

POSSIBLE ROLE OF THE MOLECULAR CHARACTERISTICS OF THE SODIUM CHANNEL INACTIVATION SYSTEM IN IMPULSE CODING

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Abstract

The three-state, constant-dipole model of the Ranvier node sodium channels inactivation system helped reveal the fact that its two transitions were accompanied by constant changes in dipole moment equivalent to transferring a charge q_1 and q_2 through the entire potential drop across the membrane. These charges, being important characteristics of the gating system on a molecular level, may determine adaptational properties of the nodal membrane. A modified version of the Dodge-Hille model was used to predict a new mechanism of spike frequency adaptation. It was suggested that the effective charge distribution in the inactivation system might be a cause of different accommodative properties of motor and sensory fibres.

1. Introduction

Transmission of signals in the nervous system is accomplished by the discrete impulse code. The first element which converts generator current into impulse responses of the reflex arc afferent part is an electrically excitable membrane of the receptors. Within a wide range of receptor structures this coding function is provided by the Ranvier node membrane in sensory fibres while in motor fibres a proximal Ranvier node converting its impulse activity in accordance with the changes of synaptic current acts as an analog-digital converter. Conceptual results have been derived in earlier papers dealing with comparative studies of properties of motor and sensory fibres. Motor fibres in response to constant current were capable of producing short trains of impulses and sensory fibres responded to excitation by prolonged rhythmic activity (Erlanger and Blair, 1938).

Nerve impulses arise on electrically excitable membranes, a mathematical description of which was proposed by Hodgkin and Huxley (H-H) (Hodgkin and Huxley, 1952). They analyzed kinetics of ionic conductance responsible for generation of action potential by the squid giant axon membrane. Their model did not contain definite conclusions on molecular mechanisms underlying this process and left open

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such questions as whether ions cross the membrane through pores or by the way of forming complexes with carriers. Later Hodgkin and Keynes put forward the concept of the membrane ionic channel (Hodgkin and Keynes, 1955). A detailed molecular description of ionic channels is still not quite clear although in the last few years our picture on ionic channels has become clearer. An ionic channel is the macromolecular complex in which one part forms so-called gating mechanism controlled by the transmembrane potential difference while another part (a selectivity filter) controls passing the ions of definite dimensions through the membrane (for reviews see Hille, 1970; Khodorov, 1979; Kostyuk and Kryshal, 1981). The description of the operation of an electrically excitable membrane is based on important postulates of the ionic theory. One is that voltage-dependent gating systems have a two-state kinetics (Hodgkin and Huxley, 1952).

While considering the mechanism of accommodation Hodgkin and Huxley assumed that processes of activation of K channels and inactivation of Na channels were the basis of this phenomenon (Hodgkin and Huxley, 1952). Further studies confirmed this suggestion. The most pronounced accommodative properties of motor fibres (Schmidt and Stämpfli, 1964; Vallbo, 1964a; Bergman and Stämpfli, 1966) result from a higher inactivation level of Na channels (Frankenhaeuser and Vallbo, 1965; Vallbo, 1964b). On the other hand, the higher activation level of K channels observed in motor fibres compared with sensory fibres is reflected by sensitivity to tetraethylammonium (TEA) (Schmidt and Stämpfli, 1964; Bergman, Stämpfli, 1966) and the shift of the activation curve in a hyperpolarizing direction (Bretag and Stämpfli, 1975). Of interest is the fact that authors studying one of the aspects of the problem, for example, the difference of K membrane systems of motor and sensory fibres, came to the conclusion that special attention should be given to specificity of Na channels to explain the different responses of these two membrane types (Palty *et al.*, 1980; Dubois, 1982).

The present paper deals with the investigation of a model of the sodium channels *h*-system of the Ranvier node, the behavior of which does not depend on activation but is governed by the second order kinetics (Chiu, 1977). The model leads to relations between the thermodynamic characteristics of the inactivation system and the adaptation properties of an electrically excitable membrane.

2. Methods

For computations of rhythmic activity of the node of Ranvier a slightly modified (Hille, 1967) Dodge model (Dodge, 1963) for myelinated fibres of *Rana pipiens* was used. The fourth order Runge-Kutta method was employed to solve the system of differential equations involved. An integration step of 8×10^{-4} ms, ensured that the error of the method did not exceed 25 μ V. Computations were carried out in the Leningrad Research Computing Centre of the USSR Acad.Sci. on a BESM-6 computer with a FORTRAN program. Calculations which did not require a wide range of operations were performed in the computing centre of the Pavlov Institute of Physiology of the USSR Acad.Sci. on a Wang computer with a BASIC program.

3. Results and Discussion

As has been mentioned above, one of the major postulates of the H-H formalism is the assumption that gating mechanism of each ionic channel controlled by the potential can be described by the single-energy barrier model. As far as gating systems of ionic channels present a population of charged particles, not interacting with each other and moving in a thermodynamically closed system, then their behavior can be examined by the methods of statistical physics and chemical kinetics.

The rate of change of the sodium inactivation variable follows a first order kinetic process and be described by the equation

$$(1) \quad \frac{dh}{dt} = a_h(1-h) - \beta_h h$$

The rate constants a_h and β_h depend on the transmembrane potential difference, and at the "potential-dependent equilibrium", i.e. at $dh/dt=0$ we obtain the equality according to the Boltzmann distribution theory

$$(2) \quad \frac{\beta_h}{a_h} = \exp\left\{-\frac{qe(E-\bar{E})}{kT}\right\}$$

where q is the effective charge (Almers, 1978) in units of the electronic charge of each particle not interacting with one another and involved in the *h*-system, e is the absolute value of the electronic charge, E is the membrane potential difference (intracellular potential minus extracellular potential), k is the Boltzmann constant, T is the absolute temperature, \bar{E} is the potential at which charges of inactivation system particles are equally distributed between open and closed states.

As far as the a_h and β_h in the H-H type model based on the first order kinetics equations failed to be described by exponential functions (Hodgkin and Huxley, 1952; Dodge, 1963), the magnitude of an effective charge appears to be dependent in this case on the membrane potential difference (Chapman, 1980; Gnetov and Krylov, 1983). Physical interpretation of this fact leads one to assume either the presence of the nonlinear profile of potential within the membrane (Chapman, 1980) or to consider the picture on gating particles polarization (Hill and Chen, 1972; Stevens, 1978). In the first case we had to discard the constant field hypothesis (Goldman, 1943) underlying the membrane ionic theory while in the second case a physical meaning of possible decrease of the dipole moment at the intensified electrical field (for detail see, Almers, 1978) remains unclear. For the present, we ignore these complications and assume that the *h*-system has second order properties. Then we imagine a population of macromolecules which can exist in three states 1, 2 and 3, depending on the membrane potential,

$$(3) \quad 3 \frac{a_{32}}{a_{23}} 2 \frac{a_{21}}{a_{12}} 1$$

Let us assume that inactivation gates are open in the state 1 and the sodium channel is

able to pass ions provided that independently functioning activation gates of the channel are also open. The states 2 and 3 are closed (inactivated) states. Assuming further that rate constants are exponential functions of potential

$$(4) \quad a_{ij} = \exp(\alpha_{ij}E + \beta_{ij}).$$

where α_{ij} , β_{ij} are constants not dependent on E , $i, j = 1, 2, 3$. At equilibrium according to Eqn. (2) we obtain

$$(5) \quad \begin{aligned} a_{12}/a_{21} &= \exp\{-q_1(E - \bar{E}_{12})e/kT\}, \\ a_{23}/a_{32} &= \exp\{-q_2(E - \bar{E}_{23})e/kT\}, \end{aligned}$$

where q_1 is an effective charge transfer which accompanies the transition between open and closed states, q_2 that between two closed states, \bar{E}_{12} and \bar{E}_{23} are potentials at which $a_{12} = a_{21}$ and $a_{23} = a_{32}$, respectively.

From Eqn. (4) and Eqn. (5) follows

$$(6) \quad \begin{aligned} q_1 &= (a_{21} - a_{12})kT/e, \quad \bar{E}_{12} = (\beta_{21} - \beta_{12})/(a_{21} - a_{12}), \\ q_2 &= (a_{32} - a_{23})kT/e, \quad \bar{E}_{23} = (\beta_{32} - \beta_{23})/(a_{32} - a_{23}). \end{aligned}$$

The main usefulness of the relations (6) is that they permit one to turn from empirical kinetic constants (a_{ij} , β_{ij}) to the description of the h -system at the level of its molecular characteristics including the charges q_1 and q_2 , potentials \bar{E}_{ij} and energy profile. One of the more important consequences of the equations is that an effective charge transferred in the second order h -system does not depend on the potential.

Such an approach is in agreement with the theory of Rojas and Keynes (1970). They proposed describing gating processes by equations based on postulates of classic thermodynamics.

Chiu (1977) was the first to experimentally determine rate constants corresponding to the scheme (3), i.e. for the case where the membrane inactivation system of the node of Ranvier in *Rana pipiens* has the second order properties. The values of these rate constants (in ms^{-1}) for one of the nodes studied at 4.5°C assume the form

$$(7) \quad \begin{aligned} a_{12} &= \exp(0.05E + 1.0), \\ a_{21} &= \exp(-0.015E - 2.96), \\ a_{23} &= \exp(0.013E - 1.4), \\ a_{32} &= \exp(-0.102E - 11.9). \end{aligned}$$

This means according to Eqn. (6) that an effective charge equal to -1.56 is transferred at the transition between open and closed states while at transition between two closed states of the h -system the magnitudes q_2 is -2.75 . Thus, the major transfer of the charge in the sodium channel inactivation system in *Rana pipiens* occurs between closed states. The nodal inactivation system in *Xenopus laevis* is also governed by the second order kinetics (Kniffki *et al.*, 1981).

The voltage dependences of its rate constants can be given by the equations

$$(8) \quad \begin{aligned} a_{12} &= \exp(0.022E - 0.13) \\ a_{21} &= \exp(-0.092E - 6.463) \\ a_{23} &= \exp(0.019E - 1.45) \\ a_{32} &= \exp(-0.025E - 4.092) \end{aligned}$$

while effective charges are distributed vice versa:

$$q_1 = -2.75, \quad q_2 = -1.06.$$

Returning to the scheme (3) it should be noted that each transition is accompanied by a constant change in the dipole moment equivalent to transferring a charge q_i ($i = 1, 2$) through the entire potential drop across the membrane. Then, according to Eqn. (5) the fractional occupancy $h_{1\infty}$ of the conducting state 1 can be calculated as

$$(9) \quad \begin{aligned} h_{1\infty} &= \left(1 + \exp\left\{-\frac{q_1 e(E - \bar{E}_{12})}{kT}\right\}\right) \left[1 + \exp\left\{-\frac{q_2 e(E - \bar{E}_{23})}{kT}\right\}\right]^{-1} \\ &= \left(1 + \exp\left\{-\frac{q_1 eE + W_{12}}{kT}\right\}\right) \left[1 + \exp\left\{-\frac{q_2 eE + W_{23}}{kT}\right\}\right]^{-1} \end{aligned}$$

where,

$$(10) \quad \begin{aligned} W_{12} &= -\bar{E}_{12}q_1e = (\beta_{12} - \beta_{21})kT/e, \\ W_{23} &= -\bar{E}_{23}q_2e = (\beta_{23} - \beta_{32})kT/e, \end{aligned}$$

the meanings of which become evident by considering Fig. 1.

In Eqn. (9) the values

$$(11) \quad \begin{aligned} q_1 eE + W_{12} &= \epsilon_{12}, \\ q_2 eE + W_{23} &= \epsilon_{23} \end{aligned}$$

have dimensions of energy and in accordance with the model are equal to the free energy levels difference of the h -system at its transitions $1 \rightarrow 2$ and $2 \rightarrow 3$. Experimental data obtained for the nodal membrane of *Rana pipiens* (Chiu, 1977) as well as for the nerve fibre of *Xenopus laevis* (Kniffki *et al.*, 1981) permit us to present the voltage dependences of these quantities (Fig. 1A and Fig. 1B, respectively). Thus, if we let $E = 0$, then we get a proper energy profile of the h -system (Fig. 1, the inserts). In this case practically all gate particles would be in the state 3. At "switching on" of the field an energy profile is changed and redistribution of the particles occurs among states. Thus at the potentials

$$(12) \quad \begin{aligned} E = \bar{E}_{12} &= -W_{12}/q_1, \\ E = \bar{E}_{23} &= -W_{23}/q_2 \end{aligned}$$

relevant differences of the energy levels became equal to 0 (Fig. 1), which is equivalent to identical occupation of the latter ones. It is natural to require for normal

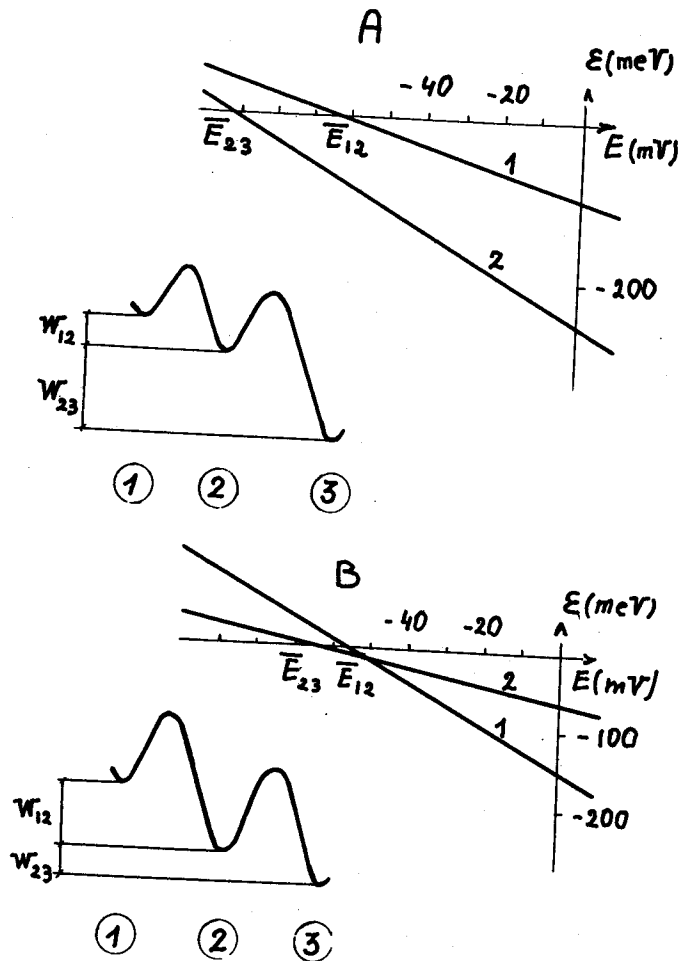


Fig. 1. Energy characteristics of the sodium channels inactivation system. Dependences were plotted using the data from Chiu (1977) for *Rana pipiens* (A) and from Kniffki *et al.* (1981) for *Xenopus laevis* (B).

1 — the dependence $\varepsilon_{12}(E)$ for the transition 1→2,

2 — the dependence $\varepsilon_{23}(E)$ for the transition 2→3 (Scheme (3)).

E_{12} and E_{23} are the potentials at which occupations of the corresponding levels of the *h*-system are equiprobable.

Inserts — Energy profiles of the inactivation systems. Membrane potential is 0 mV. $W_{12} = -95$ meV, $W_{23} = -251$ meV (A); $W_{12} = -153$ meV, $W_{23} = -64$ meV (B).

functioning of the *h*-system that magnitudes \bar{E}_{ij} fall within the physiological region of the potentials $-100\text{ mV} < \bar{E}_{ij} < 50\text{ mV}$. Only in this case will it be effectively controlled by potential. At the same time this requirement imposes limitations on the main parameters of the inactivation system, q_1 and W_{ij} (Eqn. (12)). For the node of Ranvier membrane of *Xenopus laevis* the potentials \bar{E}_{ij} are closely located (Fig. 1B) which may be interpreted as the "tuning" of the *h*-system for a certain local area of potentials. This assumption becomes more significant if we take into account that the critical potential of initiation of the node of Ranvier repetitive responses takes place at this area (55 ± 5 mV). The relation between these potentials for the nerve fibre membrane of *Rana pipiens* is quite different (Fig. 1A). \bar{E}_{12} and \bar{E}_{23} differ almost by 30 mV, and therefore the *h*-system of this fibre is controlled within a wider range of potentials so as to affect the shape of single action potential (see below).

At resting potential ($E = -75$ mV) the parameters involved in the relations (9) have definite values which can be easily found on the basis of experimental data (Chiu, 1977; Kniffki *et al.*, 1981). If all parameters except effective charge magnitudes are fixed, then the dependences $q_1 = f(q_2)$ can be obtained which allows one to estimate the level of freedom in the alteration of the latter ones and to understand the physical meaning of the relation of their magnitudes. Fig. 2 presents two dependences with fixed values of $h_{1\infty, 12}$, W_{23} , $E(E = -75$ mV) (Eqn. (9)). The resultant curves have the following common properties. At first, it should be emphasized that the

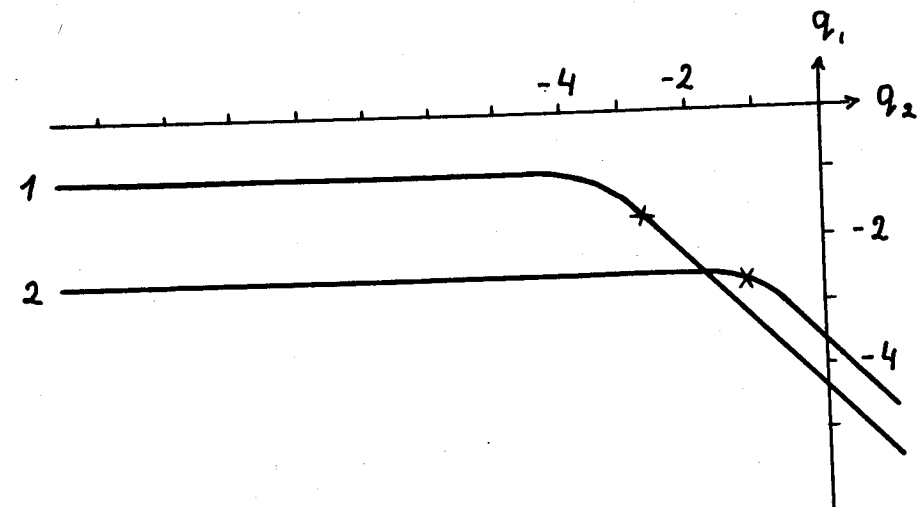


Fig. 2. Dependences between effective charge magnitudes of the inactivation system when the energy levels and the probability of its being in conducting state are fixed.

q_1 — an effective charge transferred at transition 1→2,

q_2 — an effective charge transferred at transition 2→3.

1 — the curve was plotted for the *Rana pipiens* membrane (Chiu, 1977).

2 — the curve was plotted for the *Xenopus laevis* membrane (Kniffki *et al.*, 1981).

Checks were calculated according to the Eqn. (6) effective charge magnitudes.

magnitude of the effective charge carried between open and closed states cannot be arbitrary: it is positively limited. Thus, for example, in order that the occupancy of the open state might compose 0.82 at resting potential (Fig. 2, curve 2, *Xenopus laevis*), q_1 should not be greater than -2.55 . Secondly, when q_1 reaches its boundary value, the magnitude becomes uncertain, and in fact ambiguous. Thus, in this case, when q_1 fits its boundary value within the accuracy of decimal per cent fractions, q_2 should be equal, for example, to -3 , -4 , etc. It should be emphasized here that the magnitudes q_1 and q_2 no doubt must be limited because a gate particle presents a real protein complex. Thirdly, the right branches of the curves under consideration have an interesting characteristic property: the sum of effective charge magnitudes is constant here. This, for example, means that rearrangement of q_1 and q_2 in the given region does not change the fractional occupancy of the conducting state. Furthermore, at the intersection of the ordinate axis and the theoretical curve there is a point $q_1 = q_1^*$, $q_2 = 0$, corresponding to the h -system in which the charge transfer does not occur between closed states. Such a formal treatment of these states permits us to regard this model as a single energy-barrier. For example, fractional occupancy of the conducting state ($h_{1\infty}$) at resting potential (-75 mV) is identical for the following two systems: $q_1 = -1.56$, $q_2 = -2.75$ and $q_1 = -4.31$ and $q_2 = 0$. The difference between them is probably established by the transition kinetics in the h -system. Finally, real values of effective charges calculated by Eqn. 6 are in non-linear regions of the considered curves (Fig. 2, checks). The reason why inactivation systems of the sodium channels "chose" magnitudes q_1 and q_2 located just in these regions remains unclear.

The only difference in the curves under investigation which in our opinion is of principal importance is that the main charge in the inactivation system of *Rana pipiens* is transferred between two inactivated states while in the h -system of *Xenopus laevis* the charge is transferred between the open and inactivated states. As has been mentioned above the estimated magnitudes of effective charges in the cases discussed come to: $q_1 = -1.56$, $q_2 = -2.75$ in *Rana pipiens* and $q_1 = -2.75$, $q_2 = 1.06$ in *Xenopus laevis*.

The peculiar distribution of charges in the sodium channels of the h -system of the node of Ranvier in *Rana pipiens* allows us to assume that in a given case generation of impulse activity may differ from excitable membrane responses in which according to the H-H model the whole charge is carried between the open and closed states. In other words, an additional closed state of the h -system may influence the ability of the electrical excitable membrane to generate both single action potential and trains of impulses.

In order to elucidate the possible physiological role in the impulse coding of more complex inactivation mechanism of the sodium channels, the Dodge model will be applied (Dodge, 1963). According to the scheme (3) the inactivation process can be described by the following linear differential equation system

$$(13) \quad \begin{aligned} dh_1/dt &= a_{12}h + a_{21}, h, \\ dh_2/dt &= a_{12}h_1 - (a_{23} + a_{21})h_2 + a_{32}h_3, \\ dh_3/dt &= a_{23}h_2 - a_{32}h_3, \end{aligned}$$

under the condition that $h_1 + h_2 + h_3 = 1$. Here, as in the previous schemes, a_{ij} are rate constants of transitions, h_1 corresponds to the fraction of inactivation particles in the conducting state 1, h_2, h_3 correspond to particles fractions in inactivated states 2 and 3. The solution of the equation system (13) in response to voltage step assume the form

$$(14) \quad h_i - h_{i\infty} = A_i \exp\{-t/\tau_h\} + B_i \exp\{-t/\tau_h^*\},$$

where A_i and B_i ($i = 1, 2, 3$) are the potential-dependent amplitude coefficients, $h_{i\infty}$ are the steady-state distributions. Just as the amplitude coefficients they are determined by the values of the rate constants

$$(15) \quad h_{1\infty} = a_{21}a_{32}/c_1, \quad h_{2\infty} = a_{12}a_{32}/c_1, \quad h_{3\infty} = a_{12}a_{23}/c_1,$$

$$\text{where} \quad c_1 = a_{21}a_{32} + a_{32}a_{12} + a_{23}a_{12}.$$

The time constants of the transition are given by the equations

$$(16) \quad \begin{aligned} \tau_h &= 2/(c_2 - \sqrt{c_2^2 - 4c_1}), \\ \tau_h^* &= 2/(c_2 + \sqrt{c_2^2 - 4c_1}), \end{aligned}$$

$$\text{where} \quad c_2 = a_{21} + a_{12} + a_{32} + a_{23}.$$

Thus, knowing the experimental values of the rate constants the behavior of the inactivation system can be reconstructed both under voltage clamp [Eqn. (14-16)] and at free conditions (Eqn. 13).

Fig. 3 shows the computed firing behavior for the case when the h -system has second order properties. Chiu's equations were taken to calculate the values of the rate constants (Chiu, 1977). The temperature coefficient Q_{10} was chosen as being equal to 2 (Kniffki *et al.*, 1981), so the maximum values of τ_h and τ_h^* will be approximately equal to 9 ms and 1 ms, respectively. The initial value of the variable h_1 is 0.82 which is necessary for the occurrence of rhythmic activity in the theoretical node. This means that $h_i - E$ curves are shifted by 20 mV in the depolarizing direction. The shifts change only potentials \bar{E}_{12} and \bar{E}_{23} but do not affect the charge magnitudes. Computations show that generation of repetitive responses to maintained current is accompanied by a decrease in firing frequency with time (Fig. 3A). The cause of adaptation lies in the aperiodic behavior of the inactivation system variables (Fig. 3B). Each variable which changes rapidly in accordance with the periods of repetitive responses slowly reaches steady oscillation. These characteristic features of adaptation become more pronounced at decreased stimulating current (Fig. 4). In this case changes of rapidly varying variables towards the steady level occurs for 20 ms, which corresponds to the period in which a progressive change of interspike intervals is observed; then firing ceases. It should be noted that generation of finite spike trains is a characteristic feature of the response to maintained current both for transient receptors sensory fibres and for motor fibres, particularly. Emphasis should be also placed on the fact that the shape of the first action potential

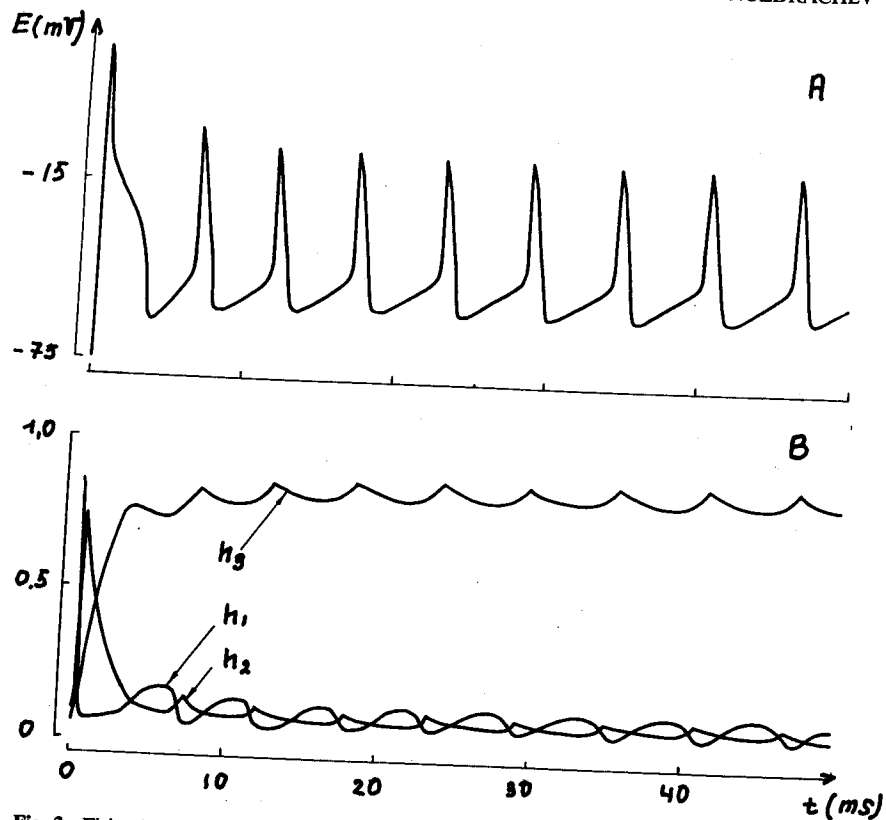


Fig. 3 Firing behavior of the nodal membrane when its h -system has second order properties. Experimental data obtained for *Rana pipiens* fibres (Chiu, 1977) were used for computations. A — rhythmic activity of the nodal membrane evoked by stimulating current equal to 0.85 nA. B — corresponding time dependences of inactivation variables describing the fractions of the particles in the open (h_1) and inactivated (h_2, h_3) states ($T=22^\circ\text{C}$).

of the considered sequence of impulses somewhat differs from the “conventional” shape obtained by computations with the unmodified model. Action potentials of this shape were recorded from motor nerve fibres, the potassium currents of which were blocked or abolished by tetraethylammonium (Bergman, 1969; Ochs *et al.*, 1981). To induce rhythmic activity the experimental values of the *Rana pipiens* membrane rate constants had to be shifted by 20 mV along the potential axis to reduce the initial inactivation level. In contrast the starting value h_{10} is a small and a theoretical node responds to a constant current step by a single action potential only. It can be assumed that the values a_{ij} [Eqn. (7)] calculated experimentally are characteristic for rapidly accommodating fibres. The shape of the first action potential typical for fibres of this kind also validates this assumption.

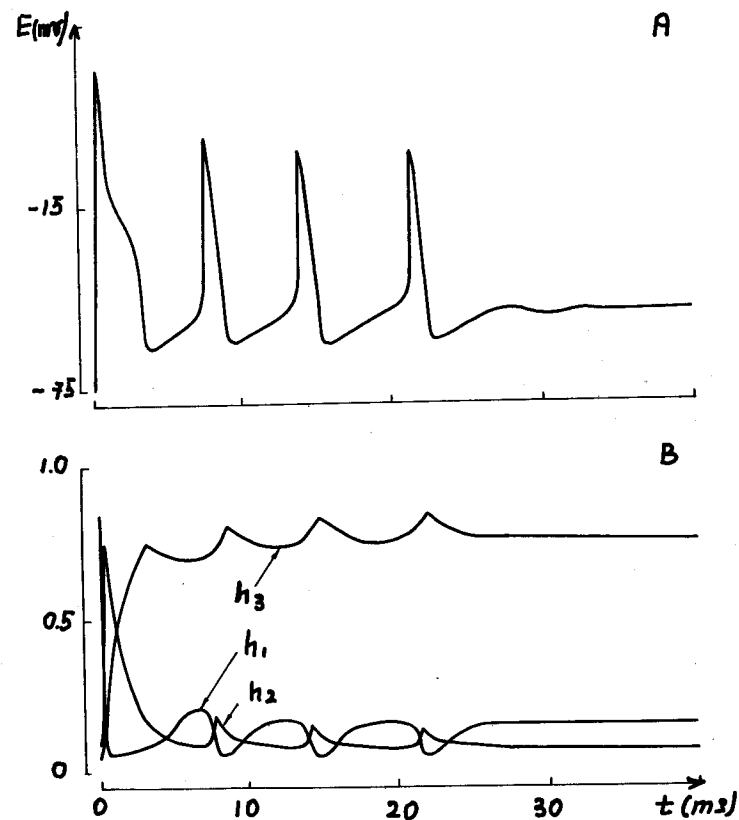


Fig. 4 Generation of a finite impulse train. A — computed action potentials in response to maintained current of 0.7 nA. B — time dependences of inactivation system variables.

Let us consider the sodium channel inactivation system of the nerve fibre in *Xenopus laevis*. In this case the initial value of the variable h_1 , i.e. its stationary value at resting potential is 0.86, which is sufficient for the appearance of rhythmic activity. Functions $h_{1\infty}(E)$, $\tau_h(E)$ and $\tau_h^*(E)$ are presented in Fig. 5. It should be noted that as in the previous case, one of the time constants approximately fits τ_h of the H-H model while another time constant with a maximum value of less than 1 ms appears due to an additional state of the inactivation system. However, despite a small value of τ_h^* the behavior of the variable $h_1(t)$ is significantly changed in this case: it reaches the maintained oscillation only 15 ms after switching on a constant current step (Fig. 6B) at the time the changes in interspike intervals are terminated (Fig. 6A). This example of adaptation behavior of the node of Ranvier membrane shows that through fast

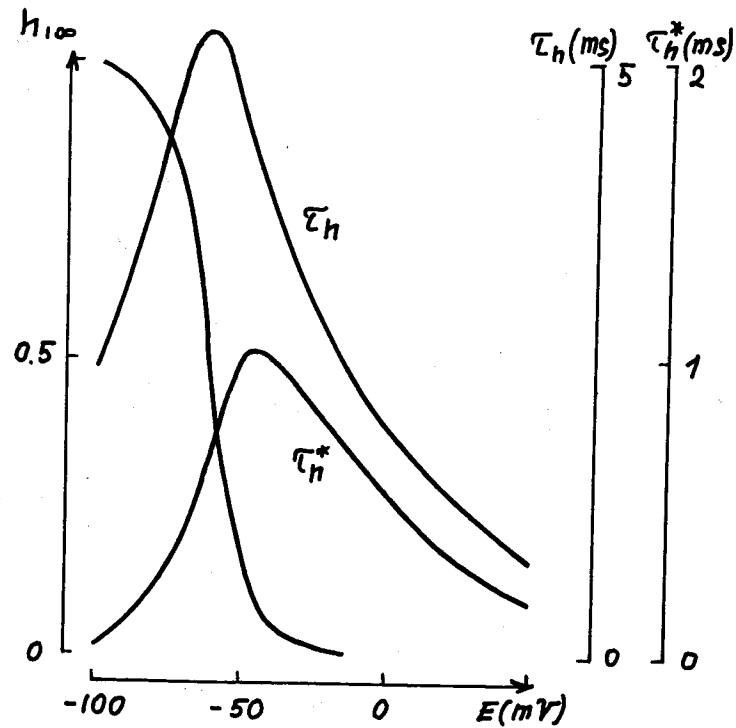


Fig. 5 Voltage dependences of time constants and steady-state values of the sodium inactivation variable in a conducting state. The curves were calculated from Kniffki *et al.* (1981) for *Xenopus laevis* nerve fibre.

molecular processes underlying the rearrangement of the membrane ionic channels voltage sensors the regulation of more slow physiologically important phenomena can be realized. In the case discussed action potentials have a regular shape. Such a node is capable to generate repetitive activity. These facts suggest that the inactivation system of the slowly accommodating fibres is composed in similar manner. Its main difference from the h -system of a fast accommodating node consists probably in different distribution of the gate charge of each transition. It has been mentioned above that the main charge of the nodal inactivation system of *Rana pipiens* is transferred between two closed states that probably leads to the delay in development of repolarization and changes in the shape of action potential. The transfer of the main charge between open and closed states in the nodal system of *Xenopus laevis* does not lead to the changes of an impulse shape.

In the previous work (Krylov and Makovsky, 1978) it was predicted that spike frequency adaptation (SFA) in amphibian nerve may probably be due to a current

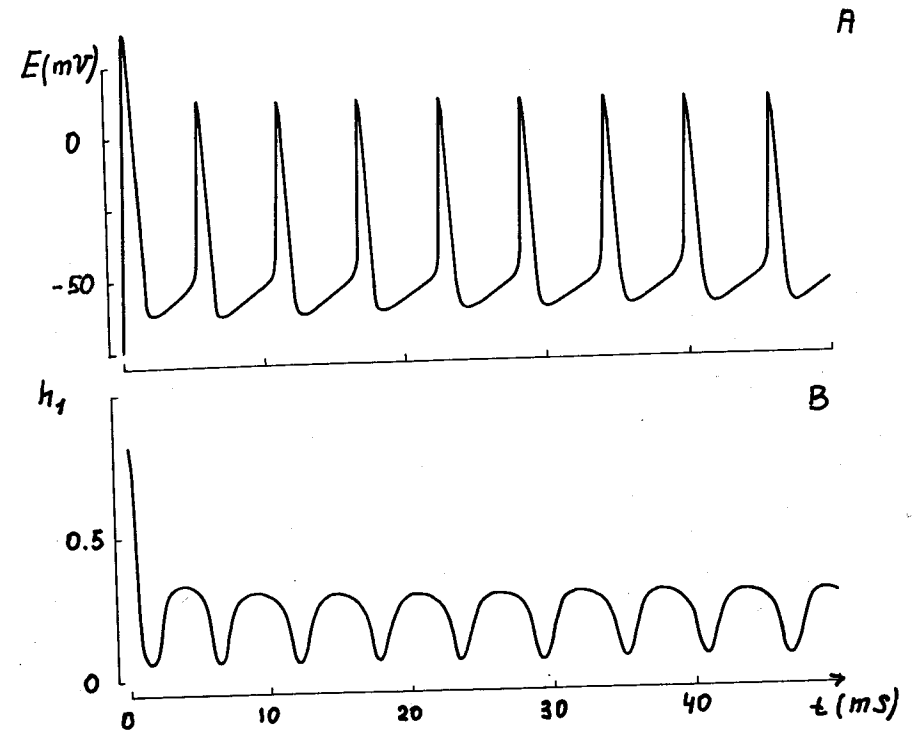


Fig. 6 Adaptational behavior of the theoretical node of Ranvier.
A — repetitive responses of the nodal membrane model modified on the basis of data presented in Fig. 5.
B — corresponding time course of the sodium inactivation variable h_1 in conducting state.

through slow potassium channels (Ilyin *et al.*, 1977; 1980). It was suggested that Makovsky's channels may also be responsible for different cases of SFA in nerve cells of various types. Dubois (1982) analysing a physiological role of the different potassium currents concluded that his results in some respect supported the idea that SFA in sensory fibres was due to a current through Makovsky's channels but the hypothesis could not explain a difference in SFA for motor and sensory fibres. Here we aimed to show that a proper distribution of effective charges in the h -systems might provide a mechanism additional to or underlying that described (Schwartz *et al.*, 1983) for sensory fibres as compared with motor fibres. We emphasize just now that the difference between the nerve cells should be elucidated on a molecular level due to the description of gating processes with thermodynamic parameters.

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