

HOW I FELL IN LOVE WITH JAPAN

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In 1956 I was working in the lab of Stephen Kuffler, at Johns Hopkins University in Baltimore, Maryland and I met Susumu Hagiwara, the first Japanese physiologist I was to know. We worked together on the crayfish stretch receptor for a few months. I enjoyed working with him. I had a car and he did not, and so I drove him to work most days. He was a very sweet and kind person, with a nice sense of humor. In addition he was more of a biologist than I was. My background was in physics, while as a child he had collected butterflies and studied birds and other animals. He had published a paper on how the time when the cicadas started to chirp in the morning depended on the level of light, and in addition he had compared the frequencies of the outputs of the frog stretch receptor with the outputs from motor units in the mammal. Afterwards he worked at UCLA and La Jolla and was a very inventive and thoughtful investigator. Best known, perhaps, for discovering and describing calcium channels, he examined many other preparations including the Mauthner's neuron of fish, both the pre- and postsynaptic sides of the squid giant synapse, the pacemaker and the follower cells of a miniature crustacean ganglion in the wall of the heart and the specialized receptors that sense electric organ discharges from the same fish. Years later I was fortunate to spend a most enjoyable few weeks with him looking at contractions in barnacle muscle.

In 1958 I moved to Salt Lake City, Utah, and during the next two years, Motoy Kuno, Koji

Uchizono and Akira and Noriko Takeuchi (she was the first women physiologist I encountered in Japan, and I met very few later), worked there. I was to meet all of them later in my travels in Japan. I moved to Minneapolis, Minnesota in 1960 and there I met Hiromasa Okada.

In 1965 I attended the International Physiological Congress in Tokyo. It was a large meeting with attendees from all over the world. I think Japan's hosting of the meeting was part of a program to show that after the World War Japan was ready to rejoin the world. Indeed the meeting followed the 1964 Olympics, also in Tokyo. I met a number of people, but I remember Yasuji Katsuki, who was Hagiwara's teacher. It turned out that Okada's father was a high official in the government of the city of Tokyo, and I was invited to a banquet where young women helped serve us and amuse us with various games during the meal. This was quite different from anything I have encountered before, or, indeed, afterwards.

After the Congress I attended two satellite meetings, one on membranes in Kyoto and one on muscle in Hakone, where I met Setsuro Ebashi, one of the leading muscle researchers in Japan, known for his work on Troponin, a basic muscle protein. I stayed in a Ryokan for the first time. My visit to Kyoto turned out to be quite significant after I started visiting the beautiful gardens in this city. I discovered a newly published book, *Kyoto, A Contemplative Guide*, which led me to visit Uji. It was somewhat difficult to get there,

but once there, I found the Byodo-In which I found be an amazingly beautiful building. At that time, one could be closer to the Amida than is permitted now. After visits to Ryoan-Ji, Kyomizudera and a number of other sites, I decided that these temples and gardens were among the most beautiful works ever made by humans.

During a later visit, I spent the day with Motoy Kuno, who after working at the University of North Carolina, had returned to Kyoto to be Chairman of Physiology at the University. We visited Uji together, and stopped at a tea stall on the way to the Temple. I received a lesson on the properties of Uji tea (he translated), which I shall never forget. Later that day we were walking around Kyoto and found a garden with the grave of Tanizaki Junichiro and Kuno showed me the grave of his father in the same garden.

In 1978 Yutaka Oomura and I organized an international conference on the Structure and Function of Receptor and Ion Channels in Biological Membranes at the National Institute of Physiological Sciences in Okazaki. There were 25 papers offered by scientists from 5 countries. Carpenter (AFRI, Bethesda) reported on the actions of putative transmitters in *Aplysia* neurons, Edwards (Albany NY) had used a variety of cations of various sizes to look at the size of acetylcholine controlled channel at the frog end-plate, Maeno, Sawada and Enomoto (Shimane Univ.) looked at the action of a quaternary compound on *Onchidium* neurons, Takahashi (Tokyo Univ.) examined the membrane channels in unfertilized tunicate eggs, Hagiwara (UCLA) did similar studies on starfish eggs, Akaike, Yasui and Brown (Univ. Texas), Kostyuk, Kristhal, Pidoplichko and Shakhvalov (Acad. Sci. Ukrainian) looked at the channels in single neurons of *Helix*, Klee (Max-Planck-Inst.) looked at slow, outward currents in *Aplysia*, Llinas, Steinberg, and Walton (New York Univ.) investigated the calcium currents underlying



Photo-1. The international conference at Okazaki in 1978.

transmitter release at the squid giant synapse, Yamagishi (Okazaki), reported on calcium currents in the squid giant axon, Zachar and Heneck (Slovak Acad. Sci.) used voltage clamp to investigate the four conductances present in crayfish muscle, Ritchie (Yale Univ.) used radioactive saxitoxin to measure the numbers of Na^+ channels, Takenaka, Yoshioka, Horie, Inoue, and Hori (Yokohama City Univ.) looked at the properties of the membrane of the squid giant axon, Oomura, Maruhashi, Shimizu and Kato (Kyushu Univ.) investigated the presence of certain amino acids in the GABA activated channels in *Onchidium* and Sato, Maruhashi and Yai (Iwate Med. Univ.) did similar studies on *Aplysia* ganglion cells, Tasaki (NIMH, Bethesda) carried out spectral analyses of the signals in the squid giant axon membrane, Watanabe and Nagano (Tokyo Med. Dent. Univ.) looked at the effects of various cations on the same responses, Kobatake (Hokkaido Univ) examined chemotactic responses in protozoa, the possible restrictions of movements of ions through channels were investigated by Hille and Schwartz and Hagglund, Enos and Eisenman (UCLA) and Paul Mueller (Eastern Pennsylvania Psy. Inst.) reported on the properties of channels in bi-layers.

In 1981 I was awarded a fellowship from the Ja-

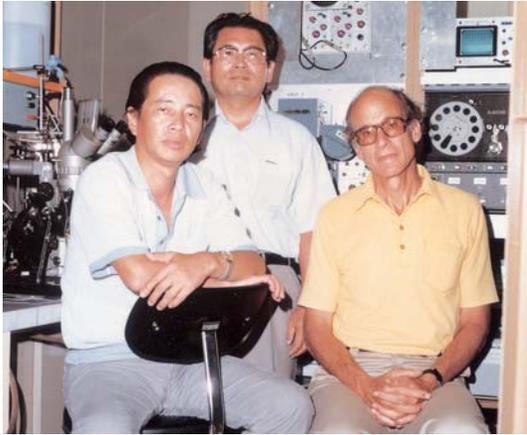


Photo-2. Sawada, Maeno and Edwards at Shimane in 1981.

pan Society for the Promotion of Science (Nihon Gakujutsu Shinkokai). I spent one month at Kyushu University (Yutaka Oomura), one at Shimane Medical University (Takashi Maeno), and one month visiting other labs, attending meetings and seeing a little bit of the country, especially Kyushu and southern Honshu. At Kyushu, we investigated the selectivity of the chloride channel in frog spinal ganglion cells (with Norio Inomata, Oomura and Norio Akaike) and that of acetylcholine and voltage activated channels in Onchidium neurons. At Shimane Ko-ichi Enomoto, Takashi Maeno and I examined the effects of guanethidine on transmitter release at the frog neuromuscular junction.

The labs I visited included Juntendo University where Akira Takeuchi was looking at the effects of glutamate at the crayfish neuromuscular junction, and Noriko Takeuchi was examining the effects of various substances on the release of acetylcholine at the frog neuromuscular junction, Tokyo Medical and Dental University, where Taro Furukawa was looking at transmitter release from the goldfish hair cell, Tokyo University, where Jun Fukuda was growing guinea pig spinal nerve cells in culture, while at the Brain Insti-

tute of Tokyo University Kunitaro Takahashi was examining the developing tunicate egg with electrophysiological techniques, at Kinki University Shiko Chichibu was looking at the sensory hairs on various areas on the surface of the crayfish, at Osaka City University Shiushi Matsuura was investigating the mechanisms underlying the adaptive changes in firing of auditory fibers, at Hiroshima University Issei Seyama, in the Medical School, was doing a structure-function study of grayanotoxin and related compounds, and Yoshinobu Kanno in the Dental School was interested in electrical communication between epidermal cells in culture, Makoto Kobayashi was studying the cross striated muscles of the local mollusk, at Kawasaki Medical School in Kurashiki, Hiromasa Okada was looking at neural control of defecation and urination, and Motoo Matsumura was looking the effects of strontium on crayfish muscle contraction, at Shiga University of Medical Science Hiroshi Kitasato was looking at the effects of insulin on muscle membrane potential, at Kumamoto University, Katsuhide Nishi was investigating calcium currents in snail neurons, at Kurume University, Kyozo Koketsu was studying calcium currents in bullfrog sympathetic ganglion cells while Shogoro Nishi was looking at possible transmitters in slices of cat lateral horn cells, at Kyoto University, Motoy Kuno, newly arrived, was looking at membrane properties of spinal motor neurons in newborn rats, at Kyushu University, Yutaka Oomura was interested in the role of the hypothalamus in feeding behavior and Hiroshi Kuriyama and colleagues were studying various aspects of the physiology of smooth muscle, and at the National Institute for Biological Sciences in Okazaki, Koji Uchizono was looking at a sleep promoting substance, Akira Watanabe was investigating changes in optical properties of the squid giant axon during an action potential, and Hiroyuki Sugiyama was

comparing the properties of junctional and extra junctional acetylcholine receptors in denervated rat muscle.

In a report I wrote on my return I noted that there was good support for basic physiological research in Japan and much of the work was of top quality. The research space was adequate and reasonably well equipped. Each department received basic funding for research, with the possibility of increased funding by applying for a grant. I noted that while many Japanese scientists had worked in the US with local support, there was little support for foreign trainees in Japan and so their numbers were small. Several Japanese scientists have made careers in the US, in particular Motoy Kuno at the University of North Carolina, who did return in Kyoto, Toshio Narahashi at Duke University, Ichiji Tasakai at the National Institute of Health, Kiyomi Koizumi at SUNY School of Medicine in Brooklyn, Kyozo Koketsu at the University of Illinois College of Medicine and Hiroshi Asanuma at the Rockefeller University.

In other trips to Japan, I met additional physiologists including Masao Ito (I was on the Editorial Board of his journal, *Neuroscience Research*, at one point), Nakaakira Tsukahara and Akimichi Kaneko. Over the years several Japanese scientists have worked in my lab, including Takashi Maeno, Ko-ichi Enomoto and Sonoko and Kishio Furuya.

I continued to edit some of Hagiwara's manuscripts over the years, and in time I started editing manuscripts for others. In the 1990s I edited the abstracts for the Annual Meeting of the Ja-

pan Physiological Society. This procedure was somewhat cumbersome, and was soon discontinued. I did post a sample abstract online, but I have no idea whether anyone has ever looked at it. I led two workshops on writing *Neurophysiological Papers in English*. In each, papers were submitted before the meeting, and I selected a paragraph from each submission to be examined by the conferees.

Several years ago, my wife and I were finally able to get to Japan to see Sakura first hand, and it was trip I shall never forget. Our friend, Miyuki Kuno helped us to select the date of travel and we hit it correctly. After several days in Tokyo to get over jet lag and to see Ueno Park we went to Kyoto. In the next ten days we visited as many gardens and temples as we could, each one more beautiful than the previous one. We discovered also that several sites are open only during that period.

We have many other fine memories of Japan, such as the gracious hospitality of the people, being buried under the warm sand on the beach in Kyushu, seeing Mt Aso (from a distance), seeing how several persimmons are left on the trees in the fall for the birds, walking the streets of Kyoto on New Year's Eve where people were carrying ropes with burning ends, watching the Gion parade in Kyoto from our hotel room, the gardens of Kyoto, especially the stone beach at the Sento Goshō, the "wedding rocks" at Futamigaura, the temple at Ise especially the giant *Cryptomera* trees and visiting several of the major ceramic areas, including Hagi, Kyoto (Raku), Bizen and Imari.