COGITATIONES

Minimum Entropy Production as a Design Criterion for Breathing

The idea that the entropy balance of an organism is the critical requirement in maintaining life has been discussed in popular science since the time of Boltzmann. SCHRÖDINGER[1] emphasizes this idea in the essay, *What is Life?* He points out that the energy and material content of an organism remain constant during metabolism, whereas the entropy content increases. The organism must continually draw negative entropy from its environment in order to maintain itself at a stationary entropy level.

In their comment on the organization found in life, PRIGOGINE and WIAME[2] make a comparison between biological and physical systems. In some physical systems under boundary conditions that impose a transport through the system, the steady state of the system is characterized by the condition that the entropy production is a minimum. The authors point out some examples of evolutionary trends which have led to a decrease in the entropy production. They even suggest that evolution, in analogy with physical processes, is just a tendency toward the state of minimum entropy production.

Both of these discussions emphasize the importance of analyzing biological processes in terms of entropy production and entropy flux. In this paper, a model foı a particular mechanism, the respiratory system in man is analyzed. The ventilation is one of the parameters in this model. It is shown that over the range of oxygen consumption which can be maintained for extended periods the observed value of the ventilation is the value which makes the entropy production a minimum and the negative entropy flux to the organism a maximum. Minimum entropy production can be said to be the design criterion which characterizes this process. An unusual aspect of this problem is the fact that the entropy production due to mixing and diffusion is of the same order as the entropy production due to the metabolism associated with the process, and the previously proposed principle of minimum metabolism or minimal effort is not adequate in this case.

The average oxygen concentration in the alveoli is a function of the rate of air exchange and the rate of oxygen consumption. This average concentration can be found by equating the amount of oxygen entering the alveoli to the amount leaving the alveoli.

$$(F_{I_{O_2}} - F_{A_{O_2}})\,(\dot V - f\,V_D) = \dot V_{O_2}$$

where

$F_{I_{O_2}}$ = 0.21, the fraction of the inspired air that is oxygen;

F_{A_O} = the fraction of the gas in the alveoli that is oxygen;

$\dot V$ = the ventilation, the amount of air breathed in l/min;

f = breathing rate in breaths per min;

V_D = 0.13 l, volume of the dead space in the passages to the alveoli;

$\dot V_{O_2}$ = amount of oxygen entering the blood in l/min.

Only $(\dot V - f\,V_D)$ liters of air per min actually reach the alveoli. At each breath, air is mixed with the gas in the alveoli and the expired gas has the average oxygen concentration of the gas in the alveoli, $F_{A_{O_2}}$. The amount of oxygen left behind as the air is inhaled and then exhaled is $(F_{I_{O_2}} - F_{A_{O_2}})(\dot V - f\,V_D)$, and this must equal the amount of oxygen entering the blood stream, $\dot V_{O_2}$.

$$F_{A_{O_2}} = F_{I_{O_2}} - \frac{\dot V_{O_2}}{(\dot V - f V_D)} \qquad (1)$$

Therefore, $F_{A_{O_2}}$ increases with increasing ventilation.

The carbon dioxide concentration in the alveoli can be found in the same way.

$$F_{A_{CO_2}} = \frac{r\,\dot V_{O_2}}{(\dot V - f\,V_D)} \qquad (2)$$

where

$F_{A_{CO_2}}$ = the fraction of the gas in the alveoli that is carbon dioxide;

r = the respiratory quotient, the ratio of the amount of CO_2 exhaled to the amount of O_2 consumed.

Entropy is convected to the body by the oxygen entering the blood stream and from the body by the carbon dioxide leaving the blood. The entropy s of a gas depends on the pressure P and temperature T of the gas

$$s = K(T) - R \ln P\,. \qquad (3)$$

The entropy flux to the body $\dot S$ is equal to

$$(\dot V_{O_2}\, s_{O_2} - r\,\dot V_{O_2}\, s_{CO_2})$$

and is a function of the ventilation because the pressure of the gases being exchanged is a function of the ventilation. Equation (4) gives the change in the entropy flux to the body with a change in ventilation at a fixed oxygen consumption.

$$\frac{d\dot S}{d\dot V} = -R\,\dot V_{O_2}\left(\frac{1}{F_{A_{O_2}}}\,\frac{dF_{A_{O_2}}}{d\dot V} - \frac{r}{F_{A_{CO_2}}}\,\frac{dF_{A_{CO_2}}}{d\dot V}\right)$$

$$= -\frac{R\,\dot V_{O_2}}{(\dot V - f\,V_D)}\left[\frac{(1-r)\,\dot V_{O_2} + r\,F_{I_{O_2}}(\dot V - f\,V_D)}{F_{I_{O_2}}(\dot V - f\,V_D) - \dot V_{O_2}}\right] \qquad (4)$$

where

$\dot S$ = the entropy flux to the body in calories per degree min;

R = 0.09 calories per degree liter STP, the universal gas constant.

The net entropy flux to the body due to the gas exchange decreases with increasing ventilation.

The quantity $d\dot S/d\dot V$ given by equation (4) is also the rate of change with ventilation of the entropy production due to mixing processes that take place in the gas. This can be seen by noticing that the oxygen in the air has a given entropy. Any change in the entropy that it carries by the time it enters the blood stream must have been produced in the mixing processes that take place in the lung. Similarly, the entropy level which the carbon dioxide finally reaches in air is fixed. It must gain the amount of entropy that is the difference between this fixed level and the amount it carries when it leaves the blood stream.

[1] E. SCHRÖDINGER, *What is Life?* (The MacMillan Company, New York 1945).

[2] I. PRIGOGINE and J. M. WIAME, Exper. 2, 451 (1946).

The other contribution to the change in entropy production associated with a change in ventilation is the increase in metabolism that is required to provide the work of increasing the ventilation. The oxygen consumption required for breathing alone has been measured by CAMPBELL, WESTLAKE, and CHERNIACK[3]. They find that 0.25 ml of oxygen is required per liter of ventilation. This requirement is independent of the value of the ventilation up to a ventilation of 45 l/min after which the cost of ventilation rises sharply. Metabolism releases 5 calories of energy per ml of oxygen consumed and this energy is eventually dissipated into heat at a temperature T. The change of entropy production with ventilation is therefore

$$\frac{d\dot{S}}{d\dot{V}} = \frac{H}{T}\,\frac{d\dot{V}_{O_2}}{d\dot{V}} \qquad (5)$$

where $H = 5$ calories per ml, the energy released per ml of oxygen consumed;

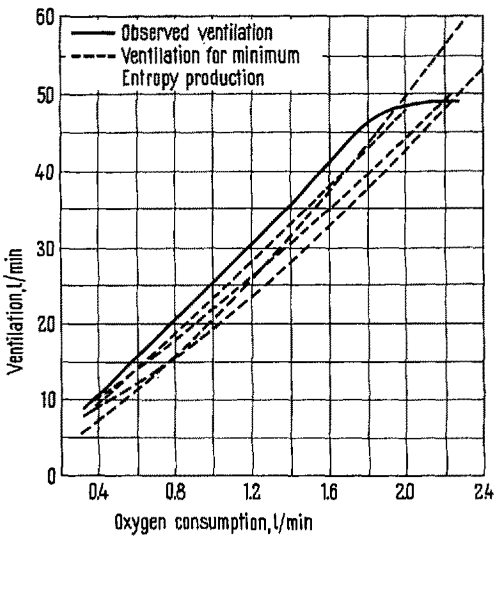
$T = 300°K$;

$d\dot{V}_{O_2}/d\dot{V} = 0.25$ ml/l.

The entropy produced by this process increases with increasing ventilation.

It is assumed that the terms given by equations (4) and (5) are the major contributions to the change in entropy production with a change in ventilation. All other variables such as the blood flow and the oxygen consumed apart from that used in breathing are held constant while the ventilation is varied. The heating of the inspired air is not considered because it is assumed that, at a given metabolic rate, a given amount of heat must be conducted from the body and that this heat would be lost by other means if it were not used to heat the inspired air.

The sum of the right sides of equations (4) and (5) can now be set equal to zero in order to find the ventilation at which the total entropy production in this process is a minimum. This value will depend on the level of oxygen consumption, the respiratory quotient, and the breathing rate. The curve of optimum ventilation or ventilation for minimum entropy production is shown in Figure 1 along with the observed ventilation of four subjects as reported by BOCK, VAN CAULAERT, DILL, FÖLLING, and HURXTHAL[4]. For an oxygen consumption below 2 l/min, the calculated and observed values of the ventilation can be said to agree within the accuracy of the data and the variation between individuals. Above 45 l/min of ventilation, the calculated curve changes character because of the increase in the oxygen consumption required by the ventilation.



The result can be expressed in two ways. The observed ventilation can be said to be either that value which makes the entropy production a minimum or that value which makes the net supply of negative entropy to the body a maximum.

Several authors have described processes which operate so as to minimize the metabolic rate. For instance, OTIS, FENN, and RAHN[5] have modeled another part of the breathing process. At a fixed alveolar ventilation, i.e. fixed O_2 and CO_2 pressure in the alveoli, they compare the work done at various breathing frequencies and find that the observed breathing frequency corresponds to the frequency for 'minimal effort'. The only processes that are considered are various kinds of work and, since the energy used in this work is all eventually dissipated as heat, the minimum-entropy-production criterion is general enough to cover this case; whereas the minimum-effort criterion cannot be applied to cases such as the one described in this paper where several different thermodynamic processes are involved.

The single problem treated here is not sufficient to discriminate between all thermodynamic functions which may have an extremum at the observed operating point. For example, the value of the net free energy flux to the body is a maximum at the observed ventilation. The variation of the free energy convected with the O_2 and CO_2 flux is only due to the variation in the entropy flux. The enthalpy change when the oxygen is burned to provide the work for breathing dominates the entropy change in this part of the process. As a result, the net free energy available to the body is a maximum at the point where the entropy production is a minimum. The problem has been described in terms of entropy production because this is the more fundamental thermodynamic quantity and because this is the principle that has been proposed in the literature referred to in the introduction. Other biological processes must be investigated in which different thermodynamic processes are involved in different proportions in order to define the principle precisely and to describe the limits and framework within which a single design criterion is applicable.

Résumé. La production d'entropie associée à la respiration est calculée en fonction d'une ventilation variable. En suite, pour le cas d'un métabolism donné, on évalue la ventilation qui minimise la production d'entropie due au mélange des gaz respirés et à la dissipation d'énergie associée à l'acte respiratoire. Cette ventilation optimum s'accorde avec celle observée pour des taux de métabolismes inférieurs à la consommation de 2 l d'oxygène par min.

TH. A. WILSON

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[3] E. J. M. CAMPBELL, E. K. WESTLAKE, and R. M. CHERNIACK, J. appl. Physiol. *11*, 306 (1957).
[4] A. V. BOCK, C. VAN CAULAERT, D. B. DILL, A. FÖLLING, and L. M. HURXTHAL, J. Physiol. *66*, 136 (1928).
[5] A. B. OTIS, W. O. FENN, and H. RAHN, J. appl. Physiol. *2*, 592 (1950).