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## *Application of Neural Network Models*

Dear Sir:

One can hardly help but be impressed by the elegance and completeness of model neural network studies such as the one described by Harth and Edgar (1967); however, it seems that perhaps the technique of neural modeling could be used in a somewhat more mundane manner to study economically the consequences of some of the hypotheses presented in the interpretation of recent experimental results. In particular, some of the different hypotheses concerning the biochemistry of learning and memory could perhaps be modeled and studied. An example of how this might be done is given here.

First, a basic network would be needed in which to incorporate the model memory system. Roberts (1968) described a rather simple computer neural network model which seems reasonably adequate. Very briefly, the model is a 10 × 10 array of abstract elements, whose values are 0, 1, or 2, depending on whether the element is inactive, refractory, or active. The program cyclically calculates the state of each element as a function of the element states of the previous cycle and external stimulation. The stimulus felt by any element is proportional to first, the proximity of its active neighbors; second, a factor determined by the postulated memory mechanism; and third, a random stimulus which produces, in effect, a fluctuating threshold. If the calculated stimulus exceeds a preset threshold, the element becomes active in that cycle, refractory in the following cycle, and then can be again active or inactive two cycles later. Network instability (continuous alteration by all elements between the active and refractory state) is avoided by allowing activity to pass only unidirectionally from a row of 10 "input" elements to a row of 10 "output" elements and by use of a certain percentage of inhibitory elements, i.e., elements which contribute a negative stimulus. For more details of the model, see the original description by Roberts (1968).

The next step would be to design a memory storage system which would model some of the experimental interpretations. For example, Hyden (1967) believes that the observed changes in RNA during training are due to the expression of genes stimulated by the electrical activity accompanying the training. The protein coded by the new RNA forms a specific executive substance of all the neurons throughout a particular set or network of neurons. The protein formation leads to increased differentiation, a modulation of the protein pattern of the cells. Roberts and Flexner (1969) apparently hold essentially the same view as Hyden. They maintain that a certain plasticity remains in the state of differentiation of the neurons in certain areas of a nervous system and that in response to the electrical activity associated with learning, different genes are expressed which ultimately alter the neuronal interactions. Thus Hyden (1967) and Roberts and Flexner (1969) apparently feel that the permanent memory of an event resides in altered neuronal interactions within sets of neurons and these alterations occur as a result of the altered patterns of gene expression of the individual neurons. In addition, the experimental results apparently show an initial stage of temporary memory during which continued training activity is required for consolidation into permanent memory.

The above interpretation of the biochemical changes associated with learning and memory is reduced to a model memory storage mechanism for the 100-element computer network in the following manner. Initially, to each element of the array is assigned a unique seven-digit number made up of combinations of the numerals 0 and 4. During operation the 0's may be 1, 2, 3, or 4 as explained below. The stimulus imparted to an element by its active neighbor is then proportional to the number of places in the two seven-digit numbers which correspond either by both having 0's or by both having a finite number (i.e., each place represents a particular gene and its numerical value denotes the "state" of expression). Specifically, suppose that the element whose stimulation is being calculated has the number 0400402 and the active neighbor element considered has the number 0444004. The two numbers correspond in the

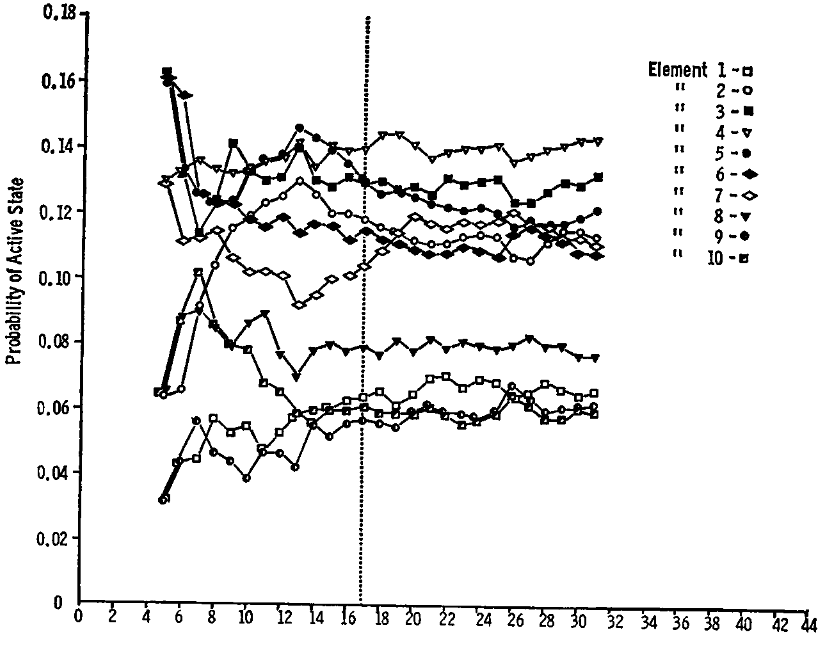

FIGURE 1 Probability of active state occurrence in output elements as a function of training.

first, second, sixth, and seventh places, or a total of four places. The stimulus of this neighbor is then calculated as four times the product of the geometrical factor (function of proximity) and a suitable constant. To this product is affixed the preset plus or minus sign (inhibitory or excitatory). This comparison is made between the stimulated element and each of the active neighbors, and all of the individual stimuli calculated. All of the individual stimuli are then summed and a random number added to the sum to get the total stimulus felt by the stimulated element.

If the calculated stimulus is greater than threshold, the memory of the stimulated element may be altered in the following manner. The summed stimulus felt by the stimulated element (less the random part) may be divided into seven parts. Each part is that subtotal of the total stimulus due to the correspondence between a particular digit in the memory number of the stimulated element and that same digit in the memory numbers of *all* the active neighbors (e.g., that portion of the total stimulus due to the correspondence between the 0 first digit of the stimulated element and say, three active neighboring elements having 0 as the first digit). Each of these seven subtotals is tested to see if it is greater or less than some fixed value. If it is smaller and if the particular digit of the stimulated element is 0, then the value of the digit is increased by 1. If the digit is 1, 2, or 3, it is decreased by 1. If the digit subtotal is greater than the prefixed value and the digit is 0, no change occurs, but if it is equal to 1, 2, or 3, the digit is increased. If the digit is 4 or becomes 4, it cannot change. This indexing of the digits provides a temporary or short-term memory change since in the digit comparison process for stimulus calculation, the digits correspond if they are merely both finite numbers or are both 0. If the total stimulus felt by the stimulated element is below threshold, the element remains inactive and each digit of the memory number equal to 1, 2, or 3 decreases by 1.

Fig. 1 illustrates representative results obtained with the 100-element computer model and the above memory storage mechanism. Each trial consists of a computer run in which the network operates for a maximum of 19 cycles. External stimuli were applied to input elements 2 and 3 for the first seven cycles of each trial. In trials 1–17, whenever output elements 2 and 3 became active, an additional stimulus was automatically applied to input elements 2 and 3. For trials 17–31, the trials differed only in that input elements were automatically stimulated when output elements 7 and 8 were active and inhibited when output elements 2 and 3 were active. The results are given as the instantaneous probability that, when an active state occurred in the 10 output elements, it would be in the particular element. Permanent memory changes occurring during the trials passed on to subsequent trials and were monitored after each trial.

These results are, of course, quite primitive but they do illustrate that this network and memory storage mechanism responds to a form of training. Variations in the particular output elements favored in the training schemes have resulted in fundamentally similar results. Memory mechanisms based on other hypotheses are being designed for comparison studies. It would be most interesting to expand the network somewhat and study the response to the more classical conditioned response training schemes.

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# *Quantitative Measurement of 1/f Noise and Membrane Theory*

Dear Sir:

In a recent note (1) I showed that electrical "noise" whose power spectrum varies reciprocally as the frequency ($1/f$ noise) should be generated when ions cross a potential barrier to enter or leave a membrane. Thus such noise would be expected, e.g. in the axonal membrane, and its *existence* cannot be used as evidence for or against any given membrane model.

Poussart (2) has now published an experimental examination of the quantitative variation of $1/f$ noise with the steady-state membrane current, assumed to be $K^+$. His results can have important implications in deciding between membrane models.

By my theory of membrane $1/f$ noise, the total noise power should be directly proportional to the total number of ions which cross the membrane interfaces per unit time. In a model which well represents many phenomena of the excitable membrane the permeability is primarily controlled at the external interface (3). As treated by activation energy, the flow of ions of species $i$ across the external interface to enter the membrane is

$$J_i\,(\rightarrow) = k_0\delta\tau_0 C_{i0}\exp\,(-\alpha_i + \varphi_0\delta/2) \qquad (1)$$

while the flow leaving the membrane across this interface is

$$J_i\,(\leftarrow) = -k_0\delta\tau_0 C_{i1}\exp\,(-\beta_i - \varphi_0\delta/2). \qquad (2)$$

$\tau_0$ is the fractional time ions can traverse the interface, being otherwise blocked by absorbed $Ca^{++}$. I have computed $\tau_0$ by essentially the Langmuir isotherm (3):

$$\tau_0 = k_1/[1 + k_2 C_{Ca}\exp\,(-2V_0)]. \qquad (3)$$

$\alpha_i$ and $\beta_i$ are the heights of the interface potential barrier in the two senses; $\delta$ is the width of the barrier; and $C_{i0}$ and $C_{i1}$ are the concentrations just outside and inside the barrier, respectively. The electric field at the interface is $\varphi_0$, which corresponds to an interface potential $V_0$. (All potentials are measured in units of $RT/F$.) $C_{Ca}$ is the $Ca^{++}$ concentration in the external solution, and the $k$'s are constants.

The net flow across the interface, for each species, is the

$$J_i = J_i\,(\rightarrow) - J_i\,(\leftarrow), \qquad (4)$$

while the total *absolute* flow (the number of ions crossing the interface in either sense) is

$$\bar{J}_i = J_i\,(\rightarrow) + J_i\,(\leftarrow). \qquad (5)$$