Biol. Cybern. 89, 163–169 (2003)
DOI 10.1007/s00422-003-0424-8

Biological
Cybernetics

Function of brainstem neurons in optimal control of respiratory mechanics

Fleur T. Tehrani

College of Engineering and Computer Science, California State University, Fullerton,
800 North State College Boulevard, Fullerton, CA 92831-3599, USA

Received: 14 March 2002 / Accepted: 6 May 2003 / Published online: 30 June 2003

Abstract. An optimization control procedure is developed to describe the function of the human respiratory controller in determination of the respiratory frequency, the expiratory reserve volume, and the physiological dead space volume at all levels of human activity. The required level of alveolar ventilation is considered to have been determined based on the inputs from the peripheral and central chemoreceptors. The proposed procedure describes the mechanical control of breathing in which the excitation signals are adjusted and transferred from the neuron pools in the brainstem to the respiratory muscles to control the rate and depth of breathing. The criterion of minimum average respiratory work rate is used to find the optimal characteristics of respiration. The respiratory frequency, physiologic dead space volume, and expiratory reserve volume are used simultaneously as the optimization variables to minimize the average respiratory work rate. The optimization procedure has been applied by using different airflow patterns at various levels of ventilation. The theoretical results of the study have been compared with the experimental data in exercise taken from the literature. The results show a close agreement between the experimentally measured data and the theoretical values found by the optimization control procedure. The findings attest to the validity of the minimum average work rate criterion and the proposed multivariable optimization procedure compared with other procedures suggested in the literature in control of respiratory mechanics.

1 Introduction

During the past several decades various hypotheses have been presented to describe the function of the respiratory controller in determination of the respiratory variables in mechanical control of breathing. The way in which the respiratory controller adjusts the drive signal to the respiratory muscles has been the subject of investigation by a number of researchers. The criterion of minimum average respiratory work rate was presented by Rohrer (1925) and later by Otis et al. (1950) to explain the experimental results of the human respiratory system. According to this criterion, frequency of breathing is optimized to minimize the average rate of energy expenditure in the breathing movement. Another hypothesis based on minimization of average force of the respiratory muscles was proposed by Mead (1960) for the same purpose. Later it was shown by Ruttiman and Yamamoto (1972) that the human airflow pattern during exercise can be better explained by the minimum work rate criterion. Yamashiro and Grodins (1973) used the minimum work rate hypothesis to optimize the respiratory frequency. In their study, the expiratory reserve volume (ERV) was first optimized by minimizing the added inspiratory and expiratory elastic works. Based on the calculated value of ERV, the breathing frequency was then optimized on the basis of the minimum average work rate criterion. The volume-pressure curve of the lung was approximated by two linear characteristics above and below the relaxation volume, and dead space was not included as an optimization variable.

In another study (Yamashiro et al. 1975), ERV, the respiratory frequency, and the relative durations of inspiration and expiration were optimized on the basis of the minimum average work rate hypothesis. The researchers assumed respiratory braking and included the effect of negative work by the respiratory muscles in exercise. The lung volume-pressure curve was presented by two linear characteristics above and below the relaxation volume. Dead space was not one of the optimized variables but was assumed as a function of tidal volume. There were considerable differences between the theoretical and experimental results in their study, especially with regard to minute ventilation and ERV.

Correspondence to: F. T. Tehrani
(e-mail: ftehrani@fullerton.edu,
Tel.: +1-714-2782658, Fax: +1-714-2787162)

In another article (Hamalainen and Viljanen 1978), a model was presented to predict the respiratory airflow pattern. The breathing frequency, dead space volume, ERV, and durations of inspiration and expiration were assumed to be fixed. The model was designed solely to predict the shape of the airflow. The model could not reproduce the asymmetry observed in the airflow pattern in inspiration, and the simulation results were not compared to any experimental data.

Later another model was presented in which minute ventilation was controlled by minimizing the sum of two functions. One, a function of the square of the difference between the arterial partial pressure of CO_2 and a desired threshold value, and the other, a logarithmic function of the minute ventilation that was considered as an indicator of the degree of the subject's comfort level (Poon 1987, 1991). The dynamic behavior of the controller was not investigated, and the system was not designed to predict respiratory frequency, tidal volume, dead space, or ERV in these studies.

In another paper (Oku et al. 1991), a model of the respiratory system based on control of CO_2 was presented. In this model, the CO_2 signal was enhanced in exercise. The simulation results for ventilation and CO_2 level were in general agreement with the experimental data. The model was not designed to predict breathing frequency, physiological dead space, or ERV.

In another article (Johnson 1995), the hypothesis of equalization of inspiratory and expiratory pressures to predict the values of ERV in exercise was presented. Determination of the respiratory frequency and the dead space was not included in this study, and it was concluded that ERV is not optimized in the same way as other respiratory variables.

In another study (Tehrani 1998), a two-level hierarchical control system was presented to determine the respiratory variables in exercise. In this study, breathing frequency was determined in the first stage of control on the basis of minimum average work rate criterion, while dead space was a linear function of alveolar ventilation. In the second stage of control, ERV was found by using the hypothesis of equalization of maximal inspiratory and expiratory pressures. The results were in general agreement with the experimental observations in low to moderate exercise. The theoretical and experimental values deviated from each other as the rate of activity was increased in exercise.

In this paper, a hypothesis is presented to describe the way in which the excitation signals from the neuron pools in the brainstem are adjusted to control respiratory mechanics. Alveolar ventilation is considered given based on the responses of the arterial and central chemoreceptors and is an input to the controller. Breathing frequency, f, the physiologic dead space volume, V_D, and the expiratory reserve volume, ERV, are all optimized simultaneously and on the basis of the same criterion to minimize the average respiratory work rate. Unlike resting conditions where expiration is almost completely passive, as the rate of activity increases, more energy is spent by the respiratory muscles to overcome the elastic forces in expiration as well as inspiration. The additional effect of the elastic forces in expiration is included in this study, and no respiratory braking is assumed at higher levels of ventilation. Rectangular and sinusoidal airflow patterns are both used at a wide range of ventilation and activity. The rectangular pattern is chosen because it has been suggested to be the optimal airflow pattern in exercise (Ruttiman and Yamamoto 1972). The sinusoidal airflow pattern is used to represent the main harmonic of any nonspecific airflow shape in exercise. The theoretical results are compared with the experimental data in the literature to assess the validity of the control scheme.

2 Methods

Since the chest and lungs are elastic elements, some of the energy of the muscles is used to overcome the elastic forces in tissue expansion. At rest, expiration is almost entirely passive and results solely from relaxation of the respiratory muscles and recoil of the lungs. But in exercise and higher levels of ventilation, expiration is also accelerated by contraction of the muscles in the chest and abdomen. Therefore, the total work required to overcome the elastic forces in respiration is described as:

$$W_{el} = W_{el(insp)} + W_{el(exp)} = \int_{0}^{V_T+ERV-V_r} P\,dv' - \int_{ERV-V_r}^{0} P\,dv' \tag{1}$$

In the above equation, V_r is the lung relaxation volume (at which $P = 0$), V_T is the tidal volume, and ERV is the expiratory reserve volume.

$$V' = V - V_r \tag{2}$$

where V is the lung volume. The elastic pressure P in Eq. 1 is described as:

$$P = K'(V - V_r) \tag{3}$$

where K' is the respiratory elastance. A list of the symbols used in the equations is also provided in the Appendix. Since $dv' = dv$, Eq. 1 can be rewritten as:

$$W_{el} = \int_{V_r}^{V_T+ERV} K'(V - V_r)\,dv - \int_{ERV}^{V_r} K'(V - V_r)\,dv \tag{4}$$

Therefore:

$$W_{el} = 0.5K'(V_T + ERV - V_r)^2 + 0.5K'(V_r - ERV)^2 \tag{5}$$

Part of the energy of the muscles is dissipated in the airways because of the existence of dead space and airway resistance. Ignoring the energy dissipated in respiration due to air turbulence and inertia, which is small compared to elastic and viscous energies, the total work in respiration can be described as:

$$W = W_{el} + W_{res} \tag{6}$$

where W_{res} is the work required to overcome airway resistance. This energy is found as follows:

$$P_g = R\mathrm{d}v'/\mathrm{d}t \tag{7}$$

where R is the airway resistance and P_g is the pressure to overcome the air viscosity in respiration.

$$\mathrm{d}W_{res} = P_g\mathrm{d}v' = R\mathrm{d}v'(\mathrm{d}v'/\mathrm{d}t) \tag{8}$$

and

$$W_{res} = \int_{\mathrm{ERV}-V_r}^{V_i-V_r} R[\mathrm{d}v'/\mathrm{d}t]\mathrm{d}v' \tag{9}$$

where V_i is the maximum volume of the lungs in inspiration. For a rectangular airflow pattern:

$$\mathrm{d}v'/\mathrm{d}t = a \tag{10}$$

where a is the peak airflow rate. By substituting Eq. 10 in 9:

$$W_{res} = \int_{\mathrm{ERV}-V_r}^{V_i-V_r} aR\mathrm{d}v' = aRV_T \tag{11}$$

But for a rectangular airflow pattern:

$$V_T = aT/2 = a/2f \tag{12}$$

and

$$a = 2fV_T \tag{13}$$

where T and f are the breathing period and frequency, respectively. By substituting Eqs. 5 and 11 into Eq. 6 and multiplying both sides of the resulting equation by f, the average rate of respiratory work can be found:

$$W^\bullet = 0.5K'f[(V_r - \mathrm{ERV})^2 + (V_T + \mathrm{ERV} - V_r)^2] + aRV_Tf \tag{14}$$

By substituting Eq. 13 into the above:

$$W^\bullet = 0.5K'f[(V_r - \mathrm{ERV})^2 + (V_T + \mathrm{ERV} - V_r)^2] + 2Rf^2V_T^2 \tag{15}$$

But:

$$V_T = V_D + V_A^\bullet/f \tag{16}$$

where $V_A^\bullet$ is the alveolar ventilation in l/s, f is breathing frequency in breath/s, and V_D is the dead space in liters.

By substituting V_T from Eq. 16 into Eq. 15:

$$W^\bullet = 0.5K'f[2V_r^2 + 2\mathrm{ERV}^2 - 4V_r\mathrm{ERV} + 2(\mathrm{ERV} - V_r)(V_D + V_A^\bullet/f) + (V_D + V_A^\bullet/f)^2] + 2Rf^2(V_D + V_A^\bullet/f)^2 \tag{17}$$

The expression for $W^\bullet$ in Eq. 17 is the objective function for a rectangular airflow pattern. In the next step of this procedure, f, ERV, and V_D in Eq. 17 are computed to minimize this objective function. The modified method of feasible directions for constrained optimization (Vanderplaats 1984; DOT User's Manual 1999) is used for this purpose. Figure 1 shows the main steps of the optimization procedure. In this method, an objective function is defined in terms of several independent variables. The optimum values of the variables are determined in an iterative procedure to minimize the objective function subject to certain constraints. In each iteration, gradients of the objective function and the critical constraints are computed, a suitable search direction is found, and the incremental step-size along the search direction to update the variables is computed. The new variables are calculated, and a convergence check is performed at the end of each iteration. If the algorithm has converged (meaning that the objective function has been minimized subject to the defined constraints), then the program is stopped. Otherwise, a new iteration is followed as shown in the diagram and the procedure continues until the optimum values of the variables are found. If the algorithm does not converge after a maximum number of iterations, the procedure is terminated. The details of how the search direction and the incremental step-size are determined and other specifications of the procedure can be found elsewhere (Vanderplaats 1984; DOT User's Manual 1999) and are not repeated here for brevity.

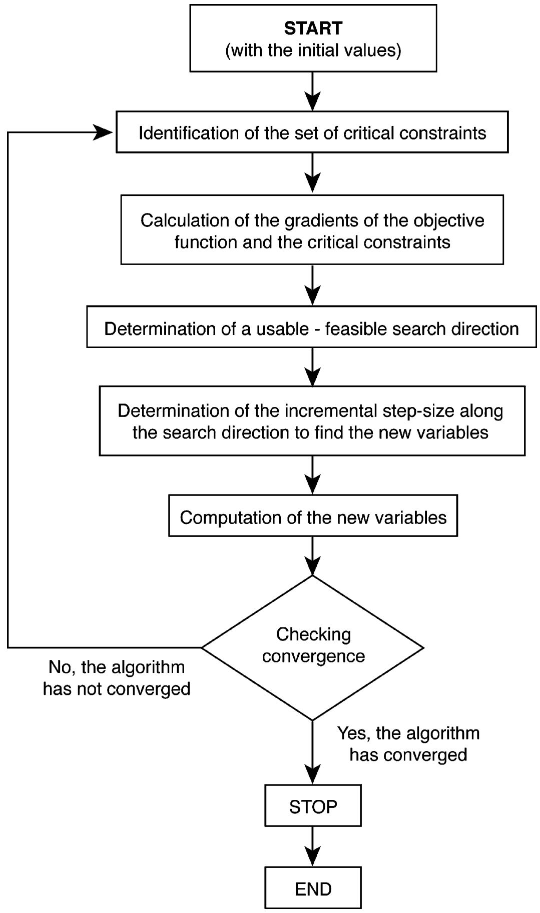

Fig. 1. The main steps of the optimization procedure

In minimizing the objective function expressed by Eq. 17, the optimization algorithm is constrained by the physiological range of dead space V_D. The relationship between the mean value of the dead space and alveolar ventilation, which is based on the experimental measurements at different levels of ventilation, is the following linear equation (Asmussen and Nielsen 1956; Fincham and Tehrani 1983; Hey et al. 1966):

$$V_D(\text{mean}) = 0.1698 V_A^\bullet + 0.1587 \tag{18}$$

The standard deviation of the data points taken from the literature that were used to derive this equation is about ±20%. Therefore, the search window for V_D in the optimization algorithm was chosen as:

$$\text{Range of } V_D = V_D(\text{mean})(1 \pm 0.2) \tag{19}$$

The lower and upper limits of the variables were defined by their physiological limits in the algorithm. Frequency was limited between 6 to 54 breaths/min, the physiological dead space was limited in the range of 0.14 to 0.7 l, and the range for ERV was defined from 0.6 to 2.5 l. Therefore, the optimization algorithm was subject to the following additional side constraints:

$$6 \le F \le 54 \qquad (F \text{ is breathing frequency in breaths/min and is } 60f) \tag{20}$$

$$0.14 \le V_D \le 0.7 \tag{21}$$

$$0.6 \le \text{ERV} \le 2.5 \tag{22}$$

The effect of a sinusoidal airflow pattern was also evaluated in this study. The respiratory work to overcome viscous forces is calculated for a sinusoidal airflow pattern as follows:

$$\mathrm{d}v'/\mathrm{d}t = a \sin 2\pi f t \tag{23}$$

By substituting in Eq. 8:

$$\begin{aligned} dW_{\text{res}} &= P_g \mathrm{d}v' = R[\mathrm{d}v'/\mathrm{d}t]\mathrm{d}v' \\ &= R[\mathrm{d}v'/\mathrm{d}t]^2 \mathrm{d}t = Ra^2 \sin^2 2\pi f t \mathrm{d}t \end{aligned} \tag{24}$$

Therefore:

$$W_{\text{res}} = \int_0^{T/2} Ra^2 \sin^2 2\pi f t \mathrm{d}t = a^2 RT/4 \tag{25}$$

But:

$$V_T = \int_0^{T/2} a \sin 2\pi f t \mathrm{d}t = a/\pi f \tag{26}$$

thus:

$$a = \pi f V_T \tag{27}$$

By substituting Eq. 27 into Eq. 25:

$$W_{\text{res}} = R\pi^2 V_T^2 f/4 \tag{28}$$

Substituting Eqs. 5 and 28 into Eq. 6 yields:

$$\begin{aligned} W &= 0.5K'[V_r - \text{ERV}]^2 \\ &\quad + 0.5K'[V_T + \text{ERV} - V_r]^2 + R\pi^2 V_T^2 f/4 \end{aligned} \tag{29}$$

Multiplying both sides of this equation by f and expressing V_T in terms of $V_A^\bullet$, f, and V_D from Eq. 16, the following equation for the average work rate in breathing for a sinusoidal airflow pattern will result:

$$\begin{aligned} W^\bullet &= 0.5K' f [2V_r^2 + 2\text{ERV}^2 \\ &\quad - 4V_r\text{ERV} + 2(\text{ERV} - V_r)(V_D + V_A^\bullet/f) \\ &\quad + (V_D + V_A^\bullet/f)^2] + (R\pi^2 f^2/4)(V_D + V_A^\bullet/f)^2 \end{aligned} \tag{30}$$

The expression for $W^\bullet$ in Eq. 30 is the objective function for a sinusoidal airflow pattern to be minimized. Using the modified method of feasible directions for constrained optimization (Vanderplaats 1984; DOT User's Manual 1999), f, ERV, and V_D were computed to minimize the respiratory work rate described by Eq. 30. The same constraints that were used for the variables for a rectangular airflow were also applied for a sinusoidal airflow pattern.

3 Results

The optimization algorithm was applied under various test conditions at different levels of respiration. Table 1 shows the summary of the optimization results. F, V_D, and ERV are the independent variable outputs, while V_T, V_E, and V_i depend on the first three. Rectangular and sinusoidal airflow patterns have both been applied. Average values reported in the literature (Mead 1960; Otis et al. 1950) for R (airway resistance) and K' (respiratory elastance) for healthy subjects have been used in the study. In Table 1, R is 5.6 cm H_2O.second.liter^{-1} while K' is either 8.52 or 5.5 cm H_2O.liter^{-1}, resulting in respiratory time constants of 0.011 min and 0.017 min, respectively. The lung relaxation volume V_r is 2.5 l, and the vital capacity of the lungs VC is 4.8 l. The optimization results are compared with the experimental data in the literature. These data are from healthy individuals in exercise while breathing the ambient air. The same experimental data have been used by several researchers on the same subject (Yamashiro and Grodins 1973; Yamashiro et al. 1975; Johnson 1995; Tehrani 1998). In the figures that follow, the optimization results are compared to the experimental data to assess the validity of the control procedure.

In Fig. 2, the theoretical values of breathing frequency are compared with the experimental results of Silverman et al. (1951). The theoretical results are shown for $RC = 0.011$ min for both rectangular and sinusoidal airflow patterns. The theoretical and experimental results are seen to be in close agreement. The theoretical values lie within one standard deviation of the experimental data reported in the article by Silverman et al. (1951). There is no significant difference between the results obtained for two different airflow patterns as shown in Fig. 2.

Table 1. Summary of the optimization results. $R = 5.6$ cm H_2O.second.liter^{-1}, $V_r = 2.5$ l, and $VC = 4.8$ l

Input variables				Optimized output variables					
	V_A	K'	RC	F	V_D	ERV	V_T	V_E	V_i
Rectangular airflow pattern	5.88	8.52	0.011	14.00	0.14	2.16	0.56	7.90	2.72
	7.74	8.52	0.011	16.30	0.15	2.12	0.62	10.17	2.74
	13.13	8.52	0.011	21.10	0.16	2.03	0.78	16.61	2.81
	21.36	8.52	0.011	25.70	0.19	1.88	1.02	26.17	2.90
	30.48	8.52	0.011	28.60	0.21	1.72	1.28	36.59	3.00
	62.93	8.52	0.011	32.30	0.31	1.07	2.25	72.84	3.31
	5.88	5.50	0.017	11.50	0.14	2.10	0.65	7.54	2.75
	7.74	5.50	0.017	13.50	0.15	2.06	0.72	9.76	2.78
	13.12	5.50	0.017	17.30	0.16	1.94	0.92	15.96	2.86
	21.36	5.50	0.017	20.30	0.19	1.74	1.24	25.17	2.98
	30.46	5.50	0.017	21.40	0.21	1.46	1.63	35.00	3.10
	62.86	5.50	0.017	28.80	0.31	0.99	2.48	71.66	3.47
Sinusoidal airflow pattern	5.88	8.52	0.011	12.80	0.14	2.14	0.60	7.73	2.74
	7.74	8.52	0.011	15.10	0.15	2.10	0.66	9.98	2.76
	13.13	8.52	0.011	19.10	0.16	1.98	0.85	16.27	2.83
	21.37	8.52	0.011	23.30	0.19	1.83	1.10	25.75	2.93
	30.50	8.52	0.011	25.00	0.21	1.61	1.43	35.84	3.04
	62.90	8.52	0.011	30.10	0.31	0.99	2.40	72.17	3.40
	5.88	5.50	0.017	10.50	0.14	2.06	0.70	7.40	2.76
	7.74	5.50	0.017	12.00	0.15	2.00	0.79	9.53	2.79
	13.13	5.50	0.017	15.60	0.16	1.88	1.00	15.68	2.88
	21.37	5.50	0.017	18.50	0.19	1.66	1.34	24.85	3.00
	30.50	5.50	0.017	19.50	0.21	1.30	1.87	34.66	3.17
	62.80	5.50	0.017	26.70	0.30	0.92	2.66	71.00	3.58

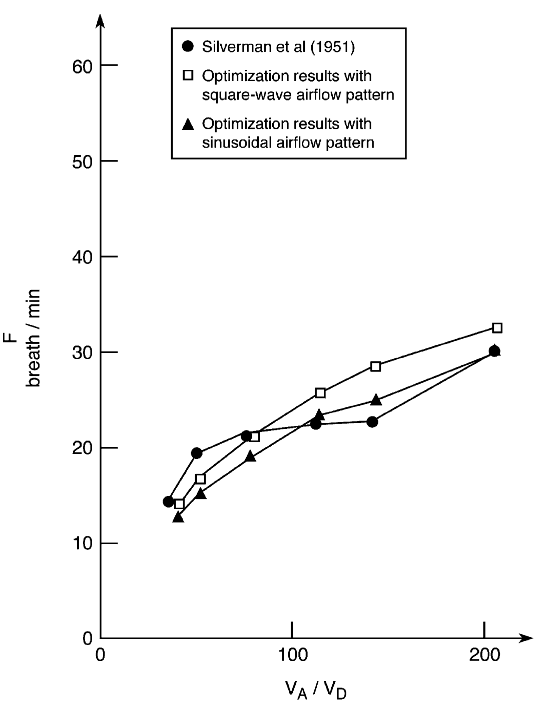

Fig. 2. Comparison of the theoretical results of the respiratory frequency with the experimental data of Silverman et al. (1951)

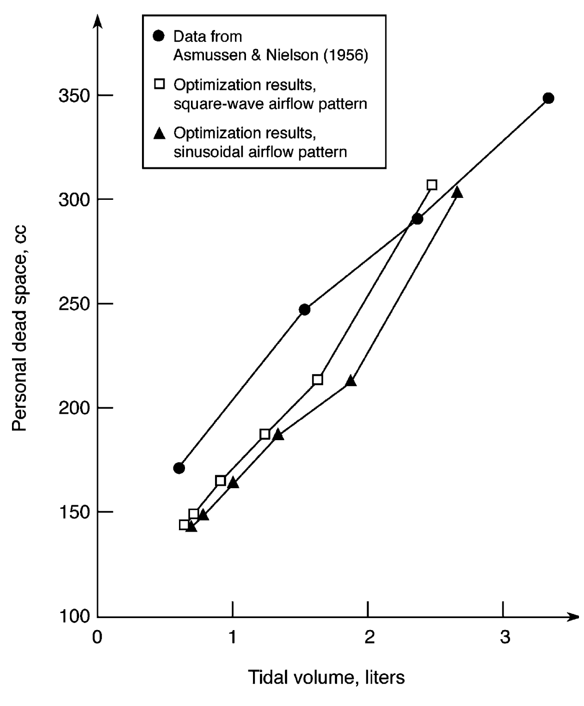

Fig. 3. Theoretically predicted optimization results for the dead space compared to the experimental values reported by Asmussen and Nielsen (1956)

Figure 3 shows the optimization results of V_D in comparison to the experimental data from Asmussen and Nielsen (1956). The theoretical results are shown for both airflow patterns while RC is equal to 0.017 min. The experimental and theoretical results are in general agreement, as shown in the figure. The predicted values are within one standard deviation of the reported experimental data. There is no significant advantage associated with either of the two waveforms in this test.

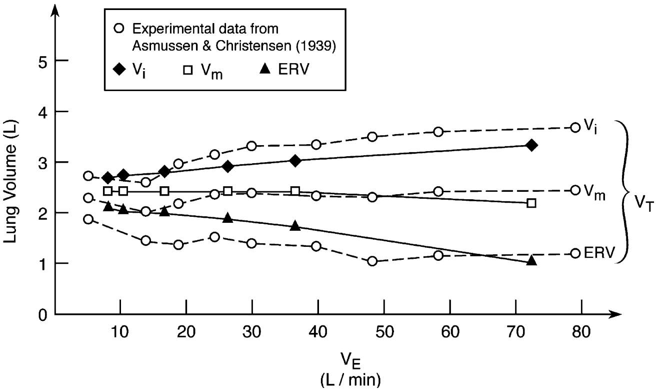

Fig. 4. Comparison of the theoretical results for ERV, V_i, V_m, and V_T with the experimental data of Asmussen and Christensen (1939). A rectangular airflow pattern is assumed to find the theoretical results

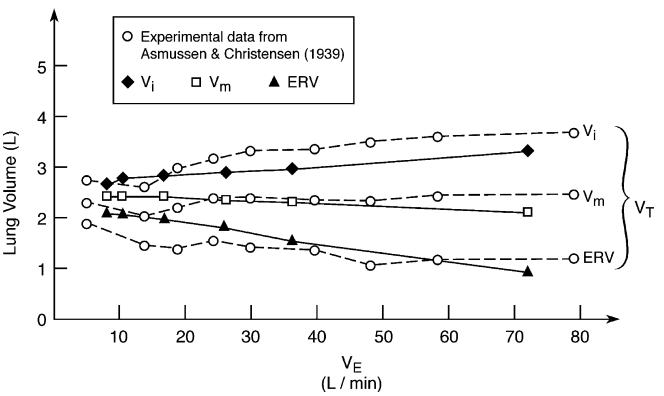

Fig. 5. Theoretical results of ERV, V_i, V_m, and V_T compared to the experimental data of Asmussen and Christensen (1939). A sinusoidal airflow pattern is applied to find the theoretical values

In Figs. 4 and 5, the optimization results for ERV, V_T, V_i, and V_m are compared with the experimental data of Asmussen and Christensen (1939). In Fig. 4, a rectangular airflow pattern is applied, and in Fig. 5 this pattern is sinusoidal. In both figures, *RC* is equal to 0.011 min. The theoretical results are seen to be in close agreement with the experimental data. Once again, different airflow patterns do not seem to have significantly affected the optimization results.

4 Discussion

An optimization control procedure is presented to describe the function of the respiratory controller in mechanical control of breathing. The optimization procedure is designed to control the respiratory frequency, the expiratory reserve volume, and the physiologic dead space volume in humans at different levels of ventilation. These variables are optimized simultaneously to minimize the average respiratory work rate. The effect of the work performed by the respiratory muscles in expiration at higher levels of activity has been included in this study. The elastic work in inspiration is divided into two parts: the work spent to inflate the lungs above the relaxation volume and the work performed to overcome elastic forces to increase the lung volume from ERV to the relaxation level. The latter part is assumed to be passive and due to recoil of the lungs. The elastic work spent in expiration is also divided into two sections: the work done to bring lung volume back to the relaxation value and the work spent to further deflate the lungs to the ERV level. The first section is assumed passive and due to recoil of the lungs, and the second part is added to the total elastic work in inspiration to include the energy spent in contraction of the muscles in exhalation. The effect of respiratory braking is ignored in this study since the significance of braking decreases considerably as the rate of exercise increases. The energy spent to overcome viscous forces in inspiration is added to the total elastic work to find the total energy in respiration. Other types of work such as those spent to overcome turbulence forces and inertia are ignored compared to the elastic and viscous energy.

To investigate the effects of different airflow patterns, rectangular and sinusoidal waveforms have been used in this study. The rectangular pattern was chosen since it has been suggested in the literature (Ruttiman and Yamamoto 1972) to be the optimal airflow pattern in exercise. However, according to earlier experimental observations reported in the literature, the airflow pattern was found to be widely different and posture dependent in different individuals (Morrow and Vosteen 1953; Proctor and Hardy 1949). Regardless of the specific pattern of airflow, a sinusoidal pattern can be considered as its first and most important harmonic. Therefore, the sinusoidal airflow pattern was also used in this study to represent a nonspecific/generic airflow shape in exercise. The $I : E$ ratio is less than unity at rest. Prediction of the exact airflow shape under resting conditions would require consideration of the variations in this ratio. However, the $I : E$ ratio rises sharply in exercise and approaches unity as respiratory braking diminishes at higher rates of activity. This ratio on the average ranges from about 0.9 to 1.05 at high levels of activity according to early data in the literature (Silverman et al. 1951). The same trend was also observed in later experimental observations (Poon 1989). Therefore, since the focus of this study was on exercise, and prediction of the exact airflow shape was not one of its objectives, the $I : E$ ratio was assumed to be unity in applying both rectangular and sinusoidal airflow patterns. Application of these two patterns has not made any significant difference in the results. This indicates that there may not be an optimal airflow pattern in exercise. This result is consistent with some of the experimental observations reported in the literature that have indicated different patterns of airflow for different individuals. Even for the same individual, since physiological testing is not precisely repeatable, the airflow pattern is subject to some variation at different times.

In summary, breathing frequency, the physiologic dead space volume, and the expiratory reserve volume have all been optimized simultaneously and on the basis of the same criterion to minimize the average respiratory work rate. The optimization results have been compared to and found to be in close agreement with the experimental data. Contrary to Johnson's hypothesis (Johnson 1995), it is shown here that ERV is optimized with the breathing frequency and dead space to minimize the mean respiratory work rate. No additional, hierarchical procedure seems to be involved in the determination and adjustment of these variables. ERV, like the other respiratory variables, is optimized to keep the average respiratory work rate at the minimum level.

In conclusion, the results of this study attest to the validity of the minimum average work rate criterion and the proposed multivariable optimization procedure for control of respiratory mechanics.

Appendix
Glossary of symbols

Symbol	Definition	Unit
a	peak airflow rate	liter/second
ERV	expiratory reserve volume	liter
f	breathing frequency	breath/second
F	breathing frequency	breath/minute
K'	respiratory system elastance (the reciprocal of compliance)	cm H_2O/liter
P	pressure	cm H_2O
P_g	pressure to overcome air viscosity resistance	cm H_2O
R	air viscosity resistance	cm H_2O/liter/second
RC	respiratory time constant (product of resistance and compliance)	minute
t	time	second
T	breathing period	second
V	lung volume	liter
V_A	alveolar ventilation	liter/minute
$V_A^\bullet$	alveolar ventilation	liter/second
VC	vital capacity of the lungs	liter
V_D	physiologic dead space	liter
V_E	total ventilation	liter/minute
V_i	maximum lung volume in inspiration	liter
V_m	lung midposition	liter
V_r	lung relaxation volume	liter
V_T	tidal volume	liter
W	energy	cm H_2O.liter (0.098. Joule)
W_{el}	work to overcome elastic forces	cm H_2O.liter (0.098. Joule)
W_{res}	work to overcome resistive forces	cm H_2O.liter (0.098. Joule)
$W^\bullet$	average work rate of breathing	cm H_2O.liter/second (0.098. Watt)

References

Asmussen E, Christensen EH (1939) Die Mittelkapazität der Lungen bei erhöhtem O_2-Bedarf. Skand Arch Physiol 82: 201–211

Asmussen E, Nielsen M (1956) Physiological dead space and alveolar gas pressures at rest and during muscular exercise. Acta Physiol Scand 38: 1–21

DOT User's Manual (1999) Vanderplaats research and development, Inc. Colorado Springs, CO

Fincham WF, Tehrani FT (1983) A mathematical model of the human respiratory system. J Biomed Eng 5: 125–133

Hamalainen RP, Viljanen AA (1978) Modelling the respiratory airflow pattern by optimization criteria. Biol Cybern 29: 143–149

Hey EN, Lloyd BB, Cunningham DJC, Jukes MGM, Bolton DPG (1966) Effects of various respiratory stimuli on the depth and frequency of breathing in man. Resp Physiol 1: 193–205

Johnson AT (1995) The change in initial lung volume during exercise. IEEE Trans Biomed Eng 42(3): 278–281

Mead J (1960) Control of respiratory frequency. J Appl Physiol 15: 325–336

Morrow PE, Vosteen RE (1953) Pneumatographic studies in man and dog incorporating a portable wireless transducer. J Appl Physiol 5: 348–360

Oku Y, Saidel GM, Chonan T, Altose MD, Cherniack NS (1991) Sensation and control of breathing: a dynamic model. Ann Biomed Eng 19: 251–272

Otis AB, Fenn WO, Rahn H (1950) Mechanics of breathing in man. J Appl Physiol 2: 592–607

Poon CS (1987) Ventilatory control in hypercapnia and exercise: optimization hypothesis. J Appl Physiol 62(6): 2447–2459

Poon CS (1989) Effects of inspiratory resistive load on respiratory control in hypercapnia and exercise. J Appl Physiol 66(5): 2391–2399

Poon CS (1991) Optimization behavior of brainstem respiratory neurons. A cerebral neural network model. Biol Cybern 66: 9–17

Proctor DF, Hardy JB (1949) Studies of respiratory airflow. Bull Johns Hopkins Hosp 85: 253–280

Rohrer F (1925) Physiologie der Atembewegung. In: Bethe A et al (eds) Handbuch der normalen und pathologischen Physiologie, vol 2. Springer, Berlin Heidelberg New York, pp 70–127

Ruttiman VE, Yamamoto WS (1972) Respiratory airflow patterns that satisfy power and force criteria of optimality. Ann Biomed Eng 1: 146–159

Silverman L, Lee G, Plotkin T, Sawyers IA, Yancey AR (1951) Airflow measurements on human subjects with and without respiratory resistance at several work rates. Arch Ind Hyg Occup Med 3: 461–478

Tehrani FT (1998) Optimal control of respiration in exercise. In: Proceedings of the 20th IEEE conference of the Engineering in Medicine and Biology Society, Hong Kong, 20: 3211–3214

Vanderplaats GN (1984) An efficient feasible directions algorithm for design synthesis. AIAA J 22(11): 1633–1640

Yamashiro SM, Daubenspeck JA, Lauristen TN, Grodins FS (1975) Total work rate of breathing optimization in CO_2 inhalation and exercise. J Appl Physiol 38: 702–709

Yamashiro SM, Grodins FS (1973) Respiratory cycle optimization in exercise. J Appl Physiol 35: 522–525