that they will eventually be shown to cross over with each other.

The stocks used were vermilion eye color (*v*), forked bristle (*f*) Bx^3 *ma-l*, which was made from the *ma-l* strain at the California Institute of Technology, and *v* $ma\text{-}l^{bz}$, made from the bronzy (*bz*) stock kindly made available by Fahmy. The eye color of these stocks is yellow-orange; the presence of *v* facilitates their separation from the complementing flies (*v f* Bx^3 *ma-l*/*v* $ma\text{-}l^{bz}$) which have a bright red eye color. The wild-type stock used was an Oregon-R stock originally derived from the strain kept at Johns Hopkins University.

The results indicate that the phenotypes of *ma-l* and $ma\text{-}l^{bz}$ are similar (*12*). Both mutants have a diminution of the red pteridine components of the eye color and our investigation reveals that $ma\text{-}l^{bz}$, like *ma-l*, is deficient in xanthine dehydrogenase. There is a consequent absence of the enzyme's reaction products, while the enzyme's substrates accumulate. Both mutants are nonautonomous (*14*), and we have been able to show that both are maternally affected if their female parent contains $ma\text{-}l^{+}$ (*15*). However, it is of interest that neither *ma-l* nor $ma\text{-}l^{bz}$ is maternally affected if the mother was *ma-l*/$ma\text{-}l^{bz}$, a fact which indicates a functional relationship between these genes.

On the other hand, we find that females heterozygous for both genes (*ma-l*/$ma\text{-}l^{bz}$) have a normal eye color, indicating that the functional deficiencies of *ma-l* are not identical with those of $ma\text{-}l^{bz}$, and that one mutant can complement the functional losses of the other (*13*). This complementation, however, is not complete, since the amount of xanthine dehydrogenase present in *ma-l*/$ma\text{-}l^{bz}$ flies is only approximately 5 percent of that of the wild-type (Fig. 1); this small amount of enzyme is reflected by low amounts of uric acid and isoxanthopterin (the enzyme products) which we observe on paper chromatograms. The low enzyme level is further reflected in the fact that hypoxanthine, which is usually present in only trace amounts in wild-type flies, accumulates in *ma-l*/$ma\text{-}l^{bz}$ flies.

Other workers have also reported that the levels of enzyme found in complements are much lower than that found in the wild type (*4*, *5*). The general picture found in *ma-l*/$ma\text{-}l^{bz}$ flies resembles that found in maternally affected *ma-l* males in which relatively small amounts of enzyme restore the normal eye pigmentation while only a small effect is observed on the rest of the biochemicals involved (*15*). Why this should occur is not understood, since we do not know the reactions which lead to the formation of the red pigment. Nor do we understand the mechanism behind the complementation phenomenon, which presumably occurs as a "recombination of parts" of either the template or of the enzyme. Woodward (*16*) has reported in vitro complementation when mycelial extracts of mutants which give in vivo complementation are mixed, but attempts to repeat this with our system have been negative thus far (*17*).

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6. The symbols used in this paper are as follows [based on (*7*)]: Bx^3, Beadex wing; *f*, forked bristle; *ma-l*, maroon-like eye color; $ma\text{-}l^{bz}$, bronzy allele of maroon-like; $ma\text{-}l^{+}$, the wild-type allele of *ma-l*; *ry*, rosy eye color; *su-f*, suppressor of forked bristle; *v*, vermillion eye color.
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17. Part of this research was carried out in the Zoological Institute of the University of Zurich while one of us (E. G.) was a postdoctoral fellow of the National Institutes of Health. We would like to thank Prof. Hadorn, Prof. Chen, Prof. Burla, Dr. Ursprung, and Dr. Anders for their kindness and help.

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Analysis of Firing Patterns in Single Neurons

Abstract. The use of a high-speed digital computer for investigation of neural firing patterns is described. The high sensitivity of the method permits detection of stimulus-response relations buried in a background of spontaneous activity.

The firing pattern of a neuron in a sensory system is generally more complex than a simple all-or-none response that occurs shortly after the delivery of a stimulus. Frequently, neurons exhibit spontaneous firings, and the change of a stimulus parameter may simultaneously affect (i) the total firing rate and its distribution in time, (ii) the interspike intervals, and (iii) the latency between the stimulus and the first spike of a burst. Visual inspection of oscilloscopic displays is most appropriate for the detection of type (iii) pattern changes. The observer who relies on such limited response criteria selects a biased sample from the total population of neurons available for observation. A more representative sampling of the population can be obtained by broadening the response criteria with a more quantitative description of the total firing patterns.

Compilation of such results from single-unit data has usually involved tedious "hand and eye" measurement of strip-film records (*1*), although some schemes have been developed for automatic display of the repetition of very constant and simple patterns of firing (*2*). In the present study the TX-O (*3*), a fast, general-purpose digital computer with a flexible input-output system, was used for the analysis of more complex firing patterns.

The TX-O computer was programed to perform two complementary analyses of tape-recorded data. The results are presented as two displays: (i) a time histogram—a histogram of the distribution of action potentials in time relative to the instant of stimulus presentation (summed over many stimulus presentations), and (ii) an interval histogram—a histogram of the occurrence of various interspike intervals (that is, time intervals that separate two successive action potentials). A peak on a time histogram shows preferred time of firing relative to the stimulus; a peak on an interval histogram shows a preferred interval between firings.

Note that both of these analyses involve time averages and therefore yield a time average of the firing pattern rather than single sequences of unit events in the pattern. The second form of analysis, the interval histogram, is mathematically similar to the autocorrelation function for a time function that is a train of pulses. Thus a Fourier transform of the smoothed interval histogram is related to a power spectrum (power as a function of frequency) of the trains of the cell firings. (It would be interesting to examine the order in which the "bins" in each of the two histograms are filled. Unfortunately, the relatively small number of events that can be observed in an experiment of reasonable length makes these fractional analyses statistically impractical.)

In our processing system, neuronal spikes and stimulus pulses from tape are picked out by discriminators and

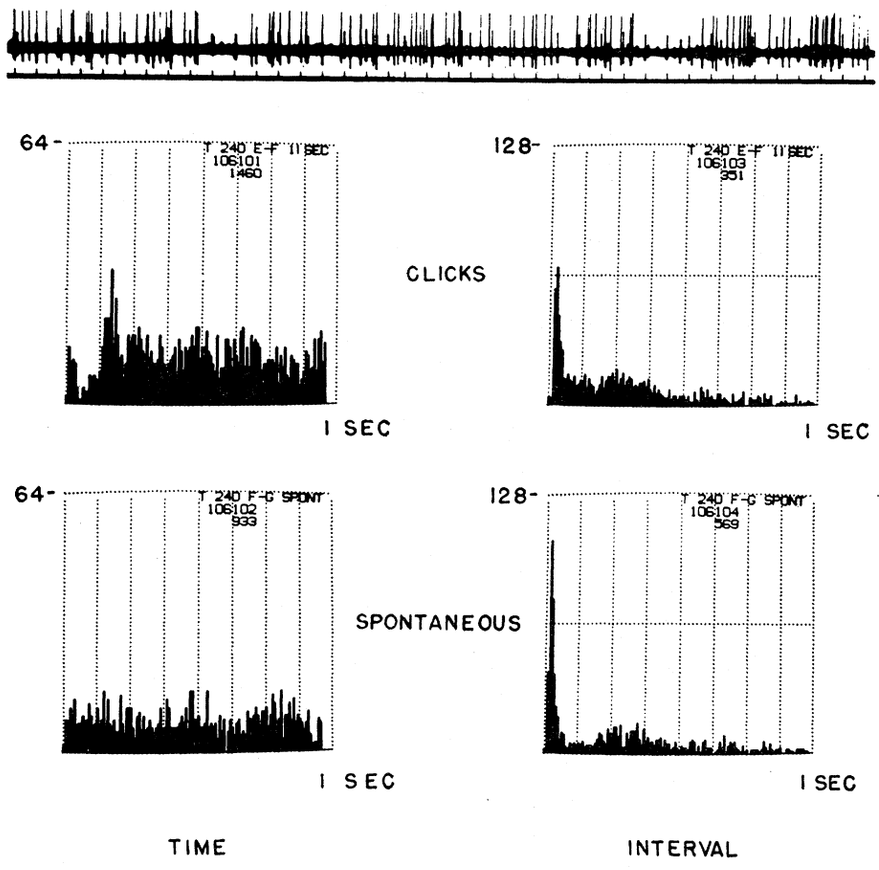

Fig. 1. Top trace, film strip of a cell's firing pattern. Lower trace, stimulus markers at 1 sec intervals. Below: time (left) and interval (right) histograms for 10 minutes of data from this unit. The stimulus condition is indicated at the upper right of each histogram (bin width, 8 msec).

Schmitt triggers, formed into standard TX-O computer pulses (by DEC digital test units), and fed directly into an available register of the computer. Detailed analog-digital conversion of the data waveforms is not used. The TX-O program senses the proper portion of the stimulus pattern, keeps internal time, and compiles the necessary histograms. The output of the processing program is a display of a histogram with various typewriter-controlled titling provisions; the display is photographed with a Polaroid camera. All relevant constants of the computation are available to the operator on toggle switches. The maximum resolution available in real processing time is 0.5 msec per bin. Better effective resolution can be obtained by playing back the data tape more slowly than it was recorded. If coarser resolution is used, the tape can be played back faster than it was recorded, and the processing time shortened.

The computer program accommodates tape-recorded experiments that involve repeated (cyclic) presentation of several different stimulus conditions. Each condition lasts for an arbitrary length of time and comprises an arbitrary number of repetitions of a basic stimulus. Such an experimental format allows meaningful comparison of the various stimulus conditions because data for all stimulus conditions are similarly affected by physiological changes of state of the preparation.

This processing system has been applied in a study of the firing patterns of single cells in the auditory cortex of lightly anesthetized cats (Nembutal). Single-neuron and slow-wave activity were observed by standard methods with 5 to 10 μ tungsten microelectrodes. In order to minimize the pulsatile motion of the brain the electrodes were moved in a closed oil-filled chamber threaded into the skull (*4*). Acoustic clicks were presented to the preparation in a repeating pattern of 15 seconds of stimulation followed by 15 seconds of silence. Both the electrical activity and the stimulus pattern were recorded with an FM tape system for later processing.

Results obtained for a cortical cell of a frequently encountered type are shown in Fig. 1. At the top is an ordinary strip-film presentation of the cell firing. The large pulses on the upper trace indicate firing of the neuron under study; the lower trace shows stimulus markers at 1 sec intervals. Below are time and interval histogram analyses of about 10 minutes of such data, for both the stimulated and spontaneous conditions. The time histograms show clearly that the cell's firings are depressed for approximately 150 msec after the delivery of the stimulus and then briefly enhanced. The interval histograms show less contrast between spontaneous and stimulated conditions. However, we note the distribution of interspike intervals is more uniform during stimulation. Since the cell is firing only about three times per second, it is extremely hard to "see" any of this behavior on the strip film.

Obvious extensions of these data-handling methods can lead to techniques that will be useful in investigating the complex relations between graded and discrete aspects of electrocortical function (*5*).

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Vivax-Type Malaria Parasite of Macaques Transmissible to Man

Abstract. Transmission of *Plasmodium cynomolgi bastianellii* from rhesus monkeys to two human subjects by *Anopheles freeborni* and the occurrence of attacks of malaria in two other laboratory workers not exposed to human malaria suggests the existence of an animal reservoir of infection complicating malaria control and eradication.

Plasmodium cynomolgi subspecies *bastianellii* was recently described by Garnham (*1*), who found distinct morphological and immunological differences between it and typical *P. cynomolgi*. The new subspecies was isolated from a *Macara irus* monkey from Malaya (*1, 2*). Garnham sent this parasite to us for study, and we have done many experiments with it in rhesus