High-resolution measurement of current flowing through isolated membrane patches from nerve and muscle cells

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High-resolution current measurements employing black lipid membranes have shown that the current contributions from individual ionic channels embedded in the membrane (e.g. Gramicidin A channels) can be well resolved (1). The pattern of switching of the channels gives very detailed kinetic information on the molecular rearrangements that occur during opening and closing (2). Analysis of the single channel conductance as a function of ionic concentrations or voltage allows the ion permeation process to be studied.

In biological membranes, ionic channels of similar properties control a number of important physiological functions such as nervous excitation, neuronal transmission, muscle contraction, etc. (for review see (3)). Unfortunately, the conditions of measurement in biological preparations are very different from those of the black lipid membrane. Therefore, the traditional methods of current recording in biological membranes (voltage-clamp) carry high background noise. The background noise is about two orders of magnitude higher than would be required for the resolution of single channel currents. This is mainly due to the large size of cells used in standard measurements. For single channel resolution the membrane area on which the measurement is performed should be made smaller than 1000 μm^2. We achieved this by electrically isolating a small patch of membrane for current measurement (4). This was done by placing a polished micropipette onto the clean surface of a cell and measuring the current that flows through the pipette.

The success of such a measurement depends critically upon the establishment of good contact between glass and membrane, otherwise the electrical shunt between pipette interior and bath fluid leads to excessive background noise. Recently, we have found ways to improve this contact such that background noise is good enough to resolve most of the ionic channels of interest (5). The improvement of contact also allows membrane patches adhering to the pipette tip to be physically removed from the cell by withdrawal of the pipette (6). Then, a membrane patch of microscopic dimensions spans the opening of the pipette. It has both of its surfaces exposed to fluid, the ionic composition of which can be changed at will. Thus, current measurements can be performed under conditions very similar to those prevailing during measurements on model membranes.

Examples will be given of recordings from nerve, muscle and chromaffin cells. The latter ones, responsible for the release of adrenaline in stress situations, possess all the ionic mechanisms characteristic of neurons which are: a conductance activated by a neurotransmitter (Acetylcholine); Na- and K-

specific channels for nerve impulse generation, and Ca-specific currents mediating transmitter release.

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