Granit writes that he can well remember how deeply he was stirred when he first read of Adrian's early contributions in the physiology of neurons. He says "it suddenly became clear that both sense organs and neurons delivered a message of repeated brief electrical impulses." But in 1934, it could not have been clear how basic and influential these early findings were to become. Later the "all-or-none law" was developed more thoroughly by Hartline, Erlanger, Gasser, Granit, Zotterman, and numerous others interested in neuron system information processing. The patterns of peripheral unit discharge were found to agree with psychophysically defined sensory functions. In the few cases (Hensel, Zotterman, and their co-workers) where direct comparison between human sensation and unit data could be obtained, the correlation was truly impressive.

Application of the newly developed microelectrode technique to mammalian retinal physiology by Granit in the late 1930's was pursued by many during the period ending in 1968 with K. T. Brown's classic monograph. The findings absent from this research may be of particular importance. In retrospect, there had been a notable failure of numerous investigators to record all-or-none potentials in retina during this 40-year period. Analysis of ganglion cell fields was initiated elegantly by Kuffler, and subsequently explored by many other researchers, but only ganglion cells had shown the spike potentials which are now accepted as commonplace in the peripheral nervous system literature. Recently, new techniques for intracellular recording and marking have been applied by Werblin and Dowling in this country, and Kaneko and his colleagues in Japan. These studies demonstrated that, at least in some vertebrates, the ganglion cells are indeed the only cells in the retina which consistently produced potentials which could be identified as regenerative action potentials. In this respect, the retinal cells appear distinct from peripheral nervous system neurons. However, the retina is not peripheral in embryonic origin but is an outgrowth of the primitive ectoderm of the forebrain. It may not be surprising then that the granular and perhaps other cells in the olfactory bulb have been found to function in the absence of regenerative spike potentials. It is curious that processing by graded potential in the absence of propagated action potentials has not been examined heavily in the densely packed brain nuclei where many cells have processes as short as those found in the mammalian retina.

It is possible that brain nuclei and the retina do not process information in the same way. If this is the case, extensive re-thinking may be in order for numerous other generalizations from relatively peripheral systems to assumed strategies of brain function. On the other hand, it seems equally likely that brain physiology is much in the same state as retinal knowledge between 1940 and 1968. That is, progress has been slowed by the Lorelei call of all-or-none, spike potential producing cells which are selectively recorded by researchers.

Over the last two years, I have been tak-
ing an informal opinion poll. We are fortunate, many times a year, but particularly in the winter to have visitors to our campus who present lectures in brain neurophysiology. I have had the opportunity to put to most of them, the question: "Assuming that the usual graded synaptic potentials are present, do you think that brain interneuronal processing may occur in the absence of unit spike potentials?" Surprisingly, I have found that the replies may be sorted into a geographic pattern. The majority who were trained in the west feel that this is a reasonable possibility, and that more research involving intracellular recording and cell marking is required to look into it. The visitors who received their training in the central states and east coast generally respond that it is almost unthinkable that neural tissue could process information in the absence of unit spike potentials. Most of our visitors who work outside of the retina were unfamiliar with the recent findings in the vertebrate retina and were quite surprised at the accumulating evidence supportive of graded potential processing.

If it should turn out that processing between closely opposed cells throughout the nervous system (both brain and retina) is normally accomplished in the absence of regenerative spikes, a most interesting and highly flexible communication system may be conceived. Informally it might be characterized as a combination analog-digital processor. That is, the actual processing of information in areas where there is high cellular density and short processes might be accomplished entirely on an analog (graded potential) basis. While information which must be carried over relatively long distances, a few millimeters or more, would proceed by discrete "digital" code, the all-or-none spike potential. My engineering colleagues tell me that a digital system for processing would provide high precision but with a sacrifice of component efficiency. Conversely, the analog approach incorporates high spatial efficiency and low numbers of processing elements but with a sacrifice in precision. Although they may be instructive, it is not wise to push these analogies too far since their artificiality cannot be overstated. However, the basic question remains, "Does normal interaction among neural cells require the presence of regenerative spike potentials?" If intracellular marking and recording techniques applied to brain cells produce a finding similar to those previously reported in the retina, the repercussions will be profound indeed.

Where interaction is by graded potentials alone (the analog model) a most stable and efficient form of processing would require feedback around the active elements. Such a model is familiar in the engineering world in the form of the operational amplifier, whose characteristics are determined by its feedback loop, and are readily changed by relatively small alterations in the loop's components. As time is measured in science, a long time ago Rushton proposed a human retinal control function which could be accomplished by feedback. Recently, independent findings on mammalian retinas as diverse as cat and dolphin have shown cells situated in the inner layers of the retina with processes spanning to the outer layers in such a way that the necessary feedback pathways could be provided.

William W. Dawson