Upsala Journal of Medical Sciences

ISSN: 0300-9734 (Print) 2000-1967 (Online) Journal homepage: http://www.tandfonline.com/loi/iups20

Swelling of Nerve Fibers during Action Potentials

I. Tasaki & K. Iwasa

To cite this article: I. Tasaki & K. Iwasa (1980) Swelling of Nerve Fibers during Action Potentials, Upsala Journal of Medical Sciences, 85:3, 211-215, DOI: 10.3109/03009738009179190

To link to this article: http://dx.doi.org/10.3109/03009738009179190

Published online: 17 Mar 2010.

Upsala J Med Sci 85: 211–215, 1980

Swelling of Nerve Fibers during Action Potentials

I. Tasaki and K. Iwasa

National Institute of Mental Health, Bethesda, Maryland and Marine Biological Laboratory, Woods Hole, Massachusetts, USA

ABSTRACT Nerve fibers swell concomitantly with the initiation of an action potential. Pronounced shrinkage follows the phase of swelling. These mechanical changes are attributed to the movement of water predicted by Teorell.

INTRODUCTION In Teorell's electrohydraulic nerve analog (3), three forces are in operation: salt concentration gradient, electric potential gradient and pressure gradient. The cooperation of these forces gives rise to periodic or rhythmical fluxes water and solutes. In a review published in 1962, Teorell (4) made the following statement:

> "It is not likely that biological membranes are rigid; they may rather be distendable and elastic. Thus forces, balancing a possible electroosmotic pressure, may be developed within the membrane structure itself. Different layers in the composite membrane may have varying charge densities and hydraulic permeability.... It might perhaps be possible that this (membrane) structure can be subject to swelling or shrinkage, in the sense we have dared to suggest here.

Teorell's point of view as to the structure of the nerve membrane and his imaginary process of swelling of the membrane structure during excitation are schematically depicted in Figure 1. Up to the present, however, no one has published direct experimental evidence in support of Teorell's viewpoint.

Last year, we have constructed new devices for measuring small, rapid mechanical changes and succeeded in demonstrating minute movement of the nerve membrane during excitation (1, 2). The present paper describes the methods and the results of our experiments demonstrating that many aspects of the remarkable prediction made by Teorell a long time ago have actually been realized.

MATERIAL AND METHODS Giant axons taken from squid available in Marine Biological Laboratory, Woods Hole, Mass., were used after extensive cleaning

of a 4 mm long middle portion. The axon was kept under tension in a nerve chamber with a convex bottom (1). Action potentials were induced repetitively in the axon by introducing into the chamber a low Ca-salt solution containing 4 mM $CaCl_2$ and 500 mM NaCl. Detection of mechanical changes of the axon was carried out during repetitive firing of action potentials in the middle portion of the axon. Simultaneously, action potentials were observed using a pair of extracellular platinum electrodes located 4 mm away from the site of mechanical recording.

A Fotonic sensor, purchased from Mechanical Technology, Inc. Latham, New York, was incorporated in our device for measuring small displacements of the axon surface. The sensor consists of two bundles of fine optical fibers mixed at one (sensing) end: one bundle for carrying white light from a source (quartz-iodine lamp) to the surface of the axon and the other for transmitting the light from the axon surface to a photo-detector (Pin-10, United Technology, Inc., Santa Monica, Cal.). To enhance the reflectivity of the axon surface, a small piece of gold leaf (about 100 μm in diameter) was placed on the axon. With this arrangement, the intensity of the light detected depends strongly on the distance between the gold leaf on the axon and the sensor. The time-course

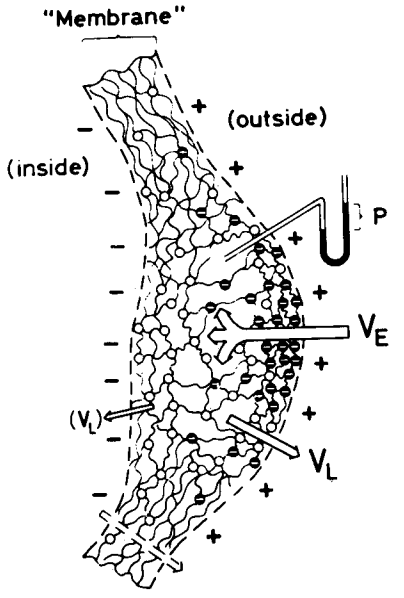

Fig. 1. A hypothetical excitability unit localized in a negatively charged, elastic membrane structure. (From T. Teorell, Biophys. J. 2: supplement, 1962, with permission).

of the displacement of the axon surface could be determined by measuring the variation of the light intensity associated with production of action potentials.

A piezo-ceramic bender (model R050S, Gulton Industries, Inc., Metuchen, N.J.) was employed for detection of small changes in the swelling pressure of the axon. Used in conjunction with a voltage-follower, the sensitivity of this mechano-electric transducer is about 0.5 mV per mg. When driven with a condenser microphone, the bender can follow mechanical vibrations up to 10 kHz. To pick up pressure changes in the axon, a small stylus (1 mm in diameter and about 5 mm in length) was attached to the free (sensing) end of the bender.

The outputs of both the voltage-follower and the photo-detector were amplified by a factor of 1,000 with a conder-coupled amplifier. A signal averager (Model SW-71B, Nicolet Instrument Corp., Madison, Wis.) was used to record mechanical responses of the axon. The experiments were carried out at room temperature (20-22°C).

RESULTS Figure 2 shows an example of the records obtained by using the Fotonic sensor. The downward deflection of the upper trace in the figure represents a decrease in the light intensity produced by an outward movement of the axon surface. It is seen that a diphasic mechanical response was

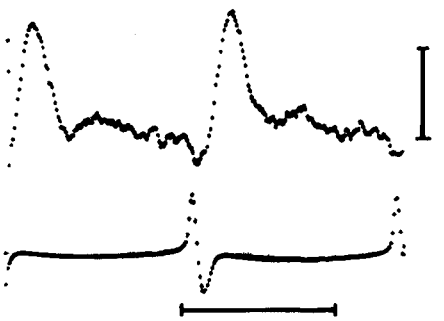

Fig. 2. Upper trace: Displacement of the axon surface associated with action potential. Lower trace: Extracellularly recorded action potential. The squid axon uder study was firing action potentials repetitively and the signal averager used for recording was triggered by the action potentials. Vertical marker indicates 1 nm, and horizontal marker 5 ms.

produced at the time when the axon developed an action potential. The first phase of the mechanical response represents swelling of the axon associated with the initiation of the action potential. The second phase, which represents pronounced shrinkage of the axon, was abruptly terminated shortly after the end of the spike. In the interval between two successive spikes, there was a small, gradual increase in the axon diameter.

The displacement of the axon surface revealed by this method was of the order of 10 Å in amplitude. This value is too large to be attributed to the difference in specific molar volume between Na- and K-ions which are known to exchange across the axon membrane during the course of an action potential. Invasion of water into the axon during the first phase of the mechanical responses, followed by a reverse process in the second phase, seems to be the only reasonable explanation of the finding described above.

The upper trace in Figure 3 shows an example of the records obtained with a piezo-ceramic bender. The downward defection of the trace represents a rise in the pressure exerted by the axon on the bender. Undoubtedly, the observed pressure changes are an isometric counterpart of the displacements observed with the Fotonic sensor. Again, we see that the mechanical response associated with the production of an action potential is diphasic. The first phase represents a sign of swelling which takes place concurrently with the onset of an action potential. The second phase is a manifestation of shrinkage occurring toward

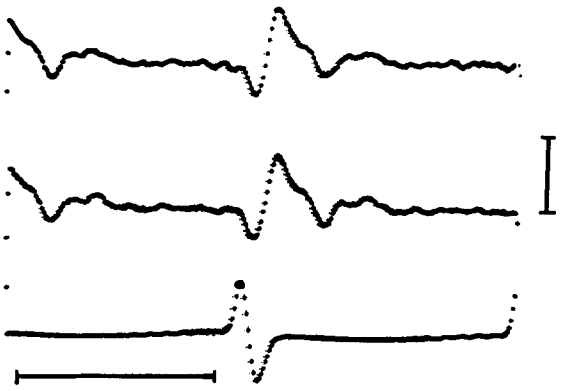

Fig. 3. Upper trace: Pressure changes in axon associated with action potential. A downward deflection represents a rise in the swelling pressure. Vertical marker indicates 5 x 10^{-2} dyn, and horizontal marker 5 ms. Lower trace: Extracellularly recorded action potential.

the end of the spike. Shortly after the end of the spike, there is a small abrupt shrinkage followed by a gradual swelling.

CONCLUSION Using squid axons, we have examined mechanical responses of nerve fibers under a variety of experimental conditions. We believe that the results obtained are quite consistent with Teorell's prediction quoted in the Introduction. We thus conclude that the macromolecules in and near the axon membrane are "distendable" and "elastic" and that the membrane structure actually "swells" and "shrinks" when an action potential is generated.

REFERENCES

1. Iwasa, K. & Tasaki, I. Mechanical changes in squid giant axons associated with production of action potentials. Biochem. Biophys. Res. Comm. (in press)
2. Tasaki, I. & Iwasa, K. Shortening of nerve fibers associated with propagated nerve impulse. Biochem. Biophys. Res. Comm. 94: 716-720, 1980.
3. Teorell, T. Electrokinetic membrane processes in relation to properties of excitable tissues. II. Some theoretical considerations. J. Gen. Physiol. 42: 847-862, 1959.
4. Teorell, T. Excitability phenomena in artificial membranes. Biophys. J. 2 (supplement) 27-52, 1962.

Received 80 08 28

Address for reprint requests:

Ichiji Tasaki
NIMH, 9000 Rockville Pike,
Bethesda, Md 20014,
USA