TRANSMISSION OF INFORMATION BY THE ARTERIAL BLOOD STREAM WITH PARTICULAR REFERENCE TO CARBON DIOXIDE

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ABSTRACT An estimate of the amount of information transmitted by way of the arterial blood stream in animals is made. Many assumptions are necessary to pose the problem in analyzable form. Taking carbon dioxide as a representative substance, a distribution of maximum entropy is developed. Three points emerge: (1) that homeostatic stability can be related to chemoreceptor sensitivity if both are given statistical interpretations consistent with concepts of information transmission, (2) that the heart acts as a filter which has considerable smoothing effect which depends in a specific fashion upon the cardiac residual volumes, and (3) a numerical estimate of channel capacity is made. The estimate is undoubtedly high. Assuming values typical of man, the calculated channel capacity for CO_2 is 3.5 to 4.7 bits per second. Since some sixty substances of communication importance occupy the blood stream simultaneously, the blood stream has a total capacity near 250 bits per second if every chemical modality has the same properties as CO_2.

In the systematic study of the physiology of metazoan organisms, it is often convenient to assign to the nervous system and to the circulatory system the roles of coordination through informative connection and coordination through material transport, respectively. This assignment seems essentially unequivocal. However, it must be recognized that in the process of maintaining a suitable environment for the cells, the circulation also plays a significant role as a communication channel. Indeed, in a sense, the whole discipline of endocrinology is a recognition of the existence of this circulatory function, wherein substances serve to regulate the activity of organs through variation of concentration levels in the circulating blood. Early physiologists emphasized this idea in the etymology of the word hormone, which derives from the concept of messenger.

The object of this study is to consider some of the properties of the circulation, abstractly, as a communication channel, with a view to setting some broad limits on its role in the transmission of information. This is of interest since the amount of traffic that the circulation carries is the amount available for the processes maintaining the internal environment of the animal, and because information measures may provide quantitative assessment of the circulation–nervous system relationship in the internal economy of the animal.

PARALLEL CHANNELS

The first and conceptually simple aspect of this channel is the coexistence of several message modalities such as the particular hormones which provide communication between an unique sending organ and one or more specific target organs. It is apparent that such an arrangement permits multiple messages to occupy the blood stream simultaneously without significant cross-talk. An example of such a modality would be ACTH liberated by the pituitary and received by the adrenal cortex. In the mammalian organism such substances may number 30 or more. In addition, one may regard every subtance which is regulated by the action of chemoreceptor mechanisms as a message modality. In such instances the transmitting source is the state of the whole animal as determined by its activity and external environment. Estimates of the number of such substances would vary greatly depending upon the prejudices of the referee. Certainly the number would not exceed the number of constituents of the blood. Conservatively, we would consider an additional 30 substances of communications importance. At the outset then, the blood stream may carry as many as 60 simultaneous conversations between parts of the body.

GENERAL CONSIDERATIONS FOR A SINGLE SUBSTANCE

We choose now to direct attention to a single substance of the second class. This choice, CO_2, is apt because of the relative rapidity with which its concentration can change. CO_2 is a relevant message-bearing substance for respiration since elevation of arterial PCO_2 leads to hyperpnea and lowering of arterial PCO_2 leads to decreased ventilation. The magnitude of the PCO_2 at any time may be regarded as a symbol. The sequence of magnitudes which varies with time constitutes the message. A suitable description is that the arterial PCO_2 is a time function of finite bandwidth (W) and finite duration (T). The frequency limitation is made because the maximum rate of change of CO_2 is limited ultimately by the physical process of diffusion. The signal duration is taken as finite since the life span of organisms is finite. It seems probable that durations much shorter than a life span may be adequate for the selection of an ergodic ensemble. A continuous function of limited bandwidth and duration is determined by its values at $2TW + 1$ sampling points. The probabilities required to describe the system are the probabilities $p(c_0, c_1, \ldots c_j \ldots c_{2TW})$ where c_j is the PCO_2 at t_j. If we assume the distribution to be continuous in all the

c_j for all j, and that the probabilities $p(c_j)$ are independent and identical for all j, then $p(c_0, c_1, \ldots c_{2TW}) = \Pi\, p(c_j)$. The entropy (Shannon 1949) is

$$H = -\iint \cdots \int p(c_0, c_1 \cdots c_n) \log p(c_0, c_1, \cdots c_n)\, dc_0\, dc_1 \cdots dc_n$$

$$= -n \int p(c_i) \log p(c_i)\, dc_i = nH_n$$

The entropy per degree of freedom, H_n, is equal to the entropy of the distribution of PCO_2 values at any time. What is needed, therefore, is some description of this distribution. A continuous distribution is assumed.

Certain fixed constraints upon the probability distribution of concentration are apparent from some elementary but fairly general considerations:

(a) that negative values of PCO_2 are not allowed

$$\int_0^\infty p(x)\, dx = 1 \tag{1}$$

(b) that on the average the internal environment shall have a specified mean PCO_2

$$\int_0^\infty xp(x)\, dx = A \tag{2}$$

and (c) that the mean squared PCO_2 is specified

$$\int_0^\infty x^2 p(x)\, dx = B^2 \tag{3}$$

An animal with good homeostasis will have $|B\text{-}A|$ very small. We seek the probability distribution subject to these constraints which will maximize the function

$$H(x) = -\int_0^\infty p(x) \log p(x)\, dx \tag{4}$$

By the method of undetermined multipliers

$$p(x) = \exp(\lambda_3 x^2 + \lambda_2 x + \lambda_1 - 1) \tag{5}$$

By appropriate manipulation the multipliers may be evaluated from equations 1, 2, 3, and 5 as follows, where $d^2 = B^2 - A^2$

$$\lambda_1 = \tfrac{1}{2} \log \frac{2(\pi - 2)}{\pi^2 d^2} - \frac{A^2(\pi - 2)}{2\pi d^2} + 2A\sqrt{\frac{\pi - 2}{2\pi^2 d^2}} + \frac{1}{\pi} \tag{6}$$

$$\lambda_2 = \frac{A(\pi - 2)}{\pi d^2} - \sqrt{\frac{2(\pi - 2)}{\pi^2 d^2}} \tag{7}$$

$$\lambda_3 = -\frac{\pi - 2}{2\pi d^2} \tag{8}$$

Eliminating the multipliers, λ_1 and λ_2 from equation 5 gives the probability density function

$$p(x) = \sqrt{\frac{2(\pi - 2)}{\pi^2 d^2}} \exp\left[\left(\frac{2 - \pi}{2\pi d^2}\right)\left(x + \left(\sqrt{\frac{2 d^2}{\pi - 2}} - A\right)\right)^2\right] \quad (9)$$

which satisfies the constraints. This distribution resembles a segment of the normal curve limited to the positive half line. The distribution is skewed, the mean exceeding the mode. Fig. 1 shows the density function for a mean PCO_2, $A = 40$ mm Hg.

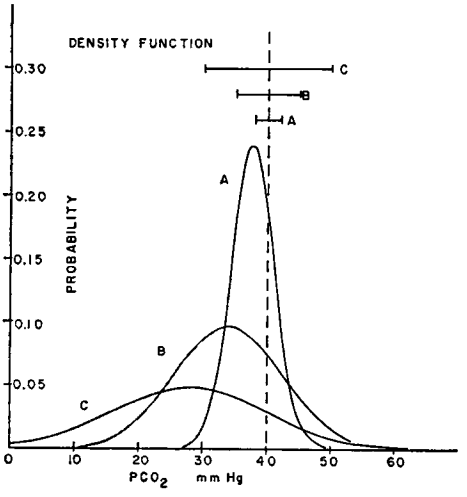


FIGURE 1 Probability density function of maximum entropy. All curves are shown for the same mean PCO_2 of 40 mm Hg, but with standard deviations of 2, 5, and 10 mm Hg indicated by bars *A*, *B*, and *C* at the upper end of the ordinate at 40 mm.

and three values of d. The entropy of the distribution calculated from the definition (equation 1) is

$$H(x) = \log \sqrt{\frac{e\pi^2 d^2}{2(\pi - 2)}} \quad (10)$$

We wish now to select an expression for information transmission which is most readily subject to physiological interpretation. The channel is characterized in terms of the message at two points, the source and the destination of the information. The relevant states of the source are the signals sent. In this instance these are represented by instantaneous PCO_2 values occurring in the pulmonary veins. The description of the family of sendable signals suitable for our computation is given by the entropy of the symbols, $H(x)$. The relevant states at the destination are the signals received, and these in turn can be described by an entropy. The signals received may not be the same as the signals sent because of the intervention of extraneous influences, noise or equivocation. For the present we shall suppose only an equivocation, $H_y(x)$. The transmission rate of a channel in these terms is defined as

$$R = H(x) - H_y(x) \quad (11)$$

Transmission rate per degree of freedom is equal to the entropy per degree of freedom of the message sent less the equivocation.

Any process leading to the mixing of temporally separated aliquots of blood

would make noise. Such processes are numerous: turbulence, streamlining, confluence, and shunting. On the arterial side of the circulation the magnitude of disturbances resulting from such processes is probably quite small. Since at the moment there is no direct way in which to describe or assign the noise in the circulation, we shall suppose that the error between PCO_2 detected and that which was actually transmitted in the pulmonary veins results from faulty detection. We shall assume the error of detection to be additive and independent of the message sent. The probability of the transmitted message being x when y is received is assumed to be normally distributed with a mean y and standard deviation c for all values of y. With such assumptions we have a situation parallel to the additive noise model of Shannon (Theorem 16) in which the conditional probability P_xy is assumed. By similar reasoning, the transmission rate given in equation 14 leads to a channel capacity

$$C = \max_{p(x)} H(x) - H(c^2) \tag{12}$$

Since the channel capacity for additive noise and that for additive equivocation are similarly formulated, one might expect that the channel capacity could be expressed readily in terms of easily identifiable parameters for equivalent noise and equivocation. Such seems not to be the case. If a Gaussian distribution is assumed for the additive component, the noise and equivocation are related through a Weierstrass transformation of the assumed message distribution. The kernel of the transformation is the assumed distribution of the additive component.

We are next faced with the problem of making a guess at the order of magnitude of c. Quite arbitrarily one could equate this to 0.075 mm Hg. PCO_2 (Haldane, 1922) which is the average value of PCO_2 change at the transmitter which leads to a consistently observable respiratory change. This is not to confuse, however, the additive noise idea with the concept of an amplitude quantized variable with a quantal step of 0.075 mm Hg. The assumption may be argued in terms of external observers. An external observer who sees only the y's (received messages) and knows the probabilities P_yx can conjecture x. If such an observer is permitted access to a sequence of y's and is required to signal the y's which are different from each other, such an observer may do so in terms of a classical statistical criterion like the critical ratio. A second observer given the values y and the response of the first observer could conjecture a value nc for the criterion of the first observer where n is an arbitrary positive number and c is the standard deviation of P_yx. Crudely, one may set the central chemoreceptor as the first observer and the physiologist as the second. The minimum difference in arterial PCO_2 which produces a ventilatory response is some multiple of the standard deviation of the equivocation. Thus the Haldane value may be assumed to be one or more standard deviations. To cover the spread of possibilities, we take the 100-fold range 1.0, 0.1, and 0.01 mm Hg. as the value c.

The channel capacity per degree of freedom is then, since $H(x)$ is maximized

$$C = \tfrac{1}{2} \log \frac{\pi}{4(\pi - 2)} + \log \frac{d}{c} \tag{13}$$

Numerical values of this channel capacity are shown in Table I.

TABLE I

CHANNEL CAPACITY FOR CO_2

Mean PCO_2 (A) = 40 mm Hg

Sensitivity c =	1.0 mm	0.1 mm	0.01 mm
Bits/degree of freedom			
for d = 2 mm	0.697	4.017	7.337
d = 5 mm	2.018	5.338	8.658
d = 10 mm	3.018	6.338	9.657

TEMPORAL SPACING OF SYMBOLS

It has already been suggested that the arterial message is a bandwidth-limited signal because any physical process can change only with finite speed. Such a statement, while certainly true, is of little value in the estimation of channel capacity per unit time. What is needed is a knowledge of how many independent symbols are emitted per unit time. The entropy per unit time in the case of bandwidth-limited ergodic ensembles is $H_t = 2WH_n$, where W is the bandwidth in cycles per unit time. One searches, therefore, for physiological processes which impose some temporal pattern upon instantaneous PCO_2 values.

The most obvious process to consider is ventilation of the lungs. Mathematical examination of the process for a stylized type of breathing indicates that ventilation imposes periodic variation in the arterial PCO_2 at the same frequency (f_s) as that of the respiratory movements (Yamamoto, 1960). Frequency components higher than the basic rate of respiration do not have appreciable amplitudes. Since respiratory activity is at best only nearly periodic, major frequency components probably exist at lower frequencies than the respiratory rate. PCO_2 changes during a respiratory cycle establish one or more values of PCO_2 which represents the interaction of the current state of ventilation, blood flow, metabolic CO_2 production, blood buffer performance, and environmental CO_2 concentration. The number of values depends upon the number of frequency components that are considered to be of appreciable magnitude. If the respiratory frequency is the maximum frequency transmitted by the arterial stream, and if 15 cycles per minute is taken as a typical repiratory rate in man, all relevant information in the arterial stream in the band 0 to f_s cycles per minute would be carried in 30 H_n bits per minute.

Another prominent physiological process intervening in the arterial blood stream between lung and brain is the beating heart. The heart isolates a volume of blood

during each beat through the action of its valves. The heart valves form subintervals of time $T = 1/f_p$ long, where f_p is the pulse rate. Intracardiac mixing produces the equivalent of one instantaneous sample. The exact instant during each pulse cycle which is presented is not constant. However, the heart may be regarded as a sampling system with somewhat irregular spacing of sampling instants. If the blood issuing in each systole is independent of the blood in adjacent systoles, one may regard the system as a sampler producing ordinary samples. Since the sampling frequency is f_p, the maximum bandwidth of signals passed is $f_p/2$. Since the sampling interval is not constant some loss of bandwidth must occur. However, sufficient information to estimate this is lacking. An upper limit to the bandwidth of signals passing the heart is set if the pulse is taken to be equally spaced. This limit is one half the pulse rate. The mammalian heart may beat as slowly as 20 per minute in large species and as rapidly as 600 per minute in the small species. The range 10 cycles per minute to 300 cycles per minute would therefore encompass the range of signal frequencies in mammals. In man, typical pulse rates lead to a bandwidth 0 to 35 cycles per minute at rest and as broad as 0 to 90 cycles per minute in exercise.

The two estimates, one based upon pulmonary ventilation and the other upon pulse, are different but not incompatible. The usual relationship between pulse rate and respiratory rate are such that respiratory frequencies are always lower than the maximum frequency passed by the heart. The frequency of respiration is variable as is the pulse rate, but in general the two vary in corresponding directions. The correlation is quite strong, and a mathematically consistent relationship between thoracic movement and cardiac rate can be derived (Clynes, 1960). Whenever the signal frequency is raised the sampling frequency is raised. Since elevations of respiratory rate and cardiac rate are characteristic of increased animal activity, it might be inferred that when the system operates more rapidly more control information becomes available. Information regarding each breath cycle is transmitted regardless of respiratory rate.

Fig. 2 shows a plot of the ratio of pulse rate to respiratory rate as a function of respiratory rate. The group of points on the left are observations on unanesthetized men at rest, exercise, inspiring CO_2, breathing through enlarged dead spaces, or breathing by metronome. The ratio ranges from 16 to 3.4. The points to the right are observations on lightly anesthetized rats at rest, or during electrically induced exercise, during intravenous CO_2 infusion, or during CO_2 inhalation. The ratio covers a similar range of values as in man. The sampling rate per breath cycle decreases as the respiratory rate increases but does not fall below the rate theoretically necessary for transmission of the fundamental component of respiratory rate frequencies. Information per unit time increases when physiological change is occurring rapidly, and diminishes during periods of physiological quiescence. The economy of variable sampling rate over fixed sampling rate is not great however. This can be seen from the smooth curves plotted for $f_p = 60$ in man and $f_p = 300$ for rat. At

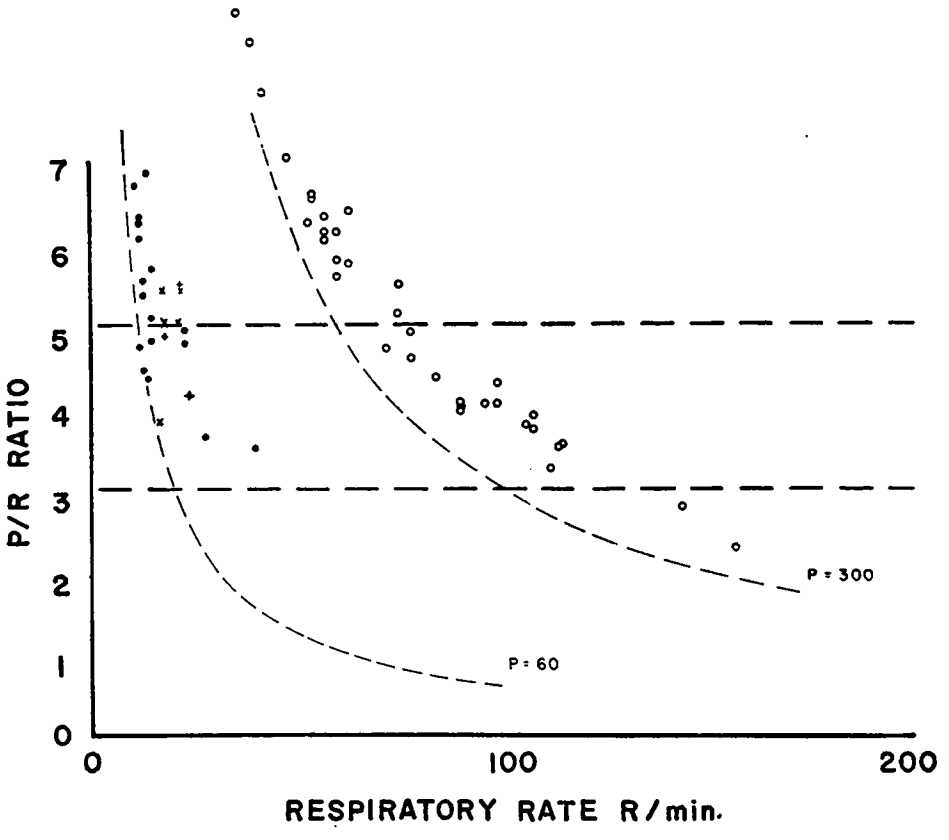


FIGURE 2 Ratio of pulse rate to respiratory rate plotted as a function of the respiratory rate. Observations in man and rat are shown. Equilateral hyperbolas for pulse = 60 and pulse = 300 are shown. Values of the ratio in excess of 9 mentioned in the text are not shown.

low respiratory rates the pulse tends to a minimum at about 60 in man and the pulse to respiratory rate ratio becomes quite large. At high respiratory rates the ratio hovers around 3. The increase in pulse rate is proportionately less than the increase in respiratory rate.

ENTROPY LOSS DUE TO FIXED CONSTRAINTS

The action of the heart as a sampler suggests that it may impose significant constraints in the frequency domain. The principal consideration is that there is usually a residual volume in the chambers of the heart. Effluent blood from a systole is not independent of antecedent systolic ejections. The transmission capabilities of the heart are less than that of an ordinary sampler. For the analysis of the heart as a pulsed filter, we shall begin with the formulation of the residual volume problem as

developed by McClure, Lacy, Latimer, and Newman (1960). The notation of these authors for the passage of a substance through the left atrium and ventricle is employed. The mass (or concentration) in the ventricle at any end diastolic instant is $M(t)$, successive end diastolic instants take the values 1, 2, 3, . . . n from some arbitrary origin. For the ventricle the stroke volume is V_E and the residual volume, V_{RV}. For the atrium the stroke volume is also V_E, and the residual volume is V_{RA}. No valvular incompetence is assumed to be present. Two secondary variables are defined as follows:

$$\alpha = V_E/(V_{RV} + V_E) \tag{14}$$

the fraction of the end diastolic volume represented by the stroke volume; and

$$\beta = V_E/(V_{RA} + V_E) \tag{15}$$

the fraction of the atrial volume at the end of systole which is ejected into the ventricle. The time sequence of events is shown in Fig. 3. All time functions are taken as

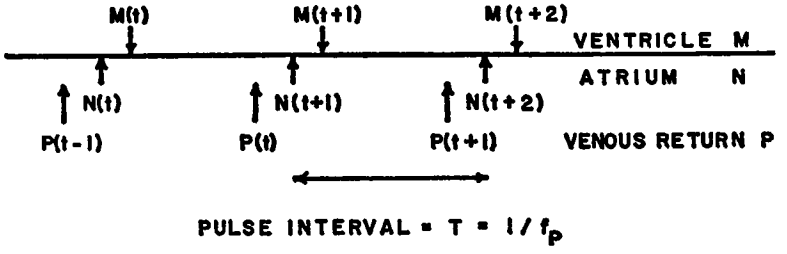


FIGURE 3 Diagram of the assumed sequence of events in the cardiac cycle. Arrows represent instant of emptying of respective chambers. Time intervals are closed to the right.

the value representative of the state before the respective chamber empties. The mass in the atrium is taken as $N(t)$, and $P(t)$ represents the venous return to the atrium during one cycle.

For the illustrated sequence of cardiac events, two difference equations may be written. For CO_2 in the ventricle at the instant $(t + 1)$ in terms of the preceeding interval (the interval is considered to be $nT < t \leq (n + 1)T$ sampled at $(n + 1)T$

$$M(t + 1) = M(t) - \alpha M(t) + \beta N(t + 1) \tag{16}$$

The corresponding equation for the atrium is

$$N(t + 1) = (1 - \beta)N(t) + P(t) \tag{17}$$

Eliminating $N(t)$ and substituting the residual fractions $a = 1 - \alpha$, and $b = 1 - \beta$

$$M(t + 2) - (a + b)M(t + 1) + abM(t) = (1 - b)P(t + 1) \tag{18}$$

Equation 18 may be regarded as the description of a pulsed filter with $M(t)$ as the output function and $P(t)$ as the input function. The weighting sequence of the filter

may be obtained by setting $P(0) = 1$; $P(n) = 0$, $n \neq 0$; $M(0) = 0$; and $N(0) = 0$. Two solutions are found:
if $\alpha \neq \beta$

$$M(n) = \frac{\beta}{\beta - \alpha}[(1 - \alpha)^n - (1 - \beta)^n] \tag{19}$$

and if $\alpha = \beta$

$$M(n) = \left(\frac{\alpha}{1 - \alpha} n\right)(1 - \alpha)^n \tag{20}$$

These equations correspond to equations 9 and 14 of the text and equation 12 of the appendix from the derivation according to McClure and his associates. Equations 19 and 20 represent the weighting sequence of the left heart as a pulsed filter seen at the left ventricle. For this sequence the sum $\sum_{n=1}^{\infty} M(n) = 1/\alpha$. The systolic ejection volume is just α times the end diastolic volume, hence the weighting function seen from the aorta is the sum $\alpha \sum_{n=1}^{\infty} M(n) = 1$. As expected, the left heart taken from the pulmonary vein through to the aorta constitutes a normalized filter.

Further characterization of the filter is conveniently performed using the z transformation (Tou, 1959). The weighting sequence in real time $n = kT$ is converted into the transfer function for the filter by the definition

$$Q(z) = \sum_{k=0}^{\infty} M(kT)z^{-k}$$

where $z = e^{Ts}$, and s is the complex variable. Then for $\alpha \neq \beta$

$$Q(z) = \frac{\beta}{\beta - \alpha}\left[\frac{z}{z - (1 - \alpha)} - \frac{z}{z - (1 - \beta)}\right] \tag{21}$$

Similarly from equation 20 for $\alpha = \beta$

$$Q(z) = (-\alpha z)/(z - (1 - \alpha))^2 \tag{22}$$

The frequency characteristics of the filter can be expressed as the gain and phase relationships as z takes the values

$$z = \cos \omega T - j \sin \omega T, \quad \text{where} \quad \omega_p = 2\pi f_p = 2\pi/T$$

$0 < \omega < \omega_p$. The gain ratio can be obtained by straightforward but lengthy algebra. For unequal residual volumes $a \neq b$

$$|Q^*(j\omega)| = \frac{1 - b}{\sqrt{(1 + a^2)(1 + b^2) - 2(a + b)(1 + ab) \cos \omega T + 4ab \cos^2 \omega T}} \tag{23}$$

For equal residual volumes $a = b$ the gain ratio is

$$|Q^*(j\omega)| = \left|\frac{1}{u + jv}\right| \tag{24}$$

where $u = (a^2\text{-}1) \cos^2 \omega T + (1 + a^2) \cos \omega T - a(1 + a)$ and $v = (1 - a^2) \sin \omega T$. The phase relationship is not of immediate interest in this context and hence

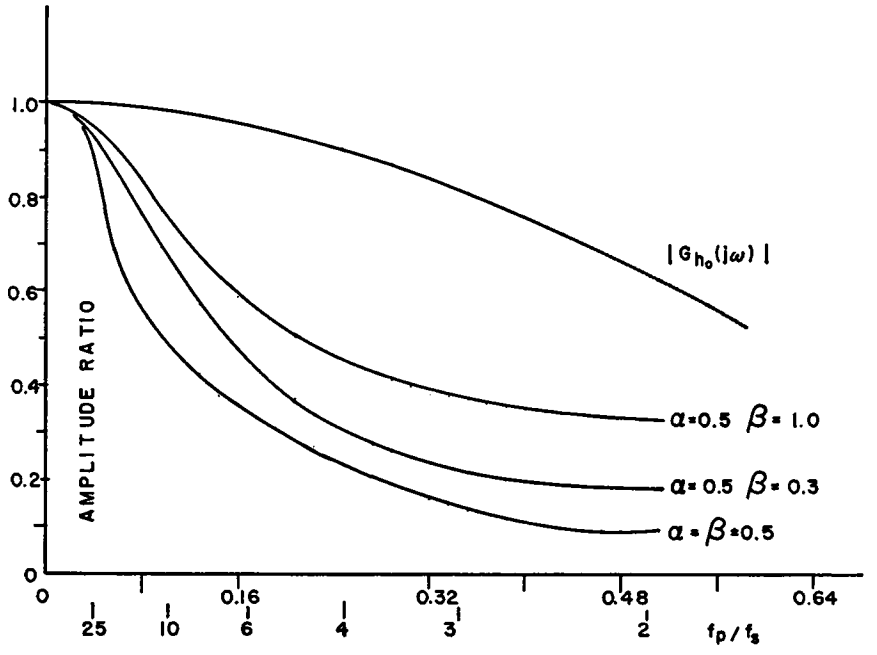
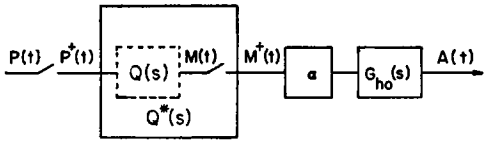


FIGURE 4 Frequency response curves of the cardiac filter. Amplitude ratio of output to input function shown as a function of relative frequency. f_p is the cardiac frequency and f_s is the respiratory frequency. The upper numbers on the abscissal scale are reciprocals f_s/f_p. α and β are stroke volumes represented as fraction of end diastolic volume. The corresponding portion of a gain *versus* frequency plot of a zero-order holding device is shown marked $G_{ho}(j\omega)$.

will be omitted here. Several plots of this function for various stroke volume ratios are shown in Fig. 4. The abscissa is shown as the ratio of signal to sampling frequency to make the curves applicable to any pulse rate.

The results of the preceding analysis define the values of the function only at times nT. To reproduce the actual events of cardiac action some additional modification is necessary. The whole model is shown in Fig. 5. The input $P(t)$ is a continuous time function and corresponds to the actual time-concentration relation of the pulmonary venous blood. A sampler forms the function $P^*(t) = \Sigma_0^\infty p(nT)\ \delta(t\text{-}nT)$; the physiological reality of this operation is not identifiable as any single



FILTER EQUIVALENT OF THE LEFT HEART

FIGURE 5 Block diagram equivalent to the operations upon pulmonary venous blood as it passes to the aorta *via* the left heart.

part of cardiac action. $Q^*(j\omega)$ is the transfer function of the two cardiac chambers in cascade. $M^*(t)$ is the time function $\Sigma_0^\infty M(nT)\ \delta\ (t\text{-}nT)$, the output of the portion of the filter represented by the two difference equations 16 and 17. A sampler at the output synchronous with the sampler at the input is necessary. The samplers in combination represent the action of the heart valves, although it is not possible to place them in one to one correspondence with the mitral and semilunar valves. The function $M^*(t)$ is passed through an ideal amplifier of gain α and through a zero order hold which normalize and reproduce the phenomenon that all the blood issuing during a systole has the same composition. The output $A(t)$ is defined for every instant and represents the continuous concentration of the substance at the orifice of the semilunar valve.

In the principal plane the overall transfer function is given by

$$\begin{aligned} G_1(s) &= A(s)/P(s) = (\alpha G_{h0} Q^*(s))/T \\ &= \frac{\alpha\beta}{\beta - \alpha} \frac{e^{Ts}(1 - e^{-Ts})}{Ts} \frac{a - b}{(e^{Ts} - a)(e^{Ts} - b)} \end{aligned} \tag{25}$$

In the frequency domain, setting $\omega_p = 2\pi f_p$

$$|G_1(j\omega)| = \alpha\beta \frac{\left|\sin \frac{\pi\omega}{\omega_p}\right|}{\frac{\pi\omega}{\omega_p}} \left(\frac{1}{\sqrt{k_1 - k_2 \cos \omega T + k_3 \cos^2 \omega T}} \right) \tag{26}$$

The entropy loss incurred in passing a continuous signal through this filter, can next be calculated. If an ensemble having an entropy of H_n per degree of freedom in band W is passed through a filter of transmission characteristic $Y(f)$, the output ensemble has an entropy H_n' per degree of freedom where

$$H_n' = H_n + (1/W) \int_0^W \log |Y(f)|\, df \tag{27}$$

(Shannon, 1949). For the heart, assume that the input function $P(t)$ is limited to the spectrum $0 \leq f \leq f_p/2$ since the sampling rate is fixed at f_p, then

$$H_n' = H_n + 2/\omega_p \int_0^{\omega_p/2} \log |G_1(j\omega)|\, d\omega \tag{28}$$

The second term on the right when fully expanded is

$$\begin{aligned} (2/\omega_p) \int_0^{\omega_p/2} \Big\{ &\log \alpha\beta - \tfrac{1}{2} \log \left(k_1 - k_2 \cos \frac{2\pi\omega}{\omega_p} + k_3 \cos^2 \frac{2\pi\omega}{\omega_p} \right) \\ &+ \log \left| \sin \left(\frac{\pi\omega}{\omega_p} \right) \right| - \log \frac{\pi\omega}{\omega_p} \Big\}\, d\omega \end{aligned} \tag{29}$$

Expression 29 may be integrated term by term.

The second term can be factored using the quadratic formula into

$$4ab\left(-\cos\frac{2\pi\omega}{\omega_p}+\frac{1+b^2}{2b}\right)\left(-\cos\frac{2\pi\omega}{\omega_p}+\frac{1+a^2}{2a}\right) \tag{30}$$

Since for $0 < a \leq 1$ and $0 < b \leq 1$, $(1 + b^2)/2b \geq 1$ and $(1 + a^2)/2a \geq 1$, the term is integrable and is

$$-\tfrac{1}{2}\log 4ab + \log 2 + \tfrac{1}{2}\log 2b - \tfrac{1}{2}\log(2 - b^2 + b^4) + \tfrac{1}{2}\log 2a - \tfrac{1}{2}\log(2 - a^2 + a^4) \tag{31}$$

The third and fourth terms are calculated readily. The entropy loss per degree of freedom is

$$H_n' - H_n = \log\alpha\beta - \log\frac{\pi}{2e} - \tfrac{1}{2}\log(2 - b^2 + b^4)(2 - a^2 + a^4) \tag{32}$$

In Fig. 6 the entropy loss is plotted as a function of the residual volume (a) of the left ventricle. While measurements of this volume in man are not certain, measurements in the dog (Holt, 1956) indicate a residual fraction between 51 and 54 per cent at heart rates near 80 per minute. The several curves of Fig. 6 are drawn

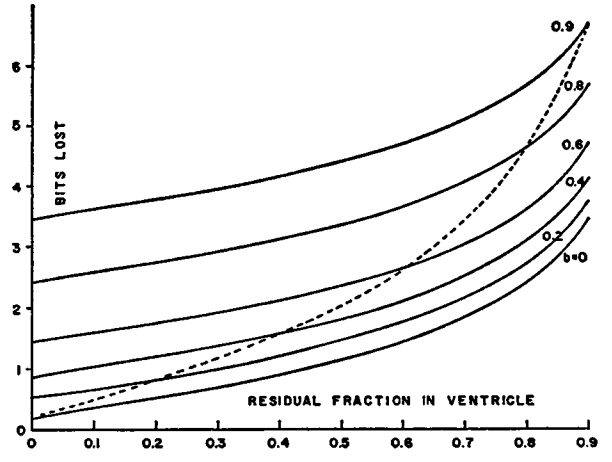


FIGURE 6 Entropy loss per degree of freedom. Cardiac filter at the aorta. The loss is shown as a function of residual fraction, (a) of the left ventricle and residual fraction, (b) of the left atrium. Ordinate is in binary measure. Broken line indicates locus of points of equal residual fractions in both chambers.

each for a different residual fraction of the atrium. Residual fractions for this chamber have not been determined. The atrium itself is a smaller chamber than the ventricle; however, at the onset of diastole not only is the atrium distended, but there is some distension of the pulmonary veins. This might imply that a chamber larger than the anatomical extent of the atrium must be considered. If the residual fraction of the atrium is less than that of the ventricle, physiologically relevant points would lie below the broken line contour which connects points of equal residual fraction.

Using the normal values for a dog, an estimate of about 2 bits per degree of freedom loss in entropy would be representative of the usual condition in passing the left heart.

REMARKS

One purpose of this study was to attempt to obtain the least upper bound to the information transmission of the arterial blood stream while utilizing as much physiological data as possible. We hoped thus not to end up with merely a number which was ample enough a tent to cover all reasonable considerations and which was not worth further debate, but to formulate the relationships in a fashion that might be relevant to certain other problems in physiology. The pertinent points are three: (1) statistical measures of the stability of homeostasis can be related to a statistical parameter of chemoreceptor activity; (2) the action of the heart is specified in a manner which may be relevant to certain problems in pathology; and (3), perhaps least, a magnitude of the channel capacity is obtained and may have relevance to problems in the application of rapid instrumentation in the study of respiration.

Information loss because of fixed constraints is independent of the considerations involved in deducing the entropy per degree of freedom which involves a measure of the stability of the internal environment. The loss is of such a magnitude, that certain combinations of homeostatic stability and regulator sensitivity are incompatible if the mechanism is to function on the basis of information received via the blood stream. The compatible systems are those in which

$$\tfrac{1}{2} \log \frac{\pi}{4(\pi - 2)} + \log \frac{d}{c} + \frac{2}{f_p} \int_0^{f_p/2} \log |G_1(j\omega)| \, d\omega \geq 0 \qquad (33)$$

Fig. 7 shows a partitioning of the plane which equation 33 affords. The shaded zone represents chemoreceptors which are not sufficiently sensitive to yield homeostatic stability indicated on the ordinate. Representative mammalian species are shown on the left, in terms of their reported homeostatic stability. One can assert, within this

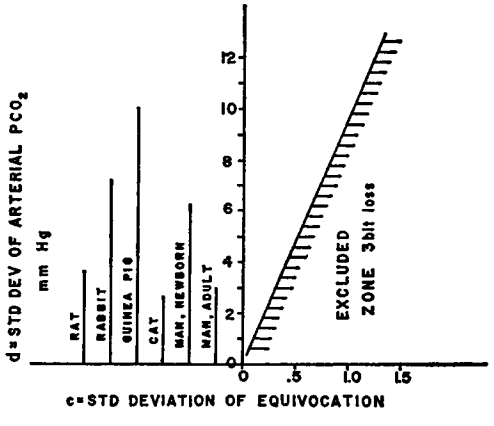


FIGURE 7 Compatible values for the standard deviations representing homeostatic stability and chemoreceptor error. Both scales are in mm Hg PCO_2. Excluded zone is the area in which chemoreceptor response is not relatable to existing internal environment.

this frame of argument, that guinea pig chemoreceptor is less sensitive to CO_2 than man's, and that the adult is more sensitive than the infant. One may further narrow the evaluation of chemoreceptors, on the speculation that homeostasis is the condition achieved by a system which maintains an existing state of activity when no information is received.

The considerations about the fixed constraints imposed by the heart, indicate a function of the pulse distinct from its role as the indicator of pulsatile flow. The heart is a filter and limits the transmission of information from lung to brain, or more generally, from any venous point to any arterial point. In a normal heart the severity of the loss per degree of freedom is about one-third to one-half, which is not as great as current thinking in respiratory physiology might indicate. The value is more compatible with the circulatory physiologists' experience with dye dilution curves and arteriograms.

One problem, not of great moment however, is the question of simulating the pulsatile flow in cardiopulmonary by-pass machines. The problem is really twofold. Gas exchangers generally operate with continuous flow rather than intermittent flow. The signal to be passed contains only very slow frequencies; hence, adding pulsatile pumping would provide no advantage, since the range of intersymbol influence in the original signal is much greater than that generated by the pump. Since the clinical procedure is usually accomplished during respiratory arrest, the second question, regarding the necessity for high frequency components in the signals for normal cardiorespiratory coordination, cannot be answered.

The filter loss is a function of the residual volume of the chambers. Cardiac dilation or valvular incompetence would lead to increased information loss such that for a given chemosensitivity the transmitted information can become inadequate. If the internal environment is regulated in terms of information received, regulation should become poorer and ultimately fail. This would be manifested as an increase in the standard deviation of random arterial blood samples in a patient. It seems possible, moreover, that this is a facet in the dyspnea of cardiac failure.

An educated estimate of the channel capacity may be made without the involved manipulation undertaken (Quastler, 1961). Consider the usually narrow span of PCO_2 observed in animals showing homeostasis and consider the span quantized into, say, 32 steps. Assuming then that the heart transmits one symbol per beat but that due to intracardiac mixing one half of the information is lost, the transmission of information is about 2 bits. At a typical ratio of pulse to respiration of 5, about 10 bits of information is transmitted per breath and about 150 per minute. This estimate is not at all discrepant with the more complexly obtained value. The estimate is undoubtedly a high one also because of the neglect of both noise and intersymbol influences in respiration. One might further conjecture that if all the information so transmitted dealt with the respiratory pattern and was utilized for the production of breaths, an unreasonable large repertory of breath types (1000)

would be required. This, of course, is not strictly correct, since the information transmitted as PCO_2 concerns not only breath pattern but also at least the external environment, the cardiac output during the breath, and the composition of the venous return. Nor is it probable, that the sole expression of the utilization of information is in terms of breath pattern. Moreover, measurements of merely the amplitude and duration of a sequence of 110,000 breaths in an unanesthetized rat at rest was found to require 30 class intervals for a histogram of amplitude and about 10 for a histogram of duration. It is not contended, however, that the large repertory exists or is used. The point is raised to show that what is important is not only to obtain a reasonable estimate, but to obtain one relatable to the body of physiological study.

The more detailed method of estimation using physiological values representative of man, yields a channel capacity for CO_2 of 3 to 4 bits per degree of freedom. At a heart rate of 70 per minute, this constitutes a time rate of 3.5 to 4.7 bits second. The channel capacity for this modality is modest in comparison with any of the common man-made systems of communication. If a similar limit is applicable to all sixty separate substances which serve as signals, the total capacity of the arterial blood stream is 210 to 280 bits per second.

In contrast, the channel capacity of a single nerve cell conceived as a system of pulse interval modulation is as great as 4000 bits per second (Rapoport and Horvath, 1960). At more commonly observed levels of spontaneous nerve fiber activity, the capacity reduces to 500 to 1000 bits per second. Another estimate based upon a model of pulse code modulation (MacKay and McCulloch, 1952) sets the maximum capacity at about 1000 bits per second. The much larger capacity of the neuron agrees with the classical assignment of the role of communication to neurons and of transport to the circulation. The larger capacity is also compatible with the requirement that information processing keep up with the rate of delivery of new information into the system. Considerable redundancy is possible not only because of the relative capacity of a neuron *versus* that of the blood, but also because many, perhaps thousands of neurons or chemoreceptor cells, usually function in parallel.

This work was supported in part by Grant G 5594 from the National Science Foundation.
Received for publication, June 19, 1961.

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