Upsala J Med Sci 85: 283–293, 1980

Impedance of the Frog Gastric Mucosa, the Teorell-Wersäll Effect

Avi Ring and John Sandblom

Department of Physiology and Medical Biophysics, Biomedical Center, University of Uppsala, Uppsala, Sweden

ABSTRACT

The small signal impedance of frog gastric mucosa has been measured from 1 Hz to 500 kHz. The results obtained in Ringer´s solution have been compared with the effect of replacing sodium with potassium on the nutrient side of the mucosa. The substitution to potassium reduces the membrane resistance and changes the impedance locus from a flat to a semicircular shape.

We have examined this effect, the Teorell-Wersäll effect, in relation to changes in membrane permeabilities. The experimental data are consistent with a model based on the electrical behaviour of transmission cables (the geometric requirement for this may be found in the gastric duct) and the observed electrical properties can be predicted from an increase in conductance of the secretory membrane when replacing sodium with potassium.

INTRODUCTION

Electrical impedance properties of epithelial membranes have generally been used to relate ionic permeabilities to structural components of the membrane.

In principle it is possible to describe the impedance of a biological membrane as a combination of elements consisting of lossy dielectrics each having an impedance Z given by:

$$Z(\omega) = \frac{R_p}{1+(j\omega\tau)^{\alpha}} \tag{1}$$

where ω is the angular frequency, R_p is the DC-resistance, τ is the time constant and α a dimensionless constant. This equation generates a semicircle in the impedance plane (2) (see Fig. 1). If $\alpha<1$ the centre is located below the abscissa.

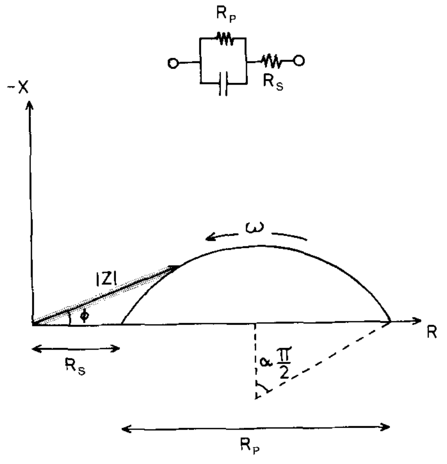

Fig. 1: Impedance locus of the circuit shown above, $|Z|$ and ϕ are the absolute magnitude and phase angle of the impedance. The depressed centre of the circle with an angle of $\alpha\frac{\pi}{2}$ is typical of lossy dielectrics.

A value of α which is less than unity implies either that the impedance arises from a series of relaxation processes with a particular distribution of time constans (3) or it arises from a frequency dependent polarization in the medium (5), for instance a membrane containing mobile sites (10).

One of the earliest impedance measurements on biological membranes was carried out by Teorell and Wersäll (11) who used Eq.(1) to describe the impedance properties of the frog gastric mucosa. They made the observation that potassium added to the secretory (mucosal) side of the membrane not only reduced the total resistance but also changed the shape of the impedance locus from that of a flat to a semicircular shape corresponding to an increase in the phase angle towards 90^{o}. This phenomenon has been referred to as the Teorell-Wersäll effect (7).

Flemström (4) concluded, from impedance measurements, that the locus contained two different dispersion regions and Rehm et al. (7) later found that each of these regions had a different dependence on potassium concentration.

Rehm et al. (7) based their analysis on measurements of transient potential responses to current steps, a method which has been claimed to be less accurate in the low frequency region (1).

We have made direct measurements of the impedance of the frog gastric mucosa for frequencies ranging from 1 Hz to 500 kHz in order to compare the behaviour with that of the different models giving rise to flat loci.

We have found that the behavior is consistent with that of a distributed capacitance, equivalent to a cable (9) and on the basis of such a model the Teorell-Wersäll effect can be explained simply as an increase in conductance of the secretory membrane when replacing sodium with potassium.

METHOD

The gastric mucosa of the species Rana Temporaria was dissected from the mucosal wall of the stomach and mounted between two chambers containing Ringer´s solution (see Fig. 2). The area of the mucosa exposed to the solutions was 0.64 cm^2. The AC-impedance was measured by passing a sinusoidal current through silver chloride electrodes and registering the potential variations close to the mucosa using an additional pair of silver chloride electrodes. To ensure a minimum distorsion of the potential response the r.m.s. value of the sinusoidal current was kept at 0.8 $\mu A/cm^2$ over the entire frequency range, which corresponded to a voltage amplitude of 5 mV (r.m.s.) at low frequencies.

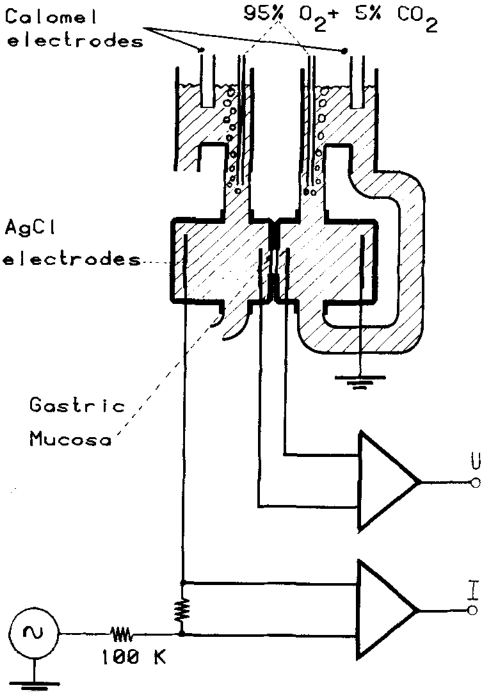

Fig. 2: Experimental arrangement for measuring the impedance of the frog gastric mucosa.

The amplitude of the current was measured by registering the potential drop across an external resistor and the phase shift between current and voltage was recorded using a phasemeter. The data were processed to give the reactive and the resistive components of the impedance as well as the magnitude and phase.

Experiments were carried out with Ringer's solution (4) (81.6 mM NaCl, 3.2 mM KCl, 1.8 mM $CaCl_2$, 0.8 mM $MgSO_4$, 0.8 mM KH_2PO_4, 17.8 mM $NaHCO_3$, 3.0 mM sodium butyrate and 2.0 mM glucose) and with a solution replacing sodium with potassium. Since the effect was more pronounced when the solution was added to the nutrient (serosal) than to the secretory side (the procedure used by Teorell and Wersäll) we present only results of adding potassium to the nutrient side.

RESULTS

After mounting, the membrane potential stabilizes in about 30 minutes. Fig. 3 shows a typical impedance locus (squares are experimental values) where two separated dispersion regions can be seen.

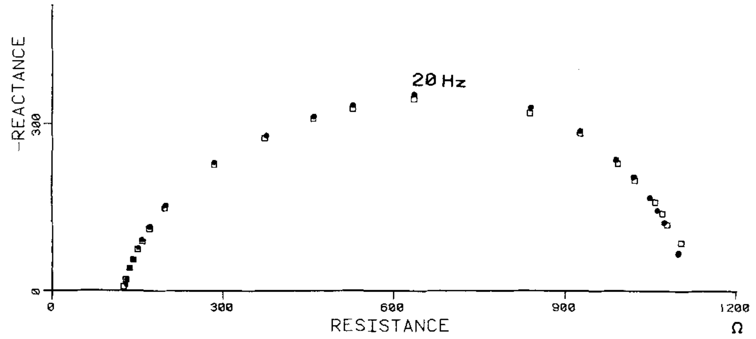

Fig. 3: Impedance locus taken after 30 min. in normal Ringer's solution. The squares are experimental values and points represent the best fit of a double RC-network.

Machen at al. (6) have studied impedance variations in relation to acid secretion and concluded that the two dispersion regions can be associated with the two sides of the epithelium. The element with the shortest time constant reflects the behavior of the nutrient side whereas the element with the longer time constant varies with acid secretion and therefore describes the electrical properties of the secretory side.

Using a description in terms of two lossy dielectrics we have obtained a best fit to the data using Simplex and Gradient type algorithms (points in Figs. 3and 4).

Fig. 4 shows the effect of adding potassium to the nutrient side of the epithelium which causes the locus to assume a more semicircular shape. In addition, the two dispersion regions have merged and are no longer clearly distinguishable.

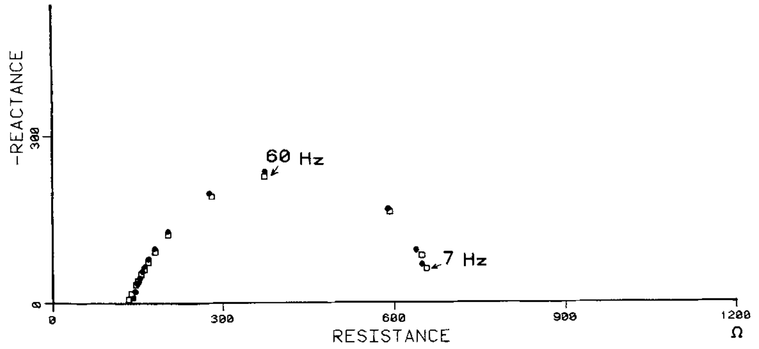

Fig. 4: Impedance locus when potassium replaces sodium on the nutrient side. The squares are experimental values and points represent the fit of a double RC-network.

This effect of potassium is also shown in the form of a Bode plot (Fig. 5) where the curves are calculated from the parameters of the above fit to the data.

Table I summarizes the results of 4 different experiments. The shape of the loci showed some variation which accounts for the scatter in the parameters obtained by the fitting procedure. However, the addition of potassium shifted the parameters in consistent directions in all experiments. A notable change, for instance, is the decrease in capacitance on the secretory side which was also noted by Rehm et al. (7). Using the model consisting of two lossy dielectrics one could conclude from this that the presence of potassium causes a considerable descrease of the area of the secretory side.

However, we suggest an alternative interpretation in terms of a fixed distributed capacitance which produces a shift in the lumped capacitance [calculated from Eq. (1)] when the membrane conductance is changed.

Table I

	R_{nut} Ω-cm^2	C_{nut} μF/cm^2	α_{nut}	R_{sec} Ω-cm^2	C_{sec} μF/cm^2	α_{sec}
Normal	270±64	1.2±0.2	0.93±0.05	220±160	10±8	0.84±0.19
K^+	51±22	1.6±0.6	0.86±0.06	290±210	1.3±0.31	0.99±0.02

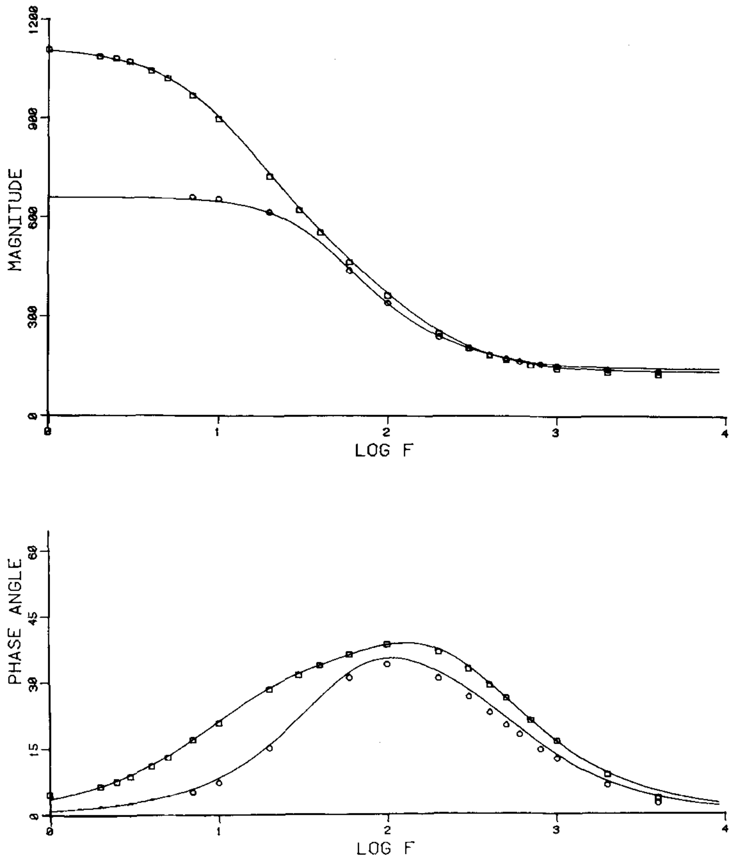

Fig. 5: Bode plot of magnitude (a) and phase angle (b) of impedance in normal (□) and potassium substituted (o). Data are from same experiments as in Fig. 3, 4. Solid lines are the best fit of double RC-network.

MODEL

The model is based on the assumption that there are conductive pathways in the gastric mucosa which behave electrically as transmission cables (9). These could be due to paracellular condition, for instance, or due to conductance via the gastric pits (ducts).

Fig. 6 shows an example of the latter situation where the current can pass through the surface membrane and across the walls of the gastric pits. The right part of the figure shows the electrical equivalent circuit.

The impedance of a gastric pit is given by the cable equation:

$$Z_c = \frac{\sqrt{z\,r'}}{\mathrm{tgh}\sqrt{\frac{r'}{z}}\;l} \qquad (2)$$

where l is the length of the pit, r the core resistance per unit length of the pit (ohm/m) and where z is the wall impedance for a unit length.

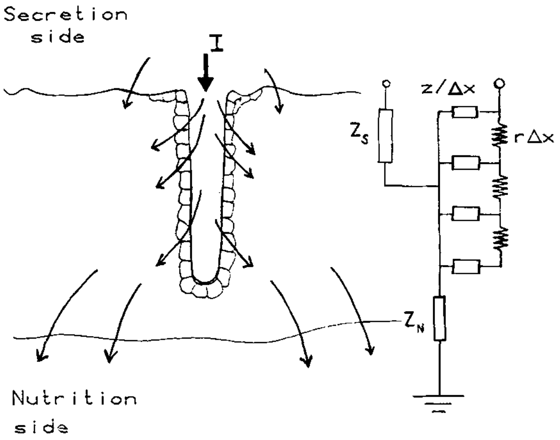

Fig. 6: Conductive pathways through the gastric mucosa and the corresponding equivalent circuit.

Eq. (2) is plotted in Fig. 7a for different values of the ratio between the wall and core resistances. The capacitance obtained by fitting Eq. (1) to each plot in Fig. 7a is shown in Fig. 7b. It is seen that as the DC-resistance decreases by a factor of 2.5 the lumped capacitance decreases by a factor of 4, and this has not involved any area changes. Also note that a uniform cable impedance gives rise to two dispersion regions in the locus.

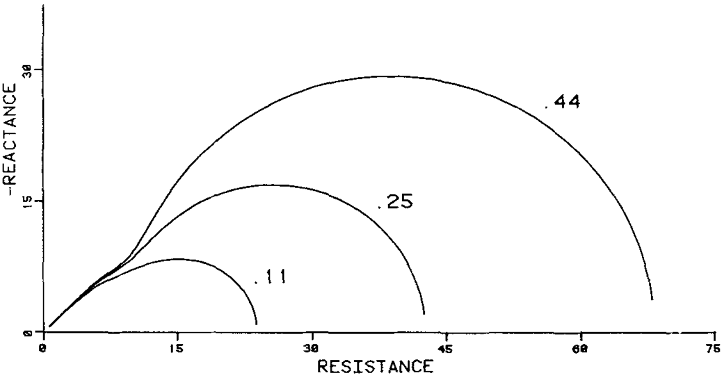

Fig. 7a: Impedance loci calculated from Eq. (2), where z is given by $z = \frac{R_m}{4(1+j\omega\tau)}$ ($\omega\tau$ is varied from 10^{-2} to 10^{2}). The factor determining the shape of two locus, R_m/rl^2, is indicated for each locus in the figure. The scaling factor is determined by the product rl and is arbitrarily set at 190.

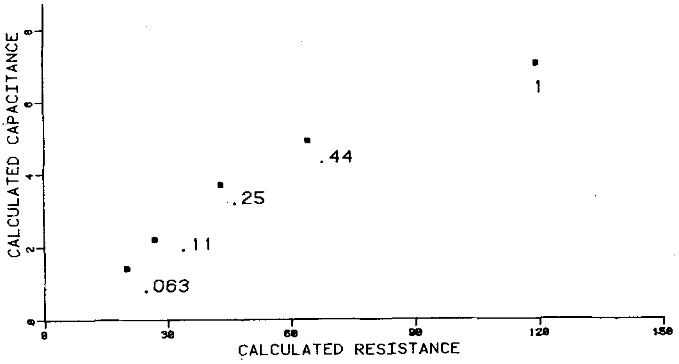

Fig. 7b: The capacitance calculated by fitting Eq. (1) to the loci in Fig. 7b are plotted against the corresponding DC-resistances.

Since the cable properties provide a possible explanation of the Teorell-Wersäll effect on the basis of changes in membrane permeability rather than area changes, we have carried out a fit to the model shown in Fig. 6 to the experimental data. The total impedance Z_T is given by:

$$Z_T = Z_N + (Z_S^{-1} + Z_C^{-1})^{-1} \qquad (3)$$

where Z_N and Z_S, the impedances of the nutrient and secretory membranes respectively, are given by simple RC-impedances [i.e. Eq. (1), setting $\alpha=1$).

Figs. 8 and 9 show a best fit of the model to the data of Figs. 3, 4 and 5.

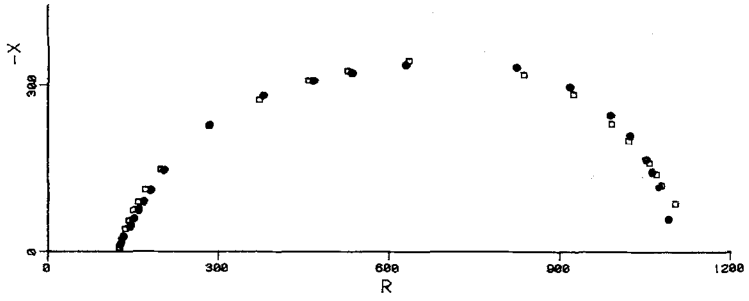

Fig. 8b: Impedance locus with same experimental values as in Fig. 3. The squares are experimental and the points are obtained by fitting the cable model to the data.

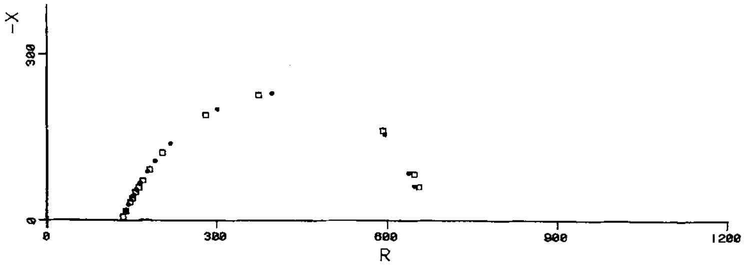

Fig. 8b: Fit of cable model to impedance locus in the presence of potassium.

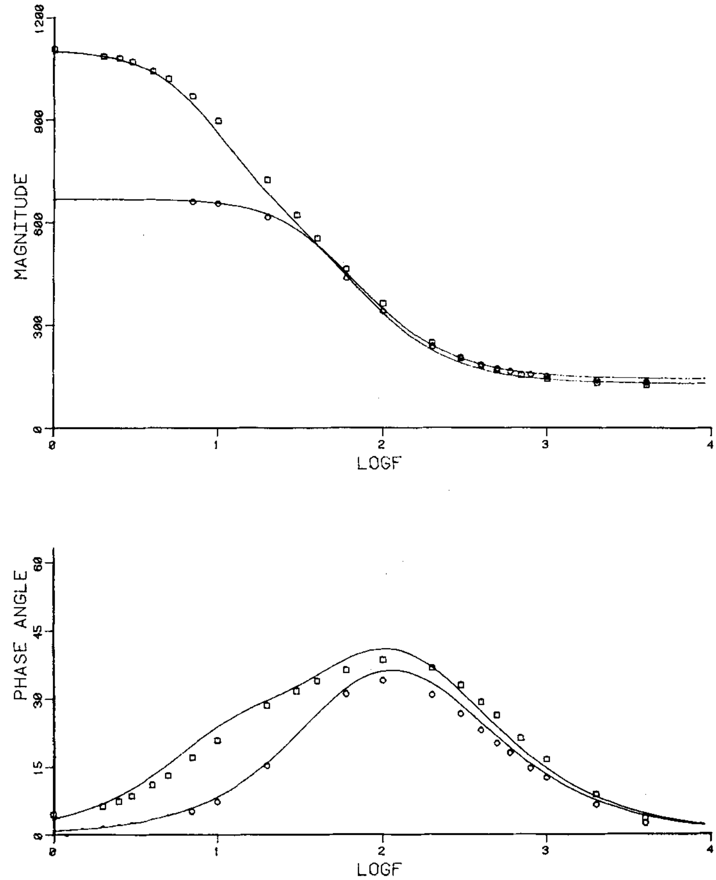

Fig. 9: Bode plot with same experimental data as in Figs. 3 and 4. The lines are theoretical curves obtained by fitting the cable model to the data, (□= normal, o=potassium).

DISCUSSION

It has been suggested by Rehm and Tarvin (8) that the large changes in capitance are associated with changes in surface area.

For example, during active acid secretion, the surface area may be effectively increased by a factor of 50-100 due to morphological changes in the parietal cells of the gastric musoca. However, since potassium is thought to increase gastric secretion on would expect the capacitance of the secretory side to increase and which is contrary to observations.

From the best fit of the data shown in Figs. 8 and 9 we can extract a set of morphological and functional parameters from the model. If we set the radius of the gastric pits to about 5 μm and the resistivity of the extracellular fluid to 100 ohm-cm then we obtain a value of 200 μm for the length of the pits, an average distance between pits of 50 μm and a value of 80 for the membrane folding in the pits (i.e. the ratio between the true surface area and the "cylindrical" area of the pit). By assuming that all membrane capacitances have the same value of 1 $\mu F/cm^2$ we calculate for the resistance of the nutrient membrane a value of 3 $kohm\text{-}cm^2$ and the tubular and surface resistances 15 $kohm\text{-}cm^2$ and 330 $kohm\text{-}cm^2$ respectively. The latter two resistances decreased by a factor of 5 (all other parameters unaltered) when potassium was added.

ACKNOWLEDGEMENTS

We thank dr. G. Flemström for valuable technical advice.

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Received 80 10 17

Address for reprint requests:

John Sandblom
Department of Physiology and Medical Biophysics,
Biomedicum,
Box 572,
S-751 23 Uppsala, Sweden