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Comparison of Two Approaches to Measurement of Electrical Impedance of Glass Microelectrodes Designed for Evaluation of Temperature Changes in Biological Tissues

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Summary

We proposed a temperature sensitive microelectrode for rapid measurements of temperature at the cellular level. In principle, the electrical impedance of the tip of the microelectrode changes with temperature. We designed an impulse measurement system (STEP) sensitive to the above changes of impedance. The system is based on a presettable negative input impedance of the current to a voltage converter. We compared the efficiency of the new STEP with the currently used RAMP system. We found following advantages of the STEP system: i) the danger of high voltage oscillations which could mechanically destroy the microelectrode tip is eliminated; ii) this system provides the opportunity to set the maximum sensitivity of the system according to the measured temperature interval. Moreover, the STEP method makes it possible to measure the resistance by using a sinusoidal stimulation signal which has to be preliminarily compensated by a rectangular signal. The shortest sampling period of the new system represents 0.1 ms with a resolution higher than 0.1 K and sensitivity better than 30 mV/K.

Key words

Microelectrode – Temperature measurement – Electrical impedance measurement

Introduction

Biological tissue experiments dealing with the temperature on a cellular level which are done in the framework of living tissue research, require a microsensor of the temperature (further microelectrode) which has a negligible influence on the temperature regime of the investigated structure as well as of its temperature field. The dimensions of this microelectrode must be below the dimensions of cells and they should not influence the normal activity of the cells. A microelectrode having suitable dimensions with regard to the cellular temperature measurements was already described by Guilbeau *et al.* 1981. In principle, this microelectrode represents the Pt – Te thermocell, the active area of whitch has a diameter of approx. 1 μm. The sensitivity of the micrcelectrode is 300 μV/K approx., with resolution of 0.25 K (equivalent noise temperature). This microelectrode achieves the steady state in 50 ms. However, an overall deformation of the temperature field caused by the temperature conductivity of the above thermocell represents the main disadvantage of this microelectrode. This problem is solved by the microelectrode which was described in our previous paper (Dittert and Rech 1988). This microsensor is represented by a glass micropipette the tip of which is filled by a glass amorphous semiconductor, the $As_2TE_3Tl_{1.5}$. It has suitable mechanical, thermophysical and electronic properties (Dittert 1988). This temperature sensitive microelectrode (TSM) functionally resembles a miniature thermistor. The principle similar to the ion sensitive microelectrode the tip of which is filled by a specific ionexchanger is exploited in the above design of the temperature microsensor. The TSM does not change the temperature field of the measured object significantly because of the properties of the glass, (amorphous glass $As_2Te_3Tl_{1.5}$) and of water are similar in terms of thermophysics. The fast measurement of the temperature in range of 0.1 ms by using the TSM which represents a temperature-impedance converter, requires specific instrumentation capable of evaluating fast frequency independent part of the electrical impedance of TSM with the temperature resolution of at least 0.1 K. Moreover, the electrical current passing through the TSM should be of very low intensity (in the range of nA) to avoid an error due to warming up the semiconductor glass in the tip of the microelectrode. This was the reason, why the impulse measurement of the microelectrode impedance by using its response to a time linear stimulating signal (RAMP, Guld 1962), which is popular in electrophysiology, is not suitable here. Moreover, the RAMP method tends to instability and oscillations (due to the decrease of impedance). The oscillations could damage the TSM due to its excessive overheating. The above facts stimulated the development and hardware implementation of a new method for impulse measurement of the resistance of the TSM and thus the temperature which will not suffer from instability that may result in the destruction of the TSM.

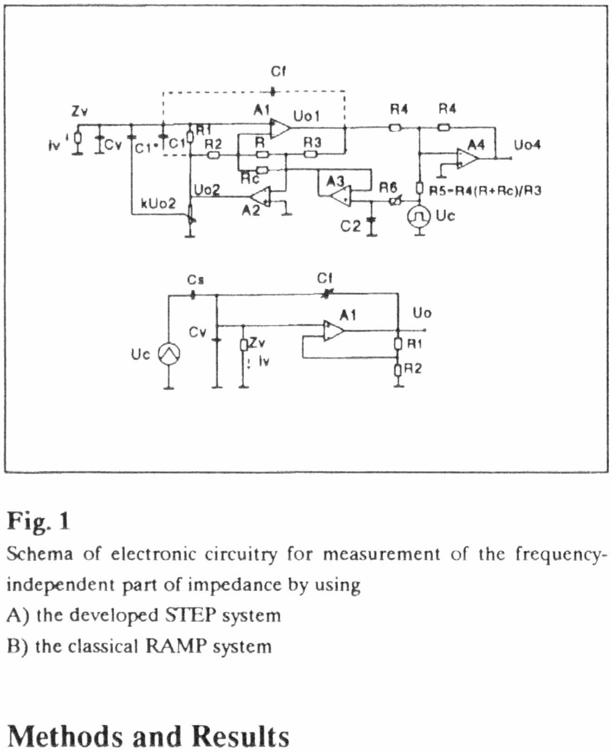

Fig. 1
Schema of electronic circuitry for measurement of the frequency-independent part of impedance by using
A) the developed STEP system
B) the classical RAMP system

Methods and Results

There exists an analytical formula in a closed form describing the impedance Z_v of a microelectrode tip with a linear profile (Dittert *et al.* 1988). In the frequency band up to 15 kHz, it is possible to describe the Laplace transform of the impedance Z_v of the TSM tip in a simple form as follows:

$$Z_v = R_v/(1+pR_vcx) \quad (1)$$

$$\text{where } R_v = 1/\sigma\pi\, r_0\, \mathrm{tg}\Phi\ [\Omega] \quad (2)$$

remains unchanged for the frequency independent part of impedance (1) which is being measured.
r_0 [m] ... radius of the tip of the TSM microelectrode
Φ [grad] ... cone of the tip
c [F/m] ... elementary cross-capacitance of the microelectrode tip
x [m] ... depth of immersion of the TSM into the measured object
σ [$\Omega^{-1}m^{-1}$].. specific electrical conductivity of the semiconductor by which the tip of the TSM is filled.

As has already been mentioned, we applied the $As_2Te_3Tl_{1.5}$ as the semiconductor located in the TSM tip. The electrical conductivity of amorphous glasses could be described in a wide temperature range by an exponential form (Mott *et al.* 1971):

$$\sigma = \sigma_{310} \exp\{B\,[(1/310) - (1273+\Theta)]\}, \quad (3)$$

where
Θ [°C] represents the temperature of the measured object.
(we found $\sigma_{310} = 0.4\Omega^{-1}m^{-1}$ and B = 4270K).

The schema of the circuitry designed for impulse measurement of the frequency independent part of impedance Z_v by using a response to the voltage step U_c (STEP method), is shown in Fig. 1A. If the gain $K = R_3/R_2$ is >1, then the dynamics of the STEP method could be described by differential equations of the 2nd order the parameters of which, except for the measured impedance and the presettable elements of the operational net, are determined predominantly by the transfer characteristics of amplifier A_1. For the sake of comparison we also evaluated the popular RAMP method of impulse impedance measurements based on the response to the linear voltage U_c increasing with slope $U_c/\Delta t$. The schema of the RAMP system is given in Fig 1B. Equations describing both methods are in Table 1. The dynamics of both compared systems are well described by a 2nd order system, with damping of the value of which could be set prior to the measurement (through the $k.U_{o2}$ in case of the STEP method and by using C_f in case of the RAMP). The Laplace transform of the response of the STEP system has a dominant transfer zero, the position of which does not depend on conditions of the measurement. It is therefore possible to compensate this zero by using a simple filter, a low frequency pass, on the input of the amplifier A_3. If the conditions $T_1 = T_2$ (where $T_1 = C_T.R_1$ and T_1 is not $f(x,\Theta)$; $C_T = C_1 + k.C_{1^*}$; $T_2 = C_2.R_6$) are satisfied then the Laplace transform of the output responses of both systems are formally mutually equal and could be expressed in the following normalized form:

$$U_o(p) = U_{os}. \quad \omega_n^2/[p.(\omega_n^2 + 2\xi\omega_n.p + p^2)]$$

ω_n[s^{-1}] ... resonant frequency of the undamped system
ξ[\] ... relative (normalized) damping
U_{os}[V] ... steady state of the response which we measure

The following parameters of both methods were compared by using their mathematical model:

a) the differential sensitivity $\partial U_o/\partial\Theta$ [V/K] in the temperature range (10 – 40) °C;

b) the resolution of the measured temperature (noise temperature) according to the formula:

$$\delta = E_{no}/(\partial U_o/\partial\Theta)\ [K]$$

Table 1

Comparison of the methods STEP and RAMP

<table>
<tr><th>STEP</th><th>RAMP</th></tr>
<tr><td colspan="2">Steady state responses as read in the steady state</td></tr>
<tr><td>$U_{os} = U_{o4} = -U_c(R_3/(R+R_c))(R_{vo}/(R_v-R_{vo}))$

where Rv is the resistance of the TSM according to (2)

$R_{vo} = R(R_1/R_2)(R_c/(R+R_c))$, R_{vo} is

parameter chosen to obey the system stability condition $R_{vo} < R_{vmin}$
(at maximal temperature: $R_v = R_{vmin}$)</td><td>$U_{os} - U_o - U_c/\Delta t \cdot (K+1) \cdot R_v C_s$,

where R_v is the resistance of the TSM according to (2)

$K - R_1/R_2$ (gain)

U_c/Δ_t [V/s] slope of the voltage increasing</td></tr>
<tr><td colspan="2">sensitivity to temperature changes</td></tr>
<tr><td>$\partial U_{os}/\partial\Theta = (U_{o4}/(1-R_{vo}/R_v)).B/(273-\Theta)^2$</td><td>$\partial U_{os}/\partial\Theta = U_o.B/(273-\Theta)^2$</td></tr>
<tr><td colspan="2">el. current during measurements and system oscillations</td></tr>
<tr><td>$i_v - U_c R/(R+R_c).(1/(R_v-R_{vo}))$

$i_{vmax} = (U_{o1max}/R_v).(R/R_3) \approx 2nA$</td><td>$i_v - (U_c \cdot C_s)/\Delta t$

$i_{vmax} - 2(\Omega_n)/\pi) \cdot u_{o1max}\, c_f \approx 1\mu a$</td></tr>
<tr><td colspan="2">resulting temperature increasing of
the TSM tip due to system oscillations</td></tr>
<tr><td colspan="2">$t = (i_{vmax}/2\pi r_o)^2((1+2\ln P/\delta\lambda) \simeq 5.10^{12}\, i^2_{vmax}$,
where
λ [W/mK] .. temperature conductivity of amorphous glass
P [/] .. external/internal radius of the amorphous glass microtip</td></tr>
<tr><td>$\Delta T_{max} \approx 10^{-5}K$</td><td>$\Delta T_{max} \approx 10K$</td></tr>
</table>

c) the value of the relative damping ξ of the system as the function of the temperature and the depth of the TSM tip immersion into the measured tissue in the range 0-2 mm.

The geometry of the discussed mathematical model of the TSM was as follows: $r_0 = 0.2\,\mu m$, $\Phi = 2^o$. The measured temperature was related to the temperature value of 30 °C and to an immersed value of 1 mm. The experimental verification was done with a thermostated volume filled by galium.

Both systems were set up as to have:

1) the critical value of the relative damping ($\xi_o = 1$)

2) equal amplitudes of the steady state responses

3) the duration of the rising slope of the response equal to 35 μs in both cases, so that the error of the reading of the steady state response is less than 5 % if the signal is sampled with a delay of 0.1 ms (settling time).

Curves in Fig. 2A confirm that both the discussed methods of impulse measurement of the impedance give similar results when considering $U_0(\Theta)$, the steady state values of the resistance, i.e. temperature. The output signal of the RAMP method increases with decreasing temperature while the STEP method shows a reverse relation.

The sensitivity as a function of the temperature (see Fig. 2B) shows a similar trend for both methods, as in the previous case (Fig. 2A). However, by choosing suitable parameter values of the STEP system its temperature sensitivity could be elevated and thus a better resolution of the measured temperature (with unchanged noise level) could be achieved in the STEP system.

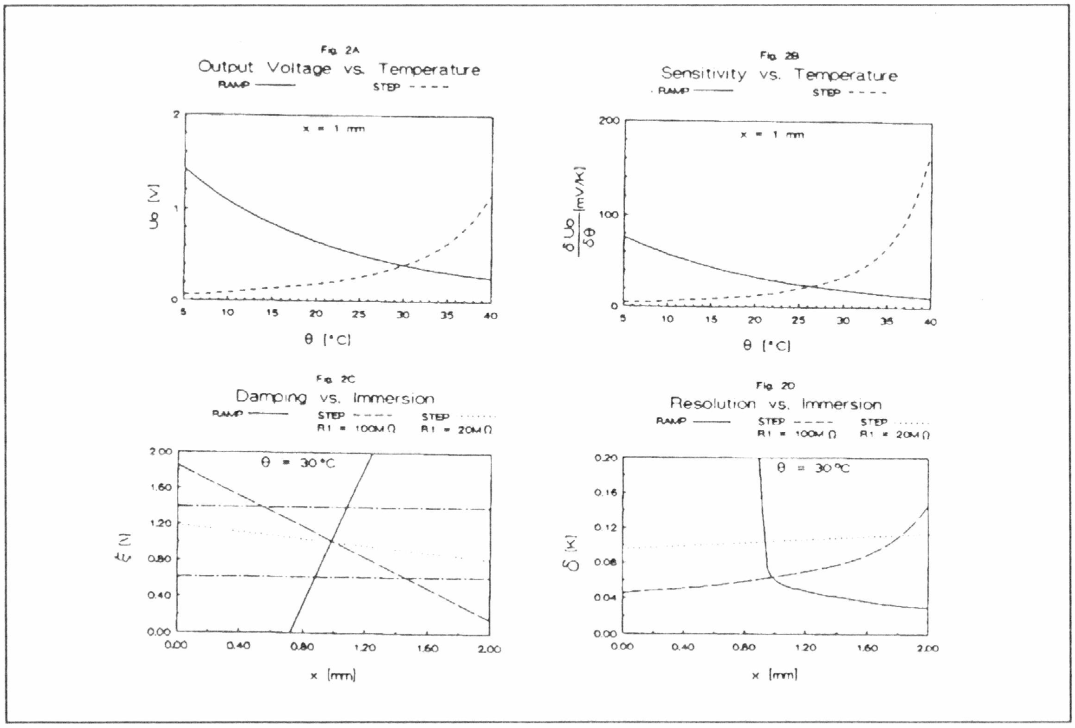

Fig. 2

Graphic comparison of parameters output of described measuring methods – A) graph of output voltage vs. temperature – B) graph of sensitivity vs. temperature – C) graph of damping vs. imersion – D) graph of resolution vs. immersion.

The critical value of the relative damping are shown by dashed lines at the level $n_{min} = 0.6$ and $n_{max} = 1.4$ (twice the value of the error of reading the U_O, i.e. 10 %).

The dynamic parameters change a little with changes of the measured temperature by both methods. The changes of dynamic parameters are more pronounced when expressed in terms of the damping of the measuring systems (Fig. 2C). The above dependence is more pronounced in the case of the RAMP method and it may result either in oscillations or in the high damping of the system. The former took place if the tip of the microelectrode is immersed less than 300 μm in the tissue and these oscillations could destroy the TSM because of the high value of the electrical current passing through its tip. The latter appears when the depth of the immersion increases in a small step. The resulting high damping of the system causes rather large error of measurements if the fixed intersampling time interval (0.1 ms) is exploited.

The relation between temperature resolution and the depth of immersion (Fig. 2D) is more linear in case of the STEP method when compared with the RAMP method.

Discussion

The dynamics of both systems are similar. However, the application of the STEP system is more convenient in practice when compared with the RAMP system. The STEP system stability and the optimal system adjustment with changes of the system parameters due to manipulation with the TSM are not critical.

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Reprint Requests

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