Functional Congruence: An Index of Neural Homogeneity and a New Measure of Brain Activity

Abstract. *Extremely high correlation between the probability that a single cell will fire and the amplitude of microelectrode electroencephalogram was established in on-line, real-time computer experiments. Such congruence between spike and wave shows orderly biological variation under sensory control. Congruence, as a measure of brain activity, provides an immediate estimate of regional neural homogeneity of function of cell populations in brain.*

There is an impressively high correlation between the probability of a spike occurring in a single cell and the wave form and amplitude of the evoked potential (*1*, *2*). The probability of a cell firing is given by the wave form of the evoked potential (recorded from the same microelectrode) throughout its extent in time, by its positivity and negativity, and by its early and late components (*1*).

Neural events, such as latency recovery cycles of single cells, are equally well predicted with the same curves and inflection points, by single-cell-firing probability or evoked potential amplitude from the same microelectrode (*2*). We have concluded that single-cell-firing probability and the evoked potential are representative of the same underlying processes of excitability and that the evoked potential is probably the summation of nearby local potentials—that is, excitatory and inhibitory postsynaptic potentials.

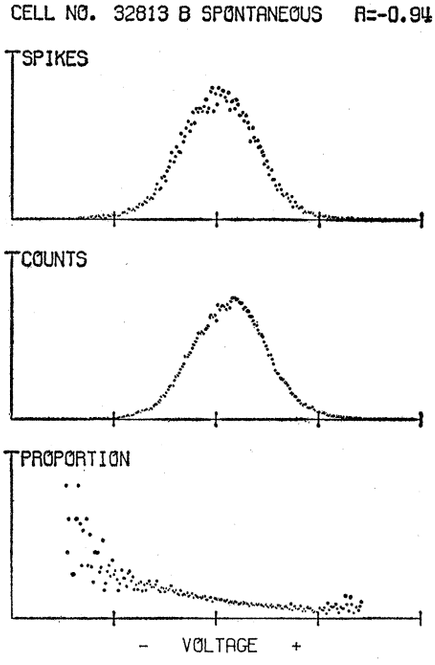

Fig. 1. Record from a single cell in visual cortex of cat. Center curve: number of occurrences of each slow-wave voltage; top curve: number of occurrences of a cell spike at each voltage in center curve; bottom curve: conditional probability of spike firing at each voltage in center curve. The R value at top gives the Pearson correlation coefficient between slow-wave voltage and spike probability. Correlations in these and all following figures are based on the middle half of the spike and slow-wave values, and all are significant beyond the .001 level. Vertical axis is arbitrary and omitted.

Our work has had major limitations. First, collection of data is time-consuming and requires large numbers of stimuli to generate an adequate sample size. Second, the obvious spike-wave relation is produced only by highly synchronous physiological stimuli in a time-locked arrangement. Third, the correlational computations after collection of data are time-consuming and tedious. This report shows that the relations are more general, including that between probability of firing of single cells and the spontaneous variation in cortical slow waves or momentary cortical excitability.

A simple on-line, real-time program for a PDP-8 laboratory computer system provided analog-to-digital conversion of the spontaneous electroencephalogram (EEG) each millisecond from a glass micropipette in the cortex of acutely prepared, curarized, and locally anesthetized cats. The slow-wave samples were stored in 256 core locations according to their voltage. That is, EEG amplitude was divided into 256 levels, and the frequency of occurrence of each voltage level was digitized, thus providing, over any period sampled, a frequency distribution of the number of times each voltage occurred. Simultaneously, each time a cell fired, a Schmidt trigger with threshold set to one-half spike amplitude provided a standard pulse to the computer. From these data, a second distribution of the number of times a spike occurred at each of the 256 voltage levels was compiled. The ratio of the number of times the cell fired at each voltage to the number of times this voltage occurred gives the conditional probabilities which were then plotted as a function of voltage. This plot provided an indication of the relation between firing probability and local slow potential.

The problem of overlap of time constants of the two signals was solved by adequate separation of the signals by the modified filters of two Tektronix 122 amplifiers. The high-frequency channel (spike channel) covered the range from 250 hz to 2 khz, and the low-frequency channel (EEG channel) covered the range from 0.1 hz to 50 hz; the filters provided 15-db attenuation at the crossover point and resulted in almost complete independence of the two signals. Both spike and wave were monitored continuously (as was the Schmidt trigger output) to assure reliability. At no time was any multiple unit recording used. Spikes used ranged in amplitude from 2 to 20 mv. In this way, 50 cortical cells and the corresponding microelectrode EEG's were studied.

The outcome for a single cell is shown in Fig. 1. The Pearson correlation coefficient between spike probability and voltage level is 0.944 and the F value for linear correlation is 1331.6. Ninety percent of all cells observed showed significant correlations between probability of firing and slow-wave amplitude. Correlations ranged from -0.98 to $+0.80$. The F values for linear correlation (Fig. 2) ranged from 6000 to 0.2 with a mean of 200, although almost half the cells observed produced significant nonlinear components ($P < .05$). Neither the oscilloscope alone nor evaluation of filmed traces revealed the dramatic stochastic relations described by the computer, even when the actual correlation was known beforehand. Failure to observe such relationships by visual inspection is not new to these studies (*3*). Any intrinsic brain activity at an electrode tip,

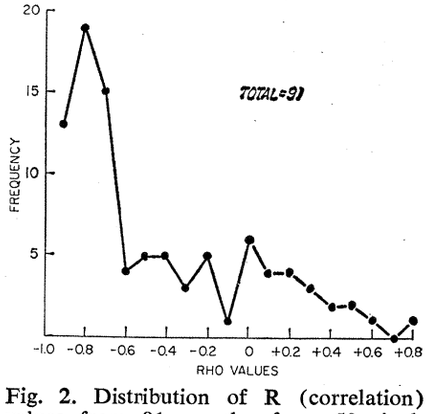

Fig. 2. Distribution of R (correlation) values from 91 samples from 50 single visual cortical cells in cat. No cell contributed more than two values. Correlations computed as before.

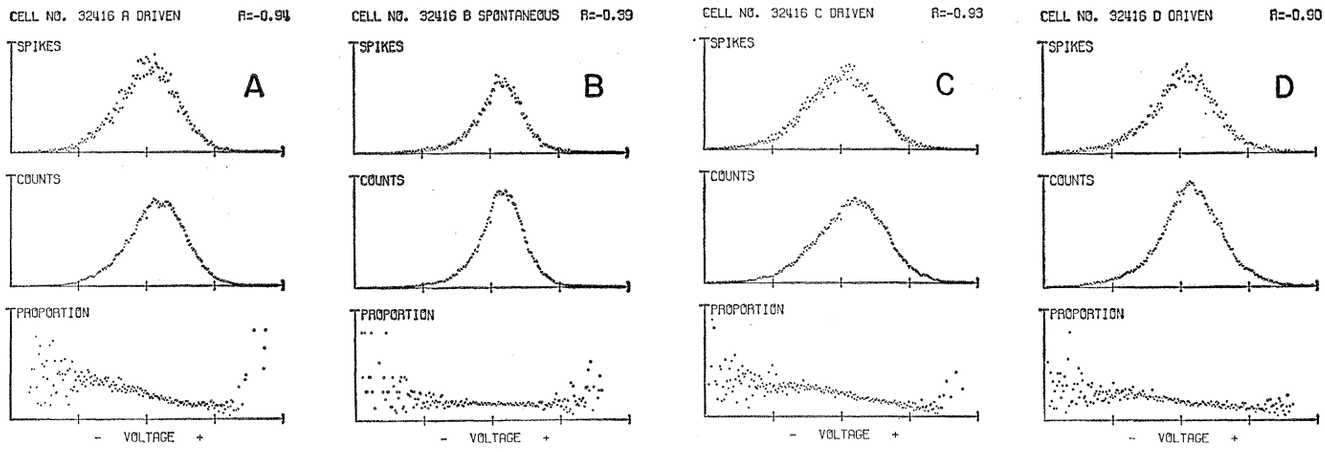

Fig. 3. An example of change in congruence with flashing light (A), without (B), and again with (C and D). Computations as before. There is an overall decrease in congruence during spontaneous (nonlight) condition as compared with the three driven (light flash) conditions, with high reliability of repeated driven measurements.

not necessarily related to afferent activity, was observed to restrict the changes in congruence reported by confounding two (possibly independent) excitability sources. Alpha activity or any hypersynchronous slow activity produced (for example, by a sleeping animal) resulted in considerable inflexibility of the congruence relationship as did drug-produced, intrinsic synchrony or any nonneural production of slow waves. Thus, spike wave forms, frequency, and slow-wave configuration were carefully monitored to assure conditions that would be as similar to physiological as possible. Sample time with constant rate or spike sample size was kept constant or adjusted appropriately under computer control to allow for application of suitable statistical procedures.

This close correspondence of spike probability and spontaneous EEG amplitude is a general phenomenon in cat cortex. It supports and extends our earlier conclusions from studies of the relation between spike probability and evoked potential properties—that the general class of brain activity which includes evoked potentials, slow activity, or EEG is representative of the momentary excitability of the brain as indicated by spike probability (*4*).

Our studies also provide partial understanding of conditions controlling the variability of correlations of spike probability and slow waves in brain. Contrary to previous expectations, based on the assumption that the relation of spike to wave is a biophysical constant, the correlation of spontaneous firing from a given cell with the EEG voltage varied from one replication (2 to 5 minutes) to another. The correlation, or congruence (*5*) of spike occurrence with EEG wave amplitude for the same cell, varied as much as 20 percent from sample to sample. This variance is more consistent with findings of studies of cortical physiology than a constant relation would be. If the field of EEG activity had been greater than anticipated, the slow activity might represent a mean excitability for the entire cell population rather than for the single cell alone. The excitability of a single cell, depending on its particular active afferents at a given moment, could be expected to deviate from the mean excitability. Congruence, then, is an expression of how well an observed cell is represented by the mean excitability. Congruence should undergo orderly biological variation under proper conditions.

Cells in the visual cortex were evaluated for orderly change in congruence. Visual stimuli (500-msec light flashes) were expected to activate common afferents to most visual cortical cells, and thereby increase the congruence, or how well the mean excitability or slow waves represented a given cell. When cells of visual cortex were driven with light, congruence or the correlation between spike firing and wave amplitude significantly increased (Fig. 3). This increase in congruence was observed in over half the cortical cells.

From the remainder of observed cells, congruence was less under driven

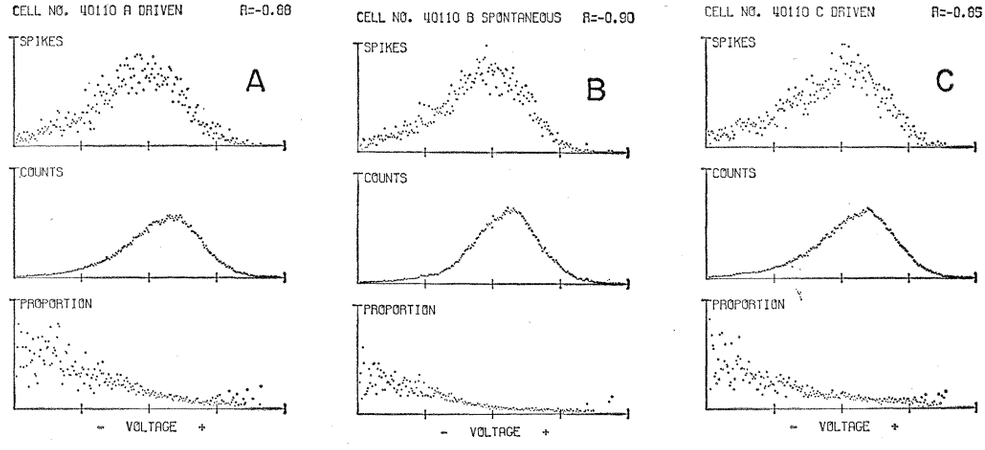

Fig. 4. Examples of change in congruence with and without light flash. This type of cell shows increased congruence during spontaneous conditions as contrasted with driven conditions. Curves A and C are driven, B is spontaneous.

conditions than it was under spontaneous conditions (Fig. 4). A small percentage of visual cortical cells are not primarily responsive to light but either respond weakly to light or respond to other stimuli (*6*). Such cells would not be represented well by mean excitability under driven conditions and would better represent the mean when all cells of the area are spontaneously active. Under driven conditions, cells with primarily visual function are dominantly responsive to visual afferents not shared by such diffusely projecting or nonprimary afferent cells. In contrast, under spontaneous conditions, these two different cell populations may have more active afferents in common.

Regardless of conditions, almost all cells remained significantly correlated with the slow-wave amplitude. These experimentally produced changes are a matter of magnitude of congruence under the specific conditions.

Congruence is an estimate of how well the mean represents a randomly sampled cell, and it provides an estimate of the relation of the momentary excitability of a given cell to that of the entire population. Congruence in our view is an index of neural homogeneity, and it represents how low the population variance around the mean excitability is. When congruence is low, one may assume that the variance of the cell population is high, and that neural homogeneity of the population is low. Thus, on the reasonable assumption that the cells studied here constituted a random sample, the common excitability or neural homogeneity can be estimated from the relation of a single cell to the accompanying slow activity from the same electrode.

This measure of congruence represents a new measure of neural activity of brain which is neither slow-wave nor spike, evoked potential nor integrated activity, but which derives instead from a second-order interaction of spike and wave. Such estimates of homogeneity can be accurately made on the basis of samples taken for as little as 1 to 2 minutes, or even a few seconds, depending only upon spike rate. This advantage raises the status of the relation of spike probability to wave amplitude from a static biophysical datum computed after the fact to a dynamic functional variable which may be evaluated moment to moment.

In pharmacological, behavioral, and other site-of-action studies, if one plots momentary correlation values simultaneously for a number of sites, the changing configuration of local structural homogeneity may be observed and will provide information about the relative internal communality of excitability or consistency of local neural function (*7*).

STEPHEN S. FOX
ROBERT J. NORMAN
Department of Psychology, University of Iowa, Iowa City

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5. We acknowledge earlier, related formulations of E. R. John [E. R. John, D. S. Ruchkin, J. Villegas, *Science* **141**, 429 (1963); ———, *Ann. N.Y., Acad. Sci.* **122**, 362 (1964); D. S. Ruchkin, J. Villegas, E. R. John, *Ann. N.Y. Acad. Sci.* **115**, 799 (1964)], who, with co-workers, developed concepts of functional correspondence based on cross correlations of evoked-potential wave shapes. John's formulation was developed to relate changes between brain areas at the same bioelectric level. Our concept of congruence applies to changes within brain structures and derives its power from measures at different bioelectric levels.
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Extinction Following Intracranial Reward: The Effect of Delay between Acquisition and Extinction

Abstract. *Rats trained to press a bar for intracranial reinforcement gave as many responses during extinction as did water-reinforced controls, when extinction came immediately after an acquisition session. However, the experimental animals gave fewer responses in extinction than water-reinforced animals when extinction was delayed for 1 hour after acquisition. The activity level of the experimental animals was high immediately after acquisition but declined markedly over the delay period, which suggests that resistance to extinction after intracranial reinforcement is primarily a function of activity level.*

Since the demonstration that electrical stimulation of the brain can serve as a reward, a number of investigators have concluded that intracranial reinforcement (ICR) and conventional reinforcement under appetitive drives may have different effects on behavior (*1*). The most noteworthy of these differences is the repeated demonstration that responses maintained by ICR extinguish faster than those maintained by food or water reinforcement (*2*). This abrupt cessation of responding when reinforcement is withheld is generally taken as the most convincing evidence that ICR is essentially different from conventional reinforcers (*3*).

Recently, however, it has been suggested that differences in response topography between ICR and conventional reinforcement may account for these reported differences in resistance to extinction (*4*). In the typical ICR situation, reinforcement is administered immediately when the subject presses a lever, while conventional reinforcement is made available at a chute or drinking nozzle some distance from the lever. Gibson *et al.* (*4*) showed that when the form of the response made for ICR and conventional reinforcement was made similar, the usual difference in resistance to extinction was not observed. They conclude that ICR is not, therefore, essentially different from conventional reinforcers.

This study is open to criticism, however. All the subjects, including those scheduled for ICR, were deprived of food during both acquisition and extinction. Since subjects had electrode implants in the lateral hypothalamus, where electrical stimulation can elicit eating (*5*), and since it has been shown that hunger increases the number of responses emitted during extinction of an ICR habit (*6*), the generality of the results of Gibson *et al.* must remain in question.

Howarth and Deutsch (*7*) have proposed that extinction following ICR is due simply to drive decay and is, there-