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Impedance Spectroscopy in Human Skin. A Refined Model

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INTRODUCTION

In our previous paper (1) an equivalent circuit describing the impedance spectrum of human cadaver skin was presented (Fig. 1a). Two novel features were introduced: replacing a capacitor with a Constant Phase Element (CPE), and adding an inductive subcircuit L-R_2. The use of the CPE led to the measurement of the fractal dimension of skin, and the inductive subcircuit was accounted for by the alignment of dipolar molecules in an alternating electric field. Here we discuss these two features in a physically more realistic context (Fig. 1b). The approach applied here agrees with earlier interpretations.

HIGH FREQUENCY BEHAVIOUR

The basic shape of a Nyquist plot (see ref. 1) of skin is a semi-circle, which is obtained with a parallel combination of a resistor and a capacitor; the diameter of the semi-circle is R. While at solid electrodes, from where this way of thinking is adopted, such a circuit has a clear physical and geometrical interpretation, its origin is not evident in the case of skin. Recently, we assumed (2) that human skin consists of aqueous pores having a charge on the pore walls (Fig. 2), and electric current flows only through these pores. This model accounted reasonably well for the iontophoretic permeation measurements. Thus, it is concluded that results obtained with electrochemical techniques are due to aqueous pores, and the lipid matrix of skin affects mainly the charged nature and geometrical structure of these pores. Therefore, the appearance of the semi-circle in the Nyquist plot also has to be related to these pores.

Consider the pore as a long (length at least two orders of magnitude greater than its diameter) insulated cable with finite conductivity. In engineering, such a cable is modelled with a **transmission line** presented in Fig. 3a. The impedance of this transmission line can be calculated if it is assumed that the impedance ‘unit’ inside the dashed line is repeated unchanged along the line, *i.e.*, the line is homogeneous. We take the first unit apart from the line and replace the rest with an unknown impedance Z_{n-1} (Fig. 3b); the impedance of this system, Z_n, is

$$\frac{1}{Z_n} = j\omega C' + \frac{1}{R''} + \frac{1}{R' + j\omega L' + Z_{n-1}} \tag{1}$$

where ω is the angular frequency and j is the imaginary unit; R’, R”, C’ and L’ are the components of the transmission line, not those in Fig 1. If the line is long enough, $Z_n = Z_{n-1} = Z$ which can be solved as

$$Z = \frac{(R' + j\omega L')}{2}\left[\sqrt{1 + \frac{4}{(R' + j\omega L')(1/R'' + j\omega C')}} - 1\right] \tag{2}$$

It must be emphasized that Z is now given per **length unit**, i.e., to calculate the impedance of the entire pore eq. (2) has to be multiplied by the pore length, l; otherwise the impedance would depend on the choice of the length of units. Separation of the real and imaginary parts of eq. (2) is quite tedious but fortunately *e.g.* FORTRAN includes complex arithmetics as intrinsic functions. The Nyquist plot of eq. (2) is indeed a complete semi-circle, as the one of an RC circuit, and furthermore, we have noticed that it converges to a constant value after only four or five units, which justifies our treatise. The diameter of the semi-circle is obtained inserting $\omega = 0$ into eq. (2). Hence, our transmission line is **mathematically equivalent to an RC circuit.**

In practice, semi-circles are always flattened which means that, in the case of solid electrodes, a capacitor in an RC circuit has to be replaced by a CPE (1): how is this accomplished in our transmission line ? The impedance of any parallel RC circuit is

$$Z_{RC} = \frac{R}{1 + j\omega RC} = \frac{R - j\omega R^2 C}{1 + (\omega RC)^2} \tag{3}$$

The product RC has the dimension of time, and therefore it is said that an RC circuit is characterized by a single relaxation time $\tau = RC$. The impedance of any parallel R-CPE circuit is

$$Z = \frac{R}{1 + (j\omega)^{\alpha} RY} \tag{4}$$

where Y is the admittance of the CPE and α is the frequency exponent which can be related to the fractal dimension (1). This circuit is characterized by a distribution of relaxation times, and the distribution density function G(τ) is proportional to $\tau^{-\alpha}$ although the distribution is non-normalizable (3). In our transmission line, there are several parallel combinations R”-C’ which correspond to a single relaxation time τ’. If instead of identical values for every R” and C’ there is a distribution of their values, a distribution of relaxation time, G(τ’), analogous to an R-CPE circuit, is obtained. Thus, we come to a conclusion that in the case of a flattened semi-circle, the values of C’ and R” perpendicular to the transmission line are varying along the line, and this kind of a transmission line is **mathematically equivalent to a circuit R_1-CPE in Fig. 1.**

Excluding L’, it is easy to find the physical interpretation of the components of this transmission line. R’ represents the ohmic resistance of the aqueous solution inside the pore, C’ is the double layer capacitance due to the charge density on the pore wall (Fig. 2) and R” is the charge transfer resistance associated to the ion exchange reaction. An inductor is a component where electric current is evolved when it is passed through a magnetic field. Because it has no

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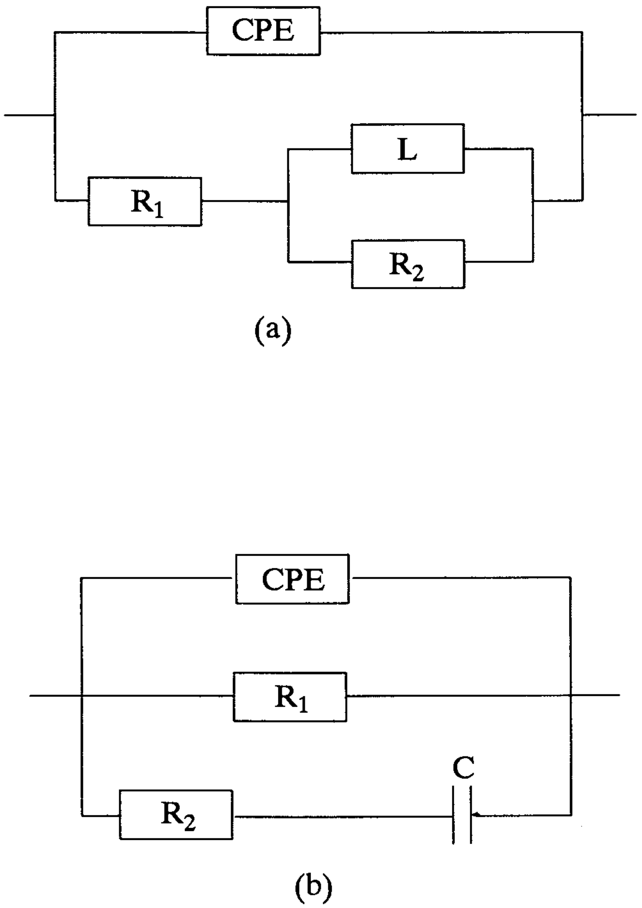

Figure 1. The alternative equivalent circuits for human skin: (a) from ref. 1; (b) presented here.

physical interpretation in ion conducting systems, and our transmission line model is adopted from an electron conductor, an inductor can be left out. This question is also addressed below.

Applying the transmission line model to a skin pore it is obvious that the R-CPE type of behaviour of skin has to be related to the structural heterogeneity of these pores, which means either a nonuniform distribution of the charges on the pore walls or a varying pore radius along the pore. This conclusion is not surprising because the transmission line model assumes a homogeneous distribution of electronic charges, while on the skin surface only discrete ionic charges are present. Formally, it is also possible that skin consists of variably sized and charged homogeneous pores each of them having their own time constants. However, since simulations of such heterogeneous systems is difficult, we have to rely on the fractal approach as described earlier (1), except that it is the heterogeneity of skin pores, not skin surface, which accounts for the observed behaviour.

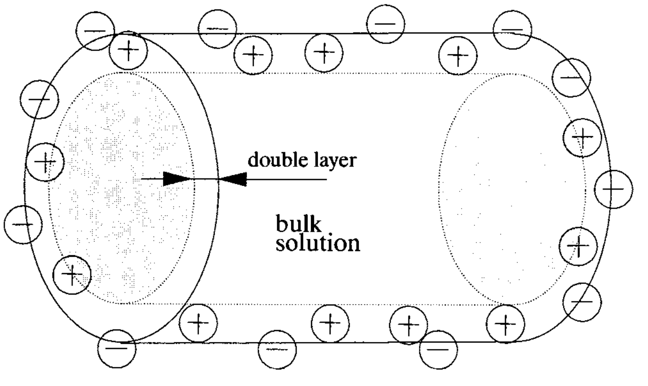

Figure 2. A schematic presentation of the pores in human skin. Pore walls has a negative charge which is balanced by positive charges in the electric double layer. In the centre of the pore there is solution with bulk properties.

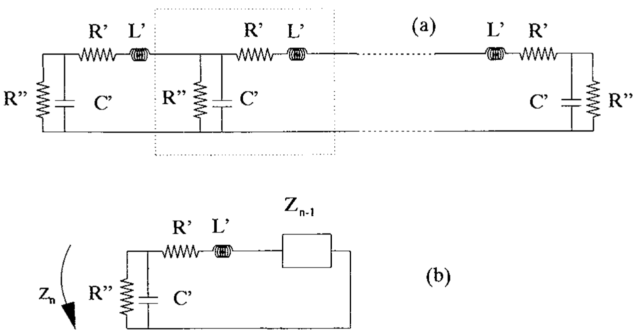

Figure 3. The transmission line model for an insulated cable with finite conductivity (a). Evaluation of the impedance of the transmission line (b).

LOW FREQUENCY BEHAVIOUR

At the low frequency region, the Nyquist plot of human skin was found to be stretching along the real axis (see Fig. 4). This phenomenon was taken into account by adding a parallel combination of an inductor and a resistor into the equivalent circuit. As discussed earlier (1), the significance of this inductor is questionable. Subsequently another equivalent circuit having practically the same effect on the Nyquist plot was found (Fig. 1b) where the inductive subcircuit is replaced by a separate branch of a capacitor and a resistor in series. Macdonald (3) applied such a circuit to a solid material where both conductive and dipolar relaxation processes are taking place; each relaxation has its own branch in the circuit; at liquid-liquid interfaces this branch is due to specific adsorption (4). Therefore, the suggested explanations for the behaviour at low frequencies are still valid (1).

In an ideal situation, as in the case of electrical components, the change of any component of an equivalent circuit

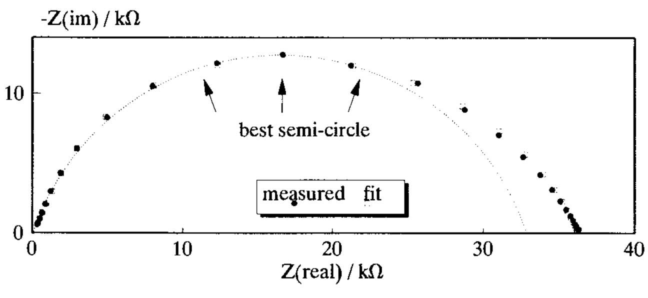

Figure 4. A Nyquist plot of human skin in 0.1 M NaCl after 16 hr hydration. f = 1.0 Hz - 10 kHz.

does not affect the other components, i.e., they are independent. In our case, a nonlinear fit (5) is carried out to find out the numerical values of the chosen components, and the components depend on each other. To demonstrate this fact, using the two equivalent circuits in Fig. 1, the results of the fits of the Nyquist plot in Fig. 4 are presented in Table I. The semi-circle has been added to emphasize the stretching along the real axis. As anticipated, small differences are obtained in the values of the other components.

Table I. Comparison of the fits into the two alternative equivalent circuits presented in Fig. 1: data from Fig. 4.

Component	Fig. 1a	Fig. 1b
$Y_{CPE}/10^{-8}\ \Omega^{-1}$	17.4	8.36
α	0.776	0.849
$R_1/k\Omega$	36.2	35.6
$R_2/k\Omega$	122	375
L/H	8.8	—
C/nF	—	18.0
$\chi^2/10^{-4}$*	3.09	2.92

* χ^2 is the function to be minimized in the fit. For a more detailed description in the case of a non-linear fit, see ref. 6.

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