does It Occur in Humans? *Am. J. Respir. Crit. Care Med.* 168: 1414–1415. [*More respiratory mechanics data.]*

Warren, J., and S. Jennings. (1984). Normal Human Airway Response to Exercise. *J. Appl. Physiol.* 53: 1686-1693. [*Exercise responses are explored.]*

Wasserman, K., J.E. Hansen, D.Y. Sue, R. Casaburi, and B.J. Whipp. (1999). *Principles of Exercise Testing and Interpretation*. 3rd ed, Lippincott Williams & Wilkins, Philadelphia, PA [*Wasserman is a well-known researcher in exercise physiology*].

Weibel, E.R., (1963), *Morphology of the Human Lung*. Academic Press, New York [*This is the classic model of human airway division*].

Whipp, B.J. (1981). The Control of Exercise Hyperpnea, in *Regulation of Breathing*, Part II, T.F. Hornbein, ed., Marcel Dekker, New York, pp. 1069–1139. [*Exercise responses are explored.]*

Whitelaw, W.A., L.E. Hajdo, and J.A. Wallace. (1983). Relationships among Pressure, Tension, and Shape of the Diaphragm. *J. Appl. Physiol.* 55: 1899–1905. [*Respiratory anatomy.]*

Wong, L.S., and A.T. Johnson. (2004). Decrease of Resistance to Air Flow with Nasal Strips as Measured with the Airflow Perturbation Device. *Biomed. Eng. Online*. 3: 38, http://www.biomedical-engineering-online.com/content/3/1/38. [*Gives respiratory resistance measurements of the nasal passages.]*

Yamashiro, S.M., J.A. Daubenspeck, T.N. Lauritsen, and F.S. Grodins. (1975). Total Work Rate of Breathing Optimization in CO2 Inhalation and Exercise. *J. Appl. Physiol.* 38: 702–709. [*This is a basic modeling paper on respiratory work.]*

Yeates, D.B., and N. Aspin. (1978). A Mathematical Description of the Airways of the Human Lungs. *Respir. Physiol.* 32: 91–104. [*This work models respiratory airways anatomy.]*

Biographical Sketch

Arthur T. Johnson attended Cornell University for his undergraduate and graduate degrees. His PhD was awarded in 1969, and he immediately began serving as an officer in the US Army, eventually serving in Viet Nam at the rank of captain. He was awarded the Army Commendation Medal and Bronze Star Medal. He joined the faculty of the University of Maryland in 1975, and was Professor from 1986 until 2009, when he became Professor Emeritus. He was cochairman of the committee to found the American Institute for Medical and Biological Engineering (AIMBE) from 1988 to 1992, and served as the Executive Director of AIMBE in 2004. He has been President of the Alliance for Engineering in Medicine and Biology (1984-1988), Institute for Biological Engineering (1998), and International Society for Respiratory Protection (2004-2006). He was the Secretary of the Biomedical Engineering Society from 2004 to 2009. He has been on the Board of Directors of the American Society for Agricultural and

Biological Engineers (1995-1997). He is a Founding Fellow of the American Institute for Medical and Biological Engineering (1992), Life Fellow of the American Society for Engineering Education (1996), Life Fellow of the American Society for Agricultural and Biological Engineers (2002), Fellow of the American Industrial Hygiene Association (2005), Fellow of the Biomedical Engineering Society (2005), Fellow of the Institute for Biological Engineering (2009), and the Life Fellow of the Institute for Electrical and Electronics Engineers (2010). He is a member of the honor societies: Phi Kappa Phi, Sigma Xi, Tau Beta Pi, and Alpha Epsilon. He has written three books: *Biomechanics and Exercise Physiology: Quantitative Modeling, Biological Process Engineering, and Biology for Engineers.* His research interests are human performance wearing respiratory protective masks, respiratory mechanics and measurement, and transport processes. He has been most recently active in teaching electronic design, transport processes, and engineering in biology courses, and working to continue development of the Airflow Perturbation Device as a noninvasive measurement of respiratory resistance.