ELECTRIC PHASE ANGLE OF CELL MEMBRANES

By KENNETH S. COLE

(*From the Department of Physiology, College of Physicians and Surgeons, Columbia University, New York*)

Höber (1910, 1912) was able to estimate the electric conductivity of the interior of red blood corpuscles from measurements made with high frequency alternating currents. Fricke (1924, 1925, a, b) greatly extended this work by careful analysis and measurements over a range of frequencies on the resistance and capacity of suspensions of these cells. He and McClendon (1926, a, b) both found the cell surface to behave like a rather good dielectric. It had an electric capacity that was practically independent of the frequency and a resistance so high as to be infinite within the limits of experimental error. But, in view of the highly specialized functions of these cells, it is not surprising to find that up to the present they seem to be the only biological systems showing these characteristics.

Measurements made at different frequencies on the alternating current impedances of various tissues by Philippson (1921), of muscle by Sapegno (1930), and of suspension of sea urchin eggs by Cole (1928, b) have indicated cell surfaces having capacities which vary with frequency. Measurements on the resistance and capacity of skin and nerve by Gildemeister and his students (1919–1928), Hōzawa (1925), Lullies (1928, 1930), and Krüger (1928), on *Valonia* by Blinks (1926) and on muscle by Fricke (1931) have further indicated a resistance which also varies with the frequency. In these latter measurements it has usually been found that the phase angle of this variable resistance-capacity combination remained more or less constant as the frequency was varied between wide limits. This resistance-capacity variation with constancy of phase angle is very similar to the phenomena of polarization capacity as found at metal-electrolyte interfaces.

641

Theory

In a previous paper (Cole, 1928, *a*) a theoretical relation was given between the alternating current reactance and resistance of an electric circuit composed of resistances and a single variable impedance element of constant phase angle.   It is proposed to give a simple derivation of this result and to test it with the experimental data of others and our own which are now available.
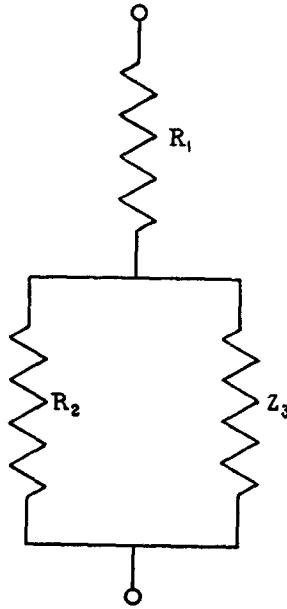

FIG. 1. Assumed equivalent tissue circuit

As was further stated, a system containing any number and arrangement of resistances with one and only one variable impedance element can be reduced to either one of two simple networks containing two resistances and one variable impedance element. For a specific example, the network of Fig. 1 will be considered. R_1 and R_2 are resistances while z_3 is a complex impedance of resistance and reactance which will presently be restricted by the assumption of a constant phase angle. By the usual methods we have for the complex impedance of this circuit,

$$z = R_1 + \frac{R_2 z_3}{R_2 + z_3} = (R_1 + R_2) \frac{\dfrac{R_1 R_2}{R_1 + R_2} + z_3}{R_2 + z_3}.$$

For the applications which we shall make, z_3 will approach infinity at the low frequencies and will approach zero at the high frequencies, so we shall make the abbreviations

$$r_0 = R_1 + R_2, \; r_\infty = R_1, \; a = \frac{R_1 R_2}{R_1 + R_2}, \; a_1 = R_2. \tag{1}$$

We then have

$$z = r_0 \frac{a + z_3}{a_1 + z_3}.$$

We may now write $z = r + jx$ and $z_3 = r_3 + jx_3$ if we consider the resistance and reactance to be in series in each case. After separating the real and the imaginary parts of the resulting equation we have the two equations

$$\text{r.p.} \quad (a_1 + r_3) r - x x_3 = (a + r_3) r_0,$$

$$\text{i.p.} \quad (a_1 + r_3) x + r x_3 = x_3 r_0.$$

At this point let us assume a constant phase angle φ_3 for z_3. Then $\tan \varphi_3 = x_3/r_3$ and we may write $r_3 = m x_3$ where $m = \cot \varphi_3$. Eliminating r_3 and x_3,

$$r^2 + x^2 - \left(r_0 + \frac{a}{a_1} r_0 \right) r + m \left(r_0 - \frac{a}{a_1} r_0 \right) x + \frac{a}{a_1} r_0^2 = 0.$$

And by equations (1) $\dfrac{a}{a_1} r_0 = r_\infty$ so

$$r^2 + x^2 - (r_0 + r_\infty) r + m (r_0 - r_\infty) x + r_0 r_\infty = 0.$$

This is however the equation of a circle in Cartesian coordinates where r and x are the variables. The radius is $\dfrac{r_0 - r_\infty}{2} \sqrt{1 + m^2}$ and the center is at the point $\dfrac{r_0 + r_\infty}{2}, \; - m \dfrac{r_0 - r_\infty}{2}$ so the slopes of the radii to r_0 and r_∞ are m and $-m$ respectively. It will be noticed that neither

the frequency nor the values of r_3 and x_3 enter explicitly into this circle diagram. It is a result of only the resistances r_0 and r_∞ and the phase factor m so all systems of the kind postulated having the same r_0, r_∞, and m will give the same circle irrespective of the distribution of the circuit elements. However, the frequency for which x is a maximum, *i.e.*, for the highest point on the circle, may be called a characteristic frequency of z_3. It is the frequency for which the magnitude, but not the phase, of z_3 is equal to $r_0 - r_\infty$. Since x is treated as the coefficient of an imaginary quantity, this locus on the r, jx plane is called the complex plane representation.

In considering biological systems we shall have reactances due only to capacities so

$$x = -\frac{1}{c\,\omega} \quad \text{and} \quad x_3 = -\frac{1}{c_3\,\omega}$$

where c and c_3 are series capacities and ω is 2π times the frequency n. In cases where the tissue has been balanced in a Wheatstone bridge by a resistance and a capacity in series, it is then only necessary to plot $1/c\omega$ *vs. r*. Where a parallel resistance-capacity combination has been used, the equivalent series circuit must be computed for each frequency. If a tissue has the equivalent of a single variable impedance element with a phase angle independent of frequency, then it must give a circle diagram. Any deviations from a circle must be due to the failure of this simple network as an electrical representation of the tissue.

Circle Diagrams

Fig. 2 is plotted from the data of Fricke and Morse (1925) on calf blood, after recomputation for the equivalent series resistance and reactance. The deviation of the points from the circle is not large in view of the difficulty of making such measurements at frequencies up to four and a half million cycles. It will be noticed that the center of the circle does not lie on the axis of resistances. Thus either m is not zero, as it would be for a perfect dielectric at z_3, or the assumption of a single constant phase angle variable impedance element is not valid. This agrees with the impedance calculation of these data (Cole, 1928, *b*). From the diagram, $m = 0.16$.

Fig. 3 is a replotting of the data of Lullies (1930) on frog nerve. Lullies gave this identical representation, but apparently did not realize its significance. He computed m analytically from r_0, r_∞, r, and x but because of the behavior near r_∞ he came to the conclusion that m varied continuously with the frequency. Our analysis tends
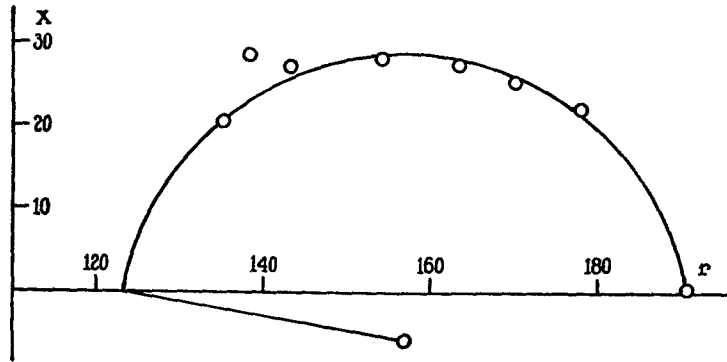

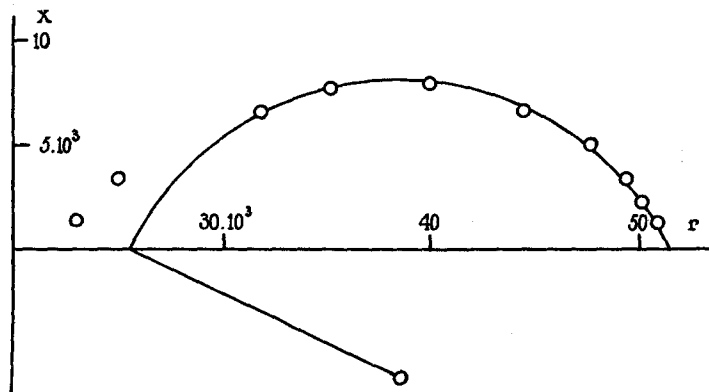FIG. 2. Reactance vs. resistance in ohms for calf blood (Fricke and Morse)

FIG. 3. Reactance vs. resistance in ohms for frog nerve (Lullies)

to show however that over the major portion of the frequency range the phase angle of a single variable impedance is sensibly constant, but with some other factor presumably entering at the highest frequencies. $m = 0.49$.

The data of Fricke (1931) on rabbit muscle have also been recom-

puted for the equivalent series combination and are shown graphically in Fig. 4. By an analytical method Fricke came to the conclusion that $m = 0.46$ which is an excellent agreement with the value obtained from the circle which best fits the data. The departure from the circle at the high frequencies is noticed here also. $m = 0.46$.
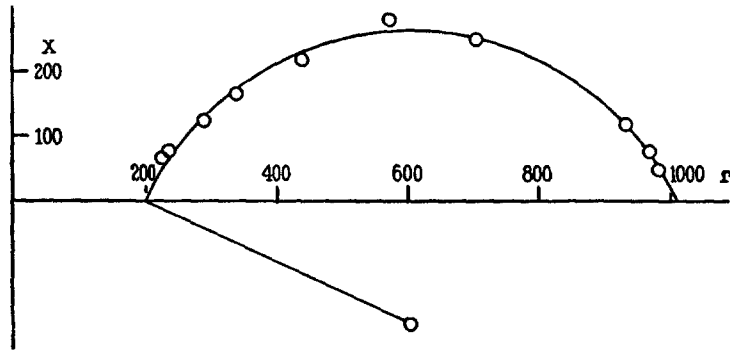
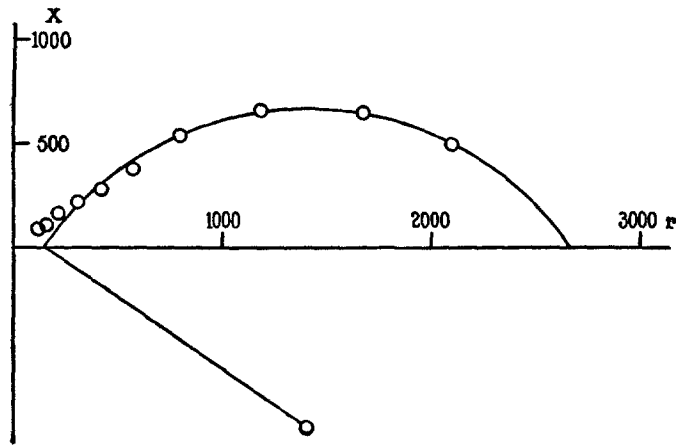FIG. 4. Reactance vs. resistance in ohms for rabbit muscle (Fricke)

FIG. 5. Reactance vs. resistance in ohms for frog skin

Fig. 5 is the diagram for a double layer of frog skin in Ringer. The effective electrode area was 0.12 cm.[2] and the frequencies range from 100 to 90,000 cycles/sec. Once again we have a rather definite circle except at the high frequency end, and it should be noted that

no resemblance of a circle was obtained for low frequencies unless the bridge current was kept low. $m = 0.69$.

Since no physiological conclusions are to be drawn, the data on an excised cat diaphragm in Ringer shown in Fig. 6 are included. The tissue was irritable but the animal had been under ether for some time and the measurements were made at room temperature. The thickness was about 2 mm. and the effective electrode area was 0.28 cm.[2] The maximum frequency was not high enough to show any deviations which might be present in the high frequency portion of the circle. $m = 0.34$.
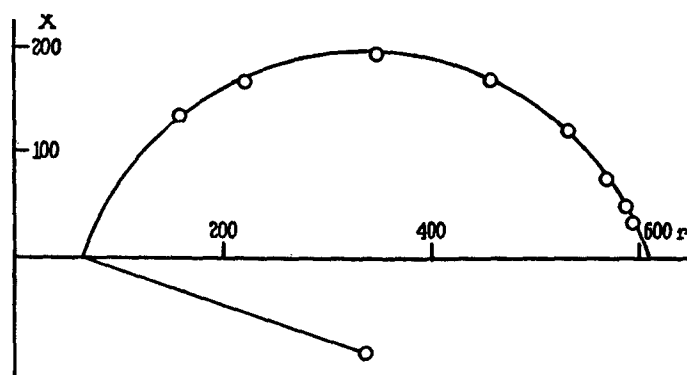

FIG. 6. Reactance vs. resistance in ohms for cat diaphragm

A slice of potato 2 mm. thick and 10 cm.[2] area in diluted sea water gave the data for Fig. 7. The sea water was diluted so that there was no appreciable change in the weight or the electrical properties. Again we cannot be sure that there would be no departure from the circle at higher frequencies. $m = 0.49$.

After a slice of potato had been boiled a few minutes in this solution, it had no measurable reactance and its specific resistance was approximately that of the solution.

The data for human skin do not extend to sufficiently low frequencies. Corresponding probably to the high frequency divergence of other materials, the measurements of Einthoven and Bijtel (1923), Gildemeister (1928), and Hōzawa (1932) give a straight line on the complex plane at frequencies above 1000 cycles. Hōzawa interprets

this as due to a static capacity in series with a polarization capacity which varies as the inverse square root of the frequency. At lower frequencies, the data indicate the possibility of an arc of a circle but Hōzawa's data to 250 cycles and our own to 50 cycles have not given a maximum for x.

On the other hand the highest frequency used in our experimental work, 90,000 cycles, was too low to give more than the initial portions of the corresponding diagrams for *Laminaria* and *Ulva*.
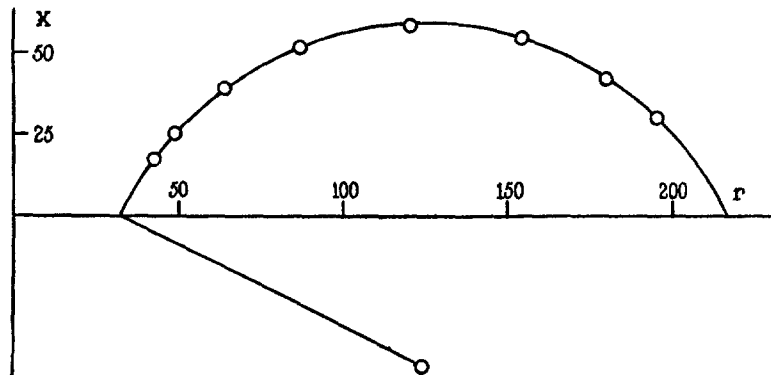

FIG. 7. Reactance *vs.* resistance in ohms for potato

DISCUSSION

In a system as complicated as tissue it might be supposed that there are at least as many variable impedance elements as there are cells. This would hardly seem to fit in with our assumption of a single element. In the less complex case of suspensions, it has been shown (Fricke, 1925, *a*; Cole, 1928, *a*) that all of the impedance elements are equivalent to a single impedance element. The evidence here presented tends to show that at least for low and intermediate frequencies, the tissues may be considered to have an equivalent single variable impedance element of constant phase angle.

The classical theory of a simple diffusion polarization capacity calls for $m = 1$ and $c_3 = \underline{c}_3\,\omega^{-\frac{1}{2}}$ where $\underline{c}_3$ is a constant. For all of the above data however m is less than unity, but the values of c_3 have not been computed without the assumption of a constant m or a value of r_∞. Fricke (1932) has shown theoretically that if $c_3 = \underline{c}_3\,\omega^{-\alpha}$ where

α is a constant, then $1/\varphi_3 = \alpha\pi/2$ or $m = \tan \alpha\pi/2$. We may compute for each tissue the value of α from the value of m for the range in which m is constant.

SUMMARY

From the theory of an electric network containing any combination of resistances and a single variable impedance element having a constant phase angle independent of frequency, it is shown that the graph of the terminal series reactance against the resistance is an arc of a circle with the position of the center depending upon the phase angle of the variable element.

If it be assumed that biological systems are equivalent to such a network, the hypotheses are supported at low and intermediate frequencies by data on red blood cells, muscle, nerve, and potato. For some tissues there is a marked divergence from the circle at high frequencies, which is not interpreted.

BIBLIOGRAPHY

Blinks, L. R., 1926, Thesis, Harvard University.

Cole, K. S., 1928, a, J. Gen. Physiol., 12, 29; 1928, b, 12, 37.

Einthoven, W., and Bijtel, J., 1923, Arch. ges. Physiol., 198, 464.

Fricke, H., 1924, Physic. Rev., 24, 575; 1925, a, 26, 678. 1925, b, J. Gen. Physiol., 9, 137. 1931, Physics, 1, 106. 1932, Phil. Mag., in press.

Fricke, H., and Morse, S., 1925, J. Gen. Physiol., 9, 153.

Gildemeister, M., 1919, Arch. ges. Physiol., 176, 84; 1922, 195, 112; 1928, 219, 89. Gildemeister, M., in Bethe, A., von Bergmann, G., Embden, G., and Ellinger, A., Handbuch der normalen und pathologischen Physiologie, Berlin, Julius Springer, 1928, 8, pt. 2, 657.

Höber, R., 1910, Arch. ges. Physiol., 133, 237; 1912, 148, 189.

Hōzawa, S., 1925, J. Biophys., 1, 185; 1932, Z. Biol., 92, 209.

Krüger, R., 1928, Arch. ges. Physiol., 219, 66.

Lullies, H., 1928, Arch. ges. Physiol., 221, 296; 1930, 225, 69.

Philippson, M., 1921, Bull. Acad. roy. Belgique, Cl. Sc., 7, 387.

Sapegno, E., 1930, Arch. ges. Physiol., 224, 187.

McClendon, J. F., 1926, a, J. Biochem., 68, 653; 1926, b, 69, 733.