PHYSICAL INTERPRETATION OF BIOLOGICAL IMPEDANCES WITH APPLICATIONS TO ELECTROSTIMULATION

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Introduction

Much work has been reported on the measurement of cell membrane impedance using microelectrode techniques. Further, the results can be related to proposed forms of the membrane structure. However, at the tissue level there have been very few attempts to relate the measured impedance to the structure. This is a difficult task which cannot be done without histological knowledge of the tissue.

Using the results of microelectrode impedance studies to determine the time-constant of individual cell membranes, and our macroscopic measurements of bladder impedance in dogs, we have developed a model which relates the components of tissue impedance to the microscopic physical structure of the tissue. Indeed, using this model, the impedance of the interstitial fluid can be studied separately. We have tested our model using the impedance measurements taken on the urinary bladder of dogs. A significant result of the model is the prediction that direct current bladder stimulation is less efficient than square wave current stimulation.

Theory

Consider the three-dimensional array of MNQ cells shown in Fig. 1(a). As a first approximation we assume that the cells in the m direction are in series and that the cells in the planes nq are in parallel. It follows from elementary circuit theory of elements in series and parallel, that:

$$R_{if} = \frac{M}{NQ} r_{if} \qquad \ldots(1)$$

$$R_m = \frac{M}{NQ} r_m \qquad \ldots(2)$$

$$C_m = \frac{NQ}{M} c_m \qquad \ldots(3)$$

$$R_{ef} = \int \frac{\rho_{ef}\, dl_m}{A(m)} \qquad \ldots(4)$$

where:

r_{if} = resistance of the intracellular fluid of one cell,
r_m = membrane resistance of one cell,
c_m = membrane capacitance of one cell,
R_{if} = macroscopic resistance due to intracellular fluid, see Fig. 1(c),
R_m = macroscopic reistance due to cell membranes,
C_m = macroscopic capacitance due to cell membranes,
R_{ef} = macroscopic resistance due to extracellular fluid.

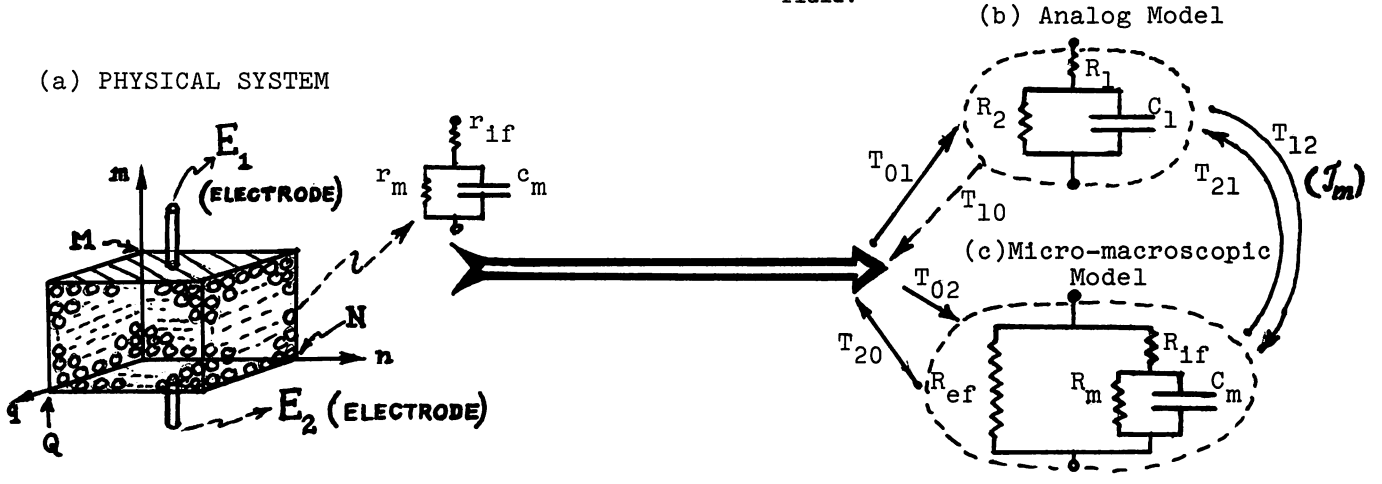

Figure 1.

(a): Schematic representation of a piece of biological tissue constituted by a three-dimensional array of MNQ cells lying between two electrodes E_1 and E_2.

(b): Analog circuit for the electrical impedance of the piece of tissue shown in (a). The elements R_1, R_2 and C_1 are independent of the frequency (Drolet, 1968).

(c): A 'Micro-macroscopic' Model, in which the components are directly related to the microscopic physical structure of the tissue. The elements R_{ef}, R_{if}, R_m and C_m are also independent of the frequency.

Note: The operations required to pass from one model to another are symbolized as follows:

T_{01}: complex operation to go from the physical system (a), to the analog model (b);

T_{02}: the transfer function to go from the physical system (a), to the 'Micro-macroscopic' Model (c);

T_{12}: the mathematical transformation to go from the analog model (b), to the 'Micro-macroscopic' Model (c);

T_{21}: the inverse of the transformation T_{12}.

A(m) =cross section area of interstitial fluid

ρ_{ef} =average resistivity of extracellular fluid

dl_m =element of length in the 'm' direction

M,N,Q=number of cells respectively in the 'm', 'n' and 'q' directions.

From (2) and (3) it is evident that the macroscopic time constant $\tau_{ma}=R_m C_m$ is equal to the microscopic time constant $\tau_{mi}=r_m c_m$. It follows that

$$\tau_{ma}=\tau_{mi}=\tau_m=R_m C_m=r_m c_m \qquad ...(5)$$

Also, (1) and (2) imply that:

$$R_{if}/R_m=r_{if}/r_m \qquad ...(6)$$

Equations (1), (2), (3), and (4) define the transformations T_{02} and T_{20} which relate the microscopic variables r_{if}, r_m and c_m to the macroscopic variables R_{if}, R_m and C_m (see Fig. 1). On the other hand, the elements R_1, R_2 and C_1 of the analog model are determined experimentally from impedance measurements (Drolet, 1968). It is most important to realize that the analog model, of Fig. 1(b), must be equivalent to the so-called 'Micro-macroscopic' Model, of Fig. 1(c). This follows since both models represent the same object--the electrical impedance of the piece of tissue shown in Fig. 1(a). From circuit theory the equivalence between these two models implies the following relationships between their elements:

$$R_{ef}=\frac{-b\pm\sqrt{b^2-4ac}}{2a} \qquad ...(7)$$

where:

$$a=-[R_1+R_2(1-\tau_m^2\omega_o^2)]$$

$$b=2R_1(R_1+R_2)(1-\tau_m^2\omega_o^2)$$

$$c=R_1(R_1+R_2)[-R_1+(R_1+R_2)(\tau_m^2\omega_o^2)]$$

$$R_{if}=\frac{R_{ef}R_1}{R_{ef}-R_1} \qquad ...(8)$$

$$R_m=\frac{-R_{if}-R_{ef}}{2}\pm\left\{\left[\frac{(R_{if}+R_{ef})}{2}\right]^2-R_{if}(R_{ef}+R_{if})(1-\tau_m^2\omega_o^2)\right\}^{1/2} \qquad ...(9)$$

$$C_m=\frac{1}{\omega_o}\left[\frac{(R_{if}+R_m)(R_{ef}+R_{if}+R_m)}{R_{if}R_m^2(R_{ef}+R_{if})}\right]^{1/2} \qquad ...(10)$$

where: $\omega_o=(1/R_2C_1)[(R_1+R_2)/R_1]^{1/2}$

Equations (7), (8), (9), and (10) define the mathematical transformation T_{12} which was introduced in Fig. 1. The transformation T_{21} is the inverse of transformation T_{12}, and can be expressed by:

$$R_1=\frac{R_{ef}R_{if}}{R_{ef}+R_{if}} \qquad ...(11)$$

$$R_1+R_2=\frac{R_{ef}(R_m+R_{if})}{R_{ef}+R_{if}+R_m} \qquad ...(12)$$

$$C_1=\left[\frac{R_1+R_2}{R_1}\right]^{1/2}\frac{C_m}{R_2}\left[\frac{R_{if}R_m^2(R_{ef}+R_{if})}{(R_{if}+R_m)(R_{if}+R_{ef}+R_m)}\right]^{1/2} \qquad ...(13)$$

Results

The 'Micro-macroscopic' Model has been verified experimentally using the results of impedance measurements made on the urinary bladder of dogs under various degrees of filling (see Table 1). From these results, it is evident that direct current bladder stimulation is less efficient than square wave current stimulation. Indeed, since $R_m >> R_{ef}$, most of the current flows in the interstitial fluid when direct current stimulation is used.

Table I.

Elements of the 'Micro-macroscopic' Model calculated from equations (7), (8), (9), and (10), using experimental values for R_1, R_2, and C_1 which are given in reference (3). Also, τ_m=8msec was used.

VOL (cm^3)	R_{ef} (Ω)	R_{if} (Ω)	R_m (Ω)	C_m (μF)
15	101.0	71.9	9,957	0.804
25	162.0	139.7	12,883	0.621
35	247.0	90.1	9,684	0.826
40	275.6	85.6	13,160	0.608
50	294.8	285.4	17,536	0.456
100	304.6	295.6	19,633	0.407
190	231.1	470.7	48,613	0.165

I am grateful to Dr. R.S.C. Cobbold for constructive criticism of the model.

This research has been supported by the MRC Grant MA 3895.

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