compatible with the suggestion of Wool that the hormone initiates the transcription of messages through combination with a repressor molecule which leads to the synthesis of specific enzymes. The known reactions of insulin with protamine, zinc, and certain quinones (*14*) may offer leads to the type of molecule which constitutes the hypothetical repressor. It is of interest that the induction of enzyme synthesis, presumably by the same mechanism noted in this study, has been reported for cortisone stimulation of liver tryptophane pyrrolase (*15*) and hepatic gluconeogenic enzymes (*16*), for insulin-dependent synthesis of liver glucokinase (*9*), for estrogen stimulated phospholipid and protein synthesis in the uterus (*17*), and for the calorigenic and increased growth rate actions of thyroid hormones (*18*).

The results of this study also demonstrate a separation of the hypoglycemic action of insulin and the hormonal induction of enzymes. This suggests that the transcellular transport of glucose stimulated by insulin is not dependent on the synthesis of new enzyme protein.

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Adaptation in Stretch Receptor Neurons of Crayfish

Abstract. *Two factors involved in the adaptation in stretch receptor cells of crayfish were separated and studied: (i) the decline of the rate of discharge during intracellular application of constant current and (ii) the decline of generator potential during sustained stretch. The change in generator potential with time was essentially identical in both rapidly and slowly adapting cells. The slowly adapting cells continued to discharge throughout the application of depolarizing currents, whereas the rapidly adapting cells stopped discharging while the current was applied. The different rates of adaptation are therefore attributable to the difference in the properties of the electrically excitable membranes rather than the properties which produce generator potentials.*

Two different causes for adaptation in sensory receptors have been suggested: one is some mechanism which leads to a gradual decline of the generator potential, the other, some effect related to the accommodation of electrically excitable membrane (*1*, *2*). Recently, the tendency has been to regard the first of these as the more important factor, because in many receptors the time course of decline of the generator potential agrees well with that of the decline of impulse discharge (*1*). In various vertebrate mechanoreceptors the decline of the generator potential in the face of a constant stimulus has been attributed largely to the mechanical properties of the coupling between the receptor and the stimulus (*3*).

Two stretch receptors which lie side by side in crustacea exhibit marked differences in adaptation (*4*); one is rapidly adapting, the other adapts very slowly. These different characteristics have been attributed (*5*) to differences in the time course of decay of the generator potential. Eyzaguirre and Kuffler (*5*) suggested that the differences might be due to differences in structural relations between the dendrites of the receptors and the muscle fibers to which they are attached. Krnjevic and van Gelder (*6*), however, examined the mechanical properties of the muscle fibers to which the two receptors are attached and concluded that these properties could not account for the differences in rate of adaptation of the receptors. Their findings suggested the possibility that the different rates of adaptation were due to different properties of the electrically excitable membranes of the receptor neurons.

In the study reported here, the link between generator potential and spike electrogenesis in the stretch receptor neurons was uncoupled by taking advantage of the different electrophysiological and pharmacological properties of electrically excitable and electrically inexcitable membrane components (*7*). The time courses of the decline of the generator potential as well as of the accommodative processes in spike electrogenesis were thus studied separately. The results show that the main difference between the slowly and rapidly adapting cells lies in the properties of the electrically excitable membrane component rather than in the mechanism of the generator potential.

Stretch receptors from the first to the third abdominal segments were isolated and mounted on a stretching device similar to that described by Eyzaguirre and Kuffler (*5*). The preparations were bathed in a crayfish saline medium (*8*). Two microelectrodes were introduced into a given neuron: one for recording potential, the other for applying a current. The current was monitored with a resistance inserted between the bath and ground, while the potential was recorded differentially. A feedback circuit was used to maintain the applied current constant.

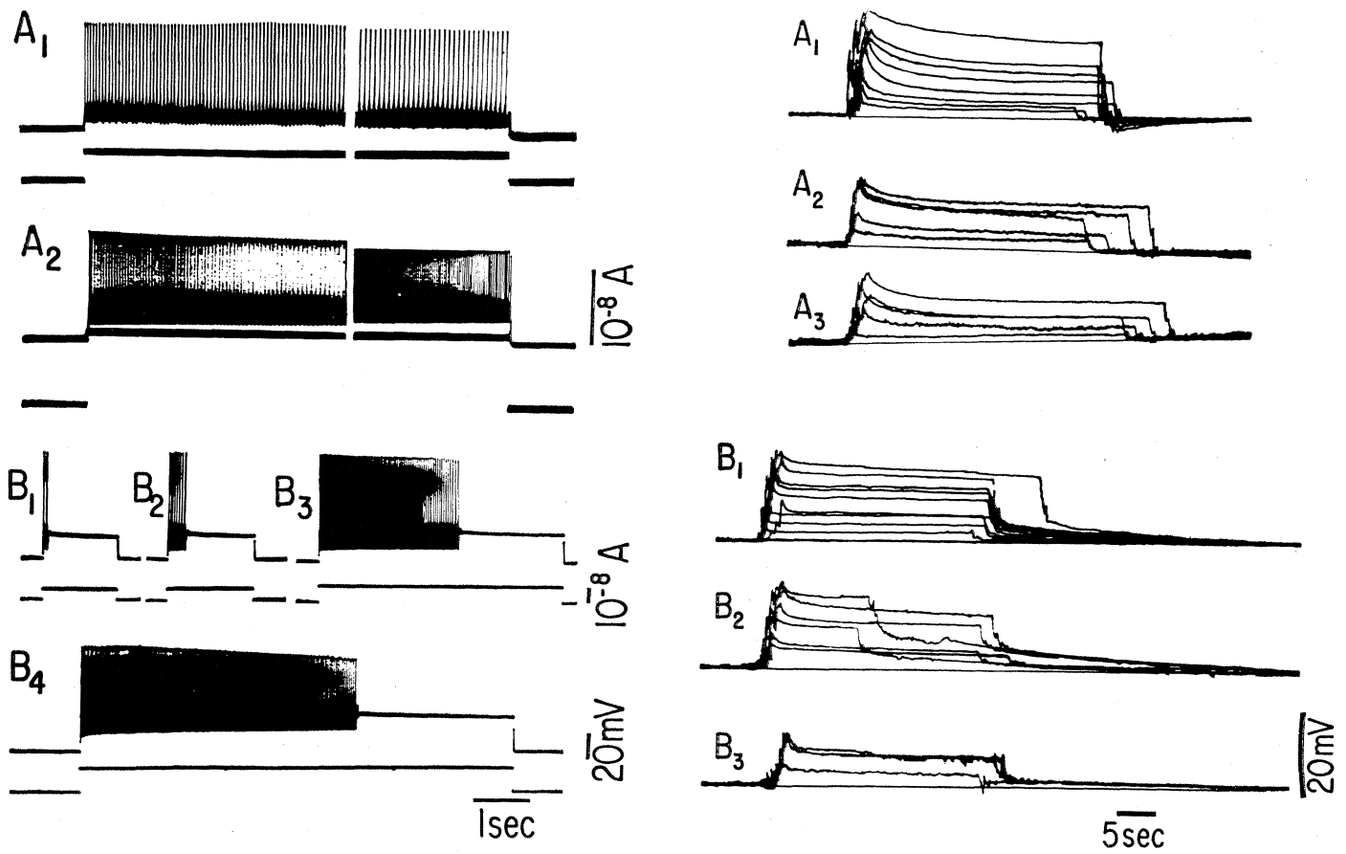
Figure 1*A* shows the repetitive firing of a slowly adapting cell during the application of long-lasting constant currents of different amplitudes. Only the initial and final parts of the sequences are reproduced, and they demonstrate the capacity of the slowly adapting receptor neuron to respond with spikes for a long time when the cell is depolarized. Figure 1*B* shows results of

the same kind of experiment with a rapidly adapting cell. The current was increased step by step through B_1 to B_4. While the duration of the repetitive firing increased with increasing current, spike electrogenesis terminated in each case while the current was still being applied. The maximum duration of repetitive discharge was not more than about 6 seconds (B_4).

There was no exception to this difference in the responses to applications of constant currents in a total of more than 30 cells. In each case, cells which had been identified as slowly adapting by microscopic observation (*4, 9*) always continued to respond with repetitive firing while the current was applied. Firing was usually observed for more than 3 minutes. When the same current was applied to a cell which was identified as rapidly adapting, the firing stopped within 30 seconds. Usually, the spike height of the rapidly adapting cells was less than that of the slowly adapting cells. However, slowly adapting cells with spikes of about 80 mv still fired repetitively, whereas rapidly adapting cells with spikes of 90 mv stopped responding quickly. Thus, the difference cannot be attributed to the possible damage of rapidly adapting cells, which are somewhat more difficult to penetrate.

Figure 2 shows the time courses of the generator potentials (*A*) in three slowly adapting and (*B*) three rapidly adapting receptor neurons during the application of various degrees of stretch. Spike electrogenesis of the cells had been blocked (*10*) by the application of tetrodotoxin to the bathing (Ringer's) solution, 10^{-7}g/ml. This drug does not affect the generator potential of crayfish stretch receptors or other varieties of electrically inexcitable activity (*11*). The lengthening of the muscle fibers by the applied stretch was observed under the microscope and was usually completed within 3 seconds. The length remained constant thereafter as long as the stretch was applied. The rate of stretch was rapid in comparison with the rate of adaptation of the rapidly adapting cells, which could generate spikes under normal conditions for as long as 20 seconds during a maintained stretch (*4*).

There was essentially no difference in the time courses of the generator potentials of the two types of cells which might account for the marked differences in their rates of adaptation. In both types of cells the generator potential declined rapidly from an initial peak, and neither the early decline nor a subsequent slow decrease in the generator potential during the maintained stretch appeared to differ significantly between the two. The only noticeable difference was that an after-hyperpolarization was often observed in the slowly adapting cells (A_1), while in the rapidly adapting cells release of the stretch always left an after-depolarization. The depolarization lasted for about 1 minute while the hyperpolarization was briefer.



Figs. 1 and 2. Fig. 1 (left). Time course of repetitive firing during the application of constant depolarizing current. (*A*) Slowly adapting cell. In A_1 the current was applied for 140 seconds, and in A_2 a larger current was applied for 26 seconds. (*B*) Responses of a rapidly adapting cell to currents of different amplitudes. At B_4 the maximum duration of repetitive firing was attained. Stronger currents than B_4 curtailed the duration of firing. Upper traces, potential; lower traces, current. Fig. 2 (right). Time course of the generator potential induced by various degrees of maintained stretch in receptor cells treated with tetrodotoxin (10^{-7} g/ml). Ink-writer recordings. Sudden onset of the generator potentials corresponds to the beginning of stretch; sudden fall of the potentials, to a release of stretch. Some irregularities at the beginning and the end of stretches are artifacts due to the mechanical property of the stretcher. (*A*) Three slowly adapting cells. (*B*) Three rapidly adapting cells.

These experiments show that the difference in adaptation rates between the two types of stretch receptor cells should be attributed to differences in the properties of their electrically excitable membrane components rather than to differences in the mechanisms of their generator potentials. However, the interplay of changes in the electrically excitable membrane with the changes observed in the generator potentials during a sustained stretch probably determine the rates of adaptation among individual neurons within each class of receptor cells.

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Replacement Rates for Human Tissue from Atmospheric Radiocarbon

Abstract. *Carbon-14, derived from the testing of thermonuclear weapons in the atmosphere of the Northern Hemisphere during 1961–62, has been found in human tissues including the brain in amounts which reflect the atmospheric concentration of carbon-14 as of several months earlier. In collagen of cartilage, the rate of uptake of carbon-14 is much slower than in other tissues; essentially no radioactive carbon was found in the collagen of 70-year-old adults that had been exposed to the comparatively high concentrations of carbon-14 in the atmosphere during the years 1954 to 1964. Individuals from the Southern Hemisphere show little increase in the carbon-14 content of their tissues at present, and detailed tests with individuals traveling to the Northern Hemisphere from the Southern allow closer scrutiny of the tissue replacement rates.*

Information on the metabolic turnover of the constituents of human tissue is of considerable importance and interest to all students of the life sciences. However, such information has been difficult to obtain because of the reluctance to use radioactive tracers in considerable dosages in normal human beings. Experiments with radioactive tracers in animals usually necessitate the administration of isotopes in micro- to millicurie quantities (3.7×10^4 to 3.7×10^7 disintegrations per second). Such quantities permit the isolation of desired compounds while maintaining a sufficient amount of radioactivity to be measured within a reasonable time and at a satisfactory statistical level in solid or liquid scintillation counters. It has been accepted generally that carbon-14 is more satisfactory as a tracer than tritium or deuterium, because of the smaller isotope fractionation effects encountered with radiocarbon.

The techniques of radiocarbon dating permit the very accurate and sensitive assessment of C^{14} in organic materials at only picocurie intensities (3.7×10^{-2} disintegrations per second). Since the amount of C^{14} in atmospheric carbon dioxide has risen suddenly in the Northern Hemisphere to almost double the reference value of 1890 as a consequence of the testing of atomic and hydrogen bombs in the atmosphere (mainly during 1961 and 1962), and because this new C^{14} has not had time to equilibrate with the biosphere, the radiocarbon can be utilized as a tracer in living things including humans.

That such studies with humans are feasible has been shown in an experiment by Broecker *et al.* (*1*), who analyzed the C^{14} content of the blood and breath of one individual, and the lung tissue of another. Their major conclusions were, first, that the interval between fixation of carbon in the average foodstuffs and their consumption is somewhat less than a year and, second, that the maximum time during which the C^{14} content of the blood lags behind that of the food is about 6 months. At present it is not possible to estimate directly the turnover rate of C^{14} in man from such measurements. However, continued measurements over a longer time interval plus supportive investigations with individuals traveling to the Northern Hemisphere from the Southern, where the increase has not occurred yet to any appreciable degree, may make such an estimate possible. Thus we have an opportunity to detail the replacement rates for tissues in humans and, thus, to better assess the possible hazards in medical use of C^{14} and the dangers of atmospheric contamination from the testing of nuclear weapons. We have investigated the C^{14} content of various human tissues, including the brain, and have studied the rates of turnover of some of the tissue components.

All tissues other than blood were obtained at autopsy from unembalmed male subjects of a single age group who had resided in Los Angeles for longer than 20 years, and who had died during January 1964 (*2*). The nature of their illnesses and causes of death are given in Table 1.

The tissues to be analyzed were dissected free from connective tissue, fat, meninges, and blood vessels, and then were frozen and lyophilized. The dried tissues were extracted with 10 volumes of hot ethanol. This was accomplished