ANOMALOUS IMPEDANCE, A PHENOMENOLOGICAL PROPERTY OF TIME-VARIANT RESISTANCE

AN ANALYTIC REVIEW

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INTRODUCTION

The subject matter of this paper is an attempt to specify the characteristics of a certain class of two terminal dissipative elements and the conditions under which such elements will display both real and imaginary components of A.C. impedance. Since it is difficult to find a systematic treatment of this subject in the biophysical literature and since the phenomena to be treated here might be important for the further interpretation of ionic phenomena in physiological membranes, a study and review were undertaken to provide a treatment which might be of use to workers in this field. It will be seen that solid state elements, such as the thermistor, and some ionic elements occurring in electrochemical systems, both physicochemical and physiological, must of necessity display this interesting property. We have chosen to call this class of resistances *time-variant resistances* for reasons that will become apparent presently. It will be assumed that the behavior of time-variant resistances can be most profitably discussed by beginning with a presentation of their general properties, especially by pointing out how they differ from time-invariant resistances. However, since the time-invariant element is more common and thus more familiar to investigators; it might be convenient to begin by recapitulating the basic characteristics of this element. Let us use current as an independent variable and proceed operationally. If a constant current of a given magnitude is applied to an element and the resulting voltage response is attained instantaneously and remains constant with time, such a resistance is *time-invariant.* (By instantaneously it is to be understood that we are *excluding* the relaxation time of most conductors which is of the order of 10^{-9} sec. Certainly with this time interval, phenomena associated with time-variant resistance would arise and, indeed, at this level all conductors must be considered to be time-variant devices.) It is clear that if the voltage response is not constant with time then the element is a *time-variant*[1] resistance. The difference between the two classes is thus established.

[1] The term time-variant has been chosen to emphasize that "time-dependent" elements are not involved here. Time dependence usually implies that the element is varied as an *independent function* of time, while the element is intrinsically time invariant. Resistance which is mechani-

A further point should be stressed with regard to establishing whether the element is purely dissipative. Upon cessation of current flow, that is, the turn-off of the step of current, if the voltage response descends instantaneously to zero, the element is, unambiguously, dissipative. If any other response of voltage is observed, the element contains either a time-variant E.M.F. or a conservative (capacitive) component, or both, in addition to the dissipative component.

It is convenient for the sake of exposition to stress two properties pertaining to the relationship of current and voltage over a wide range, namely, the linearity and symmetry of the current-voltage (*I-V*) characteristic:

Time-Invariant Elements. As regards the first property, linearity, the *I-V* characteristic is usually linear for most time-invariant resistances and such devices are referred to as "ohmic" elements (Fig. 1*a*). To be sure, non-linear elements are also encountered as will be seen presently. As for the second property, namely, whether the *I-V* characteristic is symmetrical or asymmetrical with respect to direction of current flow, most time-invariant resistances are symmetrical irrespective of whether they are linear or non-linear, the latter being referred to sometimes as varistors. (Fig. 1*a*, curves *aa* or *bb*). When the element displays an asymmetrical *I-V* characteristic, *i.e.* the *I-V* relationship differs for the two directions of current flow, the device is commonly referred to as a rectifier (Fig. 1*b*).[2]

Time-Variant Elements. The time-variant resistance–the element of prime concern in this discussion–has either a linear or non-linear *I-V* characteristic for the instantaneous state but, of course, in time, depending upon certain physical parameters, the system settles down through a sequence of states to a steady state *I-V* characteristic that is usually non-linear. As for symmetry of the *I-V* characteristic, as in the time-invariant element a symmetrical characteristic is usually found in solid state time-variant resistances (thermistor, incandescent filament. Fig. 1*c*). However, when the ionic time-variant element is encountered–as in physiological membranes–the property of asymmetry is usually seen and in this instance the term "time-delayed rectification" has been used to describe the behavior of this element (Fig. 1*d*).

To illustrate the differences let us discuss a few physical systems that display these various characteristics: Most solid state elements are time-invariant, linear, and symmetrical. However, when current flow attains sufficiently high values so that appreciable temperature changes result from the Joule's energy imparted to the system, then such well behaved ohmic elements become time-variant. They are al-

cally varied as a function of time, such as the carbon microphone, is a familiar example of the latter. The resistance discussed in this paper varies intrinsically with time by virtue of the fact that the physical state of the element changes with time; thus we have used the term "time-variant." (Note that the term "time-varying" and "time-variable" are also used by some authors as the equivalent of "time-dependent." Bennett (1) has employed the term "varying parameter" which seems the most explicit and the least ambiguous.)

[2] Since most rectifiers are non-linear elements some investigators prefer to use the term "asymmetrical varistors" for such devices and thus, for the symmetrical non-linear elements, *i.e.*, varistors just mentioned above, the term "symmetrical varistors."

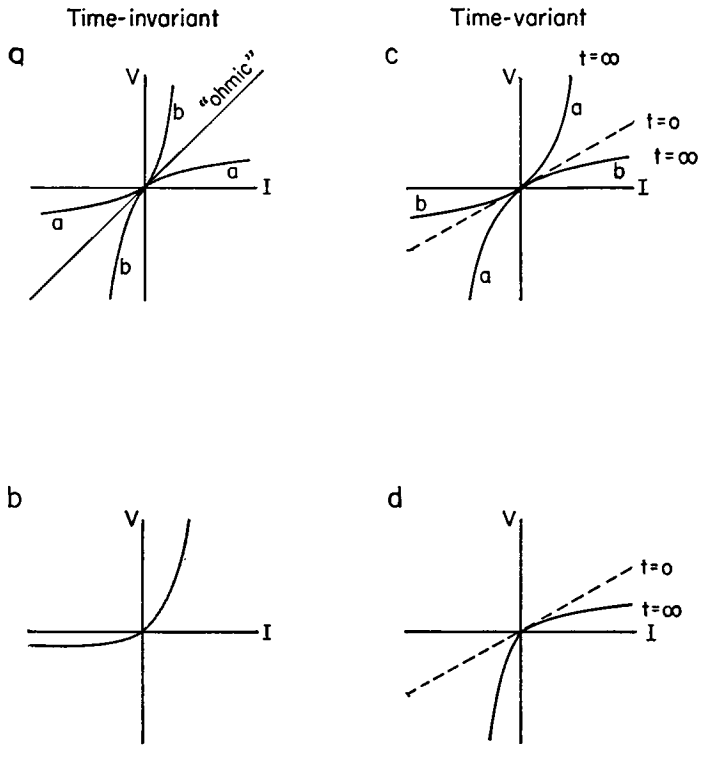

FIGURE 1 Two classes of resistances: time-invariant (1*a,b*) and time-variant (1*c,d*). The upper are symmetrical, the lower asymmetrical.

ways symmetrical since the resistivity is a unique function of temperature and not of direction of current flow. Upon establishing a current flow, depending upon whether the material displays a positive or negative temperature coefficient of resistivity, the resistance will increase or decrease with time, respectively. A well known example of the former is an incandescent lamp with a tungsten filament while the latter type is seen in the carbon filament lamp and most thermistors. Symmetrical non-linear elements are obtained by using either thyrite material or a silicon carbide-graphite mixture. Asymmetrical, non-linear time-invariant resistances constitute a most important class and are commonly referred to as "rectifiers"; *e.g.,* copper oxide, classically, and more recently the semiconductor germanium or silicon p-n junction.[8]

[8] It is important to recognize that time of relaxation of concentration profiles of injected carriers and related transport effects in solid state p-n elements, quite comparable to those to be discussed in ionic devices, can give rise to time-variant resistance properties. However, since the p-n junction element also displays genuine capacitance as a consequence of the Poisson-Boltzmann space charge region (2) and, furthermore, time-variant E.M.F. (3), and since we are concerned here primarily with systems displaying *solely* dissipative properties, this element will not concern us in detail.

An example of a time-variant, non-linear, asymmetrical resistance is very clearly seen in physiological membrane systems. Cole (4, 5) has given a description of a resistance of this type in terms of a theoretical treatment of a semipermeable ionic barrier, permeable only to K ions. Such systems were treated independently by Teorell and demonstrated explicitly in actual model systems (6). The time-variant, non-linear, asymmetrical ionic resistance of this type depends on the shifting of concentration profiles of ionic species in the barrier brought about by the current flow. The profile alteration can be brought about by two mechanisms; namely, (*a*) electrophoretic movement of ions and (*b*) electro-osmotic movement of the solution as a whole, which movements, to be sure, are superimposed upon the process of diffusion arising from the concentration gradients. The mechanisms will be discussed in more detail presently.

ANOMALOUS IMPEDANCE

The time-variant resistance is important in the treatment of physiological membrane systems and plays a role in the Hodgkin-Huxley analysis of the squid giant axon membrane. One of the interesting phenomenological properties of time-variant resistances–*the central point of this paper*–is their ability to display "reactance" as observed, for example, with an A.C. impedance measuring device, the Wheatstone Bridge.[4] This point was discussed by Cole (7) in 1941 in connection with the interesting discovery in 1940 by Cole and Baker (8) that under certain conditions the squid axon displayed positive reactance in A.C. bridge measurements. The possibility of a time-variant resistance of the ionic type being involved was expressed in more detail by Cole in 1946 (4, 5, 9) and independently in 1948 by Teorell (6, 10). Cole coined the term *anomalous reactance* (5) to specify the impedance associated with time-variant elements. The conditions under which the time-variant element displays reactance warrants some discussion. It will be seen that by specifying these conditions the meaning and the origin of the reactance effect becomes more apparent.

To display reactance, an element must permit either current or voltage to assume a zero value without both being zero identically. This is a necessary and sufficient condition for reactance. However, a *purely dissipative* element is characterized by the absence of a mechanism for the storage of electrical energy such that during one part of the cycle energy is *absorbed* from the source and during another *fed back* to the source. Thus, in a purely dissipative element the voltage and current must attain zero identically and, therefore, a pure resistance cannot introduce a phase shift between the voltage and current at the fundamenal frequency. The only possible action associated with such elements is the generation of harmonics with

[4] Another way to broach this subject might be to ask what is being measured with a bridge or Lissajous figure analysis when the element is a time-variant resistance.

respect to voltage (or current).[5] It will be seen that to observe a phase shift between voltage and current, the condition to be met is to couple the time-variant element with a source of current such that the time-variant resistance modulates a steady state of current flow. (In terms of the *I-V* plot this condition can be described by stating that the element is "biased" at an operating point and that a sinusoidal perturbation is impressed about this point.) In such a system electrical energy is being degraded to Joule's heat at every instant throughout the cycle since the element is purely dissipative.[6] The phase shift between voltage and current usually encountered in electrical systems arises from circuit elements that are conservative, namely, inductance and capacitance–the property of the circuit in this case has been defined as the impedance. It is fitting, therefore, to refer to a similar property associated with a dissipative element, *i.e.* time-variant resistance, as anomalous impedance (*cf.* Cole, 5).

Before proceeding with a quantitative treatment of a system displaying anomalous impedance, it is instructive to first describe one qualitatively. The simplest configuration of elements involving the time-variant resistance which satisfies the conditions for the reactance effect can be seen in Fig. (2*a*) in which there is a constant bias current I_0. (This configuration is especially interesting since it constitutes the basis for the circuit model used by physiologists to interpret data obtained from electrical studies of the excitable membrane of nerve and muscle cells.) The sequence of events can be seen more readily perhaps if the configuration is perturbed by a step of current. When R_t is a thermopositive element (incandescent filament), the step response to a constant current pulse I_{ab} is shown in Fig. (2*b*). For the condition of positive current I_{ab}, which divides between the elements R_t and R_{fixed}, the current flow through the time variant element R_t is reduced from the steady state magnitude I_0 by a component of I_{ab} and thus the element R_t passes through a sequence of states of decreasing resistance as it becomes cooler. The voltage response V_{ab} is that shown. For a negative current I_{ab} the current through R_t is increased from I_0 and the sequence of events occurs in reverse order giving rise to the voltage response as shown. The property, which is the key to the anomalous impedance in this instance,

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[5] While it is true that a Fourier analysis of the voltage across a time-variant resistance, *e.g.* an incandescent lamp (19), conducting a sinusoidal current indicates the presence of the fundamental and higher order harmonics with a phase shift (*i.e.* an open loop figure in terms of a Lissajous response), this is a consequence of the double valued resistance due to the time delay of the variation of resistance with respect to current throughout the cycle and *not* of energy storage, *i.e.* reactance, in the filament. This instance is perhaps a unique example in which the Fourier analysis predicts a phase shift. While this is formally correct it is without physical significance. In this regard it is useful to point out that the Lissajous response for a time-variant resistance gives rise to an open loop figure that always passes through the origin. On the other hand for a reactive element, *i.e.* an element capable of energy storage, the open loop figure never passes through the origin.

[6] It is assumed, of course, that electromotive forces due to thermoelectric phenomena are negligible.

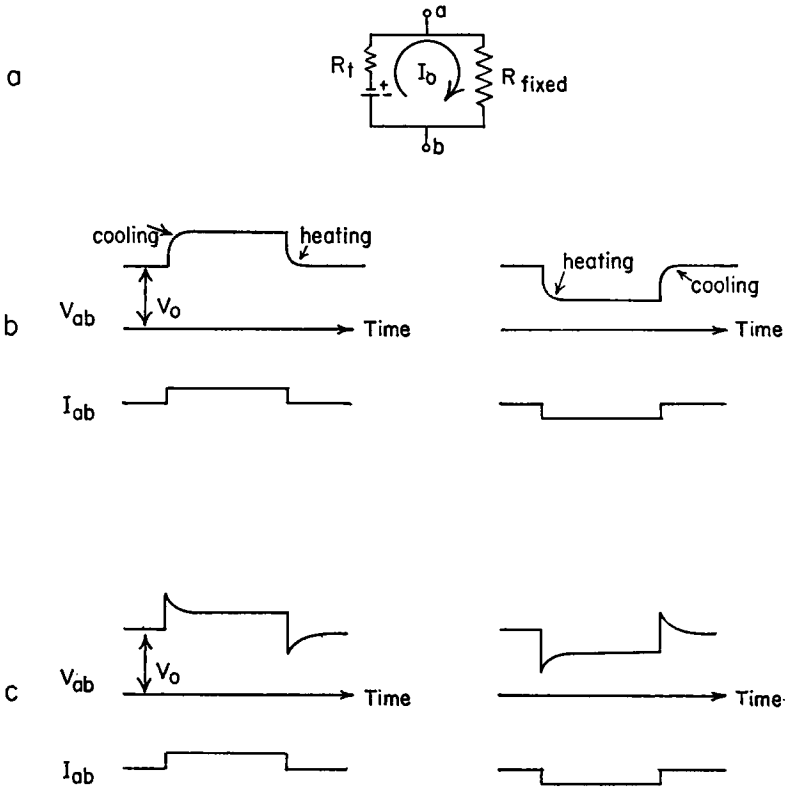

FIGURE 2*a* The basic configuration that can display anomalous impedance.
FIGURE 2*b* The small signal response of basic circuit to step of current when R_t is thermopositive.
FIGURE 2*c* The response to step of current when R_t is thermonegative.

is that the change of temperature and the related change of resistance requires a lapse of time after the onset or disappearance of the perturbing current. With a thermistor, the same thermal response occurs for a positive and a negative current pulse, respectively, except that since this element is thermonegative, the resistance will vary in the reverse sequence. The voltage response[7] is that shown in Fig. 2*c*. When these circuits are driven with sinusoidal currents, Lissajous figures are obtained indicating an *RC* and *RL* network, respectively. Such experiments show that the sinusoidal currents and voltages are out of phase and that the system displays reactance. (See page 366.) Note this would not occur if the element were perturbed in the absence of a steady state current I_0. The only effect observed would be the

[7] The responses referred to are strictly of the nature of small-signal variations. Thus the scale of V_0 with respect to the voltage responses to constant current is exaggerated in the drawing of Figs. 2*b* and 2*c*.

generation of harmonic frequencies arising from the variation of resistance throughout the cycle and the consequent distortion of the waveform of voltage. While the temperature dependence of resistivity is fairly well known as the basis for the behavior of the solid state elements, the mechanisms involved in the ionic time-variant resistances, on the other hand, are less familiar and therefore warrant a brief discussion. As mentioned above, two mechanisms have been established for ionic systems that will give rise to time-variant resistance, namely, electrophoretic and electro-osmotic distortion of the ionic profiles in a membrane.

The first ionic system to be discussed briefly is depicted in Fig. 3*a*. The system consists of a porous diaphragm (membrane), *e.g.* a sintered glass filter, which serves to separate two electrolytes, NaCl and HCl, at the same concentration. It will be convenient to stir both solutions so as to maintain the boundary conditions of concentration as indicated. The porous diaphragm thus serves only to minimize convection due to stirring. If current is established in the direction as shown in Fig. 3*b* by a set of electrodes and a source of current, the movement of ions will be such that Na^+ will move into the membrane and H^+ out of the membrane. Note Cl^- will move in the opposite direction but, since the boundary concentrations are the same, a change in profile of Cl^- will not occur. Since the mobility of the Na^+ ion is less than that of the H^+ ion the integral resistance of the membrane will increase with time approaching a limiting value associated with a preponderance of Na^+ ions in the membrane. For a current in the opposite direction (Fig. 3*c*), the concentration of H^+ ions instead will increase with time as shown and thus in this case the integral resistance will decrease with time. The general nature of the *I-V* characteristic for the steady state is indicated by Fig. 1*d*. For this mechanism to operate electrolytes must be used that, in general, consist of ionic species of different ionic conductivities.

The second system as depicted in Fig. 4 depends upon a fundamentally different mechanism for the distortion of the concentration profiles (11). It is clear that if a flow of the solution were established, *e.g.* by applying a difference in hydrostatic pressure across the membrane, the solution in the left-hand side would flow into the membrane resulting in the profile of Fig. 4*b*. A flow of solution in the other direction would result in the profile as seen in Fig. 4*c*. Although the mechanism is quite involved and thus will not be pursued here, it will suffice to point out that the bulk movement of solution can occur when a field is applied if the barrier contains mechanically fixed ionic groups (12). The simplest system that will facilitate description of this phenomenon is to imagine a population of fine uniform capillaries whose walls are covered by ionic groups. If current is established through a capillary it will be observed that in addition to the usual ionic movements which we discussed above, the solvent as a whole will move either in the direction of current flow (applied field) as shown in Fig. 4 or in opposition to the current flow. The particular direction will depend on the sign of the ions fixed to the capillary wall. This movement of the solution in the presence of the applied electric field is known as *electro-osmosis*.

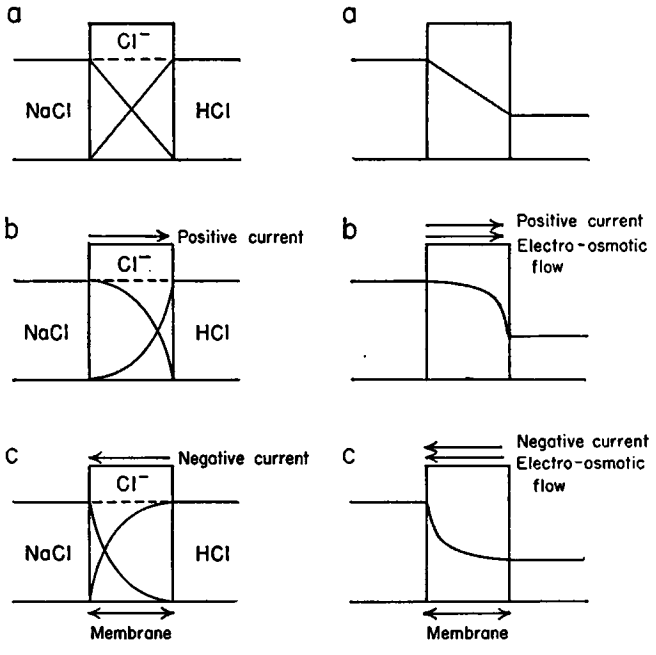

FIG. 3

FIG. 4

FIGURES 3 and 4 Steady state concentration profiles of ionic species for the condition of zero current, positive current, and negative current in the electrophoretic and electro-osmotic time-variant system, respectively.

Thus two different[8] mechanisms are available to effect alteration of the concentration profiles in a membrane and thus to establish a time-variant resistance.[9] It should be emphasized that the two mechanisms just discussed certainly do not exhaust all the possibilities and, indeed, they should not be regarded necessarily as *the* basis for the behavior of the time-variant resistance in physiological systems. The elucidation of the mechanisms involved in such systems is one of the basic and most difficult tasks confronting workers in the field of excitable membranes. For example, it would be reasonable to consider the possibility that alteration in the mechanical properties of the interface or the opening of regions or patches as a function of time is the molecular basis of the time variance of the conductance. Many different

[8] It should be pointed out that to obtain the electrophoretic time-variant resistance, *i.e.* Fig. 3, the general condition which must be satisfied is that the ions on either side must be species of differing mobilities, for this is the only way to obtain moving profiles. The electro-osmotic time-variant resistance, on the other hand, can be obtained for a single electrolyte provided of course that it is present at a concentration difference.

[9] We have assumed that the E.M.F. in either system is negligible and consequently that the elements are purely dissipative.

mechanisms might be conceived that could give rise to the I-V characteristics associated with time-variant resistance. The two mechanisms discussed here were chosen merely as concrete examples.

It would be desirable to present a general analysis of both the ionic and solid state time-variant resistance so as to obtain a complete solution as a function of V, I, and time in terms of the various physical constants of the system. Unfortunately, this is most difficult especially when the two ionic elements described above are considered. However, for the condition of small-signal perturbation an explicit solution can be obtained for the solid state element, namely, the temperature-dependent metallic filament and semiconductor (thermistor material) which will clearly show the properties of anomalous impedance. The results of this analysis can then be applied to other time-variant conductances with the same characteristics. In this way the anamolous impedance characteristics of various time variant elements can be considered without requiring knowledge of the detailed mechanisms in such elements.

The first step is to obtain an expression for the temperature since this determines the resistance. This can be done by establishing the equation for energy balance in the element. Consider an element at a temperature whose specific heat is M and dissipation constant is D, dissipating electric power IV in the steady state. Then for a small perturbation, since the rate of heat generated must be equal to the sum of the rate of heat stored and the rate of heat dissipated, we have, following the procedure of Van der Zeil (13),

$$M \frac{d(\delta\theta)}{dt} + D\,\delta\theta = \delta(IV) \tag{1}$$

For temperature-dependent resistances, in general the temperature coefficient is given by

$$\alpha = \frac{\delta R/R}{\delta\theta} \quad \text{where} \quad R = \frac{V}{I}. \tag{2}$$

Thus (1) becomes

$$\frac{M}{\alpha R}\frac{d}{dt}(\delta R) + \frac{D}{\alpha R}\delta R = \delta(IV) \tag{3}$$

and

$$\delta V = \delta(IR) - I\,\delta R + R\,\delta I$$

$$\delta R = \frac{\delta V - R\,\delta I}{I} \tag{4}$$

Inserting (4) in (3)

$$\frac{M}{\alpha R}\frac{d}{dt}\left(\frac{\delta V - R\,\delta I}{I}\right) + \frac{D}{\alpha R}\left(\frac{\delta V - R\,\delta I}{I}\right) = \delta(IV) = I\,\delta V + V\,\delta I \tag{5}$$

Rearranging

$$\frac{M}{\alpha IR}\left(\frac{d}{dt}(\delta V) - R\frac{d}{dt}(\delta I)\right) + \frac{D}{\alpha IR}\delta V - \frac{D}{\alpha I}\delta I = I\,\delta V + V\,\delta I$$

Rearranging again, we have a first order differential equation in δV and δI,

$$M\frac{d}{dt}(\delta V) + (D - I^2\alpha R)\,\delta V = MR\frac{d}{dt}(\delta I) + (DR + \alpha RIV)\,\delta I \tag{6}$$

For sinusoidal perturbation let

$$\delta V = \boldsymbol{\delta}\mathbf{V}e^{j\omega t}$$

and

$$\delta I = \boldsymbol{\delta}\mathbf{I}e^{j\omega t}$$

where $\boldsymbol{\delta}\mathbf{V}$ is the amplitude of the voltage perturbation and $\boldsymbol{\delta}\mathbf{I}$ of the current.

Thus

$$\frac{d}{dt}(\delta V) = j\omega\,\boldsymbol{\delta}\mathbf{V}e^{j\omega t}$$

$$\frac{d}{dt}(\delta I) = j\omega\,\boldsymbol{\delta}\mathbf{I}e^{j\omega t}$$

Thus from (6) we have

$$j\omega M\,\boldsymbol{\delta}\mathbf{V} + (D - I^2\alpha R)\,\boldsymbol{\delta}\mathbf{V} = j\omega M\,\boldsymbol{\delta}\mathbf{I} + (DR + \alpha RIV)\,\boldsymbol{\delta}\mathbf{I}$$

and

$$\frac{\boldsymbol{\delta}\mathbf{V}}{\boldsymbol{\delta}\mathbf{I}} = \frac{(DR + \alpha RIV) + j\omega RM}{(D - I^2\alpha R) + j\omega M} = \frac{R(D + \alpha P) + j\omega RM}{(D - \alpha P) + j\omega M} \tag{7}$$

where

$$P = IV = I^2R.$$

Rewriting (7) as

$$\frac{\boldsymbol{\delta}\mathbf{V}}{\boldsymbol{\delta}\mathbf{I}} = \frac{R(D - \alpha P) + j\omega RM}{(D - \alpha P) + j\omega M} + \frac{2\alpha PR}{(D - \alpha P) + j\omega M}$$

and finally,

$$\begin{aligned}\frac{\boldsymbol{\delta}\mathbf{V}}{\boldsymbol{\delta}\mathbf{I}} &= R + \frac{2\alpha PR}{(D - \alpha P) + j\omega M} \\ &= R + \frac{2\alpha PR(D - \alpha P)}{(D - \alpha P)^2 + \omega^2M^2} - j\frac{2\omega\alpha MPR}{(D - \alpha P)^2 + \omega^2M^2}\end{aligned} \tag{8}$$

which stresses the fact that both the real and imaginary components are frequency-dependent.

Alternatively, the above can be rewritten as

$$\frac{\delta V}{\delta I} = R + \frac{1}{\left(\frac{D - \alpha P}{2\alpha PR}\right) + j\omega\left(\frac{M}{2\alpha PR}\right)} \tag{9}$$

where it can be seen that the second term corresponds to an impedance resulting from a capacitance and resistance in parallel, namely,

$$\frac{1}{1/R_1 + j\omega C}$$

where

$$\left.\begin{aligned} R_1 &= \frac{2\alpha PR}{D - \alpha P} \\ \text{and} \quad C &= \frac{M}{2\alpha PR} \end{aligned}\right\} \tag{10}$$

The total impedance may be represented by the circuit in Fig. 5. It should be noted–to emphasize what has been stated in the discussion above in qualitative terms–that since the capacity C becomes infinite and R_1 zero for the condition of zero bias current *i.e.* $P = O$, the anomalous impedance vanishes in the absence of a steady state current.

Real Component. At this point having obtained the general impedance function, it is useful to emphasize certain subtleties of the real component of the impedance that must be recognized in measurements concerning time variant elements.

The real component of $\delta V/\delta I$ at any frequency might be termed the A.C. resistance:

$$\left(\frac{\delta V}{\delta I}\right)_{real} = R + \frac{2\alpha PR(D - \alpha P)}{(D - \alpha P)^2 + \omega^2 M^2} \tag{11}$$

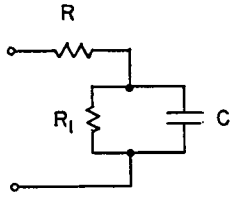

FIGURE 5 The equivalent circuit representing the impedance associated with a temperature-dependent resistance.

(*a*) At infinite frequency the real component is simply R which might be referred to as the static resistance or, the chord resistance. (In the *I-V* plot the path would be along the line connecting the point *I,V,* and the origin.) In the case of the ionic resistances which we have discussed above, this might be termed, alternatively, the

integral resistance since it depends upon the integral of the concentration function over the width of the membrane.

(*b*) At zero frequency the real component is $R + (2\alpha PR)/(D - \alpha P)$ (or $R + R_1$). This is the slope of the *I-V* characteristic at the point *I*, *V* and, accordingly, it might be called the slope resistance.[10]

In order to examine this component further it will be convenient to rearrange the above expression as follows:

$$R + R_1 = R + \frac{2\alpha PR}{D - \alpha P} = \frac{R\ D - \alpha RP + 2\alpha PR}{D - \alpha P} = R\left(\frac{D + \alpha P}{D - \alpha P}\right) \qquad (12)$$

Thus, for the case of the incandescent filament ($\alpha > 0$), *i.e.* the thermopositive element, the slope resistance is in general positive since D is usually greater than αP for most filaments. In terms of the *I-V* plot in Fig. 1*c*, this condition implies that the plot labeled *aa* does not in general bend back toward the vertical.

However, for the thermonegative element (thermistor) the range of possible relationships between D and αP is such that a bending of the characteristic can occur which gives rise to further interesting properties of such time elements.[11]

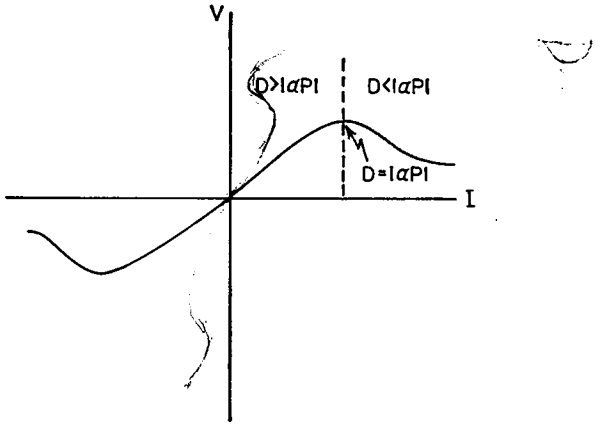

FIGURE 6 The steady state *I-V* plot of the thermonegative element extended beyond that shown in Fig. 1*c* to show the region of negative slope resistance.

Thus in Fig. 6 we see the more general *I-V* plot of the thermonegative element, *i.e.* we have extended the plot *bb* in Fig. 1*c*. Rewriting the above expression by taking into account the *negative* sign of α we have:

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[10] Ekelof and Kihlberg (14) refer to this component as the dynamic resistance.

[11] The four layer p-n diode and the Esaki diode constitute two terminal time-invariant elements that display bending of the characteristic with respect to the current and voltage axis, respectively. These facts were not included in Fig. 1*b* in order to keep the presentation as simple as possible.

$$R + R_1 = R\left(\frac{D - |\alpha P|}{D + |\alpha P|}\right) \tag{13}$$

Thus, the peak of the *I-V* steady state plot is defined by the condition $D = |\alpha P|$ or zero slope resistance. To the left of this maximum *i.e.* $D > |\alpha P|$ the slope resistance is positive while to the right it is negative.

A further significant point should be emphasized with regard to the region of operation to the right of the maximum, namely, that the frequency-dependent term in the expression for the A.C. resistance is always negative. Thus for any operating point in this region a certain frequency will exist at which the A.C. resistance is zero. This has been defined as the *critical frequency* (15).

Imaginary Component and Total Impedance. For the thermopositive element ($\alpha > 0$) we can see from the total impedance function (8) that the imaginary component is always negative and thus capacitive and vanishes at the two extremes $\omega = 0$ and $\omega = \infty$. Since we have just seen that the real component is always positive, ranging from $R + R_1$ at $\omega = 0$ to R at $\omega = \infty$, the impedance as a function of frequency is shown in Fig. 7.

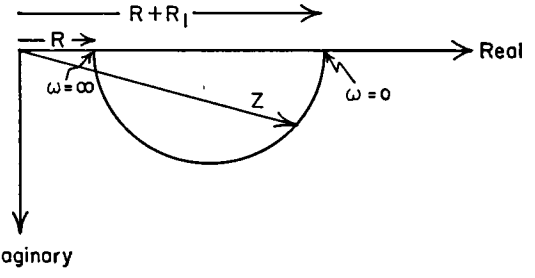

FIGURE 7 The *R,C* impedance locus applicable to any time-variant element whose resistance increases with time.

This *R,C* locus diagram is applicable to *any time variant element displaying* a *resistance* of the thermopositive type.

For the thermonegative element ($\alpha < 0$), the imaginary term is positive and in terms of the capacity, $C = M/(2\alpha PR)$, this implies a *negative* capacity, shunted by the resistance, $R_1 = 2\alpha PR/(D - \alpha P)$, which is negative. Thus the equivalent circuit is shown in Fig. 8*a*. This is a perfectly acceptable way to express the resulting impedance although it might be more convenient to transform to a circuit where the reactive element is a positive inductance since the latter is a more familiar element than the negative capacitance.

To effect this transformation three conditions must be satisfied in the new circuit:

1. At zero frequency the resistive component must be $R + R_1$.

2. At infinite frequency the resistive component must be R.
3. The electrical time constant must be R_1C.

Thus by inspection the first two conditions are satisfied as shown in Fig. 8*b*.

From the third condition we have:

$$R_1C = \frac{L}{-R_1} \quad \text{or} \quad -R_1^2C = L \tag{14}$$

Substituting for C and R_1 the equivalent inductance L is specified by:

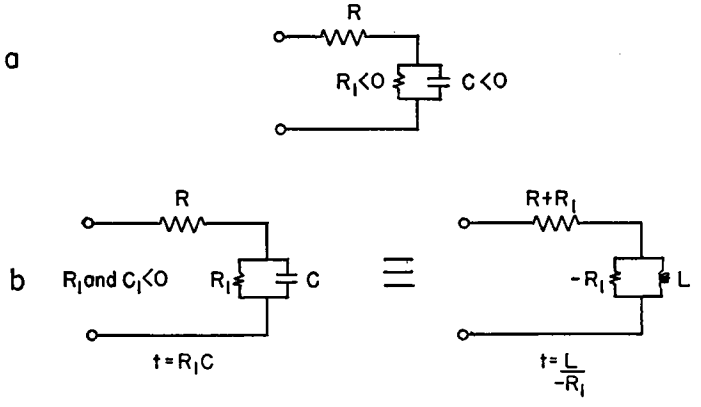

FIGURE 8*a* The equivalent circuit representing the impedance of the thermonegative element; *i.e.* R_1 and $C < O$.

FIGURE 8*b* The equivalent transformation from the negative capacitance to a positive inductance.

$$L = -\left(\frac{2\alpha PR}{D - \alpha P}\right)^2 \frac{M}{2\alpha PR} = -\frac{2\alpha PRM}{(D - \alpha P)^2} \tag{15}$$

Note, again, that the anomalous impedance vanishes as current approaches zero since the inductance L vanishes.

We must recall from our discussion of the real component of impedance in the thermonegative element that the peak of the *I-V* steady state plot is the point delimiting two different regions of operation. Thus operating to the left of the maximum, $R + R_1$, the slope resistance, is positive which results in an impedance locus diagram as indicated in Fig. 9*a*. When the thermistor is operated in the region to the right of the maximum, $R + R_1$ is negative resulting in an impedance locus as in Fig. 9*b* where it is to be noted, as discussed previously, that a critical frequency exists at which the real component vanishes. Thus at such a frequency the impedance is *purely* inductive. It should be emphasized that the *R,L* impedance locus described in Fig. 9 will apply to *any time-variant element displaying a resistance of the thermonegative type*. Thus the two generic time-variant elements have been defined.

The response of both generic elements to sinusoidal perturbations of current is summarized most conveniently perhaps by referring to the Lissajous figures as shown in Figs. 10 and 11. In Fig. 10 the instantaneous and steady state *I-V* characteristic is plotted for the thermopositive element. The trajectory of the voltage and current for sinusoidal variations about a certain steady state point is seen for low and high frequencies. At low frequencies the variations tend to follow the path along the tangent of the *I-V* characteristic thus revealing the slope resistance at that

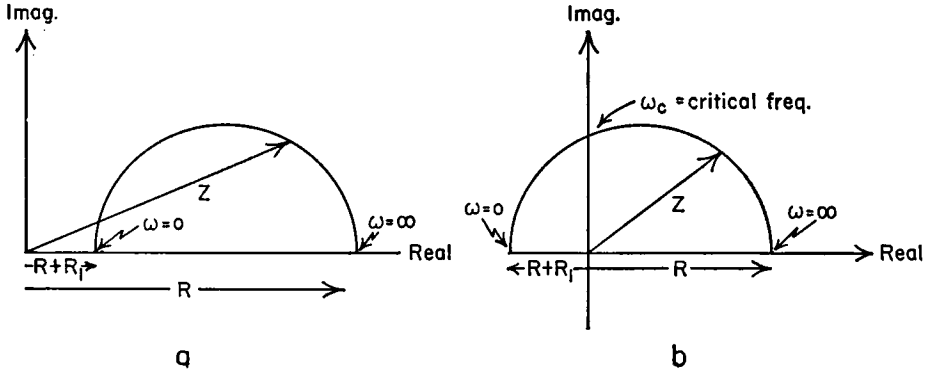

FIGURE 9 The *R,L* impedance locus applicable to any time-variant element whose resistance decreases with time. The locus to the left (Fig. 9*a*) pertains to the operating region when the slope resistance is positive, and the locus to the right (Fig. 9*b*) when it is negative.

point. As the frequency is increased the trajectory assumes an elliptical shape, being generated in a counter-clockwise direction, and the major axis of the ellipse tilts so that at higher frequencies the trajectory collapses into a straight line along the chord slope; *i.e.*, the chord resistance. (To avoid misunderstanding it should be noted that trajectories have been presented deliberately with finite ellipticity for the two extreme conditions to facilitate drawing of the figures.) In Fig. 11 the *I-V* characteristic is seen for the thermonegative element. The low frequency and high frequency response to sinusoidal perturbations is seen, again, as approaching the differential slope and the chord slope of the *I-V* characteristic, thus revealing the slope resistance and chord resistance, respectively, at the point. The phase shift between the sinusoidal perturbations of voltage and current in this instance will result in the trajectories being generated in a clockwise direction. The condition of 90 degrees phase shift between voltage and current, *i.e.* pure inductive reactance, at a critical frequency is seen in the trajectory drawn with dashed lines. It is to be recalled that this condition occurs as a consequence of the negative differential slope and thus, since the differential slope changes from positive to negative at the peak of the *I-V* characteristic, the pure inductive response is seen only in the region to the right of the peak.

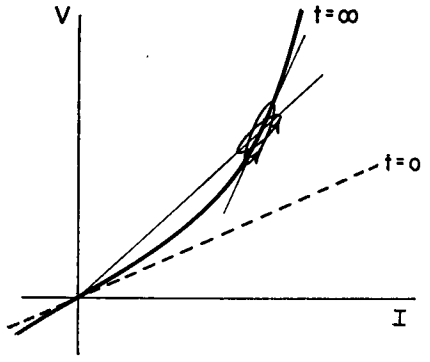

FIGURE 10 Steady state *I-V* plot of the thermopositive element and the Lissajous figures observed about a bias point for a low and high frequency perturbation. The chord and differential slopes are indicated by fine lines drawn through the operating point on the *I-V* plot.

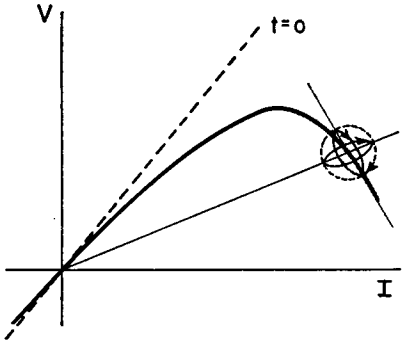

FIGURE 11 Steady state *I-V* plot of the thermonegative element. The Lissajous figures are shown only for an operating point in the region of negative slope so as to display the trajectory (dashed line) which occurs at the critical frequency; *i.e.*, 90 degree phase shift between δV and δI.

In the light of this analysis, it is worthwhile pointing out some very interesting aspects of the anomalous impedance associated with the two ionic time-variant elements described above. With the aid of Fig. 1*d*, it will be recalled that the ionic elements are intrinsically asymmetrical. Thus when operated in the direction of positive current the anomalous impedance would be of the type associated with a thermonegative-like resistance, namely, a resistive-inductive impedance. While when operated in the opposite direction of current flow the impedance would be of the type associated with a thermopositive-like resistance, namely, a resistive-capacitive impedance. The only aspect which is not seen in such simple ionic elements is the negative slope characteristic of the thermistor so that the consequences of this feature of the *I-V* characteristic, namely, negative values of A.C. resistance and a pure reactive component at a critical frequency, are not observed.

Reasoning from the point of view of general circuit theory, it is interesting to note that a combination of time-variant elements of both types must give rise to a resistive-capacitive-inductive impedance.[12] Furthermore,–as is well known from the analysis of the differential equation of a circuit containing resistance, inductance and capacitance–if one of the time-variant elements has a negative A.C. resistance, undamped oscillatory states must be possible. Accordingly, we have tried to observe oscillations in a combination of the thermistor and incandescent filament using a variety of commercially available units. Although highly damped responses have been observed, sustained oscillations have not been detected. This is undoubtedly due to the inability to obtain a suitable combination with presently available elements such that the magnitude of the negative A.C. resistance is sufficient to permit oscillatory states. At any event if the proper units are fabricated there is no doubt that the theoretical expectation of *purely dissipative time-variant elements* being capable of producing oscillatory states would be satisfied.[13]

By way of summarizing the nature of the anomalous impedance associated with time-variant resistance and, especially the necessity for the condition of steady state current, it is pertinent to point out that, in the Hodgkin-Huxley equivalent circuit of the unit area of squid membrane,–note the circuit is being considered here and not the axon itself–the time-invariant E.M.F.'s, the so-called sodium E.M.F., potassium E.M.F., and chloride E.M.F., give rise to a *finite resting current* through the respective time-variant conductances, sodium conductance, potassium conductance, and time-invariant chloride conductance. The local current must flow in the circuit because the E.M.F.'s are oppositely oriented and the resting conductances are *finite*. Thus the anomalous impedance, inductive and capacitive, reported by Cole (20) for this circuit, results from a perturbation of the resting current by applying a membrane current across the entire configuration which divides between the branches. The linear differential equation derived by Hodgkin and Huxley (16) for the axon in the quiescent state applies precisely to

[12] A series combination of a thermistor (Gulton Industries, Metuchen, New Jersey, 32CH2) and an incandescent filament (two General Electric 3 watt, 125 volt in parallel), operating at a steady state current of 4 ma., gave excellent qualitative results by means of Lissajous figures, confirming the *R,L,C* character of such a combination. Note that the significant reactive effects were observed in the range of 0.01 to 3.0 C.P.S., the equivalent capacity and inductance being in the range of several thousand microfarads and henries, respectively.

[13] The membrane oscillator model of Teorell (14) is most interesting in that a mechanical storage element, a hydrostatic column of water, is coupled mechanically to an electro-osmotic time-variant resistance. In this case the mechanical element modifies the time-variant resistance so that it no longer has a simple generic character, *i.e.* single time constant, and consequently the time-variant resistance has a resistive, inductive, capacitive quality. The *R,L,C* quality could be obtained by (electrically) coupling two generic electro-osmotic elements either by arranging the elements in parallel or in series, as in the case of the series combination of temperature-dependent elements discussed above.

The combination of an electrical conservative element, a capacitor, and a dissipative element, the thermistor, is well known with regard to the condition of oscillation and can be readily confirmed with commercially available units.

this condition of resting local current flow, obtained as we have done in the analysis above for the condition of small signal perturbation by linearizing the non-linear equation of the system which was established by applying Kirchhoff's law to the circuit. By means of this equation they have shown a damped oscillatory response for a small step of current which, as is well known, is the property inextricably related to the impedance characteristic of the system. (A simplified version of this circuit has been constructed by Dodge (22) with a time-variant Na conductance and a time-invariant K conductance by means of suitable electronic circuitry, and examined extensively in terms of its voltage and current responses as a function of time.)

At this point it is pertinent to deal with the possible meaning of the equivalent circuit in terms of a real system of ions, especially since this consideration will provide an opportunity to discuss some properties of the homogeneous *versus* heterogeneous diffusion regime of ions. By homogeneous it is to be understood that the nature of the diffusion regime does not vary as a function of the distance along the axon. Although the matter will not be pursued in detail here, it must be noted that the equivalent circuit of Hodgkin and Huxley *cannot* apply to a homogeneous diffusion regime of ions in the steady state. To be more specific, ascribing an E.M.F. and conductance in series to a given species and combining such series configurations in parallel, depending upon the number of species present, is not admissible in an homogeneous regime since this would of necessity imply not only local current flow in the volume element of the diffusion regime, but also associated phenomena such as Joule's work and a magnetic field. On the contrary these conditions do not occur in a diffusion regime. (The equivalent circuit, instead, should be an E.M.F. in series with a conductance in which *formally* both the E.M.F. and conductance is made up of as many components as the various ionic species present.) The fundamental condition which must be satisfied is that of zero current at every point x, for the case of one dimension, or r, in the case of a cylindrical geometry. This is a consequence of the fact that at every point in the regime the total flux of positive species must exist in a given direction simultaneously with the total flux of negative species of equal magnitude in the *same* direction. This condition is usually referred to as the condition of electroneutrality.[14] Integration of the total flux equation between the boundary conditions results in the diffusion potential of the regime.

The equivalent circuit of Hodgkin and Huxley implies that dissimilar ionic regimes–each with a time-invariant E.M.F. and a time-variant resistance–are acting side by side and, indeed currents are flowing locally from one micro region to another.[15] This ensemble, when perturbed by an external current, will display anom-

[14] Note this condition is basic and must be satisfied for the most general case; namely, free diffusion or steady state constrained diffusion (Planck regime).

[15] See Sollner (18) concerning heterogeneous and mosaic membranes. The view that a myraid of currents might flow in the squid axon membrane has been expressed by Marmont (21).

alous impedance and oscillatory behavior as explained in the previous discussion. Parenthetically, this argument could be considered as proof (quite independent of other considerations)–if the Hodgkin and Huxley analysis is to be adhered to–for the existence of spatially separate regions with differing E.M.F. and time-variant resistance; *i.e.*, a mosaic of distinct sodium, potassium, and chloride patches. A related comment is appropriate here with regard to the paper of Kirkwood (17) in which an attempt has been made at a general theoretical treatment of a homogeneous diffusion regime of ions in the steady state. Among other topics the author treats the subject of the A.C. impedance function and predicts, without carrying out the explicit solution, that the system will display an inductive reactance for the condition of zero current. (The condition of zero current is not only implied by the steady state but also assured by the author's stipulation that a back E.M.F. is inserted in the measuring circuit equal to the E.M.F. of the ionic system itself). If the successful solution of his equation should indicate an inductive component in the impedance function then it must be interpreted as a consequence of *time-variant* E.M.F. and not of the time-variant resistance of the regime of ions. In this case the imaginary component of the impedance function is not due to the anomalous mechanism but rather to energy storage in the system. It should be emphasized in this connection that in addition to time-variant E.M.F., which is present to some degree in most ionic regimes, it is also possible to encounter capacitive components due to Poisson-Boltzmann (diffusion double layer) regions which might arise in certain ionic elements involving fixed charges.[16] Thus the total impedance function would consist of anomalous components and of ordinary components contributed by dissipative and conservative elements, respectively.

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