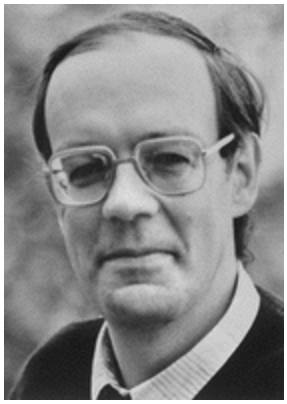
# Autobiography



I was born during the second world war in Stuttgart, the capital of Swebia, as the first of two children. My father, Bertold Sakmann, was the director of a theatre, the third son of a physician whose family had lived in southern Germany for several generations. My mother, Annemarie Sakmann, was a physiotherapist and was born in Bangkok, the second child of a Prussian physician who served as doctor to the King of Siam and was the founder of the first hospital in Siam.

During the first half of my childhood I grew up in Lindau, on Lake Constance, in a completely rural environment. There I went to elementary school, before returning to Stuttgart where I completed my Abitur at the Wagenburg Gymnasium. My only real interests at school were the physics lessons. At home I spent most of my time designing and building model motor and sailing ships as well as remote control aeroplanes. It was generally assumed that I would become an engineer. In the final year of school however I learned about cybernetics and its possible application to biology. Cybernetics fascinated me, because it seemed to me that living organisms could be understood in engineering terms.

Since I could not make up my mind between physics and biology I enrolled at the medical faculty of Tübingen University. The first two years in medicine offered a broad spectrum in biochemistry and physiology and I decided to do my doctoral thesis in electrophysiology which seemed to be closest to engineering. At the time it was common practice to study at several different medical schools and I attended schools in Freiburg, Berlin and Paris. My decision to finish medical studies in Munich was largely dictated by a beautiful young lady whose attention I was desperate to catch in Tübingen, though without initial success. Today Christiane is my wife and we have two sons and a daughter. Christiane is a highly successful ophthalmologist specializing in pediatric ophthalmology. For most of the time since we have been married I have been known in Göttingen and Heidelberg as the "eye doctor's husband".

At that time 'biological cybernetics' was a field that fascinated many students of biology and physics. Werner Reichardt's and Bernhard Hassenstein's quantitative behavioural analysis of a beetle's optomotor response promised to make brain functions understandable in terms of information theory. Otto Creutzfeldt in the Kraepelin Institute in Munich accepted me as a doctoral student to work on the electrophysiological basis of pattern recognition. Although small by today's standards, the Kraepelin Institute encompassed almost all aspects of neurobiology at the time, ranging from voltage clamp current recordings from snail neurones in Dieter Lux's department to quantitative analysis of monkey behaviour in Detlev Ploog's department. In Otto Creutzfeldt's department, great enthusiasm and optimism prevailed in trying to understand and build models of pattern recognition by the visual system, and there was close collaboration with electrical engineers and computer scientists from the Munich Technical University. After three

years of experimental work on the neurophysiological basis of light adaptation in the cat's visual system I realized that the central nervous system (CNS) was too difficult to comprehend without understanding the synaptic connections more clearly. I went to a course on basic mechanisms of vision in a summer school and I attended a lecture given by Bernard Katz on nerve, muscle and synapse, which convinced me that cellular physiology would be very helpful in trying to understand the functions of the central nervous system. To gain experience in voltage clamping I joined Dieter Lux's laboratory and learned from Erwin Neher how to voltage clamp synaptic currents in snail neurones before moving to Bernard Katz's department at University College, London.

There I worked with Bill Betz for one year, learning the basics of synaptic transmission and taking apart the neuromuscular synapse into its pre- and postsynaptic elements. During the following two years I learned, with Dale Purves, that the neuromuscular synapse is also a good model for studying long-term changes in chemical and electrical excitability. During this time Bernard Katz and Ricardo Miledi discovered 'membrane noise' and 'elementary events', and Linc Potter and Ricardo Miledi in the same department made the first attempts to count and isolate acetylcholine receptors. I was very lucky to be at University College at this particular time, when both the electrophysiology and the biochemistry of synaptic transmission became molecular. It seemed that a molecular understanding of the end-plate currents was within reach, and it became clear to me that I wanted to work on the molecular aspects of synaptic transmission, and on the development of synapses, which is what I have been doing since. The major experimental challenges were the direct recording of the elementary events that had been postulated from Katz and Miledi's experiments, the biochemical and structural characterisation of the acetylcholine receptor molecule, and the relation between structure and function of ion channels and receptors.

When Otto Creutzfeldt offered me the opportunity to run a laboratory of my own in his department at the Max-Planck-Institute for Biophysical Chemistry in Göttingen, I gladly accepted because other physicochemical and biochemically orientated departments there seemed to provide the right background for molecular physiology. Erwin Neher had moved to Göttingen as well, and we agreed to characterize different subtypes of acetylcholine activated channels with biophysical methods. This project went rather well, and it suggested to us that ion channels in denervated muscle fibres might be a good choice to try out extracellular pipettes for the recording of elementary events. Some initial success was followed by many frustrations in attempts to improve the seal resistance by choice of different preparations and treatments of pipette tips. Finally, with the help of a group of very dedicated collaborators, Owen Hamill, Alain Marty and Fred Sigworth, we succeeded in establishing patch clamp recording configurations which allowed us to investigate almost any type of channel in almost every cell type. A practical course, and the book that resulted from this course, marked the end of our primary focus on methodological problems, and allowed me to concentrate my efforts on understanding the role of ion channels in synaptic signalling at the molecular level. The resulting work was carried out with David Colquhoun and Joachim Bormann in the following years.

The next methodological step was to apply molecular biology techniques to problems of

ion channel physiology. It seemed that proper use of recombinant channels in Xenopus oocytes could only be made in combination with single channel conductance measurements. Together with Veit Witzemann we found a simple way to free mRNA-injected oocytes from their covering layers to perform the first single channel conductance measurements from heterogeneously-expressed acetylcholine receptors. Later, Shosaku Numa suggested we collaborate combining patch clamp and recombinant DNA techniques to establish structure-function relations of the acetylcholine receptor. This fruitful collaboration identified the structural basis of channel subtypes and localized domains important for ion transport. It also provided me with a strong incentive to learn recombinant DNA techniques myself. When I later established my own department, I made sure that the techniques of cellular biophysics and molecular biology were well represented. As a result, I was well equipped to follow my strong interest in structure-function relations of ion channels and in the synaptogenesis of the neuromuscular junction.

Another technical challenge, to develop new methods for recording postsynaptic currents from neurones in brain slices, was prompted by my ongoing interest in CNS synaptic physiology. Together with Tomoyuki Takahashi we developed a method to expose neurones in brain slices, so that patch clamp techniques could be applied to measure quantal synaptic currents and elementary events in the CNS. Understanding synaptic transmission in the CNS requires a close collaboration with molecular biologists, so I moved my laboratory from Göttingen, where I had been collaborating with Erwin Neher for sixteen years, to Heidelberg, one of the molecular biology centers in Germany. Here I am collaborating with Peter Seeburg to elucidate the functions and dysfunctions of CNS synapses at a molecular level, using an approach which combines the techniques of biophysics and molecular biology.

Looking back, I feel very fortunate that I began my career in two laboratories that guided me to important scientific issues that interested me for over twenty years. The scientists that influenced me most were Otto Creutzfeld, who made me decide to take up a scientific career in neurophysiology, and Bernard Katz, in whose department at University College, London I was trained in cellular biophysics, and who still remains my mentor. Later, I was fortunate to meet fellow scientists with whom I shared interests and who became good friends. With Erwin Neher I shared an exciting and wonderful sixteen years of scientific adventures and 'basteln' on new methods in the Max-Planck-Institute in Göttingen. In our collaboration it has always proven important to spend a good part of our time developing methods and instruments, and to share newly developed methods with fellow scientists.

I began my scientific career in the Max-Planck-Gesellschaft in 1966 and, with the exception of three postdoctoral years (1970-1973) at University College, London, I have remained affiliated with this organisation ever since. The ideal working conditions provided by this organisation have been invaluable. I am currently the Director of the Department of Cell Physiology at the Max-Planck-Institute for Medical Research in Heidelberg as well as, at present, the Acting Director of this Institute. Most of the major awards were given to me jointly with Erwin Neher, with whom I share also the Nobel

Prize. These earlier awards were the Bunsen Prize, the Feldberg Prize, the Spencer Prize, the Leibniz Prize, the Gross-Horwitz Prize, the Louis Jeantet Prize and the Gairdner Prize. For me the most important awards, before I shared the Nobel Prize, were the Magnes Award of the Hebrew University (1982) and Harvey Prize of the Technion (1991). I am glad to be the first German scientist to receive these awards.

From *Les Prix Nobel. The Nobel Prizes 1991*, Editor Tore Frängsmyr, [Nobel Foundation], Stockholm, 1992