The Effects of Several Alcohols on the Properties of the Squid Giant Axon

CLAY M. ARMSTRONG and LEONARD BINSTOCK

From the National Institutes of Health, Bethesda. Dr. Armstrong's present address is the Department of Physiology, University College, London, England

ABSTRACT The effects of several alcohols on the resting potential, action potential, and voltage-clamp currents of the squid giant axon have been measured. All the alcohols employed are similar in that they depress maximum sodium conductance much more than maximum potassium conductance. Octyl alcohol differs from the others (C₂ through C₅) in that it has less tendency to depolarize the axon. Depolarization is always accompanied by a decrease of gK near the resting potential, such that the ratio gK/gNAK is decreased. Steady-state inactivation of the sodium ion current is unaffected by alcohols, as is membrane capacity. Resting membrane conductance is usually decreased by alcohols. The findings are discussed in relation to work on monomolecular films.

INTRODUCTION

Alcohols have been used in many studies of narcosis, chiefly because of their simple structure and well known physical and chemical properties. A series of alcohols, furthermore, offers the possibility of correlating differences in narcotic activity with simple differences in the molecular structure of the alcohols.

For our purposes the findings in alcohol narcosis can be summarized in three statements. The oldest finding is a distinction between long and short chain alcohols on the basis of the latter's tendency to depolarize the nerve (Bishop, 1932). It has also been found that in order to achieve the same effect the thermodynamic activity of the alcohol in the fluid around the nerve must increase as the hydrocarbon chain of the alcohol grows longer (Ferguson, 1951; Posternak and Larrabee, 1951). Finally, Skou (1958) has found a close correlation between narcotic potency of several alcohols and their ability to increase the surface pressure in a monomolecular film of myelin extract.

There has been no complete study of alcohol narcosis using the voltage-clamp technique, first employed by Cole (1949). We have performed such a study on the squid giant axon, and made some observations on the effect of alcohols on the parameters of the Hodgkin-Huxley nerve equations. The results confirm an earlier report by Moore (1958) that alcohols primarily affect...
the sodium permeability of the fibers, and it appears that this may be a general rule for all narcotics acting upon nerve fibers (cf. Taylor, 1957; Hagiwara and Saito, 1959; Narahashi et al., 1964). The results also confirm the old distinction between long and short chain alcohols.

METHODS

Some of the experiments reported here were performed using a voltage-clamp apparatus similar to that of Cole and Moore (1960). The frequency response of such a system, or the rapidity with which it can impose a voltage step on the axon, is limited by two factors. First is the transconductance of the control amplifier, i.e. how much current it puts out in response to the error signal, important because of the large membrane capacity. More important is the frequency response of the potential sensor (the micropipette-preamplifier combination), which is severely limited by the high impedance of the micropipette. The limited frequency response of the potential sensor can introduce a hidden error. If the frequency response of the control amplifier and load exceeds that of the potential sensor, there occurs an overshoot of the actual membrane potential which grows in amplitude and duration as the discrepancy in frequency response grows. In bad cases the peak of the overshoot can be 250 per cent of the step amplitude, as may be observed by using a resistor and capacitor to simulate the membrane. Ordinarily the overshoot is hidden from the observer, who sees the membrane potential as distorted by the potential sensor. It is, in fact, this distortion which is responsible for the overshoot.

The first of these problems was largely solved by making the control amplifier a solid state amplifier of high transconductance and wide band width. To improve the frequency response of the potential sensor, a coaxial electrode (i.e., pair of electrodes) was devised to serve as both current electrode and as internal potential electrode. The inside of the large pipette (100 microns) shown in Fig. 1 measures the potential of the inside of the axon. This signal is fed into a simple cathode follower via a Ag-AgCl junction. An electrically floating platinum wire through the narrow part of the pipette lowers the impedance several fold, but does not disturb the dc stability of the electrode. The pipette is filled with 0.5 M KCl. Platinum foil, subsequently platinized, is wrapped around the outside of the pipette to serve as current electrode. (The foil has no direct electrical connection with the inside of the pipette.) This potential electrode-cathode follower combination attenuates high frequency signals somewhat, but the attenuation can largely be compensated by adjusting the phase lead network \( q \) (Fig. 2).

The current-measuring electrode and amplifier are similar to that described by Moore (1959). The output of amplifier \( C \) is proportional to membrane current density. The proportionality constant is determined by the setting of potentiometer \( r \).
Potentiometer \( S \) allows adjustment of the signal fed back to compensate for the resistance \( R_s \) (cf. "compensated feedback," Hodgkin, Huxley, and Katz, 1952). This signal was zero in most of the experiments reported here; i.e., there was no compensation for \( R_s \). The remainder of the system is similar to that of Cole and Moore (1960). The complete system can impose voltage steps of 10 \( \mu \)sec. rise time on the axon. Current density through the axon membrane, however, is considerably less than with the micropipette technique.

The following sequence of potential changes was imposed on the axon. (a) A conditioning pulse of 7 to 30 msec. duration. Unless noted otherwise it was a hyperpolarization of 40 or 50 mv to remove sodium inactivation. (b) The test step. (c) Return to the resting potential. To determine steady-state inactivation, the test step was held constant and the conditioning step was varied (Hodgkin and Huxley, 1952b).

Membrane resistance was measured by applying hyperpolarizing voltage steps of 10 to 40 mv to the membrane and measuring the current as soon as possible after the capacity transient. This procedure had certain difficulties which are described below. "Instantaneous" current-voltage curves (i.e., a curve whose zero current intercept is determined by the equilibrium potential of the ion to which the membrane is permeable at the instant of measurement, and the slope of which is determined by the resistance to the movement of that ion) were measured by the same
method. In this case the ionic current (as opposed to the capacity current) could be measured 30 μsec. after the step.

Membrane capacity was determined from the area under the current curve during application of a hyperpolarizing voltage ramp.

The axon was continuously perfused externally with artificial sea water of pH near 7.4. Composition of the artificial sea water in mM was: Na⁺, 430; K⁺, 10; Cl⁻, 560; Ca⁺⁺, 10; Mg⁺⁺, 50. The alcohols (Fisher certified reagent except for ethyl alcohol, which was ordinary 95 per cent laboratory alcohol) were introduced via the perfusion fluid. 8 or 10 minutes were allowed for equilibration and washout. Thermodynamic activities were calculated from the coefficients of Butler et al. (1935). Temperature was measured by a thermistor-bridge arrangement (Cole, 1957), and usually varied less than 1° for coherent sets of measurements. Temperature range was 3–13°C. The thermistor was in the measuring chamber.

**RESULTS**

*Resting Membrane Potential, Conductance, and Capacitance*

Short chain alcohols (C₂ through C₆) depolarize at all the concentrations employed. The depolarization is roughly proportional to the concentration, and is 7 or 8 mv at concentrations that reduce the maximum sodium conductance by 60 or 70 per cent. The depolarization effected by these alcohols precedes in time any change of the action potential.

Octyl alcohol hyperpolarizes by about 2 mv at concentrations that decrease the sodium current by 60 or 70 per cent. Higher concentrations depolarize the axon by 10 mv or more. With octyl alcohol the effect on the action potential precedes in time the effect on the resting potential.

The resting membrane conductance of two axons was determined before, during, and after treatment with n-propyl and octyl alcohols at two concentrations. If the alcohol depolarized, a long conditioning step of voltage was applied to return the membrane to the untreated resting potential, and conductance was then determined. The current declined as a function of time following application of the test step, reaching a fairly constant level after 0.6 msec. The conductance depended very much on the time after the step that the measurement was made. As determined 100 μsec. after the step, alcohol treatment caused a modest decrease of membrane conductance (average, from an initial 0.48 mmho/cm² to 0.42 mmho/cm²), while as determined 600 μsec. after the step the decrease was larger (average, from 0.38 mmho to 0.26 mmho). The currents involved in this determination were so small that considerable error could result from prolongation of the capacity current; e.g., prolongation by the slow polarization of a component of the membrane dielectric. Since this is very likely (Curtis and Cole, 1938; Hodgkin, Huxley, and Katz, 1952), we consider the determination at 0.6 msec. more meaningful. As calculated from the time constant of decay of the K⁺ current following a
TABLE I

<table>
<thead>
<tr>
<th>Alcohol</th>
<th>Concentration</th>
<th>Before</th>
<th>During</th>
<th>After</th>
</tr>
</thead>
<tbody>
<tr>
<td>n-Propyl</td>
<td>0.13 M</td>
<td>0.42</td>
<td>0.28</td>
<td>0.61</td>
</tr>
<tr>
<td></td>
<td>0.13 M</td>
<td>0.31</td>
<td>0.19</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.26 M</td>
<td>0.19</td>
<td>0.30</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.26 M</td>
<td>0.41</td>
<td>0.25</td>
<td>0.44</td>
</tr>
<tr>
<td>Octyl</td>
<td>0.37 mM</td>
<td>0.39</td>
<td>0.38</td>
<td>0.42</td>
</tr>
<tr>
<td></td>
<td>0.96 mM</td>
<td>0.61</td>
<td>0.31</td>
<td>0.41</td>
</tr>
</tbody>
</table>

Figure 3. Action potentials in ASW (9.5°C) and in 510 mM ETOH (9.5°C). The axon was space-clamped, and stimulated by means of the internal current electrode. Marks indicate the stimulus duration.

hyperpolarizing step (Hodgkin and Huxley, 1952 c), $g_K$ at this time is about 75 per cent of its initial value. The results of the 0.6 msec. determination before, during, and after alcohol treatment are shown in Table I.

Membrane capacity (see Methods) is not significantly changed by alcohol treatment. We estimate that we could have seen a change of 10 or 20 per cent.

Action Potential

Low concentrations of all alcohols decrease the action potential peak much more than the following hyperpolarization (Fig. 3). Higher concentrations also decrease the hyperpolarization.

Sodium Currents and Conductance

The peak $Na^+$ current was determined as seen in the inset of Fig. 4, and is plotted in Fig. 4 as a function of $V_m$ (voltage of the inside potential electrode with outside potential electrode zero) during the test depolarization. The peak sodium conductance (Hodgkin and Huxley, 1952 a) at any voltage is the slope of the chord joining the sodium equilibrium potential to the peak current curve at that voltage, or, $g_{Na} = I_{Na}/(V_m - E_{Na})$. (Hereafter $g_{Na}$ will be used to mean peak $g_{Na}$.) $E_{Na}$, the sodium equilibrium potential, or the $V_m$...
where Na⁺ current is zero, is not significantly changed by alcohol treatment. $g_{Na}$ from several experiments is plotted as a function of $V_m$ during the test step in Fig. 5. In each case the magnitude of $g_{Na}$ is considerably reduced by alcohol treatment and the reduction is most marked for small depolarizations, so that maximum $g_{Na}$ for the treated axon is reached when the axon is more depolarized. The extent of this shift of the $g_{Na} - V_m$ relation was found to be a function of the magnitude of the current decrease effected by the alcohol, and is undoubtedly in part an artifact caused by the resistance between the electrodes in series with the membrane, $R$, in Fig. 2 (cf. Taylor et al., 1960; Cole and Moore, 1960). Inward current produces a voltage in $R$, that makes the actual membrane potential positive (i.e., the axon depolarized) with respect to the command voltage, $V_m$. Membrane potential and $V_m$ are the same only if current is zero or if the voltage across $R$, is compensated for.

The value of $R$, cannot be determined exactly and it is difficult to know what part of the $g_{Na} - V_m$ shift is artifact. The following experiment, suggested to us by Dr. Fred Dodge, indicates that most of the shift is artifact. The Hodgkin-Huxley equations imply that a conditioning step changes the magnitude of $g_{Na}$ (by changing the factor $h$) but does not alter the dependence of $g_{Na}$ on membrane potential; i.e., there is no shift along the voltage axis. If this is so,
any shift of the $g_{Na} - V_m$ relation as the conditioning pulse varies can be attributed to $R$, and eliminated by the proper compensating signal. This procedure at least provides a useful basis for comparison. In the experiment performed the conditioning pulses were a 40 mv hyperpolarization and a 5 mv depolarization. Maximum peak Na+ currents were respectively 1.75 ma/cm² and 0.81 ma/cm². Shift of the $g_{Na} - V_m$ curve was eliminated by setting potentiometer $S$ (see Methods). Following this procedure, alcohol treatment produced only a small shift of the $g_{Na} - V_m$ curve, about 5 mv, implying that the larger shifts of Fig. 5 are mostly artifact.

The reduction of the sodium conductance was measured in another way, by determining the instantaneous current-voltage curve during the period of

Figure 5. a-c $g_K$ (upper curves) and $g_{Na}$ (lower curves) as functions of membrane potential during the test step. a, micropipette technique. b, c, axial potential electrode. Test step was preceded by a 40 mv hyperpolarizing step to remove Na+ inactivation. d, See text. Depolarization is to the right.
high sodium conductance. The conductances estimated from such curves (Fig. 4) agree well with the maximum $g_{Na}$ obtained by the other method. The zero current intercept for the instantaneous curve differs from that of the peak current mainly because the instantaneous curve is not corrected for leakage current, which was not determined explicitly in this experiment. The filled circles in Fig. 4 give the instantaneous curve after correction by the approximate method applied to the peak current curves (inset of Fig. 4: leakage current is taken as the instantaneous step of outward current).

Steady-state inactivation as a function of $V_m$ was examined in several experiments (see Methods). No consistent change was found.

**TABLE II**

<table>
<thead>
<tr>
<th>Alcohol</th>
<th>Concentration</th>
<th>$g_{leak \ \alpha}$</th>
<th>$g_{leak \ \alpha}$</th>
<th>$g_{K \ \alpha}$</th>
<th>$g_{K \ \alpha}$</th>
<th>R.P.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>(ASW)</td>
<td>(ASW)</td>
<td>(ASW)</td>
<td>(ASW)</td>
<td></td>
</tr>
<tr>
<td>n-Propyl</td>
<td>0.13 M</td>
<td>0.75</td>
<td>0.13</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.13 M</td>
<td>0.50</td>
<td>0.13</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isobutyl</td>
<td>0.06 M</td>
<td>1.00</td>
<td>0.13</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.06 M</td>
<td>0.33</td>
<td>0.19</td>
<td>-54</td>
<td>-45</td>
<td>-56</td>
</tr>
<tr>
<td>Octyl</td>
<td>0.37 mM</td>
<td>0.86</td>
<td>0.19</td>
<td>-51</td>
<td>-49 to -46</td>
<td>-49</td>
</tr>
<tr>
<td></td>
<td>0.52 mM</td>
<td>1.8</td>
<td>0.19</td>
<td>-56</td>
<td>-60</td>
<td>-56</td>
</tr>
</tbody>
</table>

* LiCl replaced NaCl in ASW.

**Potassium Current, Conductance, and Resting Membrane Potential**

The potassium current was obtained as shown in the inset of Fig. 4. The potassium conductance is defined (Hodgkin and Huxley, 1952 a) by $g_K = I_K / (V_m - E_K)$. Because of the investment of the axon by the Schwann cell (Frankenhaeuser and Hodgkin, 1956) $E_K$ can only be estimated. In these experiments this is not a serious difficulty. If $E_K$ is unchanged by alcohol treatment, and we assume this to be so, the ratio of the treated and untreated currents at a given voltage is the ratio of the conductances, unless there is a large difference in current density. If there is, accumulation of potassium in the Schwann cell space will cause the conductance to be underestimated for the larger current flow.

In plotting Fig. 5 it was arbitrarily assumed that $E_K$ was equal to the resting potential of the untreated nerve. The potassium conductance is affected by alcohol in three ways. Fig. 5 a shows very little effect on $g_K$. ($g_K$ will be used to mean steady-state $g_K$. See inset of Fig. 4.) Such a pattern was seen only with octyl alcohol ($G_o$) in low concentration and was not associated with a depolarization. In one experiment (Table II) octyl increased $g_K$ near the resting potential. There was an accompanying hyperpolarization. In Fig. 5 b $g_K$ is
decreased for small depolarizing steps. This pattern was seen with concentrations of octyl that were more than sufficient to block, or with concentrations of alcohols C₄ through C₆ just sufficient to block. The constancy of this association argues for a fundamental difference in action between alcohols C₂ through C₆ and C₈ (cf. Bishop, 1932; and Crescitelli, 1948). In all cases this pattern is associated with a depolarization roughly proportional to the decrease in gₓ. In Fig. 5 c, gₓ is depressed over the entire voltage range. This is seen with high concentrations of all alcohols, and is associated with a large depolarization (more than 10 mV). The distinction between C₂ through C₆ and C₈ is emphasized by Fig. 5 d. It is clear that C₈ depolarizes much less for a given decrease of maximum gₙa.

Leakage Current

The leakage current was taken as the current flowing at Eₙa following a hyperpolarizing conditioning step (Adelman and Taylor, 1961). The effect of three alcohols on gₗeak is shown in Table II. (Average gₗeak for the untreated axon was 0.33 mmhos/cm².) Also shown is the effect, simultaneously determined, on the resting potential, and on gₓ as near the resting potential as it could be measured (usually about 20 mV depolarized). Examination of the curves of Fig. 5 indicates that the effect on gₓ at the resting potential was probably greater. In all cases a depolarization was accompanied by a decrease of the ratio gₓ/gₗeak.

Maximum Conductances As a Function of Alcohol Concentration

Fig. 6 is a composite of most of our results, showing the depression of maximum gₙa and maximum (observed) gₓ as a function of the thermodynamic activity of the alcohol in the perfusion fluid. The curves are an approximate fit of the points for n-propyl alcohol. The figure illustrates two facts. First, low concentrations of alcohols affect maximum gₙa much more than maximum gₓ. Similar results have been reported for procaine (Taylor, 1957), for urethane (Hagiwara and Saito, 1959), and for tetrodotoxin (Narahashi et al., 1964). Second, the thermodynamic activity for equivalent effect rises as the length of the alcohol's carbon chain increases. Thus, the first points for isobutyl alcohol are at thermodynamic activity slightly above 3 × 10⁻², while equivalent points for octyl alcohol are slightly above 7 × 10⁻².

DISCUSSION

Our results are in general agreement with those of Ferguson (1951) and Posternak and Larrabee (1951) regarding the increase in thermodynamic activity required to block as the chain length of the alcohol increases. Knowledge of the blocking thermodynamic activity, however, is really no more helpful than knowledge of the blocking concentration. From neither is it possible
to calculate the concentration of alcohol molecules in the membrane without knowledge of the sea water/membrane partition coefficient for the various alcohols. There is no direct way of determining this coefficient as the precise character of the membrane is not known. Mullins has attempted to guess the coefficient from data on narcosis (1954). Another approach is that of Skou, who made monomolecular films of myelin extract and measured the rise in surface pressure of these films as a function of narcotic concentration. Evidence that these films are similar, at least in some ways, to the axolemma of a frog sciatic axon is the close correlation between the surface or spreading pressure of the narcotic-treated film and the potency of the narcotic (Skou, 1954, 1958).

![Figure 6](image_url)

**Figure 6.** Depression of maximum $g_{Na}$ and maximum (observed) $g_{K}$ as functions of the thermodynamic activity of the alcohol in the perfusion fluid. Dashed lines approximately fit the points for n-propyl alcohol.

If we conclude that these films are similar in composition to the squid axon membrane, it is possible to calculate (Skou, 1954) from the data of Skou (1958) the number of alcohol molecules in the membrane for a given alcohol concentration in the aqueous phase. (The alcohol concentrations we employed were similar to those used by Skou, but we made no attempt to determine the minimum blocking concentration.) Calculated in this way, the number of molecules in the membrane at blocking concentration rises by a factor of 1.3 as the hydrocarbon chain of the alcohol increases in length from C2 to C6, beyond which Skou has no data. The number of molecules required to give a 9.3 dynes/cm rise in surface pressure increases by about the same factor.

In the following discussion it is assumed for simplicity that alcohols effect the same increase in spreading pressure of the axolemma that they effect in a myelin extract film. It may, of course, be impossible to increase the axolemmal...
C. M. ARMSTRONG AND L. BINSTOCK  

Effects of Alcohols on Squid Axon  

spreading pressure: membrane molecules may simply be squeezed into another phase, with no increase in pressure. Such an occurrence would not change the argument in principle.

The data presented obviously cannot be explained by the variation of a single parameter, such as surface pressure. Alcohols C₂ through C₆ do not decrease \( g_{Na} \) appreciably without decreasing the resting potential. Octyl alcohol, on the other hand, does.

The literature of monomolecular films suggests another possible variable, namely the tendency of a penetrating molecule to disrupt the cohesive forces of a film. An increase in spreading pressure of a film can arise from two factors: an increase in the occupied surface area (i.e., addition of molecules to a film at constant area), and disruption of the intermolecular attractive forces that keep the film from spreading (Davies and Rideal, 1961). In the present case one would expect that octyl alcohol, having a longer hydrocarbon chain than the other molecules tested, would interact more with the membrane molecules through van der Waals attractive forces and thus disrupt cohesion less. There is some evidence for this. Extrapolation of Skou's data to octyl indicates that more octyl molecules must be present in the membrane to block (or to increase surface pressure a given amount) than, say \( C₄ \) molecules. Octyl is thus less efficient in increasing spreading pressure than \( C₄ \). Both molecules have the same cross-sectional area, so to achieve the same effect with fewer molecules, \( C₄ \) must be more effective at disrupting membrane cohesion. In connection with this it is interesting that branching of the hydrocarbon chain decreases the requisite number of molecules (Skou, 1958).

There is another aspect of the increased alcohol-membrane cohesion as chain length increases. The energy required to move a \(-\text{CH}_2-\) group from a non-polar substance into water is approximately 600 cal/mole. Thus it would require 1800 cal more to move a mole of octyl from a non-polar membrane to water than would be required for \( C₄ \). Since this is about three times the random thermal energy, octyl molecules must leave the membrane much less frequently than \( C₄ \) molecules, making the octyl-filled membrane much less subject to small random reorganizations than is the case with \( C₄ \).

If the resting membrane potential is to be explained solely in terms of passive ion fluxes, octyl must affect resting membrane permeability differently from the other alcohols. Complete specification of the permeabilities determining the resting potential has not yet been achieved. It is generally thought that the ratio \( g_{K}/g_{leak} \) is the determining factor, where \( E_{leak} \) is somewhere between \( E_K \) and zero. There is evidence for the myelinated frog fiber that the leakage current is largely carried by \( K^+ \) ions (summarized by Dodge, 1963). For the squid axon the evidence is less conclusive, but the experiments of Adelman and Taylor at least make two other possible carriers, \( Na^+ \) and \( Cl^- \), unlikely. In the absence of evidence to the contrary, it might be supposed that
the leakage channel is specific for K⁺ ions, but that the specificity is limited, perhaps favoring K⁺ to Na⁺ by three to one. Evidence has been presented above that depolarizing concentrations of alcohols decrease the ratio $g_K/g_{\text{leak}}$, while low concentrations of octyl do not appreciably affect either conductance. Our data are not conclusive, but seem to indicate that a decrease of this ratio is largely determined by a decrease of $g_K$ (near the resting potential). This rules out an appealingly simple proposition, that C₂ through C₄ increase $g_{\text{leak}}$ by disorganizing the membrane. How disorganization of the membrane might be related to a decrease of $g_K$ near the resting potential is a matter for speculation.

The data are consistent with the idea that the conductance of the K⁺ specific channels is a small fraction of total membrane conductance at the normal resting potential (Baker, Hodgkin, and Shaw, 1962). Treatment with 0.13 m n-propyl alcohol, for example, decreases $g_K$ near the resting potential tenfold. Our resting $g_m$ measurements (0.6 msec.) reflect 75 per cent of this decrease, or roughly a sevenfold decrease of $g_K$. $g_{\text{leak}}$ is reduced twofold. These changes are accompanied by a twofold decrease of resting $g_m$ (not determined on the same axon), indicating that $g_{\text{leak}}$ is the major conductance of the normal resting axon. Indeed, $g_{\text{leak}}$ as determined at $E_K$ more than accounts for resting $g_m$, a reflection of rectification of the leakage current-voltage curve (Adelman and Taylor, 1961).

The authors gratefully acknowledge the helpful discussions of Dr. K. S. Cole and Dr. R. E. Taylor. We are indebted to Dr. Fred Dodge for many helpful suggestions regarding the manuscript.

Received for publication, January 29, 1964.

REFERENCES

C. M. ARMSTRONG AND L. BINSTOCK  Effects of Alcohols on Squid Axon
c


Ferguson, J., 1951, Relations between thermodynamic indices of narcotic potency and the molecular structure of the narcotic, in Mechanisme de la narcose, Centre National de la Recherche Scientifique, Paris.


Skou, J. C., 1958, Relation between the ability of various compounds to block nervous conduction and their penetration into a monomolecular layer of nerve tissue lipoids, Biochim. et Biophysica Acta, 30, 625.
