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This Week's Citation Classic

Hodgkin A L & Huxley A F. A quantitative description of membrane current and its application to conduction and excitation in nerve.
J. *Physiol. London* **117**:500-44, 1952.
[Physiological Laboratory, University of Cambridge, Cambridge, England]

The changes in sodium and potassium permeability which underlie the nerve impulse can be described quantitatively by equations which are consistent with the idea that movement of membrane charges or dipoles, produced by changes in electric field, control gates to Na^+ and K^+. When these equations are solved, they account quantitatively for the shape and velocity of the propagated impulse and the associated conductance change and ionic movements, as well as several puzzling subthreshold phenomena. [The *SCI*® indicates that this paper has been cited over 1,970 times since 1961.]

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"This paper concludes a series describing experiments which we carried out with B. Katz in the summers of 1948 and 1949 on the giant nerve fibres of the squid. The method we used was introduced in a simplified form by K.S. Cole, who started experiments with it in 1947.[1,2] Our version required us to insert two metal wires down the axis of a nerve fibre —to avoid electrode polarization effects, separate wires were used for passing current and for sensing the resulting changes of potential. We did this by winding two 20 µm silver wires in a double helix round an 80 µm glass rod and then pushing the assembly down a track predrilled with a smooth capillary by the method that we introduced in 1939.[3] A feedback amplifier sends through one wire whatever current is needed to make the other wire undergo a step-like change of potential, and the time course of this current through the membrane is recorded. This is much easier to interpret than the results of simpler procedures such as recording voltage at constant current or, as in most previous experiments,' of applying a stimulus and letting the nerve take charge.

"Carrying out a good voltage-clamp experiment is rather like climbing a beautiful mountain by a difficult route. Of course there is no danger, but you have to go through a whole series of tricky operations over five or six hours and a single mistake can wreck all the hard work done by your colleagues and yourself. A cleaned squid nerve fibre with a double spiral of wire inserted correctly down its axis is really a most satisfying object and it is a pity that so few people have the opportunity of repeating these experiments. Perhaps some of the aesthetic pleasure and excitement associated with the experiments have crept into the dry pages of a scientific journal and have attracted a wider range of readers than usual.

"Another reason why our paper has been widely read may be that it shows how a wide range of well-known, complicated, and variable phenomena in many excitable tissues can be explained quantitatively by a few fairly simple relations between membrane potential and changes of ion permeability —processes that are several steps away from the phenomena that are usually observed, so that the connections between them are too complex to be appreciated, intuitively. There now seems little doubt that the main outlines of our explanation are correct, but we have always felt that our equations should be regarded only as a first approximation that needs to be refined and extended in many ways in the search for the actual mechanism of the permeability change's on the molecular scale."

1. **Cole K S**. Dynamic electrical characteristics of the squid axon membranes. *Arch. Sci. Physiol.* **3**:253-8.
2................. *Membranes, ions and impulses.* Los Angeles. CA: University of California Press. 1968. p. 241-69.
3. **Hodgkin A L 4 Huxley A F.** Action potentials recorded from inside a nerve fibre. Na*ture* **144**:210-11. 1939.

* The experimental work on which this article is based was largely done at the Laboratory of the Marine Biological Association, Plymouth, during 1948 and 1949.