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Ion channels: their discovery, their function, and their role in medicine and pharmacology

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'Bioelectricity' has been viewed for a long time as a phenomenon observable only in 'excitable tissue' such as nerve or muscle as demonstrated by Luigi Galvani and Alessandro Volta already in the late 18th century. Arguably the nerve impulse or 'action potential' is the most spectacular manifestation of bioelectricity and much effort was directed in the 19th and 20th century towards understanding its physico-chemical basis. In 1902 Julius Bernstein published his 'Membrane Theory', which posits, that electrically excitable cells are surrounded by a membrane and that electrical signals across this membrane are due to its ion-specific permeability. Finally, in the early 1950s the British physiologists Alan L. Hodgkin and Andrew F. Huxley were able to show that the nerve impulse is caused by changes in this permeability, which lead to fluxes of the most abundant cations of our body fluid: Sodium (Na+) and potassium (K+).

When Bert Sakmann and myself started to address the question what causes permeability changes in nerve membrane, we still thought that an answer would resolve not more than an issue related to nerve excitability. We wanted to prove that 'ion channels' or pores in the nerve membrane open and close in order to provide the precisely timed current pulses, that make the nerve impulse go. To provide this proof, we had to develop a method for the measurement of current across biological membranes, which is 100 times more sensitive than previously existing methods. This method allowed us to register discrete current changes, when ion channels open for short times, and this way for the first time allowed us to observe dynamic changes of such biological nanostructures in real time.

The possibility to measure small membrane currents, however, not only provided proof of the ion channel concept, but also revealed that ion channels are present in basically all cell types of our body, where they fulfill a variety of functions. They are present in our sensory organs, where they transduce physical quantities, such as sound, taste, smell touch, and temperature and convert them into electrical signals. Other types of channels are present in the kidney, where they control fluid flow, or in bones, where they sense stress and induce growth. Ion channels, as regulators of cell function, turned out to be prime targets for pharmacological intervention. A small number of drug molecules interacting with a small number of ion channels are able to inhibit or stimulate the function of a whole cell. Thus, ion channel research has become an important element of drug development. Unfortunately ion channels also turned out to be the cause for a variety of congenital diseases, when their function is compromised by mutations.

In this lecture I will briefly touch on the history of bioelectricity, review some classical findings regarding surface properties of membranes in aequeous media, report about our experiments, which led to the discovery of ion channels, and briefly summarize more recent biological findings.