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# A STUDY OF MEMBRANE PERMEABILITY CHANGES DURING NERVE ACTION POTENTIAL BY MEANS OF COMPUTER SIMULATION

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**We wish to report a new method of analytical description of single nerve action potential suitable for computer simulation, with which we have beeu able to calculate the sodium and potassium permeability changes postulated by Hodgkin and Katz (1949).**

**Using the data from the paper by Oshima, Makimo and Kondo (1988) a new formula which describes the single nerve action potential for $Na^+$ and $K^+$ ions in nerve membrane was derived (Wrzeciono, Gorzelańczyk & Markiewicz-Wrzeciono, 1990):**

$$E_m(t) = 26\ mV \ln \left[ \frac{1 + \left(\frac{r-1}{r+1}\right) e^{-\alpha\xi(t)ft}}{1 - \left(\frac{r-1}{r+1}\right) e^{-\alpha\xi(t)ft}} \right]$$

**where $r = P_{Na^+}/P_{K^+}$, $f = [2r/(r^2-1)]\ln r$, $\alpha = P_{K^+}(1+r)A/V$, $E_m(t)$[mV] — siugle nerve action potential, $P_{Na^+}$[cm/s], $P_{K^+}$[cm/s]-absolute membrane permeability of $Na^+$ and $K^+$ ions, $A$ - membrane area, $V$ - considered volume, $\xi(t)$ - newly iutroduced parameter.**

**As starting data of our simulatiou program we used the experimental course of $E_{me}(t)$ for the single nerve actiou potential and approximate valnes for $r(t)$. By the simulation procedure an approximation error $\Delta E = |E_m(t) - E_{me}(t)|$ was minimized during each step until the decrease of total $\Delta E$ valne was less than $1.10^{-7} mV$ (Wrzeciono *et al.*, 1990).**

**On the basis of our simulation we obtained the exact numerical values of absolute membrane permeability $P_{Na^+}(t)$[cm/s] and $P_{K^+}(t)$[cm/s]. Our numerical results agreed with experimental data (Hodgkin & Katz, 1980).The numerical program preseuted was found useful to calculate $P_{Na^+}(t)$, $P_{K^+}(t)$ as a combinatiou of experimental $E_{me}(t)$ and modelling data.**

## INTRODUCTION

The fundamental unit of information transmitted from one part of the nervous system to another is a single action potential. The shape of each impulse is the same, with an amplitude of about 100 mV and a fixed duration of about a millisecond. As in most living cells, the interior of the axon is rich in potassium ions and poor in sodium ions and the body fluids outside the axon are rich in sodium ions and poor in potassium ions. Because of this unequal distribution of ions, together with the fact that the membrane, in its resting state, is much more permeable to potassium than to sodium ions,

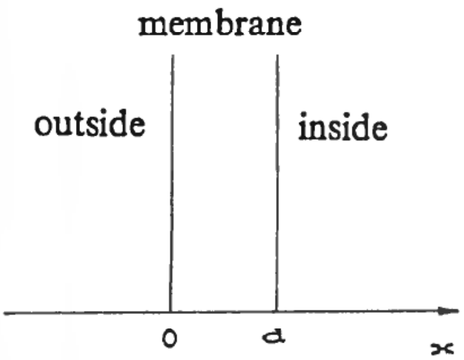


Fig. 1 A membrane of area $A$ ($10^{-4}$ $m^2$) and thickness $d$ separating two solution compartments — outside and inside of a neuron.

the nerve has a resting potential ranging from −60 to −70 mV, the inside being electrically negative with respect to the outside (Keynes, 1979).

This situation is diametrically changing during an action potential. This is a rapid alteration in membrane potential, which may last only about 1ms; during this time the membrane potential changes from −70 mV to +30 mV and then returns to its original value. During an action potential the permeability of the membrane to sodium and potassium is markedly altered. In the rising phase of the action potential, the membrane permeability to sodium ions undergoes a several hundred-fold increase and sodium ions rush into the cell. As the membrane becomes more positive inside, sodium inactivation causes the sodium permeability to decrease towards its resting value. However, the repolarisation process is speeded up by a simultaneous increase in potassium permeability which causes more potassium ions to move out of the cell. These two events, sodium inactivation and increased potassium permeability, allow potassium diffusion to regain predominance over sodium diffusion and the membrane potential rapidly returns to its resting level (Hodgkin & Huxley, 1952; Hodgkin, Huxley & Katz, 1952; Weidmann, 1951).

## THEORY

In our model the membrane separates two solutions having a distinct concentration of sodium and potassium ions. We have made the assumption about the absence of an external electric field under a quasi-steady state condition.

We have considered a quasi-steady flow of elecrolyte ions: sodium and potassium across a planar neural membrane of thickness $d$ and area $A$ separating two solution compartments: outside and inside of the neuron, the volumes of which are $V_1$ and $V_2$ respectively. We have taken the $x$-axis perpendicular to the membrane, its surfaces being placed at $x=0$ and $x=d$ (see Fig. 1).

In the present paper, membrane properties are described by the following parameters: $b_{K+}$ and $b_{Na+}$ which are the partitition coefficients of ions $K^+$ and $Na^+$ between the membrane and solution phases and $P_{K+}$ and $P_{Na+}$ which are the membrane permeabilities of potassium and sodium ions.

These parameters are given by the following formulas (Hodgkin & Katz, 1980; Oshima, Makimo & Kondo, 1980).

$$C_{oK+}(+0)=b_{K+}C_{oK+} \quad (1)$$

$$C_{oNa+}(+0)=b_{Na+}C_{oNa+} \quad (2)$$

and

$$C_{iK+}(d-0)=b_{K+}C_{iK+} \quad (3)$$

$$C_{iNa+}(d-0)=b_{Na+}C_{iNa+} \quad (4)$$

and

$$P_{K+} = \frac{RT}{Fd} u_{K+} b_{K+} \quad (5)$$

$$P_{Na+} = \frac{RT}{Fd} u_{Na+} b_{Na+} \quad (6)$$

where: $C_o$ and $C_1$ are respectively ion concentrations in solution outside and inside of the axon, $C_o(+0)$ and $C_1(d-0)$ are concentrations within the membrane, $R$ — gas constant, $F$ — Faraday constant, $u$ — mobility of ions, $T$ — temperature.

To describe the time-dependent nerve action potential we have used the formula given by Oshima, Makimo and Kondo (1988):

$$E_m(t) = \frac{kT}{ze} \ln \left| \frac{(1-\varphi)(1+r)+[r\varphi-(1-\varphi)]e^{-\alpha ft}}{(1-\varphi)(1+r)+[\varphi-r(1-\varphi)]e^{-\alpha ft}} \right| \quad (7)$$

where: $E_m(t)$ is time dependent membrane action potential, $k$ — Boltzman's constant, $T$ — the absolute temperature, $e$ — elementary elect-

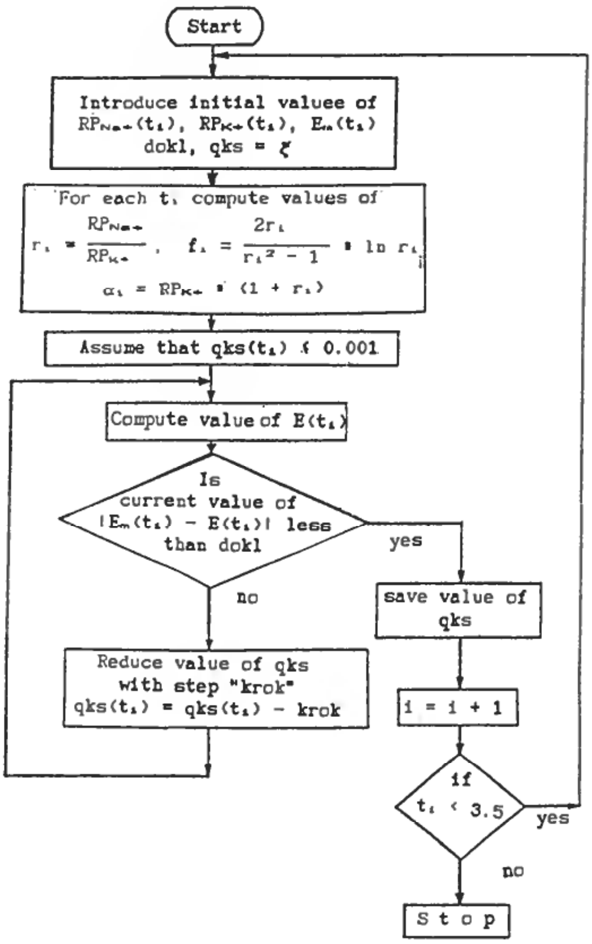


Fig. 2 Simplified flow diagram for the program organization where dokl-accurancy of numerical calculation and krok — the fixed calculation step.

ric charge, $t$ — time, and:

$$\varphi = \frac{V_2}{V_1 + V_2} \tag{8}$$

$$\alpha = P_{K+}\,(1+r)\frac{A}{V} \tag{9}$$

$$r = \frac{P_{Na+}}{P_{K+}} \tag{10}$$

$$f = \frac{2r}{r^2-1}\ln r \tag{11}$$

The formula (7) was derived with the assumption that $r = \frac{P_{Na+}}{P_{K+}}$ is constant and is not changing at the time (Oshima, *et al.*, 1988).

As is known, during the action potential the membrane permeabilities for sodium and potasium ions are changing. Therefore, we have modified the formula (7) taking the time dependent permeability changes into consideration. We have made the following assumptions:

$V_1 = V_2 = V = 10^{-6}\,\mathrm{m}^3$ (ass. 1)

$\varphi = 0{,}5$ (ass. 2)

$A = 10^{-4}\,\mathrm{m}^2$ (ass. 3)

$T = 300$ K (ass. 4)

and introduced a new parameter $\xi(t)$, which describes time dependent changes of the expres-

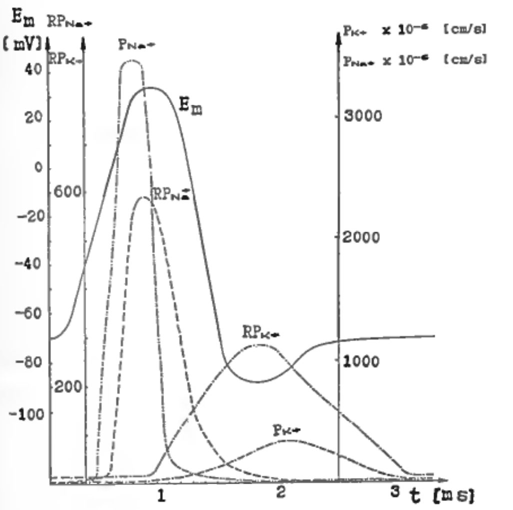


Fig. 3 Changes in absolute and relative sodium and potassium permability during action potential.
$RP_{Na+}$, $RP_{K+}$ — relative permeability (data)
$P_{Na+}$, $P_{K+}$ — absolute permability (results)
$E_{m}$ — membrane potential (data)

sion $\alpha\xi(t)/f$.

Taking into account all these assumptions we find:

$$E_m(t) = 26\,mV \ln \left[ \frac{1+\left(\frac{r-1}{r+1}\right)e^{-\alpha\xi(t)/t}}{1-\left(\frac{r-1}{r+1}\right)e^{-\alpha\xi(t)/t}} \right] \quad (12)$$

Flexibility and compactness of the formula (12) suggested for use in computer simulation of time-dependent nerve action potential.

## RESULTS AND DISCUSSION

Formula (12) describes a very complicated non-linear high-order function which is very difficult to disentangle.

In order to obtain numerical results, we have assumed an initial course of relative membrane permeabilities of $Na^+$ and $K^+$, respectively $RP_{Na+}(t)$ and $RP_{k+}(t)$, using the experimental data obtained by Hodgkin and Katz (3). We have used an experimental course of action potential of a Sepia fibre given by Weidmann (1951).

On the basis of the above data and assumptions and by means of the algorithm presented in Fig. 2 the program in Turbo Pascal 4.0 has been written on IBM Personal Computer .

It allowed us to find time courses of the absolute membrane permeabilities of $Na^+$ and $K^+$ ions, respectively $P_{Na+}(t)$[cm/s] and $P_{K+}(t)$[cm/s]. Fig.3 illustrates the obtained results.

An interpretation of the newly introduced parameter $\xi(t)$ may be presented:

$$\alpha\xi(t) = P_{K+}\left[1 + \frac{P_{Na+}}{P_{K+}}\right]\xi(t) \quad (13)$$

(see formulas 9 and 10 and ass. 1 and 3). After transformation we get

$$\alpha\xi(t) = (P_{K+} + P_{Na+})\xi(t) \quad (14)$$

So we can present $\xi(t)$ in the following way:

$$\alpha\xi(t) = P'_{K+}(t) + P'_{Na+}(t) \quad (15)$$

Therefore, the parameter $\xi(t)$ is exactly connected with the time course of $P_{K+}(t)$ and $P_{Na+}(t)$.

Formula (12) describes the relationship between $P_{Na+}(t)$, $P_{K+}(t)$ and $E_m(t)$ well, only when the value of the membrane potential for $t=0$ being:

$$E_m(t) = 26 \text{ mV} \ln r \quad (16)$$

would be used at the beginning of the computer simulation. For $t=0$ we obtain the resting potential.

For example, for resting potential $E_m(0) = -70$ mV an adequate value of $r$ should be calculated. We have found:

$$r = \frac{P_{Na+}}{P_{K+}} = \frac{1}{15}$$

This value may be accepted. It is comparable with Hodgkin and Katz's results (Hodgkin & Katz, 1949).

The magnitude of the membrane potential $E_m(t)$ tends to 0 as $t \to \infty$

$$\lim_{t\to\infty} E_m(t) = 0 \quad (17)$$

Therefore, formula (12) is valid only within a limited time span. The duration of an action potential is short enough to use the formula (12). We can calculate the value of the membrane potential for $t=2{,}9$ or $3{,}0$ ms after its return to fixed conditions. For the moment when membrane potential returns to its resting level we have got $P_{K+} = 1.7 \cdot 10^{-6}$ cm/s and

$P_{Na^+} = 0.1133 \cdot 10^{-6}$ cm/s. These numerical results correspond with experimental data given by Hodgkin and Huxley (1949).

Taking into account all the above considerations we can say that the formula (12) is adequate to describe a single time-dependent nerve action potential.

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