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This Week's Citation Classic

Toyoda J, Nosaki **H & Tomits T.** Light-induced resistance changes in single photoreceptors *of Necturus* and *Gekko. Vision Res.* **9**:453-63, 1969.
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Vertebrate photoreceptors respond to light with hyperpolarization, namely, with an inside negative potential change. Studies on their membrane properties indicate that the receptors are kept depolarized in the dark, as is common in nerve cells at their excited state, and become repolarized toward the resting membrane potential upon illumination. [The SC/® indicates that this paper has been cited over 180 times since 1969.]

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"First of all, I would like to say how pleased we are to learn that our paper is listed as one of the most-cited articles in its field.

"The experiments described in this paper were performed using ordinary neurophysiological techniques and the results obtained were analysed on the basis of the neurophysiological principles widely accepted. In this respect, the paper is not especially epoch-making. The reason why it is cited so frequently is probably in its simple but unexpected conclusion that the vertebrate photoreceptors are excited in the dark and return to the resting state upon illumination. Generally, the membrane potential of the nerve cells is inside negative at the resting state, but shifts to positive upon excitation due to an increase in the permeability of the membrane to sodium ions which then tend to enter the cell. This positive potential change is called depolarization.

"The intracellular recording from vertebrate photoreceptors was first reported in 1965[1] It was shown that they respond to light with hyperpolarization in contrast to most invertebrate photoreceptors which are known to re spond to light with depolarization. This first attempt to record the intracellular response from photoreceptors met with many difficulties. The main problem was that even with microelectrodes of tip diameter less than 0.1 um, the retinal cells easily escaped from the tip when the electrode was inserted gently into the retina. One of us, T. Tomita, tried to solve this problem by giving high acceleration to the electrode advancement. However, he happened to think of giving a high frequency vibration to the retina instead of giving an acceleration to the electrode. This method was found very effective. Even with the aid of such a jolting method, however, it took almost three months before we finally had the first sign of intracellular recording.

"The unusual response polarity of vertebrate photoreceptors immediately led us to the present experiments to solve the mechanisms underlying the response. The major problem was the size of the receptors. In order to study the permeability change of the membrane it was necessary to use double-barreled electrodes, with one barrel for recording the potential change and the other for passing electric current. The carp receptors we used at the beginning were too small to allow intracellular recording with such electrodes. The mud puppy and gecko, known to have large photoreceptors, were finally found to meet this purpose.

"The concept that the outer segment membrane of vertebrate photoreceptors becomes impermeable to sodium ions in response to illumination is now commonly cited in standard textbooks and monographs.[2] It served as one of the stepping-stones for later studies on the function of photoreceptors."

1. **Tomita T.** Electrophysiological study of the mechanisms subserving color coding in the fish retina. *Cold Spring Harbor Symp.* **30**:559-66, 1965.
2. **Rodieck R W.** *The vertebrate retina. Principles of structure and function.* San Francisco. CA: W. H. Freeman. 1973. 1044 p.