Generalia

Electrophysiological Studies on Gland Cells*

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Introduction

The physiology of nerves and muscles, as we know it today, could never have been developed without the extensive use of electrophysiological methods. In the physiology of gland cells, electrical methods have until recently only been used occasionally, a fact that explains the paucity of precise information on membrane events in secretory cells. Yet without such information we can hardly expect to get insight into the basic mechanisms of secretory processes. Fortunately, in recent years an increasing amount of papers describing electrophysiological aspects of gland cells have appeared. Because of the relatively small size of gland cells, as compared to nerve or muscle cells, a number of technical problems exist and have probably influenced the results of many reports. The present survey is not a review of gland cell electrophysiology, although a number of important results will be mentioned, but rather a critical examination of the methods currently in use.

Type of preparation

In the terminology of this review, cell electrophysiology means measurement of cell membrane potential and possibly cell membrane resistance. As discussed in a following section, this must be done with the help of glass micro-electrodes puncturing the cells. Several tissue preparations are at hand: a) in vivo, b) perfused glands, c) superfused segments or superfused slices, d) isolated or cultured cells. The choice of preparation depends, among many things, on the particular tissue under investigation and on the other parameters, besides the electrical ones, which are to be measured simultaneously (fluid secretion, enzyme output, hormone output, metabolism etc.).

a) The in vivo preparation will frequently provide the starting point, since it often appears to be the easiest to handle. This unfortunately frequently turns out not to be the case. One problem is movement of the tissue due to the blood circulation and the respiratory movements of the animal. Manipulations of the ionic composition of the extracellular fluid are very restricted, and the results obtained from studies where close arterial infusion of ions or chelating substances has been attempted are not always clear1. The main advantage of this preparation is that gland stimulation can be carried out using the natural nerve supply, and important information on physiological aspects of the type of innervation has been obtained2,3. It is also the duty of physiologists to measure electrical parameters under conditions as close to those in the intact living organism as possible, and especially in the salivary glands excellent results have been obtained4.

b) This classical physiological preparation has repeatedly been the object of electrophysiological investigations, especially in the case of the salivary glands and the pancreas5–8. This preparation has many advantages, mainly because of the easy manipulation of the extracellular ionic composition, but the stability of the membrane potential recording is not very good. Close arterial injection of the appropriate physiological secretory stimulant (frequently acetylcholine (ACh)) often results in movements of vascular smooth muscles causing movements of the tissue. It is therefore only rarely possible to record the full time course of a stimulant-induced change in membrane potential, and in the perfused pancreas it is even difficult to record the initial effect of ACh or cholecystokinin-pancreozymin on the membrane potential9. Therefore, in spite of the fact that in this preparation a correlation between fluid secretion from an exocrine gland and changes in membrane potential is possible, there are severe limitations precluding a more detailed analysis of the electrical properties of the gland cell membrane.

c) The superfused slice preparation has frequently been employed and has properties similar to the superfused gland segment preparation. In the slice preparation, the micro-electrode impalement occurs through a cut surface, whereas in the segment preparation the natural surface of at least part of the gland is untouched and the impalement occurs through an undamaged

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surface. The main advantage of these types of preparations is that it allows very stable membrane potential measurement and also easy manipulation of the ionic environment. In the liver, the pancreatic islets, the exocrine pancreas, the adrenal cortex and the salivary glands, this technique has been successfully employed. This type of preparation in some cases also allows simultaneous recording of membrane potential and output of the secretory product.

Measurement of membrane potentials

In excitable tissues different techniques for measuring membrane potentials exist: 1. Capillary glass micro-electrodes which are inserted into the cell by puncturing the cell membrane. 2. Larger micro-electrodes inserted axially into long cable-like structures with a large diameter (squid axons). 3. The sucrose gap technique used on tissues composed of long cells with large diameters (myelinated nerve, smooth muscles). Of these techniques only the first can be applied to the exocrine gland cells, since these are small cuboid structures. The fact that gland cells generally are much smaller than nerve and muscle cells, however, presents difficulties even for the micro-electrode technique and this has influenced many results unfavourably.

It has been realized since the beginning of the micro-electrode era that membrane potentials measured with this technique tend to give too low values, and this is true especially in the case of small cuboid cells. All electrophysiologists face the problem of selection of data and therefore a discussion of the criteria used for such a selection is pertinent. If a sudden small advancement of the micro-electrode tip in a tissue causes a rapid change of the electrical potential of the electrode, which is stable within at least a few seconds, and the potential suddenly returns to the preadvancement level upon withdrawal of the electrode, this will often be considered a satisfactory cell impalement. However, as pointed out by Frömter, there appears to be a positive correlation between the stability and the magnitude of the membrane potential. In my view, the key point is the stability of the recorded potential, and generally one should require that membrane potentials are stable in the range of minutes rather than seconds. Previously it was considered essential that the potential change upon micro-electrode impalement should be sharp. Unfortunately the term sharp is not well defined. Therefore it may be better to avoid this criterion since it is relative and mainly dependent on the speed of the pen recorder paper or the sweep of the oscilloscope beam. With standard equipment it is anyway impossible to know what happens in the first milliseconds following the micro-electrode impalement. The essential question is whether the potential following the impalement, observed on a minute time scale, is declining, remaining, or increasing and then stabilizing. The two latter patterns will represent satisfactory impalements. In Figure 1 examples of different types of impalements are given.

There has been some discussion over the meaning of the absolute value for the membrane potential obtained from micro-electrode work. It has been correctly pointed out that such a measurement from the standpoint of a physicist is meaningless. However,