tained consist chiefly of weekly Sedgwick-Rafter counts of phytoplankton and analyses of total phosphorus from water samples taken the same day. A number of estimates of nannoplankton and analyses of soluble phosphorus were also made during the study, which covered three summer months.

While the phytoplankton populations were relatively low, there was considerable variation in numbers from week to week, and several minor blooms were observed. As was expected, total phosphorus also varied considerably, increasing in all ponds after heavy rains.

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5 November 1958

Artificial Neuron

Abstract. An electronic model is described for simulating many of the gross operational functions which are believed to hold for living nerve cells. Synaptic growth is not included. Despite difficulties in drawing very rigorous analogies between the biological cell and its model, a sufficient number of rough similarities exist to make systemic experimentation interesting. Several approaches are mentioned.

Although the complete transmission properties of living nerve cells are not known, many gross behavioral aspects are reasonably well understood. The logical properties of neurons are thought to be generally similar throughout a wide variety of organisms; major differences between different types of cells seem to involve time and level parameters. (A neuron is defined here to include the cell body plus all of its dendritic and axonal appendages.) Using models to simulate the functions of nervous tissue may be useful in understanding or in predicting neurological behavior. Because of the incomplete state of our knowledge of neurophysiology and neuroanatomy, such simulations can be at best only vague and approximate. Nevertheless, these models may be useful as research tools. Several neuron simulations have been previously specified (*1*). This report describes an electronic simulation of a neuron and indicates some of the research which is made possible by such modeling.

To put it in the simplest terms, a neuron may be considered to be an electrochemical black box, essentially a binary-output transducer, having two kinds of input and one output. It is binary only in the sense that, for a given internal state and set of input conditions, it either fires (transmits an output signal) or it does not. It is a transducer in the sense that, independent of the nature of the input signal (it may be electrical or chemical, for instance), a unique standardized electrical output is produced if any output occurs at all. The two types of input are excitatory and inhibitory. Because of complex interacting properties internal to the element, it cannot be considered to be a simple binary switch. It is in fact these very properties which give rise to the complicated behavior we wish ultimately to understand.

The gross properties of a neuron, vastly oversimplified, are described below. These are the functions incorporated in the electronic model.

Input. (i) Inhibition: A particular input connection to a neuron can, while energized, inhibit firing of the neuron by other inputs. (ii) Excitation: Other input connections to a neuron will, if sufficiently energized, always fire the neuron if certain conditions are met. These conditions are described below. (iii) Threshold: A neuron may be fired if the triggering energy supplied to it exceeds a certain threshold value within a time limit. There are input pulses which have insufficient amplitude to cause firing no matter how long they last. This threshold is variable, being a function of the previous history of firing of the neuron. (iv) Refractory period: Immediately after firing, a neuron's threshold rises effectively to infinity and for a period on the order of a few milliseconds, no input signal can fire the neuron again. This absolutely refractory period is followed by a relatively refractory phase. During this second phase a decreasing threshold is observed, approaching the prefiring threshold and reaching it after a few tens of milliseconds. (v) Summation: Two or more input pulses, each of insufficient energy to excite a neuron, can be integrated by the cell so that firing occurs. To be successful, this summation must occur within a maximum time, typically on the order of a millisecond or so. Since these inputs may arrive via different pathways, there can be both spatial and temporal summation.

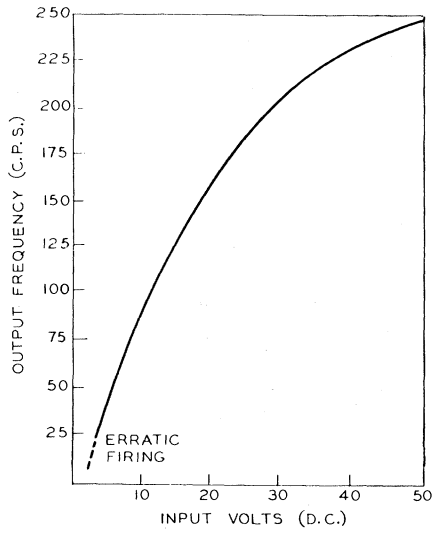

Fig. 2. Typical output firing frequency as a function of input excitatory voltage.

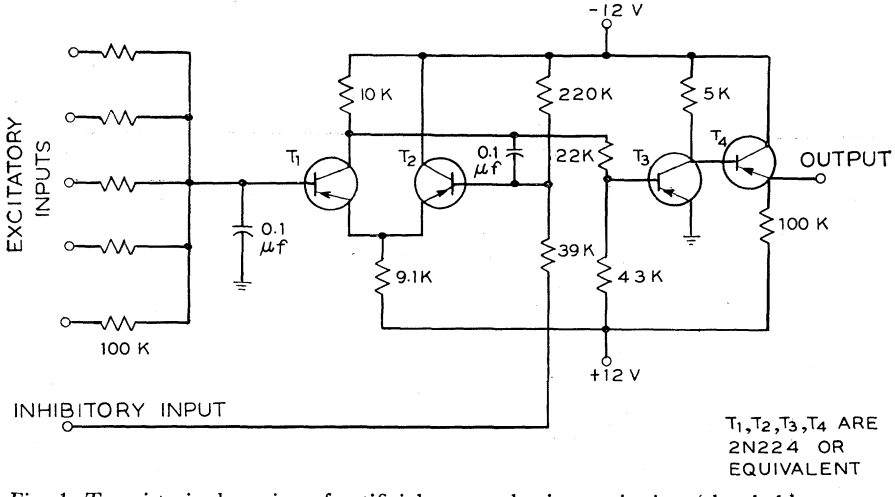

Fig. 1. Transistorized version of artificial neuron having excitation (threshold, summation, refractory) functions, inhibition, and all-or-none output, as described in text.

Output. The output of a neuron is "all-or-none." If firing occurs, then a pulse of standard amplitude and duration is produced. There are exceptions, but as a first approximation we may consider the energy per output pulse to be constant.

A model which realizes these functions can be easily made with electronic circuits. One version is shown in Fig. 1 (*2*). This four-transistor device exhibits the properties of excitation, inhibition,

summation, variable threshold, and all-or-none output, as described.

The model has an integrating time constant of 2 msec and a refractory time constant of about 10 msec, approximating corresponding values in the biological neuron. Quiescent threshold is from 1 to 5 volts (depending on the number of inputs connected), while the output pulse level is 10 volts. These levels are many times greater than those found in nerve tissue (there thresholds are typically 5 to 10 mv; output spike potentials are approximately 50 mv), but the *ratios* between threshold and output levels are commensurate. These ratios in part determine input summation characteristics when several cell outputs combine. The output pulse duration is approximately 4 msec; this is considerably greater than the action spike length found in biological nerve, but it can be shortened at will by use of a suitable differentiating network. The output characteristics are compatible with the input (excitatory and inhibitory) requirements such that a chain or network can be readily assembled. One unit will drive up to 100 others without serious deterioration of output wave form or output level.

This circuit can be used to give either single pulse outputs or variable frequency pulse trains, depending on the nature of the input. A typical direct-current input versus frequency output characteristic is shown in Fig. 2. This mode of operation is useful for simulating peripheral receptors, such as retinal elements, when used in conjunction with suitable transducers.

Photoresistive cells (for example, cadmium selenide) and these neuron models have been used to simulate some of the simple structures and functions of the retina. "On," "off," and "during" receptors are easily produced, as are flicker-fusion phenomena. Mutual inhibition of cells in an array, resulting in spatial differentiating of optical images, is also readily arranged. Similar experiments in audition are contemplated.

The relative simplicity and low unit cost (less than $10) of this model makes feasible network experiments in which large numbers of cells are used. Simple circuit changes to obtain other input and refractory time constants or excitation and inhibition thresholds can be easily made if desired.

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2. I gratefully acknowledge the work of R. M. Wolfe for the basic circuit design.

20 October 1958

Isotope Dilution Method for Assay of Inagglutinable Erythrocytes

Abstract. The number of cells that remain free in the presence of agglutinin is usually much larger than the number of inagglutinable cells. The true inagglutinable proportion can be found by successive agglutinations of a labeled population in the presence of unlabeled carrier cells. By this means it is shown that group A persons possess non-A erythrocytes in proportions of the order of 10^{-3}.

Estimation of small proportions of inagglutinable cells has hitherto presented insurmountable difficulties. Ashby (*1*) found a range of 0.03 to 3.5 percent of free cells in human anti-A or anti-B agglutinations. It was uncertain whether the cells remained free because they were truly inagglutinable or because of some other limitation of the reaction. McKerns and Denstedt (*2*) reasoned that if free cells were inagglutinable they would accumulate with successive additions of fresh cells to the reaction mixture. Since successive additions did not increase the free-cell count, the free cells are mainly agglutinable. In these circumstances the count does not reveal the proportion of inagglutinable cells or even if any such cells are present.

If cells are radioactive, they can be distinguished from unlabeled cells added later. Thus initial cells can be traced through many agglutinations with unlabeled "carrier" cells. This eventually removes the labeled agglutinable cells, and the remaining activity represents inagglutinable cells.

An experiment with known mixtures of agglutinable and inagglutinable cells labeled in vitro with sodium Cr^{51}-chromate (*3*) illustrates the feasibility of the method. About 0.03 ml of labeled O cells and 2 ml of unlabeled AB cells were mixed with 25 ml of saline and 10 ml of lima bean extract (*4*) having an anti-A titer of 1:128. A 1-ml sample was removed for Cr^{51} counting. The remainder was agglutinated at 4°C in a 7- by 9-in. pan. The mixture was transferred to a separatory funnel and allowed to settle 5 minutes, and the agglutinated mass separated from the supernatant. One milliliter of supernatant was removed for counting. The remaining volume was noted and returned to a pan with 3 ml of added agglutinin and 3 ml of 66 percent suspension of unlabeled AB carrier cells. This was repeated six times, then 0.5 ml of labeled AB cells was added with the usual carrier and agglutinin. This reaction mixture was sampled for counting, and the experiment continued through five more stages. The supernatant sample at each stage was immediately centrifuged, and the pellet was washed once with saline and counted in a well-type scintillation counter while it was in the centrifuge tube. Preliminary dilutions of reaction mixture and supernatant samples of stage 7 were required to bring them within counting range. In Fig. 1, corrected sample activity is plotted against stage. The inagglutinable cells remain in the system while agglutinable cells added midway in the experiment are swept out.

The dilution owing to additions of agglutinin and carrier was noted at each stage, and the activity was corrected by the cumulative product of prior individual dilution factors. An individual dilution factor does not include the packed-cell volume of carrier which is, in effect, both added and removed between samplings. One might suppose the proper factor to be the ratio of reaction mixture volumes after and before the fluid additions. Reconstruction experiments corrected in this manner, however, showed a paradoxical increase of inagglutinable cells. If the data for Fig. 1 had been so treated, for example, the proportion of labeled cells would have seemed to double within eight stages. Evidently agglutination does not entrap inagglutinable cells but excludes them locally, thus tending to concentrate such cells in the supernatant. We infer that agglutinated cells possess an extracellular volume inaccessible to free cells. Under our experimental conditions this associated volume was about one-third the total volume of the agglutinated mass, since omission of *all* the 66 percent carrier from the calculations for Fig. 1, rather than just its packed-cell volume, nearly compensated for the concentration effect. This unexpected exclu-

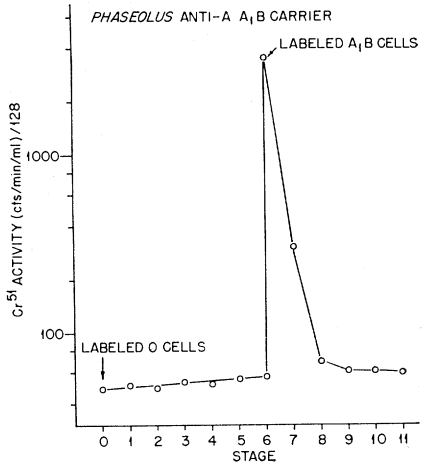

Fig. 1. Reconstruction experiment with inagglutinable O cells and agglutinable AB cells. The point on the left is the initial reaction mixture in which only the O cells are labeled. The following six points are supernatants of successive agglutinations with unlabeled AB carrier cells. The high point is the reaction mixture of stage 7 after the addition of labeled AB cells. The remaining five points are supernatants as before.