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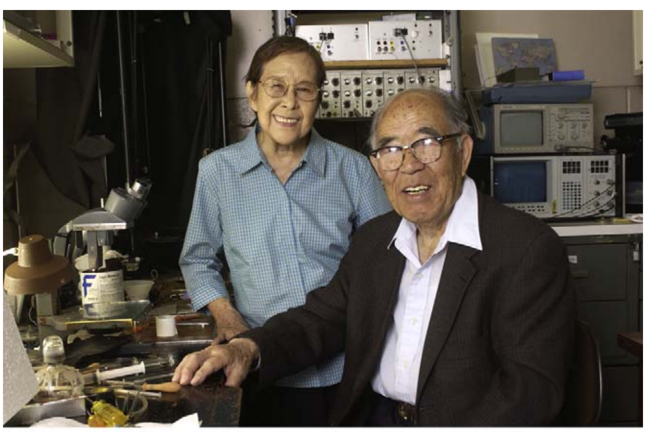
# Obituary: Dr. Ichiji Tasaki

Dr. Ichiji Tasaki, who has made a number of discoveries in the mechanisms of the conduction of electrochemical signals in nerve cells, died on January 4 in 2009 in Bethesda, Maryland, USA at the age of 98. Up until just a few days before he had been very active mentally as well as physically, but on a stormy day he fell as he was walking near his Bethesda home heading to his lab at the National Institutes of Health (NIH).



Dr. Ichiji Tasaki at his lab with his wife, Mrs. Nobuko Tasaki.

Dr. Tasaki was born in Fukushima, Japan in 1910. He studied medicine at Keio University Medical School in Tokyo, Japan and received his M.D. for his initial study on the electrophysiological properties of nerve fibers in 1938. After World War II, he extended his research in England and Switzerland through a Rockefeller Fellowship. In 1951 he moved to the United States to work at the Central Institute for the Deaf at Washington University in St. Louis. In 1953, Dr. Tasaki began his career at the NIH as a senior scientist at the National Institute of Neurological Disorders and Blindness (NINDB). In 1961 he moved to the National Institute of Mental Health (NIMH). From 1966 to 1984, he was chief of the Laboratory of Neurobiology at the NIMH and subsequently a senior researcher. Since 1998 he was a senior researcher at the National Institute of Child Health and Human Development (NICHD) until he retired as scientific emeritus in 2008, and continued to work in that capacity until his death.

During his long research career at the NIH, Dr. Tasaki spent most days in his laboratory with his wife of nearly 70 years, Mrs. Nobuko Tasaki, carrying out a wide range of extremely delicate and ambitious experiments in order to understand the signaling mechanisms of the electrical excitation and signal conduction in nerve cells and their axons. Dr. Tasaki mentored a number of prominent researchers including Dr. Gen Matsumoto (group director at RIKEN Brain Science Institute, until he passed away in 2003) and Dr. Susumu Terakawa (professor at Hamamatsu University School of Medicine). He was officially the supervisor of Dr. Robert Wurtz who then became a laboratory chief at the National Eye Institute (NEI). I came to know Dr. Tasaki in early 1980s when I was working with Dr. Wurtz in the first floor of Building 36 at the NIH.

By studying the peripheral nerves of the frog electrophysiologically, Dr. Tasaki discovered that the action potentials conduct along the axon very quickly by jumping from one discrete position to the next, a phenomenon called ‘saltatory conduction’. This is now a fundamental fact in neuroscience. In many animals (but not all) the peripheral nerve fibers or the central axons are enclosed by a membranous structure called the myelin sheath. Although its existence had been known since the 19th century, the function of the myelin sheath had been unclear until Dr. Tasaki’s discovery. Using elegant and sophisticated electrophysiological methods, Dr. Tasaki first demonstrated that electrically excitable points are sparsely and regularly distributed along a single nerve fiber and those points correspond to the nodes of Ranvier, breaks of myelin sheath. He then demonstrated that an action potential literally jumps from one node of Ranvier to another, while the intervening myelin sheath functions as the electrical insulator.

One of the most important discoveries in neuroscience is that information is carried along the axon in the form of spiky electrochemical waves which are called action potentials or impulses. The axons are like electric cables and the brain is like an integrated electric circuits. However, the speed of impulse conduction is nowhere nearly as fast as that of the signals in electric cables, and this posed a problem for animals which needed quick escape or attack reactions, especially as the animals became larger during evolution. Saltatory conduction revolutionalized the way in which neuronal signals are conveyed. Owing to the insulating effect of the myelin sheath, the signal conduction became much faster, more reliable, and less influenced by external noise. It became much more cost-effective because energy expenditure was minimized. In order to achieve an equivalent level of performance without saltatory conduction with the myelin sheath, our brain would need to be probably 100 times larger and would need much more oxygen and energy. In this sense, the saltatory conduction represents a big leap in evolution, and its discovery by Dr. Tasaki was a historical event in neuroscience.

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The huge advantage of saltatory conduction implies that animals are at risk of losing it. In various neurological disorders the myelin sheath is destroyed (demyelination) as seen in multiple sclerosis, Guillain–Barré syndrome, and mercury poisoning, or defective (dysmyelination) as implicated in leukodystrophies. The wide spectrum and severity of the symptoms in these patients demonstrate the importance of the myelin sheath, and recognizing saltatory conduction as a major function of the myelin sheath was an important step toward the cure of these neurological disorders.

Dr. Tasaki came to the idea of saltatory conduction in 1938 in the experiments conducted at Keio University in Tokyo, and submitted a manuscript to the American Journal of Physiology in 1939. Unfortunately, however, it coincided with the beginning of World War II, and the manuscript was not published. Unfazed by such a difficult situation, Dr. Tasaki repeated and extended his earlier observations, and wrote two manuscripts in German. The manuscripts were first sent to Frankfurt via Siberian rail-road. But the Siberian route became unavailable in 1941, and the manuscripts were then sent to Frankfurt by submarine via South America. A long time after the end of the war, it was found that the manuscripts sent to Germany had been accepted and published in Pflügers Archiv in 1941. This is the story that Dr. Tasaki told me when I was studying at the NIH. More details are described in his own recent article (Tasaki, 2007).

Saltatory conduction was a start of Dr. Tasaki's scientific endeavor. During his career in England, Switzerland, and USA, he developed models of membrane excitability using highly sophisticated methods which seemed beyond the scope of a single individual researcher. His goal was to understand the fundamental nature of nerve cell excitation as physicochemical phenomena of nerve cell membranes. The cell membrane is a lipid bilayer in which large protein molecules are embedded. Based on a series of experiments Dr. Tasaki concluded that rapid changes in the conductance of univalent ions across the nerve cell membranes, particularly sodium ions, are caused by the rapid conformational transitions of the protein molecules which are caused by the changes in the state of its cross linkage with calcium ions. His model is summarized in his book (Tasaki, 1982).

In 1952 Hodgkin and Huxley published a series of papers and proposed a model explaining how action potentials in neurons are initiated and propagated. Specifically, action potentials are caused by reversible alterations in sodium and potassium permeability arising from changes in membrane potential. Implicit in this model was the concept of 'ion channels', which later was confirmed using various methods. The Tasaki model at least superficially appeared to contradict the Hodgkin–Huxley model, and for that reason has not attracted much attention. Retrospectively, however, Dr. Tasaki's model had gone one step beyond the Hodgkin–Huxley model, because it was later demonstrated that protein molecules constitute the ion channels and undergo conformational transitions which gate the ionic fluxes.

Dr. Tasaki's obsession in the physical and chemical nature of nerve cells led him to a different horizon in neuroscience. He was a pioneer in measuring changes in mechanical, thermal, and optical properties of single nerve axons and structures innervated by the axons (e.g., skin). Optical recording is now one of the most successful new technologies in neuroscience. In 1968 two research groups came to the basic idea of optical recording, and Tasaki's group was one of them (see Tasaki et al., 1969). Dr. Tasaki probably had no intention to apply the optical recording method to visualize the pattern of neural activation in the brain of behaving animals or humans, but this shows a typical relationship between science and technology: Applied science or technology is often born out of basic science unintentionally. In this sense, Dr. Tasaki's mission is still ongoing. His basic observations on the mechanical or thermal changes associated with neural activation may turn out to be another successful technology some time in future.

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