The Nobel Prize in Physiology or Medicine 1991

Presentation Speech

Presentation Speech by Professor Sten Grillner of the Karolinska Institute

Translation from the Swedish text

Your Majesties, Your Royal Highnesses, Ladies and Gentlemen,

Our cells constitute the small working units of the body. Each organ consists of a bewildering number of cells. The nervous system alone has a larger number of nerve cells than there are human beings on earth. Every little cell is surrounded by a thin membranous wall, like a soap bubble. This membrane surrounds the interior of the cell in which there is a high level of activity; large and small molecules are being manufactured. Each cell has power plants of its own, which produce chemical packets of energy for the cell factory. The interior of the cell is very sensitive to change, it is demarcated by the cell membrane. The cell must continuously make new molecules, distribute its different products, and handle its waste products efficiently. Therefore, the cell membrane contains a number of specific transport systems, which bring different agents in and out of the cell. *This year's Nobel Prize is concerned with such a transport system - the ion channel system*. It transports electrically charged atoms, commonly called ions. The body fluids consist mainly of sodium, potassium, and chloride ions. The interior of the cell has a high concentration of potassium ions, whereas sodium ions dominate on the outside. This leads to a difference in electric potential between the inside and the outside of the cell, which can amount to as much as a tenth of a volt. This membrane potential is used for a number of different tasks. It permits, for example, nerve cells to send rapid electrical signals along their processes, and many of the cells in the body to communicate with each other.

Ions are transported through ion channels, which can be specific to one type of ion like sodium or potassium. Every single ion channel consists of one protein molecule or a molecular complex, which forms the walls of a thin channel, connecting the interior of the cell with its exterior. The ion channel has such a small diameter that it corresponds to the width of only one single ion, and it is thus incredibly small. The ion channel is opened or closed as its molecule changes shape. When, for example, the ion channel molecule for sodium is opened, sodium ions in a long row will pass through the minute ion channel into the cell, because there are more sodium ions outside the cell than on the inside. Since ions are electrically charged, an electric current will also pass through the open ion channel. This year's Laureates, Erwin Neher and Bert Sakmann, succeeded in making a conclusive demonstration that ion channels exist, by developing a technique by which the miniscule currents, flowing through a single ion channel molecule, could be measured. These are currents of a thousandth of a billionth of an ampère. The technique is nevertheless, in principle very simple. A thin glass-tube filled with fluid is used as a recording electrode. The tip of the tube is pulled out to a width of only some thousandth of a millimeter. When it is brought in very close contact with the cell membrane, they form as it were, a chemical unity with each other. The ion channels, which are present in the cell membrane under the pipette opening, will then form the only connection between the interior of the cell and its outside. When one of the channels is opened a very small current will flow, which can be measured through the ingenious technique of Neher and Sakmann. We can thus measure exactly when a single ion channel is opened or closed, that is when a single molecule changes its shape. *This is a totally unique level of resolution*. This technique was combined with the new methods for biochemical microsurgery on single molecules, through which different parts of the ion channel molecules can be modified or exchanged. Through this procedure, it has been possible to elucidate the function of the different parts of the molecule, for instance, what makes an ion channel select only one type of ion, or be sensitive to a particular type of chemical transmitter. This technique has in one single blow changed our ability to study the different ion channels, which influence the life of every little cell. Thousands of laboratories throughout the entire world now use this technique to understand the roles ion channels may play in different tissues in animals or plants. Ion channels are, for instance, engaged when the cells in the pancreas secrete insulin, when the heart is contracting, or when we think or remember something. A number of diseases are either influenced or caused by a modified ion channel function. Many drugs act directly on the specific type of ion channel, which is of importance in a particular disease. Examples include, anxiety, cardiovascular disease, epilepsy, and diabetes. Our life as a unique individual actually starts with an activation of the ion channels in the egg cell by the sperm at the instant of conception. This prevents other competing sperms from gaining access to the egg cell.

Professors Neher and Sakmann,

On behalf of the Nobel Assembly at the Karolinska Institute I wish to convey to both of you our warmest congratulations for having enabled us to understand how ion channel molecules function. They are a prerequisite for biological life. You will now receive the Nobel Prize from the hands of His Majesty the King.

From Nobel Lectures, *Physiology or Medicine 1991-1995*, Editor Nils Ringertz, World Scientific Publishing Co., Singapore, 1997