DIELECTRIC PARAMETERS OF HUMAN BLOOD SERUM IN THE RANGE 1–30 Mc/s*

V. A. Konovalenko and V. A. Yamshanov

Petrov Research Institute of Oncology, Leningrad

The dielectric properties of blood serum in the frequency range 1–30 Mc/s are chiefly deter-mined by the salts present in it. The contribution of the proteins to the complex dielectric constant (c.d.c.) of blood serum may be found on lowering the concentration of the salts to 0·01 N. The "Sel'kov–Balygin phenomenon" in this frequency range within the limits of ex-perimental error is not found. On study of solutions with high ionic strength in the frequency range considered by us in some cases an important role may be played by polarization phe-nomena.

ONE of the ways of studying biological specimens is to investigate their dielectric para-meters. A number of studies have been published concerned with the dielectric properties of blood serum. Thus, it was found that as a result of heating the serum for 30 min at $t = 56°$ its dielectric parameters change [1]. The greatest changes were observed in normal humans. In patients they are less. There is a correlation between the value of change in the dielectric parameters and the character of the illness. This observation provided the basis of a method of diagnosing a number of diseases including malignant tumours [1–4]. Unfortunately, it is not quite clear from the published work at which frequency the measurements were made and secondly, which parameters were deter-mined.

The measurements of complex dielectric constant of human blood serum over the range 100–500 Mc/s are described in [5]. Changes were observed in the real part of the complex dielectric constant on thermal treatment of the serum of normal donors. But in the blood of cancer patients this was not observed. The value of the effect observed in the serum of healthy donors rose with fall in the working frequency. At a frequency of 200 Mc/s it was from 1·5 to 4·5 per cent.

We carried out measurement of the complex dielectric constant (c.d.c.) of water, solutions of NaCl, the serum of healthy (and in some cases also sick) persons and the serum of animals over the range 1–30 Mc/s. The aim of the work was to study the effect of heating on the dielectric parameters of the blood serum and also to elucidate the contribution of the c.d.c. of the salts dissolved in it.

The measurements were made with an E-10-2 bridge intended for investigating the total conductivity of various specimens. In working out the technique we abandoned the "non-contact" method of measurement recommended by a number of authors.

The point is that the calculated formulae using this method in the case of our test objects in the given frequency range have a very complex form. Work by this method in addition requires a large number of calibration measurements. All this makes the non-contact method very laborious. We applied the contact method which in this case is considerably simpler. A special check showed that the non-contact and contact methods give practically the same results.

The test object was in a cuvette of special design thermostatted at 20°. To exclude the chemical influence of the material of the cuvette on the test fluids the electrodes were made of polished tantalum and the shell of teflon. The design of the cuvette was intended to ensure inhomogeneity of the field in the volume of the sample of not more than 10^{-3}. Allowance for the inductance of the ring of the cuvette together with the inductance of the co-axial–plug transition of the instrument was based on the formulae given in the description of the instrument.

$$g_x = g_0(1 - \omega^2 L C_x)^2,$$

$$C_x = (C_0 + g_x^2 L)\left[1 - \omega^2 L (C_0 + g_x^2 L)\right],$$

where g_x, C_x—true values of conductivity and capacitance; g_0, C_0—measured values; L—total inductance equal to $4 \cdot 7 \times 10^{-8}$ H; ω—frequency.

Since the analytical solution of the set of these equations is difficult it was solved graphically for each individual case by means of a set of previously calculated parametric curves. The error of the measurement of total conductivity was 3 per cent and the error of the graphic calculation was 3 per cent for the reactive and 1 per cent for the active component. This graphic method of calculation was used both for checking the pick-up detector and during the measurements.

The first step in our work was experiments in order to elucidate the working characteristics of the pick-up. It was necessary for us to measure the working and parasitic capacitances of the cuvette, its inductance and also to establish the effect of the polarization phenomena on the results of the measurement.

The pick-up was checked with binary mixtures of dioxane–water and solutions of NaCl of varied concentration.

A number of authors have shown that in study of dielectrics with high ionic conductivity one is bound to run into polarization phenomena due to the presence of free charge carriers [6, 7]. The presence of polarization phenomena is manifest in practice in an increase in the measurable capacitance of the test fluid. The value of the capacitance due to polarization phenomena depends on many factors including the concentration of ions, the working frequency and the material of the electrode.

In our conditions there were two factors the consequence of which might be increase in the role of polarization phenomena. Firstly, there was the high content of the salts in the blood serum. Secondly, increase in the role of polarization phenomena is also promoted by the properties of the electrode material. A cuvette with electrodes of polished tantalum with a potential of several volts possesses practically zero conductivity with direct current. The absence of electrolysis due to this promotes the maintenance

of high concentrations of ions in the near-electrode zones. Thus, the electrodes of polished tantalum ensure minimum influence on the specimen but at the same time increase the contribution of the polarization phenomena.

To make an experimental study of the role of polarization phenomena in our conditions we measured the total conductivity of the cuvette with solutions of NaCl of different concentrations. The results obtained are presented in Fig. 1. They may be
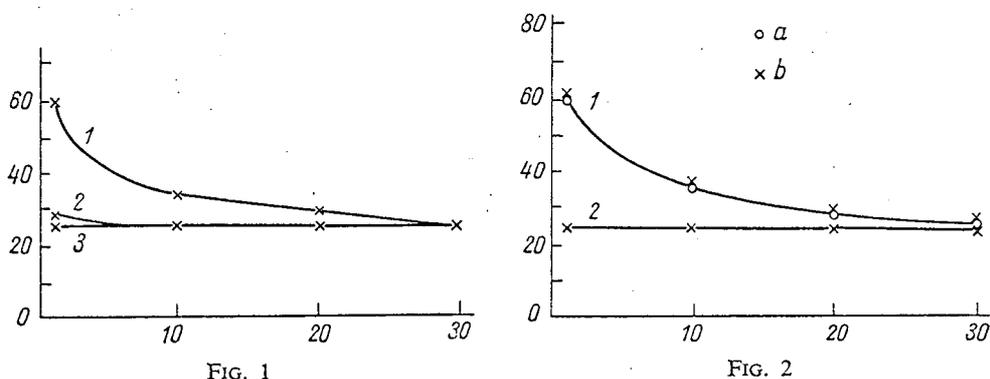
FIG. 1.

FIG. 2.

FIG. 1. Dependence of capacitance of solutions of NaCl on frequency: 1—0.1 N NaCl ($\kappa = 9.8$ mmho × × cm^{-1}); 2—0.05 N NaCl ($\kappa = 4.8$ mmho·cm^{-1}); 3—0.01 N NaCl ($\kappa = 1.08$ mmho·cm^{-1}). Abscissa — frequency Mc/s; ordinate — $C - C_0$, pF.

FIG. 2. Dependence of capacitance of solutions on frequency: 1—a—native blood serum, averaging over three samples ($\kappa = 10.1 \pm 0.2$ mmho·cm^{-1}); b—0.1 N NaCl; 2—distilled water. Abscissa and ordinate as in Fig. 1

interpreted as follows. According to the findings of Schwan aqueous solutions of salts must possess a dielectric constant close to that of water (up to frequencies of the order of 10^9 c/s) [8]. The permeability of water in this region remains constant. Consequently, the reactive components of the total conductivity need not depend on frequency. Such results were obtained by us for water and solutions of NaCl of low (0.01N) concentration. In these cases the polarization phenomena did not influence the results of the measurement. With increase in the concentration the frequency dependence of the capacitance of the sample became increasingly important (it first appeared at low frequencies). Finally, for 0.1 N solution of NaCl this dependence was already observed over the whole range. The active component of conductivity remained independent of frequency for all the solutions studied. The frequency dependence of the capacitance of the sample over our frequency range may consequently be explained only by polarization phenomena.

Thus, in studying specimens with high concentrations of salts in condition ensuring the minimum chemical and electrochemical action on the specimen it is necessary to reckon with polarization phenomena at frequencies up to 30 Mc/s.

As is known, the concentration of salts in the blood serum is equivalent to a concentration ~ 0.15 N. From the above-outlined experimental findings it is clear that already at a concentration in water of 0.1 N over the whole frequency range studied by us well marked phenomena are observed due to the dissolved salt. Consequently, it may be

expected that in measurements of the c.d.c. of serum the role of the salts must be considerable. To elucidate the contribution to the c.d.c. of the salts present in the serum and the proteins we compared the dielectric properties of the serum and solutions of NaCl. We measured the active and reactive components of the conductivity of the native serum from three healthy donors, from one cancer patient and from preserved horse serum. The values obtained for the various samples of serum of the healthy persons, the patient and the horse were practically indistinguishable (the deviations did not go beyond the error of measurement). The results obtained were compared with the corresponding data for aqueous solutions of NaCl of different concentrations. Figure 2 presents the measured values of capacitance for the serum, 0·1 N NaCl and water. Over the entire range studied the values of the reactive conductivity from which we calculated the value of the real part of c.d.c. of native serum completely concurred with this parameter for 0·1 N NaCl.

From the comparisons made we may conclude that the real part of the c.d.c. of blood serum is practically completely determined by the salts dissolved in it.

The values of the active conductivity of the blood serum and 0·1 N solution NaCl remained constant over the entire frequency range and coincided. This indicates that the imaginary component of c.d.c. of blood serum is also due to the salts present in it.

The next series of experiments was concerned with the conditions in which it is possible to detect dielectric parameters of serum proteins over the frequency range considered. For this purpose the samples of serum available were dialysed against solutions of NaCl of different concentrations. It was found that the minimum permissible concentration of NaCl in solution is 0·01 N. Further fall in the concentration of the salt led to partial denaturing and then to coagulation of the serum globulins. Therefore, in subsequent experiments we worked with serum samples dialysed against 0·01 N solution of NaCl. The measurements showed that the reactive component of total conductivity of these samples (corresponding to the real part of the c.d.c.) like the corresponding parameter for 0·01 N solution of NaCl does not depend on the frequency and coincides in value with the reactive conductivity of water. This indicates that the polarization phenomena in the serum with such a concentration of salts are negligibly small.

Quite different behaviour is shown by the active conductivity of the samples of serum studied. As can be seen in Fig. 3 it considerably exceeds the active conductivity of 0·01 N NaCl at all frequencies. This excess can be due only to the proteins present in solution. As shown by our measurements, the active losses in water over the frequency range used are practically undetectable. The solution of 0·01 N NaCl has the same specific conductivity at all frequencies over our range (Fig. 3). Consequently, the observed frequency dependence of the active conductivity of the dialysed blood serum can also be explained only by the presence in the solution of proteins.

In order to test the earlier assumption on the decisive role of the salts in c.d.c. of native serum the samples of serum dialysed against 0·01 N were subjected to "back dialysis" against physiological saline. The measurements then made of the parameters of the samples thus obtained showed that their dielectric properties coincided with those

of native serum. Thus, with fall in the concentration of salts in blood serum to a level of 0·01 N its dielectric parameters are determined in the main by proteins. This is confirmation of the conclusion drawn from the preceding series of experiments that the c.d.c. of native serum are determined in the main by the salts present in it.
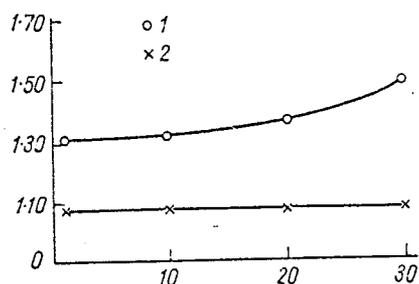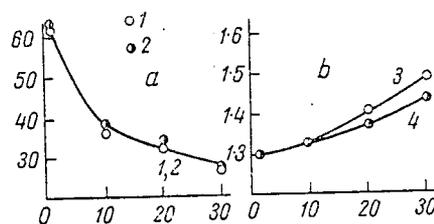

FIG. 3

FIG. 4

FIG. 3. Frequency dependence of specific conductivity: *1*—dialysed blood serum (against 0·01 N NaCl); *2*—0·01 N NaCl. Abscissa—frequency Mc/s; ordinate—conductivity, mmho·cm^{-1}.

FIG. 4. Effect of heating on dielectric parameters of blood serum: *a*—*1*—native serum; *2*—heated at 60°C for 30 min; *b*—*3*—native serum dialysed against 0·01 N NaCl; *4*—dialysed, heated. Abscissa—frequency Mc/s; ordinate—*a*—C–C$_0$, pF; *b*—conductivity, mmho·cm^{-1}.

The next task of our work was to elucidate the possibility of observing the Sel'kov and Balygin effect [1–4] in our frequency range. This phenomenon consists in change in the parameters of blood serum as a result of heating. We made a comparative study of c.d.c. of blood serum before and after 30 min heating at 60°C. Since in [1–4] the authors describe the maximum effect in the blood of healthy donors we also carried out the investigation chiefly on the serum of healthy humans. In our experiments we used the blood of three donors. In addition, we investigated the blood of one cancer patient. The results of the investigation of all samples were identical (see Fig. 4). Curves *1* and *2* respectively show the change in the reactive component of conductivity of native and heated sera. As can be seen from the Figure, the curves for heated and unheated serum almost completely coincided. The observed minor differences in the measured values do not go beyond the bounds of experimental error. The native and heated sera also do not differ in specific conductivity.

Thus, in the frequency range studied by us an "Sel'kov–Balygin effect" exceeding the experimental error could not be detected.

Figure 4 also presents the results of measurement of the parameters of the serum of a healthy person before and after heating dialysed and against 0·01 N NaCl. The curves *3* and *4* indicate the frequency dependence of the specific conductivity of the unheated and heated dialysed sera respectively. Although as indicated above, the contribution of protein to the c.d.c. of dialysed serum is quite considerable, above the experimental error, differences in the properties of unheated and heated sera of healthy donors could not be detected. The blood sera of cancer patients in our frequency range do not differ from those of healthy persons.

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BIOPHYSICS OF COMPLEX SYSTEMS. MATHEMATICAL MODELS

PROBLEM OF DYNAMIC MODELLING OF MICROBIOLOGICAL PRODUCTION PROCESSES*

YA. KOZHESHNIK

Czechoslovakian Academy of Sciences, Prague

The mathematical principles of modelling microbiological processes are outlined in the systems: biomass–substrate–inhibitor; examples are given of analysis of the models with use of analogue computer devices.

I. INTRODUCTION

THE problem concerns the design of mathematical models of systems in which together with a large number of molecules of different chemical substances the reaction involves the biomass, the cells of which multiply, grow and die.

The meaning of such models is that of verifying the hypotheses underlying the models or verifying the phenomena which appear to be phenomenologically probable. Work of this kind has already appeared in the literature [1–4]. Characteristic of the present time is the appearance of the practical need to investigate the interaction of the biomass and the surrounding medium; the consequence of this interrelationship is the arrest of growth or conversely, the growth of the biomass, the appearance of some substances and the consumption of others as a result of biochemical processes.

For the initial and final stages of the reactions when the number of microorganisms is small, it may be necessary to use stochastic models; in other cases the processes may be described by differential equations (dynamic models).