Minimizing the Influence of the Series Resistance in Potential Clamped Ranvier Nodes

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Abstract. Series resistance artifacts in ionic current measurements on single myelinated nerve fibres are commonly minimized by reducing sodium currents. Doing this some deviations from the predictions of the Hodgkin-Huxley-Frankenhaeuser formalism become evident. In the present investigation two methods to reduce sodium currents were used with and without compensated feedback to examine the influence of the nodal series resistance. Changing the availability of sodium permeability by appropriate prepulses peak sodium current-voltage relations obeyed the Hodgkin-Huxley-Frankenhaeuser formalism only provided the amount of compensated feedback was set to give minimum of the current-voltage relation near $E = 0$. For reduced sodium concentration in the bathing fluid the so-called independence principle predicts a shift of the minimum of the current-voltage relation on the potential axis in negative direction as compared to ordinary Ringer solution, if the effective series resistance is sufficiently small. This was confirmed by experiments only if the above mentioned amount of compensated feedback was used. The results suggest that the „$E = 0$"-criterion indicates optimum compensation of the influence of the series resistance.

Key words: Node of Ranvier — Compensated feedback — Potential clamp — Independence principle — Sodium inactivation

Introduction

The problem of series resistance artifacts in ionic current measurements does exist in various preparations, e. g. nonmyelinated nerve fibres (Hodgkin et al. 1952; Goldman and Schauf 1972; Waxman 1978; Bezanilla et al. 1982; Shrager et al. 1983; Moore et al. 1984), myelinated nerve fibres of cold and warm blooded vertebrates (Drouin and Neumcke 1974; Chiu 1980; Zaciu et al. 1981; Neumcke and Stämpfli 1982; Koppenhöfer et al. 1984; Dubois and Benoit 1985), skeletal muscle fibres (Hille and Campbell 1976) and heart muscle fibres (Beeler et al. 1970; Trautwein 1973).

without compensated feedback ($k = 0$), squares those derived with compensated feedback. Optimum compensation was achieved at $k_{opt} = 0.067$. Without compensated feedback the minimum of the sodium current voltage curve was shifted to the right, when currents were reduced by increased sodium inactivation (compare open and filled circles). As shown by the dotted line, there was no shift under compensated feedback (compare open and filled squares). Note that the shift is less pronounced with $h_\infty < 1$ (filled symbols), compared to the corresponding curve derived under $h_\infty = 1$ (open symbols), according to the current proportional influence of R_S. Similar results have been described by Dubois and Benoit (1985).

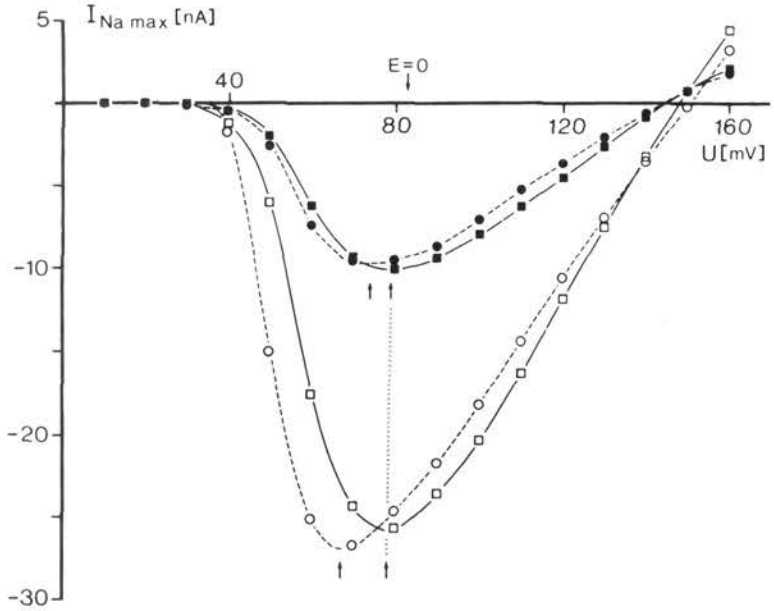

Fig. 1. The influence of sodium inactivation on the position of peak sodium current-voltage curves with and without compensated feedback. Abscissa: test pulses U in mV. Ordinate: peak sodium currents $I_{Na\,max}$ in nA. Squares: under optimum compensation (k_{opt}). Circles: without compensation ($k = 0$). Open symbols: with hyperpolarizing prepulses of -40 mV in amplitude and 50 ms in duration. Filled symbols: with depolarizing prepulses of $+20$ mV in amplitude and 50 ms in duration. ($1—h_\infty$): steady state value of sodium inactivation at the end of the prepulses. Optimum compensation yielded a series resistance of 370 kΩ in this experiment. Holding potential, $E_H = -82.7$ mV. The curves were calculated using spline interpolation. Arrows indicate curve minima.

B. Decreasing sodium currents by low sodium concentration

The dependence of peak sodium currents on the sodium concentration in the bathing fluid was investigated first by Hodgkin and Huxley (1952a,c). They

derived a formal description of their experimental results, the so-called „independence principle", which enables to predict sodium currents, I'_{Na}, in low sodium, c'_a, from current at normal sodium concentration (I_{Na}, c_a):

$$\frac{I'_{Na}}{I_{Na}} = \frac{(\alpha' \cdot c'_a / \alpha \cdot c_a) \cdot \exp((E - E_{Na}) \cdot F/(R \cdot T)) - 1}{\exp((E - E_{Na}) \cdot F/(R \cdot T)) - 1} \quad (1)$$

where E is the membrane potential, E_{Na} is the sodium equilibrium potential; F, R and T have their conventional meanings. α and α' are activity coefficients, considering the different activities of the respective solutions (Adam et al. 1977). Under the assumption that the activities close to the membrane match those in free solution and neglecting the influence of choline ions on the activity of the sodium ions $\alpha'/\alpha = 1.085$ for the experimental conditions chosen (Robinson and Stokes 1959).

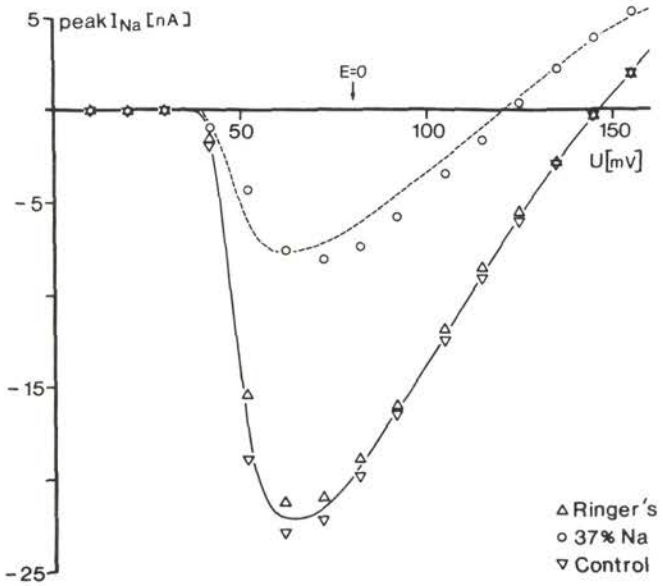

Fig. 2. The influence of external sodium concentration on peak sodium currents. Abscissa: test pulses U in mV. Ordinate: peak sodium currents $I_{Na\,max}$ in nA. Triangles: 100 % Na before and after application of 37 % Na (circles). The continuous curve was calculated using spline interpolation, from which the interrupted curve (for 37 % Na) was calculated by Eq. (1). No compensated feedback ($k = 0$). $E_H = -81$ mV.

Although the independence principle was considered as a „cornerstone" of the ionic hypothesis (Cahalan and Begenich 1976), its validity for myelinated nerve fibres is still controversial. Dodge and Frankenhaeuser (1959) found the in-

dependence principle to be a fairly good description for changes in peak sodium currents induced by changes in sodium concentration of the bathing fluid. Other authors observed deviations from the independence principle and attributed them at least in part (Hille 1975) or fully (Brismar 1980) to the influence of the series resistance. In particular, with reduced sodium concentration, the minimum of the peak sodium current-voltage curve is often shifted to the right as compared to the corresponding curve in ordinary Ringer solution (Drouin and Neumcke 1974). This observation initiated investigations on the influence of the nodal series resistance on the validity of the independence principle (Wiese 1985).

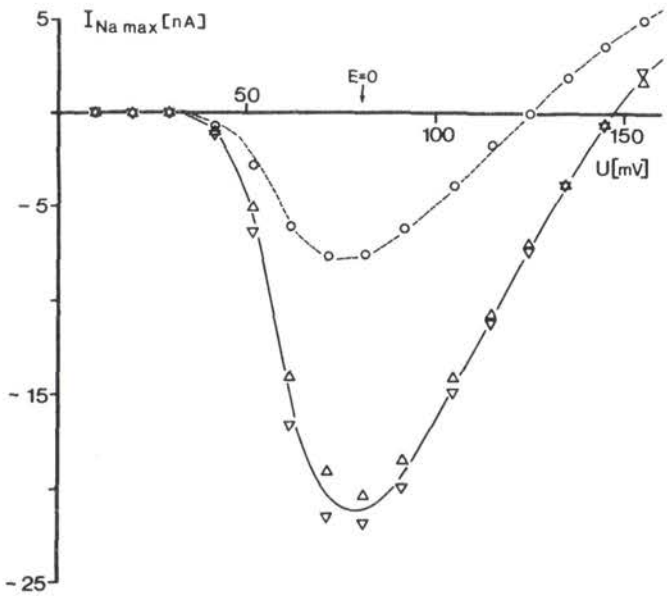

Fig. 3. The influence of external sodium concentration on peak sodium currents. The same experiment as in Fig. 2 but under optimum compensation of the influence of the series resistance ($k_{opt} = 0.067$; $R_S = 400\,k\Omega$). $E_H = -81$ mV.

Figure 2 shows sodium current-voltage curves measured in normal sodium (100 % Na, triangles) before and after exposure to low sodium (37 % Na, circles) without compensated feedback ($k = 0$). The continuous curve was calculated using spline interpolation, from which the interrupted curve was derived using equation (1). The following results are obvious:

i) The minimum of the peak sodium current-voltage curve in 100 % Na is on the left of $E = 0$.

ii) The minimum of the sodium current-voltage relation measured in 37 % Na (circles) is on the right of that in 100 % Na but still left of $E = 0$.
iii) The minimum of the interrupted curve, calculated for 37 %Na, is on the left of that of the continuous curve (100 % Na).
iv) There is a clear discrepancy between the measured and the calculated curve for 37 % Na.
In subsequent runs on the same axon the influence of optimum compensated feedback ($k = k_{opt}$) was tested. The following results were obtained (Fig. 3):
i) The minimum of the sodium current-voltage curve in 100 % Na is very close to $E = 0$.
ii) The minimum of the values measured in 37 % Na is on the left of that in 100 % Na.
iii) The minimum of the calculated curve for 37 % Na is still on the left of that in 100 % Na.
iv) The minima of both the measured values and the calculated curve for 37 % Na fall together.
As expected, these results varied with the amount of positive feedback employed (Table 1):

Table 1. Shift of the minima of the peak sodium current-voltage curves upon changes in sodium concentration at various amounts of compensated feedback. k_{opt}: optimum compensation using the „$E = 0$"-criterion. Shifts are given in mV ($\pm$ S. E. M.; $n = 11$).

Amount of compensation	$k = 0$	$0.5 \cdot k_{opt}$	k_{opt}	$1.25 \cdot k_{opt}$
100 % Na, measured — 37 % Na, measured	-6.6 ± 1.1	0.8 ± 1.6	4.8 ± 1.1	10.3 ± 1.7
100 % Na, measured — 37 % Na, calculated	1.6 ± 0.3	3.6 ± 0.6	4.6 ± 0.6	6.4 ± 1.7
37 % Na, measured — 37 % Na, calculated	8.2 ± 1.1	2.9 ± 1.8	-0.1 ± 0.8	-3.9 ± 1.2

Without compensation ($k = 0$) the minimum of the measured sodium current-voltage relation in 37 % Na is shifted to the right with respect to the curve in 100 % Na, whereas with $0.5 \cdot k_{opt}$ almost no shift is detectable. With optimum compensation (k_{opt}), however, there is a shift to the left which becomes even larger if the compensation is increased beyond k_{opt} ($1.25 \cdot k_{opt}$). The curve calculated for 37 % Na is shifted to the left with respect to the curve measured in 100 % Na at any setting of positive feedback and increases with increased amount of compensated feedback. The third line shows that in 37 % Na the measured values fall together with the respective calculated curve only under optimum compensation. Otherwise the calculated curve is shifted to the left ($k = 0$, $k = 0.5 \cdot k_{opt}$) or to the right ($1.25 \cdot k_{opt}$).

If compensated feedback is employed the minimum of the peak sodium current-voltage curve is always shifted to the right with respect to the corresponding curve measured without compensation (compare Fig. 1). This holds both for 100 % Na and 37 % Na and is shown in Table 2 for k_{opt}. The values of the series resistance measured in individual experiments were pooled in three groups, mean values for each of them are given. The third line shows the mean value of the shift measured in 100 % Na, the fourth line that in 37 % Na. Evidently the shift increases with increasing series resistance. In 37 % Na the shift is always less than in 100 % Na, but still detectable, as expected from the findings of Gillespie and Meves (1980), who found an influence of R_S on currents of only one fifth of their normal value.

Table 2. Mean value of the shift (in mV) of the minimum of the peak sodium current-voltage curve due to compensated feedback ($k = k_{opt}$) for 100 % Na and 37 % Na in relation to the mean series resistance R_S (in kΩ) of three arbitrarily chosen series resistance ranges.

	$R_S < 350$	$350 \leq R_S \leq 450$	$R_S > 450$
Series resistance (kΩ)	188	391	615
Number of experiments	2	6	3
Shift in 100 % Na (mV)	6	19	25
Shift in 37 % Na (mV)	1	7	10

Both Figure 2 and 3 show that the minimum of the calculated curve for 37 % Na is on the left of the corresponding curve in 100 % Na. The question was, whether the independence principle itself implicates this finding. Obviously equation (1) does not consider any influence of the series resistance. Nevertheless, without positive feedback the currents measured in normal sodium (c_a) are influenced by the series resistance to an unknown extent. Therefore, it is impossible to decide whether the observed shifts of the current voltage curves in low sodium (c_a') result from the independence principle itself or have to be attributed to the influence of the series resistance.

For any peak sodium current-voltage curve its slope is zero at the minimum of the curve. Comparing the slope of the current-voltage curve in reduced sodium concentration (c_a') at the minimum of the corresponding curve in ordinary Ringer solution (c_a), it can be decided whether the independence principle itself implies a shift of the curve or not.

After some straightforward calculations and with $dI_{min}/dE = 0$, $I = I_{min}$ and $E(I_{min}) = E_{Imin}$ one arrives at:

$$\left.\frac{dI'}{dE}\right|_{Imin} = I_{min}\frac{F/(R\cdot T)\cdot\exp(E_{Imin}\cdot F/(R\cdot T))\cdot(1-\alpha'\cdot c'_a/\alpha\cdot c_a)}{\exp(E_{Imin}\cdot F/(R\cdot T))^2}$$

$$dI'/dE|_{Imin} = 0 \qquad \text{for } \alpha'\cdot c'_a = \alpha\cdot c_a \tag{2}$$

$$dI'/dE|_{Imin} > 0 \qquad \text{for } \alpha'\cdot c'_a < \alpha\cdot c_a$$

Bearing in mind that the slope of peak sodium current-voltage curves is positive on their right branch, the independence principle implies a shift of the minimum of the corresponding curve in low sodium to the left as compared to ordinary Ringer solution.

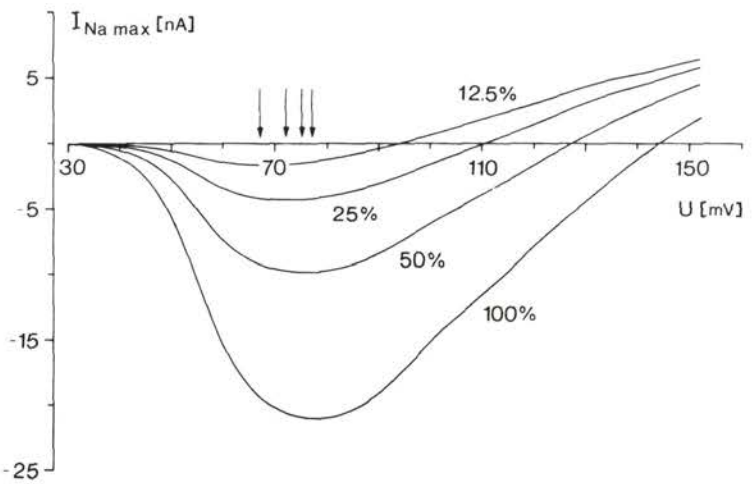

Fig. 4. The influence of external sodium concentration on the position of the peak sodium current-voltage curve as calculated by the independence principle. Abscissa: test pulses U in mV. Ordinate: Peak sodium currents $I_{Na\ max}$ in nA. 100 %: interpolated curve for ordinary Ringer solution of Fig. 3. 50 %, 25 %, 12.5 %: calculated curves from curve „100 %" by Eq. (1). Arrows indicate curve minima.

Figure 4 shows a peak sodium current-voltage curve measured in normal sodium concentration (100 % Na) under compensated feedback ($k = k_{opt}$), from which the curves corresponding to several concentrations (50 %, 25 %, 12.5 %) were calculated using equation (1). Arrows indicate the position of actual curve minima. As expected from equation (2), they are shifted to the left with decreasing sodium concentration.

Discussion

The commonly used methods for reducing the influence of the series resistance result in a diminution of the current proportional potential drop across R_S by diminishing the ionic currents.

If sodium currents are reduced by tetrodotoxin (TTX), their kinetic parameters become changed (Neumcke and Stämpfli 1982; Benoit et al. 1985) and the minimum of the sodium current-voltage curve is shifted on the potential axis in positive direction (Narahashi 1971; Neumcke and Stämpfli 1982). Both effects can qualitatively be attributed to the reduced influence of R_S (compare Koppenhöfer et al. 1984, Figs. 1 and 3). Therefore it remains unclear, whether these changes are effects of R_S alone or if there is an additional pharmacological effect of TTX on the kinetics of sodium currents.

Sodium currents may be reduced by applying appropriate prepulses as well. Without compensated feedback increased inactivation results in a shift of the minimum of the current-voltage curve on the potential axis in positive direction (Fig. 1, circles). Under compensated feedback, using the criterion of Koppenhöfer and coworkers (1984) for k_{opt}, no shift is detectable (Fig. 1, squares). This finding agrees with the predictions of the Hodgkin-Huxley-Frankenhaeuser formalism. Even under increased sodium inactivation optimum compensation causes a shift of the minimum of the peak sodium current-voltage curve (Fig. 1, filled symbols). Furthermore, reduction of sodium currents cannot enhance the loading of the membrane capacitance which remains delayed by the series resistance (Wiese 1982; Wiese et al. 1982; Wiese and Koppenhöfer 1983). Therefore, the time interval between the beginning of a test pulse and the moment when the membrane potential has settled at the new level can effectively be shortened only by compensated feedback (Salzberg and Bezanilla 1983).
The intersection of the sodium current-voltage curve with the potential axis is shifted by positive feedback as well (Fig. 1, open symbols). The holding current, the potential dependent leakage current and potassium current passing potassium channels are not zero at the intersection point and cause a potential drop across R_S, which qualitatively explains the shift (Koppenhöfer et al. 1984). Similar results have been shown for non-myelinated nerve fibres (Taylor et al. 1960).

Furthermore, the intercept of the curves measured at $h_\infty < 1$ (filled symbols) was 5—10 mV left of that measured at $h_\infty = 1$ (open symbols). This is due to the fact that potassium currents were not blocked by specific potassium blockers like tetraethylammonium chloride to avoid any pharmacological effect on sodium currents (Bromm et al. 1978; Koppenhöfer 1967; Schönle and Koppenhöfer 1981, 1983; Stanfield 1983). Calculation of the point of intersection of the peak sodium current-voltage curve with the potential axis using standard data of

myelinated nerve fibres (Frankenhaeuser and Huxley 1964) revealed a shift by 8 mV to the left if h_x was reduced from 1.0 to 0.3. This agrees satisfactorily well with the experimental results shown in Fig. 1. In the potential range of the minimum of the sodium current-voltage curve these potential dependent effects are negligibly small.

Another method of decreasing sodium currents is to lower the sodium concentration in the bathing fluid. The independence principle gives a formal description between Na-currents in normal and reduced sodium concentration. If no compensated feedback is used (Fig. 2) there are clear differences between the points measured in 37 % Na (circles) and the calculated curve. The minimum of the latter is shifted to the left, while the measured values are shifted to the right with respect to the curve in 100 % Na. This is due to the influence of the series resistance depending on the current strength (compare open and closed circles in Fig. 1). The shift of the calculated curve in opposite direction, however, is predicted by the independence principle and increases with the difference in concentrations (compare Fig. 4).

Figure 3 shows that differences between measured and calculated curves for 37 % Na disappear, if compensated feedback is employed, using the criterion for optimum compensation (Koppenhöfer et al. 1984). In this case the minima of both curves are shifted to the left with respect to the curve in 100 % Na. In this connection two points have to be considered:

i) If in experiments under reduced sodium concentration, the sodium current-voltage curve is shifted to more positive potentials as compared to the corresponding curve in Ringer solution (Drouin and Neumcke 1974) and even if no shift is detectable (Dodge and Frankenhaeuser 1959), the influence of the series resistance cannot be disregarded (Wiese 1985).

ii) The independence principle is good description of sodium currents I at reduced sodium concentration only provided the effective series resistance is negligibly small, either by a genuine small series resistance (Koppenhöfer et al. 1987) or by optimum compensation for its current proportional voltage drop.

The present paper shows that some deviations of the experimental data from the predictions of the Hodgkin-Huxley-Frankenhaeuser formalism can be attributed to the series resistance artifact. Using the criterion for optimum compensation proposed by Koppenhöfer and coworkers (1984), compensated feedback proved to be a suitable tool to escape such problems.

Acknowledgement. We thank J. Wittig for help with the experiments.

References

Adam G., Läuger P., Stark G. (1977): Physikalische Chemie und Biophysik. Springer Verlag, Berlin, Heidelberg, New York

Attwell D., Cohen I. (1977): The voltage clamp of multicellular preparations. Progr. Biophys. Mol. Biol. **31**, 201—245

Beeler G. W., Reuter H. (1970): Voltage clamp experiments on ventricular myocardial fibres. J. Physiol. (London) **207**, 165—190

Bellman R., Kashef B. (1972): Application of spline and differential quadrature to partial differential equations of the Hodgkin-Huxley type. Computers in Biomedicine: Proceedings supplement. Proceedings of the fifth Hawaii International Conference on System Sciences, Supplement

Benoit E., Corbier A., Dubois J. M. (1985): Evidence for two transient currents in the frog node of Ranvier. J. Physiol. (London) **361**, 339—360

Berthold C. H., Rydmark M. (1983): Electrophysiology and morphology of myelinated nerve fibres. VI. Anatomy of the paranode-node-paranode region in the cat. Experientia **39**, 964—975

Bezanilla F., Vergara J., Taylor R. E. 1982): Voltage clamping of excitable membranes. In: Methods of Experimental Physics, Vol. 20, (Eds. Ehrenstein G., Lecar H.), pp. 445—511, Academic Press, New York

Brismar T. (1980): Potential clamp analysis of membrane currents in rat myelinated nerve fibres. J. Physiol. (London) **298**, 171—184

Bromm B., Ochs G., Schwarz F. R. (1978): Is tetraethylammonium chloride a specific blocker of the potassium channel? J. Physiol. (London) **284**, 150—151P

Cahalan M., Begenisich T. (1976): Sodium channel selectivity. Dependence on internal permeant ion concentration. J. Gen. Physiol. **68**, 111—125

Chiu S. Y. (1980): Asymmetry currents in the mammalian myelinated nerve. J. Physiol. (London) **309**, 111-125

Chiu S. Y., Ritchie J. M. (1980): Potassium currents in nodal and internodal axonal membrane of mammalian myelinated nerve fibres. Nature **284**, 170—171

Dodge F. A., Frankenhaeuser B. (1958): Membrane currents in isolated frog nerve fibre under voltage clamp conditions. J. Physiol. (London) **143**, 76—90

Dodge F. A., Frankenhaeuser B. (1959): Sodium currents in the myelinated nerve fibre of *Xenopus laevis* investigated with voltage clamp technique. J. Physiol. (London) **148**, 188—200

Drouin H., Neumcke B. (1974): Specific and unspecific changes at the sodium channels of the nerve membrane. Pflügers Arch. **351**, 207—229

Dubois J. M., Benoit E. (1985): Permeabilité au sodium de la fibre nerveuse myelinisée: hyphothéses et conclusions. Funkt. Biol. Med. **4**, 37—41

FitzHugh R., Cole K. S. (1973): Voltage and current clamp transients with membrane dielectric loss. Biophys. J. **13**, 1125—1140

Frankenhaeuser B. (1959): Steady state inactivation of sodium permeability in myelinated nerve fibres of *Xenopus leavis*. J. Physiol. (London) **148**, 671—676

Frankenhaeuser B., Huxley A. F. (1964): The action potential in the myelinated nerve fibre of *Xenopus laevis* as computed on the basis of voltage clamp data. J. Physiol. (London) **171**, 302—315

Gillespie J. I., Meves H. (1980): The time course of sodium inactivation in squid giant axons. J. Physiol. (London) **299**, 289—307

Goldman L., Schauf C. L. (1972): Inactivation of the sodium current in Myxicola giant axons. Evidence for coupling to the activation process. J. Gen. Physiol. **59**, 659—675

Greville L. (1969): Splinefunktionen, Interpolation und numerische Integration. In: Mathematische

Methoden für Digitalrechner II, (Eds. Ralston A., Wilf H. F.), pp. 249—267, Oldenbourg, München

Hille B. (1966): The common mode of action of three agents that decrease the transient charge in sodium permeability in nerves. Nature **210**, 1220

Hille B. (1968): Pharmacological modifications of the sodium channels of frog nerve. J. Gen. Physiol. **51**, 199—219

Hille B. (1975): Ionic selectivity, saturation, and block in sodium channels. A four barrier model. J. Gen. Physiol. **66**, 535—560

Hille B., Campbell D. T. (1976): An improved vaseline gap voltage clamp for skeletal muscle fibres. J. Gen. Physiol. **67**, 265—293

Hodgkin A. L., Huxley A. F. (1952a): Currents carried by sodium and potassium ions through the membrane of the giant axon of *Loligo*. J. Physiol. (London) **116**, 449—472

Hodgkin A. L., Huxley A. F. (1952b): The components of membrane conductance in the giant axon of *Loligo*. J. Physiol. (London) **116**, 473—496

Hodgkin A. L., Huxley A. F. (1952c): The dual effect of membrane potential on sodium conductance in the giant axon of *Loligo*. J. Physiol. (London) **116**, 497—506

Hodgkin A. L., Huxley A. F. (1952d): A quantitative description of membrane current and its application to conduction and excitation in nerve. J. Physiol (London) **117**, 500—544

Hodgkin A. L., Huxley A. F., Katz B. (1952): Measurement of current-voltage relations in the membrane of the giant axon of *Loligo*. J. Physiol. (London) **116**, 424—448

Koppenhöfer E. (1967): Die Wirkung von Tetraäthylammoniumchlorid auf die Membranströme Ranvierscher Schnürringe von *Xenopus laevis*. Pflügers Arch. **293**, 34—55

Koppenhöfer E., Vogel W. (1969): Die Wirkung von Tetrodotoxin und TEA an der Innenseite der Schnürringsmembran von *Xenopus laevis*. Pflügers Arch. **313**, 361—380

Koppenhöfer E., Schumann H. (1979): Sodium currents in the node of Ranvier with compensation of the effect of the series resistance. Pflügers Arch. **382**, R37

Koppenhöfer E., Schumann H. (1981): A method for increasing the frequency response of voltage clamped myelinated nerve fibres. Pflügers Arch. **390**, 288—289

Koppenhöfer E., Wiese H., Schumann H., Wittig J. (1984): Experimente zum Einfluß des Serienwiderstandes auf die Natriumspitzenströme des Ranvierschen Schnürrings. Funkt. Biol. Med. **3**, 61—64

Koppenhöfer E., Sommer R. G., Froese U. (1987): Effects of benzocaine and its isomers on sodium permeability and on steady state sodium inactivation in the myelinated nerve, obtained by an improved dissection technique. Gen. Physiol. Biophys. **6**, 209—222

Moore J. W., Hines M., Harris E. M. (1984): Compensation for resistance in series with excitable membranes. Biophys. J. **46**, 507—514

Narahashi T. (1971): Neurophysiological basis for drug action: ionic mechanism, site of action and active form in nerve fibres. In: Biophysics and Physiology of Excitable Membranes, (Ed. Adelman W. J.), pp. 423—462, Van Nostrand, New York

Neumcke B., Stämpfli R. (1982): Sodium currents and sodium current fluctuations in rat myelinated nerve fibres. J. Physiol. (London) **329**, 163—184

Rámon F., Anderson N., Joyner W., Moore J. W. (1975): Axon voltage clamp simulations. IV. A multicellular preparation. Biophys. J. **15**, 55—69

Ritchie J. M., Rogart R. B. (1977): The binding of Saxitoxin and Tetrodotoxin to excitable tissue. Rev. Physiol. Biochim. Pharmacol. **79**, 1—50

Robinson R. A., Stokes R. H. (1959): Electrolyte Solutions. Butterworths, London

Salzberg B. M., Bezanilla F. (1983): An optical determination of the series resistance in *Loligo*. J. Gen. Physiol. **82**, 807—817

Schmidt H., Stämpfli R. (1966): Die Wirkung von Tetraäthylammoniumchlorid auf den einzelnen

Ranvierschen Schnürring. Pflügers Arch. **287**, 311—325
Schönle C., Koppenhöfer E. (1981): On the influence of purified tetraethylammonium chloride on Na-currents of voltage clamped Ranvier nodes. Pflügers Arch. **391**, R38
Schönle C., Koppenhöfer E. (1983): Zur Selektivität der Wirkung gereinigten Tetraäthylammoniumchlorids am Ranvierschen Schnürring. Funkt. Biol. Med. **2**, 49—52
Schumann H. (1980): Kompensation der elektrischen Auswirkungen des perinodalen Zugriffswiderstandes bei Ionenstrommessungen am Ranvierschen Schnürring. Thesis, Kiel
Schumann H., Koppenhöfer E. (1981): Compensation of the low-pass filter properties of the current measuring internode in voltage clamped myelinated nerve fibres. Biophys. Struct. Mechanism **7**, 317
Schumann H., Koppenhöfer E., Wiese H. (1983): Compensation of the low-pass filter properties of the current measuring internode in voltage clamped myelinated nerve fibres. Gen. Physiol. Biophys. **2**, 287—295
Shrager P., Starkus J. C., Mei-Ven C. L., Peracchia C. (1983): The periaxonal space of crayfish giant axons. J. Gen. Physiol. **82**, 221—244
Sigworth F. J. (1980): The variance of sodium current fluctuations at the node of Ranvier. J. Physiol. (London) **307**, 97—129
Stämpfli R., Hille B. (1976): Electrophysiology of the peripheral myelinated nerve. In: Frog Neurobiology, (Eds. Llinas R., Precht W.), pp. 3—32, Springer, Berlin
Stämpfli R., Uhrik B. (1980): Membrane area and series resistance computed from serial sections of nodes of Ranvier. J. Physiol. (London) **308**, 15—16P
Stanfield P. R. (1983): Tetraethylammonium ions and the potassium permeability of excitable cells. Rev. Physiol. Biochim. Pharmacol. **97**, 1—68
Taylor R. E., Moore J. W., Cole K. S. (1960): Analysis of certain errors in squid axon voltage clamp measurements. Biophys. J. **1**, 161—203
Trautwein W. (1973): Membrane currents in cardiac muscle fibres. Physiol. Rev. **53**, 793—835
Waxman S. G. (1978): Variations in axonal morphology and their functional significance. In: Physiology and Pathophysiology of Axons, (Ed. Waxman S. G.), pp. 169—190, Raven Press, New York
Wiese H. (1982): The influence of different parameters on the capacity current in potential clamped Ranvier nodes. Pflügers Arch. **392**, R34
Wiese H. (1985): Die Anwendbarkeit des Hodgkin-Huxley-Frankenhauser Formalismus zur Beschreibung der Natriumkanals elektrisch erregbarer Membranen. Thesis, Kiel
Wiese H., Koppenhöfer E. (1983): On the capacity current in myelinated nerve fibres. Gen. Physiol. Biophys. **2**, 297—312
Wiese H., Koppenhöfer E. (1985): Optimum compensation of the series resistance artifact in potential clamped Ranvier nodes. Pflügers Arch. **405**, R53
Wiese H., Stüning D., Koppenhöfer E. (1982): Capacity currents in potential clamped Ranvier nodes. Pflügers Arch. **394**, R47
Wiese H., Wittig J., Koppenhöfer E. (1984): The effect of compensated feedback on peak sodium currents of Ranvier nodes in low sodium. Pflügers Arch. **400**, R57
Zaciu C. (1982): Analysis of certain errors in voltage clamp measurements on myelinated nerve fibre. J. Biomed. Eng. **4**, 331—333
Zaciu C., Tripsa M., Vasilescu V. (1981): Computer simulation of the effect of the nodal gap resistance on ionic current measurements in the node membrane. Biophys. J. **36**, 797—802

Final version accepted August 20, 1987