PROGRESS IN BRAIN RESEARCH

VOL. 7

SLOW ELECTRICAL PROCESSES IN THE BRAIN

N. A. ALADJALOVA

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BY

N. A. ALADJALOVA

Institute of Biophysics, Academy of Sciences, Moscow (U.S.S.R.)

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INTRODUCTION

Many phenomena in animal nerve tissue are accompanied by electrical processes. These processes are largely due to mechanisms of nervous activity. They provide special opportunities for studying those aspects of nervous activity which generally do not lend themselves to other research techniques.

Conversion of the energy of cell metabolism to a specific neuronal function is responsible for molecular and ionic changes, which are associated with the appearance of electrical potentials and changes in electrical constants of the tissue — its electroconducting and dielectric properties.

The electrical potentials that arise in the brain have a varied origin. These include the brief impulses lasting 0.2-3 msec that follow excitation of the neuron and the slower potentials lasting 10-20msec that reflect the processes of local excitation in the cell body and in its dendritic processes. Slow potential oscillations with periods ranging from 50-500 msec are shown in the electrocorticogram (ECoG). Considerable information is now available on their origin and relationship with the electrical potentials that arise in different segments of the neuron, but the subject is still moot in many respects.

Electrical phenomena of an entirely different order and origin are also recorded in the brain structures, namely, infraslow rhythmic potential oscillations. By "infraslow" rhythmic oscillations (Aladjalova, 1956a, b; 1957a, b) are meant the potential oscillations which are similar sinusoidal in form, with a period of 7-8 sec and an amplitude of 0.3-0.8 mV and with a period of 0.2-2 min and an amplitude of 0.5-1.5 mV; there are also intermediate values of the oscillation periods. Consequently, the oscillations range from a frequency of 7-8 to 0.5-2 per min.

Electrical phenomena of the infraslow order are determined by processes connected with slow changes in excitable properties. They do not reflect direct shifts in response to excitation, although they are inseparably connected with them. The excitability of a neuron in the brain varies both with the impulses reaching it from other excited elements and with processes that are stimulated by humoral factors and the metabolic mechanism of nervous tissue. There are several types of interaction of nervous and humoral regulation. Certain humoral substances are released into the circulatory system under the influence of certain parts of the nervous system; circulating in the blood, they may influence the nervous system. In addition, excitation of an individual axon causes chemical substances to be released locally near the synapse. Consequently, the effect of humoral substances on nerve cells

may be either localized or generalized in character. This effect is often selective with respect to the properties of individual components of the neuron. "We are unaware at present of any nervous regulation without the participation of humoral factors in some degree or form, nor are we aware of any humoral regulation that is not more or less connected with nervous regulation" (Orbeli, 1935).

In the neurohumoral chain of phenomena, the nerve cell and the neuroglial cell must be regarded as a single functional unit. Intimate relations exist between these cells which are based on chemical processes and which are facilitated by the presence of a structural relationship resembling that between Schwann cells and nerve fibers.

The humoral factors may effect the excitability of the neuron, acting through its dendrites, which possess high chemical sensitivity; the electrical manifestation of these processes may be very slow rhythmic changes in potential.

Electrophysiology has at its disposal data on slow recordings of electrical potentials in the cerebral cortex of a steady characteristic (Kaufman, 1912; Libet and Gerard, 1941; Beritov; 1948b; Rusinov, 1953, 1958; Aleksanyan and Demirchoglyan, 1955; Leão, 1944a, b, 1951; Bures, 1954a, b, 1955, 1957; Goldring and O'Leary, 1951a, b, 1954, 1957; and others). However, in most of the familiar observations these changes are aperiodic, being directly related in time to a stimulating effect on the nervous tissue.

Our main task was to investigate the phenomenon of the infraslow rhythmic potential oscillations that are found in various brain structures of warm-blooded animals, the origin of which could not be directly linked to concurrent nervous excitation.

Infraslow potential oscillations are manifested differently in the various brain structures, which may be divided into two categories accordingly. In the rabbit, infraslow rhythmic potential oscillations may arise in the cerebral cortex and hypothalamus, chiefly in the dorsomedial nucleus and premammilary region. Infraslow potential oscillations are not found in the nuclei of the thalamus, in the central gray matter around the walls of the aqueduct of Sylvius, or in the brain stem reticular formation.

Slow oscillations that take a long time to become extinguished are characterized by the manifestation of vital activity at different stages in evolution. The existence of these oscillations is ensured by the fact that the actual process is controlled by the inflow of energy required to maintain it, and for this reason we call it an auto-oscillary process.

Auto-oscillations are also encountered in the simplest forms of life. They are even found at the level of plasmodium protoplasm (Kamiya and Abe, 1950) and in some muscle structures (Koshtoyants, 1957).

Auto-oscillatory processes appear in the form of a cyclic change in mechanical properties in some structures and in the form of physicochemical changes in others (Aladjalova, 1950b; Aladjalova and Mertsalova, 1954). The frequency of oscillations is influenced by physicochemical and chemical factors, *e.g.* by epinephrine (Aladjalova, 1950b) and acetylcholine (Bülbring, 1957) in smooth-muscle structures,

by acetylcholine in ciliary movement (Bülbring *et al.*, 1953), and by serotonin in rotation of mollusc embryos (Manukhin and Buznikov, 1960). Hormones influence the parameters of certain auto-oscillatory processes in the tissues of higher animals. This is also shown by an increase of the infraslow potential oscillations in the rabbit brain after activation of the animal's hormonal functions.

Living structures may be divided into those in which very slow oscillations of electrical potential appear in the course of normal activity and those in which this process arises only under certain conditions (chronic denervation, exposure to chemical agents). The first type includes several types of smooth muscles and some types of nerve cells in the ganglia of invertebrates. The second type includes the skeletal muscles, nerve fibers, and certain types of nerve cells.

It is interesting to note that the magnitude of the infraslow rhythmic process in central nervous system structures is largely proportional to the sensitivity of these structures to certain chemical factors in the environment.

Infraslow cerebral activity is probably intensified by the occurrence of certain chemical gradients in nervous tissue and in this respect reflects the activity of the slow controlling system that ensures control of the level of activity in relation to the operation of the mechanisms that maintain stability and homeostasis.

Much slower periodic processes are also to be found in the brain. Specifically, cycles of activity arise after external perturbation in several structures with 20-30 min periods and last for several hours ("hour-long oscillations"). Assuming that the control systems of the brain are subdivided into high- and low-speed infraslow activity and "hour-long oscillations" should be regarded as a manifestation of slow system control.

Since the phenomenon of infraslow rhythmic potential oscillations was not previously investigated, we thought it worthwhile to subject it to a detailed analysis using a variety of experimental techniques. It was necessary to find answers for the following questions. What brain structures are characterized by the phenomenon of infraslow rhythmic changes in potential? How are they related to the overall excitability of nervous tissue? Are all kinds of neurons equally involved in this phenomenon? What influences effect the frequency and amplitude of infraslow potential oscillations in the brain? What is the role of neuroendocrinal relations in this phenomenon?

It was important to obtain some idea of the possible mechanisms governing the origin and regulation of the infraslow rhythm and of the nature of the processes reflected in the infraslow potential oscillations. If these processes are of significance for the integrative activity of the brain, they should change regularly as new temporary connections are formed. It was therefore important to investigate this phenomenon in the human brain.

Neurohumoral interactions in the cerebral cortex are reflected not only in the phenomenon of infraslow rhythmic potential oscillations, but also in the physicochemical properties of nervous tissue which determine its electroconductivity. Measurements of the electrical

impedance may help to elucidate the mechanism of these ionic shifts.

Impedance of the cerebral cortex can be investigated *in vivo* in wakeful animals by means of implanted electrodes (Aladjalova, 1953a, 1954a, 1955a). Two factors are responsible for a change in cortical impedance. One characterizes the general level of ionic mobility in nervous tissue and changes more or less simultaneously with a change in the metabolic level of the cortex and physiological condition of the animal. The other characterizes the local ionic shifts in the upper layers of the cortex and undergoes slow oscillatory changes. These changes are closely related to the nature of the electrical activity of the cortex and seem to occur largely (depending on the arrangement of the electrodes) in the layer of the apical dendrites.

A change in the physicochemical conditions of the dendritic area precedes a change in excitability of the neuron bodies. This raises the question of the part played by the exchange between dendrites and the environment in regulating the metabolic level of the neurons.

In studying the mechanism of the biological action of physical agents, drugs, etc., the various approaches that have been suggested seem promising. For example, investigation of the slow electrical processes in the brain following exposure to ionizing radiation made it possible to distinguish two types of cortical neurons by their response to irradiation, to identify the dendrites as the most reactive element of the neuron, and to broaden the analysis of the origin of the phases of post-radiation changes (Aladjalova, 1957).

Since it has been shown that infraslow potential oscillations reflect certain chemical processes in nervous tissue, specifically those connected with neurohormonal relations and with the function of the neuroglia, recording of these oscillations may add new information to our knowledge of the function of the brain. In view of the fact that changes in neuroglial activity play a part in the pathology of brain metabolism, it is fair to assume that the proposed method will find application in medical practice.

CHAPTER I

RECENT DATA ON THE STRUCTURE AND FUNCTION OF NEURONS IN THE CEREBRAL CORTEX

The structure and function of nerve elements of the cerebral cortex are being investigated at three levels: (1) cellular constituents — nucleus, cytoplasm, and surface layer; (2) the neuron as a whole and its connections with other neurons; (3) nerve complexes linked together by influences that often encompass whole divisions of the nervous system.

We shall briefly describe recent knowledge of this field, emphasizing those aspects that are pertinent to our investigation.

NERVE ELEMENTS AND GLIA

Sarkisov and Polyakov (1949) distinguished various types of neurons in the cerebral cortex.

Pyramidal neurons have a cell body from 10-40 μ or more in diameter and two types of dendritic branches: apical dendrites several millimetres long extending upward to the pia mater and basal dendrites with branches near the base of the cell body in an area with a radius of 150-200 μ (Fig.1). One neuron can have more than 50 dendritic branches.

Pyramidal neurons may be further subdivided according to the course of their axons. The axon may emerge from the center of a cell body and in certain neurons travel through the white substance of the hemispheres to other parts of the nervous system. In other neurons it turns toward the surface of the cerebral cortex; or it ramifies and its processes return to the region of their own basal dendrites where they make synaptic contacts (recurrent collaterals).

Stellate neurons with dendrites ramifying near the neuron body. The axons and dendrites branch out in all directions and sometimes extend into neighboring areas of the cortex. Many axons coming from the white substance terminate around these stellate cells.

Other types of neurons, spindle shaped, spider, etc., are varieties of these basic cells.

Distribution of the neurons in the cortex varies from layer to layer. The deeper one proceeds in the inner third of the cerebral cortex, the more numerous the larger neurons are.

The number of stellate cells decreases in the deeper layers while the number of pyramidal cells increases. Finally, the stellate cells with their locally distributed axons are again common among the pyramidal cells in the bottom layer.

The density of the neurons in the cerebral cortex varies from layer

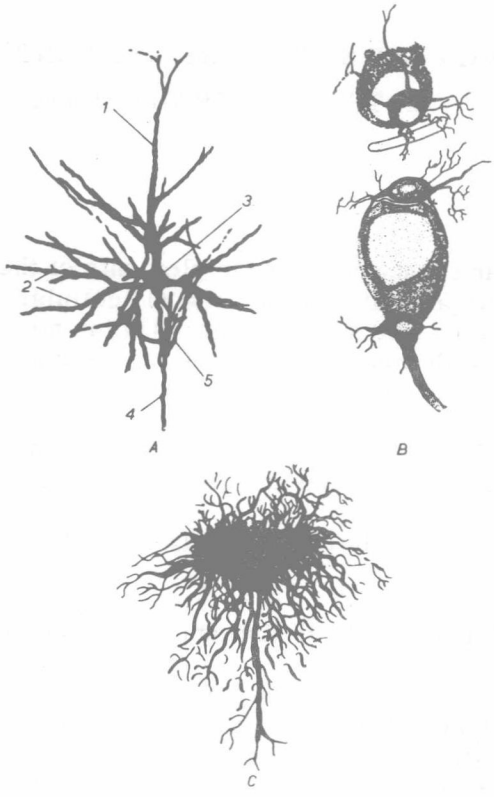

Fig. 1. (A) Pyramidal neuron from the sensorimotor cortex of the cat: 1 = apical dendrite; 2 = basal dendrites; 3 = cell body; 4 = axon; 5 = recurrent collateral of axon; (B) oligodendroglia immediately adjacent to the neuron (satellite cells) (Penfield, 1924); (C) neuroglial cell stained by Golgi's method (Glees, 1955).

to layer. Figures for the cat visual cortex by Sholl (1956) are presented in Table I.

Due to the neuron density in the cerebral cortex and the abundance of axonal connections between them, the activity of a single neuron may

TABLE I

DENSITY OF NEURONS IN THE CAT VISUAL CORTEX (SHOLL, 1956)

Depth (in μ from the pia mater)	*No. of cells per 0.001 mm³*	*Depth (in μ from the pia mater)*	*No. of cells per 0.001 mm³*
0-150	-	1150	46
250	106	1250	83
350	97	1350	97
550	43	1550	46
650	40	1650	57
750	66	1750	26
850	69	1850	80

effect the excitability of 4000 other neurons through the synaptic contact:

The axons of the associative neurons that emerge from different regions of the cortex proceed to other regions and terminate in all layers except the most superficial one (Sarkisov, 1956).

The specific afferent fibers, which are part of the classical sensory pathway from the receptors through the specific nuclei of the thalamus, proceed through the lowest layer of the cortex and enter the central part of the cortex in the region of the stellate cells. For example, afferent fibers from the lateral geniculate body may ramify into 12 branches (the distance between the furthest branches is about 650 μ) and end at different depths in the region of the stellate cells of the visual cortex. Along the pathway of such branches 5000 neurons may be encountered. The excitation threshold of these branches is often changed by afferent impulses. Some 25,000 afferent and 75,000 efferent fibers pass through a 1 mm^2 cross section of visual radiation in a cat (Sholl, 1956). The distance between the centers of the fibers is no more than 0.4-1.9 μ (Bok, 1959).

Such density of conduction pathways requires them to be fairly well insulated from one another. Otherwise, the excitation impulses arising in some conductors could change the excitability of the adjacent fibers by influencing the electrical field. The neuroglia may partly function as insulation.

Numerous axonal endings approach the dendrites from other neurons. The receiving surface of the cell body is known to constitute only 10% of the receiving surface of the dendrites (Sholl, 1956). The decrease in density of the basal dendrites with distance from the cell body limits the receiving area of the neurons in the region of the basal dendrites to a radius of about 100 μ.

Most of the apical dendrites enter layer I, which contains both myelinated and small unmyelinated fibers that proceed a considerable distance parallel to the cortical surface. These fibers are the axons of different neurons in the subjacent layers. The dendrites differ from the axons in physical and chemical properties as well as in mechanism of excitation.

A major problem in the histology of the cerebral cortex is to elucidate the organization of the synaptic endings. Unlike the motor neurons of the spinal cord, the cortical cells have not yet been definitely proved to have special axonal endings on the cell body. Cases have been observed in which the axons seem to entwine the cell body. Axons are frequently parallel and very close to dendrites. It is also known that the apical and basal dendrites are interspersed with gemmules which, according to Sarkisov and Polyakov (1949), may function as synaptic contacts.

On the basis of anatomical and physiological data, Chang (1951a, b) divided synaptic contacts in the cerebral cortex into two categories: pericorpuscular and paradendritic. The former are formed on the cell body, the latter on the dendrite. The high density of the pericorpuscular synapses makes it very probable that postsynaptic potentials develop in the cell body.

The number of axons approaching the cells and their methods of contact

with the cell bodies and dendrites have a bearing on the distribution of information through the cortical neurons. They integrate the information coming from different sources and control the excitability of the cell.

Palade and Palay (1954, 1955) detected some details of the fine structure of synapses of different cells by means of investigation with the electron microscope. Within the synaptic ending could be seen vesicles 300 Å in diameter which were at times in direct contact with the membrane, while at other times they were adjacent to the mitochondria. The presence of mitochondria in a synaptic ending is evidence of high metabolic activity therein. It is believed that the vesicles contain a chemical substance (acetylcholine) that takes part in the transmission of excitation through the synapse (Robertson, 1956).

Neurons interact as a result of chemical processes in the synapse and neuroglia. There are two main types of neuroglia: macroglia and microglia. The former consists of protoplasmic and fibrous astrocytes (Fig. 1) with a large nucleus and many branching processes as well as oligodendroglia cells (with a small nucleus), which were once thought to have no branches until Penfield (1930) demonstrated the opposite to be true. The microglia consists of long branching cells.

The astrocytes are about 10 μ in diameter. Their processes approach and parallel the blood vessels for a distance of 5-7 μ. The astrocytes come in contact with the neuron and oligodendrocytes through their heavily branched network.

The oligodendroglia is located very close to the nerve cells (Fig. 1). It is indirectly connected with the blood vessels through the astrocytes. Certain cells of the oligodendroglia are approached by a few axon collaterals, which either terminate at the body of the oligodendrocytes or touch them and then travel on (M. and A. Scheibel, 1958). Multiple contacts exist between the oligodendroglia and dendrites.

In the rabbit (Glees, 1955), fibrous astrocytes with short branches can be easily seen in the upper layers of the cerebral cortex; their ramifications terminate on blood vessels or on the pia mater. Heavily branched fibrous astrocytes with a large nucleus are frequently found in the deep layers of the cortex. In layers II and III glial cells lie very close to one another.

Protoplasmic astrocytes occur in layers IV and V. Their number decreases from the surface of the cortex to the white substance, while the number of oligodendroglia cells increases. Oligodendrocytes in the white substance acquire long branches, which proceed along the nerve fibers.

Neuroglial elements are more strongly developed in man and monkey than in animals standing lower on the evolutionary ladder (Achucarro, 1918). Some authors assumed that the ratio of the number of glial cells in the cerebral cortex to the number of nerve cells indicates the stage of brain development. However, this view was refuted by the discovery that this ratio is higher in whale than in man. The ratio of glial cells to nerve cells most likely increases with the size of the brain because the neuron density decreases at the same time: in mice: 142.5 neurons per 0.001 mm^3 of cerebral cortex; in rabbits: 43.8; in dogs: 24; in men: 10.5; in whales and elephants: 6.8 (Tower, 1954).

The close apposition of the glia to the blood vessels makes it likely that the glia constitutes a unique barrier between nerve elements and the blood system. The surface of the cortex has a layer of glia in the pial region that separates nervous tissue from the fluid compartment in the subarachnoidal space (Zavarzin and Schelkunov, 1954).

It has been conjectured that the distance between the cell body and synaptic endings of the incoming axons may change as the glia swells and thus influence conduction in the synapse. However, Palay and Palade (1954) concluded, on the basis of an electron microscope study, that there is no neuroglia between the synaptic endings and the cell body. The role of the neuroglia in synaptic transmission may be manifested through its effect on neuron metabolism (Snesarev, 1926).

The neuroglia has an active metabolism, the rate in the oligodendroglia being higher than in the other forms of glia. The neuroglia may supply the neuron with nutrients synthesized by its metabolism. This is probably the function of the satellite cells. The neuroglia can therefore be regarded as a mechanism that ensures the metabolic level needed to excite the neuron. This mechanism may well be working through the axon-oligodendrocyte synaptic system (M. and A. Scheibel, 1958). Hence the inflow of information through the collaterals of the axons to the oligodendroglia may serve to prepare the neuron for activity.

According to a hypothesis of Galambos (1961), oligodendroglial cells may become storehouses of information, which is imprinted chemically as a result of signals from the axons.

The earlier theory that the neuroglia provides mechanical support for the nerve elements was recently contradicted by new findings. It was found that the position of the neuroglia is not permanently fixed (Horstmann, 1954) and that its processes change position, increasing or decreasing their sphere of influence. Moreover, the cell body of glia (oligodendroglia) pulsates rhythmically in a tissue culture (Lumsden and Pomerat, 1951). The glial cell may contract in response to electrical stimulation (Chang and Hild, 1959) with a latent period of 1.5-4 min; length of contraction: 1.4-3.4 min, relaxation: 6-16 min.

Glial cells possess a resting membrane potential of the order of 50 mV recorded with an intracellular electrode (Hild *et al.*, 1958). The glial cell membrane is depolarized in response to strong electrical stimulation, the potential decreasing by $\frac{1}{e}$ of its magnitude* for 4 sec, *i.e.* 1000 times longer than in neuron excitation.

The neuroglia in the ganglia of some invertebrates contains protein granules (Scharrer, 1941), a neurosecretory substance** liberated very close to the nerve cells and participating in their metabolism.

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* e - the base of natural logarithms ($e \approx 2.7$) serves as the characteristic to determine the time constant.

** Neurosecretion has now been found in many nerve structures. For example, spherical inclusions of different sizes have been noted in the nerve cells of the earthworm nerve cord (De Robertis and Bennett, 1955) and they participate in synthesis of the secretion (presumably epinephrine). Neurosecretory cells have also been described in several subcortical nuclei (hypothalamus, amygdaloid nucleus, etc.) in vertebrates (Barry, 1954a, b, c; 1956).

Secretory material is also present in neuron cytoplasm in the form of granules 400-2000 Å in diameter. The cytoplasm has tiny vacuoles (0.5-1 μ in diameter) filled with homogeneous material and solid masses 200 Å thick lying alongside. The structure of neuron protoplasm includes molecules of nucleic acids arranged in such a way that desoxyribonucleic acid is concentrated in the nucleus and ribonucleic acid in the cytoplasm (Hydén, 1943).

Differentiation of cytoplasm into a system of membranes of different kinds facilitates the organization of enzymatic reactions and is a controlling factor in cell metabolism.

POTENTIALS ON THE NEURON SURFACE

Measurement of the electrical resistance of cytoplasm has shown that, despite the structural heterogeneity of the latter, it is very low compared with the resistance of the surface membrane of the cell. Consequently, most authors regard cytoplasm as an isopotential system. Yet there is evidence of a potential drop of about several millivolts between different parts of the cytoplasm in neurons. This drop was measured in a giant nerve cell of the mollusc *Aplysia* (Arvanitaki and Chalazonitis, 1956). This potential difference is of a lesser magnitude than on the surface membrane on which it reaches 70 mV in a resting state (negative on the inside). It is assumed that this potential difference on the surface membrane of the cell body is virtually the same all over the membrane. However, points on the surface membrane far away from the cell body, *e.g.* on the smaller dendrites, will nevertheless have different potential values because the diameter of the dendrite causes it to have a high electrical resistance (Coombs *et al.*, 1955a, b). Thus a shift in potential on the cell body when it is excited spreads only to the segments of the dendrites nearest to the body, thereby embracing an area with a radius of about 70-100 μ. Some difference in potentials arises between this area and an area with a diameter of 300 μ to which the dendrite branches extend.

The potential generated by the cell body upon excitation apparently does not reach the branches of the apical dendrites, but it may activate the basal dendrites (Clare and Bishop, 1955a). The potential generated by the apical dendrites is caused by the excitation reaching the branches of the synaptic endings. The resultant postsynaptic potentials are summed and a dendrite potential is created. Dendrite potentials do not generate an impulse and they spread only electrotonically (Clare and Bishop, 1955a, b).

The membrane potential of the cell body is measured with a microelectrode 0.2-0.5 μ in diameter impaled in the cell, with an indifferent electrode at a remote point. The membrane potential is 60 mV for a pyramidal cell of the cat cerebral cortex (Phillips, 1955, 1956a, b), whereas it is somewhat larger (70 mV) for a spinal cord motor neuron in the same animal (Frank and Fuortes, 1955). The lowest membrane potential has been recorded in the ganglion cell of the snail (from 30 to 60 mV) (Tauc, 1954). The membrane potential of the axon in this

animal is equal to the cell body potential of the same neuron (Eyzaguirre and Kuffler, 1955).

Regarding the motor neuron (Eccles, 1957), a high-voltage action potential (80-100 mV) is generated in the cell body membrane and adjacent portions of the dendrites by a complex series of processes. The threshold of this membrane is much higher than the threshold of the membrane of the axon hillock or the so-called "initial segment" of the axon. It has been shown that a spike potential arises first in this segment, and a similar potential being generated on the somadendritic membrane later on.

EXCITATORY AND INHIBITORY SYNAPSES

Neuron excitation and inhibition are caused by synaptic processes that may evoke or facilitate the formation of an action potential or, contrariwise, prevent it from developing. A presynaptic stimulus results in the formation of a local postsynaptic potential. An action (spike) potential arises as a result of a triggering impulse, *i.e.* a depolarization potential that has reached a critical magnitude. On the other hand, comparatively slight hyperpolarization (postsynaptic hyperpolarization) blocks an action potential.

The magnitude of the action potential of the cat cortical pyramidal cells is 80 mV (Phillips, 1956a, b) while its duration is 1 msec.

It has been conjectured that depolarization of the postsynaptic membrane requires the formation of a current that enters the cell body near the synapse. It has been calculated for the cat motor neuron that such an incoming current caused by electrical processes in the presynaptic terminals increases to a maximum in 0.5 msec and then decreases after 1.2 msec (Coombs *et al.*, 1956). At the same time the postsynaptic potential reaches a maximum only after 1 msec, *i.e.* when the incoming current of presynaptic origin has become virtually imperceptible, and then slowly decreases after 10 msec or more. These facts can be explained not by the hypothesis of electrical transmission in a synapse, but by the hypothesis of chemical transmission.

The electrical transmission hypothesis likewise fails to account for the hyperpolarization of the postsynaptic membrane which is caused by inhibiting impulses (Brock *et al.*, 1952). There is as yet no confirmation of Vorontsov's assumption that the inhibiting synapse has a special structure that permits hyperpolarization of the postsynaptic membrane by the mechanism of electrical transmission.

An inhibitory stimulus increases the permeability of the cell body membrane for potassium and chloride ions, which causes hyperpolarization of the entire membrane. This increase in ion permeability reduces the effectiveness of the excitatory stimulus.

A relatively long inhibitory postsynaptic potential creates the conditions for the summation of inhibitory influences. The effectiveness of this mechanism also depends on the antagonistic process of depolarization created by exciting stimuli. A neuron creates an action potential only when the effect of exciting stimuli is dominant at some particular

moment and causes depolarization above a critical level. This critical level is 10 mV for the initial segment of the axon and about 20 mV for the soma and dendrites (Eyzaguirre and Kuffler, 1955). These values were also determined in experiments in which depolarization was caused by a current from an artificial source (Araki and Otani, 1955).

The application of a direct current through microelectrodes (intracellular and extracellular) causes the potential to change simultaneously on the cell body membrane, in the proximal region of the dendrites, and in the initial segment of the axon (Eccles, 1957). The remote regions of the dendrites are less exposed to the effect of this current. The greater the strength of the depolarizing current, the lower the threshold and the shorter the latent period of generation of an action potential in response to natural or artificial stimulation. Meanwhile the amplitude of the exciting postsynaptic potential decreases. A hyperpolarizing current causes changes of the opposite kind. Thus, the application of current from an external source may cause the same changes in membrane potential as natural stimulation.

Hyperpolarizing postsynaptic potentials were also detected by extracellular recording of cortical cells (Phillips, 1956a and b) and by means of pharmacological analysis of cortical dendrites (Purpura and Grundfest 1957). The existence of hyperpolarizing postsynaptic potentials in the dendrites is usually masked by the presence of depolarizing potentials. A selective blockade of the latter by γ-aminobutyric acid unmasks the hyperpolarization. Purpura and Grundfest (1957) think that inhibitory and excitatory potentials exist separately in the cerebral cortex. A primary blockade of the inhibitory synapses creates the conditions for the appearance of excitation. For example, the exciting effect of strychnine and moderate doses of *d*-tubocurarine is the result of a blockade of the inhibiting synapses.

According to Grundfest (1957a), the cell membrane apparently has two mechanisms. One is excited only by chemical means, and it reacts by producing local postsynaptic potentials. The local currents that arise at this time activate, in turn, the other mechanism, one that has already been excited electrically, and which generates a spreading action potential.

The basis for the assumption that nerve cells possess a heterogeneous membrane, some parts of which yield a postsynaptic potential while others yield a spike potential, was determined experimentally in the lobster cardiac ganglion, where a spike potential arises at some distance from the point of origin of the postsynaptic potential (Hagiwara and Bullock, 1957).

There is some indication that pharmacological agents can be used to block the excitation of a chemically excitable postsynaptic membrane, whereas an electrically excitable membrane retains its capacity to generate an action potential. After employing this technique, Grundfest (1956, 1957b) concluded that dendrite potentials have a chemical postsynaptic mechanism and are not excitable electrically.

Dendrites differ from axons in many respects. Dendritic potentials do not follow the "all or none" law; they spread decremental; they are capable of summation; they lack refractoriness. Dendrites are not