

Dielectric properties of glucose solutions in the millimetre-wave range and control of glucose content in blood

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Abstract

The measurement of the dielectric properties of sugar solutions, as well as blood imitators and blood, in the millimetre-wave range allows one to obtain valuable information on the possibility of real-time control of glucose concentration in blood. These measurements are also of interest for other applications, for example, in wine industry and for the determination of water content in oil, oil products and other liquids.

Keywords: dielectrics, solutions, blood, skin, millimetre, waves

(Some figures in this article are in colour only in the electronic version)

1. Introduction

To determine the complex permittivity, i.e. ε' and ε'' , of a medium by noninvasive methods, one has to measure two parameters of the reflected electromagnetic wave. Usually (see, for example, [1]), one employs sophisticated and expensive vector network analysers and measures the modulus, $|r|^2$, and phase, φ , of the reflection coefficient, $R^* = |r|^2 \exp(i\varphi)$ ($|r|^2$ is the power reflection coefficient and $i = \sqrt{-1}$). However, the measurement of the phase of the reflection coefficient is a rather difficult problem, and the measurement error amounts to $\pm 5\%$. For this reason, common measurement techniques cannot be applied to the noninvasive determination of small concentrations of glucose in water. In the present study, we use a sufficiently simple scheme for determining ε' and ε'' of a medium, which consists in measuring the modulus, $|r_{\min}|^2 = R_{\min}$, and the frequency, f_{\min} , of a millimetre (MM) wave (f_{\min} corresponds to the minimum of the reflection coefficient R_{\min}) reflected from the following structure: a plane-parallel matching plate made of a low-loss dielectric—a medium under measurement with high losses. We developed computer programs to calculate the dielectric properties of the medium under test using the measured $|r_{\min}|^2$ and f_{\min} as well as the relevant experimental setups.

2. Measurement method

To determine the real ε' and imaginary ε'' parts of the complex permittivity of a medium under test, we used a simple scheme that consists in measuring the modulus, $|r_{\min}|^2 = R_{\min}$, and the frequency, f_{\min} , of MM waves that correspond to the minimum of the reflection coefficient from the following structure: a plane-parallel matching plate made of a low-loss dielectric—a medium under test with high losses (water, solutions, blood and human skin).

Figure 1 shows the power reflection coefficients of two media (e.g., a reference medium (water) and water with $\chi\%$ of glucose) against the frequency of the incident MM wave. In figure 1, $R_{\min,0}$ and $f_{\min,0}$ represent the minimal power reflection coefficient and the corresponding frequency of the reference medium (pure water), respectively. When $\chi\%$ of glucose is added to the reference medium, one can see that the power reflection coefficient and the corresponding frequency are changed from $R_{\min,0}$ and $f_{\min,0}$ to $R_{\min,\chi}$ and $f_{\min,\chi}$, respectively. We can calculate $\varepsilon'_{m,\chi}$ and $\varepsilon''_{m,\chi}$ using $R_{\min,\chi}$ and $f_{\min,\chi}$ and the well-known expression (1) for the reflection coefficient r^* from such a structure [2]:

$$r^* = \frac{\left(\frac{1-n_p^*}{1+n_p^*}\right) + \left(\frac{n_p^*-n_m^*}{n_p^*+n_m^*}\right) \exp[2i\beta^*l_p]}{1 + \left(\frac{1-n_p^*}{1+n_p^*}\right) \left(\frac{n_p^*-n_m^*}{n_p^*+n_m^*}\right) \exp[2i\beta^*l_p]} \quad (1)$$

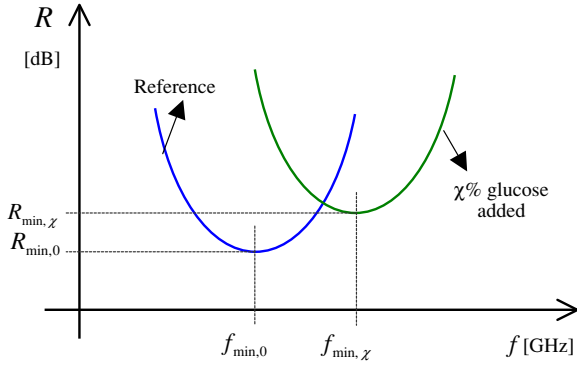


Figure 1. The power reflection coefficients of two media (a reference medium and a medium with $\chi\%$ of glucose) versus the frequency of the incident MM wave.

Here, n_m^* is the complex refractive index of the medium under test and n_p^* and l_p are the complex refractive index and the thickness of the plane-parallel matching plate, respectively. ε' and ε'' are related to n and k by the formulae

$$\varepsilon' = n^2 + \kappa^2, \quad \varepsilon'' = 2n\kappa. \quad (2)$$

β^* is the propagation constant given by

$$\beta^* = \frac{2\pi}{\lambda_0} n_p^* = \frac{2\pi f}{c} n_p^* = \frac{2\pi f}{c} (n_p + i\kappa_p). \quad (3)$$

Here, λ_0 and c are the free-space wavelength and the speed of light in free space, respectively. If the reflection coefficient in equation (1) is 0 at a given frequency $f_{\min,0}$, the thickness, l_p , and the refractive index, n_p , of the plane-parallel matching plate must be

$$n_p = \left(n_m + \frac{\kappa_m^2}{n_m - 1} \right)^{1/2} \quad (4)$$

$$l_p = \frac{(2s + 1) \cdot c}{4n_p f_{\min,0}} - \arctan \left(\frac{2n_p \kappa_m}{n_m^2 + \kappa_m^2 - n_p^2} \right) \frac{c}{4\pi n_p f_{\min,0}}. \quad (5)$$

Here, s is an integer, $s = 0, 1, 2, \dots$

Two types of measurement methods have been developed for the frequency range from 30 to 100 GHz. The first one is a waveguide method (WM), in which a plane-parallel matching plate is inserted into a single-mode rectangular waveguide with H_{10} mode. The second is a quasi-optical method (QM), in which a plane-parallel plate is placed between a horn and the media under test. For the plates available, $|r_{\min,0}^*|^2$ for the structures with pure water was measured to be less than -20 dB. The values of ε'_w and ε''_w for pure water that are needed for calculation were borrowed from [3].

3. Experimental setup and measurement of solutions

The measuring setup based on SWR and attenuation panoramic meters is shown in figure 2. Using the setup shown in figure 2, we measured the properties of glucose solutions in water and blood imitators (physiological solution: 0.9% NaCl in water) in the millimetre wave band for small glucose concentrations

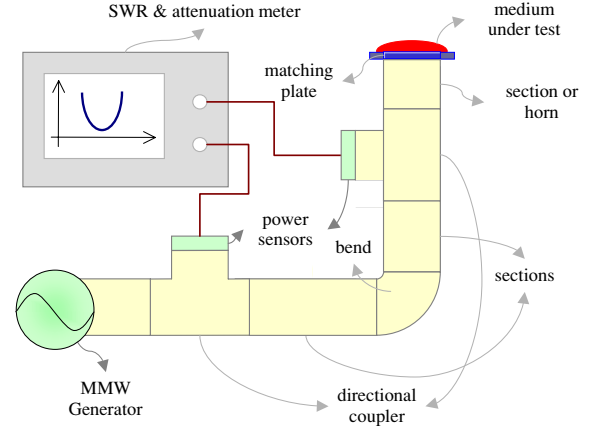


Figure 2. Schematic diagram of the experimental setup.

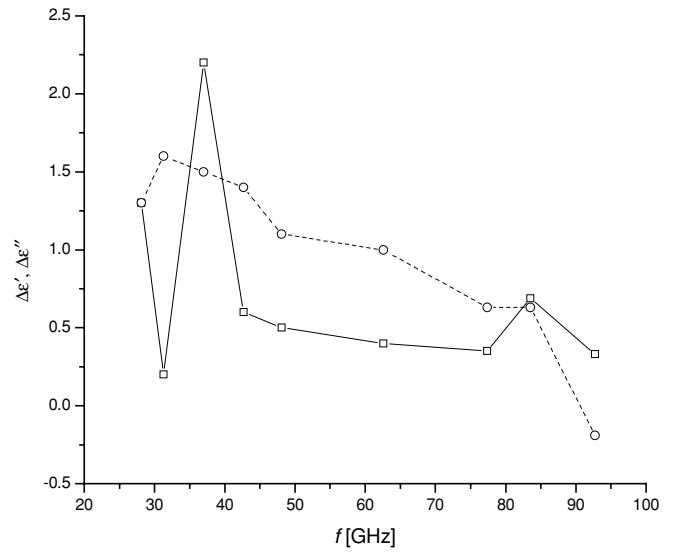


Figure 3. Difference between the permittivity of water and 3 wt% glucose solution in water as a function of frequency; $\Delta\varepsilon' = \varepsilon'_w - \varepsilon'_{3\%}$ is the difference between the real parts of the permittivity (solid line) and $\Delta\varepsilon'' = \varepsilon''_w - \varepsilon''_{3\%}$ is the difference between the imaginary parts of the permittivity (dashed line).

W ranging from 5 to 0.25 weight% (wt%). The setup was a standard scalar network analyser with standard waveguide components for appropriate frequency bands. This setup enables one to measure the reflection coefficient R_{\min} and the frequency f_{\min} with error of 0.2 dB and .01 GHz, respectively. Some results obtained from the measurements carried out in the frequency range from 28 to 93 GHz are represented in figures 3 and 4. These figures show the differences between the permittivity of water, ε'_w and ε''_w (figure 3), and of physiological solution, ε'_{ph} and ε''_{ph} (figure 4), and a 3 wt% glucose solution in water and in physiological solution, $\varepsilon'_{3\%}$, respectively; the solid and dashed curves refer to the real and imaginary parts of permittivity, respectively.

Our measurements have shown that the values of ε'_w and ε''_w are in good agreement with the results of [3, 7]. For comparison, the measurements of the dielectric permittivity of physiological solution and glucose in physiological solution carried out in [5] at frequencies from 35 to 38 GHz give for $W = 3\%$ wt. values ranging from -1 to 2 (1.5 ± 0.5) for

Table 1. Variation of blood parameters with time (measured at a frequency of 42 GHz).

N	Hb (g l ⁻¹)	T ₁ ; t = 32–34 °C				T ₁ + 40 min; t = 36 °C				T ₁ + 120 min; t = 36–37 °C			
		W (mmol l ⁻¹)	Ch (mg)	R (dB)	f (GHz)	W (mmol l ⁻¹)	Ch (mg)	R (dB)	f (GHz)	W (mmol l ⁻¹)	Ch (mg)	R (dB)	f (GHz)
1	150	3.9	253	37.4	42.71	6.1	247	39.6	42.74	3.9	253	38.2	42.75
2	142	3.6	332	37.9	42.77	4.3	309	40.5	42.73	3.9	295	38.8	42.75
3	136	3.7	268	39.1	42.74	4.4	265	39.5	42.74	3.6	244	<40	42.77
4	140	3.7	367	39.0	42.74	5.3	355	39.6	42.74	3.9	346	39.6	42.74

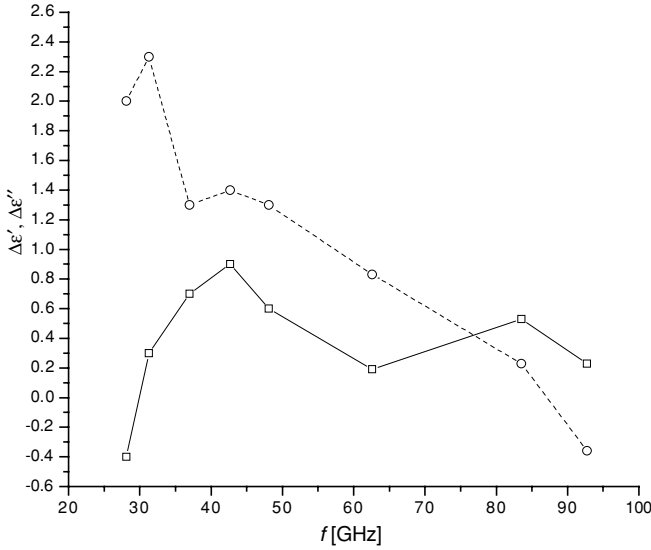


Figure 4. Difference between the permittivity of physiological solution and of 3 wt% glucose in physiological solution as a function of frequency; $\Delta\epsilon' = \epsilon'_{\text{ph}} - \epsilon'_{3\%}$ is the difference between the real parts of the permittivity (solid line) and $\Delta\epsilon'' = \epsilon''_{\text{ph}} - \epsilon''_{3\%}$ is the difference between the imaginary parts of the permittivity (dashed line).

$\Delta\epsilon' = \epsilon'_{\text{w}} - \epsilon'_{3\%}$ and from +0.7 to 1.5 (1.1 ± 0.4) for $\Delta\epsilon'' = \epsilon''_{\text{w}} - \epsilon''_{3\%}$. The main conclusions of our measurements are as follows.

- (1) The dielectric properties of glucose solutions in water and in a solution of NaCl in water are measured for the first time in a wide range of frequencies from 10 to 93 GHz for glucose concentrations of $W \leq 5$ wt%.
- (2) It is established that, for frequencies below 80 GHz, the values of ϵ' and ϵ'' for 0.9% NaCl are less than those for water. In the frequency interval from 80 to 93 GHz, the difference between these values substantially decreases and becomes comparable with the absolute error of measurement $\Delta\epsilon'$ and $\Delta\epsilon''$, which is on the order of 0.1.
- (3) Depending on the glucose concentration W in water up to $W = 5\%$, one observes a decrease in ϵ' and ϵ'' in the entire range of frequencies except for frequencies of 92–93 GHz, where the values of ϵ'' slightly increase with W .
- (4) Note that the studies of glucose concentrations in physiological solutions carried out by Japanese scientists [4, 5] in the frequency range 30–40 GHz showed that the values of ϵ' increase with the glucose concentration, in contrast to our results, whereas the values of ϵ'' decrease,

like in our experiments. The measurements carried out in [4] and [5] showed different behaviour in the frequency dependence of ϵ' . These facts can be attributed to the significant error in measuring the phase by a vector network analyser, which amounts to at least 5%.

- (5) The maximum sensitivity (change the minimal power reflection coefficient) of the method for measuring ϵ' and ϵ'' to the glucose concentration was observed in long part of millimetre wave range and was about 2.2 dB/0.5 wt% in water and 0.9 dB/0.2 wt% in a physiological solution. The extrapolation of these results allows us to suggest that a sensitivity of about 0.1 dB/0.04 wt%, i.e. of about 2 mmol l^{-1} , can be attained with the plates available.
- (6) Note that the general behaviour of $\Delta\epsilon''$ as a function of frequency (figure 3) for a 3 wt% glucose solution in water agrees with the results of [6] (figure 8 in [6]), which were obtained by molecular dynamics simulation. In [6], the total absorption in a glucose solution in the MM-wave region results from the contributions of the absorption by the molecules of the first solvation shell (S1), i.e. the molecules having at least one polyhedral face in common with solute, glucose molecules (G) and bulk water (B). The latter two contributions are characterized by a maximum of ϵ'' at higher frequencies than absorption in bulk water; it is this fact that is responsible for the decrease of $\Delta\epsilon''$ with increasing frequency in figure 3. As regards the variation of $\Delta\epsilon'$ in the frequency range 28–37 GHz by more than ± 1 , this fact can be attributed to the superposition of the above-mentioned absorption regions S1 and G; the behaviour of $\Delta\epsilon'$ in this frequency interval looks like a strongly damped resonance, which requires additional investigation.

4. Investigation of blood

These experiments were carried out in a thermostatically controlled chamber when a drop of blood taken immediately from the fingertip of a test person was placed on a matching plate. The measurements were carried out with a waveguide of cross section $5.2 \times 2.6 \text{ mm}^2$ (operating frequencies 41–42 GHz), which was completely covered by a drop of blood. Typical results of one of experiments in a thermostatically controlled chamber carried out with four persons are shown in table 1.

Here, W is the content of glucose in mmol l^{-1} , Ch is the content of cholesterol in mg, Hb is the content of haemoglobin in g l^{-1} and T_1 is the moment of time when persons 1–4 took 50 g of glucose on an empty stomach. This table shows that the reflection coefficient (R , -dB) increases for all four persons in 40 min after taking glucose, when the content of glucose

Table 2. Variation of blood parameters with time (measured at a frequency of 66 GHz).

N	T_1				$T_1 + 20$ min				$T_1 + 60$ min				$T_1 + 80$ min			
	W (mmol l ⁻¹)	R (dB)	f (GHz)	t (°C)	W (mmol l ⁻¹)	R (dB)	f (GHz)	t (°C)	W (mmol l ⁻¹)	R (dB)	f (GHz)	t (°C)	W (mmol l ⁻¹)	R (dB)	f (GHz)	t (°C)
2	5.9	27.2	66.35	36.0	6.6	27.8	66.34	36.5	6.1	27.6	66.30	37.0	4.9	27.8	66.22	38.0
3	4.8	27.6	66.37	36.5	6.3	27.8	66.32	36.5	4.3	26.7	66.29	37.0	3.9	27.6	66.22	36.0
4	6.1	28.8	66.31	36.0	7.2	29.9	66.29	36.5	6.6	28.0	66.25	37.0	5.1	28.8	66.22	36.0

in blood increases. Later, in 120 min after taking glucose, when the glucose content in blood decreases to values close to those measured at the moment T_1 , persons 1 and 2 show a considerable increase in R , whereas persons 3 and 4 do not show such an increase in R . In all the cases, the resonance frequency f of the reflection minimum is changed slightly. Thus, in all four test persons, an increase in the glucose content between T_1 and $T_1 + 40$ min is detected by millimetre waves. However, the situation is not so definite as the glucose content W decreases. Persons 1 and 2 clearly show a decrease in R , whereas, in person 4, R remains virtually unchanged and, in person 3, R is less than -40 dB, i.e. it cannot be precisely measured against the background of noise.

Thus, the data of table 1 show the following.

- (1) The dependence of R on W has an individual character; however, all persons show a decrease in R after taking glucose.
- (2) The inverse process of decreasing W , which is recorded by the variation of R , is not so clearly pronounced. This fact can be attributed to the physiological processes that take place in blood as the glucose concentration decreases.
- (3) There is no obvious effect of haemoglobin (which was constant during the measurements).
- (4) The content of cholesterol may be responsible for the difference between the functions $R(W)$ measured as W decreases or increases.

Using the data of table 1 together with the parameters of the matching plate and the values of R and f for water ($R = 25.2$ dB and $f = 42.93$ GHz at temperature close to the temperature of a human body), we determined ϵ' and ϵ'' of blood. It follows from the measurements that $\epsilon' = 18.1 \pm 0.2$ and $\epsilon'' = 23.8 \pm 0.2$, i.e. the difference between ϵ' and ϵ'' for different persons is small. Note that the data on ϵ' and ϵ'' of blood (not *in vivo*) that are available in the only publication [8] (which were measured at 25 °C: $\epsilon' = 13 \pm 3$ and $\epsilon'' = 20 \pm 3$) are in agreement with our data when temperature corrections are introduced by an analogy with the temperature dependence of ϵ' and ϵ'' of water. Note that persons with greater Hb (persons 1 and 2) have slightly greater values of ϵ'' . It is important that, for the maximal range of values of R amounting to 3 dB, we had small variation in permittivity. This fact points to the high sensitivity of the method developed and used in the project for measuring ϵ' and ϵ'' of blood by measuring the minimal reflection coefficient R from a matching plate.

We also carried out experiments with a new matching plate on persons 2, 3 and 4 at a frequency of about 66 GHz. The new plate guaranteed R_{\min} of about $-(27-30)$ dB for measurements of blood in a thermostatically controlled chamber at temperatures 36–37 °C. The measurements were carried out on an empty stomach and after taking 4–5

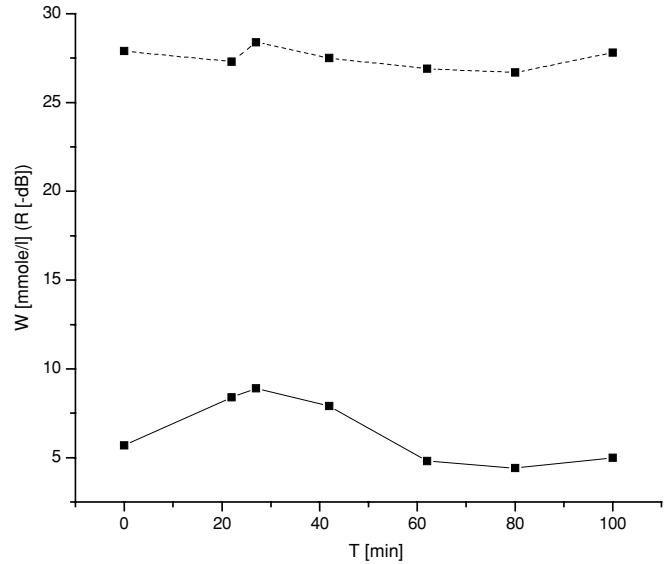


Figure 5. Correlation between variations in the glucose concentration in blood W (solid line) and the reflection coefficient R (dashed line) as a function of time elapsed since a test person took 4–5 teaspoonfuls of sugar.

teaspoonfuls of sugar. The results of these measurements are shown in table 2.

The basic conclusions are as follows.

- (1) There is a difference between the values of blood parameters for different test persons.
- (2) The sensitivity to the glucose concentration at 66 GHz is lower than that at 42 GHz, although the resonance minima R_{\min} differ insignificantly.
- (3) There is a clear correlation between R_{\min} and W as W increases, as well as a correlation between R_{\min} and W at $T_1 + 60$ min as W decreases.
- (4) At $T_1 + 80$ min, the dependence of R_{\min} on W is reversed on all test persons as W decreases. Note that the frequency f_{\min} always decreases during the measurements; the greatest variation (of 0.03–0.08 GHz) is observed during the last 20 min in all test persons. This fact requires additional medico-biological investigations.

We carried out a repeated experiment with person 2 at a frequency of 66 GHz. The results of this experiment are presented in figure 5.

This figure shows a clear correlation between W measured by a glucometer and R_{\min} at all points except for $T_1 + 27$ min. To find possible sources of error, we performed three successive measurements of W and R_{\min} at 11:19, 11:31 and 11:38 a.m. respectively on an empty stomach. We obtained the following values of W and R_{\min} : $W = 5.6, 5.7$ and 5.7 mmol l⁻¹, and $R_{\min} = 28.1, 27.6$ and 27.9 dB at $f = 66.31,$

Table 3. Correlation between W and R_{\min} .

T_1			$T_1 + 27 \text{ min}$			$T_1 + 90 \text{ min}$		
W	R (dB)	f (GHz)	W	R (dB)	f (GHz)	W	R (dB)	f (GHz)
5.4	28.9	66.29	8.4	29.9	66.25	4.4	28.6	66.22

Table 4. Variation of blood parameters with time.

ΔT (min)	R (dB)	f (GHz)	W_1
0	28.0	66.35	5.7
2	29.8	66.31	5.7
3	32.3	66.28	5.7

66.30 and 66.29 GHz, respectively. The results of another experiment with person 2 are presented in table 3. In this case, the first drop of blood was removed from the fingertip, the second drop was placed on a strip of a glucometer and the third was placed on the measurement plate.

Table 3 again shows a correlation between W and R_{\min} . The data of table 3 are in good agreement with those of figure 5 at appropriate time points.

In addition, we investigated the effect of the time delay ΔT between the moment when a drop of blood taken from a fingertip is placed on the measurement plate and the moment when the parameters R_{\min} and f_{\min} are measured. The investigations have shown a substantial variation in the parameters of blood within 1–3 min at a fixed temperature. This result is illustrated in table 4.

If we recall that similar parameters for water at the same temperature (37.5 °C) are $R_{\min} = 18.4$ dB and $f_{\min} = 66.42$ GHz, we can see that the processes that occur in blood (possibly, the coagulation of blood) are such that the values of R_{\min} and f_{\min} of blood become more and more different from those of water. Therefore, one has to guarantee that the temperature and the time intervals between the moments when blood is taken from a fingertip and the values of R_{\min} and f_{\min} which are measured should be identical for all measurements and all test persons.

5. Investigation of skin

From the electro-dynamical point of view, skin and adjoining blood-filled tissues represent a much more complicated object of study than blood. Many authors (see, for example, [9]) pointed out that the parameters of skin, such as thickness, blood richness, sweat and moisture, depend on a test person, his age and a place on his body. Moreover, the blood richness and moisture depend on external factors such as temperature, humidity and illumination, and internal factors

such as physical and intellectual stresses and a general state of health. Therefore, at the first stage, we measured R_{\min} and f_{\min} for different parts of body at different frequencies. As was expected, fingertips, palms, wrists, forearms and earlobes have substantially different values of the reflection coefficient. When we used the matching plates that guaranteed a deep minimum R_{\min} for water and blood, the maximum reflection R_{\min} (the minimal value of $|R_{\min}|$) was attained on fingertips and palms. The best matching was achieved on earlobes and forearms. Therefore, further measurements of R_{\min} were carried out on forearms. Just as in [10], where the measurements were carried out in the infrared band, for different persons we observed different values of R_{\min} and f_{\min} at equal values of glucose concentration. We also found that the values of R_{\min} and f_{\min} depend on the pressure of the matching plate to the forearm and its position on the forearm. To minimize these effects, we carried out systematic measurements in the long-wavelength region of the millimetre-wave band, where, as is well known (see, for example, [9] and our skin data presented in table 5), the penetration depth of the wave $d \approx 1/\alpha$ (the skin depth) is maximal and, as a result, the wave interacts with the parts of body that are richer in blood.

Table 5 shows that ε' and ε'' monotonically decrease as frequency increases. The penetration depth d of the wave into the skin equals approximately $1/3\alpha$ and ranges from 0.7 mm for 30 GHz to 0.36 mm for 77 GHz at 36–37 °C. These values are close to those of water at the same temperature. The results of table 5 are obtained by averaging the results of more than 20 measurements at $W = 4\text{--}5 \text{ mmol l}^{-1}$. Note that these values of ε' at frequencies 30–40 GHz are in satisfactory agreement with the results of [9], whereas ε in our experiments is substantially greater than that in [9].

As for the measurements of R_{\min} and f_{\min} as a function of W , just as in the case of the measurements of blood at a frequency of 43 GHz, we observed a correlation between R_{\min} and W as W increased after taking glucose (sugar) on an empty stomach. At a frequency of about 60 GHz, a variation in R_{\min} was much smaller than that at 42 GHz, which is likely to be attributed to the smaller penetration depth d . Note that, in the afternoon (after 3–4 p.m.), a variation in R_{\min} for close values of W in a normal situation (without taking additional glucose) was much greater than that before the noon. This fact points to certain physiological changes in skin at the depth d that are associated with the vital functions of the organism such as movements, nourishment and tiredness, which were also pointed out in [10].

To reduce the effects of the position and the pressure of the matching plate and the above-mentioned physiological phenomena in a person, we carried out repeated measurements of R_{\min} in a modified setup. In this setup, the diameter of the

Table 5. Dielectric properties of skin.

f (GHz), $\tan \delta, \alpha$	$\tan \delta, \alpha$	$\tan \delta, \alpha$ (1 cm ⁻¹)	$\tan \delta, \alpha$	$\tan \delta, \alpha$ (1 cm)	$\tan \delta, \alpha$	$\tan \delta, \alpha$ (1 cm ⁻¹)	$\tan \delta, \alpha$	$\tan \delta, \alpha$ (1 cm ⁻¹)
Water: 37 °C	$\varepsilon = 34.05 + i34.3$	1.0 14.5	$\varepsilon = 23.1 + i30.5$	1.32 21.3	$\varepsilon = 13.87 + i23.29$	1.68 30.9	$\varepsilon = 11.7 + i20.7$	1.8 34.4
Skin	$\varepsilon = 13.0 + i34.2$	2.63 18.7	$\varepsilon = 10.6 + i23.5$	2.2 21.4	$\varepsilon = 7.86 + i12.7$	1.62 22.9	$\varepsilon = 7.6 + i10.3$	1.4 22.4

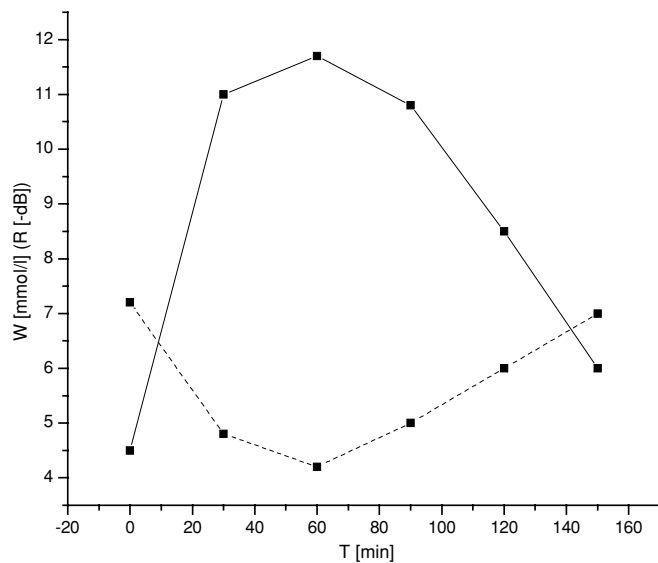


Figure 6. Same as in figure 5 measured on a modified setup.

contact area between skin and the measurement plate was increased to 35 mm to reduce the effect of the position of the plate on the skin, the measurements were fulfilled at a fixed frequency near 35 GHz, and the test person took only glucose and was at rest during the whole period of measurements. The results of one experiment are shown in figure 6.

Here, W is the glucose content measured by a standard invasive glucometer and R is the reflection coefficient measured by the MM setup. Figure 6 shows a clear correlation between the reflection coefficients R and W .

6. Conclusions

A new method has been applied to measure the dielectric properties of glucose solutions in water and in a blood imitator. The measurements have been carried out for the first time in the frequency range from 28 to 93 GHz for glucose concentrations W ranging from 5 to 0.5%. A sensitivity of up to 2.2 dB per 0.5 wt% of glucose concentration was realized. Extrapolation of these results shows that the sensitivity may be increased to 0.04 wt% (2 mmol l^{-1}). These results may serve a basis for the design of a laboratory or industrial equipment for controlling small concentrations of glucose (sugar) in water and in the physiological solution.

The dielectric properties of blood have been measured *in vivo* (without preservatives) for the first time with a sufficiently high degree of accuracy (the measurement accuracy of ϵ' and ϵ'' is ± 0.2) at frequencies of 42 and 66 GHz. The method developed in the project allows a real-time determination of glucose content in blood using a single drop of blood.

The reflectivity of skin on various parts of human body has been measured at frequency intervals from 30 to 80 GHz. It has been established that, for close values of W , fingertips, on one hand, and forearms and earlobes, on the other, have substantially different values of R_{\min} and f_{\min} . As for the noninvasive determination of the glucose concentration W , we have obtained a good correlation between W and the output MM-wave signal of a device that was in contact with skin in the case when W increases after taking glucose on an empty stomach.

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