Neuromimes: Action of a Reciprocally Inhibitory Pair

Abstract. *Two electronic neuron models (neuromimes) connected to a common excitatory input and having both self- and mutual-inhibition were used to simulate the pulse patterns which control wing musculature in certain insects. With variation of stimulus frequency, firing patterns changed in discrete steps. Pattern change was found to be hysteretic: the pattern elicited by a given stimulus frequency depended on whether that frequency was approached from above or below. Pattern selection could be controlled by the injection or deletion of a single pulse in the stimulus pulse-train as well as by smooth frequency change.*

In discussing the neurophysiology of flight-control systems in locusts, Wilson (*1, 2*) suggests that the commonly seen alternate double firings (in wing elevator-depressor reciprocation) may arise from the action of two reciprocally inhibiting neurons (or pools of motoneurons) which have a common source of excitation. Described herein are the results of experiments with a pair of neuromimes (*3*) arranged to produce such patterns.

The conjecture that reciprocally inhibiting pairs of neurons could be responsible for the control of antagonistic muscular systems was first made in 1903 by McDougall (*4*). He proposed that the rhythmic alternate contractions and relaxations responsible for locomotion might arise from the action of pairs of single units with crossed inhibitory axon collaterals. Several years later Sherrington (*5*) discussed similar notions.

More recently there have been studies of reciprocal inhibition in arrays of neurons in sensory systems (*6*), and of recurrent inhibition in small ensembles for central control (*7*). Investigations of the behavior of only two coupled neurons, however, have been relatively infrequent, though extremely interesting, particularly as they reflect McDougall's and Sherrington's early ideas. Retzlaff and Fontaine (*8*) demonstrated that a pair of teleost Mauthner cells behave as a "flip-flop" because of their reciprocal inhibition. Reiss (*9*) investigated the reciprocating action of two cross-inhibited model neurons under common excitatory stimulus; he showed several interesting classes of alternating firing patterns which emerged from an asymmetrical pair—that is, where one unit was dominant.

Wilson's suggestion that the insect flight-control patterns he observed might arise from neuron pairs operating in a flip-flop manner prompted our present work for two reasons. First, it is of theoretical interest to determine the modes of action available to such configurations. Second, Wilson (*1*) had just demonstrated that a novel input-output firing characteristic predicted by earlier experiments with neuromimes (*3, 10*) indeed held under some conditions for real neurons. It seemed that further experiments along this line might be profitable.

In order to simulate with neuromimes the pulse patterns seen in the locust neuromuscular system, two units (*A* and *B*) were connected as indicated at the top of Fig. 1. The configuration is similar to that suggested by Wilson, in which neurons *A* and *B* might control antagonistic muscles, their common input excitation being supplied by a constant or nearly constant central stimulus. In the neuromime experiments the common excitatory stimulus was a continuous pulse train of constant frequency. The recurrent outputs, led back to inhibitory inputs, provided both mutual and self inhibition. The three inputs to each unit (one excitatory and two inhibitory) were given simple configurations of diodes, resistors, and capacitors to simulate synaptic isolation and postsynaptic integration (*11*).

Records of neuromime activity were made with conventional pen recorders; the input stimulus pulses and output firing patterns in Fig. 1 are redrawn from those records for clarity. The model's input-output relationships shown under f_1 reproduce the alternate double firings found in the insect flight motor system (*1, 2*). The cir-

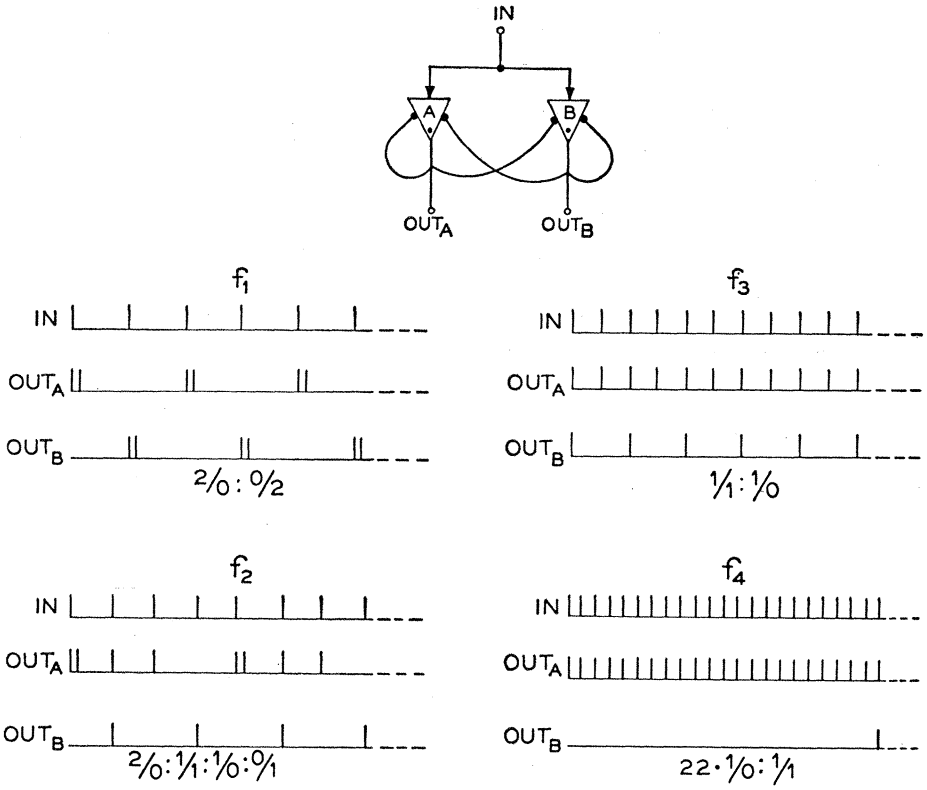

Fig. 1. Four typical firing patterns derived from a pair of reciprocally inhibiting neuromimes driven in common by a constant-frequency spike train. All patterns repeat indefinitely. f_1, Alternate double firings similar to neuromuscular patterns in insect flight motor systems. The name given to the response pattern is *A*/*B*:*A*/*B*: . . ., each colon marking one stimulus period, and the entire name representing the response period; thus, 2/0:0/2 indicates that, for the first stimulus impulse, unit *A* fires twice and unit *B* not at all, while for the second stimulus impulse, *A* is silent as *B* fires twice, and then this pattern repeats. f_2, At a slightly higher common input frequency the pattern of *A* becomes more complex, and *B* fires on alternate input stimuli. f_3, For still higher input frequency, unit *A* fires with each stimulus spike while *B* fires on alternate ones. f_4, At a relatively high frequency, *A* fires 22 times while *B* remains silent; *B* then fires once (as does *A*), and the cycle repeats.

cuit was arranged to produce this pattern over an input range of about 8 to 22 pulses per second (pps), which is similar to the physiologically observed range. The double firings for each stimulus pulse occur because the time course of self-inhibitory buildup is sufficiently long that no significant threshold shift occurs until after the second response.

If we examine the action of the circuit in which input frequency is the only variable (that is, time constants are unchanged), a number of different output patterns emerge. Consider the result shown (Fig. 1) for f_2 (which is slightly higher than that for f_1). Unit *A* fires twice-once-once for three consecutive input pulses and misses the next, the pattern then repeating, while unit *B* fires in response to every other input pulse. At every fourth stimulus time *A* and *B* fire simultaneously.

At a still higher input frequency, f_3, unit *A* fires synchronously with the input train while unit *B* continues its count-of-two frequency division. At relatively high frequencies (for example, 40 to 90 pps for the constants employed in this series of experiments), a remarkable change in activity is observed; the pattern depicted under f_4 is typical. Dominant unit *A* continues to follow the input pulses one-for-one, while unit *B* remains silent for long intervals. In this case *A* fires 22 times while *B* remains silent. Then both units fire in unison, and the pattern repeats.

As the frequency of the input pulse train is continuously increased, a sequence of many different output patterns is generated; Fig. 2*a* shows a typical sequence. The patterns range from 1/1, in which both units fire synchronously with the input, through a set of rather intricate patterns, to a series of responses in which unit *A*, firing synchronously, increases its dominance as unit *B*, firing less and less frequently, is finally suppressed completely. Each pattern is stable over some range of input frequencies—that is, within limits a given pattern is locked-in despite input frequency variation. Above about 40 pps the "staircase treads" tend to shorten smoothly and to become quite small.

In Fig. 2*b* the plot of the patterns versus stimulus frequency is continued. At about 90 pps unit *B* fires once for every 33 input spikes while unit *A* continues to follow one-for-one. Just beyond this, *B* ceases to respond, and for all higher stimulating frequencies *A* alone fires. Up to approximately 200 pps the slope of the function is unity, —that is, *A*'s response continues to be one-to-one. For all input frequencies above 200 pps, however, the firing frequency of unit *A* increases very little. (This is due to the fact that the intervals between stimulus pulses are now short compared to the circuit time constants, and an essentially constant driving function appears at the neuromime's input terminals.)

It is interesting that for a fixed structure and set of temporal parameters the effect of increasing the frequency of the stimulus is to change the network activity from patterned and phasic to tonic in the dominant unit, and from patterned and phasic activity to quiescence in the non-dominant unit.

While the detailed dynamics of this system are relatively complicated, the fundamental interactions are rather simply described. Suppose that a train of normally suprathreshold stimulus impulses is injected into the common excitatory input. At very low stimulus rates, simultaneous firing of both units is possible over a range in which all the time constants for inhibition are short compared to the stimulus pulse period; hence, both units can return to resting threshold before the next stimulus pulse arrives. While mutual inhibition serves, in general, to suppress the higher-threshold unit, instantaneous lock-out is impossible because of firing latency in the active unit

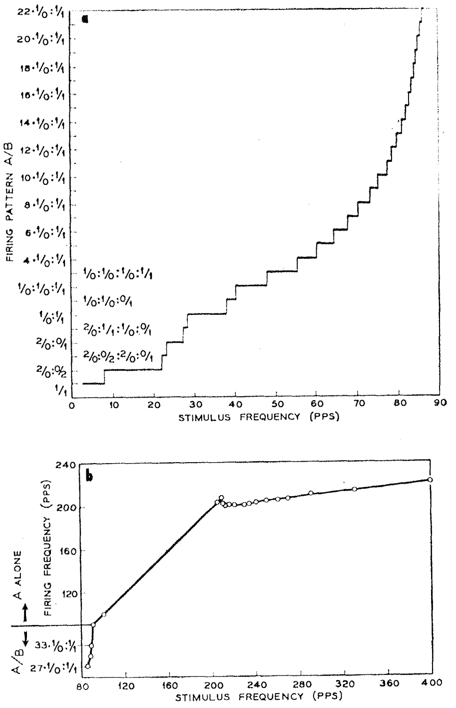

Fig. 2. (*a*) Family of firing patterns obtained as the stimulus frequency is increased. Each pattern, which repeats indefinitely, is stable over a range of stimulus frequencies, discontinuously changing at the extremes of the range. (*b*) Continuation of Fig. 2*a*. Above about 90 pps, unit *B* ceases firing; *A* fires alone then, following each stimulus pulse one-for-one up to about 200 pps. Beyond 200 pps, *A* fires with approximately constant frequency.

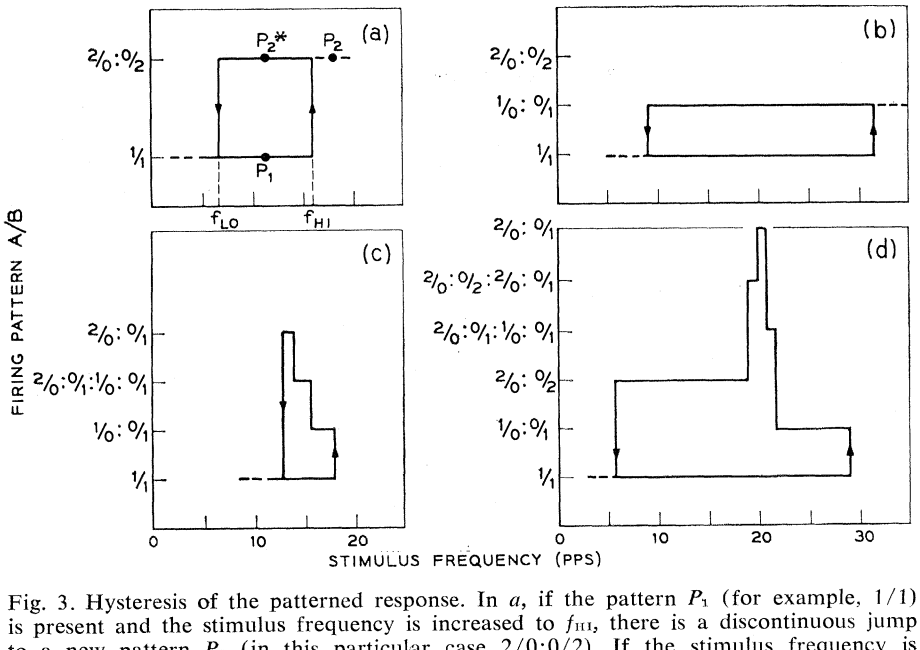

Fig. 3. Hysteresis of the patterned response. In *a*, if the pattern P_1 (for example, 1/1) is present and the stimulus frequency is increased to f_{HI}, there is a discontinuous jump to a new pattern P_2 (in this particular case 2/0:0/2). If the stimulus frequency is then decreased the pattern remains, even though the frequency is lowered almost to f_{LO}. At f_{LO} there is an abrupt switch to the original pattern. In *b*, *c*, and *d* other types of hysteresis loops are shown which are obtained from the same pair of units with different time constants of reciprocal inhibition.

and of synaptic delay in the cross-inhibitory pathway.

For intermediate rates where the interval between pulses is commensurate with the self-inhibitory time constants, firing alternates between the two units. This is made possible either by an innate circuit asymmetry (since precise equivalence of threshold is practically impossible), or by any noise fluctuation which permits one unit to become momentarily dominant. In the steady state, a given excitatory impulse finds the unit that has just fired still relatively refractory (that is, the self-inhibitory time course has not yet run out). But the opposing unit, well recovered from self-inhibition two input periods back, is now dominant because of lower threshold, and it fires. Thus, firing activity in the pair alternates.

The alternating activity described so far depends only on self-inhibition—that is, refractoriness—and not on reciprocal suppression. However, at high stimulus rates, where the interval between pulses is commensurate with the time constants for reciprocal inhibition, the dominant unit becomes more effective in suppressing the opposing unit because of accumulated cross-inhibition. In the limit, at sufficiently high rates, complete and sustained dominance is possible.

A rather surprising result is obtained if the frequency of the stimulus is decreased. Consider Fig. 3*a*. Let us assume operation at some point between f_{LO} and f_{HI}, producing pattern P_1 (in this case 1/1). As was seen earlier, this pattern will persist with increasing stimulus frequency until f_{HI} is reached, at which time there will be a discontinuous jump to a new pattern P_2. Now, if the frequency of the stimulus is decreased, the original path is not retraced. Instead, the new pattern P_2 persists, even though the stimulus frequency lies between f_{LO} and f_{HI} (for example, the operating point indicated by P_2*), for which stimulus the pattern P_1 was previously elicited. The "captured" pattern P_2 continues as the stimulus frequency decreases until f_{LO} is reached and pattern P_1 reappears.

Hysteresis, in which the approach path to a particular stimulus uniquely determines the response, is seen for all patterns shown in Fig. 2. Moreover, a number of radically different hysteresis loops can be produced by modifying the circuit's temporal parameters. For example, the loops of Fig. 3, *b*, *c*, and *d*, were obtained by changing both of the time constants for mutual inhibition by factors ranging from 0.5 to 4.0. The arrangement of the ordinate response patterns follows the natural ordering with increasing stimulus frequency (as in Fig. 2). The classes of patterns change somewhat with different circuit constants.

One may speculate that if such hysteretic switching action were used by real nervous systems then a similarly simple, economical control of pattern states might be expected. For example, may only a transient shift of stimulus frequency be required in order to go from one state to another—that is, can a change in pattern be obtained merely by injecting an extra pulse into the stimulus train? Such indeed is the case for the model. The hysteresis loop shown in Fig. 3*a* is readily traversed by single-pulse control; for a fixed stimulus frequency between f_{LO} and f_{HI}, a single intercalated spike causes P_1 to change to P_2, while a single deleted impulse (or an injected inhibitory spike) triggers the converse change.

Neither hysteretic action nor its control (as described) has yet been demonstrated physiologically, but a seemingly similar effect is found in some crustacean nerve-muscle preparations (*12*). In those experiments, a given muscular tension produced by a background stimulus of constant frequency applied to a single motor fiber can be triggered into a state of greatly increased tension simply by intercalating a single extra shock. Further, Katz (*13*) suggests that prompt relaxation without reduction of background activity might be obtainable by injecting a few inhibitory impulses. However, the available evidence does not suggest, nor does it seem very likely, that these results depend on effects like those described herein. Clearly, though, physiological latching mechanisms exist which do not depend on elaborate neural networks.

The ubiquity of recurrent and reciprocal inhibition makes flip-flop action in nervous systems at least plausible. It may well be that Renshaw cells, for instance, produce effects similar to those described here, but the brief antidromic volleys commonly used as probing stimuli are inappropriate for disclosing such effects. Furthermore, stimulus frequency is not often used as an experimental variable, while at least for the class of experiments reported here it is a revealing parameter. If hysteresis actually occurs in nature then appropriate neurophysiological experiments may disclose entirely new modes of information-processing at the single-cell level.

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Electroencephalographic Correlates of Binocular Rivalry in Man

Abstract. *Under conditions of ocular rivalry, changes in the rhythmic brain response to flicker stimulation of one eye correspond closely to the subject's report of changes in the perceptual dominance of that eye.*

When the fields of view for the two eyes are similar they are combined by a central fusion process, forming a single unified perception of the visual field. If the stimuli presented to corresponding parts of the two retinas differ markedly, however, a binocular rivalry occurs in which the visual image of one eye alternates with or suppresses that of the other (*1*). The degree of suppression and rate of alternation de-